

Mental health care guide for licensed practitioners and mental health professionals

Prepared by the Mental Health Clinical Advisory Group

Schizophrenia

Oregon
Health
Authority

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Section 1. Mental Health Clinical Advisory Group (MHCAG) assessment and treatment flow charts for schizophrenia

Figure 1. Acute psychosis flow chart

<p>Clinical considerations</p>	<p>The clinician should be aware of possible early subclinical/prodromal symptoms that may indicate an increased risk of developing schizophrenia in youth and younger adults.</p>		
<p>1 Assess for safety.</p>	<p>A. Suicide: For adults, use the Columbia Suicide Severity Rating Scale and Triage for Use in Primary Care (see pages 30–31); for adolescents, use the ASQ tool (see page 32).</p>	<p>B. Violence toward others (see pages 28–29): Consider risk factors for violence.</p>	<p>C. If risk cannot be quickly mitigated: Call county behavioral health (see Appendix of county resources; see pages 114–118) or dial 9-1-1.</p>
<p>2 Begin initial workup.</p>	<p>A. Administer psychosis screener: CAPE-P15 (see page 35).</p> <p>B. History and physical</p> <ol style="list-style-type: none"> 1. Patient history (medical, psychological and substance use). Use substance use screeners: SBIRT, DAST, AUDIT (see page 32). 2. Neurological and mental status exams, including an AIMS (see page 32) baseline 	<p>C. Conduct labs including:</p> <ul style="list-style-type: none"> • CBC with differential • CMP (with liver enzymes, electrolytes, BUN, Cr, calcium) • RPR • Urine drug screen • Thyroid screen (TSH, reflexive T4) • HcG 	<p>D. Consider neuroimaging in first episode psychosis (see page 46) when focal neuro deficits are present and with new onset psychosis.</p> <ul style="list-style-type: none"> • A1c • Lipids (baseline and annually if using antipsychotic medications) • As appropriate, the physician may request urinalysis with microscopy • B-12 and folate
<p>3 Conduct initial treatment intervention.</p>	<p>Social</p> <p>Access community resources:</p> <ol style="list-style-type: none"> Refer to specialty provider (psychiatrist, neurologist, PMHNP). Refer to the psychosocial assessment and intervention flow chart (see page 4) in this guide. 	<p>Psychological</p> <ol style="list-style-type: none"> Learn more about psychological interventions used in treating schizophrenia. Refer to a therapist (See Considerations when choosing a therapist, page 22). 	<p>Biological/medical</p> <ol style="list-style-type: none"> Consider medications and refer to the medication algorithm. Consult with the Oregon Psychiatric Access Line for prescribing providers: 503-346-1000.
<p>Diagnosis of schizophrenia</p> <p>Positive symptoms: florid hallucinations (commonly auditory or visual but can be olfactory, tactile or, in some cases, masqueraders), delusions, paranoia, disorganized thinking and behavior.</p> <p>Negative symptoms: social withdrawal and isolation, flattened or blunted affect, low motivation, low energy, paucity of thought or speech.</p>		<p>Notes</p> <p>Consider differential diagnoses of psychotic symptoms. Please refer to the DSM-5 (see Diagnostic criteria for schizophrenia, pages 33–34) for a complete list of diagnostic criteria.</p> <p>Schizophrenia affects approximately 1% of the population. Psychosis is more common than schizophrenia.</p>	

Figure 2. Stabilization and management of schizophrenia flow chart

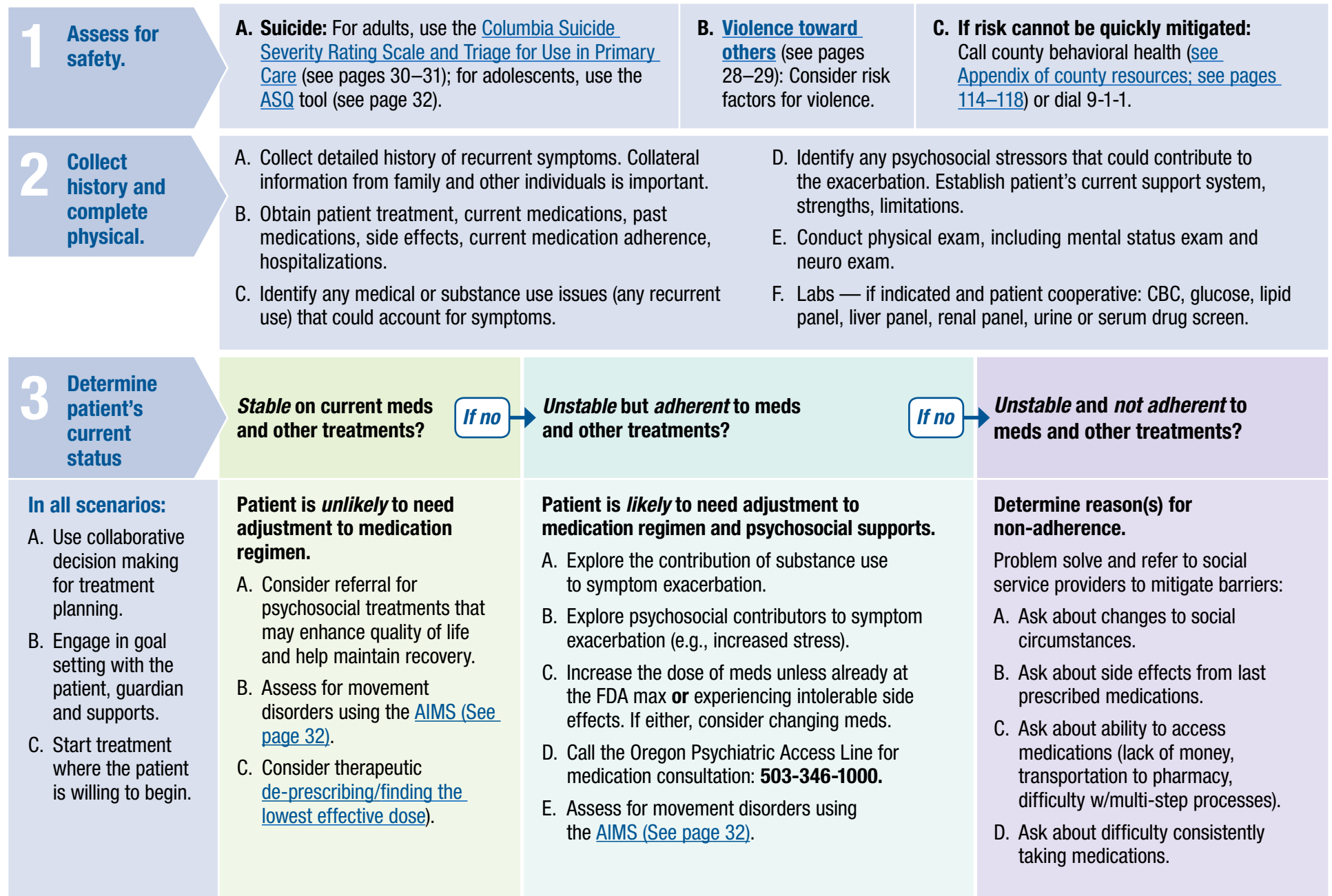


Figure 3. Psychosocial assessment and intervention flow chart

Engagement and assessment

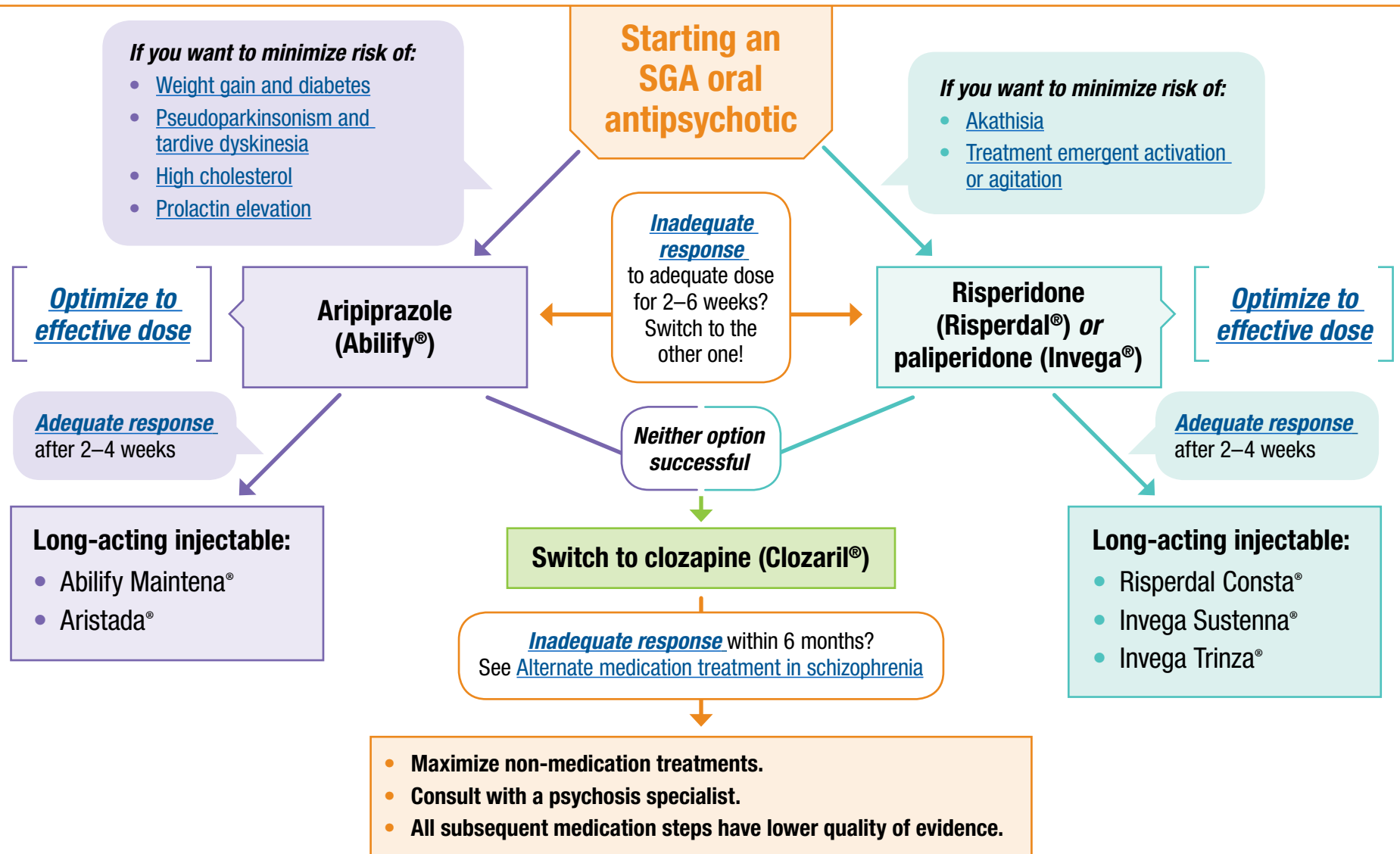
<p>First, stabilize and address any safety concerns that may be present.</p>	<p>Build trust. Establish and maintain a therapeutic alliance. Maintain an environment with a trauma-informed care (TIC) approach.</p>	<p>Assess for symptom changes and changes to social circumstances. Address social factors contributing to symptom exacerbation either immediately or by referral, depending on urgency and severity.</p>	<p>Be aware of Common Barriers to Treatment for those with a diagnosis of Schizophrenia. Problem solve.</p>	<p>When patients have a guardian, involve the guardian in all treatment-related decisions. Incorporate patient supports in treatment care plan.</p>
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Planning and intervention

<p>A. Work collaboratively with the patient, guardian and supports to create immediate, short- and long-term goals.</p>	<p>B. Choose interventions that have demonstrated effectiveness in the treatment of schizophrenia and can assist the patient in meeting their goals.</p>		<p>C. Develop a crisis plan.</p>	<p>D. Consider medications if necessary.</p>
<p>Consider using the SMART goals format to create immediate, short- and long-term goals.</p>	<p>Wraparound intervention/support programs including</p> <ul style="list-style-type: none"> For youth/young adults: Early Assessment and Support Alliance (EASA) For adults: Assertive Community Treatment (ACT) 	<p style="text-align: center;">OR</p> <p>Other psychosocial interventions including psychoeducation, cognitive behavioral therapy, supported housing, social skills training, peer-delivered services, cognitive remediation, intensive case management, occupational therapy, supported employment, substance abuse and co-occurring disorders treatment</p>	<p>Create a crisis plan with the patient, guardian and supports.</p>	<p>If medication is indicated, refer to the medication algorithm or contact the Oregon Psychiatric Access Line (OPAL) for consultation for prescribing providers.</p>

Ensure that treatment care planning is patient-centered, and the treatment care plan is responsive to emerging needs.

Figure 4. MHCAG recommended medication algorithm: Starting second generation antipsychotic (SGA) medication treatment in schizophrenia



For information about maintenance, medication adjustments and tolerability, refer to these links:

[Inadequate response](#) (see page 112)

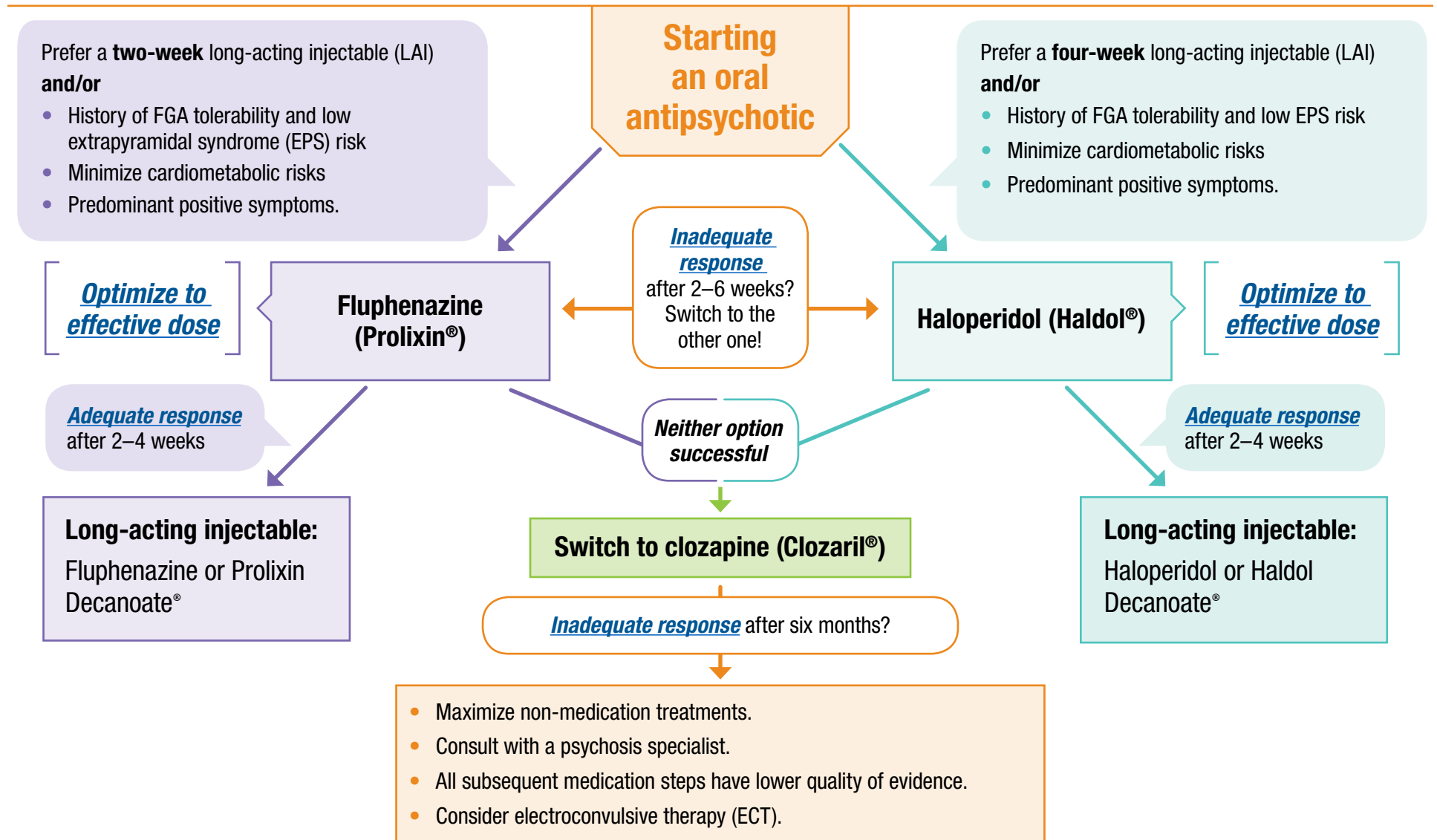
[Adequate response](#) (see page 112)

[Finding the lowest effective medication dose in psychotic disorders](#) (see pages 41–43)

Positive Cardiometabolic Health Resource: <https://mentalhealthpartnerships.com/wp-content/uploads/sites/3/pchr.png>

Movement disorders: <http://n.neurology.org/content/neurology/81/5/463.full.pdf>

Figure 5. If first generation antipsychotic (FGA) preferred medication algorithm for treatment in schizophrenia



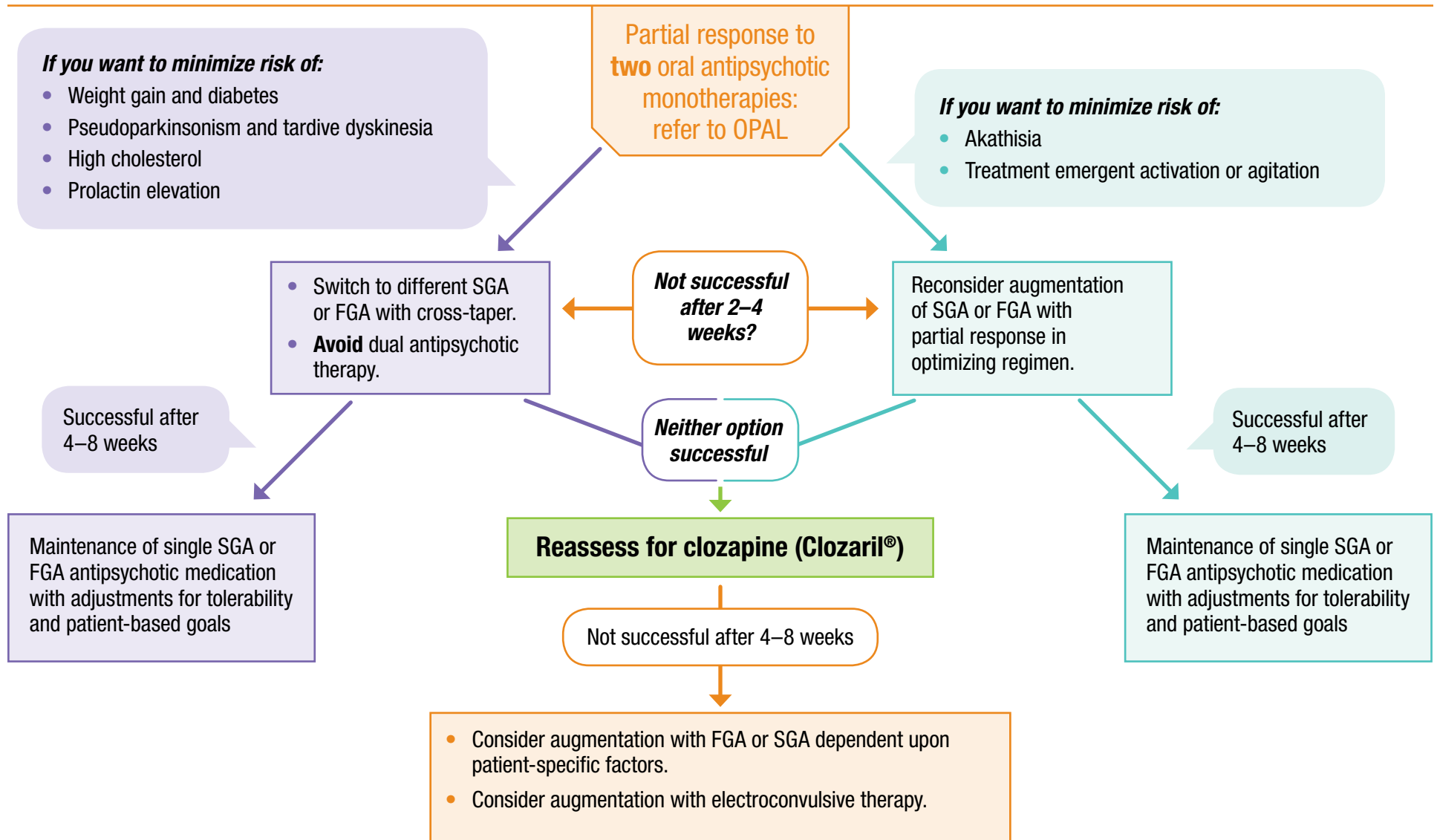
For information about maintenance, medication adjustments and tolerability, refer to these links:

[Finding the lowest effective medication dose in psychotic disorders \(see pages 41–43\)](#)

Positive Cardiometabolic Health Resource: <https://mentalhealthpartnerships.com/wp-content/uploads/sites/3/pchr.png>

Movement disorders: <http://n.neurology.org/content/neurology/81/5/463.full.pdf>

Figure 6. Alternate medication treatment in schizophrenia



For information about maintenance of single SGA or FGA antipsychotic medication with adjustments for tolerability and patient-based goals:

[Finding the lowest effective medication dose in psychotic disorders \(see pages 41–43\)](#)

Positive Cardiometabolic Health Resource: <https://mentalhealthpartnerships.com/wp-content/uploads/sites/3/pchr.png>

Movement disorders: <http://n.neurology.org/content/neurology/81/5/463.full.pdf>

Figure 7. Antipsychotic-related side effects

Parkinsonism

- Resting tremor (4–6Hz, slower than physiologic or intention tremor)
- Pill-rolling of hand
- Bradykinesia
- Rigidity
- Shuffling gait
- Stooped posture

Options

- A. Reduce antipsychotic dose.
- B. Switch to antipsychotic with less parkinsonism risk.
- C. Maintain antipsychotic; treat side effect with:
 - Benztropine 1–2mg twice a day (BID)
 - or**
 - Diphenhydramine 25–50mg BID

Acute dystonia

- Involuntary upward gaze
- Facial grimacing
- Laryngeal spasms
- Neck spasms
- Abdominal wall spasms
- Spine spasms

Options

- Urgent medical treatment!
- Intramuscular/intravenous (IM/IV) benztropine 1–2mg
- or**
- IM/IV diphenhydramine 25–50mg

Akathisia

- Feels restless
- Trouble standing still
- Paces
- Feet constantly moving or rocking

[Barnes Akathisia Rating Scale is recommended.](https://cpnp.org/ed/movement-disorders#scales)

Options:

- A. Reduce antipsychotic dose.
- B. Switch to antipsychotic with less akathisia risk.
- C. Maintain antipsychotic; treat side effect with:
 - Propranolol 10–30mg BID (titrate response, BP, HR) **or**
 - Clonazepam (0.5 to 1mg BID) **or**
 - Lorazepam (1mg two to three times a day) **or**
 - Clonidine (0.1mg TID).

Tardive dyskinesia

Repetitive, involuntary, purposeless movement of:

- Face, mouth or tongue
- Upper or lower extremities
- Trunk

Abnormal Involuntary Movement Scale (AIMS) is expected: <https://cpnp.org/ed/movement-disorders#scales>.

- Evaluate medications and medical conditions for other causes of dyskinesia.
- Consider referral to neurology, ideally a movement disorder specialist.

Treatment

- A. Trial reduction of antipsychotic dose
- B. Quetiapine monotherapy switch in addition to clozapine monotherapy
- C. Trial of clonazepam augmentation
- D. Switch to clozapine
- E. Use of other non-medication treatment modalities such as electroconvulsive therapy

Section 2. Medication tables and resources for schizophrenia

The MHCAG recommends a collaborative evidence-based approach with providers and patients selecting medications that may provide the greatest value and cost-effectiveness. Please refer to Medication pricing information, page 40 in the Resources for Clinicians section.

Table 1: MHCAG recommended antipsychotic medications, indications and general information

Drug	Form.	t _{1/2} *	Adult dose	FDA indications	Pediatric approval	Drug-specific considerations	Former FDA pregnancy category	Possible CBD/THC	Possible tobacco smoke interaction
Second generation (“atypical”) antipsychotics (SGAs)									
Aripiprazole (Abilify®)	Oral	75~94	2–15 mg/day QD	Autistic disorder	≥ 6 year	Schizophrenia: efficacy not significantly greater for doses > 15mg/day	C	Y (CBD inhibition of 3A4 pathway)	Unlikely
			10–30 mg/day QD	Bipolar disorder, maintenance and acute treatment +/- lithium or valproate	≥ 10 year				
			2–20 mg/day QD	Tourette’s Syndrome	≥ 6 year				
			2–15 mg/day QD	Major depressive disorder (adjunct)	No				
			10–30 mg/day QD	Schizophrenia	≥ 13 year				
(Abilify Maintena®)	LAI	29.9–46.5 d	400 mg once monthly (≥ 26 days)	Schizophrenia	No	~Missed dose schedule 2nd/3rd dose: > 5 weeks since last dose, restart oral aripiprazole for 14 days; ≥4 doses: > 6 weeks since last dose, restart oral			
(Abilify Aristada®)	LAI Aristada®	53–57 days	300 mg once monthly for adverse effects	Bipolar I disorder, maintenance	No				

Table 1 continued

Drug	Form.	t _{1/2} *	Adult dose	FDA indications	Pediatric approval	Drug-specific considerations	Former FDA pregnancy category	Possible CBD/THC	Possible tobacco smoke interaction
	Oral, IM	23	3–12 mg/day QD	Schizophrenia	No ≥ 12 year	Mild renal impairment t _{1/2} = 24 hours; moderate renal impairment t _{1/2} = 40 hours; severe renal impairment: t _{1/2} = 51 hours	C	Unknown	Unlikely
LAI – (Invega Sustenna®) [1 month]	LAI	25–49 d	39–234 mg once monthly		No				
(Invega Trinza®) [3 months]	LAI (Trinza®)	84–95 d, 118–139 d	273–819 mg every 3 months 273–819 mg every 3 months 273–819 mg every 3 months	Schizophrenia Major depressive disorder Bipolar Disorder	No No ≥ 10 acute for mania	Oral → LAI dose: 3 mg/day → 39–78 mg monthly 6 mg/day → 117 mg monthly 9 mg/day → 156 mg monthly 12 mg/day → 234 mg monthly			
Risperidone	Oral, solution ODT	3–20 ~21–30	0.25–3 mg/day QD (initial 0.5 mg when ≥ 20 kg) 2–6 mg/day QD 2–8 mg/day QD	Autistic disorder, irritability Bipolar I disorder Schizophrenia	≥ 5 year and ≥ 15 kg ≥ 10 year ≥ 13 year	Renal: CrCl ≤ 30 mL/min initiate at 0.5 mg BID for bipolar and schizophrenia; Hepatic: Child-Pugh Class C initiate at 0.5 mg BID for bipolar and schizophrenia	C	Y (CBD inhibition of the CYP 3A4 pathway)	Unlikely
LAI – (Risperdal Consta®)	LAI	3–6 d ~8 d	25–50 mg IM every 2 weeks	Bipolar I disorder Schizophrenia Schizophrenia	No No No				

Table 1 continued

Drug	Form.	t _{1/2} *	Adult dose	FDA indications	Pediatric approval	Drug-specific considerations	Former FDA pregnancy category	Possible CBD/THC	Possible tobacco smoke interaction
Clozapine (Clozaril®)	Oral,	12 (4–66)	25–900 mg/day; dose based on tolerability and CBC	Treatment resistant schizophrenia	No	Black box warnings for severe neutropenia, orthostatic hypotension, seizures, myocarditis, cardiomyopathy and mitral valve incompetence	B (floppy baby syndrome and	Y (THC inhibition of CYP 1A2 pathway; CBD inhibition of CYP 3A4 and 2C19 pathways)	Y (induction of CYP 1A2 pathway by smoke tobacco)
			5–20 mg/day	Schizophrenia, recurrent suicidal behavior	No				
			5–18 mg/day	Schizophrenia	≥ 13 year				
			Flu: 20–50 mg/day	Major depressive disorder, with fluoxetine	≥ 10 year				
First generation (“typical”) antipsychotics (SGAs)									
	Oral, IM, elixir	12.2	PO: 2.5–40 mg/d Q6–8 hour IM: 1.25–10 mg/d Q6–8hr	Schizophrenia	No	Contraindicated with large doses of hypnotics, liver damage and subcortical brain damage	N	Unknown	Unlikely
LAI — (Prolixin)	LAI	14–26 days	12.5–100 mg SubQ Q4–6 weeks	Schizophrenia, chronic	No	12.5 mg Q3weeks = 10mg oral daily Titrate to effectiveness (max 100mg)			
Haloperidol (Haldol®)	Oral	14–37	2–5 mg BID-TID	Schizophrenia	≥ 3 year	Not approved for IV administration, monitor EKG if given IV (higher risk of QT prolongation)	C	Y (CBD inhibition of CYP 2D6; THC Inhibition of 1A2)	Y (induction of CYP 1A2 pathway by tobacco)
			0.5–5 mg BID-TID, no max	Severe problematic behavior in children	≥ 3 year				
			0.5–5mg BID-TID	Tourette’s syndrome	≥ 3 year				
LAI — (Haldol)	LAI	21 d	10–20 x PO dose monthly	Schizophrenia, chronic	No	Doses over 450mg per month have limited clinical evidence			

* Half-life reported in hours unless otherwise specified; ~ = active metabolite

Legend: t_{1/2} = Half-life; LAI = Long-acting injectable; IM = Intramuscular; Inh = Inhalation; SL = Sublingual
IR = Immediate release; ER = Extended-release

FGA= First generation antipsychotic

SGA= Second generation antipsychotic

Table 2: Side effects for additional antipsychotic medications

Drug	Trade name	Weight gain	Hyper-	EPS/TD	Prolactin	Sedation			QTc
Second generation (“atypical”) antipsychotics (SGAs)									
Asenapine	Saphris®	++	-	++	++	++	-	+	+
Brexipiprazole	Rexulti®	+	+	+	-/+	+	-/+	-/+	-/+
Cariprazine	Vraylar®	+	-/+	++	-/+	+	-/+	-/+	-/+
lloperidone	Fanapt®	++	++	-/+	-/+	+	+	+++	++
Lurasidone	Latuda®	-/+	-/+	++	-/+	++	-	+	-/+
Olanzapine*	Zyprexa®	++++	++++	+	+	++	++	+	+
Quetiapine	Seroquel®	+++	+++	-/+	-/+	++	++	++	+
Ziprasidone	Geodon®	-/+	-/+	+	+	+	-	+	++
First generation antipsychotics (“typical”) (FGAs)									
Chlorpromazine	Thorazine®	+++	+	+	++	+++	+++	+++	+
Loxapine	Loxitane®	++	ND	++	++	++	+	+	+
Perphenazine	Trilafon®	++	ND	++	++	++	+	-	ND
Thioridazine	Mellaril®	++	ND	+	+++	+++	++++	++++	+++
Thiothixene	Navane®	++	ND	+++	++	+	+	+	+
Trifluoperazine	Stelazine®	++	ND	+++	++	+	+	+	ND

* = Long-acting injectable agent available

Table 3. Pharmacokinetics and dosing of MHCAG recommended medications

Drug	Form.	t½*	Tmax	Metabolism	Oral BA	Dosing considerations
Second generation (“atypical”) antipsychotics (SGAs)						
Aripiprazole (Abilify®)	Oral	75 ~94	3–5	Extensive hepatic metabolism via CYP2D6 and CYP3A4	87%	See Table 1 for LAI missed dose schedule Concurrent strong CYP2D6 or CYP3A4 inhibitors reduce dose by 50% For LAI 400 mg → 200 mg and 300 mg → 160 mg
(Abilify Maintena®)	LAI	29.9–46.5 days	4–7 days			
(Aristada®)	LAI	53–57 days	4–7 days			
(Aristada Initio®)	LAI	15–18 days	27 days	Same as other aripiprazole formulations	Same as other aripiprazole formulations	Administered as a single dose for initiation of treatment at the same time as a 30 oral dose of aripiprazole and the first Aristada® injection

Table 3 continued

Drug	Form.	t _{1/2} *	Tmax	Metabolism	Oral BA	Dosing considerations
Clozapine (Clozaril®)	Oral	12 (4–66)	2.2–2.5	Extensive hepatic metabolism via CYP1A2 (primary), CYP2C19, CYP3A4, CYP2D6	27–60%	Monitoring: REMS for severe neutropenia. ANC > 1500/mcL (>1000/mcL with benign ethnic neutropenia) required for initiation CBC: weekly for 6 months; then every other week for 6 months; then monthly thereafter
Paliperidone (Invega®)	Oral, IM	23	24	P-glycoprotein Limited hepatic metabolism	28%	Mild renal Impairment t _{1/2} = 24 hour; Moderate renal impairment t _{1/2} = 40 hour; Severe renal impairment: t _{1/2} = 51 hour
LAI – (Invega Sustenna®)[1 month]	LAI (Sustenna®)	25–49 days	13 days			
(Invega Trinza®) [3 months]	LAI (Trinza®)	84–95 d, 118–139 d	30–33 days			
Risperidone (Risperdal®)	Oral	3–20 ~21–30	1 17 (PM)	Extensive hepatic metabolism via CYP2D6	70% 94% (ODT)	Dose adjustments with renal or hepatic impairment or with concomitant use of CYP3A4 inducers or CYP2D6 inhibitors Oral → LAI dose: 3 mg/day → 90 mg monthly 4 mg/day → 120 mg monthly
(Risperdal Consta®)	LAI	3–6 d ~8 d	29–31 d			
Risperidone (Perseris®)	LAI	7–11 days	4–6 hours	Same as other risperidone products		
First generation antipsychotics (“typical”) (FGAs)						
Fluphenazine (Prolixin®)	Oral	12.2	PO: 2 IM: 1.5–2	No well-defined metabolic pathway	20–50%	High volume of distribution: 10,580–61,924 L/kg Variable oral absorption Contraindicated with liver damage
LAI - (Prolixin Decanoate®)	LAI	14–26 days	34–65			
Haloperidol (Haldol®)	Oral	PO: 14–37 IM: 20	PO: 3–6 IM: 20min	50–60% glucuronidation CYP2D6 and CYP3A4 activity	60–86%	Do not administer IV due to high risk of QT prolongation resulting in torsades de pointes Administer initial doses > 100 mg 3–7 days apart
LAI - (Haldol Deca-noate®)	LAI	21 days	6 days			

* t_{1/2} = Half-life reported in hours unless otherwise specified; ~ = active metabolite; wks = weeks

**Paliperidone 3-month extended release LAI

^ Active metabolite half-life

CYP = Cytochrome P540; UGT = UDP-glucuronosyltransferase

Oral BA = Oral bioavailability

IR = Immediate release; ER = Extended release

PM = Poor metabolizer

AUC = Area under the curve; C_{max} = Maximum concentration

T_{max} = Time to maximum concentration (absorption), reported in hours unless otherwise specified

Inh = Inhalation; SL = Sublingual

CBC = Complete blood count; ANC = Absolute neutrophil count

Table 4. Pharmacokinetics and dosing of additional medications

Drug	Form.	t½*	Tmax	Metabolism	Oral BA	Dosing considerations
Second generation (“atypical”) antipsychotics (SGAs)						
Asenapine (Saphris®)	Oral (SL)	24	0.5–1.5	Hepatic via CYP1A2 and UGT1A4	35%	Use contraindicate in severe hepatic impairment (Child-Pugh Class C)
Brexpiprazole (Rexulti®)	Oral	91	4	Hepatic via CYP3A4 and CYP2D6	95%	CYP2D6 poor metabolizers reduce dose to 50% (reduce to 25% if concomitant strong inhibitors of CYP3A4 as well)
Cariprazine (Vraylar®)	Oral	2@4 days ~1–2 days ~1–3 wks	3–6	Extensive hepatic metabolism via CYP 3A4	50%	Reduce dose to 50% with concurrent strong inhibitor of CYP3A4
lloperidone (Fanapt®)	Oral	18–33 ~26–37 ~13–31	2–4	Extensive hepatic metabolism via CYP2D6 and CYP3A4	96%	Weak inhibitor of P-glycoprotein. Use not recommended in severe hepatic impairment: Child-Pugh Class C
Lurasidone (Latuda®)	Oral	18	1–3	Hepatic via CYP3A4 (active metabolite)	9–19%	Take with food, at least 350 calories. Renal: CrCl ≤ 50 mL/min = max 80 mg/day. Hepatic: Class B max 80 mg/day. Hepatic: Class C max 40 mg/day.
Olanzapine (Zyprexa®)	Oral, IM	30	1–8	Hepatic via CYP1A2 and CYP2D6	Rapid	40% removed via first pass metabolism
LAI – (Zyprexa Relprevv®)	LAI	30 days	7 days			
Quetiapine (Seroquel®)	Oral	6 (IR) 7 (ER) ~12	1.5 (IR) 6 (ER)	Primarily CYP3A4 (active metabolite)	100%	Rapid absorption with high fat meals (800–1,000 calorie) increase Cmax 8% and AUC 2% of ER formulation
Ziprasidone (Geodon®)	Oral	7	6–8	Hepatic metabolism via CYP3A4 and CYP1A2	60%	Take with ≥ 500 calories of food. Increase oral BA up to 2-fold
First generation (“typical”) antipsychotics (FGAs)						
Chlorpromazine (Thorazine®)	Oral, IM, IV	6 ~30	PO: 2.8 IM: 1–4 IV: 2–4	Extensive hepatic metabolism: glucuronidation and CYP2D6	32%	No renal or hepatic dose adjustments
	LAI	21 days	6 days			
Loxapine (Loxitane®)	Oral	Initial: 5 Final: 19	1.5–3	Extensive liver metabolism: CYP1A2, CYP2D6, CYP3A4 substrates	100%	Inhibitor of P-glycoprotein Active and inactive metabolites
Inh - (Adasuve®)	Inh	7.6	1.1 min			Contraindicated for asthma or COPD

Table 4 continued

Drug	Form.	t _{1/2} *	Tmax	Metabolism	Oral BA	Dosing considerations
Molindone (Moban®)	Oral, IM	1.5	1.5	Hepatic (36 active metabolites)	-	Duration of action:24–36 hours
Perphenazine (Trilafon®)	Oral, IM	9–12 ~10–19	1–3	CYP2D6, glucuronidation and sulfoxidation	-	Poor CYP2D6 metabolizers may have prolonged half-life
Prochlorperazine (Compazine®) (Procot®) Rectal (Compro®)	Oral, IM, rectal	6–22	0.5–1	Hepatic (active metabolite)	12.5%	No renal or hepatic dose adjustments
Thioridazine (Mellaril®)	Oral	21–24	1–4	Extensive hepatic metabolism	25–33%	Do not use with QT prolonging medications or inhibitors of thioridazine metabolism (see Table 1)
Thiothixene (Navane®)	Oral	34	-	CYP1A2 metabolism	Erratic	High lipophilicity
Trifluoperazine (Stelazine®)	Oral	3–12	1.5–6	In the gut and liver (active)	Erratic	Onset 2–4 weeks

* t_{1/2} = Half-life reported in hours unless otherwise specified; ~ = Active metabolite; wks = weeks

**Paliperidone 3-month extended release LAI

^ Active metabolite half-life

CYP = Cytochrome P540; UGT = UDP-glucuronosyltransferase

Oral BA = Oral bioavailability

IR = Immediate release; ER = Extended release

PM = Poor metabolizer

AUC = Area under the curve; Cmax = Maximum concentration

Tmax = Time to maximum concentration (absorption), reported in hours unless otherwise specified

Inh = Inhalation; SL = Sublingual

CBC = Complete blood count; ANC = Absolute neutrophil count

Table 5. Medication and medical monitoring resource

	Baseline (or with change of treatment)	Every visit	Every 3 months of	Every 6 months of	Every 12 months of	As clinically indicated
Assessment/monitoring						
Height, weight (with percentiles), BMI, waist circumference	X	X				
Blood pressure and heart rate	X	X				
Family history (special focus on family experience with psychotropics and metabolic/medical issues with impact on medication risks)	X				X	
Adherence assessment and discontinuation reasons (Assess prior treatment adherence at baseline)	X	X				
Assessment of social risk factors relevant to treatment	X	X				
AIMS/EPS and akathisia assessment	X	X		X		X
Parkinsonism and akathisia	X					
Sexual function question	X		X		X	X
ECG (for ziprasidone or others prone to QTc prolongation)	X			One time @ 6 months		
Assessment/lab monitoring						
CBC (REMS guidance takes precedence if applicable)	X			X		
Fasting (or random) blood glucose and HbA1C	X		>5% change in waist or weight	X		
Liver function testing — minimally AST, ALT, GGT (consider also lipase/amylase if specific risks for pancreatitis)	X				X	
Cholesterol (Total, LDL, HDL and triglycerides)	X			X		
TSH and T4	X				X	
Pregnancy test	X	As clinically indicated				
Prolactin (Assess urgently for sexual dysfunction, gynecostasia or spontaneous lactation)				High D2 receptor affinity agent	X	X

Section 3. MHCAG schizophrenia resources for individuals, caregivers, families and teachers

Support, education and navigation organizations

These organizations provide general education, support and navigation services to individuals living with mental illness and families affected by mental illness. They have knowledge of treatment and support services in local communities, and they can often assist individuals and families in deciphering the mental health system and identifying pathways for help. They are a good place to start for any individuals and families seeking information and support.

Oregon Family Support Network

The Oregon Family Support Network (OFSN) is a statewide nonprofit organization that supports families raising school-age children with significant mental health challenges. OFSN offers wraparound services to eligible families and children on the Oregon Health Plan. OFSN also offers information, support and trainings to families seeking help, such as trainings in collaborative problem solving and in navigating individual education plans (IEPs).

Summary of services

- Information and support for families, such as navigation questions
- Wraparound family partner program for eligible families on the Oregon Health Plan
- Support, education, training and recreational programs in multiple Oregon communities.

Call: 503-363-8068

Web: www.ofsn.org

National Alliance on Mental Illness of Oregon

The National Alliance on Mental Illness of Oregon (NAMI Oregon) is a statewide nonprofit organization with 15 chapters across Oregon that serve individuals and families living with mental illness. Services include education, support and policy advocacy services. NAMI offers navigation services and free education classes, support groups, and public workshops that address the lifespan and include individuals living with mental illness as well as their families and other loved ones.

Summary of services

- Navigation helplines for all people affected by mental illness
- Free education classes and support groups
- Free public education presentations and workshops.

Call: 503-230-8009, 800-343-6264

Web: www.namior.org

Mental Health Association of Oregon

The Mental Health Association of Oregon (MHAO) is an organization led by adults with lived experience in the mental health system. MHAO provides technical support and education to organizations across Oregon that offer peer services. MHAO provides peer services for adults in several Oregon communities and trainings for peer support specialist certification. MHAO can also refer individuals to organizations around Oregon that are peer-led or that provide peer services for adults in various local communities.

Summary of services

- Technical support to peer-led organizations
- Peer support specialist certification trainings
- Trainings and workshops for adults living with mental illness.

Call: 503-922-2377

Web: www.mhaoforegon.org

Organizations addressing disabilities

These organizations provide support, education, and navigation services for individuals and families living with developmental disabilities.

FACT Oregon

FACT Oregon (Family and Community Together Oregon) is the federally designated parent training and information center for families raising school-age children with disabilities. FACT Oregon assists families in navigating and advocating for education services and disability services in general. FACT Oregon also connects parents with other parents with lived experience in raising school-age children with disabilities.

Summary of services

- Resource and navigation line for families via family resource specialists
- Workshops and other trainings on the developmental disabilities system
- Trainings and information on special education and individualized education program plans
- Parent support and networking opportunities.

Call: 503-786-6082, 888-988-3228

Web: factoregon.org

Autism Society of Oregon

The Autism Society of Oregon is a nonprofit advocacy organization that provides resources, education, advocacy and support for individuals and families living with autism. The website lists chapter contacts in most Oregon regions along with support groups and other activities of interest to families affected by autism.

Summary of services

- Parent-to-parent support and mentoring opportunities
- Support groups in multiple Oregon communities with local representative contact information
- Event calendar with information and trainings of interest offered by other organizations.

Call: 888-288-4761

Web: <http://autismsocietyoregon.org>

Brain Injury Alliance of Oregon

The Brain Injury Alliance of Oregon is a statewide nonprofit organization that serves individuals and families affected by traumatic brain injuries through resources facilitation, education and support services.

Summary of services

- Information, referrals and a clearinghouse for community resources
- Peer mentoring and support for families and individuals living with brain injuries
- Holds conferences, workshops and trainings in various Oregon communities.

Call: 800-544-5243

Web: www.biaoregon.org

Support organizations for adults

David Romprey Oregon Warmline

The David Romprey Oregon Warmline is a toll-free warmline that provides one-on-one support for individuals living with mental illness. The warmline features specially trained responders with lived experience who provide support and connection to callers struggling with a mental health condition. The warmline is operational daily; hours can vary.

Note: The warmline is not a crisis line. It is designed for individuals seeking peer support.

Call: 800-698-2392

Web: <http://communitycounselingsolutions.org/warmline/>

Dual Diagnosis Anonymous of Oregon Inc.

Dual Diagnosis Anonymous of Oregon (DDA) is a specialized 12-step group designed to support individuals living with both a mental illness and a substance use disorder. DDA groups add an additional five steps around mental health and are understanding of individuals who need support in an environment that addresses co-occurring conditions. Support groups are available across Oregon.

Call: 503-222-6484, 877-222-1332

Web: www.ddaoforegon.com

Depression Bipolar Support Alliance

The Depression Bipolar Support Alliance (DBSA) is a nationally recognized support group model specially designed for people living with depression or bipolar disorder. DBSA offers groups in several Oregon communities and provides a real-time online support group accessible through its website.

Call: 877-222-1332, 503-222-6484

Web: www.dbsalliance.org

Support organizations for youth

Youth ERA

Youth ERA is a support organization designed by and serving youth and young adults living with mental illness and related conditions. Youth ERA operates drop-in centers in several Oregon communities, including Salem, Medford, North Bend and Milwaukie. The centers feature peer support specialist services, among other offerings. Youth ERA also offers trainings and other programs to help young people become knowledgeable advocates.

Call: 971-334-9295

Web: www.youthera.org

Legal advocacy organizations

Disability Rights Oregon

Disability Rights Oregon (DRO) is Oregon's federally designated protection and advocacy system organization charged with upholding the civil rights of individuals living with disabilities, including individuals living with serious mental illness. DRO assists with legal problems directly related to disabilities.

Key services include:

- Information, tools and referrals that help empower self-advocacy on numerous topics such as education, employment, housing and guardianships
- General information on legal rights and other resources via appointments with intake advocates.

Call: 503-243-2081, 800-452-1694

Web: droregon.org

Youth, Rights & Justice

Youth, Rights & Justice is a Portland-based nonprofit law firm that provides court-appointed attorneys who represent children in foster care, parents in the child dependency system and youth in the juvenile court system. Youth, Rights & Justice provides services in the Portland metropolitan area but offers helpful information on its website for both youth and parents.

Call: 503-232-2540

Web: www.youthrightsjustice.org

Suicide prevention hotlines and text lines

Lines for Life

Lines for Life is an Oregon-based nonprofit that operates 24-hour crisis lines. Lines for Life offers help and hope to individuals and their loved ones when in crisis or when needing confidential help for drug addiction, alcohol abuse, thoughts of suicide and other mental health issues. Lines for Life staff and volunteer crisis intervention specialists are highly trained and help thousands of individuals each year. The organization also has specialty crisis lines for veterans and teenagers.

Web: www.linesforlife.org

Suicide Lifeline

800-273-8255 (24 hours)

Text 273TALK to 839863 (8 a.m.–11 p.m. Pacific time daily)

Alcohol and Drug Helpline

800-923-4357 (24 hours)

Text RecoveryNow to 839863 (8 a.m.–11 p.m. Pacific time daily)

Military Helpline

888-457-4838 (24 hours)

Text MIL1 to 839863 (8 a.m.–11 p.m. Pacific time daily)

YouthLine

Teen-to-teen crisis and helpline. Teens available daily 4–10 p.m. Pacific time. Lines for Life answers off-hour calls. Call 877-968-8491.

Text teen2teen to 839863.

Chat at www.oregonyouthline.org.

Other specialty services

Early Assessment & Support Alliance

The Early Assessment & Support Alliance (EASA) is a care model designed to intervene in the first episode of psychosis for youth and young adults. EASA programs are available in most Oregon counties, although access and eligibility may vary from county to county. Early intervention that provides wraparound services to young people experiencing psychosis and their families and/or other support networks is an evidence-based approach that has proven highly successful in keeping young people on a normal life path.

Web: www.easacommunity.org

Considerations when choosing a therapist

Types of mental health providers, types of treatment and what to expect:

Mental Health America: <http://www.mentalhealthamerica.net/finding-right-care>

Questions to ask a provider: <http://www.mentalhealthamerica.net/questions-ask-provider>

Section 4. Schizophrenia assessment and treatment resources for clinicians

Oregon Psychiatric Access Line (OPAL) for medication consultation for prescribing providers

The Oregon Psychiatric Access Line (OPAL) is a service of Oregon Health & Science University that provides free, same-day child and adult psychiatric phone consultation to primary care providers in Oregon. The program expands the availability of high-quality mental health treatment to Oregon youth and adults via timely psychiatric consultation, medical practitioner education and connections with mental health professionals throughout the state.

Individuals and families living with mental illness may benefit from their medical providers registering with OPAL. Once registered, providers have access to child and adult psychiatrists Mondays through Fridays (excluding major holidays) from 9 a.m. to 5 p.m. Only providers may use OPAL.

Call: 503-346-1000 (provider inquiries only)

Web: <https://www.ohsu.edu/xd/education/schools/school-of-medicine/departments/clinical-departments/psychiatry/divisions-and-clinics/child-and-adolescent-psychiatry/opal-k/index.cfm>

Safety intervention and crisis plans

Safety intervention plan on the following pages provided by Yamhill County Behavioral Health.

Safety intervention plan

Effective Date:

Client Information

Name (First / MI / Last): **DOB:**
County of Residence: **Case #:** **Phone:**
Support persons (family, advocate, peer support, sponsor) who you want called in a crisis
Name: **Relationship:** **Phone:**
Name: **Relationship:** **Phone:**
Name: **Relationship:** **Phone:**

Medical Information

Counselor/Case Manager: **Phone:**
Agency: **Phone:**
If you are taking mental health medications, who prescribes them?
Name: **Phone:**
Primary Care Physician: **Phone:**
Person who has a list of your current medications:
Medications that have been helpful in emergencies:
Medications to avoid and why:
Allergies/adverse medical effects:
Mental Health Conditions:
Substance use issues:
Medical Conditions:
 I have completed a Declaration for Mental Health Treatment. It is available at:
 I have completed a Law Enforcement Data Systems(LEDS) Medical Database. It is available at:

Personal Action/Crisis Prevention Planning

Some things I want from my life are:
Signs that I'm doing OK:
Early signs that I'm not feeling well:
What I can do to help myself:
Ways that others can help me:
What I don't want – What doesn't help:
I know I need to get help when:

In a crisis I need to know I have help with Pets Children Transportation
 Other: (explain):

In a crisis situation I will do this:

Optional: My provider or other support person agrees to do this:

- I would like to request a trauma survivor peer support volunteer (if you're on the Oregon Health Plan)
 I would like more information about peer support services

Oregon state law allows healthcare providers to share your confidential information to the extent necessary to help you during an emergency. *Oregon Revised Statutes 179.505 (4)(a)*

Ideas to help spark your thinking when filling out your plan

Pick any ideas that fit for you – Add your own ideas – Use your own words

Signs that I'm doing okay:

- I can laugh at myself; find my sense of humor
- I feel that life is good; I am grateful
- I have confidence in myself; I'm not ashamed or afraid
- I can balance both positive and negative aspects of my life
- I can think things through and am in control of my actions, thoughts, feelings
- I make time to see friends; I feel sociable, safe, secure
- I participate in meaningful activities or work; I feel connected to society
- I feel energetic, calm and strong
- I take time to exercise
- I don't feel nervous or anxious; I'm curious, interested, not bored
- I am focused; I can concentrate; I'm not easily distracted
- I enjoy sound sleep; I like waking up

Early signs that I'm not feeling well:

- Changes in sleep habits: fatigue, insomnia; wanting to sleep all the time
- Changes in eating; stop eating or eat compulsively
- More sensitivity to what I see, hear, smell or touch
- Seeing figures, hearing voices
- I stop taking care of myself
- I start believing that people are against me, but know that my thinking is off
- I am bothered by thoughts I can't get rid of
- I feel like harming myself or others
- I think about getting back into addictive behavior
- I feel more anxious or depressed; I experience more panic
- I get confused or have increased difficulty with memory
- I experience racing thoughts
- I'm more irritable or angry; I disagree with people a lot
- I stop answering the phone or knocks at the door; I don't open my mail

What I can do to help myself:

- Hum; sing; read; lie down and rest; take a nap; talk with friends
- Tell the voices to go away; think "STOP"
- Watch TV or a video; to a movie, listen to music
- Help other people
- Debate with the voices
- Exercise; take a walk; clean a room
- Journal; write a letter; do my hobby
- Take a bath or shower; soak my feet; fix my fingernails
- Let someone know that I am having symptoms and what they are
- Use my mindfulness skills
- Safely release my anger or frustration
- Use alternatives to harming myself

- Make myself a treat or a good meal or buy a flower
- Pet my dog or cat
- Breathe
- Take time to be myself
- Call somebody who understands; call a peer support person

Ways others can help me:

- Listen to my story long enough to really hear what I'm saying
- Talk to me; encourage and reassure me; show me my successes
- Encourage me to pace or move around; to listen to my music; to draw or paint
- Call my peer support person
- Remind me of my goals; my interests; my connections
- Hold me; breathe with me; help me become aware of what is happening
- Ask me if I am hearing voices and how loud they are
- Tell me that you want to help; ask me what I want from you
- Accept and respect me; understand that I am doing the best I can
- Treat me the same as when I am not having problems; take me seriously
- Give me space; leave me alone
- Treat me gently, calmly; slow me down
- Help me communicate my needs to professionals
- If you give me any instructions, make them clear and write them down
- Problem solve with me on concrete things I can do to take care of myself
- Be aware of how the volume of your voice affects me
- Ask me if I've eaten; feed me

What I don't want – What doesn't help:

- Keeping me waiting
- Dismissing, forgetting, or ignoring what I tell you
- Asking immediately whether I'm a danger to myself or others
- Talking to me
- Touching me
- Not listening to me; making assumptions about what I need
- Telling me what to do or what not to do; nagging me; lecturing me
- Judging me, or criticizing me, or labeling me
- Trying to control me or threatening me
- Making me sign a safety contract
- Putting me in the hospital
- Taking my choices away; taking my clothes away
- Putting me in restraints
- Overwhelming me or pushing me to do things I'm not ready for
- Patronizing or talking down to me

I know I need to get help when:

- There are too many voices and sounds; I can't focus on what I want to hear
- A voice (not my own) tells me to do things and I can't ignore it
- I am convinced that people are out to get me
- What I see in the mirror is not me
- I talk in ways that don't make sense to others
- It feels like something is crawling on my skin
- I have a plan to hurt myself or others
- I feel out of control
- I can't stand myself
- I engage in addictive behavior
- I can't stand how I feel – I have to do something now!

Client- Print Name:	Client/Parent Signature:	Date:
Parent/Guardian- Print Name:	Parent/Guardian Signature:	

Staff - Print Name/Credentials:	Staff Signature:
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Violence toward others assessment

Risk factors for violence against others (1)

- Comorbid substance use disorder diagnosis*
- History of polysubstance abuse*
- Recent history of use or misuse of drugs or alcohol*
- Non-adherence to medication and other recommended treatment modalities*
- Hostile behavior
- History of violent victimization
- History of conviction for a violent crime
- History of childhood physical or sexual abuse
- History of parental criminal involvement
- History of parental alcohol misuse

*Indicates strong association with risk of violence if present

- History of homelessness (recent and longitudinal)
- Recent history of arrest for any offense
- Co-morbid anti-social personality disorder
- Positive symptoms of psychosis (paranoia)
- Higher general symptom scores
- Higher PANSS (positive and negative symptom scores)
- Previous suicide attempts
- Being male
- Poor impulse control
- Poor insight into mental health and substance use conditions
- **Interventions targeted at dynamic risk factors offer the most opportunity for risk mitigation.**

Protective factors are generally the opposite of the risk factors for violence.

Included factors with strong or moderate association with violence. Weak associations not included.

Suicide assessment

Adults

Columbia-Suicide Severity Rating Scale and triage for use in primary care (2)

COLUMBIA-SUICIDE SEVERITY RATING SCALE

Screen with Triage Points for Primary Care

Ask questions that are in bold and underlined.	Past month	
	YES	NO
Ask Questions 1 and 2		
1) <u>Have you wished you were dead or wished you could go to sleep and not wake up?</u>		
2) <u>Have you had any actual thoughts of killing yourself?</u>		
If YES to 2, ask questions 3, 4, 5, and 6. If NO to 2, go directly to question 6.		
3) <u>Have you been thinking about how you might do this?</u> e.g. "I thought about taking an overdose but I never made a specific plan as to when where or how I would actually do it....and I would never go through with it."		
4) <u>Have you had these thoughts and had some intention of acting on them?</u> as opposed to "I have the thoughts but I definitely will not do anything about them."		
5) <u>Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?</u>		
6) <u>Have you ever done anything, started to do anything, or prepared to do anything to end your life?</u> Examples: Collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump; or actually took pills, tried to shoot yourself, cut yourself, tried to hang yourself, etc. If YES, ask: <u>Was this within the past 3 months?</u>	Lifetime	
	Past 3 Months	

Response Protocol to C-SSRS Screening

Item 1 Behavioral Health Referral
Item 2 Behavioral Health Referral
Item 3 Behavioral Health Consult (Psychiatric Nurse/Social Worker) and consider Patient Safety Precautions
Item 4 Behavioral Health Consultation and Patient Safety Precautions
Item 5 Behavioral Health Consultation and Patient Safety Precautions
Item 6 Behavioral Health Consult (Psychiatric Nurse/Social Worker) and consider Patient Safety Precautions
Item 6 3 months ago or less: Behavioral Health Consultation and Patient Safety Precautions

Columbia-Suicide Severity Rating Scale screening version — since last contact

COLUMBIA-SUICIDE SEVERITY RATING SCALE Screening Version – Since Last Contact

SUICIDE IDEATION DEFINITIONS AND PROMPTS	Since Last Contact	
Ask questions that are bold and <u>underlined</u>	YES	NO
Ask Questions 1 and 2		
1) <u>Have you wished you were dead or wished you could go to sleep and not wake up?</u>		
2) <u>Have you actually had any thoughts of killing yourself?</u>		
If YES to 2, ask questions 3, 4, 5, and 6. If NO to 2, go directly to question 6		
3) <u>Have you been thinking about how you might do this?</u> <i>E.g. "I thought about taking an overdose but I never made a specific plan as to when where or how I would actually do it...and I would never go through with it."</i>		
4) <u>Have you had these thoughts and had some intention of acting on them?</u> <i>As opposed to "I have the thoughts but I definitely will not do anything about them."</i>		
5) <u>Have you started to work out or worked out the details of how to kill yourself and do you intend to carry out this plan?</u>		
6) <u>Have you done anything, started to do anything, or prepared to do anything to end your life?</u> Examples: Collected pills, obtained a gun, gave away valuables, wrote a will or suicide note, took out pills but didn't swallow any, held a gun but changed your mind or it was grabbed from your hand, went to the roof but didn't jump; or actually took pills, tried to shoot yourself, cut yourself, tried to hang yourself, etc.		

- Low Risk
- Moderate Risk
- High Risk

*For inquiries and training information contact: Kelly Posner, Ph.D.
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Adolescents

The Ask Suicide-Screening Questions (ASQ) Toolkit from the National Institute of Mental Health (NIMH). An initial screener for adolescent suicide risk

<https://www.nimh.nih.gov/labs-at-nimh/asq-toolkit-materials/index.shtml>

NIMH Toolkit: Outpatient: Brief Suicide Safety Assessment

https://www.nimh.nih.gov/labs-at-nimh/asq-toolkit-materials/outpatient/pdfs/bssa_155415.pdf

Alcohol and drug use screeners

SBIRT – Screening and Brief Intervention and Referral to Treatment

<http://www.sbirtoregon.org/wp-content/uploads/Brief-screen-English-pdf.pdf>

Use first when screening for possible substance use. This is an alcohol, drug and depression screener. Follow-up with the Alcohol Use Disorders Identification Test (AUDIT) for alcohol abuse or Drug Abuse Screening Test (DAST) for drug abuse if SBIRT indicates a need for additional screening.

AUDIT – Alcohol Use Disorders Identification Test

<http://www.sbirtoregon.org/wp-content/uploads/AUDIT-English-pdf.pdf>

Use after SBIRT for more in-depth alcohol screening.

DAST – Drug Abuse Screening Test

<http://www.sbirtoregon.org/wp-content/uploads/DAST-English-pdf.pdf>

Use after SBIRT for a more in-depth drug screening.

Movement disorder scales

AIMS – Abnormal Involuntary Movement Scale

http://cqaimh.org/pdf/tool_aims.pdf

BARS – Barnes Akathisia Rating Scale

<https://www.outcometracker.org/library/BAS.pdf>

Labs and tests

Early Assessment and Support Alliance (EASA) lab recommendations

<http://www.easacommunity.org/PDF/Practice%20Guidelines%202013.pdf>

Diagnosis

Diagnostic criteria for schizophrenia

The Diagnostic and Statistical Manual of Mental Disorders 5th Edition (DSM-5) (3) lists the following criteria:

(A) For a diagnosis of schizophrenia:

There must be two criteria present for a “significant portion of time during a one-month period (or less, if successfully treated)”. Of these criteria, at least one must be:

(B) For a significant time since onset, the functional level must have deteriorated “markedly below” the level reached before onset in one or more areas of work, interpersonal relations, self-care, etc.

(C) Continuous signs of difficulties persist for at least six months and must include at least one month of symptoms (less if successfully treated) that meet criteria A.

(D) Schizoaffective disorder and depressive or bipolar disorder with psychotic features have been ruled out.

(E) Symptoms are not explained by the physiological effects of a substance or other medical condition.

(F) If there is a history of autism spectrum disorder or other communication disorder with childhood onset:

- The additional diagnosis of schizophrenia is made only if prominent delusions or hallucinations, and
- The other required symptoms of schizophrenia are present for at least one month (or less, if successfully treated).

- **Delusions**
- **Hallucinations**
- **Disorganized Speech**
- **Grossly Disorganized, or**
- **Catatonic Behavior, and**
- **Negative Symptoms (e.g. diminished emotional expression or volition)**

Common misdiagnoses and comorbidities

The DSM-5 also notes some common psychiatric diagnoses that masquerade as schizophrenia which include:

- Major depressive disorder with psychotic features
- Bipolar disorder with psychotic features, and
- Schizoaffective disorder (among others).

Drug and alcohol use is a common comorbidity with schizophrenia and other mental illnesses. Tobacco use is particularly common among those with a diagnosis of schizophrenia.

Psychosis scales

Community Assessment of Psychiatric Experiences- Scale Description (4)

Important notes about the CAPE-P15:

- Time to administer is five minutes
- Sensitivity = 73 percent, specificity = 58 percent
- Positive predictive value of 66 percent, negative predictive value of 66 percent
- The study sample was comprised of young adults ages 18-25 from a university population.
 - » 46 percent report family history of a mental disorder, and
 - » 8 percent reported a family history of psychosis.
- Compared to CAARMS interview:
 - » Psychometrics: internal consistency ($\alpha=0.79$).
 - » Good fits root mean square error of approximation (RMSEA) $<.05$. Comparative fit index (CFI) (.976).
- Review: <http://www.psychiatry.cam.ac.uk/blog/2017/04/04/cape-p15-lifesaver-timesaver/>
- “The CAPE-P15 shows promise as a measure of positive, psychosis-like experiences,* but further validation of this measure is required in community samples.” (5)

*Brief screening for psychosis-like experiences | Request PDF. Available from: https://www.researchgate.net/publication/247155640_Brief_screening_for_psychosis-like_experiences

Community Assessment of Psychiatric Experiences (CAPE-15) Scale

In the past three months have you:

1. Ever felt as if people seem to drop hints about you or say things with a double meaning?
2. Ever felt as if some people are not what they seem to be?
3. Ever felt that you are being persecuted in any way?
4. Ever felt as if there is a conspiracy against you?
5. Ever felt that people look at you oddly because of your appearance?
6. Ever felt as if electrical devices such as computers can influence the way you think?
7. Ever felt as if the thoughts in your head are being taken away from you?
8. Ever felt as if the thoughts in your head are not your own?
9. Ever had thoughts so vivid you were worried other people would hear them?
10. Ever heard your thoughts being echoed back at you?
11. Ever felt as if you are under the control of some force or power other than yourself?
12. Ever felt as if a double has taken the place of a family member, friend or acquaintance?
13. Ever heard voices when you are alone?
14. Ever heard voices talking to each other when you are alone?
15. Ever seen objects, people or animals that other people can't see?

Total "yes" responses = _____

Total "yes" responses for items 1-5 = _____ (Persecutory ideation)

Total "yes" responses for items 6-12 = _____ (Bizarre experiences)

Total "yes" response for items 13-15 = _____ (Perceptual abnormalities)

Total scores = 0-45 (M= 20.56 young adults)

Perceptual abnormalities = 0-9 (M = 3.38 young adults)

Persecutory ideation = 0-15 (M = 8.48 young adults)

Bizarre experiences = 0-21 (M = 8.69 young adults)

Programme for Improving Mental HealthcarE (PRIME)

Important notes about the PRIME (6):

- Time to administer three to five minutes
- Adolescents and young adults help-seeking referred to a clinical high-risk clinic
- Self-report format:
 - » Mean age 19 years.
 - » 74 females, 108 males (validated for a non-clinical Kenyan population)
- Recommended cutoff for a positive screen:
 - » Three 5s , or
 - » One 6 on items 19, 20
- Validity (sensitivity and specificity) for at least three items with a rating of 5 or 6. Responses of 4 or 5 did not demonstrate validity.
- The higher the score, the more likely the true positive.
- There were only minor changes from the original PRIME screen questionnaire on item 9 and 12. Was compared to the standard psychosis-risk syndromes (SIPS).
- Developed by researchers at Yale. The same group that developed the Patient Health Questionnaire (PHQ).

Composite risk questionnaire (7)

- Participants were help-seeking high and low-risk and non-psychotic outpatients.
- Ages 16-32
- Takes five minutes to administer.
- Public domain
- 15-item screener developed from original 231 items.
- **The best sensitivity and specificity are responses between three and seven total yes responses**
- **A “yes” to items 1, 2 and 3 is considered higher sensitivity.**

- **Greater than seven “yes” responses are an indication of a need for further evaluation for psychosis.**
- The 15 items fall into four categories:
 - » Interpersonal difficulty or social anxiety (items 2, 5, 7, 8, 12)
 - » Self-depreciating (items 1, 4, 9)
 - » Negative symptoms (items 3, 10, 11), and
 - » Subthreshold psychotic-like experiences (items 6, 13, 14, 15).
- Construct validity established with structural interview of schizotypy and data from non-psychotic relatives.

Treatment resources

Shared decision-making references

<https://www.ahrq.gov/sites/default/files/wysiwyg/professionals/education/curriculum-tools/shareddecisionmaking/tools/sharefactsheet/share-approach-factsheet.pdf>

Resources for implementing trauma informed care

<https://traumainformedoregon.org/>

Common barriers to treatment for people with a diagnosis of schizophrenia*

- Lack of insight, poor motivation and other negative symptoms
- Lack of a therapeutic alliance with a provider
- Mismatch of provider skills and patient needs
- Difficulty accessing and using transportation to attend appointments
- Trauma (including trauma experienced while receiving mental and physical health care)
- Treatment fatigue (if chronically unable to reach or maintain recovery goals, unmet expectations, social service system failures)
- Inadequate social supports
- Insufficient income

*This is not an exhaustive list. Some patients may encounter few barriers. Other patients will encounter many.

- Inadequate housing or homelessness
- Difficulty navigating social service systems with their often-conflicting eligibility and access requirements
- Difficulty independently managing medications
- Reluctance to participate in blood draws for medication monitoring
- The cumulative biopsychosocial impact of co-morbid physical, mental and substance use disorders

Goal-setting

Consider using the SMART goals format to create goals that are:

Specific: What is your goal? What are the specific components of your goal? E.g., If your goal is to “get in shape,” what will that look like? Does it mean you need to lose weight, inches around your waist? Gain weight? Add muscle? Define your goal with as much detail as possible.

Measurable: How are you going to measure your success? If your goal is to lose weight you could measure your progress by weighing yourself each week.

Achievable: Are you able to do the goal with the resources and skills you have? Do you need help to achieve your goal? If so, from whom?

Realistic: Is your goal reasonable? Is the goal too much of a stretch right now or is it just not something that can be done? For example, if you are a 35-year-old adult and you stated you wanted to grow a foot taller, that is not realistic. But if you wanted to gain a ¼ inch in height, you may be able to acquire custom made lifts for your shoes which would make you appear slightly taller.

Time-bound: What is your deadline for achieving your goal? Do you want to complete it within 30 days, six months, a year?

Set goals:

Immediate (during the appt or within the next week):

Short-term (within the next one to six months):

Long-term (within six to 12 months)

Medication adherence

Medication adherence is a significant and complex issue. It must be actively addressed to successfully manage schizophrenia.

Prevalence: It is estimated that one in five prescriptions in the United States is not filled at all. Of those filled, about 50 percent are not taken according to the instructions. (1) The cumulative effect of these missed medications accounts for 100-300 billion of health care expenditures. (2)

Causes: There is a wide variety of drivers for non-adherence, but the most common factor is simply inattention and forgetting to take medications. Other factors can include:

- Cost
- Side effects
- Stigma
- Perceived ineffectiveness
- Running out of medications
- Difficulty getting to the pharmacy, and
- Cultural barriers.

Strategies to intervene: Evidence on medication adherence is widely varied. Broad reviews are unable to determine any consistently effective interventions. (3) Populations studied are heterogeneous and interventions often complex and multifaceted.

Medication adherence must be directly assessed and explored at regular intervals. Evidence shows that proactively addressing adherence and exploring possible barriers, such as cost and out-of-pocket expense results in increased adherence, a lasting effect. (4)

Other strategies can include education. This includes motivational interviews, exploration of ambivalence about medications and culturally appropriate medication education.

Inclusion of care team members can be of benefit. This includes pharmacists, case workers and community health workers.

Reminder systems, such as pill boxes, phone or text alerts have been shown to be effective. However, the effect stops when the intervention stops.

Interventions must be tailored to the individual's need. That is why the most important aspect is a regular and thorough assessment of medication adherence.

Medication pricing information

Medication pricing information is available at:

- www.goodrx.com for pricing for a broad audience, and
- www.opdp.org to check Oregon prescription drug prices

Oregon Health Plan Drug List

- www.orpdl.org/drugs for those on Medicaid fee-for-service.

General social services resource information

Toll free, dial 2-1-1 or visit www.211info.org

Principles of the recovery model

Principles of the recovery model: <https://store.samhsa.gov/system/files/pep12-recdef.pdf>

Assertive community treatment (ACT)

<http://oceact.org/assertive-community-treatment/>

“Assertive Community Treatment (ACT) is an Evidence-Based Practice (EBP) designed to provide comprehensive treatment and support services to individuals who are diagnosed with serious mental illness. ACT services are provided by a multidisciplinary team and are designed to be provided in the most integrated setting possible to maximize independence and community integration. (8)”

As of Dec. 14, 2018, the Oregon Center for Excellence for Assertive Community Treatment programs are available in many Oregon counties. Go to <http://oceact.org/programs/> to search for available programs and contact information.

Guidelines for long-acting injectables

http://www.sussexpartnership.nhs.uk/sites/default/files/documents/long_acting_antipsychotic_guidelines_-_ver_4_final_may_140.pdf

Positive Cardiometabolic Health Resource

https://www.rcpsych.ac.uk/docs/default-source/improving-care/ccqi/national-clinical-audits/ncap-library/national-audit-of-schizophrenia-document-library/nas_round-2-report.pdf?sfvrsn=6356a4b0_2 (pages 165-166)

Safe deprescribing of inappropriate medication therapies

<http://www.deprescribing.org>

Finding the lowest effective dose in psychotic disorders

Most people who experience a psychotic episode do not develop Schizophrenia. Also, many will not experience recurrent psychotic symptoms after their first episode resolves. (1, 2) In addition, doses of antipsychotic medications can often be lowered after resolution of the acute or initial stages of a psychotic episode. Furthermore, a subset of people who do develop Schizophrenia learn to manage their psychotic symptoms without medication use or have a higher quality of life when not taking medications. (2, 3, 4) Given the physical health risks of long-term antipsychotic use (tardive dyskinesia, weight gain, diabetes mellitus, cardiovascular disease, etc.), a trial of tapering down on medications, with a goal of discontinuing medications, should be considered. The goal of this tapering process is not one of decreasing side effects of medications, which is an important but separate issue. The goal of this tapering process is to establish if a lower dose of medication is enough to address and manage the patient's symptoms. Also, if a patient needs to continue medications at all.

A thorough cost and benefit analysis of tapering medications, conducted jointly by the provider and the patient, is highly recommended before starting such a process. This analysis needs to be considered carefully in individuals with a history of high-risk symptoms or behaviors, as the sequelae of recurrent symptoms for these individuals can bring significant social or legal consequences. Regardless of risks, the provider and patient should create a list of shared goals (e.g., decreased side effects, improved energy and concentration, maintenance or improvement of work or academic performance, minimal to no recurrent symptoms, etc.), to better assess the effectiveness of the medication taper.

The potential risks and benefits of a medication taper will vary by individual, but generally include the following concerns:

Potential benefits	Potential risks
Decreased side effect burden	Recurrent symptoms
Decreased long-term health risks	Potential social dysfunction related to recurrent symptoms
Decreased polypharmacy (if applicable)	Potential academic or employment issues related to recurrent symptoms
Decreased potential for medication interactions (if applicable)	

Such a trial of tapering off medications can be considered after six to 12 months of clinical stability (5), even if medications were modified or changed during this six to 12-month period of clinical stability. Tapering can be considered sooner than six months in cases where the psychosis appears related to exogenous etiologies, such as substance induced psychosis.

No clear guidelines exist for how to conduct such a taper. However, general recommendations are to slowly and consistently decrease the medication dose over one to three months, depending on the initial medication dose (lower initial doses can be tapered off over a shorter period). The taper should continue apace until the medication is discontinued, or psychotic symptoms recur or worsen. Should psychotic symptoms recur or worsen, all attempts should be made to maximize non-pharmacologic supports (e.g., sleep hygiene, sobriety, physical activity, etc.) to stabilize symptoms before medications are increased again. If these efforts are not effective to decrease symptoms, the medication should be increased to the lowest dose at which symptoms were better managed. After three months of attaining stability again, the taper can be resumed. Although a slower taper schedule should be considered. If symptoms consistently recur when medication is decreased to a certain level, consider continuing the medication long-term at this dose. If the patient is taking multiple medications, tapering should start with just one medication as agreed upon by the provider and the patient. That medication should be tapered off, or tapered as low as possible, before attempting to taper a second medication.

Pearls

- A maintenance dose is often lower than an acute treatment dose!
- Establish shared goals collaboratively with the patient.
- Consider taper after six to 12 months clinical stability.
- Taper medication dose over one to three months (or even longer!).
- During a taper, increase contact with the patient.
- Maximize non-medication treatments.
- Feel free to call OPAL with any questions!

Care should be taken when tapering off long acting injectable medications. These medications have extremely long clinical half-lives and clinical changes often lag one to three months behind dosing changes. As such, the pace of tapering should slow down accordingly. The oral supplementation should be used if symptoms recur during the taper, to control symptoms more quickly. Injection dosing can also be increased. However, it will not produce a clinical effect for one to three months. Similarly, some oral antipsychotics have long half-lives. This includes aripiprazole and brexpiprazole, with clinical changes occurring two to six weeks after dosing changes. In addition, some medications, such as clozapine, are associated with rebound psychosis (6), especially when tapered quickly. As such, tapering of such oral medications should be done slowly and with caution.

When proceeding with a medication taper, the patient should have increased contact with their treatment providers and trusted individuals in their social support network to monitor progress and assess stability. The odds of a successful taper off antipsychotic medications are improved if the client participates in other treatment modalities or health maintenance activities (therapy, occupational therapy, physical activity, social activity, sleep hygiene, healthy diet, sobriety, etc.) while tapering off medications.

The definition of an adequate dose

For primary care clinicians, the adequate dosing of antipsychotics for schizophrenia should be based on four factors:

1. Duration of treatment
2. Level of psychotic symptoms
3. Level of adverse reactions, and
4. FDA maximum recommended daily dose.
 - As the patient can tolerate (adverse reactions), the dose of medication should increase up to the FDA maximum dose, if debilitating (cannot function independently) psychotic symptoms persist.
 - Doses should not exceed FDA recommended maximum dose.
 - Duration should be at least six to eight weeks up to maximum tolerated dose without significant amelioration of psychotic symptoms, before being considered an adequate trial.
 - Even at low or starting doses, intolerable (patient says they won't take medication) adverse reactions would indicate adequate dosing has been completed.

Increasing and optimizing antipsychotic medication doses

Oral antipsychotic medications: Prescribing psychotropic medications is often difficult. Effective doses may vary between individuals and may vary for an individual over time. In addition, medications with the same clinical indication may not produce similar clinical responses. For example, one patient may be responsive to any antipsychotic medications, another may respond only to a subset of these medications and a third patient may respond only to one or two specific medications. Unfortunately, providers cannot predict which patients will respond to which medications. This frequently leads to a trial and error pattern of prescribing until “the right” medication and dose is found.

In general, as antipsychotic medications are more or less equally effective (with the exception of clozapine, which is generally more efficacious but often more difficult to tolerate), medication choice should initially be guided by side effect profiles. For example, a patient with sleep difficulty and anxiety in addition to psychosis may benefit most from an antipsychotic with a side effect profile that includes sedation. Whereas a patient with psychosis and low energy or depression may benefit more from a medication with more activating effects. Similarly, a patient at high-risk for metabolic syndrome may wish to avoid antipsychotics that have a high potential to increase that risk and may prefer medications with a lower metabolic risk. Of course, in many cases, a medication may present a mixed side effect profile for a patient, offering some side effects that could be helpful, but others that could be difficult to tolerate. In such instances, a joint decision by the provider and the patient, weighing the options and risks against each other, offers the best opportunity for success. Whenever possible, generic medication is preferred over brand medication, assuming both are equally clinically indicated, as this will decrease cost of treatment by up to 90 percent.

After an antipsychotic medication is chosen, a decision needs to be made about the starting dose. In determining the starting dose, the urgency for symptom improvement must be weighed against the risk of intolerable side effects. If a patient is willing to accept more potential side effects to experience improvement more quickly, a higher starting dose is acceptable. Alternately, patients who cannot tolerate excessive side effects, or who have no urgency to address their symptoms, may do best on a lower starting dose (10-50 percent of the lowest therapeutic dose). While this approach may lengthen the time to response, it may lead to better long-term tolerance of the medication. A similar approach can be taken to titrating the dose to a therapeutic level (assuming the starting dose is not a therapeutic dose). Patients feeling urgency to address their symptoms may be willing to tolerate an increased risk for side effects and can titrate up more quickly (either by bigger steps up or a quicker pace of adjustments). Patients who benefit from minimizing side effects are better served with a slow titration (either by smaller steps up or a slower pace of adjustments).

Once a therapeutic dose is reached, a sufficient amount of time must pass to assess the patient's response. For oral antipsychotic medications, side effects may present in the first one to five days of use (one to 10 days for aripiprazole, given its long half-life), and decrease over one to two weeks as the patient accommodates to the medication. The exception is metabolic side effects, which may take two to 12 weeks to appear. Therapeutic effects may present in two to seven days (four to 14 days for aripiprazole, given its long half-life). It will continue to increase over the next 30-90 days.

Patients should be re-assessed after two to seven days of antipsychotic use in urgent scenarios. Patients can be assessed after 14-60 days of use in non-urgent scenarios. When re-assessed, adjustments should be made by assessing the therapeutic response, weighed against the goal of minimizing side effects. In general, one of seven scenarios will happen:

1. Good therapeutic response with minimal side effects. In such a case, medications should continue without change.
2. Partial therapeutic response with minimal side effects. In such a case, medications can either be increased as tolerated (usually by ten to 50 percent of the lowest therapeutic dose), or maintained at the current dose, hoping more time on that dose will bring a better response. Patients should be re-assessed per the above recommendations.
3. No therapeutic response with minimal side effects. In such a case, the patient should be managed as per #2 above, with a higher likelihood that the medication dose should be increased.
4. No therapeutic response with significant side effects. In such a case, the medication should be discontinued, and an alternate medication should be started. Such "failed trials" are often helpful, as they help determine which side effects the patient is prone to. In addition, which side effects are tolerable or intolerable for that person.
5. Partial therapeutic response with significant side effects. In such cases, medications can be decreased, hoping a lower dose will alleviate side effects while more time on the medication will lead to a therapeutic response. However, if the dose is already sub-therapeutic, the patient may be better served by changing to an alternate medication as per #4 above. Alternately, the patient can maintain on the current dose of medication, in hopes of a decrease in side effects and an increase in therapeutic effects over time. Patients should be re-assessed per the above recommendations.
6. Good therapeutic response with significant side effects. In such cases, medication should be decreased (by 10-50 percent of the lowest therapeutic dose), hoping that side effects will decrease as therapeutic response is maintained. Patients should be re-assessed per the above recommendations.
7. Any or no therapeutic response with intolerable side effects. In such cases, the medication should be discontinued, and an alternate medication started. Patients should be re-assessed per the above recommendations.

Long acting injectable (LAI) antipsychotic medications: Long acting injectable antipsychotic medications should not be started unless the patient:

- Has used the oral form of the medication before, and
- Experienced:
 1. Benefit, and
 2. No or tolerable side effects.

Otherwise, the patient is at risk for a lengthy period of uncomfortable side effects with no recourse but to allow the serum medication level to decrease as time passes. Generally, a two to three-day trial of oral medication is enough to determine if the client has a severe or allergic reaction to the individual medication. However, treatment with an oral agent until an effective dose is identified is the best strategy. Once an effective dose is identified, an equivalent dose of the LAI formulation of the medication can be approximated. Depending on the LAI medication used, oral medications may be discontinued immediately, or may need to be continued for two to four weeks.

After starting LAI antipsychotic medication, the dose may need to be adjusted due to effectiveness or side effects. If so, it may take two to four weeks, depending on the individual medication, before effects of the adjustment may be seen. During this transition period, consider temporary use of oral antipsychotic medication to more quickly address symptoms. Otherwise, consider temporary use of adjunct medications to more quickly address side effects.

Once an antipsychotic dose is found that is effective and adequately tolerated, the medication dose should be maintained (barring clinical changes or emergent side effects). Do so for three to five months before considering tapering off medications.

Neuroimaging in first episode psychosis

Structural neuroimaging (either CT or MRI) is commonly ordered during a workup of first-episode psychosis. National guidelines vary significantly:

Pro

- Recommend MRI specifically (Royal Australian and New Zealand College of Psychiatrists, 2016)

Consider

- Consider CT or MRI if clinically indicated, with MRI preferred given “the subtle nature of neuropathological findings in schizophrenia” (American Psychiatric Association, 2004)

- Consider CT or MRI if specifically indicated by history, neurological exam or neuropsychological testing. MRI if suspicious for autoimmune encephalitis, e.g. rapid progression of memory deficits, focal CNS findings, new seizures (Canadian Psychiatric Association, 2017)

Against

- **Not** recommended as part of initial investigations for first episode psychosis (National Institute for Health and Care Excellence (NICE), 2013)

These disparate recommendations reflect that data are limited in this area. Structural lesions contributing to psychosis are rare. It is complex to weigh the financial and morbidity cost of neuroimaging that does not change psychosis management (i.e. the vast majority of cases) vs. the impact of uncovering a diagnosis and treatment-altering finding. Neuroimaging cannot be actively recommended in all cases, imaging with either CT or MRI should be considered when the patient's symptoms or age are atypical for first episode psychosis. MRI is preferred if autoimmune neuroinflammation is a possible etiology.

Clozapine Support Service Program Handbook

Clozapine Support Service Program Handbook on the following pages provided by the Oregon State Hospital Pharmacy

Clozapine Support Service Program Handbook

Overview: This handbook is intended to provide guidance to the clinical pharmacist administering the Clozapine Support Service. It is a guidebook to assist the clinical pharmacist in patient monitoring and providing recommendations to the treating provider. This document is not intended to serve as prescriptive policy on the use of Clozapine at OSH and should not be construed as such. This protocol establishes the Clinical Pharmacist as an agent of the Treating Provider. It is the intent of this protocol that the Clinical Pharmacist should serve in the role of an advisor to the Treating Provider and not as an independent practitioner. Working under his or her direction, the Clinical Pharmacist shall provide monitoring of medication side effects, tolerability, and safety, as well as provide recommendations on the safe and effective use of clozapine according to the guidance herein.

Background and Need at OSH

1. There is good reason to believe that Clozapine remains underutilized at OSH:
 - The rate of utilization of Clozapine at Oregon State Hospital, as of April 2015, is 15.3%.
 - Whereas the rate of treatment-resistant schizophrenia in the general schizophrenia population is 20-30%,^{1,2} the inpatient state hospital system carries a disproportionate load of patients with treatment resistant schizophrenia.
2. The barriers to starting and keeping patients on clozapine are generally cited as^{3,4,5,6}:
 - Unfamiliarity with its use
 - Patient refusal of blood draws
 - Concern for the increased monitoring that is required
3. It is evident that a higher rate of preventable discontinuations is contributing to lower rates of clozapine utilization at OSH:
 - A review of clozapine discontinuations at Oregon State Hospital in 2013 revealed that 44% (12 of 27 cases) of discontinuations were due to preventable central nervous system and autonomic side effects.
 - Additional reasons for discontinuation included myocarditis (one case), weight gain (one case) and patient refusal of blood draws (two cases). Five cases had unclear reasons or no documentation.
 - Discontinuations due to autonomic and CNS side effects such as sialorrhea, orthostatic hypotension, constipation and sedation can be prevented with adequate pharmacological and non-pharmacological interventions.

Purpose

The purpose of the Clozapine Service is to:

1. Increase the appropriate utilization of clozapine at Oregon State Hospital by decreasing preventable discontinuations and mitigating the barriers to its use.
2. Increase the safety in the use of Clozapine by more systematically and consistently monitoring for side effects

Goals of the Clozapine Service: Increasing Utilization

1. Increase rates of clozapine utilization where it is indicated
2. Increase the safety of the use of clozapine by:
 - Providing value-added patient monitoring by a clinical pharmacist

- Promoting evidence-based dosing and titration for clozapine
 - Providing evidence-based recommendations to the Treating Provider regarding the use of clozapine
3. Increasing the tolerability and acceptance of clozapine for patients by:
 - Providing side effect monitoring for routine side effects and making recommendations about the use of adjunct medications and dosing/titration strategies
 - Providing evidence-based recommendations to the Treating Provider regarding the use of clozapine

Clinical Pharmacist Duties – Summary

1. Visit with patient regularly to monitor for side effects and tolerability
2. Inform the Treating Provider or a covering provider when the primary treating provider is unavailable, of relevant findings, observations and urgent matters via direct communication.
3. Document relevant finding and observations in the electronic medical record.
4. Provide recommendations to the Treating Psychiatrist where indicated, or requested, for the safe and effective use of clozapine in accordance with this protocol
5. Receive and transcribe telephone orders from the Treating Provider when necessary

Definitions

1. Treating Psychiatrist: The primary psychiatrist or psychiatric mental health nurse practitioner responsible for the treatment of the patient
2. Medical Physician: The primary medical physician responsible for treatment of the patient
3. Treating Provider: The Treating Psychiatrist or the Medical Physician
4. Clinical Pharmacist: Pharmacist responsible for managing the Clozapine Service, working under the direction of the treating psychiatrist and the medical physician
5. Refractory: failure to respond to at least two adequate trials of antipsychotic medications, at least one of which must have been a second-generation antipsychotic (SGA), given at least at standard therapeutic doses for a minimum period of 4 weeks

I. Clozapine Indications

- A. Clozapine is indicated in the following cases
 - 1. Refractory schizophrenia or schizoaffective disorder
 - 2. Individuals with schizophrenia or schizoaffective disorder with high risk of suicide, unmitigated by other treatment approaches^{7,8}
 - 3. Individuals with schizophrenia or schizoaffective disorder with chronic assaultiveness unresponsive to behavioral intervention and alternative pharmacotherapy⁹
 - 4. Treatment resistant bipolar mood disorder refractory to treatment with alternative antipsychotics¹⁰

- B. Additional cases where clozapine may be indicated:
 - 1. Individuals needing antipsychotics with moderate to severe tardive dyskinesia or intolerable EPS or drug induced parkinsonism
 - 2. Symptomatic hyponatremia with other antipsychotics^{11,12}
 - 3. Individuals with Parkinson's disease requiring an antipsychotic agent

II. Contraindications and Precautions

- A. Clozapine is contraindicated in the following cases:
 - 1. Prior history of clozapine-induced agranulocytosis (defined as an absolute neutrophil count < 500)
 - 2. Severe central nervous system depression or delirium
 - 3. Coma
 - 4. History of clozapine-induced myocarditis or cardiomyopathy; re-challenge may be appropriate in some instances

5. Pretreatment absolute neutrophil count (ANC) less than 1500 cells/cubic mm³. In cases of documented benign neutropenia, the baseline ANC must be a minimum of 1000 cells/cubic mm.³
 6. Non-adherence to required laboratory monitoring
 7. Uncontrolled seizure disorder
 8. Uncontrolled medical conditions that are likely to result in patient injury with clozapine treatment. Examples: acute narrow angle glaucoma, bowel obstruction, paralytic ileus, unstable hypotension, unstable tachyarrhythmias
 9. Allergy to clozapine
- B. The Clinical Pharmacist is responsible for alerting the Treating Provider of the following circumstances, which may require additional work-up, including referral and consultation by a specialist, if appropriate:
1. Use of therapy or any other medications or therapies that suppress bone marrow production or function. Examples include:
 - a) Anti-neoplastic drugs
 - b) Anti-retroviral medications
 - c) Carbamazepine
 - d) Propylthiouracil
 2. Use of certain antiarrhythmics, type 1C agents in particular, such as
 - a) Propafenone
 - b) Flecainide
 - c) Encainide
 - d) Quinidine
 3. Pregnancy or breast feeding
 4. Serious medical illnesses such as uncontrolled diabetes, heart failure, morbid obesity, etc.
 5. Seizure disorder
 6. History of hypersensitivity to loxapine or amoxapine
 7. Other serious drug interactions, which are identified

- C. Additional monitoring, precautions and management strategies may be warranted in certain cases. The Clinical Pharmacist is responsible for alerting the treating provider and making suggestions or recommendations, if appropriate, in the following cases:
1. History of seizure disorder: Consider initiation of a prophylactic antiepileptic agent, such as lamotrigine or valproate, prior to or concurrently when commencing clozapine. The Clinical Pharmacist is to provide additional patient monitoring at the direction of the Treating Provider and alert nursing of the need to watch for signs or symptoms of seizure disorder, including observation for myoclonic jerks.
 2. Present cardiovascular disease or history of myocarditis or cardiomyopathy (not related to clozapine treatment): Consider extended monitoring of troponin and CRP measurements.
 3. Evidence of significant hepatic or renal disease: Consider additional clozapine plasma level measurements to avoid toxicity.
 4. Prostatic enlargement or narrow angle glaucoma: Recommend minimizing use of additional anticholinergic agents, when possible.
 5. History of paralytic ileus, frequent constipation, or bowel obstruction: Recommend initiating a prophylactic bowel care regimen and minimizing use of additional anticholinergic agents, when possible.
 6. Family or personal history of obesity, dyslipidemia, or diabetes: Closer monitoring of weight, lipids and fasting blood glucose. Consider referring for dietary consult early in treatment.
 7. Pregnancy (Category C) or breast feeding
 8. Concurrent use of
 - a) Anticholinergic medications: Discontinue and minimize whenever possible
 - b) Antihypertensive medications: Consider use of alternatives with lower propensity to induce hypotension
 - c) Highly protein-bound drugs such as digoxin and warfarin: Clinical Pharmacist to provide additional monitoring of these medications, e.g. more frequent INR's
 - d) Central nervous system depressants, barbiturates or benzodiazepines, especially in the first week of clozapine titration: Recommend discontinuing or minimizing if clinically appropriate. Consider more frequent monitoring of blood pressures, including orthostatic blood pressures
 - e) CYP-450 1A2 inhibitors: Lower dose targets may be used since CYP1A2 inhibitors increase clozapine levels.¹³
 - (1) Fluvoxamine (substantial)
 - (2) Ciprofloxacin
 - (3) Ethinyl Estradiol
 - (4) Atazanavir
 - (5) Cimetidine
 - (6) Zileuton
 - f) CYP-450 1A2 inducers: Higher dose targets may be necessary. Consider patient's smoking status and plan accordingly if discharging from the hospital as smoking decreases plasma levels by up to 50%¹⁴
 - (1) Smoking (substantial)
 - (2) Barbiturates
 - (3) Primidone
 - (4) Carbamazepine
 - (5) Rifampin

- g) Although not as significant, agents that inhibit or induce CYP3A4, CYP2C19 and CYP2D6 (e.g. fluoxetine) also produce an interaction with clozapine. The Clinical Pharmacist is to advise the Treating Provider of any such interactions.

III. Pre-Treatment Workup: The Clinical Pharmacist to ensure these have been completed and documented in the medical record when ordered:

- A. Recommended within 7 days prior to beginning clozapine treatment
1. Vitals, including temperature, pulse, respiration rate and blood pressure. If missing, Clinical Pharmacist to have nursing obtain on initial visit.
 2. Orthostatic blood pressure (BP taken lying >5 min and standing at 3 min) if patient reports dizziness or lightheadedness upon standing or recent history (<4 weeks) of fall(s). An abnormal result (postural drop >30mmHg; SBP drop \geq 20 mmHg or DBP drop \geq 10 mmHg) should prompt consultation and referral to the Medical Physician for evaluation.
 3. Patient interview and documentation of symptoms in the electronic medical record per the Clozapine Monitoring Checklist (**Appendix A**)
 4. Complete blood count with differential (ANC required per registry guidelines)
- B. Recommended within 30 days prior to beginning clozapine treatment
1. BMI. If missing, Clinical Pharmacist to have nursing obtain on initial visit.
- C. Recommended within 3 months prior to beginning clozapine treatment
1. Fasting blood sugar and HB A1C
 2. Lipid panel
- D. Recommended within 12 months prior to beginning clozapine treatment
1. Complete physical examination
 2. Comprehensive Metabolic Panel
 3. Electrocardiogram (ECG)

IV. Initial and Subsequent Visits with the Clozapine Service Clinical Pharmacist

- A. On the initial visit with the Clinical Pharmacist, the patient will be assessed using the Clozapine Monitoring Checklist (**Appendix A**). Nursing should be enlisted to obtain missing baseline measures including BMI, vitals, and blood pressure and documented in the medical record. Further assessments obtained at baseline for comparison include:
1. Gastrointestinal symptoms, including an assessment of bowel frequency
 2. Cardiovascular symptoms
 3. Other symptoms commonly implicated as side effects in clozapine treatment
 4. All observations should be documented in the Electronic Medical Record using a progress note
- B. Follow-up visits and monitoring with the Clinical Pharmacist are to occur twice weekly in the initiation phase of clozapine treatment (typically 4 weeks). Monitoring may be continued in the case of an extended titration or abnormal findings, as directed by the Treating Provider.

- V. Monitoring during the Initiation and Continuation Phases: Clinical Pharmacist to ensure missing parameters are obtained and documented in the medical record**
- A. Monitoring provided by the Clozapine Service is divided into the Initiation Phase (typically 4 weeks), during which the patient is being titrated onto clozapine therapy and the Continuation Phase, during which the patient has achieved a stable clozapine dose with no outstanding issues necessitating further dose titration or modification.
 - B. Weight and BMI
 1. Weight and BMI is recommended to be obtained at baseline, week 4 and quarterly thereafter. An increase in any parameter greater than 5% in the first month or 10% in a 3-month period warrants referral for dietary consultation and patient counseling on dietary and lifestyle modification.
 - C. Temperature, Pulse, Respiration Rate, and Blood Pressure
 1. Recommended twice weekly during the Initiation Phase and as needed once stable dose is achieved or after 4 weeks, whichever is greater.
 - D. Orthostatic Blood Pressures
 1. As directed by the Treating Provider, orthostatic blood pressure (BP taken lying >5 min and standing at 3 min) before and 2 hours after initial dose(s) may be indicated in patients:
 - a) Older than 65 years old
 - b) Who are medically unstable or debilitated
 - c) With pre-existing hypotension
 - d) With a history of postural hypotension
 - e) At high risk of falls and hypotensive side effects
 - E. Side effect assessment by the Clinical Pharmacist
 1. A complete side effect assessment visit with the Clinical Pharmacist is recommended twice weekly during the Initiation Phase of clozapine treatment. Such assessment includes a patient interview to assess cardiovascular, gastrointestinal, and other symptoms commonly attributable to clozapine (See Clozapine Monitoring Checklist, **Appendix A**).
 - F. Hematological Monitoring (CBC's)
 1. Frequency of hematological monitoring during clozapine treatment is to be conducted as dictated by the Clozapine Registry guidelines (See Pharmacy Protocol 3.002 Clozapine Management System)
 2. Hematological monitoring: Standard (1) venipuncture with a CBC and complete 5-part differential
 3. Hematological monitoring may be waived through the national registry in cases of terminal illness and hospice care.
 - G. Additional Recommended Lab Monitoring
 1. Monthly for the first three months: fasting blood sugar
 2. Quarterly: fasting blood sugar, HB A1C, and lipid panel

3. Annually: comprehensive metabolic panel, electrocardiogram, and full physical exam
4. A KUB is recommended in the following case:
 - a) Unreliability in reporting bowel movements and suspicion of constipation
5. Troponin and CRP measurements are to be obtained as directed by the Treating Provider. Tachycardia is an indication for closer monitoring of cardiovascular parameters and related symptoms. One or more cardiac symptoms (dyspnea, fever, chest pain, palpitations, fatigue, s/sx characteristic of heart failure) indicates the need for prompt evaluation by the Medical Physician.

VI. Dosing and Titration per Pharmacy Clozapine Service Protocol

A. Overview

1. This section details the target dose and titration schedule that the Clinical Pharmacist will employ if directed by the Treating Psychiatrist to initiate an individual on clozapine. A specific target dose must be specified by the Treating Psychiatrist.
2. Many side effects due to clozapine that lead to intolerance and preventable discontinuation are dose related (e.g. sedation, sialorrhea, constipation and seizures). Furthermore, significant inter-individual variation exists in clozapine metabolism and effective serum levels relative to a particular daily dose. Consequently, the aim of the recommended titration schedule below is to achieve a generally effective and tolerable dose at which time a serum clozapine level can be obtained to guide further titration decisions.
3. The threshold clozapine serum level of 350 µg/mL^{15,16,17} is generally recognized as the cutoff differentiating between the majority of responders and non-responders in clozapine population studies. However, a minority of individuals do respond at lower plasma levels.
4. The method of titration, target dose, and titration schedule described herein prioritizes minimizing side effects and adverse events. If more rapid titration is indicated clinically, a target dose and titration schedule should be selected as directed by the Treating Provider.
5. Many different clinical factors unique to the individual may justify an entirely different approach to clozapine titration and target dose. The dose and titration protocol herein should not be construed as prescriptive for all providers or cases in which clozapine is used.
6. The Clinical Pharmacist may employ a different titration schedule and target dose if directed to do so by the Treating Provider.

B. Therapeutic Drug Level Monitoring Past the Target Dose

1. The combination of clozapine and norclozapine is useful in assessing side effect burden and seizure risk. However, only the clozapine level should be used to assess adequate plasma levels. It is noteworthy that norclozapine demonstrated no benefit as an antipsychotic versus placebo in a double-blind randomized placebo controlled phase II trial aimed at its development as an antipsychotic (Acadia Pharmaceuticals ACP-104 Phase IIb trial).¹⁸
2. A clozapine level >350 µg/mL, based on equally divided BID-TID daily dosing, indicates that no further dose titration may be necessary. It is recommended that an adequate trial of clozapine should be maintained (>4 weeks) prior to reevaluating the need for dose escalation.

3. A clozapine level <350 µg/mL does not necessarily indicate the need for further dose titration. Limited data exists to suggest that a level of 200 µg/mL may be effective for acute response¹⁷ as well as in preventing relapse¹⁹. Consequently, the decision for further dose escalation should be made by the Treating Psychiatrist based on an assessment of the patient’s psychopathology, side effects, and initial response.

C. Initial Recommended Target Dose

1. Men <65 years old: 250 mg/day
2. Women, individuals > 65 years old and individuals with chronic disease: 200mg/day
3. Debilitated or acutely ill: as directed by the Treating Psychiatrist

D. Recommended Initial Titration Schedule

1. On titration to the initial target dose, clozapine should be commenced at 12.5mg and the dose increased no more frequently than 25mg/day (**Table A**).
2. If daytime sedation becomes a problem, the dose can be weighed more heavily towards the evening with a 25%/75% split. However, clozapine plasma levels should be interpreted in context of the disproportionate influence from the evening dose²⁰ (e.g. a 25-50% adjustment in the level may be appropriate) (**Table B**).
3. Upon achieving 3-5 days (corresponding to about 5 half-lives necessary for steady state levels) of the initial target dose (see below), a clozapine level should be obtained.

Table A	Target 200mg/day		Target 250mg/day	
	AM	PM	AM	PM
Day 1		12.5		12.5
Day 2		25		25
Day 3	25	25	25	25
Day 4	25	50	25	50
Day 5	25	75	25	75
Day 6	50	75	50	75
Day 7	50	100	50	100
Day 8	75	100	75	100
Day 9	100	100	100	100
Day 10	""	""	100	125
Day 11	""	""	125	125

Table B	Target 200mg/day		Target 250mg/day	
	AM	PM	AM	PM
Day 1		12.5		12.5
Day 2		25		25
Day 3		50		50
Day 4	25	50	25	50
Day 5	25	75	25	75
Day 6	25	100	25	100
Day 7	50	100	50	100
Day 8	50	125	50	125
Day 9	50	150	50	150
Day 10	""	""	50	175
Day 11	""	""	75	175

E. Titration beyond the Initial Target Dose

1. Final Target Dose should be selected as directed by the Treating Psychiatrist after an evaluation of clinical symptoms and plasma clozapine levels, if available.
2. It is recommended that dose escalation above the initial target dose occur in increments of 50mg every two days towards the final target unless clinical factors dictate otherwise, as determined by the Treating Psychiatrist.
3. Approximate dose targets needed to achieve a plasma level of 350 µg/mL (rounded by 25mg) have been derived from population studies conducted by Rostami-Hodgeman et al.²¹ and are presented below (**Table C**) as a general reference for the final target dose that may be required.

a) **Table C: Approximate Total Daily Dose Needed to Achieve 350 µg/mL**

Age	Male (80kg)	Female (70kg)
20	375	300
30	350	275
40	325	250
50	300	250
60	275	225

**Dose estimates based non-smoking status; rounded by 25mg.*

VII. Monitoring of Specific Clozapine Adverse Events and Side Effects by the Clinical Pharmacist

A. Myocarditis and Tachycardia^{22,23,24,25}

1. Clozapine has been associated with an increased risk of fatal myocarditis, especially during, but not limited to, the first month of therapy.
2. The Clinical Pharmacist shall notify the Medical Physician and the Treating Psychiatrist of any instance of:
 - a) An individual reporting or experiencing: dyspnea, tachypnea, fever, chest pain, palpitations, unexplained fatigue, edema in the extremities, persistent cough or wheezing, fluid retention or abdominal swelling
 - b) Recommend to the Treating Physician that a troponin or CRP be drawn and notify the treating physician if the results come back as abnormal.
3. About 25% of individuals treated with clozapine evidence a benign tachycardia, with an average increase of 10 to 15 beats per minute. This effect is dose dependent and is independent of reflex tachycardia.
 - a) However, tachycardia is also a common presenting symptom in individuals with myocarditis. Patients with tachycardia during the first month of clozapine treatment should be monitored more closely for any of the above symptoms (2a).

B. Eosinophilia^{22, 23}

1. Eosinophilia is defined as $>4 \times 10^9$ Cells/L and is implicated in clozapine-induced eosinophilic colitis syndrome and eosinophilic cardiomyopathy. The incidence rate for clozapine induced eosinophilia in the United States has been estimated to be as high as 7% in males and 23% in females.
2. The manufacturer label recommends that clozapine be stopped if eosinophil levels exceed 3×10^9 Cells/L, however most cases of eosinophilia are apparently benign and resolve over time.
3. Re-challenge is recommended when levels drop below 1.0×10^9 Cells/L
4. When eosinophilia is identified, the Clinical Pharmacist will notify the Medical Physician and the Treating Provider
5. At the direction of the Treating Provider, additional symptom tracking may be initiated, including monitoring of constitutional and cardiac symptoms

C. Orthostatic Hypotension^{22, 23}

1. The incidence of orthostatic hypotension in clozapine treated patients is approximately 9%, with the majority of cases occurring early in treatment. Tolerance to this side effect develops over 4-6 weeks. Patients with specific risk factors for orthostatic hypotension and falls should be screened by checking an orthostatic blood pressure upon dose initiation.
 - a) If orthostatic hypotension is identified, it is recommended that clozapine titration be paused and continued at a slower rate.
 - b) Dose reduction, dividing doses more equally throughout the day, and modification of target dose should also be considered.
 - c) Non-pharmacological interventions include counseling on the need to rise slowly from sitting or lying position and increasing salt intake if medically appropriate.
 - d) The incidence of orthostatic hypotension is approximately 9% in clozapine treated individuals. Use of benzodiazepines, which can exacerbate hypotension, should be minimized during titration whenever clinically appropriate.

D. Seizures^{22, 23}

- a) Seizure risk increases in proportion to the speed of clozapine titration ($>25\text{mg}/\text{day}$) and the total daily dose. In population studies, seizure risk doubles for doses over 300mg per day and triples for total daily doses exceeding 600mg/day.
- b) An antiepileptic agent such as valproic acid may be considered as a prophylactic agent to mitigate seizure risk.
- c) The observation of seizure or myoclonic jerks should be immediately reported to the Treating Psychiatrist and Medical Physician for evaluation. If myoclonic jerks are observed, dose reduction and/or initiation of an antiepileptic agent are recommended.

- E. Sedation^{22,23}
- a) Up to 39% of individuals treated with clozapine experience excessive sedation. Tolerance to this side effect develops slowly and may be incomplete.
 - (1) Recommendations:
 - (a) Weighing doses towards nighttime may reduce this side effect. However, it is important to note that excessively large single doses of clozapine increase the risk of seizures at peak plasma concentrations.
 - (b) Assess clozapine plasma level and consider dose reduction if level (>350 µg/mL) and/or clinical response is adequate.
- F. Hyperthermia^{22,23}
- a) Benign hyperthermia occurs in approximately 5% of clozapine treated individuals, typically early in the course of treatment and resolving over time.
 - (1) Recommendations:
 - (a) Notify the Treating Provider and Medical Physician
 - (b) Initiate closer monitoring for symptoms of myocarditis/cardiomyopathy; obtain troponins and/or CRPs as directed by the Medical Physician.
 - (c) Consider antipyretics (e.g. ibuprofen or acetaminophen)
- G. Persistent Neutropenia not progressing to Agranulocytosis^{26, 27, 28}
1. A subset of individuals are neutropenic or borderline neutropenic at baseline prior to initiating clozapine. Benign Ethnic Neutropenia is the typical manifestation and is characteristic of individuals with African or Middle Eastern ancestry. Benign ethnic neutropenia should be documented as such in the medical record, at which time the lower ANC threshold of 1000 cells/ mL³ can be used to allow for continued clozapine therapy.
 2. Although evidence demonstrating the effective use of lithium as an adjunct to treat/prevent neutropenia is limited, anecdotal evidence exists to recommend its use for benign neutropenia with the aim of preventing interruptions in clozapine therapy. If employed, lithium levels should be monitored as usual. If upon initiation, no benefit is seen after 30-60 days of use, discontinue lithium.
- H. Constipation^{22, 23}
- a) Constipation, defined as less than three bowel movements per week, occurs in approximately 14% of clozapine treated individuals and can lead to bowel obstruction and death. Chronic dehydration and concurrent anticholinergics are risk factors for bowel obstruction. The bowel care management protocol is a multi-step protocol for assessing and managing the bowel care regimen. The Clinical Pharmacist is responsible for recommending bowel care medications according to the bowel care management protocol (see below) when constipation is identified.

Bowel Care Management Guidance^{29,30,31,32}

Preliminary: Assess fluid and fiber intake (Recommend 40-48 oz. of fluid/day and 20-35 g/day of fiber/day). If inadequate, recommend diet modification and increase in fluid intake.

Liquid Option	Pill Option
Step 1 (Standard Prophylactic) Docusate 100 mg po BID MOM 30 mL po every 24H PRN if no BM in 48H	
Step 2 PEG 17g mixed with 8 oz. of fluid po every other day MOM 30 mL po every 24H PRN if no BM in 48H	Step 2 Docusate 100 mg po BID Senna 2 tabs (17.2 mg) po Q HS MOM 30 mL po every 24H PRN if no BM in 48H
Step 3 PEG 17 g mixed with 8 oz. of fluid po daily MOM 30 mL po every 24H PRN if no BM in 48H	Step 3 Docusate 100 mg po BID Senna 3 tabs (25.8 mg) po Q HS MOM 30 mL po every 24H PRN if no BM in 48H
Step 4 PEG 17 g mixed with 8 oz. of fluid po BID MOM 30 mL po every 24H PRN if no BM in 48H	Step 4 Docusate 100 mg po BID Senna 4 tabs (34.4 mg) po Q HS MOM 30 mL po every 24H PRN if no BM in 48H
Step 5 PEG 17 g mixed with 8 oz. of fluid po daily Senna 2 tabs (17.2 mg) po Q HS MOM 30 mL po every 24H PRN if no BM in 48H	
Step 6 PEG 17 g mixed with 8 oz. of fluid po BID Senna 2 tabs (17.2 mg) po Q HS MOM 30 mL po every 24H PRN if no BM in 48H	

I. Sialorrhea^{22, 23,33,34,35}

- a) Up to 31% of clozapine treated individuals experience excessive salivation, which can lead to significant discomfort and clozapine discontinuation. While anticholinergics have been the mainstay of treatment, these agents increase the risk of constipation and urinary retention as well as contribute to cognitive impairment. The Clinical Pharmacist will make recommendations based on the following Sialorrhea Management Protocol to provide evidence-based intervention.

b) **Sialorrhea Management Guidance**

- (1) **Step 1:** Ipratropium Nasal Spray 0.03% – SL
 - (a) Initial: 1 spray SL once to twice daily
 - (b) If ineffective: May increase to 2 sprays SL once to three times daily
- (2) **Step 2:** Hyoscyamine 0.125 – 0.25 mg SL BID-QID OR Atropine Ophthalmic Drops 1 drop SL at HS and may increase to 2 drops SL BID
- (3) **Step 3:** Glycopyrrolate tabs: 1 mg po BID
- (4) **Step 4:** Add intervention in Step 3 with Steps 1 or 2 above

- J. Weight Gain and Metabolic Syndrome^{22, 23}
- a) Weight gain and metabolic abnormalities are a common side effect of clozapine treatment. In population studies, the average weight gain has been approximately 1.4 pounds per month in the first four years of treatment, or 67.2 lbs. after four years. The metabolic syndrome is also a common side effect of clozapine treatment and is characterized by central obesity, weight gain, hyperlipidemia, and glucose intolerance. Where weight gain and metabolic syndrome is evident and progressing, the Clinical Pharmacist will:
- (1) Consider referral for dietary consultation if there is an increase in any parameter greater than 5% in the first month or 10% in a 3-month period
 - (2) Reinforce lifestyle and dietary modification goals with the patient at each visit
 - (3) Recommend the use of metformin or topiramate where appropriate
 - (4) Recommend statins where appropriate to improve dyslipidemia
- K. Glucose Intolerance^{22, 23}
- a) Glucose intolerance develops commonly in clozapine treated patients. Clozapine has been found to be associated with a 7% per year increase in the prevalence of diabetes mellitus per year of clozapine exposure. Where elevated fasting plasma glucose is identified, the Clinical Pharmacist will:
- (1) Monitor fasting plasma glucose and alert the Treating Psychiatrist and Medical Physician of dramatic and progressive changes
 - (2) Recommend the use of metformin to mitigate glucose intolerance when appropriate

Appendix A: Clozapine Monitoring Checklist

Assessments	Baseline	Initiation/Titration (Weeks 1-4)	Continuation (>Weeks 4)
VITALS ASSESSMENT			
Weight/BMI/Waist Circumference	w/in 30 days	x 1 at Week 4	Quarterly
Temp/Fever since last visit?	w/in 7 days	x 2/Week	PRN as directed†
Respirations (beats/min)			
Blood Pressure (sitting)/Pulse			
Orthostatic Blood Pressure	PRN as directed†	PRN as directed†	
SIDE EFFECTS ASSESSMENT			
C/V Disease or Family History	w/in 7 days	x 2/Week	PRN as directed†
ECG Results (abnormal?)			
Palpitations/Tachycardia/Chest Pain			
Hypotension			
Dizziness/Falls/Lightheadedness			
Blurred vision			
Weakness/Fatigue/Sedation			
Sialorrhea			
Swallowing			
Fever/Chills			
Sore Throat			
Mouth Ulcers			
Nausea/Vomiting			
Constipation/BMs (how often?)			
Dyspnea/Tachypnea			
Constant Cough/Wheezing			
Fluid Retention/Edema/Abnormal Swelling			
Myoclonic Jerk			
INTERACTING MEDICATIONS			
1A2 , 3A4, 2C19, 2D6 inhibitors/inducers			
Constipating Meds: anticholinergics/opiates			
Adherence: Check MAR/Interview med-giver)			
LABS			
CBC w/Complete Differential (Venipuncture)	w/in 7 days	Weekly	Per Registry Guidelines
CBC 3-part Differential (Finger-stick)			
FPG/Lipid Panel	w/in 3 months	FPG x 1 at Week 4	Quarterly
CMP	w/in 12 months		Annually
ECG	As per standard OSH protocol (annually)		
Full Physical Exam			
KUB		As Indicated*	
Troponin + CRP		Weekly	Weekly PRN**

† If symptomatic, at Treating Provider's request, dose escalation, or other significant medication changes

*Concern for constipation and patient unreliable in reporting bowel frequency

**Tachycardia is an indication for closer monitoring of cardiovascular parameters and related symptoms. One or more cardiac symptoms (dyspnea, fever, chest pain, palpitations, fatigue, s/sx characteristic of heart failure) indicates need for immediate evaluation by Medical Physician and weekly troponins/CRP as directed.

Sources Note: Substantial reference made to the California Department of State Hospitals Psychotropic Medication Policies, Chapter 13.²² Dr. Ted Williams provided personal guidance from his experience in a pharmacist managed Clozapine Service at the Department Veteran Affairs.³⁶

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Treatment resources: Extrapyramidal symptoms (eps)

Table 1. Tardive Dyskinesia

Drug	Form	t _{1/2}	Dosing	FDA Indication	Pediatric Approval	Side Effects (>10%) and Drug Specific Considerations	Cost
Central Monoamine-Depleting Agents and Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors							
Valbenazine (Ingrezza)	Oral	15-22	40 mg QD x 1 wk; 80 mg QD	Tardive Dyskinesia	No	Side Effects: <i>Somnolence, Akathisia, Sedation</i> QT Prolongation (especially with CYP2D6 or CYP3A4 inhibitors)	\$\$\$\$\$\$
Deutetrabenazine (Austedo)	Oral	~9-10	6-48 mg/d BID	Tardive Dyskinesia	No	Side Effects: <i>Somnolence, Diarrhea, Xerostomia, Fatigue</i> QT Prolongation	\$\$\$\$\$
Tetrabenazine (Xenazine)	Oral	~A: 7 ~B: 5 ^^ 17.5 ^^~A: 10 ^^~B: 8	50-200 mg/d	Tardive Dyskinesia (off-label)	No	Side Effects: <i>Insomnia, Fatigue, Anxiety, Nausea, Depression, Dysphagia, Sedated</i> QT Prolongation Highest rates of adverse effects	\$\$\$\$\$\$\$

Legend: t_{1/2} = half-life

t_{1/2} reported in hours unless otherwise specified; ~ = active metabolite half-life; ^ = half-life in renal failure; ^^ half-life in hepatic failure

Estimated Average Monthly Cost based on AWP: \$\$\$\$ = 2,500-5,000; \$\$\$\$\$ = 5,000-10,000; \$\$\$\$\$\$ > 10,000

Table 2. Pharmacokinetics

Drug	Form	t _{1/2}	Tmax	%PB	Metabolism	Oral BA	Dosing Consideration
Central Monoamine-Depleting Agents and Vesicular Monoamine Transporter 2 (VMAT2) Inhibitors							
Valbenazine (Ingrezza)	Oral	15-22	0.5-1	>99% ~A:60-68	CYP3A4 – extensive CYP2D6: Alpha-HTBZ active metabolite	49	CrCl < 30: use not recommended Hepatic impairment (Mod-Sev): 40 mg/d CYP3A4 Inhibitors: 40 mg/d CYP3A4 inducers: Not recommended
Deutetrabenazine (Austedo)	Oral	~9-10	3-4	~A: 60-68 ~B: 59-63	CYP2D6 Alpha-HTBZ (~A) and Beta-HTBZ (~B) active metabolites	80%	CYP2D6 Poor metabolizer or strong inhibitors MAX 36 mg/d CI in hepatic impairment Miss > 1wk restart at initial dose
Tetrabenazine (Xenazine)	Oral	~A: 7 ~B: 5 ^^ 17.5 ^^~A: 10 ^^~B: 8	1-1.5	82-85 ~A: 60-68 ~B: 59-63	CYP2D6: extensive Alpha-HTBZ (~A) and Beta-HTBZ (~B) active metabolites	75%	CYP2D6 inhibitor: MAX 50 mg per day and 25 mg per dose

%PB = Percent Protein Binding; t_{1/2} and Tmax are reported in hours unless otherwise specified
t_{1/2}: ~ = active metabolite half-life; ^ = half-life in renal failure; ^^ half-life in hepatic failure, e = elderly

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Section 5. MHCAG methodology

In 2017, the Oregon Legislature passed House Bill (HB) 2300. This bill directs the Oregon Health Authority (OHA) to convene a Mental Health Clinical Advisory Group (MHCAG) to develop evidence-based algorithms for mental health treatments with mental health drugs based on four criteria. The criteria include:

1. Efficacy of the drug
2. Cost of the drug
3. Potential side effects of the drug, and
4. Patient's history of the drug.

To develop this algorithm, the MHCAG was tasked with using

- Peer-reviewed medical literature
- Observational studies
- Studies of health economics
- Input from physicians and patients, and
- Any other information the MHCAG deemed appropriate with an evidence base.

Additionally, the MHCAG was authorized to make recommendations to the Pharmacy and Therapeutics Committee on:

- Implementation of evidence-based algorithms
- Changes to the Prescription Drug List used by OHA, and
- Practice guidelines for the treatment of mental health disorders with mental health drugs.

The MHCAG recommends a collaborative evidence-based approach with providers and patients to select medications that may provide the greatest value and cost-effectiveness.

Process and Workgroup Methodology

The MHCAG is comprised of fifteen members that represent:

- Actively practicing psychiatrists
- Licensed clinical psychologists
- A psychiatric nurse practitioner
- Primary care providers
- Pharmacists
- Advocates
- Coordinated care organization (CCO) representatives, and
- A mental health consumer or family of a consumer.

To develop the schizophrenia treatment care guide, the full MHCAG met monthly with additional special meetings convening on an as-needed basis to:

- Collectively review scientific evidence
- Discuss systemic barriers to receiving mental health treatment for Oregonians
- Develop algorithms
- Create practice guidelines, and
- Make recommendations for inclusion in the final treatment care guide.

The recommendations contained in this treatment care guide are based on:

- Combined expertise of the MHCAG members
- Input from the public, and
- Review of the available scientific evidence.

Expert review and public consultation

Four members of industry and two members of the public with relevant clinical experience provided input on the guidelines during the year. The work of the group was conducted according to Oregon public meetings law and as such, research and draft guidelines were readily available for review by members of the public throughout the year.

Stakeholder identification and refinement*

“There is an inadequate workforce to deliver safe and effective care in outpatient and inpatient psychiatric programs. The cramped schedule leaves less time to review clinical information, provide expert guidance to the treatment team and practice up to the level of their licensure. The reduced supply and limited opportunities to expand competencies in training programs also leave the workforce less prepared to participate in the innovative models of care that are central to health care reform. These models are key features of coordinated care organizations and alternative payment mechanisms that reimburse providers on outcomes instead of volume. There is a great irony in the implementation of health care reform. On one hand, there is increasing recognition of the value of psychiatry and of behavioral health services as key components to the reduction of the total cost of care and improvement of general health outcomes concurrently there is a shortage of psychiatrists that will only worsen with integration of primary care and behavioral health and the shift to coordinated care organizations (CCOs) as part of health care reform. Due to efficient screening for mental health and substance use disorders (SUDs) in primary care, there will be growing demand for access to psychiatric services.”

To address both critical need and clinical impact, MHCAG Workgroup identified primary care teams inclusive of their patients as our key stakeholders moving forward allowing for potential to expand resources for our specialty providers.

Workgroup discussion methodology

Key clinical issues evolved from MHCAG Workgroup discussion and consensus throughout 2018 similar to the Texas Medication Algorithm Project antipsychotic schizophrenia treatment algorithm (9) however with perhaps a very different stakeholder group in consideration:

1. Should antipsychotic treatment pathways for individuals with schizophrenia differ in primary care versus specialty care?
2. When should first generation antipsychotics (FGAs) be considered in patient informed medication selection?
3. When should long-acting injectable (LAIs) antipsychotics be considered in an individual with schizophrenia?
4. How many antipsychotic (SGA or FGA) trials should precede the initiation of clozapine or referral to specialist care?
5. What is the status of augmentation strategies for patients receiving clozapine?

* Adopted from National Council for Behavioral Health (NatCon) “The Psychiatric Shortage” 2017 Position Statement, https://www.thenationalcouncil.org/wp-content/uploads/2017/03/Psychiatric-Shortage_National-Council-.pdf

Methodology for creation of MHCAG clinical decision-making pathways and clinical pearls

The work group planned the scope. Individual members drafted sections according to their area of interest and expertise, with reference to existing research literature and reviews. In addition, experts in specific areas contributed to the relevant sections. The working group considered recent international community practice groups (CPGs). (9, 10, 11)

The MHCAG workgroup then reviewed literature (as proposed by any group member) pertinent to particular clinical issues identified for workgroup discussion. Whenever possible workgroup members based their decisions on empirical evidence. However, when inadequate evidence was available panelists could draw upon expert opinion and clinical judgement with a goal of reaching consensus.

Methodology for grading of intervention-based resources

For intervention resources and publications, levels of evidence were graded using World Federation of Societies of Biological Psychiatry (WFSBP) methodology. Consensus-based clinical pearls were formulated when the work group judged that there was inadequate published evidence on a topic. Clinical pearls are based on the consensus of a group of experts in the field, and are informed by their agreement as a group, according to their collective clinical and research knowledge and experience. Where applicable, key considerations were selected from the recommendations on each topic. The whole working group reviewed this care guide. Discussion took place via a series of work group meetings and teleconferences. When members disagreed about clinical advice or interpretation of evidence, the issue was discussed until consensus was reached. This guide also refers readers to selected current documents, statements or algorithms published elsewhere; these were either developed within or by expert groups led by, or included, Oregon, United States and international experts.

The MHCAG workgroup also reached consensus about transparency and integrity of the information used to inform clinical decision-making pathway consensus. Two bibliographers were appointed to the group to evaluate and grade all literature proposed for consideration as care guide structure and development evolved during MHCAG workgroup meetings in 2018. MHCAG schizophrenia bibliographers were to achieve an independent interrelated reliability of no less than $k=.08$ for grading of intervention-based references. At the time of this draft publication their reliability was approximated at $k=.87$.

As of January 2019, our draft documentation is considered “low confidence” without completion of formal meta-analysis assessment and discussion per A MeaSurement Tool to Assess systematic Reviews (AMSTAR) 2 guidelines. *The MHCAG workgroup intends to have a rate as “moderate to high confidence” from the MHCAG bibliographers and the OHA Pharmacy and Therapeutics Committee (refer to hyperlink for AMSTAR 2 Evaluation Sheet below) by final publication of any medication pathway care guide inclusive of schizophrenia.*

AMSTAR 2

AMSTAR 2 checklist: https://amstar.ca/Amstar_Checklist.php

Research methods and reporting: <https://www.bmj.com/content/bmj/358/bmj.j4008.full.pdf>

AMSTAR 2 critical domains and MHCAG schizophrenia treatment pathway rating

- Protocol registered before commencement of the review (item 2) [Yes – partial]
- Adequacy of the literature search (item 4) [Yes]
- Justification for excluding individual studies (item 7) [Yes]
- Risk of bias from individual studies being included in the review (item 9) [Yes – partial]
- Appropriateness of meta-analytical methods (item 11) [No]
- Consideration of risk of bias when interpreting the results of the review (item 13) [Yes]
- Assessment of presence and likely impact of publication bias (item 15) [Yes]

AMSTAR 2: Rating overall confidence in the results of the review and MHCAG schizophrenia pathway

High

- No or one non-critical weakness
 - » The systematic review provides an accurate and comprehensive summary of the results of the available studies that address the question of interest.

Moderate

- More than one non-critical weakness*
 - » The systematic review has more than one weakness but no critical flaws. It may provide an accurate summary of the results of the available studies that were included in the review.

Low

- One critical flaw with or without non-critical weaknesses
 - » The review has a critical flaw and may not provide an accurate and comprehensive summary of the available studies that address the question of interest.

* AMSTAR rating tool

Critically low

- More than one critical flaw with or without non-critical weaknesses
 - » The review has more than one critical flaw and should not be relied on to provide an accurate and comprehensive summary of the available studies.*
 - » Multiple non-critical weaknesses may diminish confidence in the review and it may be appropriate to move the overall appraisal down from moderate to low confidence.

Bibliographer evaluation of literature and scientific evidence for MHCAG clinical decision-making pathways

The MHCAG workgroup also reached consensus to what grading “system” bibliographers would adopt in evaluating all materials considered. However, in doing so, the workgroup interrelated it to current criteria and methodology used by the OHA Pharmacy and Therapeutics Committee. National Institute for Health and Care Excellence (NICE) guidelines (12), which are considered a gold standard, were not selected due to the negative impact of potentially giving psychopharmacology studies with more significant flaws a higher-grade. This would be due to typical variance in psychopharmacology research methodology. (13) Because of these shortcomings of existing grading systems, we decided to adopt current World Federation of Societies of Biological Psychiatry (WFSBP) grading guidelines. The workgroup wants to provide optimal transparency for users of this guideline. Therefore, the workgroup plans to use the WFSBP grading system for categories of evidence for all future revisions of MHCAG treatment care guide documents for each guide. The workgroup also plans for updates to be provided no later than every 24 months. “Consensus guidelines may improve the overall quality of treatment (however, adherence to published guidelines is not always satisfactory). Guidelines also may have some influence on the design of future studies. By insisting on high quality standards, they can stimulate the application of rigorous methodological standards.”

On the following pages is a table with comparisons of the grading scheme for categories of evidence used by the NICE Guidelines for Anxiety Disorders (Eccles and Mason 2001) with the WFSBP Guidelines system.

* AMSTAR rating tool

Table I. Comparisons of the grading scheme for categories of evidence used by the NICE Guidelines for Anxiety Disorders (Eccles and Mason 2001) with the WFSBP Guidelines system. ¹These standards are defined in Bandelow et al. (2008, this issue).

Eccles and Mason (2001)		World Federation of Societies of Biological Psychiatry (WFSBP)	
Category of evidence	Description	Category of evidence	Description
I	Evidence from: – meta-analysis of randomised controlled trials, or – at least one randomised controlled trial	↑↑ A	Full Evidence From Controlled Studies is based on: two or more double-blind, parallel-group, randomized controlled studies (RCTs) showing superiority to placebo (or in the case of psychotherapy studies, superiority to a “psychological placebo” in a study with adequate blinding) <i>and</i> one or more positive RCT showing superiority to or equivalent efficacy compared with established comparator treatment in a three-arm study with placebo control or in a well-powered non-inferiority trial (only required if such a standard treatment exists) In the case of existing negative studies (studies showing non-superiority to placebo or inferiority to comparator treatment), these must be outweighed by at least two more positive studies or a meta-analysis of all available studies shows superiority to placebo and non-inferiority to an established comparator treatment. Studies must fulfill established methodological standards ¹ . The decision is based on the primary efficacy measure.
		↑B	Limited Positive Evidence From Controlled Studies is based on: one or more RCTs showing superiority to placebo (or in the case of psychotherapy studies, superiority to a “psychological placebo”) <i>or</i> a randomized controlled comparison with a standard treatment without placebo control with a sample size sufficient for a non-inferiority trial <i>and</i> no negative studies exist
II	Evidence from: – at least one controlled study without randomisation, or – at least one other type of quasi-experimental study	(↑) C	Evidence from Uncontrolled Studies or Case Reports/Expert Opinion
		C1	Uncontrolled Studies is based on: one or more positive naturalistic open studies (with a minimum of five evaluable patients) <i>or</i> a comparison with a reference drug with a sample size insufficient for a non-inferiority trial <i>and</i> no negative controlled studies exist
III	Evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies	C2	Case Reports is based on: one or more positive case reports <i>and</i> no negative controlled studies exist

Table I (Continued)

Eccles and Mason (2001)		World Federation of Societies of Biological Psychiatry (WFSBP)	
Category of evidence	Description	Category of evidence	Description
IV	Evidence from expert committee reports or opinions and/or clinical experience of respected authorities	C3	Based on the opinion of experts in the field or clinical experience
		↔ D	Inconsistent Results Positive RCTs are outweighed by an approximately equal number of negative studies
		↓ E	Negative Evidence The majority of RCTs studies shows non-superiority to placebo (or in the case of psychotherapy studies, superiority to a “psychological placebo”) or inferiority to comparator treatment
		? F	Lack of Evidence Adequate studies proving efficacy or non-efficacy are lacking

Section 6. Endnotes and bibliography

Endnotes

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11. OPAL-K (Oregon Psychiatric Access Line for Kids) Psychosis (2018) provided a framework for assessment and clinical management and for the choice and timing of interventions.
12. National Institute for Health and Care Excellence (NICE) guidelines (Eccles and Mason 2001)
13. Bandelow, 2008 https://www.wfsbp.org/fileadmin/user_upload/Treatment_Guidelines/Bandelow_et_al.pdf

Bibliographies and grading criteria

Inclusion and exclusion criteria for graded versus abbreviated schizophrenia bibliography

Due to the inherent limitations of currently published evidence, MHCAG consensus for bibliography inclusion was a grade of C- or higher by the appointed schizophrenia bibliographers. MHCAG also reached consensus in terms of making clinical recommendations where there was no conclusive evidence, avoiding making decisions solely on clinical consensus. Therefore, maintaining transparency in what evidence was applied as stated above. All graded resources as well as resources deemed either descriptive or supportive due to their chart are listed below under “Graded references”.

All tertiary information resources such as UpToDate®, IBM Micromedex®, Lexicomp®, etc. were excluded from grading. However, content reviewed was then cited below for transparency. All treatment care guides, protocols etc., authored by other clinical entities inclusive of Early Assessment Support Alliance (EASA), Central City Concern (CCC) and Oregon State Hospital (OSH) were reviewed in full. However, their bibliographies were cited in their current state within those respective entities. Also, their references were left intact for transparency and are listed below under “Cited references.”

Graded references

Abbreviated bibliography

(Independently graded C- or higher by 2018 MHCAG bibliographers)

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Table 6. MHCAG bibliography literature grading tool

(Adopted August 2018)

MHCAG grading Tool	MHCAG sub-workgroup(s) where publication is sited	Study citations (author, year) _____	Pharmacy & Therapeutics grade	World Federation of Societies of Biological Psychiatry (WFSBP)	MHCAG	MHCAG TOC Section 1
Questions for panel grading*		Question responses or comments (if needed)	<input type="checkbox"/> High <input type="checkbox"/> Moderate <input type="checkbox"/> Low <input type="checkbox"/> Inefficient	<input type="checkbox"/> A <input type="checkbox"/> B <input type="checkbox"/> C <input type="checkbox"/> D <input type="checkbox"/> F	<input type="checkbox"/> A <input type="checkbox"/> B <input type="checkbox"/> C <input type="checkbox"/> D <input type="checkbox"/> F	<input type="checkbox"/> Inclusion <input type="checkbox"/> Exclusion
What type of publication is being cited?						
Two or more double-blind parallel group randomized controlled studies showing superiority to placebo?			Yes = Grade A High Inclusion No = Continue grading, review remainder of WFSBP grade A study types before considering moderate evidence or grade B	Yes = Grade A High Inclusion No = Continue grading, review remainder of WFSBP grade A study types before considering moderate evidence or grade B	Yes = Grade A High Inclusion No = Continue grading, review remainder of WFSBP grade A study types before considering moderate evidence or grade B	<input type="checkbox"/> Inclusion <input type="checkbox"/> Exclusion
Limited positive evidence from controlled studies and no negative studies exist?			Yes = Grade B Moderate Likely inclusion No = Continue grading, review remainder of WFSBP grade B study types before considering insufficient evidence or grade C	Yes = Grade B Moderate Likely inclusion No = Continue grading, review remainder of WFSBP grade B study types before considering insufficient evidence or grade C	Yes = Grade B Moderate Likely inclusion No = Continue grading, review remainder of WFSBP grade B study types before considering insufficient evidence or grade C	<input type="checkbox"/> Inclusion <input type="checkbox"/> Exclusion

<p>Evidence from uncontrolled studies or case reports or expert opinion? Positive naturalistic open study with five or more patients? Expert opinion or consensus?</p>			<p>Yes = Grade C Low Possible inclusion</p> <p>No = Continue grading, review remainder of WFSPB Grade C study types before considering Insufficient evidence or grade D</p>	<p>Yes = Grade C Low Possible inclusion</p> <p>No = Continue grading, review remainder of WFSPB Grade C study types before considering Insufficient evidence or grade D</p>	<p>Yes = Grade C Low Possible inclusion</p> <p>No = Continue grading, review remainder of WFSPB Grade C study types before considering Insufficient evidence or grade D</p>	<p><input type="checkbox"/> Inclusion <input type="checkbox"/> Exclusion</p>
<p>Inconsistent results? Positive randomized controlled study (RCT) outweighed by an equal number of negative studies?</p>			<p>Yes = Grade D Insufficient Likely exclusion</p> <p>No = Continue grading, review remainder of WFSPB grade D study types before considering insufficient evidence or Grade D or F</p>	<p>Yes = Grade D Insufficient Likely exclusion</p> <p>No = Continue grading, review remainder of WFSPB grade D study types before considering insufficient evidence or Grade D or F</p>	<p>Yes = Grade D Insufficient Likely exclusion</p> <p>No = Continue grading, review remainder of WFSPB grade D study types before considering insufficient evidence or Grade D or F</p>	<p><input type="checkbox"/> Inclusion <input type="checkbox"/> Exclusion</p>
<p>How likely are research results to be realized in the real world considering population and circumstances for care?</p> <p>Is the patient similar to the study participants?</p> <p>Is the intervention feasible when one considers the patient's economic status, treatment adherence and other factors?</p>	<p><input type="checkbox"/> Yes, If yes please comment in the next column</p> <p><input type="checkbox"/> No</p> <p><input type="checkbox"/> N/A</p>					<p><input type="checkbox"/> Inclusion <input type="checkbox"/> Exclusion</p>

Table 7. OHA pharmacy and therapeutics quality of evidence grades and definitions crosswalk to MHCAG grades and definitions

OHA P and T grade	OHA definition	MHCAG grade	MHCAG definition, adapted WSFBP grading
High	<p>High confidence that the estimated effects produced in the studies reflect the true effect. Further research is very unlikely to change the estimated effect.</p> <p>Type of evidence</p> <ul style="list-style-type: none"> Evidence is based on data derived from multiple randomized controlled trials with homogeneity with regard to the direction of effect between studies <p>AND</p> <ul style="list-style-type: none"> Evidence is based on multiple, well done randomized controlled trials that involved large numbers of patients. 	A	<p>Full evidence from controlled studies is based on: two or more double-blind, parallel-group, randomized controlled studies (RCTs) showing superiority to placebo (or in the case of psychotherapy studies, superiority to a “psychological placebo” in a study with adequate blinding) and one or more positive RCT showing superiority to or equivalent efficacy compared with established comparator treatment in a three-arm study with placebo control or in a well-powered non-inferiority trial (only required if such a standard treatment exists). In the case of existing negative studies (studies showing non-superiority to placebo or inferiority to comparator treatment), these must be outweighed by at least two more positive studies or a metaanalysis of all available studies shows superiority to placebo and non-inferiority to an established comparator treatment. Studies must fulfill established methodological standards. The decision is based on the primary efficacy measure.</p>
Moderate	<p>Moderate confidence that the estimated effects produced in the studies reflect the true effect. Further research may change the estimated effect.</p> <p>Type of evidence</p> <ul style="list-style-type: none"> Evidence is based on data derived from randomized controlled trials with some conflicting conclusions with regard to the direction of effect between studies OR Evidence is based on data derived from randomized controlled trials that involved small numbers of patients but showed homogeneity with regard to the direction of effect between studies <p>OR</p> <ul style="list-style-type: none"> Some evidence is based on data derived from randomized controlled trials with significant methodological 	B	<p>Limited Positive Evidence from Controlled Studies is based on: one or more RCTs showing superiority to placebo (or in the case of psychotherapy studies, superiority to a “psychological placebo”)</p> <p>OR</p> <p>a randomized controlled comparison with a standard treatment without placebo control with a sample size sufficient for a non-inferiority trial and no negative studies exist</p>

OHA P and T grade	OHA definition	MHCAG grade	MHCAG definition, adapted WSFBP grading
Low	<p>Limited confidence that the estimated effects produced in the studies reflect the true effect. Further research is likely to change the estimated effect.</p> <p>Type of evidence</p> <ul style="list-style-type: none"> • Most evidence is based on data derived from randomized controlled trials with significant methodological flaws (e.g., bias, attrition, flawed analysis, etc.) <p>OR</p> <ul style="list-style-type: none"> • Evidence is based mostly on data derived from non-randomized studies (e.g., cohort studies, case-control studies, observational studies) with homogeneity with regard to the direction of effect between studies 	C	<p>Evidence from uncontrolled studies</p> <p>OR</p> <p>Case reports one or more positive case reports and no negative controlled studies exist</p> <p>OR</p> <p>Expert opinion</p> <p>OR</p> <p>Uncontrolled studies is based on: one or more positive naturalistic open studies (with a minimum of five evaluable patients)</p> <p>OR</p> <p>A comparison with a reference drug with a sample size insufficient for a non-inferiority trial and no negative controlled studies exist</p> <p>OR</p> <p>Based on the opinion of experts in the field or clinical experience</p>
Insufficient	<p>Evidence is not available or too limited to permit any level of confidence in the estimated effect.</p> <p>Type of evidence</p> <ul style="list-style-type: none"> • Evidence is based mostly on data derived from non-randomized studies (eg, cohort studies, case-control studies, observational studies) with some conflicting conclusions with regard to direction of effect between studies <p>OR</p> <ul style="list-style-type: none"> • Evidence is based on data derived from expert opinion or panel consensus, case reports or case series <p>OR</p> <ul style="list-style-type: none"> • Evidence is not available 	D and F	<p>Inconsistent results</p> <p>Positive RCTs are outweighed by an approximately equal number of negative studies</p> <p>OR</p> <p>Negative evidence</p> <p>The majority of RCTs studies shows nonsuperiority to placebo (or in the case of psychotherapy studies, superiority to a “psychological placebo”) or inferiority to comparator treatment</p> <p>OR</p> <p>Lack of evidence</p> <p>Adequate studies proving efficacy or non-efficacy are lacking</p>

Section 7. MHCAG glossary

Adequate response — When the patient and the treatment team collaboratively assess that the balance of mental health symptoms and treatment-related side effects is overall having a sufficiently positive effect on the patient’s quality of life.

Adverse response — A response that has any negative side-effect.

Attenuated or sub-clinical symptoms of schizophrenia — Symptoms which, if present, indicate the patient is considered at “ultra-high risk” of developing psychosis or schizophrenia.

Baseline monitoring — Labs and tests that are to be obtained prior to starting the medication.

Client-centered approach — The patient is given information, pros and cons, and the patient makes the final choice on their own with the information given. (The client has the most responsibility for their decision.)

Failure — No appreciable signs of improvement or symptom diminution.

FGA and SGA — first-generation anti-psychotic and second-generation anti-psychotic — First-generation antipsychotics (FGAs), also known as neuroleptics, conventional or typical antipsychotics, have significant potential to cause extrapyramidal side effects and tardive dyskinesia. This propensity to cause movement disorders is the primary difference between FGAs and second-generation antipsychotics (SGAs).”

Goal-setting — Determining treatment aims with the patient that are important to the patient as well as the clinician.

Inadequate response — When the patient and the treatment team collaboratively assess that mental health symptoms are insufficiently treated or there are treatment-related side effects which are having an overall negative impact on the patient’s quality of life.

Intolerable SEs — Side-effects that result in patient stopping the medication.

Maintenance monitoring — Labs and tests to be obtained periodically after medication maintenance dose is reached.

Positive response — A response that has any sign of improvement.

Shared decision making — Where both patient and physician carry responsibility for making the decision.

Timeframe — A period used to determine an effect.

Tolerable side effects — Side-effects that do not result in discontinuation of medication.

Treatment success — Improvement in symptoms that meets the aims of treatment in restoring health and function.

Section 8. Appendix of county resources

Oregon county crisis phone numbers:

<https://www.oregon.gov/oha/PH/PREVENTIONWELLNESS/SAFELIVING/SUICIDEPREVENTION/Pages/crisislines.aspx>

BAKER New Directions Behavioral Health and Wellness

General access

- 541-523-3646 (8 a.m. - 5 p.m.)

Crisis number

- 541-519-7126 (after hours)

BENTON County Mental Health Program

General access

- 541-766-6835

Crisis number

- 1-888-232-7192

CLACKAMAS County Mental Health Center

General access

- 503-742-5335

Crisis number

- 503-655-8585

CLATSOP Behavioral Healthcare

General access

- 503-325-5722

Crisis number

- 503-325-5724

COLUMBIA Community Mental Health, Inc.

General access

- 503-397-5211

Crisis number

- 503-397-5211 or 1-866-866-1426 (after hours)
- Vernonia: 503-397-5211

COOS County Mental Health Program

General access

- 541-751-2500

Crisis number

- 541-751-2550

CROOK Lutheran Community Services

General access

- 541-323-5330

Crisis number

- 541-323-5330

CURRY Community Health

General access

- Gold Beach: 541-373-8001
- Brookings: 541-813-2535
- Port Orford: 541-373-8085

Crisis number

- 1-877-519-9322

DESCHUTES County Mental Health Services

General access

- 541-322-7500

Crisis number

- 541-322-7500 (24 hours) or
1-800-875-7364

DOUGLAS Community Health Alliance

General access

- 541-440-3532

Crisis number

- 1-800-866-9780

GILLIAM Community Counseling Solutions

General access

- Condon: 541-384-2666
- Arlington: 541-454-2223

Crisis number

- 911

GRANT Community Counseling Solutions

General access

- 541-575-1466

Crisis number

- 911

HARNEY Symmetry Care

General access

- 541-573-8376

Crisis number

- 541-573-8376

HOOD RIVER Mid-Columbia Center for Living

General access

- 541-386-2620

Crisis number

- 1-888-877-9147 or 541-386-7534

JACKSON County Health and Human Services

General access

- 541-774-8201

Crisis number

- 541-774-8201

JEFFERSON County Community Mental Health Program

General access

- 541-475-6575

Crisis number

- 541-475-6575 (24 hours)

JOSEPHINE Options for Southern Oregon

General access

- 541-476-2373

Crisis number

- 541-474-5360 (24 hours)

KLAMATH Basin Behavioral Health

General access

- 541-883-1030

Crisis number

- 541-883-1030

LAKE County Mental Health Center

General access

- 541-947-6021

Crisis number

- 541-947-6021 or 1-877-456-2293

LANE County Health and Human Services

General access

- 541-682-3608

Crisis number

- White Bird Clinic: 541-687-4000 (after hours)

LINCOLN County Mental Health Program

General access

- Adults: 541-574-5960
- Children: 541-265-4179
- Lincoln City: 541-265-4196

Crisis number

- 1-888-232-7192 (24 hours)

LINN County Mental Health

General access

- 541-967-3866

Crisis number

- 541-967-3866 or 1-800-304-7468 (24 hours)

MALHEUR Lifeways, Inc.

General access

- 541-889-9167

Crisis number

- 541-889-9167

MARION County Mental Health Services

General access

- 503-588-5351
- Woodburn: 503-981-5851

Crisis number

- 503-585-4949

MORROW and WHEELER Community Counseling Solutions

General access

- Heppner: 541-676-9161
- Boardman: 541-481-2911

Crisis number

- 911

MULTNOMAH County Mental Health Services

General access

- 503-988-5887

Crisis number

- 503-988-4888
- Toll-free at 1-800-716-9769

POLK County Mental Health

General access

- Dallas: 503-623-9289
- West Salem: 503-585-3012

Crisis number

- 503-623-9289 (days)
- 503-581-5535 or 800-560-5833 (after hours)

SHERMAN Mid-Columbia Center for Living

General access

- 541-296-5452

Crisis number

- 1-888-877-9147
- 541-296-5452

TILLAMOOK Family Counseling Inc.

General access

- 503-842-8201

Crisis number

- 503-842-8201 or 1-800-962-2851

UMATILLA Lifeways, Inc.

General access

- Hermiston: 541-922-6226
- Milton-Freewater: 866-343-4473
- Pendleton: 541-276-6207

Crisis number

- Hermiston and Milton-Freewater: 1-866-343-4473
- Pendleton: 541-276-6207

UNION Center for Human Development

General access

- 541-962-8800

Crisis number

- 541-962-8800

WALLOWA Valley Center for Wellness

General access

- 541-426-4524

Crisis number

- 541-426-3111

WASCO Mid-Columbia Center for Living

General access

- 541-296-5452

Crisis number

- 541-296-6307
- 1-888-877-9147 (after hours)

WASHINGTON County Mental Health

General access

- 503-291-1155

Crisis number

- 503-291-9111

WHEELER and MORROW Community Counseling Solutions

General access

- 541-763-2746

Crisis number

- 911

YAMHILL County Adult Mental Health and Family & Youth Mental Health Programs

General access

- Adults: 503-434-7253
- Youth: 503-434-7462

Crisis number

- 1-844-842-8200



HEALTH POLICY & ANALYTICS
Office of Delivery Systems Innovation

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