Early Psychosis

Rhoshel Lenroot, MD
School of Psychiatry and Behavioral Sciences
University of New Mexico, Albuquerque, New Mexico
rlenroot@salud.unm.edu

Outline

- Overview of early psychosis
- Evaluation
- Intervention
- Take-homes and local resources

Joshua

- 15-year-old male brought in by parents at suggestion of school nurse
- Grade this semester decreased from As to Cs and Ds
- Parents noticed not seeing friends past few weeks; mostly stays in his room alone; not wanting to go out with family
- Dropped out of soccer team
- Irritable with younger sister when she is loud
- Lots of time listening to music with headphones
- Keeps curtains closed

Mental Status Exam:

- Pale, quiet, appears tired, no physical distress or evidence neurologic abnormalities
- Can’t keep up with grades because starting to have a hard time focusing on work and organizing tasks; feels depressed sometimes about this but otherwise mood ok
- Noise of other students becoming increasingly distracting and irritating
- Sometimes hears whispers, footsteps, but when looks around no one is there; he thinks must be something his mind is doing but make him anxious
- Uncomfortable in public and around open windows; has a feeling that people are looking at him; knows it doesn’t make sense but can’t shake it and so keeps windows covered and avoids leaving home
- Denies suicidality, intent to harm others, drug use
- Having difficulty falling asleep but energy ok during day
- Family history include aunt hospitalized for some mental health problem

Which one is the most likely diagnosis?

A. Attenuated psychosis syndrome
B. First episode of schizophrenia
C. Major depression with psychotic features
D. Schizophreniform disorder
E. Schizotypal personality disorder

What is Psychosis?

- Experience of altered perceptions of reality
  - Hallucinations
  - Delusions

- Disturbance in thought process and thought generation
  - Feeling others can interfere with thoughts
  - Disorganization of thoughts, speech, behavior

- Often associated with negative symptoms:
  - Cognitive difficulties: memory, attention, planning, processing speed
  - Loss of interest, motivation, or participation in social, vocational, educational activities
  - Difficulty making decisions
  - Decreased range of expressed emotions

Psychotic Symptoms Associated With Many Different Conditions

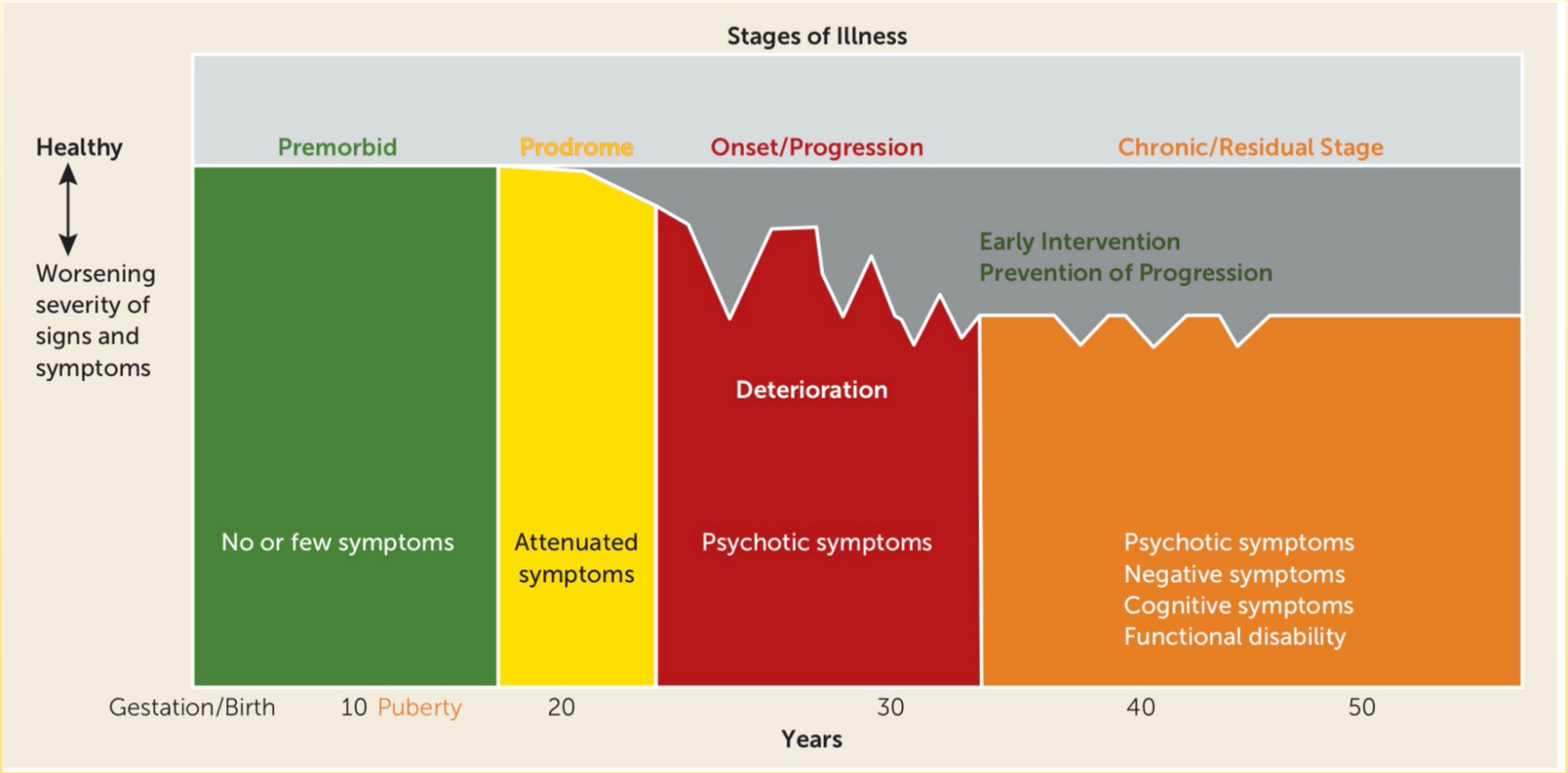
- Psychiatric disorders:
  - Schizophrenia-spectrum disorders
  - Bipolar Affective Disorder, Major Depression
  - Post-traumatic stress disorder
  - Borderline personality disorder
- Substance use
- Medical and neurologic disorders, medication side effects

Schizophrenia

- Two or more of following present for **significant portion of the time during a one-month period**
  - Delusions, hallucinations, disorganized speech, grossly disorganized or catatonic behavior, negative symptoms
- For significant portion of time since onset, level of functioning in one or more areas is significantly decreased
- Continuous signs of disturbance for at least six months – at least one month of active symptoms; may include periods of attenuated or only negative symptoms
- Not due to another cause

- Schizophrenia affects approximately 7/1000 individuals across their lifetime[1]
- Early onset schizophrenia: between ages 13-18
  - Estimated 39% males, 23% females with schizophrenia have onset by age 19[2]
  - Childhood onset: prior to age 13 – rare but not unknown
- Standardized mortality ratio due to all causes 2.6 compared to controls - individuals die on average 12-15 years earlier[1]

Why interest in early psychosis?



Schizophrenia: Prototype of idiopathic psychotic disorder

Figure from Lieberman JA, First MB. *NEJM*. 2018;379:270-280.

Psychosis-like experiences are not uncommon

- Psychosis-like experiences (PLE): hallucinations or delusions of varying levels of severity; may or may not have distress or clinical condition
- Meta-analysis of reported psychosis-like experiences (PLE) in general population from 61 cohorts (Linscott and van Os, 2013)
- Median estimated prevalence: 7.2%
- Transient for nearly 80%
- 7.4% developed psychotic disorder
- Higher rates in younger individuals: Meta-analysis from 13 community samples found in 9.83%

Linscott and van Os, An updated and conservative systematic review and meta-analysis of epidemiological evidence on psychotic experiences in children and adults. Psychological Medicine 2013;43:1133-1149

Clinical High Risk for Psychosis (CHR-P)

- **Attenuated Psychosis Syndrome – most common**
  - Delusions, hallucinations, or disorganized speech at least 1/week in past month
  - Enough severity or frequency for clinical attention, but with relatively intact reality testing
  - Onset or worsening of symptoms in the past 12 months
  - Not better explained by other condition
- **Brief Intermittent Psychosis Syndrome (BIPS):** full psychotic intensity, not sufficient frequency/intensity to meet criteria for psychotic disorder
- **Genetic Risk and Deterioration Syndrome (GERD):** first degree relative with psychosis AND significant loss of function in last year

Answer: What is most likely dx for Ted?

A. Attenuated psychosis syndrome
B. First episode of schizophrenia
C. Major depression with psychotic features
D. Schizophreniform disorder
E. Schizotypal personality disorder

Mitch

- Mitch is a 17-year-old high school senior who was brought to the emergency department by his parents after coming home early from school and telling them he could not stay at school because his teacher was a witch and he could hear the thoughts of the other students talking about him. He was upset and irritable but not violent or threatening.
- After a couple of hours he started to relax and wasn’t sure why he had had this belief. He related he had several episodes like this over the preceding three months; happening once or twice a month and lasting from a few minutes to a few hours; this was the first time it was so severe he had to leave school and had told his parents. These experiences were bothering him enough so he was starting to want to avoid going to school.

Which one is the most likely diagnosis?

A. Attenuated psychosis syndrome
B. First episode of schizophrenia
C. Brief intermittent psychosis syndrome (BIPS)
D. Genetic Risk and Deterioration Syndrome
E. Schizotypal personality disorder

Which one is the most likely diagnosis?

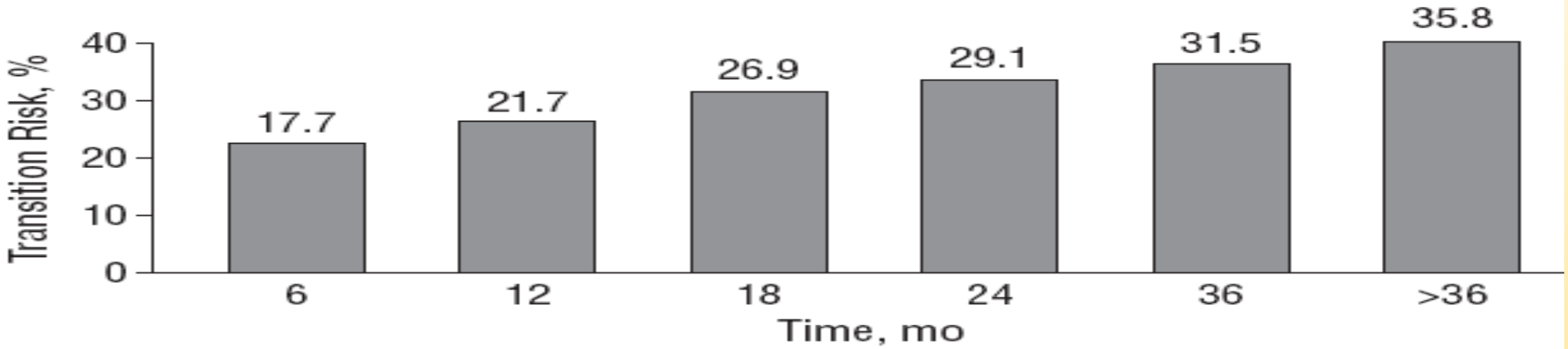
A. Attenuated psychosis syndrome
B. First episode of schizophrenia
C. Brief intermittent psychosis syndrome (BIPS)
D. Genetic Risk and Deterioration Syndrome
E. Schizotypal personality disorder

Self-Assessment Question

Based on data from the last 10 years, estimates of the percentage of individuals who meet criteria for clinical high risk for psychosis who are likely to develop a psychotic disorder within two years is:

A. 10%
B. 30%
C. 40%
D. 50%
E. 60%

Transition Risk to Psychosis Over Time (N=27, n=2502)



No. of Studies	Follow-up, mo	Transition Risks, 95% CI
9	6	17.7 (12.3-24.9)
13	12	21.7 (16.6-27.8)
4	18	26.9 (19.5-35.9)
12	24	29.1 (23.2-35.7)
6	36	31.5 (23.8-35.0)
4	>36	35.8 (29.6-42.5)

$P<.001$ for all.

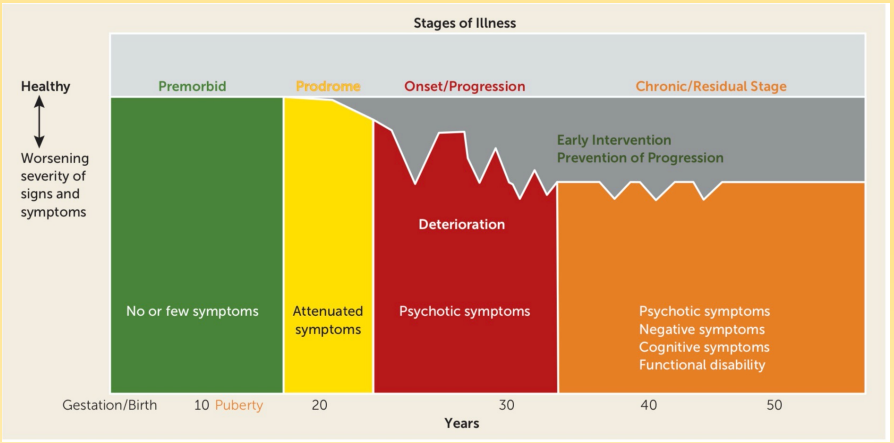
Fusar-Poli P. et al. Arch Gen Psychiatry. 2012 ;69(3):220-229.

The answer is A, 30%. The first studies in the 1990s found higher conversion rates, however these have dropped and most early psychosis centers now report between 20-30% of the general group of clinical high risk subjects convert within two years.

Studies looking exclusively at individuals under 18 are reporting lower rates of conversion, between 15-20%

Clinical staging approach for early psychosis

- Clinical staging used broadly in medicine
- Expand diagnosis to include where person is along course of development of disorder
- Framework allow more specific tailoring of intervention to specific stages[1]



Clinical Stage		Definition	Intervention
0	Premorbid	Asymptomatic Genetic Risk	Improve mental health literacy Family psychoeducation
1a	CHR-P	Negative and Cognitive sx	As above plus reduction of substance misuse
1b	CHR-P	Attenuated psychotic sx	Add vocational support, psychological therapies; treat comorbid conditions
1c	CHR-P	Brief psychotic episodes	Add close monitoring
2	Early full recovery	Full-threshold FEP	Add atypical antipsychotics and other medications; vocational rehabilitation
3a	Late/Incomp. Recovery	Single relapse	Add more emphasis on relapse prevention, early warning signs
3b	Late/Incomp.Recovery	Multiple relapses	Add emphasis on long-term stabilization
3c	Late/Incomp. Recovery	Incomplete recovery	Consider clozapine in case of treatment resistance
4	Chronicity	Severe, unremitting	Emphasis on social participation

Outline

- Overview of early psychosis
- Evaluation
- Intervention
- Take-homes and local resources

Formulation

- Biological
- Psychological and developmental factors
- Social and cultural factors
- Spiritual
- Important to find out how young person, family, or other support figures understand symptoms

Evaluation for psychosis

- Screening tools
  - Prodromal Questionnaire-Brief (PQ-B) – 21 item – large research base – ages 12 and up; recently validated version for individuals under 12[2]
  - Prime screen: 12 and 5 item versions
  - Others
- Positive screen to be followed by in-depth assessment such as SIPS (Structured Interview for Psychosis-Risk Syndromes) to assess psychotic symptoms
- Clinical evaluation to rule out other possible medical contributors and differential diagnosis

Please indicate whether you have had the following thoughts, feelings and experiences **in the past month** by checking "yes" or "no" for each item. **Do not include experiences that occur only while under the influence of alcohol, drugs or medications that were not prescribed to you.** If you answer "YES" to an item, also indicate how distressing that experience has been for you.

1. **Do familiar surroundings sometimes seem strange, confusing, threatening or unreal to you?**

   ☐ **YES** ☐ **NO** ***If YES:*** When this happens, I feel frightened, concerned, or it causes problems for me:

   ☐ Strongly disagree ☐ disagree ☐ neutral ☐ agree ☐ strongly agree

2. **Have you heard unusual sounds like banging, clicking, hissing, clapping or ringing in your ears?**

   ☐ **YES** ☐ **NO** ***If YES:*** When this happens, I feel frightened, concerned, or it causes problems for me:

   ☐ Strongly disagree ☐ disagree ☐ neutral ☐ agree ☐ strongly agree

Outline

- Overview of early psychosis
- Evaluation
- Intervention
- Take-homes and local resources

Self-Assessment Question

Which one might be best initial intervention for Joshua?

A. Aripiprazole 2mg
B. Dialectical behavior therapy
C. Escitalopram 10mg
D. Psychoeducation for Joshua and his family
E. Methylphenidate, long-acting 27mg on prescription

Coordinated specialty care (CSC)

- Family psychoeducation
- Individual therapy, CBT for psychosis
- Supported employment, education
- Peer support
- Medication
- Substance use disorder treatment
- Case management

Supporting Function

- Supported employment
- Collaborating with schools to help student stay engaged
- Advocacy
  - Psychotic disorders are included in Individuals with Disability Act (IDEA) under Emotional Disturbance – consider Individual Education Plan IIEP)
  - Also may be eligible for 504 plan
- Occupational therapy
- Peer support
- Social interactions

Psychopharmacology

- First episode psychosis:
  - Low dose antipsychotic
  - Several antipsychotics approved by FDA down to age 13
  - Young people more likely to have more severe weight gain, metabolic effects
  - Long acting injectables can be a treatment option early in course

Research

JAMA Psychiatry | Original Investigation

Effect of Long-Acting Injectable Antipsychotics vs Usual Care on Time to First Hospitalization in Early-Phase Schizophrenia

A Randomized Clinical Trial

John M. Kane, MD; Nina R. Schooler, PhD; Patricia Marcy, BSN; Christoph U. Correll, MD; Eric D. Achtyes, MD; Robert D. Gibbons, PhD; Delbert G. Robinson, MD

- PRELAPSE trial of LAI vs oral medication
- Aripiprazole once monthly compared to clinician choice
- 489 participants aged 18-35 across 39 clinical sites
- Primary outcome: time to first hospitalization
- Only 14% of potential participants declined participation because of possibility may receive long acting injectable

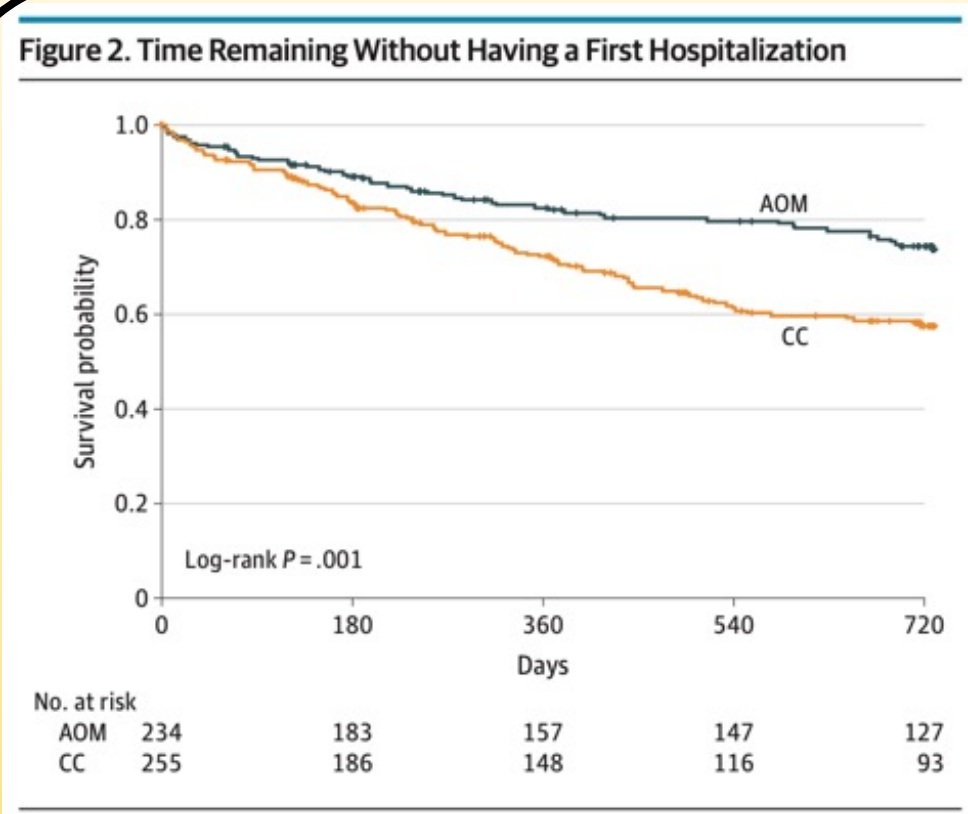


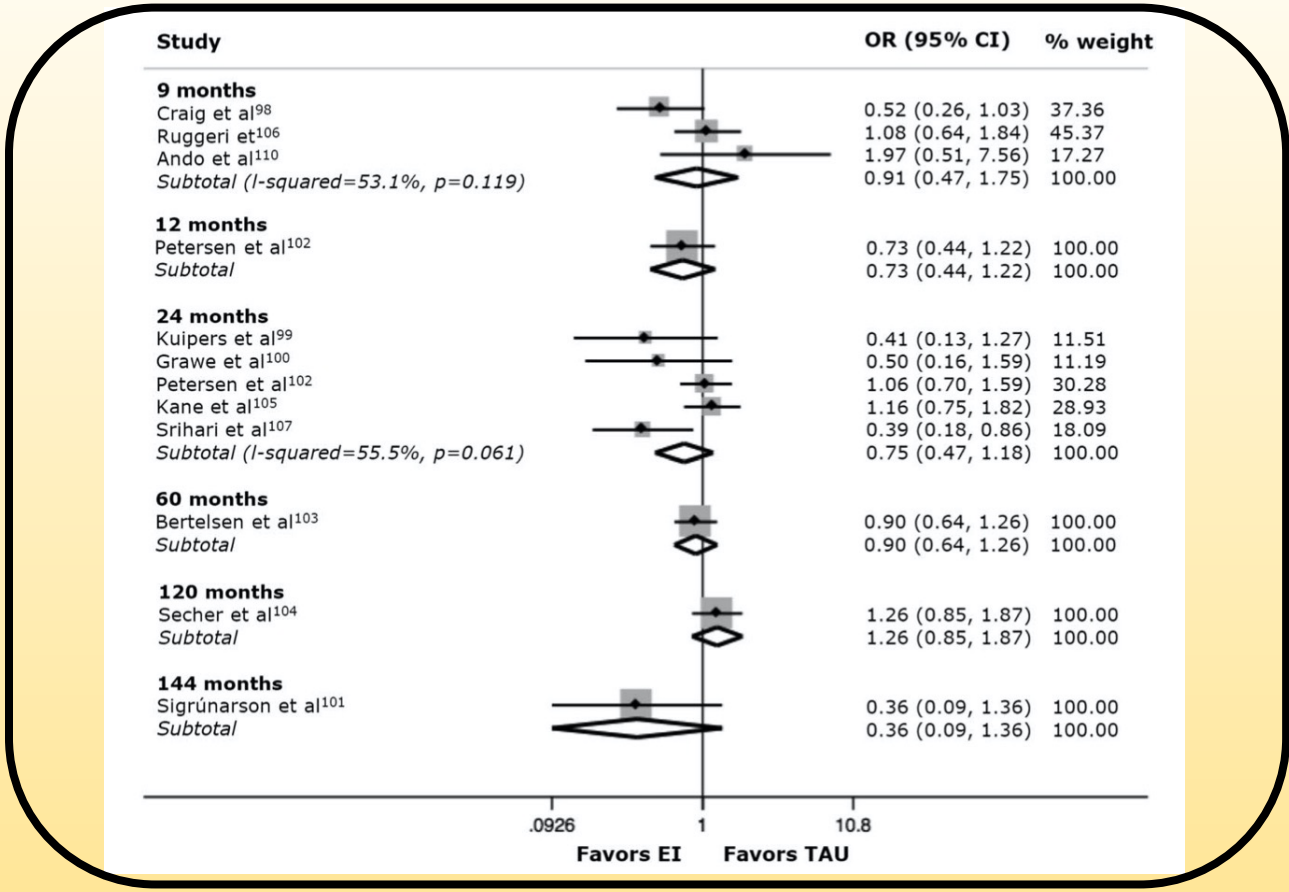
Figure 2. Time Remaining Without Having a First Hospitalization

Log rank test $\chi^2 = 11.373$; df = 1; $P < .001$. AOM indicates aripiprazole once monthly; CC, clinician's choice.

Kane et al, JAMA Psychiatry 2020:77(12);1217-1224

Coordinated specialty care

- FEP good initial response often followed by lack of adherence to treatment
- Differences in outcomes related to psychosocial aspects
- Meta-analysis of 12 trials comparing coordinated specialty care to standard care: decreased risk of relapse



Intervention	9 months (95% CI)	24 months (95% CI)	10 years (95% CI)
Standard care	14% (10-20%)	49% (29-69%)	76% (53-90%)
Coordinated specialty care	17% (13-21%)	38% (14-66%)	54% (36-70%)

Fusar-Poli et al, Improving outcomes of first-episode psychosis: an overview. World Psychiatry 2017;16:251-265

Enhancing engagement

- Attention to developmental issues
- Involving family or other support figures from the beginning
  - How do they interpret the symptoms?
- Improving adherence:
  - Offer a choice of antipsychotic wherever possible – aim for a joint agreement with patient and family
    - Choice of medication
    - Desired outcomes and how can be achieved
  - Keep as simple as possible
  - Close monitoring and quickly addressing side effects
  - Asking patient regularly how much of medication they have taken recently; their views on how well it is working and side effects
- If wish to discontinue; high but not 100% rate of relapse; work with pt/family around goals, gradual discontinuation

Current recommendations for CHR-P

- Coordinated specialty care
- Antipsychotics not first line treatment
- Low dose antipsychotic may be considered
  - If attenuated symptoms severe/frequent and distressing
  - If no response to psychosocial intervention
  - Treat as a brief intervention. Discuss this at outset with patient, family.
  - Current recommendations to choose based on side –effect profile, individual considerations
  - No medications have FDA indication for attenuated psychosis

Important to treat co-morbid conditions

- North American Prodrome Longitudinal Study (NAPLS-2): 744 CHR youth and 276 health controls, mean age 19yrs
- **Depression, anxiety** highest rates

Clinical high risk vs healthy controls

	CHR	HC	χ^2
	n = 744 (%)	n = 276 (%)	
Current SCID diagnoses			
Depression disorder	316 (42.5)	4 (1.4)	157.66***
Bipolar disorder	50 (6.7)	0 (0.0)	19.53***
Alcohol misuse	24 (3.2)	0 (0.0)	9.13**
Cannabis misuse	38 (5.1)	2 (0.7)	10.28**
Other substances misuse	7 (0.9)	0 (0.0)	2.62
Obsessive-compulsive disorder	51 (6.9)	0 (0.0)	19.94***
Post-traumatic stress disorder	16 (2.2)	0 (0.0)	6.04*
Anxiety disorder	355 (47.8)	11 (4.0)	176.69***
Somatoform disorder	8 (1.1)	0 (0.0)	3.0
Paraphilia	8 (1.1)	0 (0.0)	3.0
Eating disorder	9 (1.2)	0 (0.0)	3.37
Learning disorder	49 (6.6)	2 (0.7)	14.61***
Attention deficit hyperactivity disorder	130 (17.5)	5 (1.8)	43.16***
Developmental disorder	19 (2.6)	0 (0.0)	7.21**
Oppositional defiance disorder	22 (3.0)	1 (0.4)	6.17*

Addington et al, Comorbid diagnoses for youth at clinical high risk of psychosis, Schiz Res 2017;190:90-95

Which one might be best initial intervention for Joshua?

A. Aripiprazole 2mg
B. Dialectical behavior therapy
C. Escitalopram 10mg
D. Psychoeducation for Joshua and his family
E. Methylphenidate, long acting 27mg on prescription

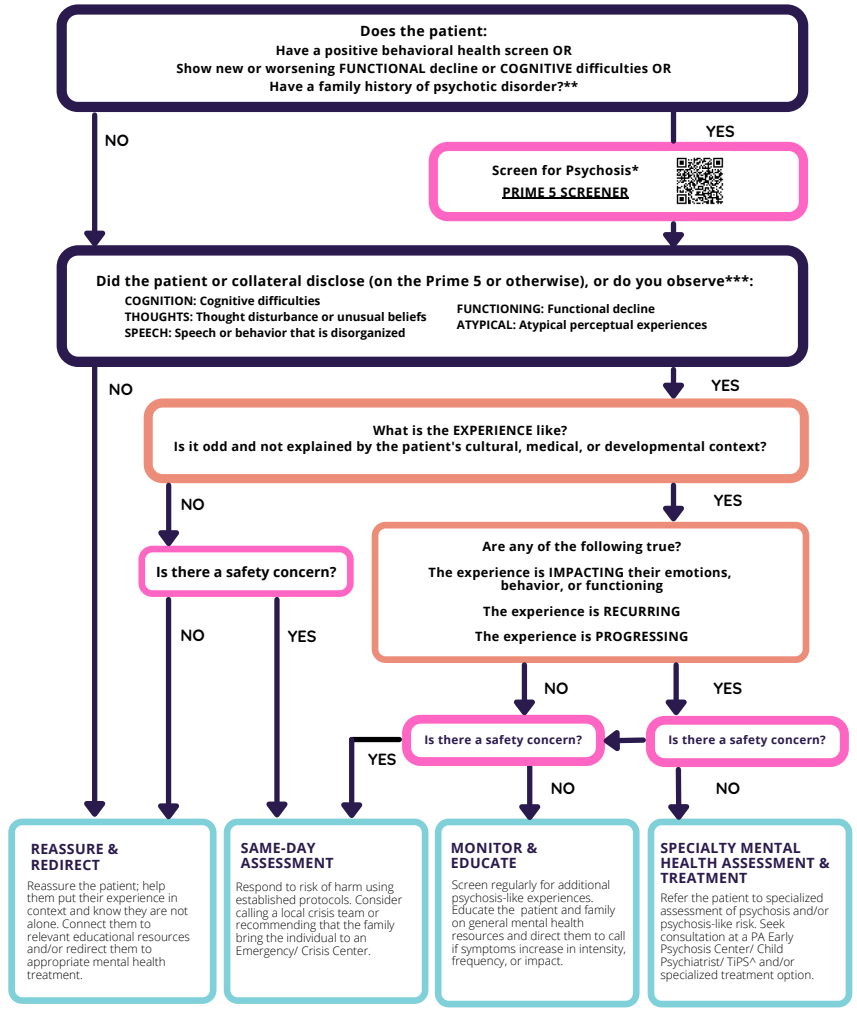
Outline

- Overview of early psychosis
- Evaluation
- Intervention
- Take-homes and local resources

HeadsUp

FLOWCHART FOR EARLY PSYCHOSIS SCREENING FOR PEDIATRICIANS & PRIMARY CARE CLINICIANS

AGES 11-35*



*

AGE CONSIDERATION: Early psychosis screening is recommended for 11-35 year olds; outside this range new-onset primary psychotic disorders are rare and different assessment approaches and referrals may be needed.

**

FAMILY HISTORY: Patients with a first/ second degree relative with a psychotic disorder should receive REGULAR SCREENING for psychosis-like symptoms regardless of mental health status. Use the "MONITOR & EDUCATE" path in the absence of other psychosis risk indicators.

***

FUNCTIONING: Marked decline in performance at school/work and/or typical activities, withdrawal, changes in sleep patterns.

ATYPICAL: Seeing things not there: e.g., shadows, flashes, figures, people, or animals. Hearing things others do not: e.g., clicking, banging, wind, mumbling, or voices. Seeing or hearing everyday experiences as unfamiliar, distorted, or exaggerated.

COGNITION: Memory, attention, organization, processing speed. Understanding abstract concepts, social cues, complex ideas.

THOUGHTS: Unwarranted suspiciousness about friends, family or strangers. Unfounded concern something is wrong with their bodies. Thinking that their body or mind has been altered by an external force. Believing others can read their mind or control their thoughts.

SPEECH: Trouble putting thoughts into words. Speaking in jumbled or hard to follow sentences. Dressing inappropriately for the weather or behaving oddly.

Adapted with permission from psychosisscreening.org

HeadsUp-pa.org

PRIME SCREEN–REVISED-5

to be administered by the provider

The following questions ask about your personal experiences. We ask about your sensory, psychological, emotional, and social experiences. Some of these questions may seem to relate directly to your experiences and others may not. Based on your experiences **within the past year,** please tell me how much you **agree or disagree** with the following statements. Please listen to each question carefully and tell me the answer that best describes your experiences.*

		Definitely Agree	Somewhat Agree	Slightly Agree	Not Sure	Slightly Disagree	Somewhat Disagree	Definitely Disagree
1	I think that I have felt that there are odd or unusual things going on that I can't explain.	6	5	4	3	2	1	0
2	I have had the experience of doing something differently because of my superstitions.	6	5	4	3	2	1	0
3	I think that I may get confused at times whether something I experience or perceive may be real or may be just part of my imagination or dreams.	6	5	4	3	2	1	0
4	I think I might feel like my mind is "playing tricks" on me.	6	5	4	3	2	1	0
5	I think that I may hear my own thoughts being said out loud.	6	5	4	3	2	1	0

*Note: Individuals can be shown a copy of this scale to assist in responding:

Definitely Agree	Somewhat Agree	Slightly Agree	Not Sure	Slightly Disagree	Somewhat Disagree	Definitely Disagree
6	5	4	3	2	1	0

There are **2 ways** to score the PRIME-5. Either way suggests a fuller evaluation for subthreshold or threshold psychosis symptoms should be considered:

1) Sum of the 5 items. To score, sum items 1-5 to obtain a total. Find the individual's age, then look at their PRIME-5 Score. A person scoring at or above the PRIME-5 score has endorsed a level of symptoms that is 2 standard deviations higher than the mean of others his/her/their age.

Age	11	12	13	14	15	16	17	18	19	20	21+
PRIME-5 Score	19	18	17	16	15	15	15	15	13	15	13

OR

2) Traditional Criteria. >=One item rated 6 (Definitely Agree) OR >=three items rated 5 (Somewhat Agree) is considered significant (i.e., warranting consideration of fuller evaluation).

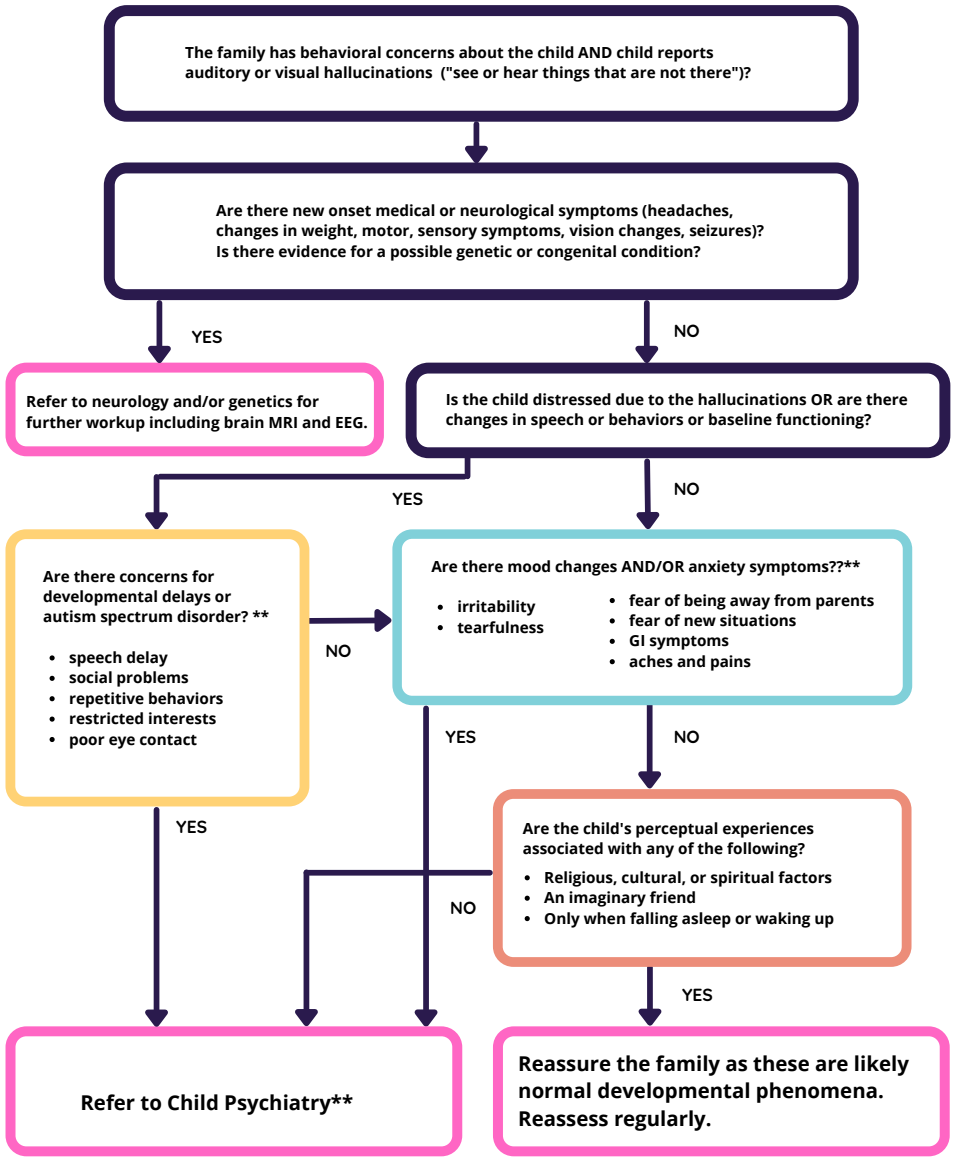
Reference: Calkins, M.E., Taylor, J., White, L., Moore, T.M., Moxam, A., Ruparel, K., Wolf, D.H., Kohler, C., Gur, R.C., Gur, R.E. (2021). "Norming" psychosis spectrum symptom endorsements: Age, sex and race standard scores for a brief screening tool in youth, in preparation.

HeadsUp

FLOWCHART FOR EARLY PSYCHOSIS SCREENING FOR PEDIATRICIANS & PRIMARY CARE CLINICIANS

AGES 10 & UNDER

ALL Safety concerns; use crisis resources & consult with Child Psychiatry



Internal:
Sandra Naigle
272:3602 (phone)
272-9843 (fax)
sanaigle@salud.unm.edu
Powerchart adhoc

External:

505-272-7806

Serving individuals…

- **Between ages 12-25**
- **Living in Bernalillo County and surrounding areas**

&

- **Determined to be at Clinical High Risk of Psychosis using the SIPS**

Serving individuals…

- Between ages 15-30
- Living in New Mexico

&

- Experiencing a first episode of psychosis within the past 12 months

Internal:
Dawn Halperin
272:3602 (phone)
272-9843 (fax)
dhalperin@salud.unm.edu
Powerchart adhoc

External:

1 (888) NM – EARLY
or
1 (888) 663 – 2759

What's next?

- Addressing heterogeneity
  - Stratification for treatment response, predicting outcomes
- Improving detection of early psychosis
  - More efficient screening and assessment tools
- Youth-friendly delivery methods and interventions
- New therapeutics

Resources

- National Association of State Mental Health Program Directors has extensive information and links regarding early psychosis on their website, https://www.nasmhpd.org/content/early-intervention-psychosis-eip
- IEPA Early Intervention in Mental Health Association; http://iepa.org.au
- International Physical Health in Youth Stream (IphYs) of IEPA Early Intervention in Mental Health – algorithms and other resources www.iphys.org.au
- PEPPNET: national network of early psychosis providers with active listserve and links to webinars: https://med.stanford.edu/peppnet.html
- AACAP Practice Parameter for the Assessment and Treatment of Children and Adolescents with Schizophrenia, DOI: https://doi.org/10.1016/j.jaac.2013.02.008

References

1. McGorry et al, *ANZJP* 2006;40:616-622
2. Loewy R et al, Schiz Research 2011;129(1):4-246
3. Karcher et al, JAMA Psychiatry 2018;75(8):853-861
4. Miller et al, Schizophr Res 2004;70(1):78
5. Brodey et al, Schizophr Res 2019;208:390-396
6. Miller et al, Schiz Bulletin 2003; 29(4):703-715
7. Florance et al, Ann Neurol 2009; 66(1):11-18
8. Engen et al, Front Psychiatry 2020;11:666
9. DeVoe et al, Early Interv Psychiatry 2019; 13(1):3-17
10. Woods et al, Schizophrenia Bulletin 2017;43(Suppl1):S58
11. McGlashan et al, American J of Psychiatry 2006;163:790-799.
12. McGorry et al, J Clinical Psychiatry 2013; 74(4):349-356
13. Amminger et al, Arch Gen Psychiatry 2010; 67:146-154
14. McGorry et al, JAMA Psychiatry 2017;74:19-27
15. Amminger et al, Biological Psychiatry 2020;87:243-252
16. Lally et al, Psychological Medicine 2016;46:3231-3240
17. Jauhur et al, Molecular Psychiatry 2018;24:1502-1512
18. Barnes et al, *J Psychopharmacology* 2019;34(1) 3-78
19. Thien et al, Schiz Res 2018;199:374-379
20. Boarati et al, CNS Disord 2013;15(3)
21. Fabrega et al, Ther Adv in Psychopharm 2015;5(5):304-306
22. Robinson et al, JAMA Psychiatry 1999;56(3):241-247
23. Bowtell et al, Schiz Res 2018;195:231-236