

Emergency Care of those Experiencing Psychosis: Common Challenges, Solutions, & the Open Dialogue Approach

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Joe's Disclosures





Early years



Middle years



Joe's Disclosures

<p>Academic</p>	<p>I attend on inpatient unit here.</p>  <p>Clinician McLean Hospital x 12 years</p>	 <p>I teach here.</p> <p>Educator MGH/McLean Harvard Med School x 12 years</p>	<p>I do this too.</p>  <p>Administrator Clinical Director, McLean x 6 years</p>
<p>Non-academic</p>	<p>Nothing yet...</p> 		

Menti Poll – Question 1

Join at menti.com | use code 5899 9202

 Mentimeter

What one word are you feeling right now?

Waiting for responses ...

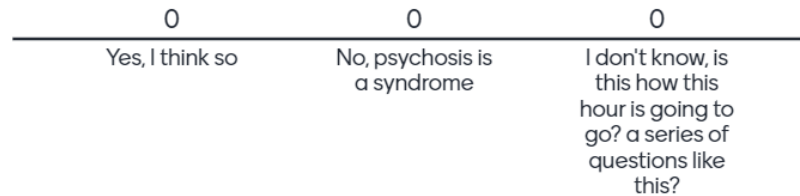


Menti Poll – Question 2

Join at menti.com | use code 5899 9202



Does every patient with psychosis have schizophrenia?



Menti Poll – Question 3

Join at menti.com | use code 5899 9202



What is the primary emotional experience of psychosis?

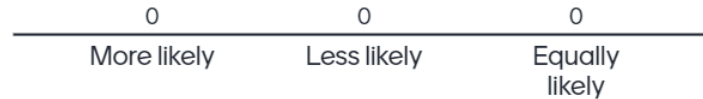


Menti Poll – Question 4

Join at menti.com | use code 5899 9202

 Mentimeter

Case: A person with schizophrenia comes to the ED with chest pain. Is it more likely, less likely, or equally likely be true cardiac?



Menti Poll – Question 5

Join at menti.com | use code 5899 9202

 Mentimeter

What antipsychotics do you use in the ED?

Waiting for responses ...



Menti Poll – Question 6

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 Mentimeter

What do you wonder about when you think about psychosis or assessing psychosis or working with people with psychosis?

Waiting for responses ...



Objectives



Describe inadequacies of the current system of care for people with serious mental illness.



Discuss principles of Open Dialogue's approach for people with psychosis.



Discuss challenges in care of the patient experiencing psychosis in emergency settings.



Discuss the approach, evaluation, and treatment of the patient with psychosis and agitation, including de-escalation techniques.

Outline

- Cases Related to Psychosis
- Current state of care for severe mental illness
- Open Dialogue Applied to an Inpatient Unit
- Approach to psychosis in the Emergency Department
- Interviewing, de-escalation, and medication selection
- Special situations
- Cases
- Q&A

Kaizen...

改善

Cases for emRIC ECHO

PAUL CHARLTON, MD
GIMC ED DIRECTOR

Case 1

35 yo M, hx bipolar disorder and methamphetamine use disorder, prior suicide attempts, multiple prior inpatient psychiatric hospitalizations for psychosis and suicidality. Prescribed Olanzapine and Clonazepam but not taking either.

On prior transport to inpatient psychiatric hospitalization, pt overpowered medical flight crew members and nearly wrested control of medical aircraft from pilot, causing emergency landing. Due to numerous incidents of agitation during transport similar to this, regional flight teams now either refuse to transport patient or require patient to be “fully sedated” prior to transport.

On prior transports, patient was so sedated upon arrival to stand-alone psychiatric hospitals that they refused acceptance and required patient to be transported by flight team to nearest ED due to high level of sedation.

Case 1 (continued)

There is no ambulance ground transportation available and there is no regional arrangement for law enforcement to transport patient between hospitals.

Today patient is in ED for suicidal thoughts and has been assessed by behavioral health evaluator to need transfer for inpatient psychiatric stabilization.

Patient is volatile, with intermittent outbursts and threats towards staff when he does not receive something he wants, but is calm between episodes.

An inpatient stand-alone psychiatric facility 2 hours away by flight has accepted the patient, but state that he cannot be overly-sedated upon arrival.

All local flight teams state that they will not transport this patient if he is volatile and a threat to take down the aircraft.

How do you approach this situation?

10 Domains of De-escalation

1. Respect personal space
2. Do not be provocative
3. Establish verbal contact
4. Be concise
5. Identify wants and feelings
6. Listen closely to what the pt. is saying
7. Agree or agree to disagree
8. Lay down the law and set clear limits
9. Offer choices and optimism
10. Debrief (pt and staff)

Goldilocks Level of Sedation for a Flight

Verbal De-escalation of the Agitated Patient

Richmond et al

Table 3. Summary of strategies for broaching the topic of medication/escalating persuasion techniques.

What helps you at times like this?	STRATEGY: Invite the patient's ideas.
I think you would benefit from medication.	STRATEGY: Stating a fact.
I really think you need a little medicine.	STRATEGY: Persuading.
You're in a terrible crisis. Nothing's working. I'm going to get you some emergency medication. It works well and it's safe. If you have any serious concerns, let me know.	STRATEGY: Inducing.
I'm going to have to insist.	STRATEGY: Coercing. Great danger, last resort.

- Maximize verbal de-escalation strategies, what's worked before, helps minimize medications needed
- Avoiding long sedation risk factors (multiple agents in one hour, long half life benzos)
- Consider oral meds before IM/IV
- Medicate just before flight again, options include:
 - Existing meds like olanzapine 10mg PO/IM for agitation/psychosis/mania
 - Risperidone 2mg/lorazepam 2mg PO
 - Haloperidol 5mg/lorazepam 2mg IV (QTc risk) or haloperidol 5mg/lorazepam 2mg/diphenhydramine 50mg PO/IM (EPS risk) (repeat in 10min, but not anticholinergic) – average total time sedated 84-126 minutes
 - Midazolam 5mg IM/IV (repeat in 10 min) – rapid onset, average total time sedation 82-105 minutes
- But, methamphetamine withdrawal involves severe hypersomnia (“sleeps for 3 days straight”) – tell accepting hospital

Methamphetamine Psychosis

Up to 40% of users affected

Self resolves in **one week** for many, but may involve agitation, violence, and delusions

For some, may **recur or eventually persist** months or convert to chronic psychotic disorder difficult to distinguish from schizophrenia

Diagnosis is based on **temporal relationship** of symptoms to meth use (consider Utox & collateral)

Consider **benzodiazepines** for agitation and **antipsychotics** for agitation/psychosis

Psychosocial treatments to prevent relapse best (CBT, contingency management, motivational interviewing, 12-step, treat co-occurring psychiatric disorders)

Methamphetamine Psychosis

No antipsychotic is definitively better than all others

Six head-to-head RCTs in network meta-analysis included 6 antipsychotics and showed:

- Quetiapine (300 mg/day) and olanzapine (20 mg/day) were superior to risperidone (4–8 mg/day) and aripiprazole (15 mg/day) for psychotic symptoms
- Aripiprazole was the big loser—it was inferior to haloperidol (6–20 mg/day) and paliperidone ER (9 mg/day), as well as to quetiapine and olanzapine.
- Thus, consider **quetiapine** and **olanzapine**, to be tapered off in a month or after psychosis resolves.

Outpatient, hyperphagia and hypersomnia resulting from methamphetamine withdrawal might compound the side effects from olanzapine and quetiapine.

Case 2

50 yo woman found at the Greyhound bus stop disheveled and mumbling incomprehensible phrases to a person not visible to bystanders. EMS brings her to the ED, where she identifies her name and that she came on the bus from Michigan but got off the bus because “the people were trying to poison me.” She endorses that she has been hospitalized for behavioral health reasons in the past but cannot provide any further information about herself and she has no medications or identifying information on her.

After your ED evaluation shows no apparent acute medical issues, normal labs, and a Utox +cannabinoids only, your hospital behavioral health consultant (LCSW) evaluates the patient and recommends transfer for inpatient psychiatric stabilization due to being gravely disabled from apparent psychosis.

Case 2 (continued)

Your BHS evaluator cannot make recommendations about whether to initiate medications or which ones to start. You anticipate the patient will likely be in your ED for 24-48 hours before transfer, with presumed working diagnosis of schizophrenia.

She is generally calm in the ED and not harming herself or threatening staff.

Would you recommend initiating any medications while she awaits transfer in your ED?

If so, which medications?

Starting Antipsychotics in the ED for Chronic Psychosis

Rule out medical causes and other active medical issues (avoid diagnostic overshadowing)

Baseline EKG for QTc, monitor VS

Consider:

- **Risperidone** 1mg-2mg day one, then up by 1mg/d toward 4-6mg (average dose 4mg)
 - Benefits of moderate risk metabolic syndrome/EPS, minimally sedating, comes in LAI, often first choice on inpatient, inexpensive.
 - But, only comes PO.
- **Olanzapine** 5-10mg day one, then up by 5mg/d toward 15-30mg (average dose 20mg)
 - Benefit of rapid acting, effective even in low doses, moderately sedating.
 - But, only PO/IM, risks of metabolic syndrome, no easy LAI access, not chosen for first break psychosis but irrelevant here.
- **Haloperidol** 5mg day one, 10mg day two then observe
 - Benefit of low risk metabolic syndrome but higher risk EPS, comes PO/IM/IV, minimally sedating, comes in LAI, inexpensive.
 - But, watch for EPS and add benztropine 1-2mg daily if needed.
- Avoid aripiprazole (because long half-life, harder for inpatient to change meds), quetiapine (because need to get to 400-800mg before has antipsychotic effect)

Inpatient Management of Established Schizophrenia – McLean 2019

Recommended daily doses of antipsychotic drugs for an acute psychotic episode or exacerbation of multi-episode or chronic psychosis are 300–1000 mg chlorpromazine (CPZ) equivalents. For **first-generation antipsychotics** (FGAs), examples are: fluphenazine 5–15 mg, haloperidol 5–15 mg, or perphenazine 24–72 mg. For **second-generation antipsychotics** (SGAs) examples are: aripiprazole up to 30 mg, olanzapine 10–20 mg, paliperidone 3–15 mg, quetiapine 300–1000 mg, risperidone 2–8 mg, ziprasidone 80–160 mg.

Clozapine should be offered to patients with a clinically inadequate response, persistent thoughts of suicide or suicide attempts, or persistent aggressive behavior (it may also help with co-occurring substance abuse). If circumstances are compelling, its use can be considered after a single trial of an antipsychotic. Three–six months at a clozapine plasma level of 250–350 ng/mL is generally considered an adequate trial.

Augmentation Strategies – If clozapine alone does not produce an adequate response, adding other treatments can be considered, such as: lamotrigine, a second antipsychotic, ECT, or rTMS. Mood-stabilizers may benefit agitation or excitement but are unlikely to help with persisting positive psychotic symptoms.

But, tell me more about the
current state of affairs in psychosis
care...

A Systematic Review of Mortality in Schizophrenia

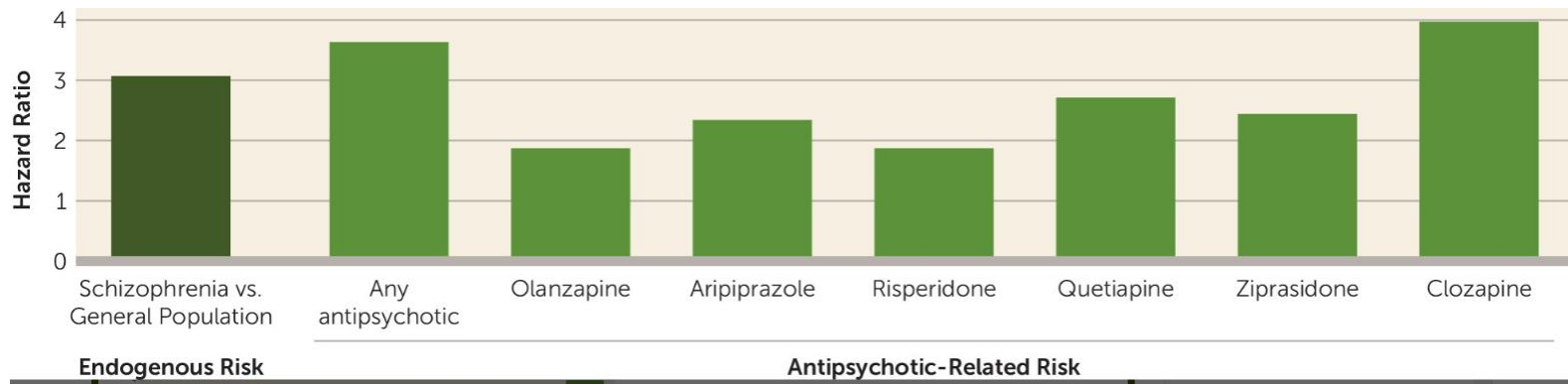
Is the Differential Mortality Gap Worsening Over Time?

Sukanta Saha, MSc, MCN; David Chant, PhD; John McGrath, MD, PhD, FRANZCP

Conclusions: With respect to mortality, a substantial gap exists between the health of people with schizophrenia and the general community. This differential mortality gap has worsened in recent decades. In light of the potential for second-generation antipsychotic medications to further adversely influence mortality rates in the decades to come, optimizing the general health of people with schizophrenia warrants urgent attention.

Arch Gen Psychiatry. 2007;64(10):1123-1131

Diabetes is associated with both schizophrenia itself and with antipsychotic drug treatment



Rajkumar et al., 2017; Andreassen 2017

Be careful with diagnostic overshadowing...

Stoklosa, MacGibbon, Stoklosa, 2017

Assaultive and belligerent?



Cooperation often begins with
HALDOL[®]
(haloperidol)
a first choice for starting therapy

Acts promptly to control aggressive, assaultive behavior

Recent studies have reported the great effectiveness of HALDOL (haloperidol) in controlling aggressive and assaultive behavior. "From the control of violent attacks reported by a group of criminal patients, 'success in control of acts of assaultiveness' was obtained substantially during treatment with HALDOL." Intensive control can be achieved quickly. "Usually within a few days after the administration has been started, control of assaultive and assaultive acts."

Usually leaves patients relatively alert and responsive

Although some instances of drowsiness have been observed, most patients with HALDOL (haloperidol) remain alert. In a report on a study with criminal patients in a hospital setting, "The patients remained alert and were available to participate in treatment." "Local investigators report that HALDOL 'normalizes' behavior and produces a positive attitude in the treatment of patients who have been difficult to manage."

Reduces risk of serious adverse reactions

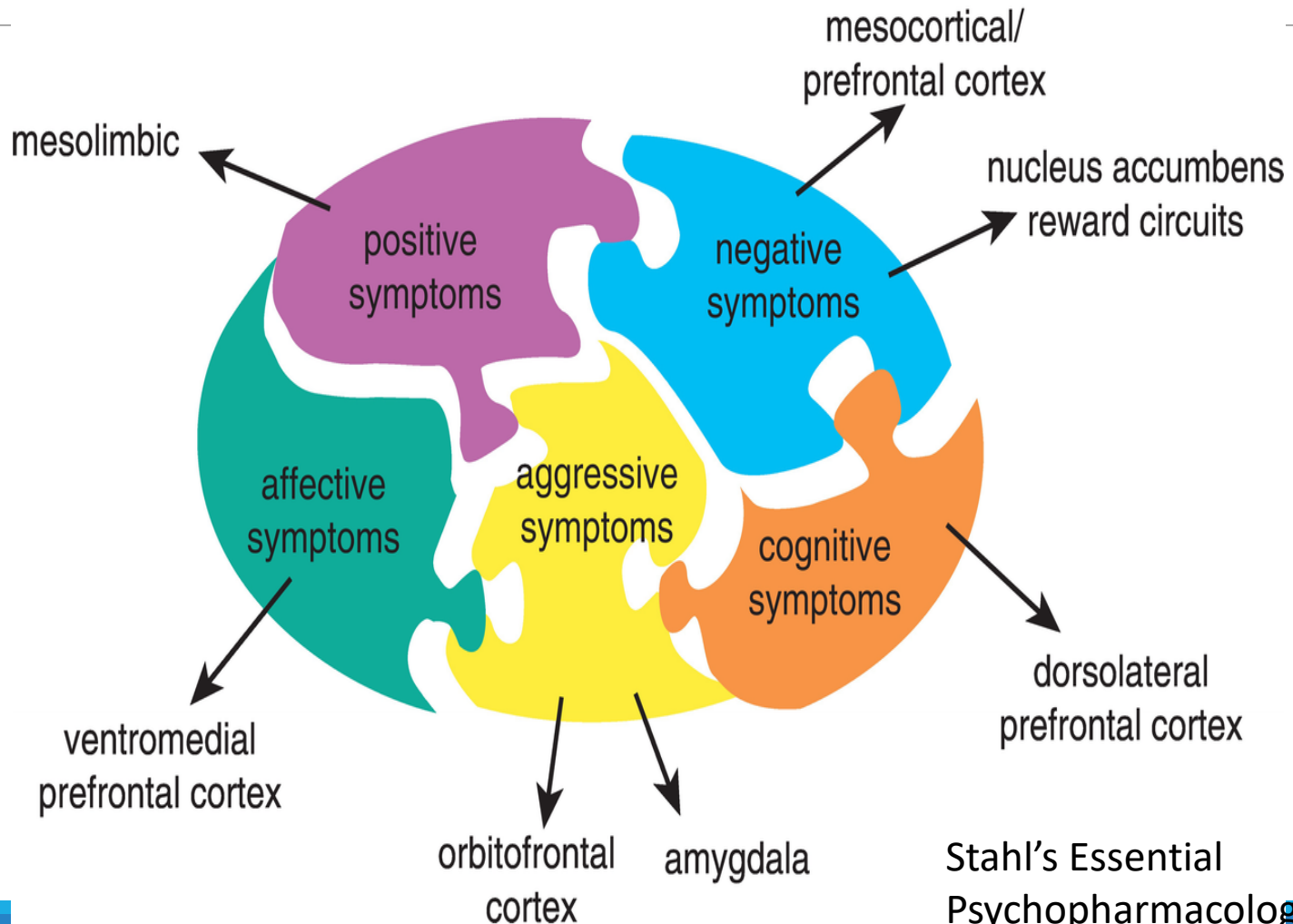
HALDOL (haloperidol) administration results in minimal levels of the patients' treatment with the psychotropic. "Treatment is safe and does not cause significant depression, but not hyperactivity." There is also the likelihood of adverse reactions such as drowsiness, weight change, and abnormal laboratory results and skin rashes. "The main adverse side effects of HALDOL (haloperidol) - extrapyramidal symptoms - are readily detected and easily controlled."

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For information relating to Indications, Contraindications, Warnings, Precautions and Adverse Reactions, please turn page.

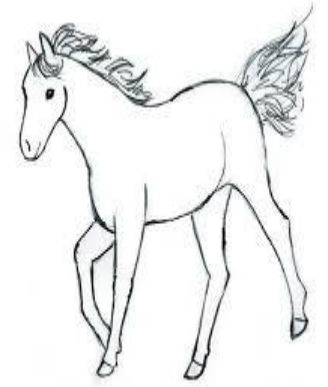
Metzel, "The Protest Psychosis: How Schizophrenia Became a Black Disease." 2010.

Match Each Symptom to Hypothetically Malfunctioning Brain Circuits





Perceptions of Psychiatry



“I decided early in graduate school that I needed to do something about my moods. It quickly came down to a choice between seeing a psychiatrist or buying a horse. Since almost everyone I knew was seeing a psychiatrist, and since I had an absolute belief that I should be able to handle my own problems, I naturally bought a horse.”

- Kay Redfield Jamison, PhD, *An Unquiet Mind: A Memoir of Moods and Madness*

Institute of Medicine's Call to Arms

Quality Chasm

Care “respectful of and responsive to individual patient preferences, needs, and values”

Psychiatry sluggish



Inspirations from the US

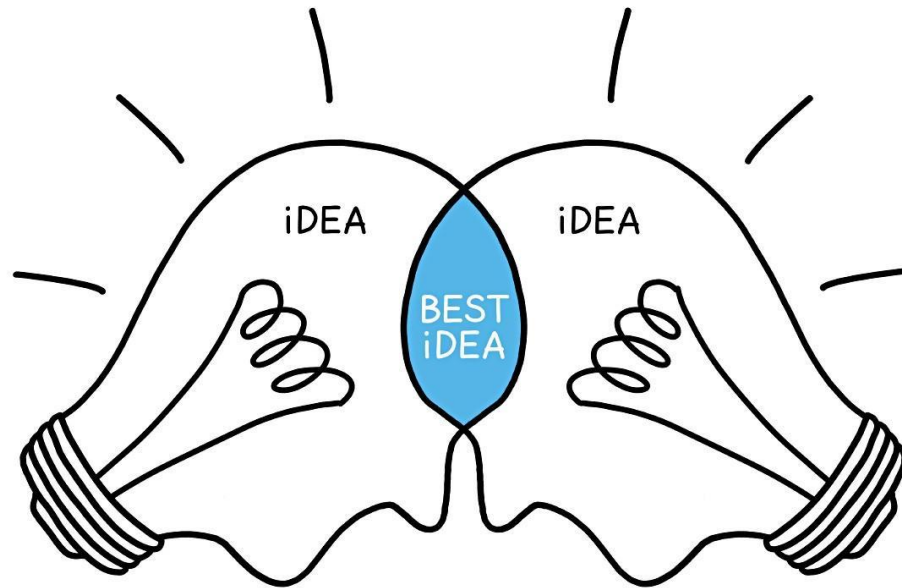
Child and Family Centered Care (CFCC)

- Multidisciplinary rounds at bedside
- Patient-friendly language
- Standard of care

Shared Decision Making (SDM)

- Share expertise and information
- Individual values and preferences
- PCORI

History of the idea to use dialogic practices at McLean



Inspiration from Abroad: Western Lapland - Finland



Maps.google.com

Open Dialogue - Impressive Results

Two-year follow up studies

- 84% returned to full time employment or studies
- 14% on disability
- 33% used antipsychotic medication

Ten-years into implementation, another two year follow up study

- Fewer patients being diagnosed with schizophrenia
- Younger age of patients coming to care
- Shorter duration of untreated psychosis (3 weeks)

Latest OD Data out of Finland

- **19 year outcomes** (Bergstrom et al. 2018)
 - 36% on antipsychotics in OD group
 - 81% on antipsychotics in CG
 - 33% receiving disability allowances in OD group
 - 61% receiving disability allowances in CG



What should I think?

Our current situation is unacceptable



**"It's not a great mission statement,
but we'll revise it if things get better."**

We need another tool

This is not the final answer, but there is something to be learned here...

What is Open Dialogue?

- Humanistic, non-medicalized, meaning-making approach to psychopathology
- Treatment system and a way of providing care within that system
- Draws upon many practices from US family and narrative therapies
- Views psychosis as a profound state of isolation
- Social network approach to care
- Egalitarian: drops the clinical and expert gaze
- Aims to alter the course of chronicity and disability



Truth is not born nor is it to be found inside the head of an individual person, it is born between people collectively searching for truth, in the process of their dialogic interaction

— *Mikhail Bakhtin* —

AZ QUOTES

Open Dialogue Fidelity

TABLE 1: The Seven Principles of Open Dialogue

IMMEDIATE HELP

SOCIAL NETWORK PERSPECTIVE

FLEXIBILITY AND MOBILITY

RESPONSIBILITY

PSYCHOLOGICAL CONTINUITY

TOLERANCE OF UNCERTAINTY

DIALOGUE (& POLYPHONY)

Seikkula et al. 2006

Open Dialogue – 7 Principles

LANGUAGE

(poetics)

Tolerance of uncertainty
Social network perspective
Dialogism



SYSTEM

(micropolitics)

Immediate help
Flexibility and mobility
Responsibility
Psychological continuity

Key Elements of Dialogic Practice

Team meeting format

- Multiple clinicians, social supports

Language and phrasing

- Open-ended questions, exact words, present

Timing and flow

- Multiple viewpoints, relational

Response to psychosis

- Normalize, stories not symptoms, reflecting teams, transparent, tolerate uncertainty

Questions and Skills

The two questions begin a dialogic meeting:

1. The history of the idea to have the meeting?

(or, whose idea was it to come in? What were they worried about?)

2. How do you want to use the meeting?

(or, what are hoping for in your visit/hospital stay today?)

The two skills to help people feel heard and connect:

- Responsive listening
- Reflecting

US Implementation

The Institute for

dialogicpracticeSM

Recovery as a function of being in life

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2017-19 International Certification Training in Dialogic Practice

- Module 1: June 12 – June 16, 2017
- Module 2: September 13 – September 17, 2017
- Module 3: November 8 – November 12, 2017
- Module 4: March 7 – March 11, 2017

Wednesday through Sunday schedule, except for Module 1, which is Monday through Friday.

[View Course >](#)

US Implementation & Beyond

Ellenhorn PACT Boston, Grady Memorial Hospital Atlanta, Howard Center in VT & UVM

Denmark, Norway, Sweden, UK, Italy, Germany, other European countries

Advocates Western MA (Gordon et al., 2016)

- 12-month feasibility study
- High satisfaction for participants, families, and providers
- Improvements in symptoms and functional outcomes
- Majority working or in school after one year

open dialogue uk



Dialogic Practice Adapted to AB2

Initially:

- Three training sessions
- Nursing, social work, mental health specialists, psychiatrists
- Workshop format

Follow up:

- Follow-up meetings (staff, in services, PIC meetings)
- Distributed handouts/resources on email/wiki

Patient Centered Communication Initiative – Phase I

Rounds:

- Combined patient and treatment rounds
- Utilizing a “reflecting team” during rounds

Family Meetings:

- Earlier family meetings
- Using a “reflecting team” during the family meeting

Culture:

- Minimize power dynamics such as using first names among both clinicians and patients or all titles
- Avoid communication about the patient when the patient is not present

First half of rounds



Second half of rounds – discussion



Second half of rounds - reflection



Patient Centered Communication Initiative – Phase II

Framing

Discussion of patient and plan

- Offer “assessment” or “reflections”
- Tentative language
- Personal reflections

Details of plan

Asking patient for reflections

Inviting more voices/opinions

Patient Centered Communication Initiative

Changes made in first 3 months

Early observations and patient stories

- Best for most acute patients
- More voices in the room
- Less need for involuntary care?
- Fewer restraints?
- Better mentalization
- Better satisfaction

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McClean adopts Dialogic Practice

See the new Harvard/McClean research study that reports positive results.

[Read More >](#)

The screenshot shows a website for 'The Institute for dialogicpractice'. The main navigation bar includes 'Home', 'Dialogic Practice', 'Open Dialogue', 'Application', 'Courses', 'About', 'News', and 'Contact'. A prominent orange button labeled 'Apply Online' is visible. Below the navigation, there is a featured article with a purple background. The article title is 'McClean adopts Dialogic Practice' and the text reads 'See the new Harvard/McClean research study that reports positive results.' A 'Read More >' link is at the bottom right of the article. The article image shows a stone sign for 'McLean HOSPITAL HARVARD MEDICAL SCHOOL AFFILIATE' with a crest and the year '1811'.

Patient Centered Communication Initiative

"I felt like I trusted you guys easier."

"I learned more about myself because I heard what you said about me everyday."

"You guys pay attention to everything! I realize that you do more than just push pills."

"It was really weird at first, but not after a while. You should keep doing it."

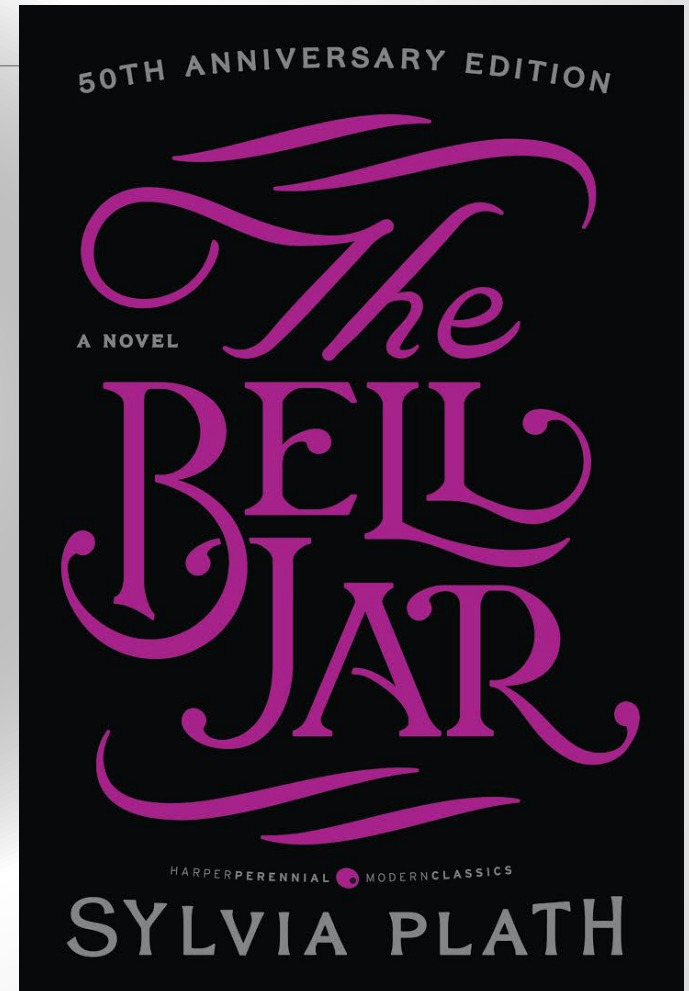
"I felt more involved in my care and the decisions being made."

PCC NAMI Study

Shattering the Bell Jar: Assessing the Impact of an Open-Communication Model on Patient-Centered Outcomes

Impact of cultural and practice change

Assess improvements in perceived quality of care and create more collaboration



McLean Perceptions of Care (PoC)

4: Did the staff explain things in a way you could understand?

5: Were you involved as much as you wanted in decisions about your treatment?

7: Did the staff listen carefully to you?

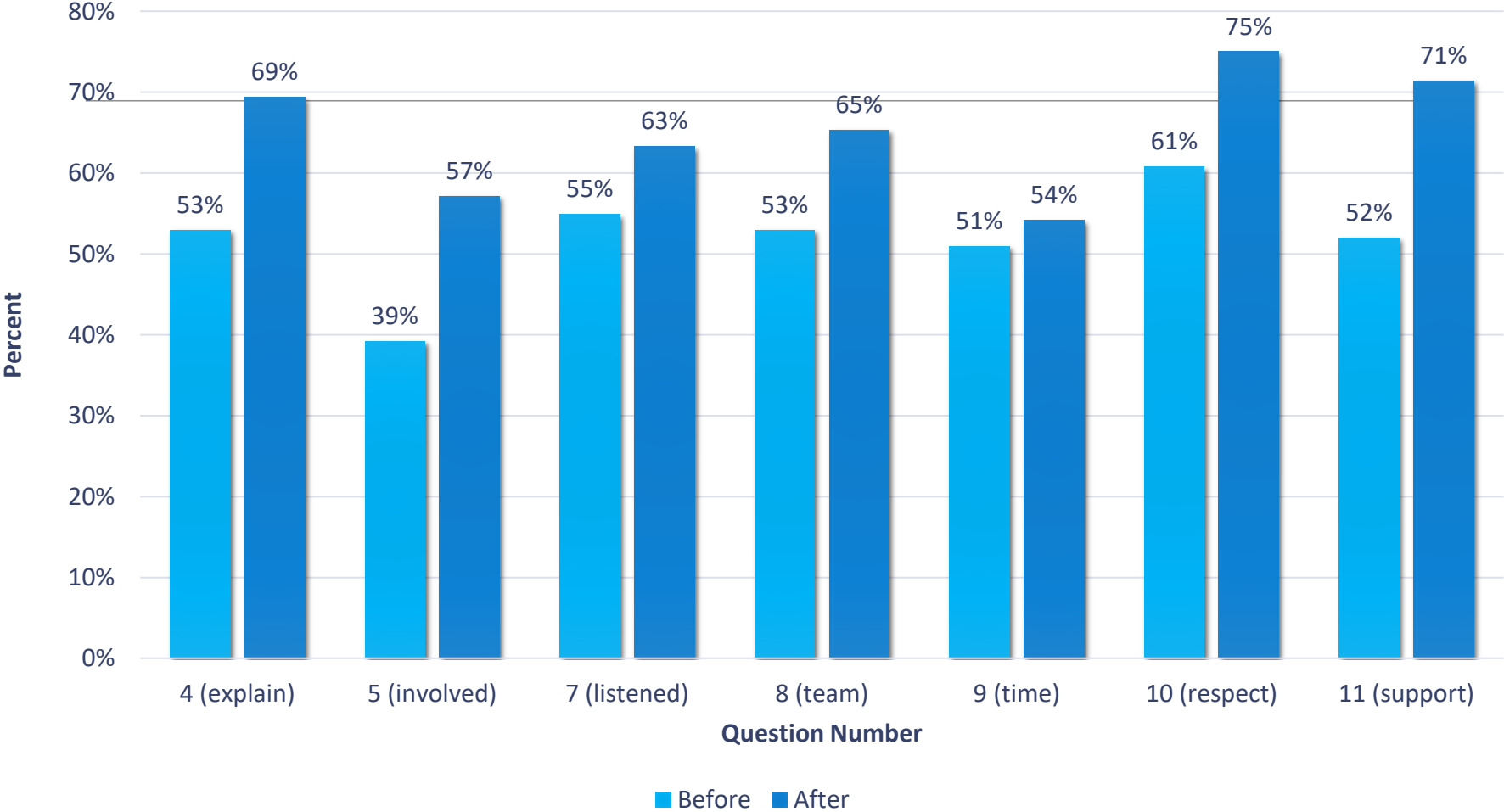
8: Did the staff who treated you work well together as a team?

9: Did the staff spend enough time with you?

10: Did the staff treat you with respect and dignity?

11: Did the staff give you reassurance and support?

Percent Choosing "Always" by Question for Team 1 on Interpersonal Domains



Results

Odds ratios

Tendency towards significance of an improvement in rating

Significant team effects

- Least heterogeneity Question 11 (support, Odds ratio 2.14, p 0.04)
 - The odds of choosing “always” is 2.14 higher after the intervention relative to before the intervention

Lessons Learned

Cultural change is hard

Sustained energy and champions

Build changes into a routine/structure

“More” the model or “less” the model

Family meetings partly shifting based on choices

Training is hard to perpetuate

Choose which values to prioritize (time)

Open Dialogue Used Clinically

The Patient-Centered Communication (PCC) Initiative on AB2

- Person-centered rounds with a “Reflecting Team”
- Earlier Family meetings, more patient reflections

McLean OnTrack (first episode clinic)

- Network meetings (intake & ongoing)

McLean Appleton (residential program for psychosis) & PACT (assertive community treatment)

- Dialogic intakes
- Dialogic consults
- Intervision



An Alternative Form of Mental Health Care Gains a Foothold

By BENEDICT CAREY

Published: Aug. 8, 2016

A movement toward largely nonmedical approaches, focused on holistic recovery rather than symptom treatment, is growing in the United States.

Dialogic Staffing Model



Resident meets with patient



Attending joins encounter
Dialogic staffing with
patient present



Collaborative discussion and
treatment planning

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ISPS THE INTERNATIONAL SOCIETY
FOR PSYCHOLOGICAL
AND SOCIAL APPROACHES TO PSYCHOSIS

ROUTLEDGE

Open Dialogue for Psychosis

Organising Mental Health Services to Prioritise
Dialogue, Relationship and Meaning

Edited by Nick Putman and Brian Martindale



SERIES EDITORS:
Anna Lavis and Andrew Shepherd

FIRST EDITION

DIALOGICAL PSYCHIATRY

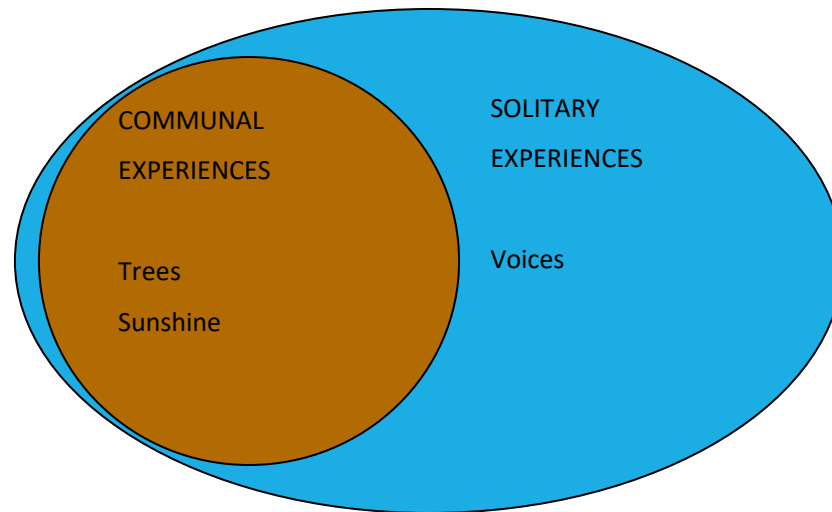
A HANDBOOK FOR THE TEACHING
& PRACTICE OF OPEN DIALOGUE



RUSSELL
RAZZAQUE

That's great, but we work in
the emergency department...

Reality vs Psychosis Pictorially



Stranger than Fiction



Still of Will Ferrell in Stranger Than Fiction

www.imdb.com

The Soloist



www.imdb.com

Initial Management of Psychosis (and Agitation) in the ED

- Triage or initial clinical assessment



- Initial psychiatric stabilization, including pharmacologic interventions and agitation management



- Diagnostic workup to evaluate medical and psychiatric conditions



- Further psychiatric evaluation



- Determining safe disposition

Initial Management of Psychosis (and Agitation) in the ED

- Triage or initial clinical assessment



- Initial psychiatric stabilization, including pharmacologic interventions and agitation management



- Diagnostic workup to evaluate medical and psychiatric conditions

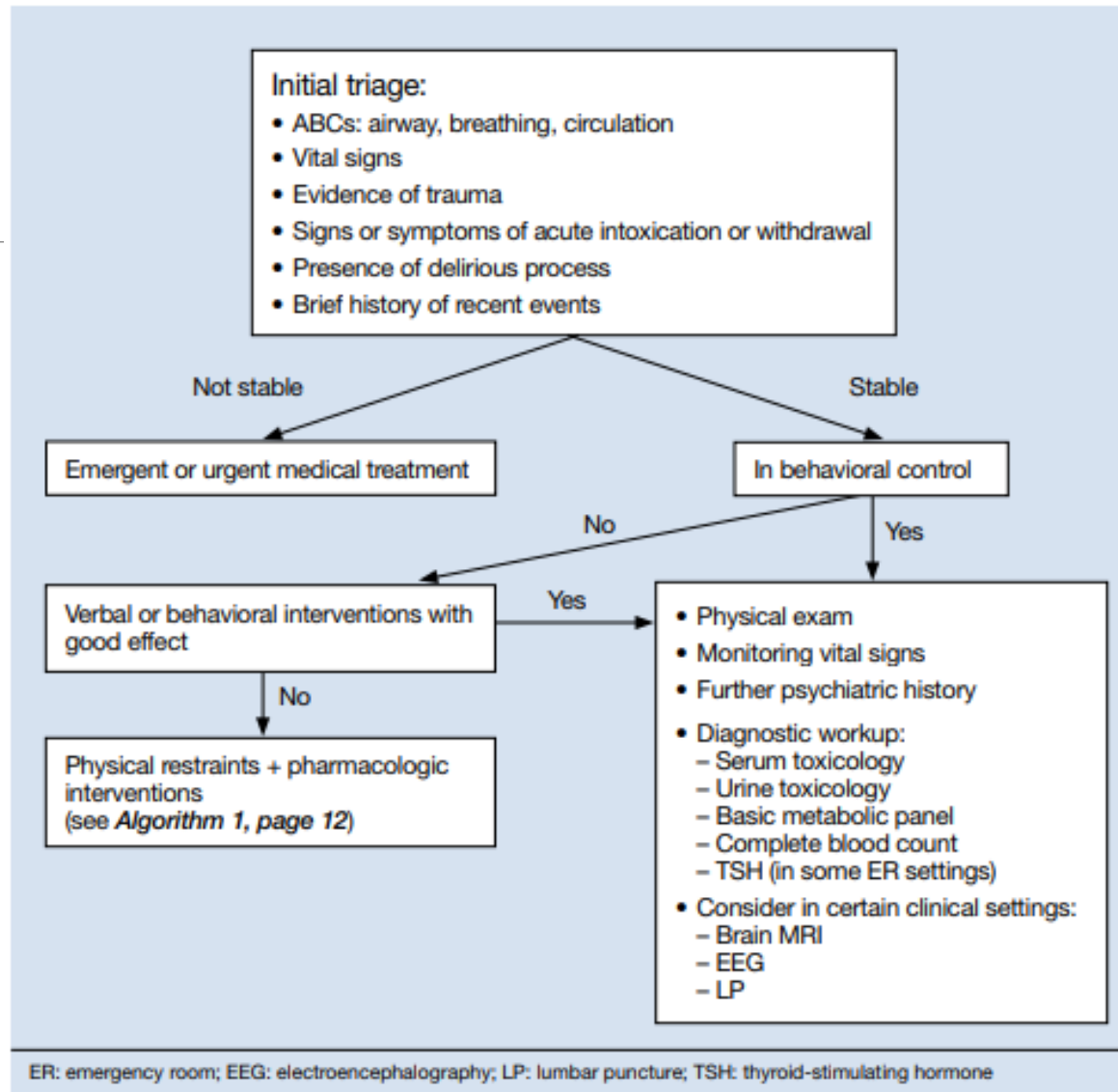


- Further psychiatric evaluation (or Emergency Department team starting antipsychotic treatment!)



- Determining safe disposition

Diagnostic workup of an acutely psychotic patient



Brown, Stoklosa, Freudenreich, 2012

First Episode of Psychosis Evaluation – McLean 2019

Psychiatric history including medical and family history

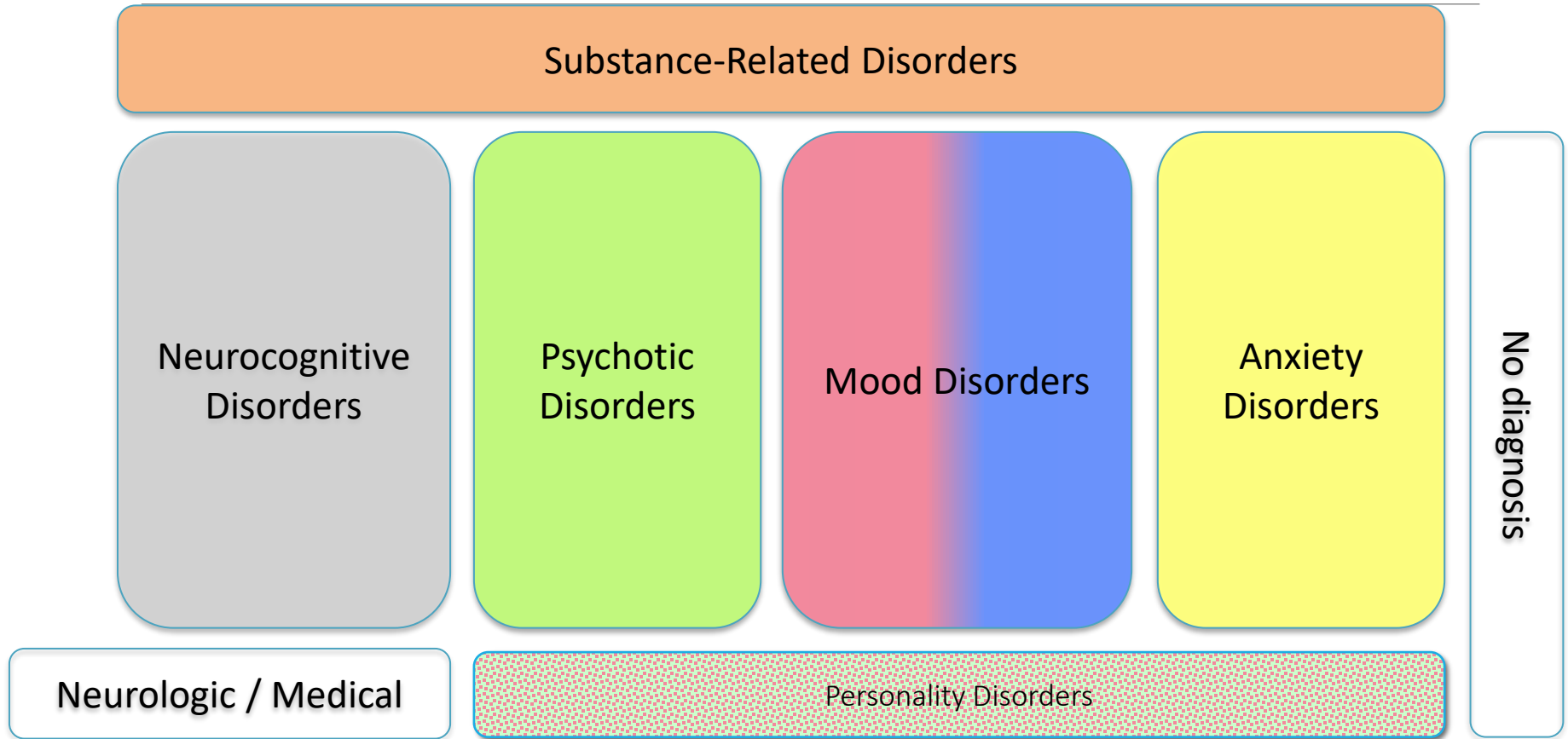
Physical examination including neurologic exam and BMI (components of routine admission assessment)

Laboratory studies: CBC and differential, erythrocyte sedimentation rate, electrolytes, liver function panel, TSH, lipid profile, HemA1c, urine toxicology screen, UA, vitamin B12, HIV antibody titers, RPR, folate, pregnancy test in women of child-bearing age

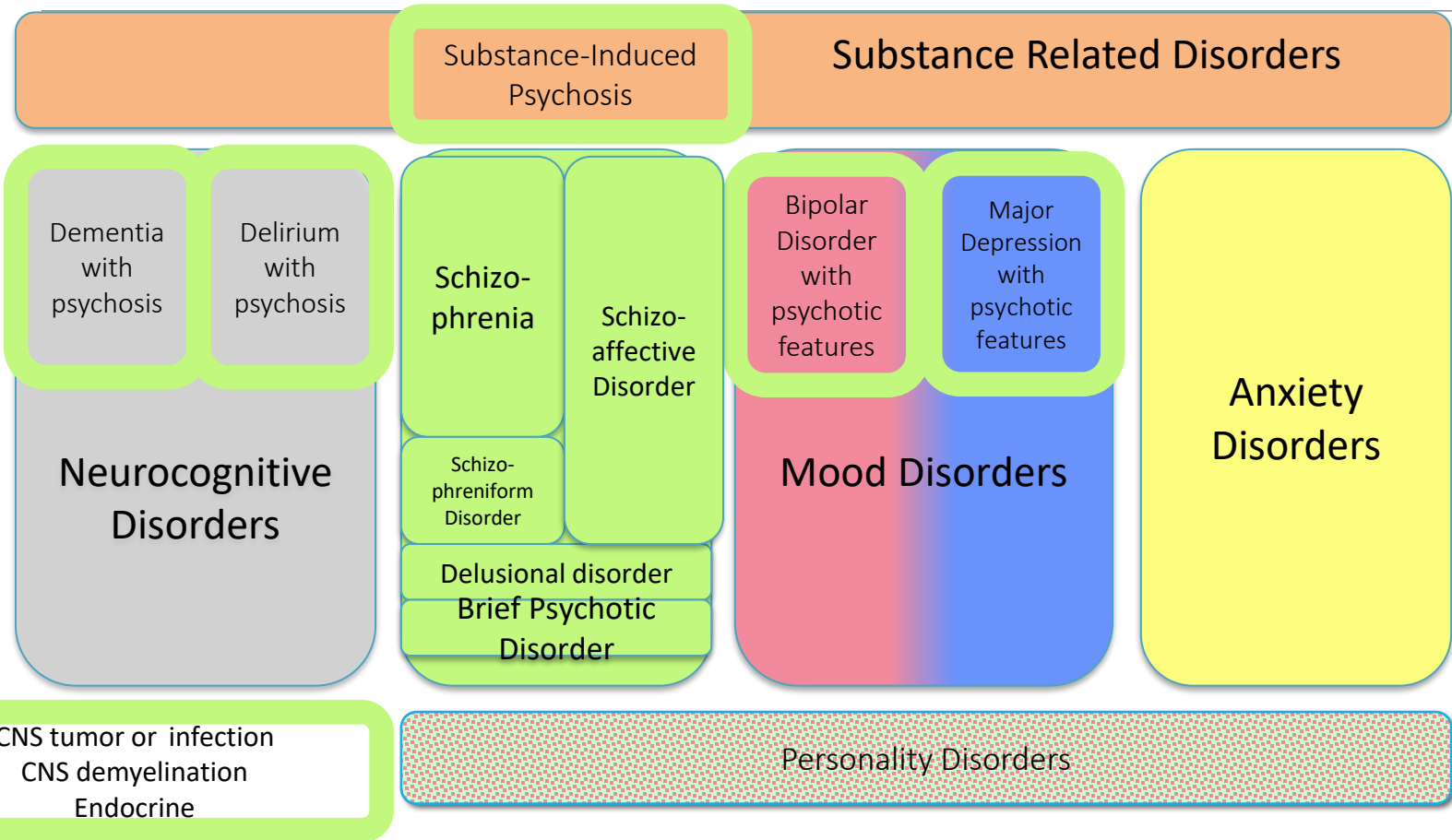
Additional tests may be appropriate when indicated by the clinical picture and family history but need not be ordered routinely.

- Brain imaging, EEG, neuropsychological testing, autoantibody titers, heavy metal screen, copper and ceruloplasmin, prolactin level, fluorescent in situ hybridization testing for chromosome 22q11 deletion, Lyme antibody titers, arylsulfatase-A levels, and cerebrospinal analysis
- Consultation with neurology should not be routine but may be warranted by an atypical history or abnormality on neurologic exam.

Psychosis Psychiatric Differential Diagnosis by the “Buckets”



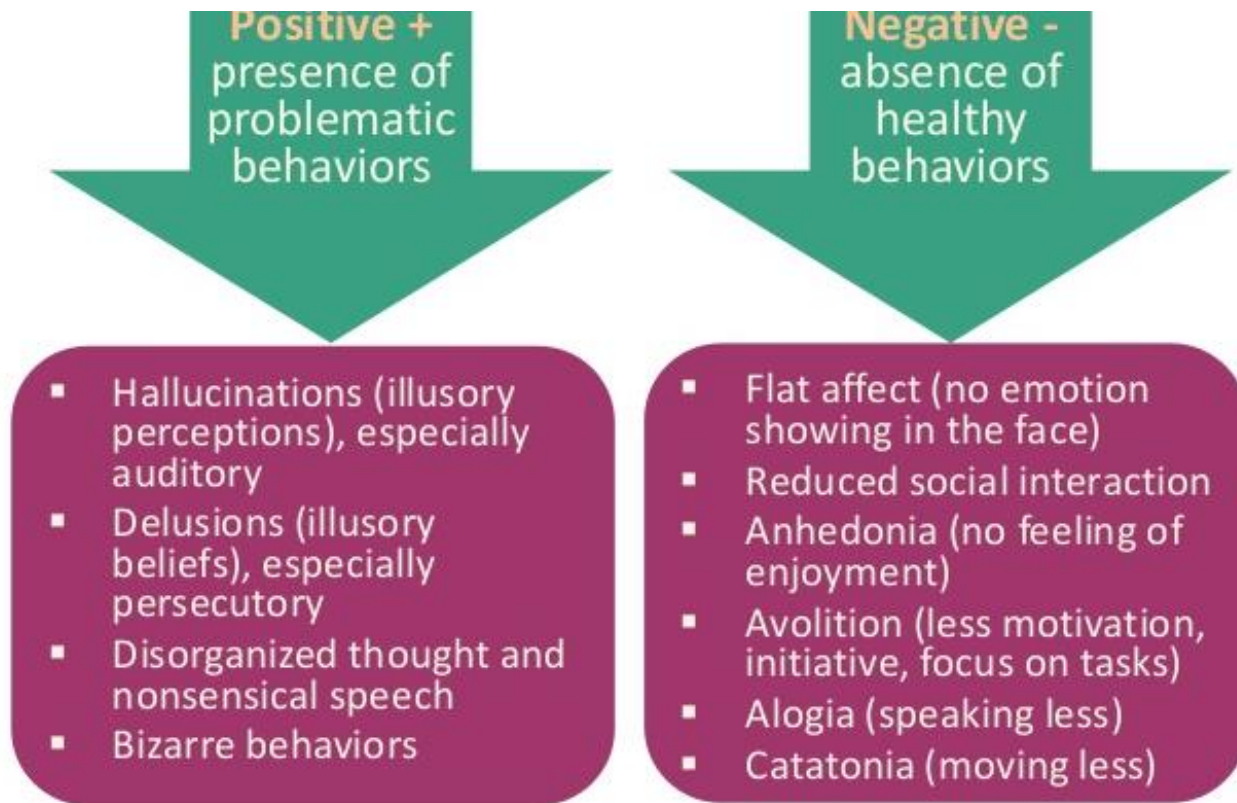
Psychotic symptoms can be present in many psychiatric disorders



Medical Causes of Psychosis

Epilepsy	Complex partial seizures (auras, automatisms)
Dementias	Alzheimer's disease (delusions > hallucinations), Dementia with Lewy Bodies (VH), HIV associated dementia (psychotic depression or mania)
CNS infection	Neurosyphilis, Neuroborreliosis (Lyme disease), Tuberculosis, Viral encephalitis (HSV, EBV, CMV, VZV, rubella, measles, including SSPE), Parasitic CNS infection (toxoplasmosis, neurocysticercosis, cerebral malaria), Cryptococcus infection, Creutzfeldt-Jakob disease
Head trauma	Psychosis following traumatic brain injury
Brain tumor	Primary brain tumors, Secondary brain metastases
Hydrocephalus	Normal pressure hydrocephalus (rare)
Stroke	Right-frontoparietal stroke (rare)
CNS structural abnormality	Midline abnormalities (corpus callosum agenesis, cavum septi pellucidi), Tuberos sclerosi, Cerebral aneurysm, Arteriovenous malformations (especially involving temporal lobe)
Demyelinating diseases	Multiple sclerosis (rare), Leukodystrophies (metachromatic leukodystrophy, X-linked adrenoleukodystrophy, Marchiafava-Bignami disease), Schilder's disease
Autoimmune diseases	Systemic lupus erythematosus (VH & tactile hallucinations especially, AH with steroids), Rheumatic fever (h/o), Myasthenia gravis, Paraneoplastic syndrome
Granulomatous disease	Neurosarcoidosis
Neuropsychiatric diseases	Huntington's disease, Wilson's disease, Parkinson's disease (visual hallucinations, especially with treatment), Familial basal ganglia calcification, Friedreich's ataxia
Sleep disorder	Narcolepsy (daytime hypnagogic/hypnapompic hallucinations)
Endocrine dysfunction	Hypoglycemia, Hyper- and hypothyroidism, Hyper- and hypoparathyroidism, Hypopituitarism, Addison's disease, Cushing's syndrome
Nutritional deficiencies	Deficiency of Mg, Zn, Niacin (pellagra), B12 (pernicious anemia), Vitamin A, Vitamin D
Metabolic diseases	Amino acid metabolism (Hartnup disease, homocystinuria, phenylketonuria), Porphyrias (acute intermittent porphyria, porphyria variegata, hereditary coproporphyria), GM-2 gangliosidosis, Fabry's disease, Niemann-Pick type C disease, Gaucher's disease (adult type)
Chromosomal abnormalities	Sex chromosomes (Klinefelter's syndrome, XXX syndrome), Fragile X syndrome, Velocardiofacial syndrome
Toxins	Carbon monoxide, Organophosphates, Heavy metals (particularly arsenic, manganese, mercury, and thallium)

Symptoms of Psychosis



Psychosis Symptoms in Cartoon Video

<https://www.mcleanhospital.org/video/mclean-ontrack-meet-amy-she-has-psychosis>

(or google “McLean” “psychosis” “Video”)

First Steps in Management in ED

- Remove potential weapons
- Give the patient space
- Distance potentially aggravating people (staff, nearby patients)
- Address basic needs (hunger, thirst, pain, nicotine withdrawal)

First Steps in Management in ED

- Remove potential weapons
- Give the patient space
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- Address basic needs (hunger, thirst, pain, nicotine withdrawal)

Article

Effect of Nicotine Replacement Therapy on Agitation in Smokers With Schizophrenia: A Double-Blind, Randomized, Placebo-Controlled Study

Michael H. Allen, M.D.

Martin Debanné, Ph.D.

Coralie Lazignac, M.D.

Eric Adam, M.Sc.

L. Miriam Dickinson, Ph.D.

Cristian Damsa, M.D.

Objective: The authors conducted a randomized, placebo-controlled study of nicotine replacement therapy for the reduction of agitation and aggression in smokers with schizophrenia.

Method: Participants were 40 smokers 18–65 years of age admitted to a psychiatric emergency service with a diagnosis of schizophrenia confirmed by the Mini International Neuropsychiatric Interview. Patients were screened for agitation with the excited component subscale of the Positive and Negative Syndrome Scale

Conclusions: The drug-placebo difference in this study was similar to that obtained in trials of parenteral antipsychotics in similar populations. This finding suggests that in patients with schizophrenia, smoking status should be included in the assessment of agitation and nicotine replacement included in the treatment of those who are smokers.

(Am J Psychiatry 2011; 168:395–399)

Interviewing - Overview

Diagnoses are based on:

- *Cross-sectional review & longitudinal review*

Clinicians' longitudinal review (history, life course) relies on collateral information as well, not only on patient recollection

- Psychosis onset usually comes as a “personality change” (social isolation, poor hygiene)

Interviewing General Tones - Empathy

While the patient wants you to “believe” their story, you don’t want to collude with delusions

- But you also want to avoid disagreeing

Instead, agree with them on what you can agree with them on – the emotional pain of their symptoms

- I’m not a detective, but what I can clearly see is that you’ve been *suffering*.
- What you’re describing sounds scary to me. I would feel *afraid*, just like you.

Empathy is not sympathy

- Avoid saying “for you”, i.e. “that’s scary”, not “that’s scary for you”

Interviewing General Tones - Curiosity and Respect

Be curious and interested throughout the interview

- Hmm. How do you know that your boss wants to kill you?

Be respectful and never laugh when presented with bizarre delusions

- Alliance comes from people feeling understood and heard
- Avoid shaming your patient

Starting the Interview

Be transparent about who you are and why you are talking to them (show i.d.)

- The predominant emotion of often fear
- Many people don't want to be here

Interviewing Someone with Psychosis

1. Do not begin by challenging delusions
2. Validate the emotion, not the psychosis
3. Explicitly state emotions and intentions
4. Reflect the patient's own words
5. Be intentional with gestures and positioning

10 domains of De-escalation

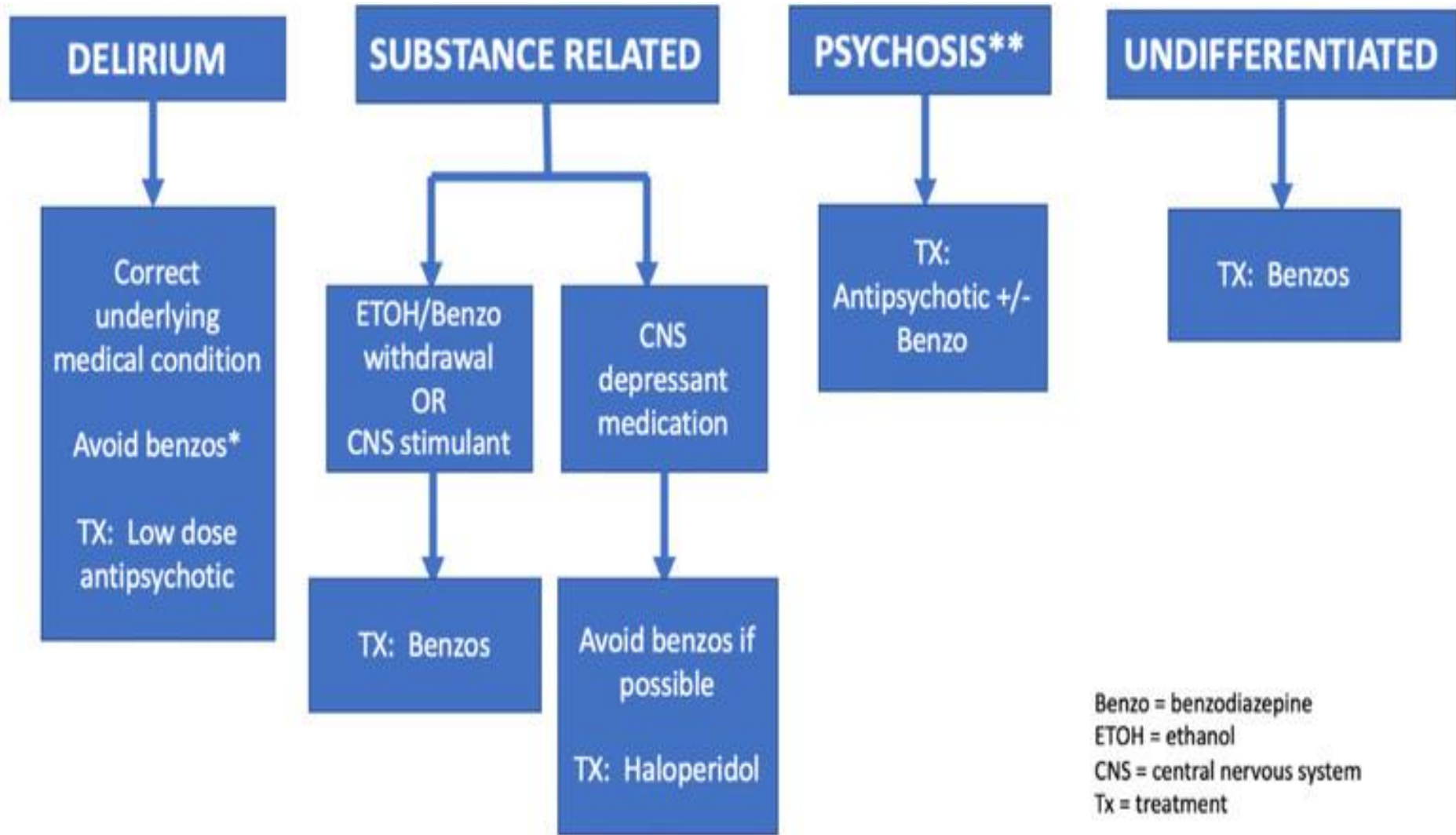
1. Respect personal space
2. Do not be provocative
3. Establish verbal contact
4. Be concise
5. Identify wants and feelings
6. Listen closely to what the pt. is saying
7. Agree or agree to disagree
8. Lay down the law and set clear limits
9. Offer choices and optimism
10. Debrief (pt and staff)

Pharmacologic Management of Agitation: How to decide?

Review patient chart

- Allergies/prior adverse reactions (EPS)
- Medical history
- EKG (specifically QTc)
- Home medications (family members & pharmacies)
- MAR (what have they already gotten and how much?)

Hypothesis of underlying cause



*Unless Benzo or ETOH withdrawal

**Hallucinations, delusions, disorganized thinking

Benzo = benzodiazepine
 ETOH = ethanol
 CNS = central nervous system
 Tx = treatment

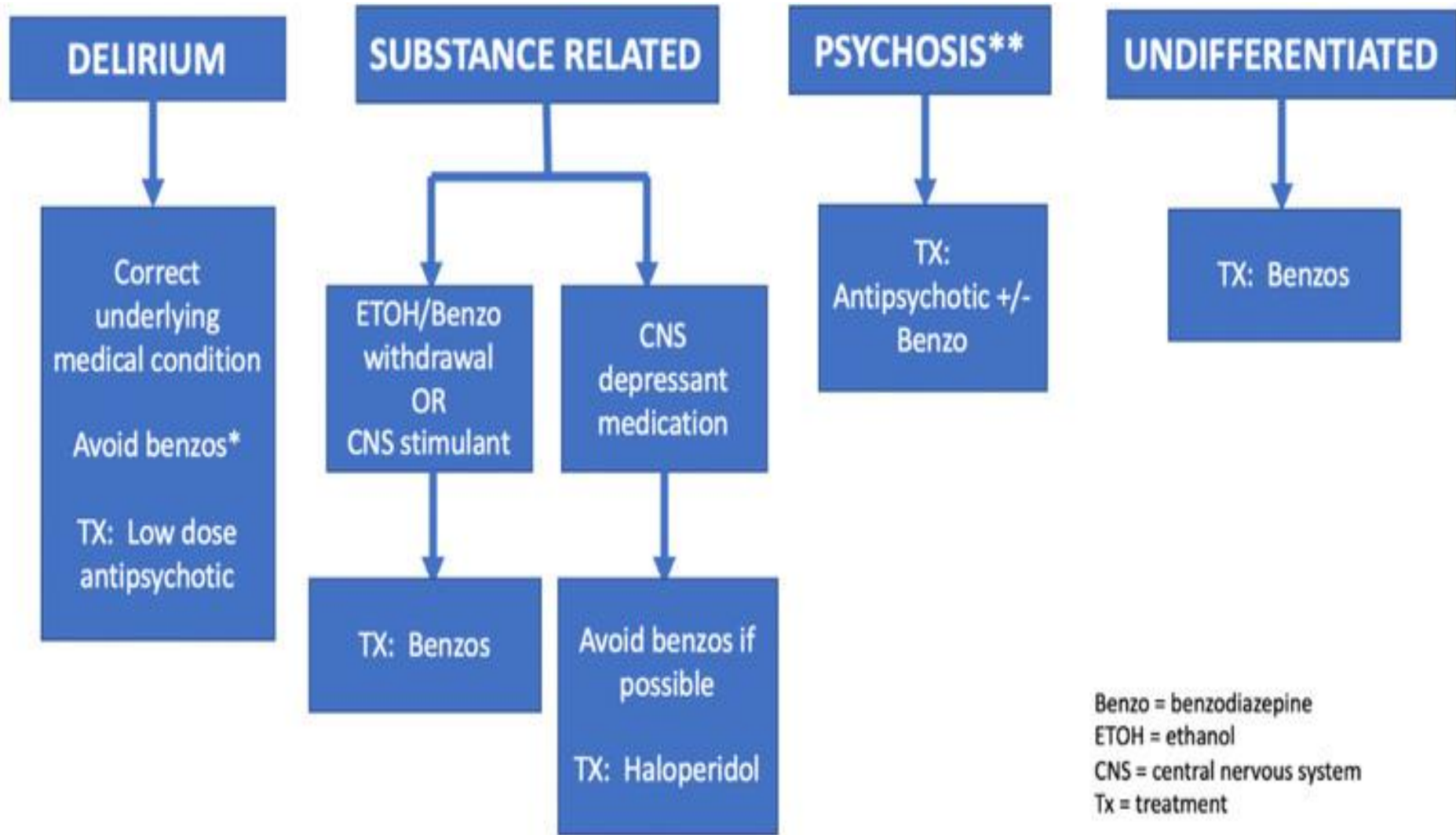
³ Roppolo et al, 2020

Emergency Room

55 yo M presents to the ED requesting alcohol detox. On arrival, patient is slurring his words. Patient is initially calm and cooperative but he becomes agitated when he is told he cannot hold onto his belongings. Patient takes quetiapine 50mg QHS and clonazepam 1mg BID at home.

What history, physical exam, labs or imaging would you like to know?

How would you manage his agitation?



Benzo = benzodiazepine
 ETOH = ethanol
 CNS = central nervous system
 Tx = treatment

*Unless Benzo or ETOH withdrawal
 **Hallucinations, delusions, disorganized thinking

³ Roppolo et al, 2020

Haloperidol (Haldol)

- Available as PO, IM or IV
- Usual dose: 1-10mg
- Peak: PO (2-6 hours), IM (30-60min), IV (15-30 min)
- Can repeat dose in 30 minutes if parenteral
- Max dose 30mg/day
- Other considerations:
 - *IM Haldol poses the greatest risk of **EPS side effects**, (never give on its own)*
 - *IV Haldol has highest (hypothetical) risk of **QTc prolongation** (replete K and Mg and check EKGs daily)*

Emergency Room

40 yo woman brought to the ED from the local airport due to agitation, disorganization and bizarre behavior. She quickly becomes agitated on arrival to the unit. Patient has no prior EMR records and engaged in very limited interview in the emergency room.

What history, physical exam, labs or imaging would you like to know?

How would you manage her agitation?

Risperidone (Risperdal)

- Available as PO or ODT
- Dose 0.5-2mg
- Peak: 1 hour
- Max dose 8mg/day
- Other considerations:
 - *Highest risk of EPS of atypical antipsychotics*
 - *Risk of hypotension*
 - Often paired with PO lorazepam for acute agitation in patients willing to take PO

Emergency Room

38 yo F with history of multiple substance use disorders (including cannabis, opioids, cocaine, methamphetamine), chart diagnosis of schizoaffective disorder (on aripiprazole), multiple prior ED presentations for aggressive behavior, and paranoia, who now presents after making violent threats towards family, and is agitated in the ED. She repeats that her neighbor is trying to kill her. BP 160/100, HR 115. Patient is diaphoretic. She refuses to give a urine sample.

How would you manage her agitation?

Lorazepam (Ativan)

- Available as PO, IM or IV
- Usual dose: 0.5-2mg
- Peak: PO (1-6 hours), IM (60-90min), IV (minutes)
- Side effects: fatigue, sedation, confusion, hyper-excitability (“paradoxical reaction” in certain populations)
- Other considerations:
 - Try to avoid in patients with intoxication from CNS depressants
 - Try to avoid in patients with delirium or risk for delirium (unless due to GABAergic withdrawal)
 - *Caution in patients with respiratory conditions (COPD, OSA)*

Emergency Room

20 yo M with a history of autism spectrum disorder, brought in from home for persistent violent behavior towards family. Patient is shouting on arrival to the ED, stating he doesn't need to be here, and unable to stay in stretcher despite frequent redirection. Upon chart review, you note he's had a previous dystonic reaction to an antipsychotic

How do you manage his agitation?

How would you treat acute dystonia should it occur?



Slide – Stephanie London, 2023

Olanzapine (Zyprexa)

- Available as PO, ODT, IM or IV
- Dose 2.5-10mg
- Peak: PO (6 hours), IM (15-45min)
- Max dose 30mg/day
- Other considerations:
 - Higher anticholinergic burden than other antipsychotics
 - Caution in those with significant respiratory compromise
 - *Do not co-administer IM/IV olanzapine with IM/IV benzodiazepines within 4 hours given risk of respiratory depression*

Chlorpromazine (Thorazine)

- Available as PO, IV or IM
- Usual dose 12.5-100mg
- First anti-psychotic developed
- Highly sedating
- Other considerations:
 - *Can lead to significant **orthostatic hypotension***
 - *Can **lower seizure threshold***
 - *Painful IM injection*
 - *Must be pushed slowly IV to avoid painful injection site reaction (“sterile abscess”). This can be a barrier when giving for acute agitation*

Emergency Room

88 yo F history of dementia, no formal psychiatric or substance use history, who is brought in by family due to worsening confusion and agitation at home. Patient lives with her son who is having trouble caring for her at home. Patient struck her home health aide earlier this week. Her only psychotropic medication is trazodone 50mg QHS.

What history, physical exam, labs or imaging would you like to know?

How do you manage her agitation?

Quetiapine (Seroquel)

- Available as PO only
- Dose 12.5-100mg
- Peak: 1.5 hours
- Often given to older adults at low doses which causes predominantly sedative effect
- Other considerations:
 - *May lead to orthostatic hypotension*

Trazodone

- Available as PO only
- Dose 12.5-100mg
- Good medication in older adults to avoid cardiac and delirium risks
- Also helpful for insomnia
- Other considerations:
 - *May lead to **hypotension***

Special populations

Children

- Mild to moderate: Clonidine PO 0.05-0.1mg (weight based)
- Severe: Zyprexa IM 1.25-5mg (weight based)
- Higher risk for paradoxical reaction to benzodiazepines

Pregnancy

- Prioritize treatment of agitation
- Generally all of our usual agitation medications are okay to use, but Haldol, Zyprexa and Ativan are the most well studied
- Avoid Thorazine due to possible hypotension and risk to fetus

Special populations

Older adults

- Mild to moderate: Serouel 12.5-25mg, Trazodone 12.5-25mg, Zyprexa 2.5-5mg PO
- Severe: Zyprexa 5mg IM or IV Haldol 2.5-5mg

Parkinson's/Lewy Body

- Mild to moderate: Seroquel 12.5-50mg, Trazodone 12.5-25mg
- Severe: Ativan 1-2mg IM or 0.5-1mg IV

ED Agitation Pathway – Mild to Moderate

Medication to PREVENT or TREAT Agitation in the ED (Updated: 2023)

Many patients are at risk for agitation in the ED, especially those experiencing anxiety, substance intoxication/withdrawal, psychosis or those with a history of agitation. These patients should have PRN medication orders written early in their ED visit, even if they do not appear currently agitated.

Level of Agitation	≤18 years of age		>18 and <65 years of age		≥65 years of age	
	Medication	Cause	Medication	Cause	Medication	Cause
At Risk for Agitation / Mild to Moderate Agitation	<p>≤ 12 years of age:</p> <ul style="list-style-type: none"> If on known anxiolytic or antipsychotic medication, or has had anxiolytic or antipsychotic medication in the past with known benefit: <ul style="list-style-type: none"> Give a dose/an extra dose of this medication If no known medication and if adequate blood pressure: <ul style="list-style-type: none"> <35 kg: Clonidine 0.05 mg PO <ul style="list-style-type: none"> May be repeated after 45 minutes. >35 kg: Clonidine 0.1 mg PO <ul style="list-style-type: none"> May be repeated after 45 minutes. 	Substance Use	<ul style="list-style-type: none"> Lorazepam (Ativan) 1-2 mg PO/IM/IV If showing any psychotic symptoms can add: <ul style="list-style-type: none"> Risperidone (Risperdal) 1-2 mg PO Haloperidol* (Haldol) 2.5 mg IM/IV 			<ul style="list-style-type: none"> If on known anxiolytic or antipsychotic medication, or has had medication in the past with known success: <ul style="list-style-type: none"> Give this medication at current or previously prescribed dose If no known medication: <ul style="list-style-type: none"> To treat current psychotic, manic or hyperactivity <ul style="list-style-type: none"> If can take PO: <ul style="list-style-type: none"> Olanzapine (Zyprexa) 2.5-5 mg PO/SL Risperidone (Risperdal) 0.5-1 mg PO (2nd line) Quetiapine (Seroquel) 12.5-50 mg PO (2nd line) If cannot take PO/parenteral preferred: <ul style="list-style-type: none"> Olanzapine** (Zyprexa) 2.5-5 mg IM/IV To treat anxiety or irritability in the absence of psychotic, manic, hyperactive features: <ul style="list-style-type: none"> Quetiapine (Seroquel) 12.5-25 mg PO Trazodone 12.5-25 mg PO Lorazepam (Ativan) 0.5 mg PO
	<p>13-18 years of age:</p> <ul style="list-style-type: none"> Substance Use (excluding suspected alcohol or benzodiazepine intoxication): <ul style="list-style-type: none"> Lorazepam (Ativan) PO 0.05 mg/kg (max 2 mg) If concern for alcohol or benzodiazepine intoxication or showing psychotic symptoms: <ul style="list-style-type: none"> Haloperidol (Haldol) PO 0.55 mg/kg/dose (max 5 mg) Agitation related to psychiatric disorder or unknown: <ul style="list-style-type: none"> If on known anxiolytic or antipsychotic medication, or has had medication in the past with benefit: <ul style="list-style-type: none"> Give this medication at current or previously prescribed dose If no known medication and to treat current psychotic or manic features, hyperactivity, anxiety, and/or irritability: <ul style="list-style-type: none"> Lorazepam (Ativan) PO 0.05 mg/kg (max 2 mg) 	Psychiatric or Unknown	<ul style="list-style-type: none"> If on known anxiolytic or antipsychotic medication, or has had medication in the past with benefit: <ul style="list-style-type: none"> Give this medication at current or previously prescribed dose. If no known medication: <ul style="list-style-type: none"> To treat current psychotic or manic features, or hyperactivity: <ul style="list-style-type: none"> If can take PO: <ul style="list-style-type: none"> Risperidone (Risperdal) 1-2 mg PO Quetiapine (Seroquel) 25-50 mg PO Lorazepam (Ativan) 1-2 mg PO If cannot take PO (Meds can be repeated in 45 min if needed): <ul style="list-style-type: none"> Olanzapine** (Zyprexa) 5 mg IM/IV Haloperidol* (Haldol) 2.5 mg IM/IV Lorazepam (Ativan) 1-2 mg IM/IV To treat anxiety or irritability in the absence of psychotic, manic, hyperactive features: <ul style="list-style-type: none"> Lorazepam (Ativan) 1-2 mg PO or IM/IV 			

ED Agitation Pathway – Severe

Medication to PREVENT or TREAT Agitation in the ED (Updated: 2023)

Many patients are at risk for agitation in the ED, especially those experiencing anxiety, substance intoxication/withdrawal, psychosis or those with a history of agitation. These patients should have PRN medication orders written early in their ED visit, even if they do not appear currently agitated.

Level of Agitation	≤18 years of age		>18 and <65 years of age		≥65 years of age	
	Medication	Cause	Medication	Cause	Medication	
Severe Agitation	<p>≤ 12 years of age or 13-18 years of age without substance use:</p> <ul style="list-style-type: none"> <25 kg: Olanzapine** (Zyprexa) 1.25 mg IM 25-70 kg: Olanzapine** (Zyprexa) 2.5 mg IM >70 kg: Olanzapine** (Zyprexa) 5 mg IM o May be repeated after 45 minutes if adequate blood pressure 	Any Cause	<ul style="list-style-type: none"> Haloperidol* (Haldol) 5 mg IM/IV PLUS Lorazepam (Ativan) 2 mg IM/IV <ul style="list-style-type: none"> o May repeat once after 10-15 minutes o Preferable for schizophrenia/psychosis or current psychosis Midazolam (Versed) 5 mg IM <ul style="list-style-type: none"> o May repeat once in 10 minutes o Preferable if sedation needed for a short period of time, such as to get an IV or imaging. o Preferable for substance use o Can follow up with IM/IV medication for mild/moderate agitation in 30-60 minutes o Time of onset <5 minutes, duration ~1 hour o Must be in Urgent or Acute: need to monitor oxygen saturation Droperidol* 5-10 mg IM/IV <ul style="list-style-type: none"> o May be repeated once after 5 minutes Ketamine 2 mg/kg IM (max 200 mg) or 1 mg/kg IV <ul style="list-style-type: none"> o May be repeated after 5 minutes o For severe agitation in patients for whom benzodiazepines or antipsychotics are contraindicated, are not effective after 1-2 doses, or are not the optimal option o Caution should be used in patients with a history of schizophrenia or psychosis, or current psychosis o Policy: https://hospitalpolicies.ellucid.com/documents/view/13249 	<p>Psychiatric</p> <ul style="list-style-type: none"> Olanzapine (Zyprexa) 5-10mg IM Haloperidol* (Haldol) 2.5-5mg IM Plus Lorazepam (Ativan) 1mg IM 	<p>Dementia</p> <ul style="list-style-type: none"> o If on known antipsychotic medication, or has had medication in the past with known success: <ul style="list-style-type: none"> o Give this medication at current or previously prescribed dose o If no known medication: <ul style="list-style-type: none"> o If can take PO: <ul style="list-style-type: none"> - Quetiapine (Seroquel) 12.5-50 mg PO - Olanzapine (Zyprexa) 2.5-5 mg PO/SL o If cannot take PO/parenteral required: <ul style="list-style-type: none"> - Olanzapine** (Zyprexa) 2.5-5 mg IM/IV - Haloperidol* (Haldol) 1-2.5 mg IM OR 0.5-1 mg IV (Do not use if a h/o Parkinson or Lewy body dementia) 	
	<p>13-18 years of age:</p> <ul style="list-style-type: none"> Substance use (excluding suspected alcohol or benzodiazepine intoxication): <ul style="list-style-type: none"> o Lorazepam (Ativan) IV/IM 0.05 mg/kg (max 2 mg) <ul style="list-style-type: none"> - May repeat after 30 minutes if adequate blood pressure Substance use from suspected alcohol or benzodiazepine intoxication: <ul style="list-style-type: none"> o Haloperidol (Haldol) IM 0.25 mg/kg (max 5 mg) <ul style="list-style-type: none"> - May repeat after 30 minutes if adequate blood pressure 		<p>Parkinson's / Lewy Body Disease</p> <ul style="list-style-type: none"> o If on known medication, or has had medication in the past with known benefit: <ul style="list-style-type: none"> o Give this medication o If no known medication: <ul style="list-style-type: none"> o If can take PO: <ul style="list-style-type: none"> - Quetiapine (Seroquel) 12.5-50 mg PO o If cannot take PO/parenteral required: <ul style="list-style-type: none"> - Lorazepam (Ativan) 0.5-1 mg IM/IV, OR - Olanzapine** (Zyprexa) 2.5 mg IM/IV (2nd line) 			

* For Haloperidol/Droperidol, monitor QTc commensurate with clinical situation.

- o Prefer an ECG prior to administration if possible.
- o ECG after administration then again at 60 minutes.
- o If QTc is prolonged patient must be on a cardiac monitor.

** For olanzapine IM/IV: Should **NOT** be administered within 60 minutes of parenteral benzodiazepine due to the potential for cardiorespiratory depression

Ketamine for Agitation

Should it Stay?	Should it Go?
Faster Onset	Vital sign changes + intubation risk
Deeper Sedation	Exacerbates psychosis
Minimal Cardiorespiratory Depression	Delirium? Catatonia? Emergency Reactions?
	Biased administration

Inpatient Pharmacologic Management of First Episode Psychosis – McLean 2019

Antipsychotic medicines, **other than clozapine and olanzapine**, are recommended as first-line treatment. Daily doses for treatment of acute, especially first-episode psychosis are typically in the range of 300–500 mg chlorpromazine-equivalents.

For **first-generation antipsychotics** (FGAs) examples include fluphenazine 5–10 mg, haloperidol 5–10 mg, perphenazine 16–32 mg, or trifluoperazine 15–30 mg.

Corresponding typical daily doses of **second-generation antipsychotics** (SGAs) are: aripiprazole 10–15 mg, paliperidone 3–15 mg, risperidone 2–4 mg, quetiapine 300–800 mg, or ziprasidone 80–160 mg.

Adjunctive treatment with **lorazepam** during the first week of treatment may help to restore sleep and reduce anxiety and hyperactivity.

Avoid use of antidepressants and stimulants.

Inpatient Management of Established Schizophrenia – McLean 2019

Recommended daily doses of antipsychotic drugs for an acute psychotic episode or exacerbation of multi-episode or chronic psychosis are 300–1000 mg chlorpromazine (CPZ) equivalents. For **first-generation antipsychotics** (FGAs), examples are: fluphenazine 5–15 mg, haloperidol 5–15 mg, or perphenazine 24–72 mg. For **second-generation antipsychotics** (SGAs) examples are: aripiprazole up to 30 mg, olanzapine 10–20 mg, paliperidone 3–15 mg, quetiapine 300–1000 mg, risperidone 2–8 mg, ziprasidone 80–160 mg.

Clozapine should be offered to patients with a clinically inadequate response, persistent thoughts of suicide or suicide attempts, or persistent aggressive behavior (it may also help with co-occurring substance abuse). If circumstances are compelling, its use can be considered after a single trial of an antipsychotic. Three–six months at a clozapine plasma level of 250–350 ng/mL is generally considered an adequate trial.

Augmentation Strategies – If clozapine alone does not produce an adequate response, adding other treatments can be considered, such as: lamotrigine, a second antipsychotic, ECT, or rTMS. Mood-stabilizers may benefit agitation or excitement but are unlikely to help with persisting positive psychotic symptoms.

Alcohol Use Disorder + Schizophrenia

Lifetime prevalence of AUD in schizophrenia of 24.3%

Leads to worse prognosis and outcomes

Consider medication for AUD: naltrexone, disulfiram, acamprosate, valproic acid, varenicline

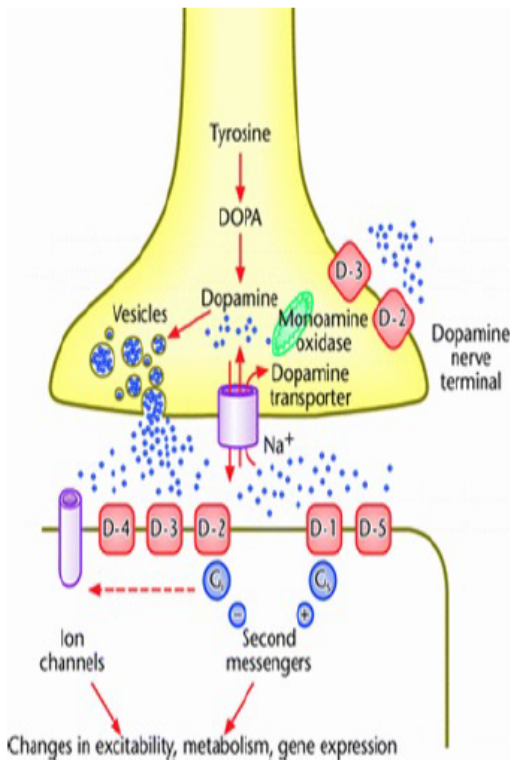
Consider long acting injectable antipsychotics (versions of **risperidone**, **haloperidol**), consider second generation antipsychotics over first generation

Psychosocial treatments that target both best (CBT, contingency management, motivational interviewing, 12-step, consider residential or ACT if available)

Typical (first generation) antipsychotics

- Classic dopamine D2 receptor antagonists

Dopamine hypothesis of schizophrenia- there is excessive dopamine neurotransmission in psychosis. DA agonists (e.g., cocaine, amphetamine) trigger/worsen psychosis; DA antagonists improve psychosis.



Generic	Trade name(s)	FDA approval
Chlorpromazine	Thorazine	1957
Trifluoperazine	Stelazine	1959
Haloperidol	Haldol, Decanoate (IM)	1967
Thiothixene	Navane	1967
Loxapine	Loxitane, Adusuve (IN)	1975
Thioridazine	Mellaril	1983
Pimozide	Orap	1984
Fluphenazine	Prolixin, Decanoate (IM)	1988
Perphenazine	Trilafon	1998

Atypical (second generation) antipsychotics

- Less strongly (more “loosely”) D2 blocking

Generic	Trade name(s)	Mechanism	FDA
Clozapine	Clozaril, Fazaclo, Versacloz, Clopine	5HT2A/D2 antagonist	1990
Olanzapine	Zyprexa, Zydys (SL), Relprevv (IM)	5HT2A/D2 antagonist	1993
Risperidone	Risperdal, M-tab (SL), Consta (IM)	5HT2A/D2 antagonist	1996
Quetiapine	Seroquel	5HT2A/D2 antagonist	1997
Ziprasidone	Geodon	5HT2A/D2 antagonist	2001
Aripiprazole	Abilify, Discmelt, Maintena (IM), Aristada (IM), Mycite (sensor)	Partial D2/5HT1A agonist; 5HT2A antagonist	2002
Paliperidone	Invega, Sustenna (IM), Trinza (q3m IM)	5HT2A/D2 antagonist	2006
Asenapine	Saphris, Secuado (TD)	5HT2A/D2 antagonist	2009
Iloperidone	Fanapt	5HT2A/D2 antagonist	2009
Lurasidone	Latuda	5HT2A/D2 antagonist	2010
Brexpiprazole	Rexulti	Partial D2/5HT1A agonist; 5HT2A antagonist	2015
Cariprazine	Vraylar	Partial D2/5HT1A agonist; 5HT2A antagonist	2015
Lumateperone	Caplyta	5HT2A antagonist; D2 antagonist; DIR-dependent glutamate modulator; SRI	2019

Atypical (second generation) antipsychotics

- Less strongly (more “loosely”) D2 blocking

Generic	Trade name(s)	Mechanism	FDA
Clozapine	Clozaril, Fazaclo, Versacloz, Clopine	5HT _{2A} /D ₂ antagonist	1990
Olanzapine	Zyprexa, Zydys (SL), Relprevv (IM)	5HT _{2A} /D ₂ antagonist	1993
Risperidone	Risperdal, M-tab (SL), Consta (IM)	5HT _{2A} /D ₂ antagonist	1996
Quetiapine	Seroquel	5HT _{2A} /D ₂ antagonist	1997
Ziprasidone	Geodon	5HT _{2A} /D ₂ antagonist	2001
Aripiprazole	Abilify, Discmelt, Maintena (IM), Aristada (IM), Mycite (sensor)	Partial D ₂ /5HT _{1A} agonist; 5HT _{2A} antagonist	2002
Paliperidone	Invega, Sustenna (IM), Trinza (q3m IM)	5HT _{2A} /D ₂ antagonist	2006
Asenapine	Saphris, Secuado (TD)	5HT _{2A} /D ₂ antagonist	2009
lloperidone	Fanapt	5HT _{2A} /D ₂ antagonist	2009
Lurasidone	Latuda	5HT _{2A} /D ₂ antagonist	2010
Brexpiprazole	Rexulti	Partial D ₂ /5HT _{1A} agonist; 5HT _{2A} antagonist	2015
Cariprazine	Vraylar	Partial D ₂ /5HT _{1A} agonist; 5HT _{2A} antagonist	2015
Lumateperone	Caplyta	5HT _{2A} antagonist/D ₂ antagonist; DIR-dependent glutamate modulator; SRI	2019

Meta-analysis of 15 antipsychotics: all are more efficacious than placebo

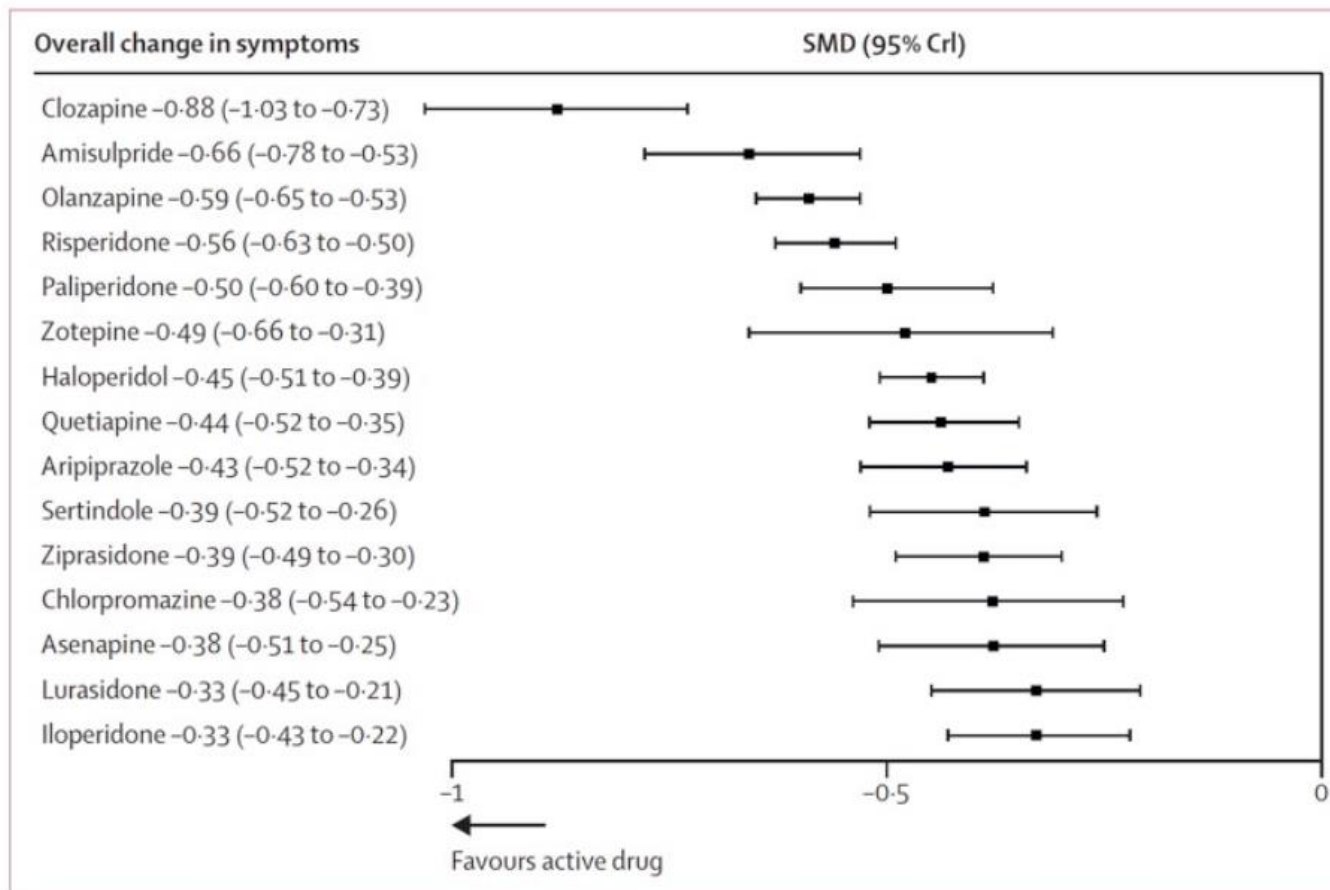


Figure 3: Forest plot for efficacy of antipsychotics drugs compared with placebo

Treatments are ranked according to their surface under the cumulative ranking (SUCRA) values (appendix p 98).

SMD=standardised mean difference. CrI=credible interval.

Leucht et al., *Lancet* 2013

Side effects associated with other targets

Side effect	Receptor /ion channel affinity	Example antipsychotics
Weight gain ^{1,2}	Higher H1	Clozapine, paliperidone, risperidone, chlorpromazine
	Higher 5HT _{2C}	Olanzapine, clozapine, asenapine, iloperidone
	Higher M ₁ , M ₃	Clozapine, olanzapine, iloperidone, chlorpromazine
Sedation ¹	Higher M ₁ , M ₄	Clozapine, olanzapine, chlorpromazine
Constipation, dry mouth, blurry vision ³	Higher M ₂ , M ₃	Clozapine, chlorpromazine, olanzapine, quetiapine
Orthostatic hypotension ⁴	Higher A ₁	Chlorpromazine, clozapine, quetiapine
QTc prolongation ⁵	hERG K ⁺ channel, Na ⁺ channel	Pimozide, thioridazine, ziprasidone

¹Olten and Bloch, *Prog Neuropsychopharmacol Biol Psychiatry* 2018; ²Kroeze et al *Neuropsychopharm* 2003;

³Migirov & Datta *NCBI StatPearls* 2020; ⁴Stroup & Gray *World Psychiatry* 2018;

⁵Silvestre et al., *J Psychopharmacol* 2014;



But... non-adherence is common in schizophrenia

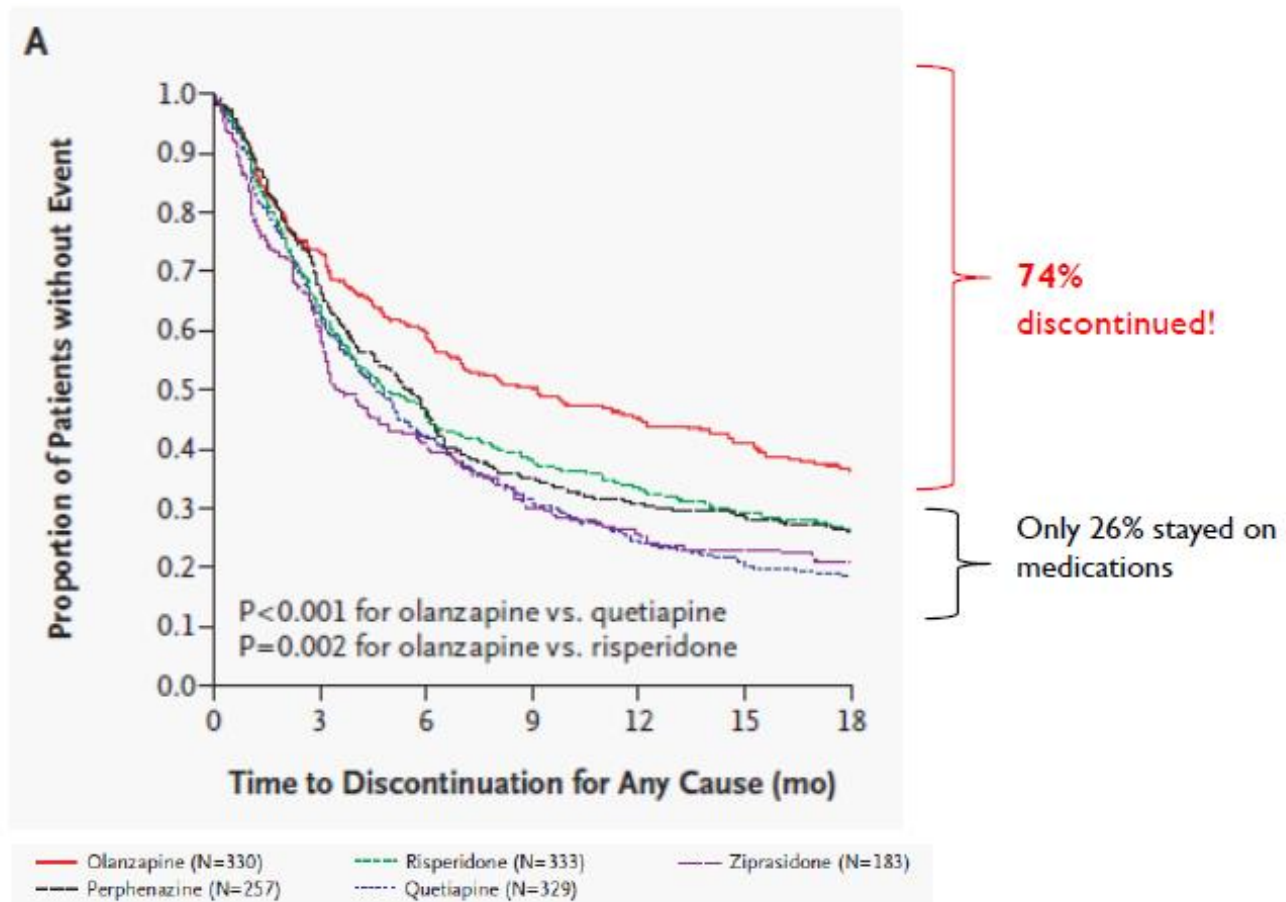


Figure from Lieberman et al., *New Engl J Med* 2005

Long-acting injectable antipsychotics (LAI's) are an important strategy for non-adherence

There are now several atypical LAI's

Trade Name	Generic	Dosing frequency	FDA approval
Risperdal Consta	Risperidone	Q2 weeks	2003
Zyprexa Relprevv	Olanzapine	Q2-4 weeks	2009
Invega Sustenna	Paliperidone	Q1 month	2009
Abilify Maintena	Aripiprazole	Q1 month	2013
Aristada	Aripiprazole	Q1-2 months	2015
Invega Trinza	Paliperidone	Q3 months	2015
Perseris	Risperidone ER	Q1 month SC	2018
Invega Hafyera	Paliperidone	Q6 months	2021

- LAI's are superior to placebo for acute and maintenance treatment of schizophrenia. (Individual LAI's similar to one another re relapse prevention.)
- LAI's can simplify the daily routine for patients.
- LAI's provide more steady blood levels of antipsychotic medications.

Correll et al., *J Clin Psychiatry* 2016 Suppl.

What is Open Dialogue?

Humanistic, non-medicalized, meaning-making approach to psychopathology

Treatment system and a way of providing care within that system

Draws upon many practices from US family and narrative therapies

Views psychosis as a profound state of isolation

Social network approach to care

Egalitarian: drops the clinical and expert gaze

Aims to alter the course of chronicity and disability

Cases for emRIC ECHO

PAUL CHARLTON, MD
GIMC ED DIRECTOR

Case 3

18 yo M high school senior with history of depression, brought by parent after aborted suicide attempt in which patient stated that he considered and prepared for hanging himself but instead sought help from family, who brought him to the ED.

He is depressed in the ED and is calm, not threatening staff or himself. He is medically cleared by the ED provider for evaluation by BHS, who recommends transfer for inpatient psychiatric stabilization.

You anticipate he will be in the ED for 24-28 hours while awaiting an accepting facility and transport.

Case 3 (continued)

Would you start medications while patient is waiting in the ED (24-48 hours)?

What other therapeutic interventions should be considered while waiting to depart the ED?

Management of the Depressed Patient in the ED

- Generally not recommended to start an antidepressant (lack of follow up, delayed onset of action)
- Rule out medical causes of depression (include EKG, TSH, B12, folate, RPR, HIV)
- Manage short term predictors of suicide, consider benzodiazepines for:
 - Mental distress – anxiety, obsessions, rumination
 - Physical distress – panic attacks or physical symptoms of anxiety, akathisia, distracted
 - Insomnia
 - Substance intoxication/withdrawal
- Ensure calm environment
- Treat with dignity & respect
- Telepsychiatry

For a Different Emergency Room Experience... The EmPATH Model

Behavioral health patients represent 15% of ED visits

EmPATH (emergency psychiatric assessment, treatment, and healing unit) delivers acute behavioral healthcare to patients in crisis in a calm, therapeutic setting

Seventy-five percent of patients treated in an EmPATH unit stabilize and return home within 24 hours

Less than 1% of patients require restraint, sedation, or other coercive treatments

Improved ED throughput, better patient & provider satisfaction

Zeller's Six Goals of Emergency Psychiatric Care

1. Exclude medical etiologies and ensure medical stability
2. Rapidly stabilize the acute crisis
3. Avoid coercion
4. Treat in the least restrictive setting
5. Form a therapeutic alliance
6. Formulate an appropriate disposition and aftercare plan

Physical Space Design

Key Take-Away: Calming environment separate from ER that prioritizes healing and access to care

- Large, open milieu space where patients can be together in the same room – high ceilings and ambient light. All can easily self-access food, drinks, linens, phones, books, games, TV. Ample room for walking about or pacing.
- Space to move about and engage in socialization, discussion, and therapy. Some feature outdoor relaxation gardens
- “Per chair” model, outfitted with recliners. Space recommendation: 80 sq ft per patient; 36 sq ft patient area around the recliners
- Open nursing station w/instant access to staff - No “bulletproof Plexiglas” separating the patients
- 1-2 Calming Rooms (unlocked spaces) - Avoid locked rooms or restraints

Zeller, 2018



Physical Space Design





Patient Benefits

Immediate care setting change from chaotic ED to a calming, “trauma-informed” environment with restraint elimination

Coercion avoided, all about engagement and individual decisions; staff available around the clock. Peer support specialists onsite.

Multi-disciplinary team treatment and resources available, discharge planning, family contact, outpatient provider connections

Rapid evaluation by a psychiatrists after arrival, comprehensive care plan development; patients may stay up to 23 hours till dispo

Hospital Benefits

EMTALA-compliant for voluntary/involuntary mental health crises; take all medically-stable patients immediately from ER

Not alternative destination to inpatient, but a separate “psych ER” where all evaluation, treatment and dispositions are made

Move behavioral health care out of the ER into more appropriate space for healing, opening up beds in the ER for medical patients

Significant reduction in admission rates, up to 80%, as patients respond very well to site and interventions

Even inpatient units benefit -- eliminate unnecessary, denied pay day inpatient admissions

Zeller, 2018

Case 4

18 yo M brought by school counselor after patient reported to counselor during a home welfare call (due to missed days from school) that he was depressed and he had considered shooting himself over the weekend and asked a cousin for access to a gun but they did not give it to him.

Patient evaluated by BHS team who felt that patient is high risk based on this story and they recommend patient be sent to inpatient psychiatric hospital.

Patient protests and said that he does not want to be admitted and that while he was suicidal this weekend, he is not suicidal now. He says, "I thought you were here to help me, and now you are sending me away? This is going to make things worse."

Case 4 (continued)

This situation appears distressing to the ED provider, school counselor, and BHS evaluator since the patient does not want to voluntarily go to inpatient psychiatric care.

How do you recommend approaching patients with who are depressed, with recent serious suicide threat, but not actively endorsing suicide today, when it feels like the process of making someone an involuntary transfer for inpatient psychiatric care may cause some harm to the patient's future trust of the medical system and even require chemical sedating medications to facilitate an involuntary transfer?

Decision Point Considerations in Involuntary Care

- Involuntary care is supposed to feel bad
- “Someone can leave when they are safe enough for whatever they are returning to”
 - Consider: level of existing psychiatric care/support, level of social supports, level of independent coping, likelihood of situation recurring
- “What changed?”
 - Consider: new supports at home, new psychiatric care supports, new biopsychosocial changes
- “How likely are they to benefit from care?”
 - Consider if first time vs 10th time, how treatable condition is
- It still feels bad: Consider treatment as an investment in someone’s future
- It feels too bad: At some point, the risk-benefit shifts

Summary

Our current system of care for people with serious mental illness leaves people dying 25 years sooner than the average population.

Open Dialogue's approach for people with serious mental illness may lead to better outcomes and serve as inspiration to grow changes in how we currently practice.

For managing people experiencing psychosis, rule out medical causes then offer people a safe non-judgmental space and start a standing antipsychotic if they will be with you a while.



Kaizen...

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Bonus Slides for Reference

If Antipsychotics Make them Worse, or if you See Odd Actions, consider... Catatonia

Catatonia is a problem with the brain's ability to choose which action, out of a huge number of possible actions, is the right one to take at a given time.

The brain has a system of gates that either open up to allow an action to proceed or stay closed and prevent that action from happening. Usually, the brain opens only one gate at a time, so that you can complete one action before moving on to the next.

In Catatonia, the mechanism that regulates the opening and closing of the gates is broken. Because of this, sometimes none of the gates can open and the person with Catatonia is unable to take any action at all. They may be unable to move, speak, talk, or eat.

Sometimes, the opposite happens, and a gate opens for no reason, leading to actions with no purpose, which can be anything from simple repetitive movements to bizarre complex behaviors.

When multiple gates open at once, the person with Catatonia may attempt to execute multiple actions at the same time, sometimes becoming indecisive or "stuck" when they are caught between two opposite or incompatible actions. An example of this, is someone who gets stuck in a doorway because the "gates" for "enter the room" and "do not enter the room" opened at the same time.

If Antipsychotics Make them Worse, or if you See Odd Actions, consider... Catatonia

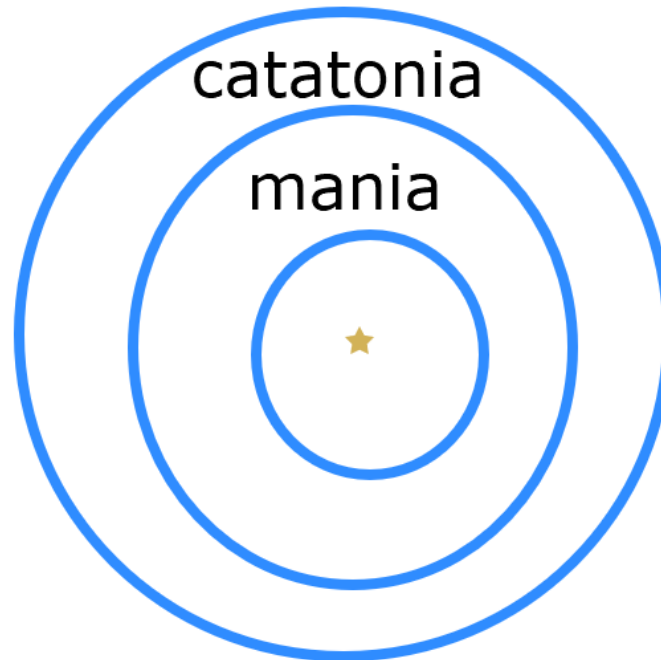
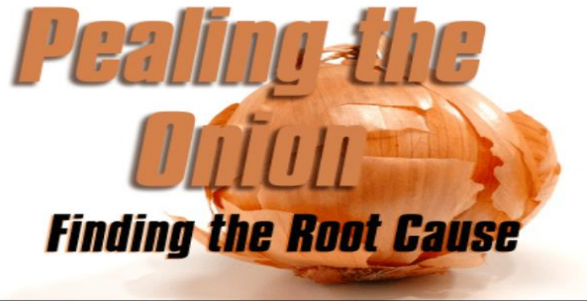
The gating mechanism is governed by two neurotransmitters, GABA and Dopamine. When the gates are broken, they need more GABA and more Dopamine to be restored to working order. This is why, we **HOLD antipsychotics** (which block dopamine) and **give people Ativan** (which increases GABA). If this is not effective enough or we need a faster response, we use **ECT** which reboots the gating system and “restores its factory settings”.

Conceptualize Catatonia

1. Catatonia is a syndrome, just like Delirium
2. Catatonia feels like the ultimate state of ambivalence or anxiety
 - Patients are frozen in indecision or anxiety (i.e. fight or flight or freeze, this is “freeze”)
3. Catatonia is a severity marker, and patients pass through phases to get sick, and in reverse to get well
 - Depression -> psychotic depression -> catatonic depression
 - Like peeling onion layers during improvement from catatonia
4. Catatonia may be all you can see at first, or you may be able to see mood or psychotic or other symptoms as well

Northoff et al, 1996. Fink & Taylor 2009. DSM-5, 2013. Fink 2011.

Conceptualize Catatonia



Onion layers during improvement

BUSH-FRANCIS CATATONIA RATING SCALE

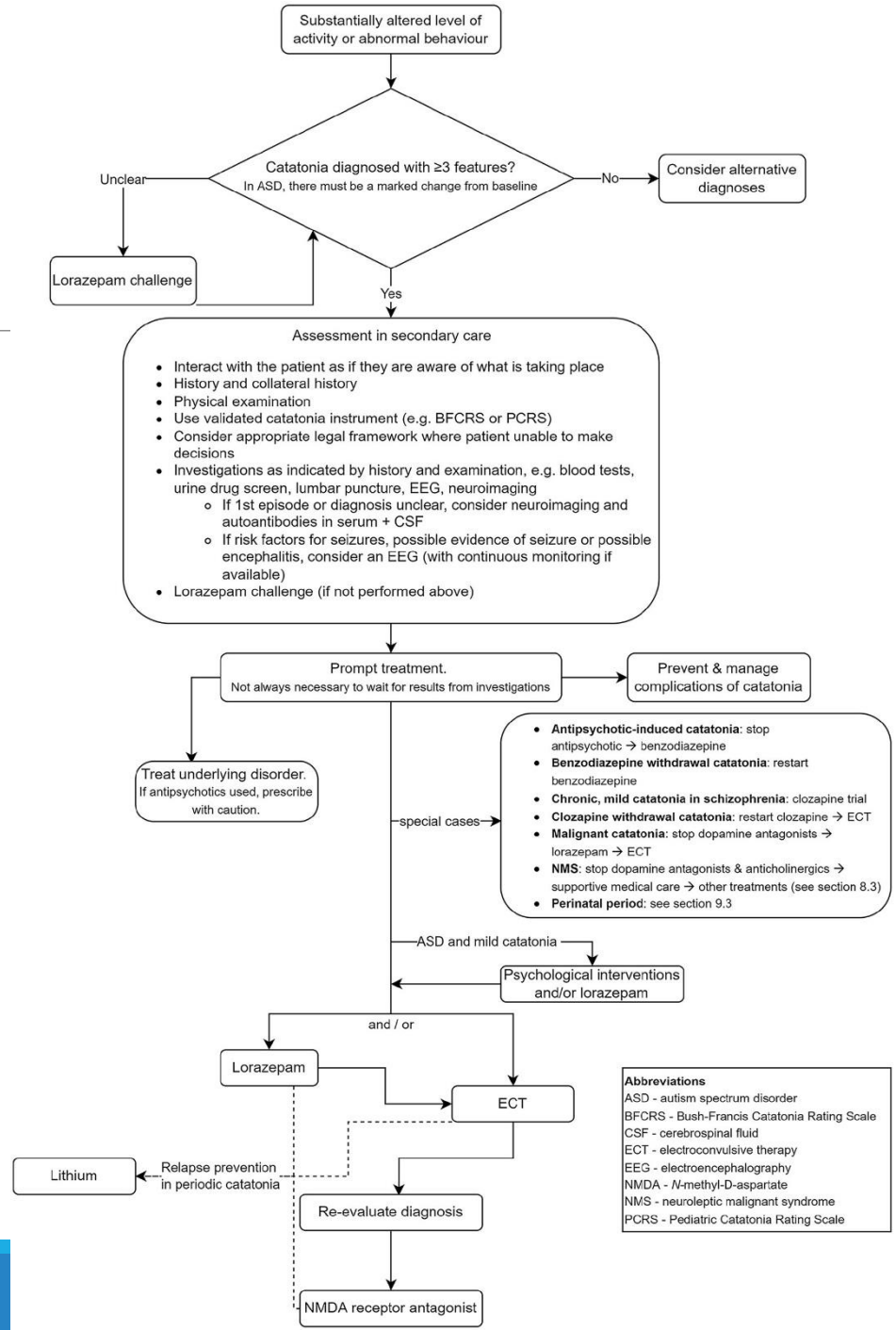
Use presence or absence of items 1-14 for screening

Use the 0-3 scale for items 1-23 to rate severity

<p>1. Excitement:</p> <p>Extreme hyperactivity, constant motor unrest which is apparently non-purposeful. Not to be attributed to akathisia or goal directed agitation</p> <p>0 = Absent 1 = Excessive motion 2 = Constant motion, hyperkinetic without rest periods 3 = Full-blown catatonic excitement, endless frenzied motor activity</p>	<p>2. Immobility/stupor:</p> <p>Extreme hypoactivity, immobile, minimally responsive to stimuli</p> <p>0 = Absent 1 = Sits abnormally still, may interact briefly 2 = Virtually no interaction with external world 3 = Stuporous, non-reactive to painful stimuli</p>
<p>3. Mutism:</p> <p>Verbally unresponsive or minimally responsive</p> <p>0 = Absent 1 = Verbally unresponsive to majority of questions; incomprehensible whisper 2 = Speaks less than 20 words/ 5 min 3 = No speech</p>	<p>4. Staring:</p> <p>Fixed gaze, little or no visual scanning of environment, decreased blinking.</p> <p>0 = Absent 1 = Poor eye contact, repeatedly gazes less than 20 seconds between shifting of attention; decreased blinking 2 = Gaze held longer than 20 seconds, occasionally shifts attention 3 = Fixed gaze, non-reactive</p>
<p>5. Posturing/catalepsy:</p> <p>Spontaneous maintenance of posture(s), including mundane (e.g. setting or standing for long periods without reacting).</p> <p>0 = Absent 1 = Less than 1 minute 2 = Greater than one minute, less than 15 minutes 3 = Bizarre posture, or mundane maintained more than 15 minutes</p>	<p>6. Grimacing:</p> <p>Maintenance of odd facial expressions.</p> <p>0 = Absent 1 = Less than 10 seconds 2 = Less than 1 minute 3 = Bizarre expression(s) or maintained more than 1 minute</p>
<p>7. Echopraxia/echoJalia:</p> <p>Mimicking of examiner's movements/speech.</p> <p>0 = Mimicking of examiner's movements/speech 1 = Occasional 2 = Frequent 3 = Constant</p>	<p>8. Stereotypy:</p> <p>Repetitive, non-goal-directed motor activity (e.g. finger-play; repeatedly touching, patting or rubbing self); abnormality not inherent in act but in frequency.</p> <p>0 = Absent 1 = Occasional 2 = Frequent 3 = Constant</p>
<p>9. Mannerisms:</p> <p>Odd, purposeful movements (hopping or walking tiptoe, saluting passers-by or exaggerated caricatures of mundane movements); abnormality inherent in act itself.</p> <p>0 = Absent 1 = Occasional 2 = Frequent 3 = Constant</p>	<p>10. Verbigeration:</p> <p>Repetition of phrases or sentences (like a scratched record).</p> <p>0 = Absent 1 = Occasional 2 = Frequent 3 = Constant</p>
<p>11. Rigidity:</p> <p>Maintenance of a rigid position despite efforts to be moved, exclude if cog-wheeling or tremor present.</p> <p>0 = Absent 1 = Mild resistance 2 = Moderate 3 = Severe, cannot be repositioned</p>	<p>12. Negativism:</p> <p>Apparently motiveless resistance to instructions or attempts to move/examine patient. Contrary behavior, does exact opposite of instruction</p> <p>0 = Absent 1 = Mild resistance and/or occasionally contrary 2 = Moderate resistance and/or frequently contrary 3 = Severe resistance and/or continually contrary</p>
<p>13. Waxy Flexibility:</p> <p>During repositioning of patient, patient offers initial resistance before allowing himself to be repositioned, similar to that of a bending candle.</p> <p>0 = Absent 3 = Present</p>	<p>14. Withdrawal:</p> <p>Refusal to eat, drink and/or make eye contact.</p> <p>0 = Absent 1 = Minimal PO intake/interaction for less than 1 day 2 = Minimal PO intake/interaction for more than 1 day 3 = No PO intake/interaction for 1 day or more.</p>

BUSH-FRANCIS CATATONIA RATING SCALE (CONT.)

<p>15. Impulsivity:</p> <p>Patient suddenly engages in inappropriate behavior (e.g. runs down hallway, starts screaming or takes off clothes) without provocation. Afterwards can give no, or only a facile explanation.</p> <p>0 = Absent 1 = Occasional 2 = Frequent 3 = Constant or not redirectable</p>	<p>16. Automatic obedience:</p> <p>Exaggerated cooperation with examiner's request or spontaneous continuation of movement requested.</p> <p>0 = Absent 1 = Occasional 2 = Frequent 3 = Constant</p>
<p>17. Mitgehen:</p> <p>"Anglepoise lamp" arm raising in response to light pressure of finger, despite instruction to the contrary.</p> <p>0 = Absent 3 = Present</p>	<p>18. Gegenhalten:</p> <p>Resistance to passive movement which is proportional to strength of the stimulus, appears automatic rather than willful.</p> <p>0 = Absent 3 = Present</p>
<p>19. Ambitendency:</p> <p>Patient appears motorically "stuck" in indecisive, hesitant movement.</p> <p>0 = Absent 3 = Present</p>	<p>20. Grasp reflex:</p> <p>Per neurological exam</p> <p>0 = Absent 3 = Present</p>
<p>21. Perseveration:</p> <p>Repeatedly returns to same topic or persists with movement.</p> <p>0 = Absent 3 = Present</p>	<p>22. Combativeness:</p> <p>Usually in an undirected manner, with no, or only a facile explanation afterwards.</p> <p>0 = Absent 1 = Occasionally strikes out, low potential for injury 2 = Frequently strikes out, moderate potential for injury 3 = Serious danger to others</p>
<p>23. Autonomic abnormality:</p> <p>Circle: temperature, BP, pulse, respiratory rate, diaphoresis.</p> <p>0 = Absent 1 = Abnormality of one parameter [excluding pre-existing hypertension] 2 = Abnormality of two parameters 3 = Abnormality of three or more parameters</p>	<p>TOTAL: _____</p>



Oldham et al,
2023

When There is Impaired Insight... LEAP

LISTEN

- Listen reflectively to delusions, anosognosia, desires
- Delay giving your opinions – “I can tell you what I think, but I’d rather understand you and your view better first.”

EMPATHIZE

AGREE

PARTNER

LEAP

Giving your opinion with the 3 A's:

- **Apologize** – “I want to apologize because my views might feel hurtful or disappointing”
- **Acknowledge fallibility** – “Also, I could be wrong and I don't know everything”
- **Agree** – “I hope we can agree to disagree. I respect your point of view and I hope you can respect mine.”

LEAP

EMPATHIZE

- Strategically express empathy for delusional beliefs, desire to prove they're not sick, and wish to avoid treatment
- Normalize the experience

AGREE

- Discuss only perceived problems/symptoms
- Review advantages & disadvantages of adherence, and reflect back the advantages & cost they perceive

LEAP

PARTNER

- Move forward on goals you both agree can be worked on together