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PSYCHIATRY ACADEMY

Long-acting injectable antipsychotics as treatment options

Sarah A. MacLaurin, PMHNP-BC
Freedom Trail Clinic of North Suffolk Community Services
Psychosis Clinical and Research Program of MGH

Disclosures

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Neither I nor my spouse/partner has a relevant financial relationship with a commercial interest to disclose.

Overview

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- What are long-acting injectable medications?
- Why would we consider using long-acting injectable antipsychotics?
- How do we decide which long-acting injectable antipsychotic to use?

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What …

are long-acting injectable antipsychotics?

Non - Pharmacologic Treatment Options

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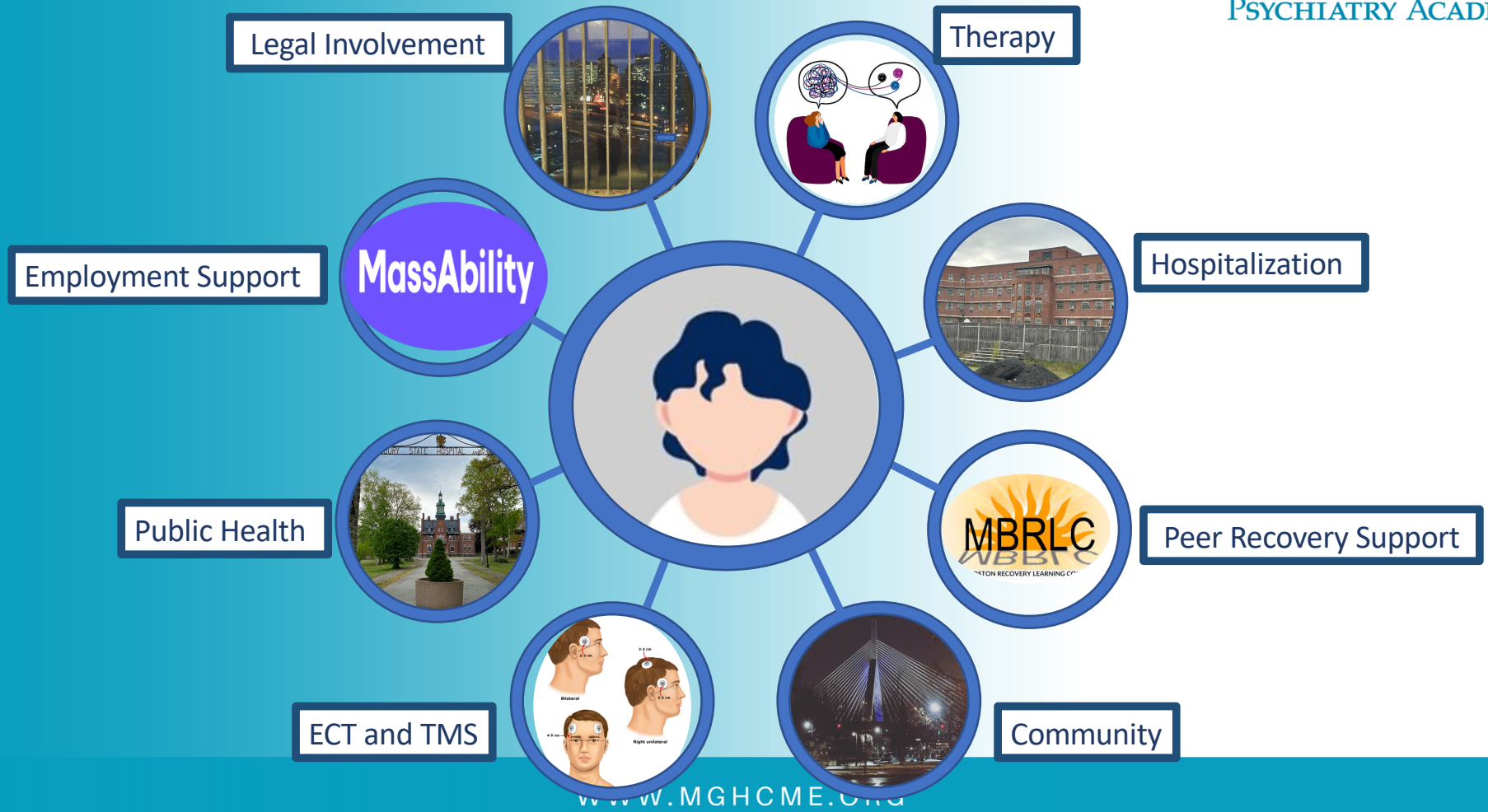

Optimal Comprehensive Care

for First Episode Psychosis (FEP)

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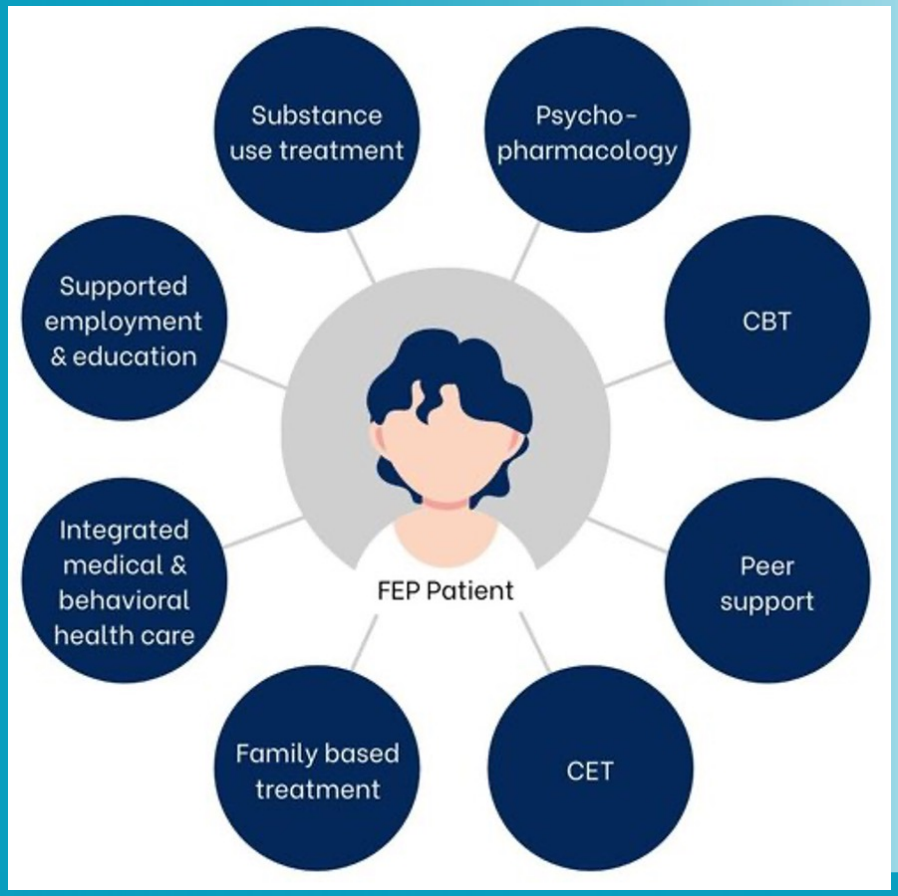

Coordinated Specialty Care:

10 programs in Massachusetts

- Individual or group psychotherapy
- Family support and education programs
- Medication management
- Supported employment and education services
- Case management

https://www.nimh.nih.gov/research/research-funded-by-nimh/research-initiatives/recovery-after-an-initial-schizophrenia-episode-raise

Pharmacologic Options

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Clozapine 1989

FGA

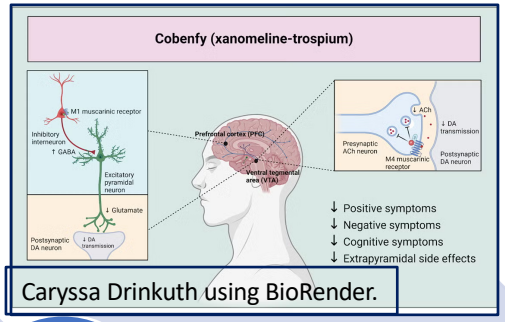
Chlorpromazine 1954
Fluphenazine 1959
Haloperidol 1967

First Generation Antipsychotics

SGA

Risperidone 1993,
Olanzapine 1996
Quetiapine 1997
Aripiprazole 2002
Paliperidone 2006
Cariprazine 2015
Lumateperone 2019

Second Generation Antipsychotics



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TGA

Xanomeline-trospium 2024

Third Generation Antipsychotic

What are long-acting injectables (LAIs)?

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Medications administered by injection lasting for a week or more

Increasingly common usage across a variety of illness states

- Diabetes
- Pain
- Birth control
- Inflammatory diseases
- HIV
- Substance use disorders
- **Psychiatric disorders**

International Treatment Guidelines:

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"Although initial treatment will be with oral medication, the possibility of switching to a **long-acting injectable** preparation **once tolerability is established should be discussed with patients early in treatment**, considering the potential benefits (easier adherence, reduced relapse risk, and improved overall mortality) and drawbacks (difficulty in making rapid dose adjustments and need for injection). The opportunity to use an long-acting injectable should be **offered in a collaborative fashion**, with care taken to avoid any perception of coercion by patients. "

McCutcheon RA, et al. 2025

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Why…

consider using long-acting injectable antipsychotics?

Risk of Non-Adherence

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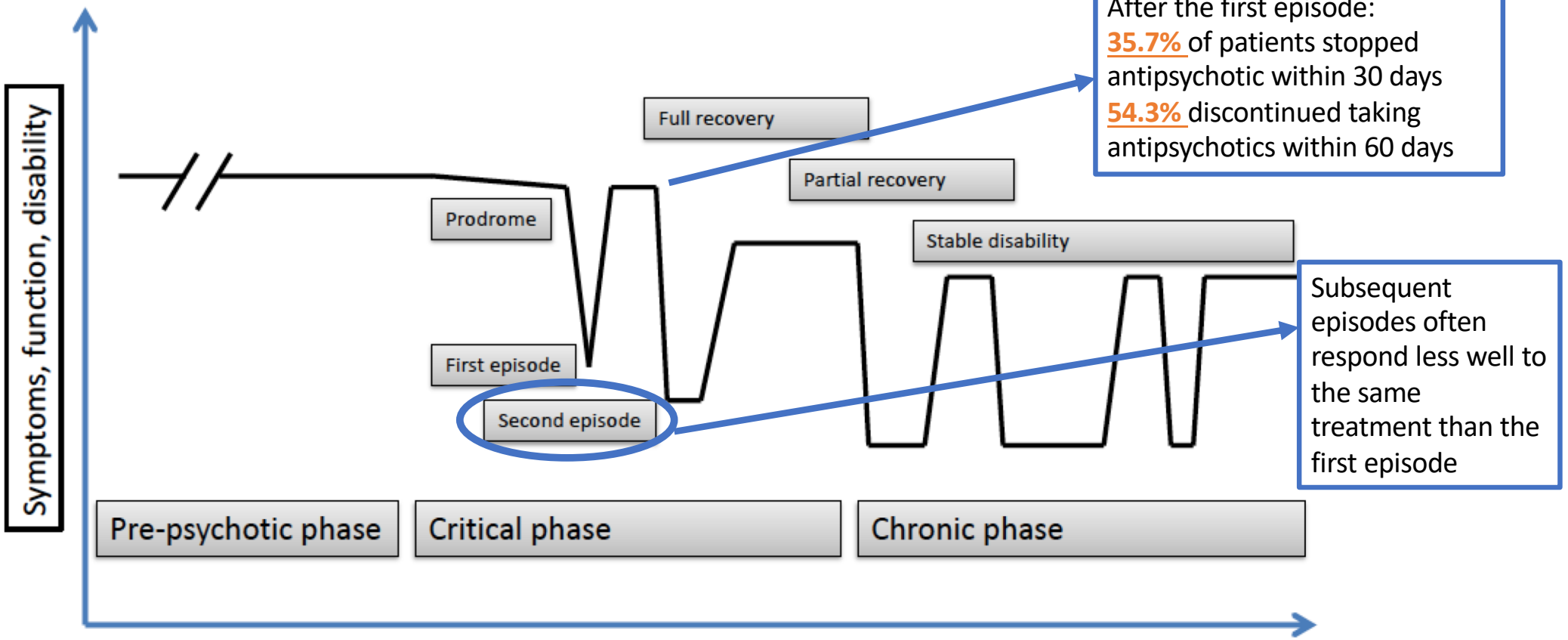

After the first episode:
35.7% of patients stopped antipsychotic within 30 days
54.3% discontinued taking antipsychotics within 60 days

Subsequent episodes often respond less well to the same treatment than the first episode

Freudenreich O. Psychotic Disorders. Springer 2020.

Tiihonen, J. (2011).

Unplanned discontinuation

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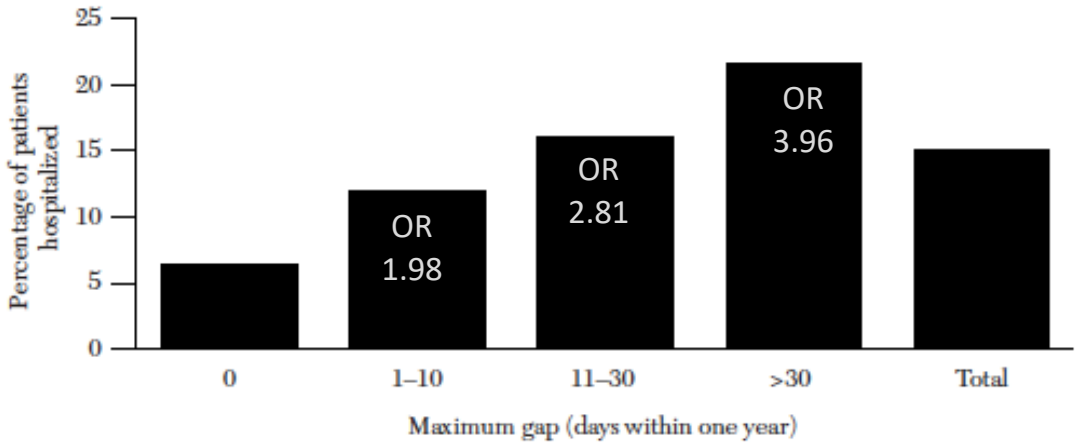
… Likely (longer) hospitalization

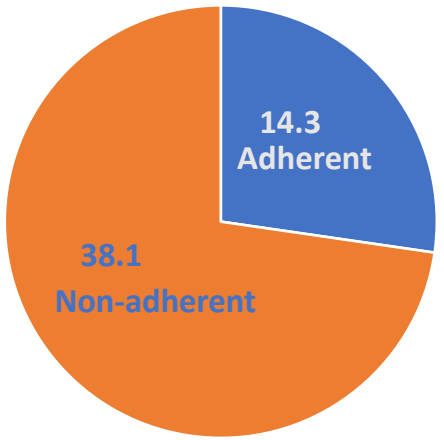
Figure 1

Percentage of patients with schizophrenia who were rehospitalized, by maximum gap in therapy[a]



[a] All pairwise comparisons were siginificant at p<.005.

Mean Number of Inpatient Hospital Days



* P < 0.001

Weiden, P. J. et al (2004).
McEvoy, J. P. et al (1984).

Relapse is likely without treatment

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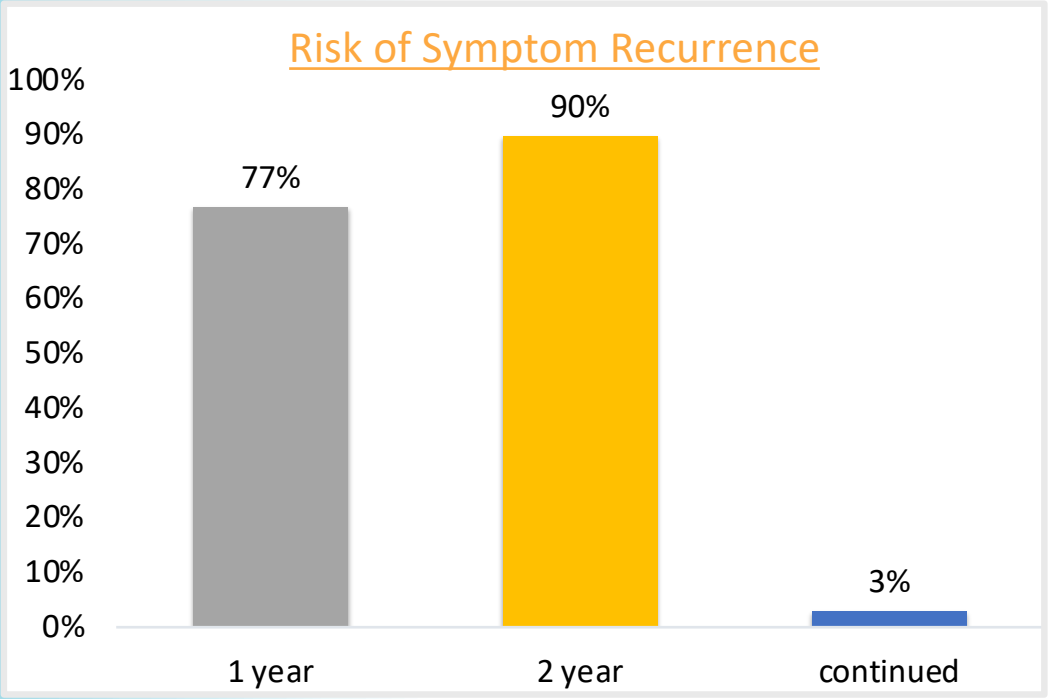
Systematic review of studies with controlled (planned) medication discontinuation.

Criteria:

(1) first episode non-affective psychosis population
(2) responded to treatment or experienced a remission of symptoms (e.g. in the maintenance phase) ≥6-months) prior to medication discontinuation
(3) the study reported symptom recurrence or worsening or relapse ≥6-months after medication discontinuation



Zipursky, R. B. et al. (2014).

Prevention of relapse in schizophrenia trial

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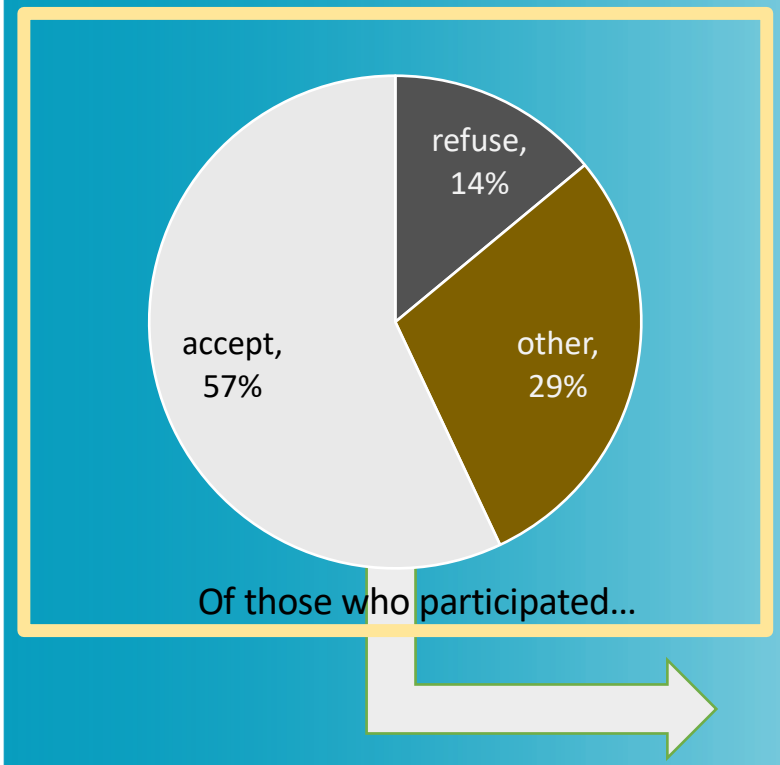
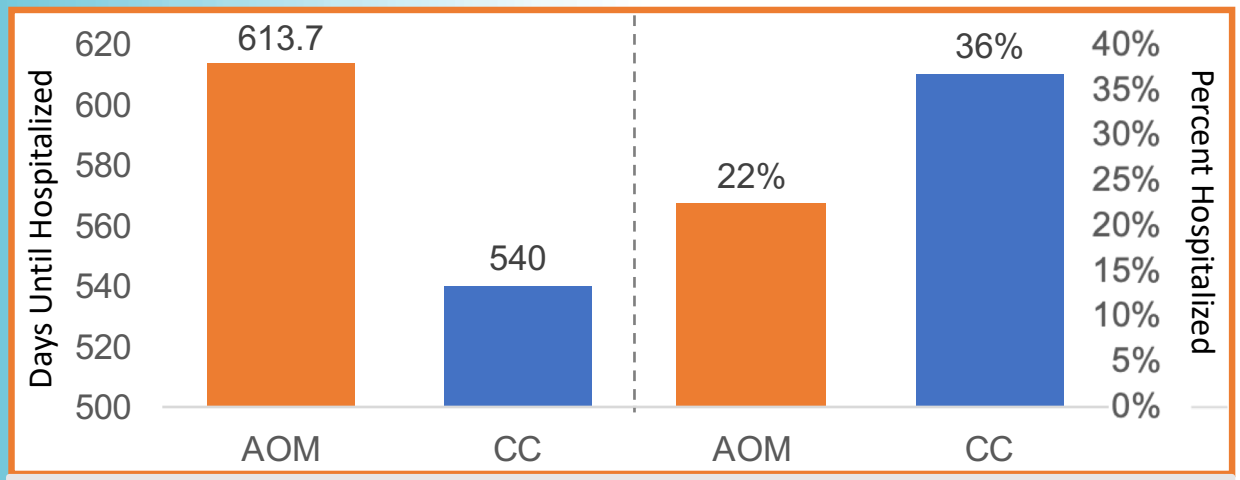


Patients are **willing** to trial LAI-antipsychotics. When offered, more than half of participants

Those accepting LAI had a significantly lower likelihood of hospitalization and length of time to hospitalization.



AOM = aripiprazole once monthly injection CC = clinician's choice

Kane, J. M. et al. (2019).
Kane, J. M et al. (2020).

LAIs reduce overall mortality

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"without mental health there can be no true physical health"

Dr. Brock Chisolm, 1953
director of the WHO

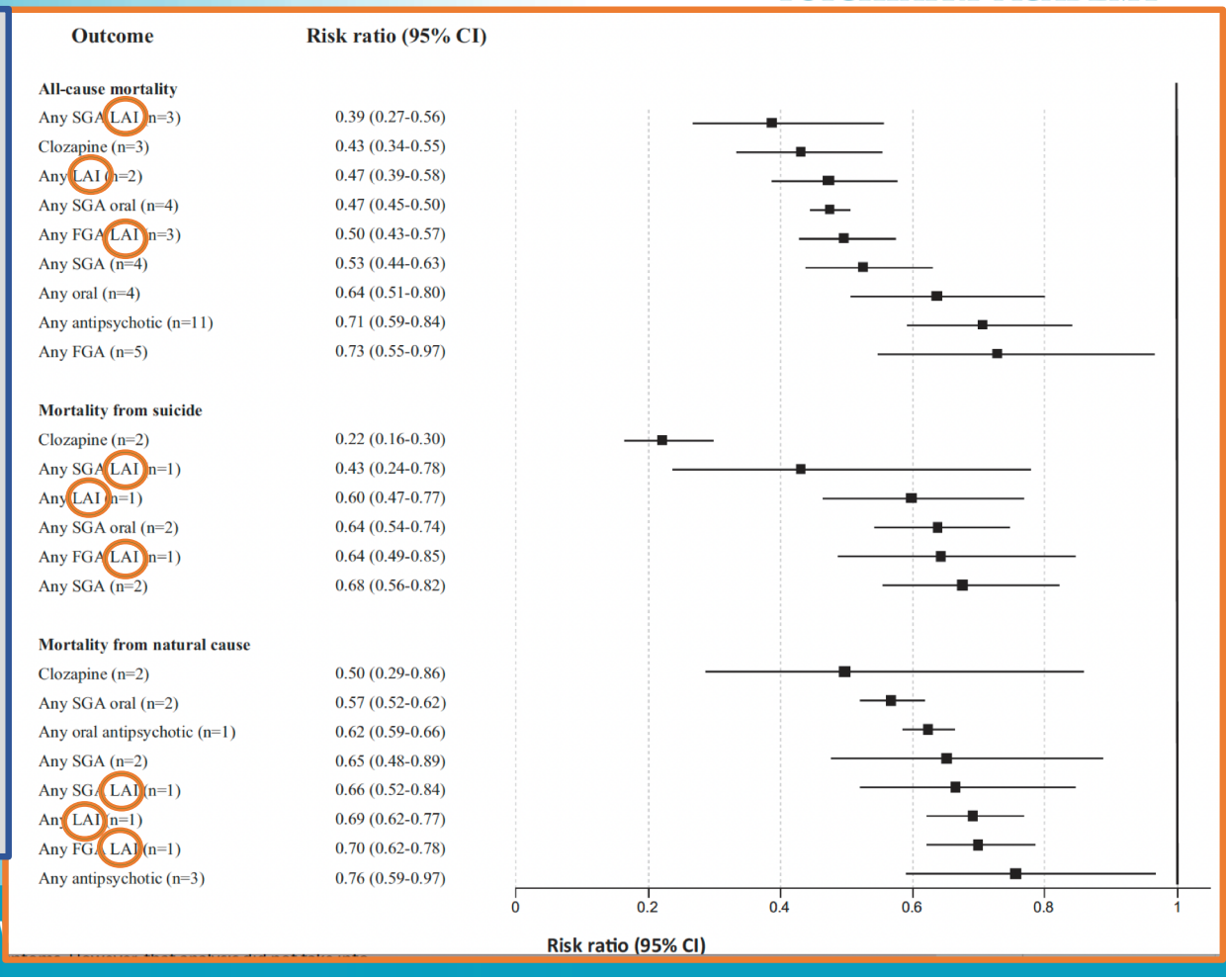
Reduced risk of death from suicide **and** death from medical disease

<u>cumulative mortality rates from a 20-year cohort study</u>

46.2% : no antipsychotic use

25.7% : any antipsychotic use

15.6% : clozapine use



Taipale H, Tanskanen A, Mehtälä J, et al. 2020
Correll CU, Solmi M, Croatto G, et al. 2022

Decrease risk of relapse

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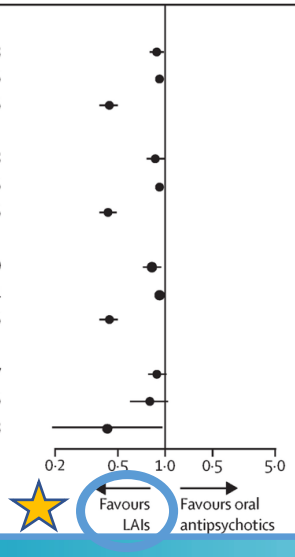
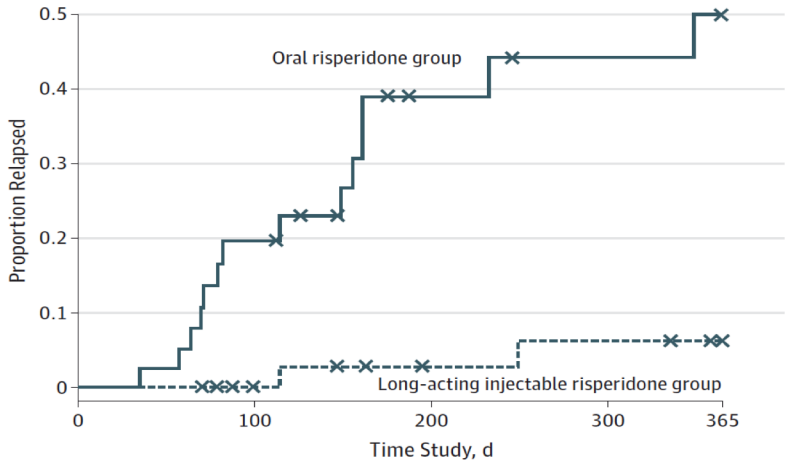
Different types of studies demonstrate superior efficacy of LAIs to prevent relapse and hospitalization

	Number of studies	Number of patients	Risk ratio (95% CI)	p value	Heterogeneity p value	Heterogeneity I^2	NNTB* (95% CI)
Hospitalisation preferential to relapse							
RCT	29	7833	0·88 (0·79–0·99)	0·033	0·092	27·0	45 (25–540)
Cohort	44	106136	0·92 (0·88–0·98)	0·0044	<0·0001	88·4	31 (19–95)
Pre–post	28	17876	0·44 (0·39–0·51)	<0·0001	<0·0001	88·7	4 (3–4)
Relapse preferential to hospitalisation							
RCT	29	7888	0·87 (0·77–1·00)	0·042	0·0007	51·9	34 (19–884)
Cohort	44	106136	0·93 (0·88–0·98)	0·0056	<0·0001	88·4	32 (19–104)
Pre–post	28	17876	0·44 (0·38–0·50)	<0·0001	<0·0001	88·5	4 (3–4)
Hospitalisation							
RCT	18	4310	0·83 (0·72–0·95)	0·0065	0·12	28·7	25 (16–82)
Cohort	38	104581	0·93 (0·88–0·98)	0·0078	<0·0001	89·6	32 (19–118)
Pre–post	28	17876	0·44 (0·39–0·51)	<0·0001	<0·0001	88·7	4 (3–4)
Relapse							
RCT	27	7407	0·89 (0·77–1·02)	0·086	<0·0001	54·5	..
Cohort	9	3286	0·80 (0·60–1·06)	0·12	0·0052	63·4	..
Pre–post	3	373	0·43 (0·19–0·96)	0·040	0·12	52·4	6 (4–76)





Relapse

Oral: 32.6%

LAI: 5.0%

NNT = 3.6

Hospitalization

Oral: 18.6%

LAI: 5.0%

NNT = 7.4

Subotnik KL, et al. (2015)
Kane JM et al. (2019)
Kishimoto et al., (2021)

Patient Perspective on LAIs

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	Advantages	Disadvantages
Patient **with** history of LAI use	+ Non-drowsy pill + Don't have to take daily + Fewer side effects + Consistent dosage + Don't need to remember to take + Sense of control over illness + Let me forget I have to be on medication	– Beginning of injection – fatigue and agitation – More anxious at the end (before injection due) – Frequent trips – Inconvenient – Tied down – Overpowering, less effective as time passes
Patient **without** history of LAI use	+ Last long + Safer + Easier to keep track of + No need to remember to take pills	– Perception that it's for non-compliant people, therefore like a punishment – Needles hurt – Harder to travel – Loss of control over dosage

Iyer S, Banks N, Roy MA, et al. (2013)

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How… do we decide,
which long-acting injectable antipsychotic to use?

Consider a LAI when …

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Based upon the patient's report, caregiver report, or prescribing record

1. The patient has missed doses since the last visit 
2. Patient is currently on more than 1 antipsychotic (not during a switch) >1
3. Patient has been on more than 2 antipsychotics in the past 12 months >2
4. Patient has been hospitalized or had a crisis visit in the past 12 months 
5. Patient is not satisfied with current level of symptom control 

Velligan, D. I., Sajatovic, M., Sierra, …& Runnels, P. (2021).

Shared Decision Making

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Pills daily or more than once a day	+	–	Long-acting medication once a month	+	–
I need to remember to take my medication every day			I need to get medication at the clinic once a month-they will give me a reminder call (I may still need to take oral medication if I am on several different kinds of pills)		
The medication will leave my system more quickly, so if I am having side effects they will decrease more rapidly			The medication will remain in my system longer, so if I am having side effects they will decrease more slowly		
I need to call for a refill and go the pharmacy to pick up my medication or have my medication delivered to my home			My medication will be at the clinic when I come		
If I forget to take my medication sometimes, it may not help me enough with my symptoms			If I forget to go to the clinic, someone will call me so I can reschedule and this may help my symptoms		
My doctor does not know how much medication I am really taking. He or she may raise my dose or add new medications for me to take because he or she will think my medication is not working well.			My doctor knows exactly how much medication I am getting and can help me decide whether to go up or down or add medication depending on how I am doing		
I may be on some medications I don't need because I don't always take my medications			I may be able to get off some of my medications because I will be on a stable dose of my antipsychotic medication.		
My medication level goes up and down in my blood. When the level is up I may get more side effects.			My medication level stays more stable and this may cause less side effects.		
I will swallow pills every day.			I will see the nurse at the clinic every month to get a shot.		
Swallowing pills is usually not difficult.			Injections can hurt.		

Pharmacologic Options:

Long-Acting Injectables

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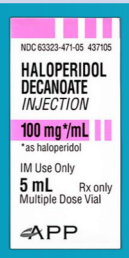
Fluphenazine decanoate

Risperdal Consta

Abilify Maintena

Invega Hafyra

1972 | 1986 | 2003 | 2009 | 2013 | 2015 | 2021 | 2023



Haloperidol decanoate

Invega Sustenna

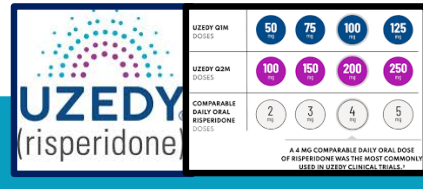
Zyprexa Relprevv

Aristada

Invega Trinza

Abilify Asimtufi

Uzedy



W GHCME.ORG

Medication	Highest Dose					Lowest Dose
Abilify Aristada	882mg q4wks	1064mg q8wks	882mg q6wks	662mg q4wks	441mg q4wks	
Abilify Maintena	400mg q4wks	300mg q4wks	300mg q4wks	300mg q4wks	200mg q4wks	
Asimtufi	960mg q8wks	720mg q8wks				
Abilify (PO)	20mg	15mg	15mg	15mg	10mg	
Fluphenzine decanoate	37.5mg q2wks	25mg q2wks	12.5mg q2wks			
Fluphenazine (PO)	20mg	15mg	10mg			
Haldol decanoate	200mg q4wks	100mg q4wks				
Haldol PO	20mg	10mg				
Invega Hafyra	1560mg q 26wks	1092mg q 26wks				
Invga Trinza	819mg q12wks	546mg q12wks	410mg q12wks	273mg q12wks		
Invega Sustenna	234mg q4wks	156mg q4wks	117mg q4wks	78mg q4wks	39mg q4wks	
Risperdal Consta			50mg q2wks	37.5mg q2wks	25mg q2wks	12.5mg q2wks
Uzedy (subcutaneous)		125mg IM q 4wks or 250mg IM q8wks ~ 5mg PO risperidone	100mg q4wks 200mg q 8wks	75mg q4wks 150mg q8wks	50mg q4wks 100mg q8wks	
Invega (PO)	12mg	9mg	6mg	3mg	1.5mg	
Risperidone (PO)	8mg	6mg	4mg	3mg	2mg	1mg
Zyprexa Relprevv	300mg q2wks	405 q4wks	210 q2wks	300mg q4wks	150mg q2wks	
Zyprexa (PO)	20mg	15mg	15mg	10mg	10mg	

Medication for Addiction Treatment
Opioid and Alcohol Use Disorders

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- Naltrexone / Vivitrol – opiate use and alcohol use disorders
  - Intramuscular
  - Every 4 weeks
  - One dose

Vivitrol®
(naltrexone for extended-release injectable suspension) 380 mg/vial

- Buprenorphine / Sublocade - opiate use disorder

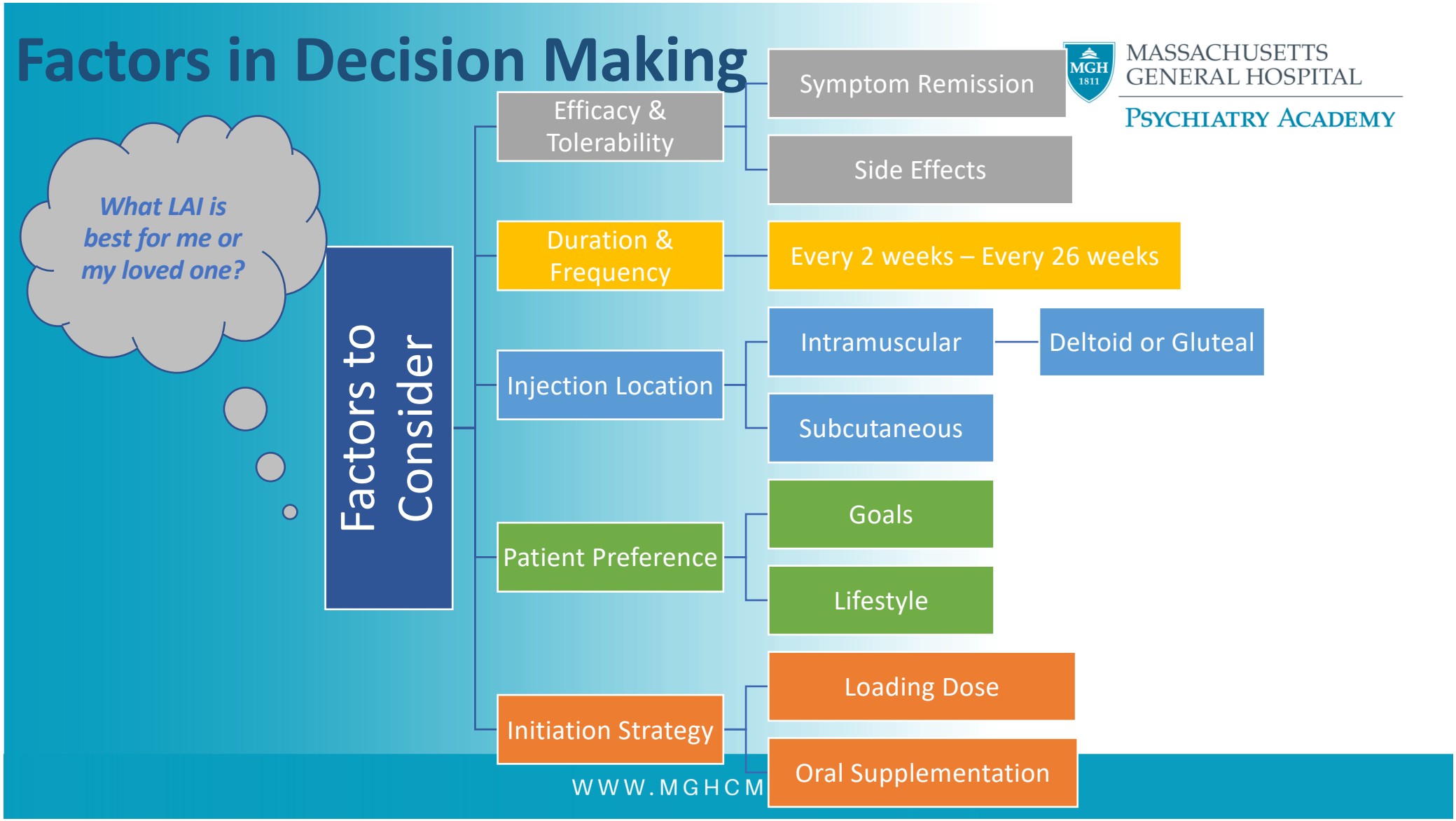
Brixadi®
(buprenorphine) extended-release injection for subcutaneous use (III)
Weekly 8 · 16 · 24 · 32 mg Monthly 64 · 96 · 128 mg

Subcutaneous
Every week:
8 – 32 mg
Every 4 weeks:
64 - 128mg

ONCE-MONTHLY
Sublocade®
(buprenorphine extended-release) injection for subcutaneous use (II)
100mg·300mg

Subcutaneous
Every 4 weeks
100mg – 300mg

Factors in Decision Making



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Improving Access

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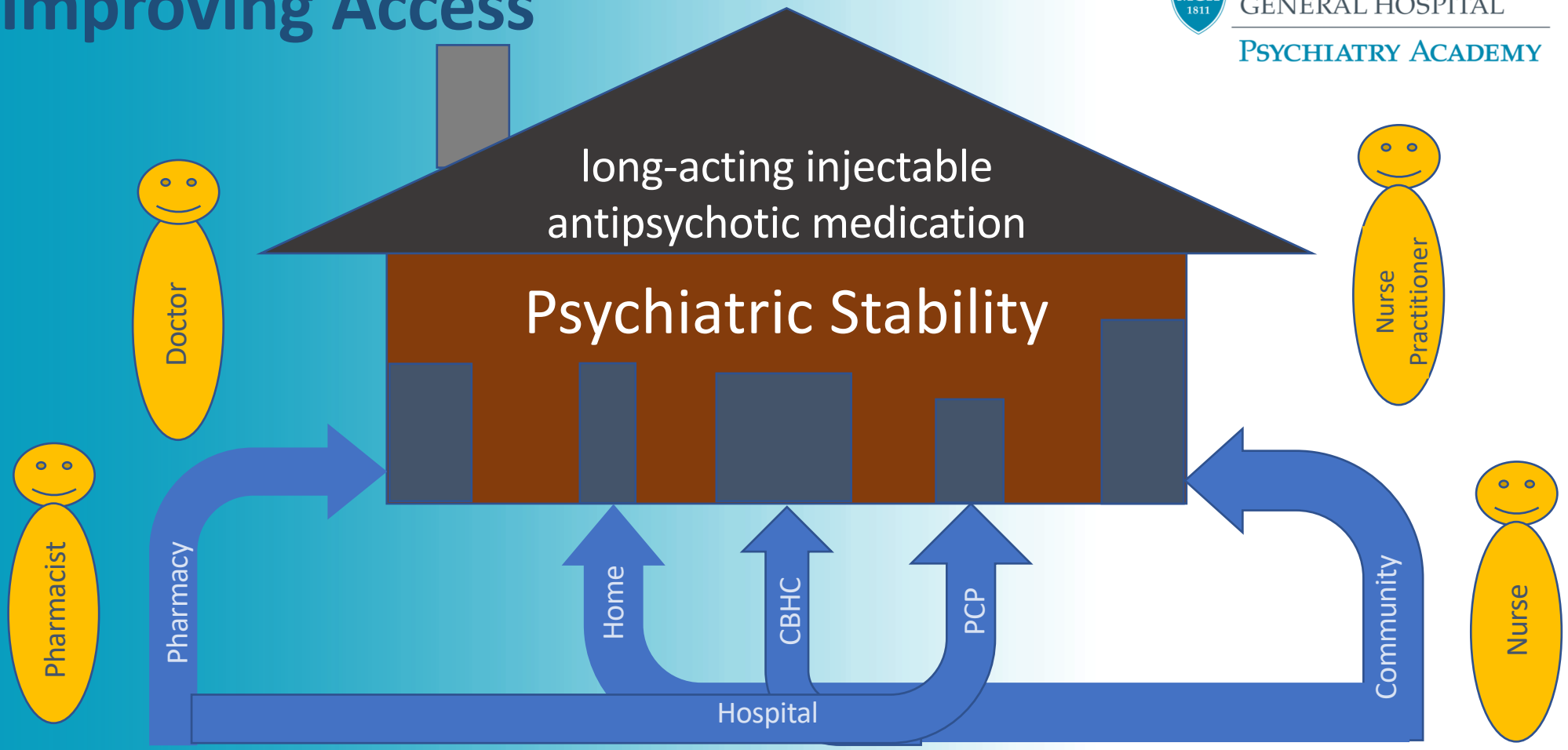

Statewide initiative, led by Dr. Foo, including Community Behavioral Health Centers and state agencies (e.g., Department of Mental Health, MassHealth).

Pharmacologic: New Agents

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Not Yet Approved:

- Olanzapine / (mdc-TJK / TEV-'749)
  - Subcutaneous
  - Every 4wks
  - Lower risk of Post-injection Delirium and Sedation Syndrome

In Development

- Ilioperidone / Fanapt
  - Similar to risperidone and paliperidone
- Xanomeline-Trospiusm / Cobenfy

Summary

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What are long-acting injectable antipsychotics?

Medications that are delivered by injection and last at least two weeks and up to six months!

Why would we consider using long-acting injectable antipsychotics?

They are effective, safe, and offer flexible dosing schedules.

How do we decide which long-acting injectable antipsychotic to use?

Prioritize factors that matter most in your recovery – duration, location, target symptoms, etc…

Long-acting injectable antipsychotics are...

A Great Option for Psychiatric Recovery!

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