

Personalizing the Pharmacotherapy approach in first episode psychosis based on patient need

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Welcome



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- For doctors and healthcare practitioners: http://epicanada.org/
- For patients and their family: https://www.earlypsychosisintervention.ca/

Social Media

• X: @EPI_Canada



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Today's Presenter



Howard C. Margolese, MDCM, MSc, FRCPC Associate Professor, Dept. of Psychiatry, McGill University Director, PEPP-MUHC, First Episode Psychosis Program



Disclosures:

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- Consultant/Paid Speaker: Abbvie, BI, HLS Therapeutics, Janssen, Newron Otsuka, Lundbeck, Teva



Objectives

- Discuss medication treatment approach in first episode psychosis
- Chose medication based on tolerability and address side effects.
- Highlight importance of treating co-morbidities
- Introduce shared decision-making concepts to improve therapeutic alliance and improve medication acceptance and adherence



First Episode Psychosis Treatment Considerations

Strategies for Engaging Patients in Treatment

Therapeutic engagement of young people with a psychotic illness:

- 1. Improves if staff do not insist that the young person accepts the diagnosis as soon as possible
- 2. Is helped if staff search for common ground to understand clients' experiences
- 3. Is helped by consistent and persistent contact with a key worker
- 4. Explores and discusses openly the young person's future goals and also their fears....their perspective
- 5. Do not be judgmental especially around the topic of drug use



What are Obstacles to Improving Outcome?

- Difficulty establishing diagnosis
- Delay in adequate treatment
- Remission not achieved or sustained
- Non-adherence to treatment
- Substance abuse
- Limited response to medication for negative symptoms, a major driver of functional outcome
- Difficulty treating cognitive and depressive symptoms



Goals of Pharmacotherapy in FEP

- Reduce DUP
- Achieve and maintain remission
- Improve quality of life
- Prevent progression of the disease



Pharmacotherapy Discussion Points with FEP patients

- Often useful to include the family in this discussion
- Discuss all treatment options with patients including LAIs and clozapine
- Most patients will refuse LAIs, but if discussed early, not seen as a punishment and can be discussed again later
- When discussing PO options, focus on side effects, tolerability, etc.
- Discuss adherence
- Discuss use of medications with ETOH and Cannabis



Pharmacotherapy Choices

Pharmacotherapy Approach

- Use metabolically favorable second or third generation antipsychotic (SGA, TGA)
 medications first
- Offer LAI early in the course of treatment discussed at very first or second visit.
- If complete or partial non-adherence is suspected, LAI re-discussed
- If 2 failed adequate trials we strongly suggest clozapine
- We prefer a trial of an LAI before clozapine to differentiate between lack of efficacy and partial/non-adherence



Pharmacotherapy: Safety First Protocol

1. Metabolically favourable SGA/TGA –

- Aripiprazole, Brexpiprazole, Cariprazine, Lurasidone, Asenapine (rarely used),
 Ziprasidone (rarely used);
- Or Arip, Risp or Palip if LAI is being considered
- Or straight to SGA/TGA- LAI Aripiprazole or Paliperidone

2. Choose

- Different MF SGA/TGA if intolerability, lack of efficacy.
- If Partial/non-adherence suspected choose SGA/TGA-LAI.
- If severe EPS consider quetiapine

3. SGA/TGA - LAI or Clozapine

4. Clozapine



Pharmacotherapy: Safety first protocol

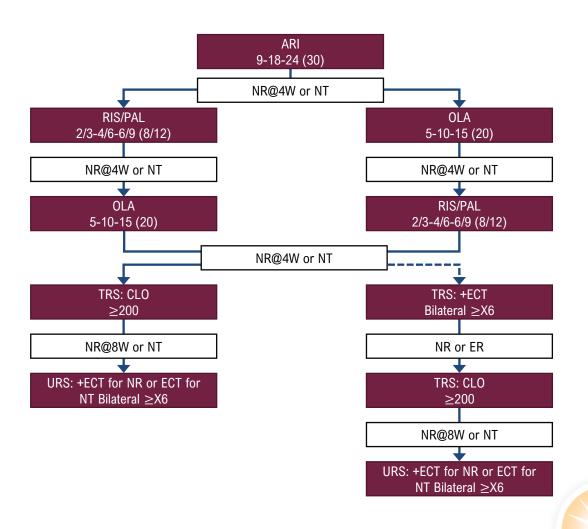
- Whatever medication is chosen first will usually work in 70-75% of patients for psychosis¹ – and even up to 87% in some studies
- Therefore, tolerability drives choice
- Goal is to treat to symptom remission
- We do not wait to increase dose; if limited or partial response after 2 weeks, we increase the dose¹
- SGA LAIs are preferred when accepted given high rates of non-adherence
- FGA are not used given negative effects on brain volumes^{1,2}

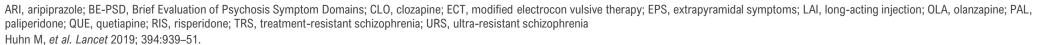


Some Experts Recommend 3rd-generation Antipsychotics as First-line Treatment for Antipsychotic-naïve Patients

Japanese Society of Clinical Neuropsychopharmacology Treatment Algorithm

- 1st-line: Aripiprazole
- 2nd-, 3rd-line: Risperidone / paliperidone or olanzapine
- 4th-line: Clozapine





If you had a Treatment Strategy that:

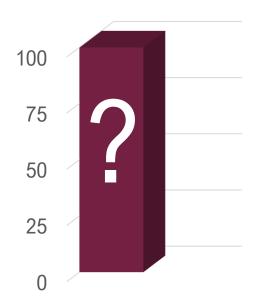
- Saved lives
- Reduced costs
- Diminished family burden
- Improved functional outcomes



If you had a Treatment Strategy that:

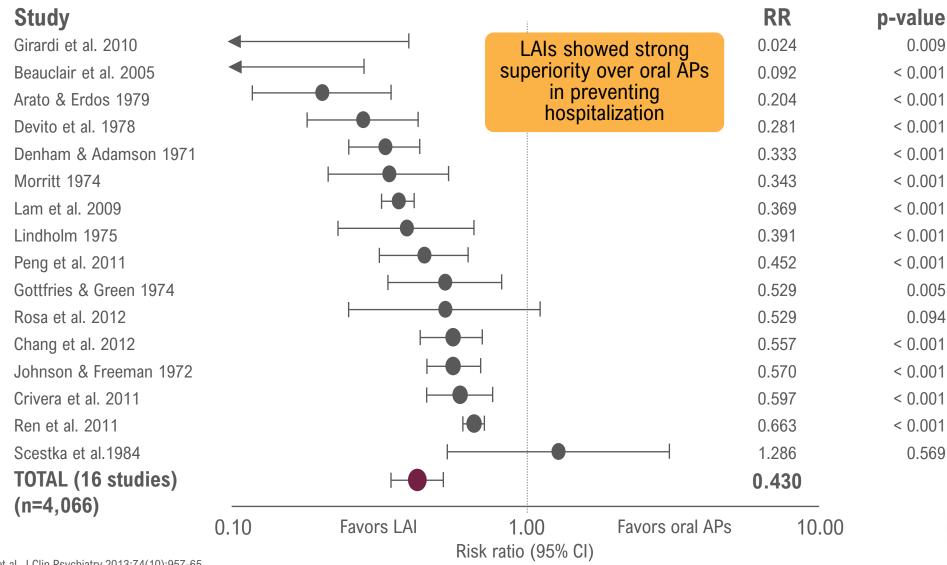
- Saved lives
- Reduced costs
- Diminished family burden
- Improved functional outcomes

In what proportion of patients would you use it?





In Mirror-Image Studies, LAIs Reduce Risk of Hospitalization Compared with Oral Antipsychotics

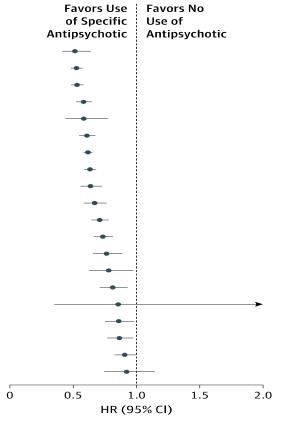


Shaping the discussion with the patient on LAI/Clozapine Decreased Risk of Rehospitalization With LAIs/Clozapine

Adjusted Hazard Ratios (HRs) and 95% Cls for Psychiatric Rehospitalisation During Monotherapy Compared With No Use of Antipsychotic in Within-Individual Analyses in the Prevalent Population



Treatment	HR (95% CI)
LAI paliperidone	0.51 (0.41-0.64)
LAI zuclopenthixol	0.53 (0.48-0.57)
Oral clozapine	0.53 (0.48-0.58)
LAI perphenazine	0.58 (0.52-0.65)
LAI olanzapine	0.58 (0.44-0.77)
LAI risperidone	0.61 (0.55-0.68)
Polytherapy	0.62 (0.58-0.65)
Oral olanzapine	0.63 (0.59-0.68)
LAI haloperidol	0.64 (0.56-0.73)
Oral zuclopenthixol	0.67 (0.59-0.76)
Oral risperidone	0.71 (0.64-0.78)
Oral aripiprazole	0.73 (0.66-0.81)
Oral levomepromazine	0.76 (0.66-0.89)
LAI flupentixol	0.78 (0.62-0.98)
Oral haloperidol	0.81 (0.71-0.93)
LAI fluphenazine	0.86 (0.35-2.08)
Other oral formulations	0.86 (0.75-0.98)
Oral perphenazine	0.86 (0.77-0.97)
Oral quetiapine	0.91 (0.83-1.00)
Oral flupentixol	0.92 (0.74-1.14)





Adverse Effects of Key Antipsychotics

	Extrapyramidal	Sedation	Weight gain	Hyperglycaemia	Anticholinergic	Orthostatic hypotension
typical antipsyc	hotics					
Risperidone	••	o initially	00	00	•	o initially
Quetiapine	O *	•••	00	000	00	00
Olanzapine	0	•••	•••	000	000	0
Clozapine	0	•••	•••	000	000	00
Amisulpride	00.	0	0	0	•	0
Aripiprazole	0	0	0	•	0	0
Ziprasidone	0	00	0	0	0	00
ypical antipsych	otics					
Haloperidol	•••	0	00	00	0	0
Chlorpromazine	00	000	000	000	000	000

Approximate frequency of adverse effects: (<2%) = negligible or absent; (>2%) = infrequent; (>2%) = moderately frequent; (>30%) = frequent. * rarely a problem at usual therapeutic doses



Pharmacotherapy of Side Effects Some Treatment Options

Prolactin elevation

Add a dopamine partial agonist e.g., aripiprazole, brexpiprazole, cariprazine

Constipation

Add stool softeners

Weight gain/metabolic syndrome

• Diet/exercise, add metformin, ? semaglutide

Sedation

Change timing of dose, look as sleep habits, r/o OSA

Insomnia

 Sleep hygiene, CBT for insomnia, then medication – many options (Trazodone, Doxepin, Z drugs, Lemborexant, Quetiapine)



Pharmacotherapy of EPS Side Effects Some Treatment Options

Akathisia

Propranolol, gabapentin, benzodiazepines, low dose mirtazapine

Parkinsonism

Benztropine, amantadine

Dystonia

• Benztropine, amantadine

Tardive Dyskinesia

• Stop anticholinergics, switch to quetiapine or clozapine, add tetrabenazine



Which medication is best for your patient?

Pharmacotherapy of Co-morbidities: Anxiety, Depression, ADHD, SUD

- Antidepressants often used for co-morbid anxiety and depression in Schizophrenia/Psychosis.
- Be aware of potential drug-drug interactions Many SSRIs will slow metabolism and raise antipsychotic blood levels
- Citalopram and escitalopram have fewer drug interactions among SSRIs;
 Desvenalfaxine (pristiq) among the SNRIs
- Pregabalin or gabapentin can be considered for anxiety as well
- Limit use of benzodiazepines
- Stimulants for ADD/ADHD only if adherence to antipsychotics is assured
- Consider naltrexone for AUD, and possibly CUD



Adherence to Treatment

- Delicate to assess strong evidence that clinicians tend to overestimate
- A variety of approaches have yielded positive results, including:
 - Family intervention
 - Psycho-education
 - Financial incentives
 - Variety of integrated care approaches
 - SMS reminders
- Experts' consensus: need for a personally tailored approach



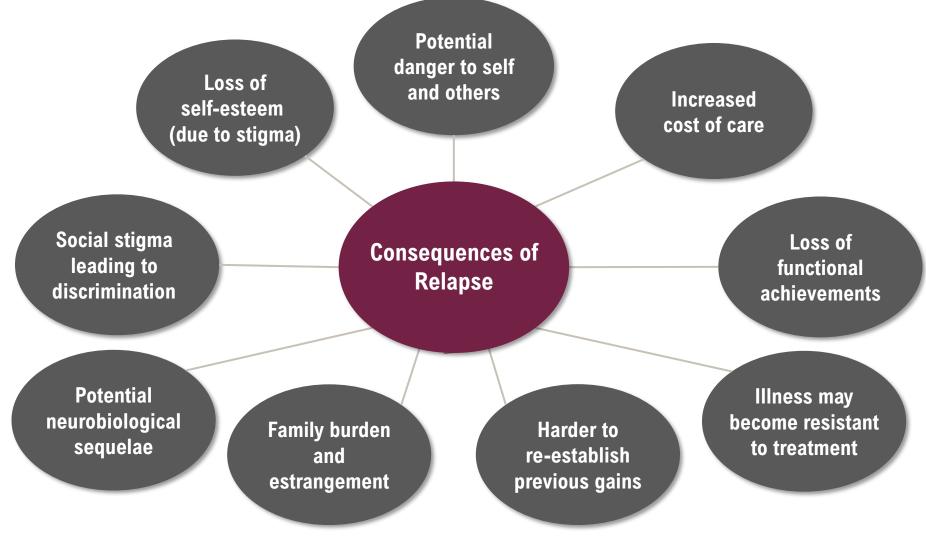
Strategies to Decrease Nonadherence with Treatment

- Ensure positive patient-physician relationship, build "therapeutic alliance"
- Develop treatment plan
- Involve caregivers/family
- Identify risk factors for nonadherence
- Choose treatment strategies promoting maximum efficacy and minimal side effects
- Follow evidence-based guidelines
- Prescribe simplest titration and dosage regimen (once-daily oral or long-acting injection)
- Use monotherapy where possible

- Manage side effects rapidly and effectively
- Provide education about illness and treatment (written and verbal)
- Discuss risks and benefits regularly
- Assess and monitor adherence regularly
- Review goals of treatment and patient expectations periodically
- Minimize disruption and inconvenience
- Ensure reimbursement of cost



Consequences of Relapse





SDM: OPTIMA and OPTICShared Decision-Making Tools

https://www.epicanada.org/tools-shareddecisionmaking

Classic SDM: Shared Decision-Making Paradigm

SIX STEPS in the shared decision-making process:

- 1. Inform the patient which decisions must be made
- Ask the patient how and to what extent he or she wants to be informed and included in decision-making
- 3. Inform the patient that different (more than one) treatment options are available
- 4. Present to the patient the different treatment options
- 5. Help the patient to find his or her own preferences
- 6. Discuss, make or defer the decision



How to Proceed with "Difficult Decisions"

One option is better than all others (according to evidence, team consensus) but there is (feared or apparent) resistance from the patient's side, e.g.:

- Take antipsychotics or not
- Medication treatment with LAI, clozapine, lithium....
- Court ordered treatment of not



Harvard Model

Basic idea: Avoid confrontation (struggle)

Goal: Create an optimal environment for a shared-decision

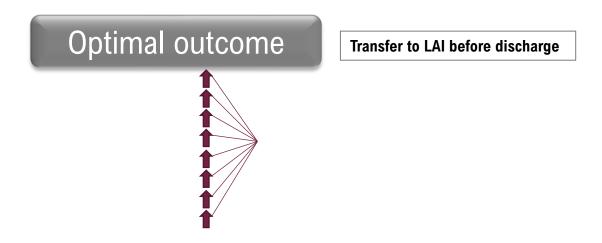
Example:

- During rounds, a patient says that they want to stop treatment immediately and leave the ward
- Problematic reaction of the HCP/team: instant (likely emotional less rational) reaction



BATNA "Best Alternative To A Negotiated Agreement"

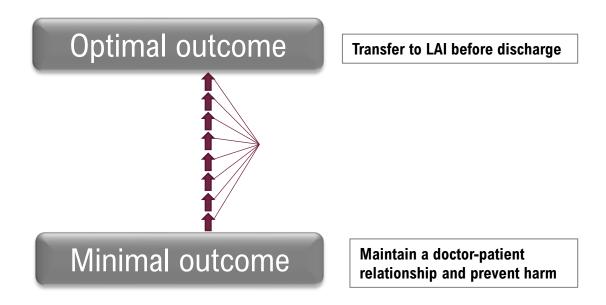
"I am not taking any treatment because I am not sick"





BATNA "Best Alternative To A Negotiated Agreement"

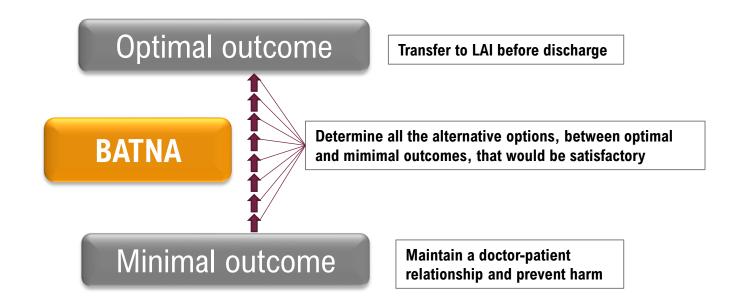
"I am not taking any treatment because I am not sick"





BATNA "Best Alternative To A Negotiated Agreement"

"I am not taking any treatment because I am not sick"





OPTIMA: A Tool for Patient Engagement



OPTIMA PATIENT DECISION AID

SHOULD YOU TAKE MONTHLY MEDICATION FOR YOUR SYMPTOMS?

A consult decision aid for people with psychotic symptoms and healthcare professionals to discuss options.

Why are you being offered monthly medication for your symptoms?

Your symptoms affect your ability to function well at home, school or work, and in your social life. Medication is a vital part of treating your symptoms and restoring your ability to take part in everyday activities. The main goal of taking medication is to help you stay well so you can stay out of hospital. Starting medication when symptoms first happen is the best way to do this.

Uninterrupted medication helps you stay well.1

- Being well is known as remission. This is shown in the graph titled "Possible Outcomes of Psychotic Symptoms".
- If you do not take medication for your symptoms, you cannot function well. You may need to be in hospital often, as you will have symptoms (relapses). Having relapses affects your brain and prevents full recovery. This is shown in the graph.



- Taking medication for your symptoms monthly provides steady levels of medication in the body, as shown in the graph titled "Monthly Medication Compared with Daily Medication Provides a Steady Level of Medication in the Body".
- This way of giving medication may decrease side effects, such as sleepiness and weight gain, compared with daily oral medication.³ Daily medication is shown in the graph.
- Monthly medication may also increase effectiveness, as it decreases the risk of recurrent symptoms, compared with oral medication.
- · With monthly medication, you receive less medication than with daily medication.



What are your options?

- 1. Take medication monthly.
- 2. Do not take medication monthly. Talk to your doctor about daily oral medication.

¹ Lieberman JA, Korean AR, Chakos M, et al. Factors influencing treatment response and outcome of fist-episode schizophrenia: implications for understanding the pathophysiology of schizophrenia. J Clin Psychiatry, 1996;57 (suppl 9):5-9.
² Sheehan JJ, Reilly KR, Fu D-J, Alphrs L. Comparison of the peak-to-trough fluctuation in plasma concentration of longacting injectable antipsychotics and their oral equivalents. Innov Clin Neurosci. 2012;9(7-8):17-23
³ Taylor D. Psychopharmacology and adverse effects of antipsychotic long-acting injections: a review. Br J Psychiatry 2009;(Suppl 53):513-9.

OFFERING PATIENTS THERAPEUTIC INFORMATION MEDICATION ALTERNATIVES (OPTIMA)

Person's Name:

BENEFITS AND REASONS TO CHOOSE MONTHLY ME	DICATION	YES	NO
When you take monthly medication rather than daily medication, you may get along at home better, be able to	Is it important to you to get along better with family and friends?		0
go to school or work, have a better social life and be more satisfied with treatment.1	Is it important to you to be able to go to school or work?		
People who switch to monthly medication say their	Is it important to you to have a better social life?		
	Is it important to you to be satisfied with your treatment?		_
Over two years, more people stay on treatment with monthly medication than daily medication.4	Is it important to you to stay on medication?		
If you need to be hospitalized with symptoms, you may spend much less time in hospital with monthly medication than with daily medication, about two-thirds less time. ⁵	Is it important to you to spend less time in hospital?		_
People who forget to take their medication daily are more likely to have symptoms and more likely to be hospitalized than people taking monthly medication. ⁶	Is it important to you to avoid being hospitalized with symptoms?		_
Over a one-year period, people taking daily medication are three times more likely to be hospitalized with symptoms than people taking monthly medication. ¹			
Relapses make it harder for you to recover. Usually, fewer relapses happen with monthly than with daily medication. Long-term treatment results are better with monthly medication. ⁷	Is it important to you to have better long term treatment result and fewer relapses?		
Some monthly medication begins to work fast ⁸ This means you may be able to recover faster and leave hospital sooner.	Is it important to you to recover faster and leave hospital sooner?		_
When you take monthly medication, you have more steady and even levels of medication in the body and may have fewer side effects, such as sleepiness and weight gain, than with daily medication.9	Is it important to you to have fewer side effects?		_
You receive less medication with monthly than with daily medication.	Is it important to you to receive less medication?		
When you take medication monthly, you do not need to worry about remembering to take medication daily.	Is it important to you not to worry about remembering to take medication?		
Taking monthly treatment may be simpler for you than taking daily.	Is it important to you to simplify your medication plan?		
If you forget to go for your monthly medication, we will reschedule your appointment with your treatment team to maintain your medication's effectiveness.	Is it important to you to stay connected to your treatment team?		_
People taking monthly medication better protect their brain from additional illness than people taking daily medication. ¹⁰	Is it important to you to protect your brain from the illness?		_

1

OPTIMA

https://www.epicanada.org/optima



OPTIMA PATIENT DECISION AID

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A consult decision aid for people with psychotic symptoms and healthcare professionals to discuss options.

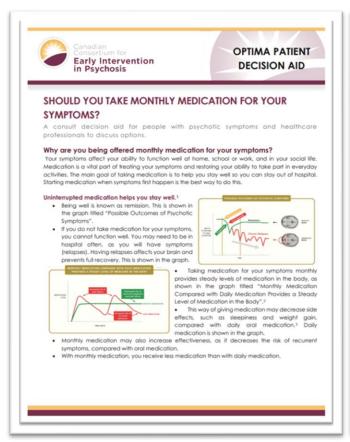
What does the acronym OPTIMA stand for?

Offering Patients Therapeutic Information on Medication Alternatives



The OPTIMA Tool has 3 Parts

Education for: 1) HCP and 2) Patient





3) Motivational Interview





Patient Handout

3 Important Sections:

- a) Should you...
- b) Why?
- c) Education on continuous treatment



OPTIMA PATIENT DECISION AID

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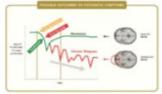
Why are you being offered monthly medication for your symptoms?

Your symptoms affect your ability to function well at home, school or work, and in your social life. Medication is a vital part of freating your symptoms and restoring your ability to fake part in everyday activities. The main goal of taking medication is to help you stay well so you can stay out of hospital. Starting medication when symptoms first happen is the best way to do this.

Uninterrupted medication helps you stay well.1

- Being well is known as remission. This is shown in the graph titled "Possible Outcomes of Psychotic Symptoms".
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- Taking medication for your symptoms monthly provides sheady levels of medication in the body, as shown in the graph filled "Monthly Medication Compared with Daily Medication Provides a Steady Level of Medication in the Body".²
- This way of giving medication may decrease side effects, such as sleepiness and weight gain, compared with daily oral medication.³ Daily medication is shown in the graph.
- Monthly medication may also increase effectiveness, as it decreases the risk of recurrent symptoms, compared with oral medication.
- With monthly medication, you receive less medication than with daily medication.



OPTIMA Questionnaire

Instructions

- Questionnaire lists benefits and risk (discomfort) of monthly medication and is the core of decision aid
- Series of questions about importance to patient of specific benefits of monthly medication
- Each question preceded by evidence statement
- Review each question to ensure patient understands
- Have patient respond Yes or No to each question
- Record response on decision aid

OFFERING PATIENTS THERAPEUTIC INFORMATION MEDICATION ALTERNATIVES (OPTIMA

Person's Name

BENEFITS AND REASONS TO CHOOSE MONTHLY MI	EDICATION	YES	NC
When you take monthly medication rather than daily medication, you may get along at home better, be able to go to school or work, have a better social life and be more satisfied with treatment.! People who switch to monthly medication say their symptoms, ability to function in their daily life, and satisfaction with treatment are much better with monthly medication.	Is it important to you to get along better with family and friends?	0	0
	Is it important to you to be able to go to school or work?		-
	Is it important to you to have a better social life?	0	-
	Is it important to you to be satisfied with your treatment?	0	-
Over two years, more people stay on treatment with monthly medication than daily medication.4	Is it important to you to stay on medication?		-
If you need to be hospitalized with symptoms, you may spend much less time in hospital with monthly medication than with daily medication, about two-thirds less time. ⁵	Is it important to you to spend less time in hospital?		-
People who forget to take their medication daily are more likely to have symptoms and more likely to be haspitalized than people taking monthly medication. ⁴ Over a one-year period, people taking daily medication	Is it important to you to avoid being hospitalized with symptoms?	0	
are three times more likely to be hospitalized with symptoms than people taking monthly medication. Relapses make it harder for you to recover. Usually, fewer relapses happen with monthly than with daily medication.	Is it important to you to have better long term treatment result and fewer relapses?	0	
Long-term treatment results are better with monthly medication. ⁷			
Some monthly medication begins to work fast* This means you may be able to recover faster and leave hospital sooner.	Is it important to you to recover faster and leave hospital sooner?		
When you take monthly medication, you have more steady and even levels of medication in the body and may have fewer side effects, such as sleepiness and weight gain, han with daily medication. ⁹	Is it important to you to have fewer side effects?	_	
fou receive less medication with monthly than with daily medication.	Is it important to you to receive less medication?		-
When you take medication monthly, you do not need to worry about remembering to take medication daily.	Is it important to you not to warry about remembering to take medication?		-
aking monthly treatment may be simpler for you than taking daily.	Is it important to you to simplify your medication plan?		-
f you forget to go for your monthly medication, we will eschedule your appointment with your treatment team to maintain your medication's effectiveness.	Is it important to you to stay connected to your treatment team?	0	_
People taking monthly medication better protect their brain from additional illness than people taking daily medication. 10	Is it important to you to protect your brain from the illness?		

1

OPTIC: Offering Patients Therapeutic Information about Clozapine, a shared decision-making tool

by Lauren Said, Pharm.D and Howard C. Margolese, MD, CM, MSc, FRCPC

Abstract

- Patients suffering from treatment resistance schizophrenia (TRS) often have an inadequate clinical response and a less favorable functional outcome. Therefore, it is important to use the most effective treatment available.
- Although clozapine has proven benefits in treating TRS compared to other antipsychotics, it is only prescribed in less than 50% of eligible patients. Clozapine's list of side effects and blood monitoring requirements give it a negative reputation amongst patients and some physicians.
- The primary focus of the OPTIC tool is to facilitate a balanced discussion between clinicians and patients that emphasizes the benefits of clozapine as the gold standard treatment for TRS. When clinicians are confident that clozapine is the best treatment for their patients, their genuine approach to offering clozapine will be better received.
- The OPTIC tool is composed of three parts, a clinician information handout, a patient handout and patient questionnaire.

developed to assist patients in deciding if clozapine is right for them. The clozapine decision aid clearly highlights the benefits of clozapine compared to other treatments for TRS and discusses how clozapine's side effects can be managed.

questionnaire uses motivational interviewing concepts to guide the discussion thereby allowing the patient to reflect on their treatment goals and determine if clozapine is suited to help them. At the end of the questionnaire the patient is invited to make a decision about taking clozapine if

effective medications? eing well is also called "remission". If the nedication you are taking does not fully unction well. You may need to be in the

ospital more often, as you will have orsening symptoms (relapses), Having relapses affects your brain health and hown in the graph to the side.

antineuchotics

people that have not shown a significan

any medication other than clozapine has a very lo hance of making you feel better, roughly 10-205 This is why we are suggesting that you try clozapine **McGill**

YES NO

CLOZAPINE **DECISION AID**

SHOULD YOU TAKE CLOZAPINE FOR YOUR SYMPTOMS?

Why are you being offered clozapine for your symptoms?

our psycholic symptoms have not responded to the medications you have taken so far. Your sumotoms your ability to function well at home, school or work, and in your social life. Medication is a vital part of fre your symptoms and restoring your ability to take part in everyday activities. Clozapine is the gold stan nedication for people who have not responded well to two different medications, such as yourself, 1 The goal of taking medication is to help you stay well so that you can function well, reach your full potential, o ourse, stay out of hospital. Taking medication that can adequately treat your symptoms, such as clozapit

What are the benefits of taking

Early Intervention

in Psychosis

OFFERING PATIENTS THERAPEUTIC INFORMATION ON CLOZAPINE (OPTIC)

When you take clozapine rather than other medication,	family and friends?			
	you may get along at home better, be able to go to school or work, have a better social life and be more satisfied	Is it important to you to be able to go to school or work?		_
	with treatment. People who switch to clozapine say their symptoms, ability to function in their daily life, and satisfaction with treatment is better. ¹	Is it important to you to have a better social life?	_	
scuss		Is it important to you to be satisfied with your treatment?	_	
	Over two years, more people stay on clozapine than other medication. ⁸	Is it important to you to stay on medication?		
affect eating ndard	People not optimally treated are more likely to have symptoms and more likely to be hospitalized than people taking clozapine.#	Is it important to you to avoid being hospitalized with symptoms?	0	0
main nd, of is the	Relapses make it harder for you to recover. Usually, fewer relapses happen with clozopine since it is the most effective treatment for your condition. Long-term treatment results are better with clozopine. If	Is it important to you to have a better long- term treatment results and fewer relapses?		_
	You are being offered clozapine because you have symptoms that are not responding to other medications	Is it important for you to take the medication with the best chance of response?	_	
	and clozapine offers the best chance of response. It is the gold standard of care for your condition.	Is it important for you to take the gold standard treatment for your condition?		_
	gold standard of care for your condition.* come patients who are now taking multiple medications might be able to take fewer medications when taking lozapime.*	Is it important to you to simplify your medication plan?	0	0
	The scheduled laboratory monitoring allows you to be more connected to your treatment team.	Is it important to you to stay connected to your treatment team?	0	_
	Since clozapine causes fewer relapses, people taking clozapine can better protect their brain compared to people taking less effective medication.	Is it important to you to protect your brain from the illness?	_	_
1				

SKS AND REASONS TO AVOID CLOZAPINE

blood tests, but most patients tolerate this well.	several by several published testing?		_
Optional question depending on availability of capillary blood	caused by regular blood testing? If you are uncomfortable with regular blood		п
testing	tests, would this device be an acceptable	_	_
If you responded NO to the previous questions	alternative for you?		
For people uncomfortable with blood tests, there is a	If yes, ask your doctor if this device is		
device that allows for regular monitoring with a simple	available in your area.		
prick of a finger. A small drop of blood is then collected			
from the tip of the finger and is used for testing.			
Blood tests are initially administered weekly then every	Are you able to tolerate the inconvenience of		
two weeks and after 1 year, every 4 weeks (monthly).**	the blood monitoring schedule?		
Clozapine side effects may include sedation (tiredness),	Are you willing to exercise, eat healthy foods		
weight gain, hypersalivation (drooling or excess saliva),	and take additional medication to manage		
constipation and palpitations. Most of these side effects	side effects if they occur?		
can be adequately managed with diet, exercise, or other			
medication.***			
Like all of the medications offered to you, clozapine does	Do you think you would be able to tolerate		
have potential side effects. To gain a better understanding	some of the potential side effects of		
of clozapine's side effects, we should discuss them in	clozapine?		
comparison with any alternative medication.			

Discussion

OPTIC provides the necessary information to initiate a balanced discussion between clinician and clozapine eligible patient. It changes the conversation from a list of clozapine's many side effects to a discussion about how its benefits on reducing TRS symptoms significantly outweigh its side effects. The main objective is for clozapine to be adequately offered systematically to people with TRS as soon as they become eligible. This tool can facilitate a positive offer and increase acceptance of clozapine. The OPTIC tool is based on the OPTIMA tool which discusses the place of LAI in treatment of psychosis.

Conclusion

We hope that the use of the OPTIC tool will facilitate positive offers of clozapine thus increasing its acceptance amongst patients with TRS as soon as they become eligible. This will hopefully be translated by an increase in the number of TRS patients effectively treated with clozapine. The OPTIC tool has not yet been distributed as it was just recently finalized, therefore its impact on clozapine prescription rates cannot be measured at this time. It will be available for free on the Canadian Consortium for Early Intervention in Psychosis website (epicanada.org)

under clinical tools.

SIRS virtual meeting On April 20th 2021

than other antipsychotics for patients with TRS. Clozapine has been shown to improve remission rates, and reduce psychotic symptoms, risk of relapse, length of hospitalization, suicidal risk, and mortality. Despite its effectiveness, it remains underused in Canada, and is often prescribed as a last resort. Physicians and patients often have negative perceptions towards the medication due to the side effects and specific laboratory monitoring requirements. However, according to Poster presented at Canadian guidelines, clozapine should be offered as a 3th line therapy, i.e., after two unsuccessful trials of adequate dose and duration using other antipsychotic medications.² This is also referred to as TRS. It is important to discuss clozapine's effectiveness in treating TRS with patients to allow 2. BENEFITS them to make an informed decision about their treatment. Clazapine should be offered to both inpatients and outpatients who have poor treatment response or lingering symptoms due to partial one particular study showed that after 3 months of treatment with clozapine, patients showed response with their current treatment. Patients who are highly suicidal, who have substance use significant improvement in symptoms, improved guality of life and greater improvement in their Submission #3007067 disorders and who present with polydipsia may also benefit from clozapine

Early Intervention

OFFFRING PATIENTS THERAPEUTIC

CLINICAL RECOMMENDATIONS ON THE USE OF CLOZAPINE

INFORMATION ON CLOZAPINE (OPTIC) ©

Patients suffering from schizophrenia often have an inadequate clinical response and less

favourable functional outcome. It is important for physicians to use the most effective treatment

possible. Although clozapine has proven its benefits for treatment resistant schizophrenia (TRS), it is

still only prescribed in 20-50% of eligible patients. The purpose of OPTIC is to provide guidance for

physicians on what information to discuss with patients when offering clozapine as a treatment option. Clozapine should be offered systematically to people with TRS as soon as they become

eligible. This tool can facilitate a positive offer and increase acceptance of clozapine by your

1. SIDE FFFFCTS Clozapine is a second-generation antipsychotic medication that has proven to be more effective

The clinician handout discusses the benefits of clozapine in TRS, how to initiate a positive offer of clozapine to patients as

well as how to best manage the side effects with lifestyle changes and medications. There is also a guide to initiating

CLINICIAN

SUPPORT TOOL

When reviewing clozapine's side effects with patients, it is important to adequately describe them so that patients can have an honest depiction of the medication. However, it should be mentioned that even though they are "common" side effects, not all patients will experience these symptoms. Furthermore, most of them can be adequately managed with a healthy lifestyle and/or pharmaceutical treatments. As for the severe side effects, given that clozanine is an older medication, a lot of information is available about its potential side effects and their ssociated risks are well documented. Also, many experts have recommended strategies to reduce the incidence of severe side effects. Therefore, they are now considered well-managed

RECOMMENDED APPROACH TO DISCUSSING CLOZAPINI

2 adequate trials with other antipsychotic medication

 People with schizophrenia that have a high risk of suicidality People with schizophrenia and a co-morbid substance abuse disorder (possibly)

People with schizophrenia who present polydipsia (possibly)?

Suggestions for initiating the discussion

other medications

antiosychotic treatments (remission)

KEY POINTS TO REMEMBER ABOUT CLOZAPINE

· Confraindications: pre-existing myeloproliferative disorder, neutropenia, know.

. "We have talked about your goals and the importance of medication to manage your symptoms. We have tried different antipsychotics and have not succeeded in treating your symptoms. Now, I would like to talk to you about clozapine, which is an effective

antipsychotic that is recommended for people like you who have not responded well to

Review and help the patient understand the benefits of clozapine after two failed

Every other trial after the second antipsychotic has a response rate of roughly 10-20%,

Question 1: Why are you being offered clozapine for your symptoms?

overall mental health compared to other antipsycholics.2

- Howes, Oliver D et al. "Treatment-Resistant Schizophrenia: Treatment Response and Resistance in Psychosis (TRRIP) Working Group Consensus Guidelines on Diagnosis and Terminology." The American journal of psychiatry vol. 174.3 (2017): 216-229. Agid. Ofer et al. "Early use of clozapine for poorly responding first-episode psychosis." Journal of clinical psychopharmacology vol. 27.4 (2007): 369-73. Williams, Richard et al. "What is the Place of Clozapine in the Treatment of Early Psychosis in Canada?." Canadian journal of psychiatry. Revue canadienne de psychiatrie vol. 62,2 (2017): 109-114
- Canadian Psychiatric Association, Clinical practice guidelines: treatment of schizophrenia. The Canadian Journal of Psychiatry, 2005;50(13):1s-57s.
- Margolese HC, Steiner W, Lalla F, Cattan C, Perillo A, Arshoff L. Development of a patient decision aid to educate patients with acute psychoses about long-acting injectable antipsychotic therapy. Institute on Psychiatri Services (IPS) 2016: The mental Health Services Conference, October 6-9 2016, Washington DC

OPTIC Consists of 3 Parts

1. Healthcare provider information brochure

Provides information about clozapine

2. Patient handout

Gives basic information about why clozapine is a good choice for them

3. Decision aid questionnaire

Uses questions to facilitate discussion of benefits and risks of clozapine vs.
 other treatments

https://www.epicanada.org/optic



Should I Continue an Antipsychotic? And if Yes, for How Long?

Benefits

- Relapse prevention
- RRR= 0.36-0.57
- Reduced mortality
- RR= 0.39-0.73



Risks

- Medication side effects
- Less recovery?



Conclusions

- When choosing your initial treatment, decide based on current and possibly future individual patient needs
- Engage patient in their treatment choice using a shared decision making (SDM) approach as this can improve adherence
- Treat both side effects and co-morbid conditions to better address individual patient needs
- Consider LAIs and when TRS is established clozapine earlier in the treatment trajectory as these medications can improve outcomes





Discussion: Questions & Comments



Evaluation

Please click on the link provided in the chat box.

Your feedback is so valuable!