

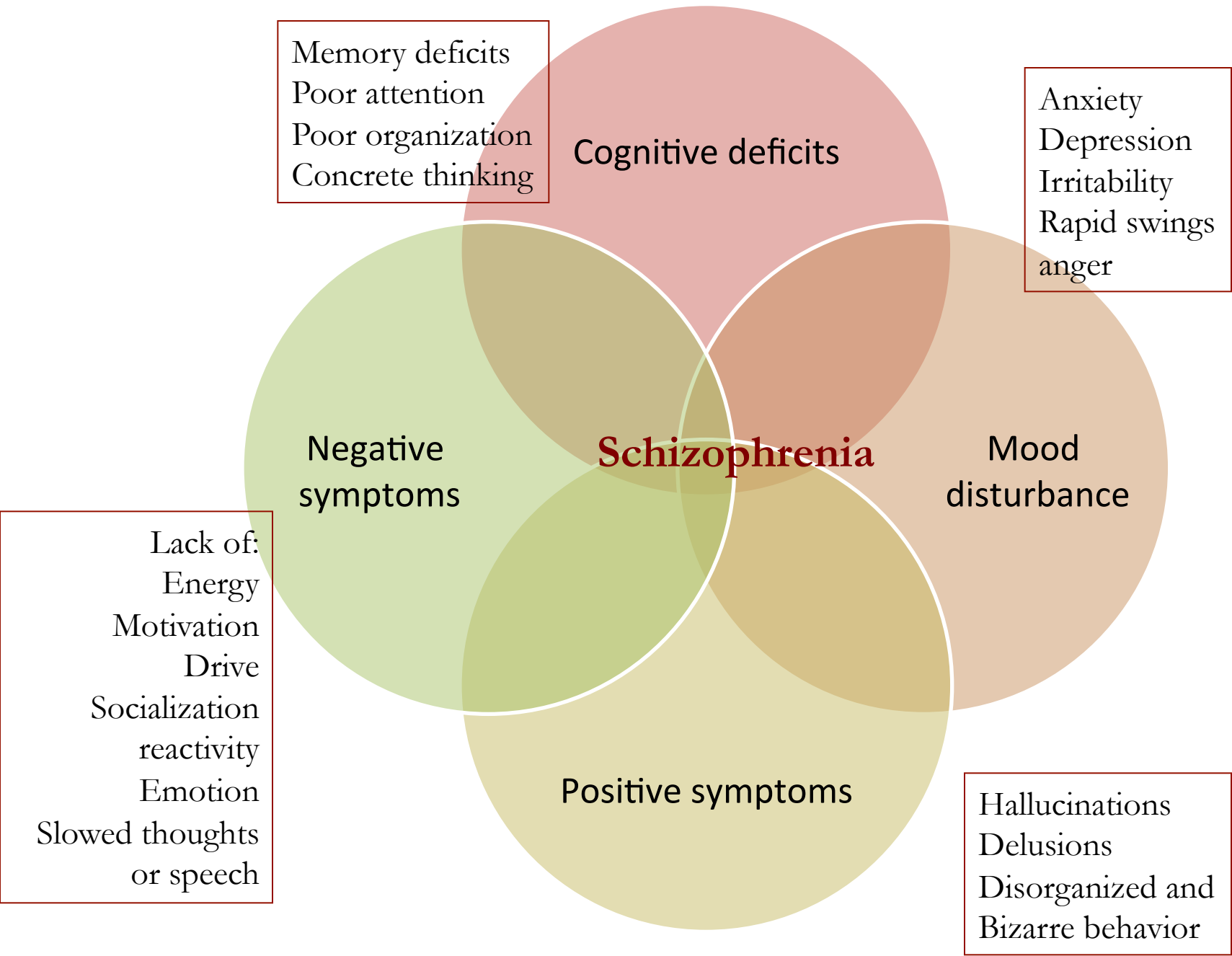
# Clinical Staging and the At-Risk Phase of Psychotic Disorder

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*Key Findings in Early Psychosis Knowledge Sharing Initiative  
Nova Scotia Early Psychosis Network*

DEPARTMENT OF PSYCHIATRY  
*Celebrating 65 years*  
1949-2014

 **DALHOUSIE**  
**UNIVERSITY**  
*Inspiring Minds*  
Faculty of Medicine



- Common among prison and homeless populations

- 80% will abuse substances during their lifetime

- 15-25x more likely to die from a suicide attempt than the general population

- 10% of patients die from suicide most often in the

- More hospital beds in Canada are occupied (8%) by people with schizophrenia than by sufferers of any other medical condition

**“Youth’s Greatest Disabler”**

World Health Report 2001 (WHO, 2002) schizophrenia and other forms of psychoses affecting **young people** rank **third** worldwide as the most disabling condition



If left untreated, there is a **continuing slow increase in impairment for years**

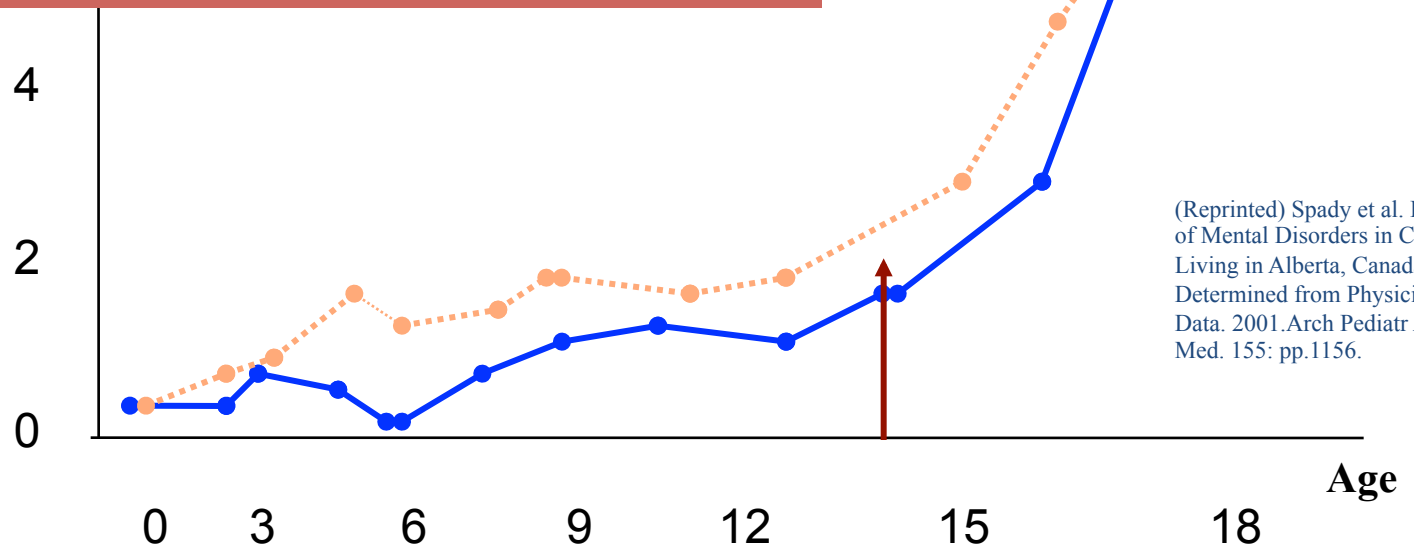
# Prevalence of Psychotic spectrum disorders per 1000 children/ adolescents

In males particularly, schizophrenia is a major disorder of adolescence

Hits adolescents in their prime – leads to a disruption in education-attainment, career building, employment

Alters relationships, family interactions, support

Alters sense of self, esteem, productivity



(Reprinted) Spady et al. Prevalence of Mental Disorders in Children Living in Alberta, Canada, as Determined from Physician Billing Data. 2001. Arch Pediatr Adolesc Med. 155: pp.1156.

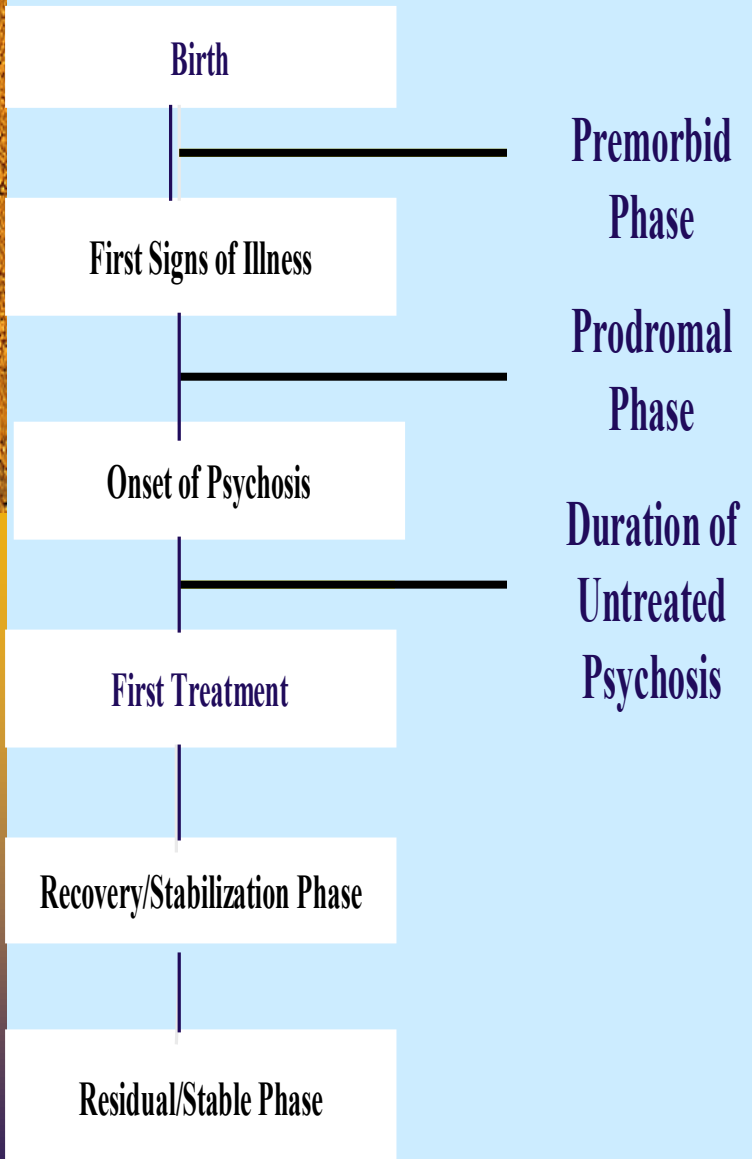
# Early Detection of Serious Mental Disorder

- Similar to familiar medical illnesses such as cancer, early detection of signs of illness prior to the development of a full neuropsychiatric disorder provides an exciting opportunity for prevention and rehabilitation.
- This is the standard for international early psychosis programs
  - Reducing the duration of untreated psychosis
    - Antipsychotic medication
    - Psychosocial and psycho-educational supports to patient and family
    - Psychotherapy & support
- Providing more comprehensive stage-specific treatment gives better results than generic 'treatment as usual' .
  - But enhanced outcomes requires ongoing stage-specific specialized treatment programs throughout the critical period.

- A substantial amount of the disability for which schizophrenia is heralded begins in the earliest stage of illness. For some, this is soon after puberty *prior* to the onset of identifiable psychotic symptoms (Hafner et al, 1995)
- This period of growing functional impairment is now referred to as the *prodrome* (retrospective) **or clinical high risk phase**\_(prospective)
- Focused effort exists now to identifying those at risk *before they convert* to reduce the morbidity and mortality associated with the onset of this illness and perhaps even delay its onset.



# Phases of Illness



# Early Detection of Serious Mental Disorder

- Akin to heart disease and cancers, psychotic disorders such as schizophrenia follow a staging process in terms of illness progression with the earliest signs of illness possibly being identifiable even before the onset of florid symptoms
- The earliest signs are also possibly the less severe or subclinical symptoms of illness that have the potential to progress
- Implications
  - Intervention (most appropriate and least invasive)
  - Prevention (indicated)

## How to identify those “at risk”:

- Criteria have been introduced for the prospective identification of people at increased risk for developing schizophrenia
  - Based on a combination of genetic risk for psychosis, the presence of attenuated symptoms and evidence of functional decline related to the symptoms
  - Studies have suggested that about 20-35% of those meeting these criteria will transition from the attenuated phase to the first episode psychotic phase of schizophrenia without treatment
    - Studies suggest the criteria are valid and reliable for predicting psychosis onset in this population



## How do we identify youth at risk?

### ■ Genetic High Risk

- No relatives with psychosis: 1-3%
- Sibling of someone with psychosis: 10%
- Child of one parent with psychosis: 13%
- Child of two parents with psychosis: 45%
- Monozygotic twin of someone with psychosis: 45-50%

### ■ Clinical High Risk (ultra high risk)

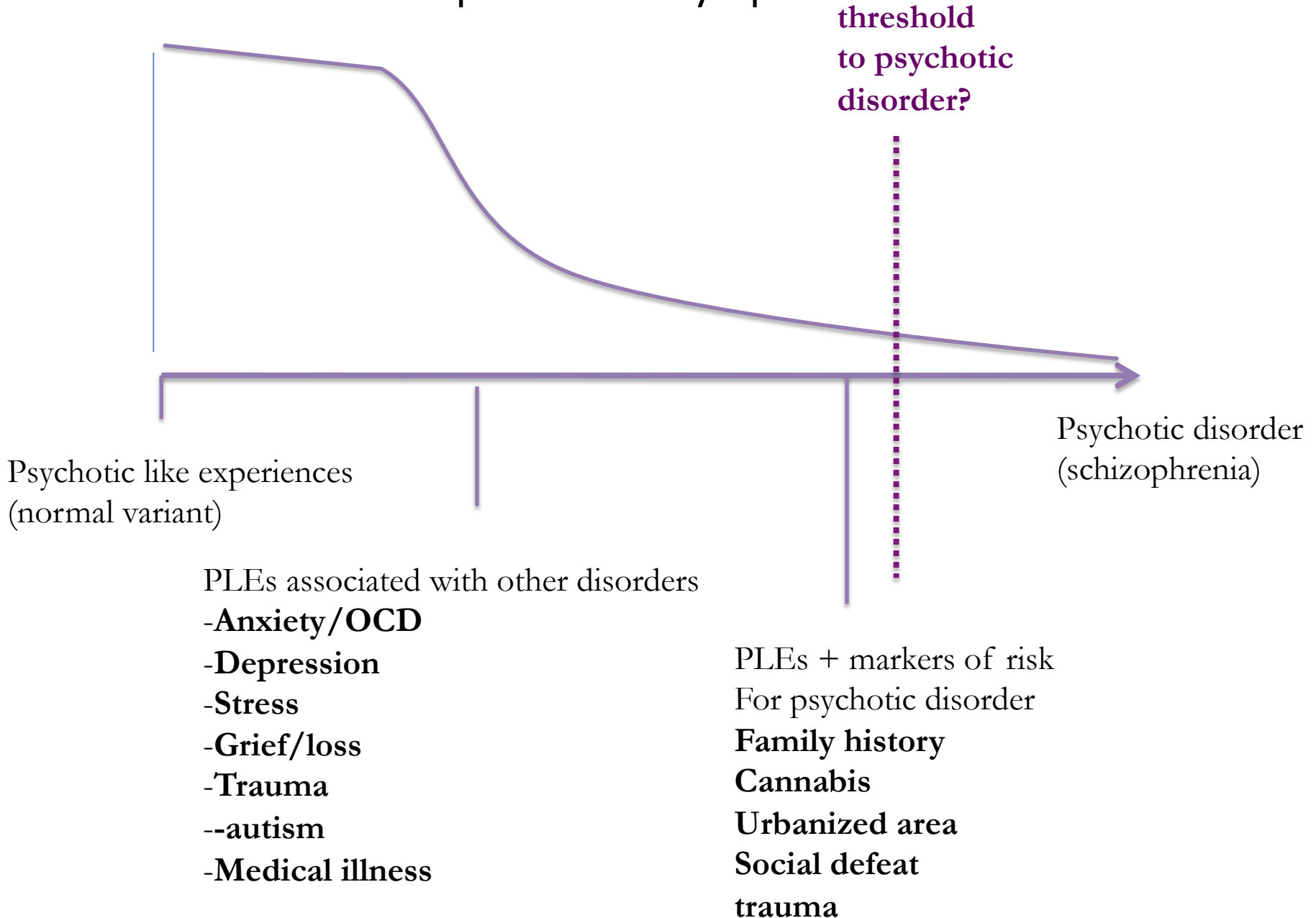
- Person has low level (sub-threshold or attenuated) psychotic experiences or brief limited psychotic experiences

### ■ Markers of functional decline

## How to identify those “at risk”:

- gene (G) X environment interaction (E) that increase susceptibility
- Psychotic outcomes are more associated with the following E risks:
  - **urbanized area**
  - **social defeat/marginalization**
  - **cannabis use**
  - **developmental trauma**
- **unusual thought content (vs perceptual disturbances)**
- risks now being further validated using prospective designs
  - **Social cognition** and **psychosis proneness**
- mental operations which guide social behavior and self in society
  - when impaired may result in psychotic symptoms
  - early childhood trauma may lead to abnormal development of this ability

# The psychosis continuum or spectrum of symptoms



- **What about the 80% who do not convert?**
  - Remit
  - Plateau
  - Convert at a later time
  - Develop another illness
- What is the significance of their psychotic experiences or PEs for which they are help-seeking?

- PEs seem to be more commonly reported in adolescents
- More than 75-90% are transitory phenomena

## **However...**

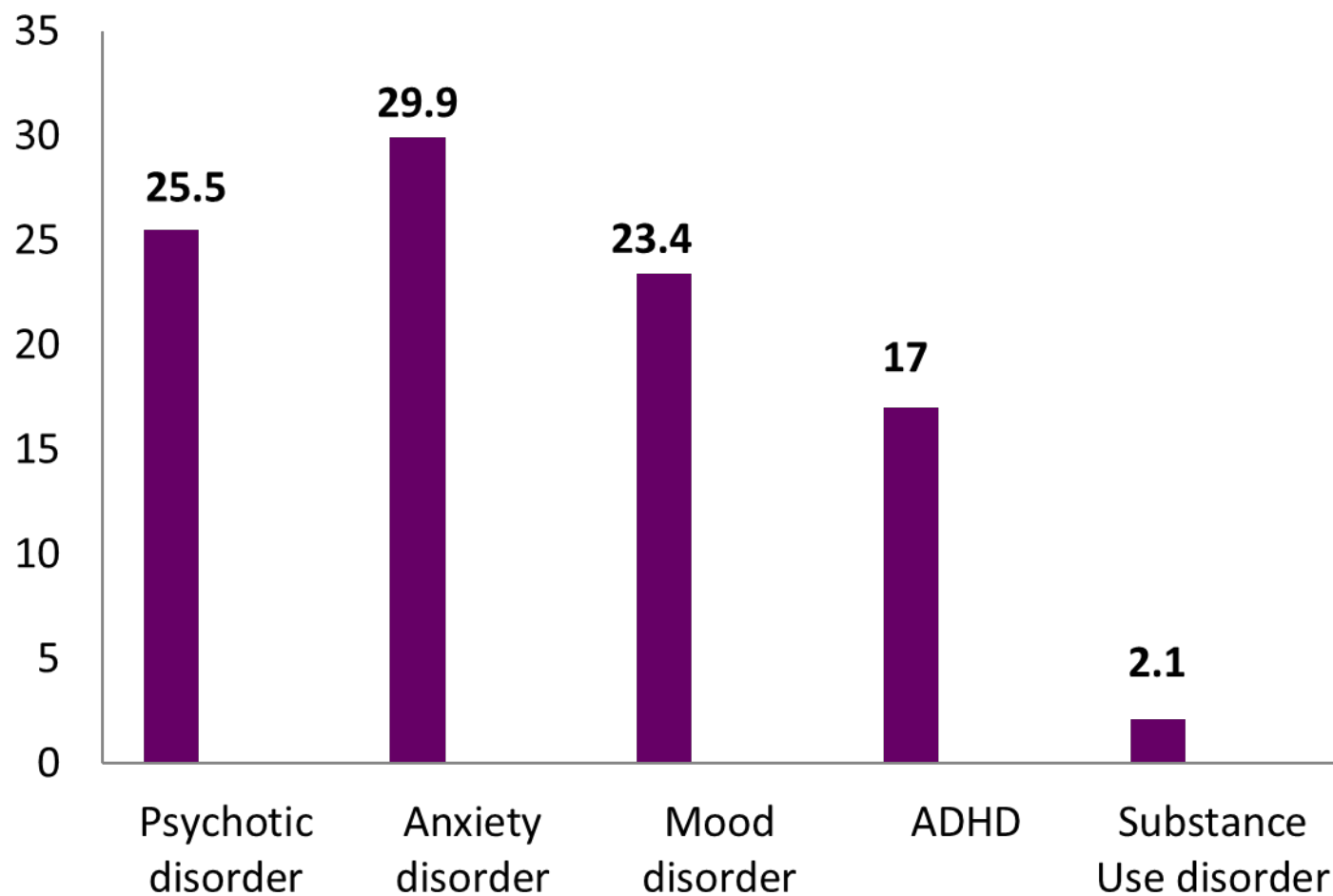
- One 15 year longitudinal study found that children with PEs have a roughly 5.1 greater chance of being diagnosed with schizophreniform disorder than those without PEs

## **The paradox is this:**

- ⦿ PEs do increase the risk of psychotic disorder (low prevalence) and yet are very common (high prevalence) in the community
- ⦿ How can we distinguish whose or which PEs confer increased at risk?
- ⦿ Do PEs confer increased risk for something else?

- In 2006 Yung et al. reviewed 140 patients between ages 15-25 who presented help seeking with PLEs to the early psychosis clinic.
- Used the Community Assessment of Psychic Experiences (CAPE), SCID and GAF.
- The 140 were identified to have clinical symptoms warranting attention but non psychotic.
  - 46% were found to have a current **mood** disorder
  - 42% were found to have a current **anxiety** disorder
  - 22% were found to have a **substance use** disorder
  - 11% were found to have an **eating disorder**
  - 11% were found to have a **disruptive behavior disorder**
    - Disorders may have been concurrent
  - Mean **GAF score was low** overall for the sample at 52.9

- Results at IWK Youth Psychosis (2010)
  - About 25% (N=47) were found to be in the first episode of a psychotic spectrum disorder (DSM-IV-TR criteria)



- Children/Youth with psychosis
- **Require ongoing focus**
  - Help-seeking
  - Unwell population
  - Heterogeneous population – PEs may herald other Axis I disorders
  - May also be at risk for worsening illness and progression to psychotic disorder



## Treatment (*indicated prevention*)

- Psychotherapeutic intervention
  - Cognitive behavioral therapy
  - Supportive therapy
  - Family therapy/education
  - Minimizing risk/monitoring
- Pharmacotherapeutic intervention
  - Antidepressant medication
  - Amino acids (glycine)
  - Omega – 3 FAs

- **Recommendations**

- No evidence at this time to use antipsychotic medicine in youth at risk
- Treating presenting problem may be indicated prevention
- Be vigilant – developing brain (critical period)
  
- Be mindful of known risk factors for development of illness (GxE interaction)
  - Cannabis
  - Isolation
  - Depression
  - Trauma
  
- **Continue research**
  - Avoids inappropriate treatment of youth with PEs
  - Avoids misdiagnosis
  - Enables us to one day intervene in the progression of serious mental illness

# Stage-specific approach to identification and treatment of results in better outcomes

- Clinical staging can provide a useful framework for understanding illness progression, identifying targets for intervention and improving illness outcome in persons with psychotic disorders
  - Research shows that in psychotic disorders
    - Pathology is more abnormal in the earlier stages
    - There is evidence of progression of pathology with transition through illness stages
    - Treatment is more effective and more benign in the earlier stages
    - **With earlier intervention progression to a first episode psychotic disorder may not be inevitable**



WHEN IS THE WORLD GOING TO REALIZE THAT  
WE KNOW EVERYTHING?!