Female Sex Moderates Association Between Asthma and Earlier Age of Onset in Schizophrenia and Bipolar Disorder

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5/3/2025

Disclosure

- Ian M. Michel has no disclosures to make.
- This study was supported, in part, by the Luther Automotive Foundation and Mayo Foundation; neither had a role in the design, conduct, analysis, or sub-mission of the study.

History of Asthma and Psychiatry

Dr. M. Murray Peshkin

Early thought on asthma viewed it as a psychosomatic disease

The establishment in Denver in 1940 of the National Home for Jewish Children, now the Children's Asthma Research Institute and Hospital, gave clinical expression to Dr. Peshkin's concepts of "intractable asthma" and "parentectomy."

In 1953, Dr. Peshkin reported that a major source of the persistent asthma suffered by 200,000 children in the nation was an unfavorable emotional environment in which the trouble was "mostly mama."

This understanding evolved as **IgE** was discovered in 1966-7 by two groups, one of which was located at the **Children's Asthma Research Institute and Hospital**, and jointly reported in 1969

Gervais L. Can Psychiatr Assoc J. 1966;11(6):497-500
Ishizaka T, et al. J Immunol. 1969;102(4):884-892..

History of Asthma and Psychiatry

- "During more recent decades, the persistent observation that symptoms of anxiety and depression occur frequently in patients with asthma has been the focus of considerable debate. If asthma was not a 'psychosomatic' disorder in the psychodynamic sense, then what was the explanation for the perception that these patients were more likely to have comorbid psychiatric symptoms?"
  - David Mrazek, Director of Pediatric Psychiatry at the National Jewish Center for Immunology and Respiratory Medicine and later Chair of the Department of Psychiatry and Psychology at the Mayo Clinic

Mrazek DA. Child Adolesc Psychiatr Clin N Am. 2003;12(3):459-471.

Background

- **Asthma**
  - Affects ~25 million people in the U.S.:
    - **6.5% of children**
    - **8.0% of adults**
  - Associated mental health findings:
    - ↑ Depressive and anxious symptoms in adolescents
    - **2x** increased risk of **anxiety** disorders
    - **Bidirectional** relationship with **depression**
    - Early adolescent asthma → ↑ risk of **major depression**

ADHD
- Significant association between asthma and **ADHD**

Childhood Trauma
- **Adverse childhood experiences** linked to asthma onset

Severe Mental Illness (SMI)
- ↑ Frequency of asthma in bipolar disorder (BD) and schizophrenia (SZ)
- Antecedent asthma is a risk factor for developing:
  - BD
  - SZ

CDC, Asthma Data 2023
Lu et al., 2012 (Pediatr Allergy Immunol)
Ye et al., 2021 (Psychol Med)
Choi et al., 2019 (J Allergy Clin Immunol Pract)
Chen et al., 2014 (J Psychiatr Res)
Kwon et al., 2014 (BMC Psychiatry)
Sun et al., 2021 (JCPP Adv)
Gaietto & Celedón, 2022 (Pediatr Pulmonol)
Wu et al., 2016 (Medicine [Baltimore])
Suetani et al., 2021 (Schizophr Res)
Lin et al., 2014 (J Affect Disord)
Wu et al., 2019 (Schizophr Bull)
Wang et al., 2017 (PLoS One)
Pedersen et al., 2012 (Schizophr Res)

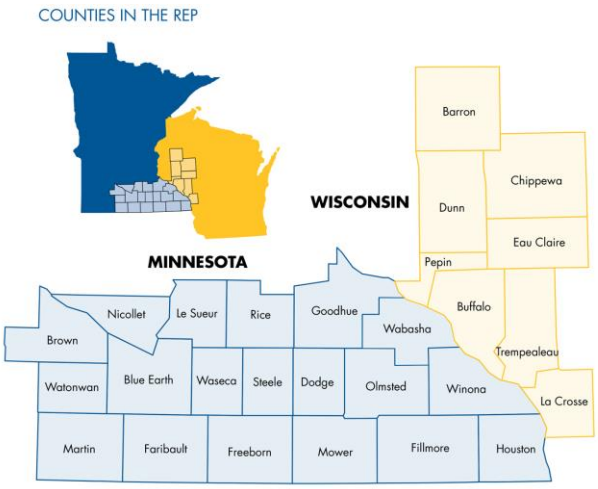
Objectives

1. To evaluate the differences in **antecedent illness trajectory** of **BD** and **SZ** with and without **antecedent asthma**.
2. Explore the potential **moderating** role of **sex** in the relationship between **asthma and BD and SZ**, particularly on **age of onset**.

Methods

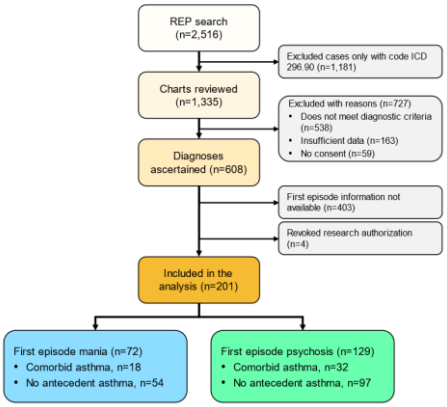
ROCHESTER EPIDEMIOLOGY PROJECT (REP)

- **Comprehensive medical records linkage system**
  - persons residing in Olmsted County, MN & surrounding counties (dynamic pop. 700,000)
  - continuously funded by NIH since 1966
  - data collected by healthcare professionals
- **The REP cohort addresses limitations**
  - observed in clinical series
  - referral bias
  - incomplete case ascertainment in administrative databases



Methods

- Patients with **first episode mania (FEM)** or **psychosis (FEP)** within the **REP**.
- **Demographics**, **psychiatric antecedents**, and **prior medical diagnoses** were collected.
- Antecedent asthma diagnoses were extracted by chart review and using ICD-9 and ICD-10 codes via REP record linkage system.



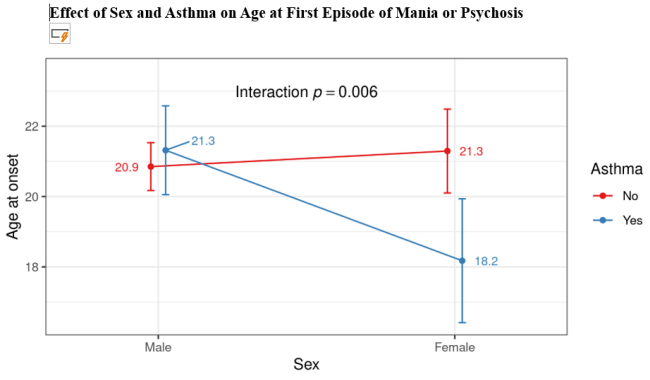
Results

- **Sample:** 201 patients with FEM (n=72) or FEP (n=129)
- Asthma **prevalence:**
  - **24.9%** (n=50) had a prior diagnosis of asthma
  - Compared to Minnesota's lifetime asthma prevalence: **12.0%**
- **No significant differences in asthma prevalence by**:
  - **Diagnosis**: 24.8% in bipolar disorder vs. 25.0% in schizophrenia (p=0.976)
  - **Sex**: 22.4% in males vs. 31.5% in females (p=0.189)
- Patients with asthma were more likely to have
  - **Any prior psychiatric diagnosis:** 88.0% vs. 68.9% (p=0.008)
  - Specifically **higher rates** of:
  - **ADHD**: 48.0% vs. 31.8% (p=0.038)
  - **Depressive disorders**: 70.0% vs. 47.7% (p=0.006)
  - **Anxiety disorders:** 48.0% vs 31.1% (p=0.030)

Characteristics	No Asthma (N=151)	Asthma (N=50)	p-value
	N (%)/ Mean (SD) or Median (IQR)	N (%)/Mean (SD) or Median (IQR)	
Age at First Episode, years	21.0 (3.5)	20.2 (4.3)	0.245
Duration of Antecedent Illness Trajectory, years	2.4 (0.0, 8.9)	5.3 (1.1, 12.2)	0.033
Antecedent Diagnoses			
Any Antecedent Diagnosis	104 (68.9%)	44 (88.0%)	**0.008**
ADHD	48 (31.8%)	24 (48.0%)	**0.038**
Intellectual Disability	7 (4.6%)	4 (8.0%)	0.365
Other Neurodevelopmental Disorder[1]	35 (23.2%)	19 (38.0%)	**0.040**
Depressive Disorder	72 (47.7%)	35 (70.0%)	**0.006**
Anxiety Disorder	47 (31.1%)	24 (48.0%)	**0.030**
Adjustment Disorders	39 (25.8%)	15 (30.0%)	0.564
Sleep-Wake Spectrum	13 (8.6%)	12 (24.0%)	**0.004**
Conduct Disorder	15 (9.9%)	6 (12.0%)	0.679
Oppositional-Defiant Disorder	12 (8.0%)	7 (14.0%)	0.205

CDC. https://www.cdc.gov/asthma/brfss/2020/tableL1.html.

Results



- **Females with asthma** had a significantly **lower mean age at first episode** (18.2 ± 3.8 years) compared to
  - **Females without asthma** (21.3 ± 3.8 years)
  - **Males without asthma** (20.9 ± 3.4 years)
  - **Males with asthma** (21.3 ± 4.1 years)

Discussion

- Evidence suggests that inflammatory processes play a critical role in the pathogenesis of mood disorders in women.
- **Earlier age of onset in females** suggests importance of
  - sex-specific inflammatory factors
  - hormonal factors
  - genetic predispositions
  - and psychosocial stressors.

- Study underscores:
  - **Increased psychiatric illness burden** in the period antecedent to FEM/P
  - **Asthma's** association with increased **psychiatric illness**.
- Future research should explore
  - Sex differences in inflammatory markers and disease outcomes.
  - Biological pathways linking asthma, inflammation, and psychiatric illness, particularly in women

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