

Likelihood of Mental Health Diagnoses Similar for Asthma Patients Prescribed Montelukast or Inhaled Corticosteroids

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Key Findings:

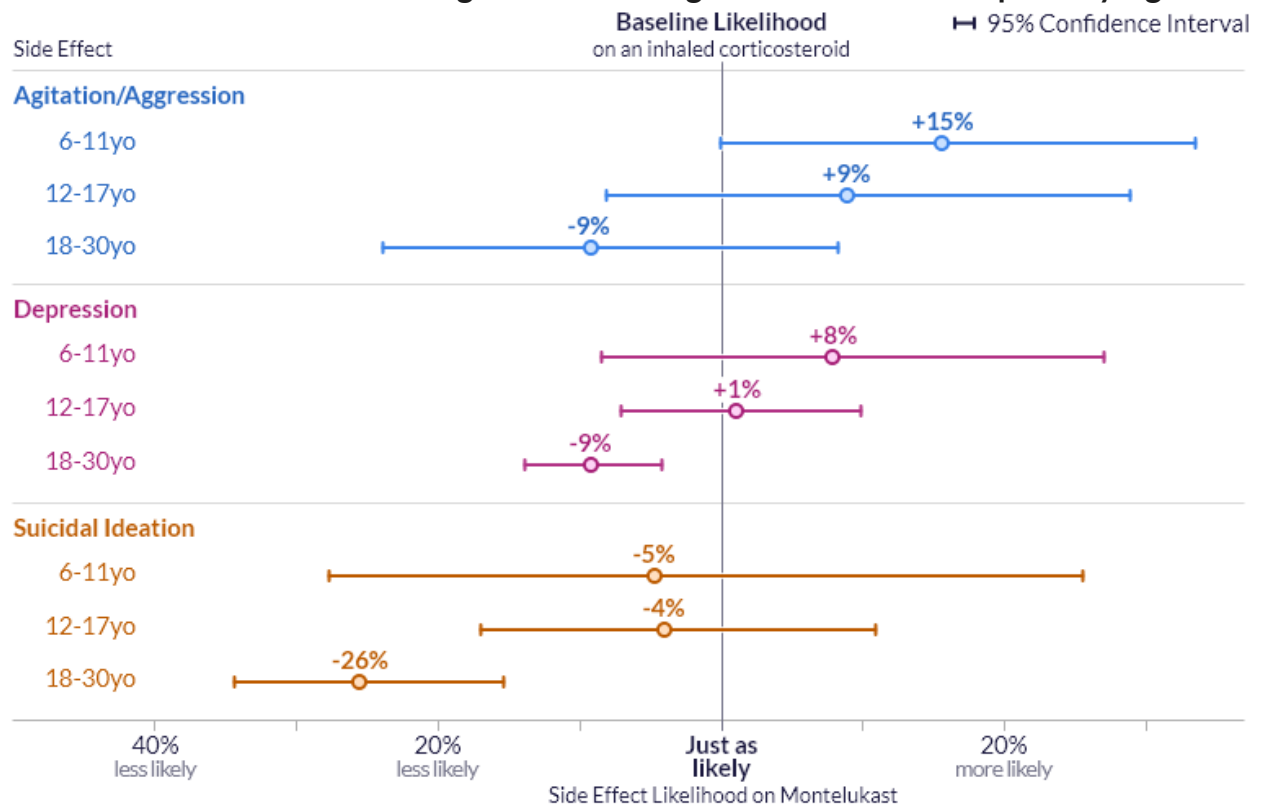
- Children aged 6 to 17 prescribed montelukast were slightly more likely to be diagnosed with suicidal ideation, depression, agitation, or aggression compared to those prescribed inhaled corticosteroids. However, that increase was not statistically significant.
- Adults aged 18 to 30 prescribed montelukast were less likely to be diagnosed with suicidal ideation or depression than adults prescribed inhaled corticosteroids.

In March 2020, the FDA issued a boxed warning for montelukast (brand name Singulair), a medication commonly used to treat allergies and asthma, citing potential mental health side effects, including changes in behavior and mood.¹ More recently, concern around these side effects has been raised by patients, their families, and the media, especially for children prescribed the medication.²

To understand the relationship between montelukast and these mental health side effects, we studied 2,596,595 million patients prescribed montelukast or an inhaled corticosteroid for the first time between January 2017 and December 2022. We then examined whether the patients had a documented diagnosis of agitation, aggression, depression, or suicidal ideation within 14 months following their initial prescription.

We found no significant difference in the likelihood of suicidal ideation, depression, agitation, or aggression for children aged 6 to 17 prescribed montelukast compared to those on an inhaled corticosteroid. The likelihood of agitation or aggression increased 15% among the 6- to 11-year-olds and 9% among the 12- to 17-year-olds on montelukast, though those increases were not statistically significant. Depression was 8% more likely in those aged 6 to 11 prescribed montelukast than in those of the same age prescribed inhaled corticosteroids, but this increase was also not statistically significant.

Likelihood of Mental Health Diagnoses Following Montelukast Prescription by Age



N=2,596,595 patients "Likelihood of Mental Health Diagnoses Following Montelukast Prescription by Age," 2024. EpicResearch.org

Figure 1. The likelihood of mental health side effects by age for patients prescribed montelukast compared to patients prescribed inhaled corticosteroids.

Among adult patients aged 18 to 30, the likelihood of depression was reduced by 9% and the likelihood of suicidal ideation was reduced by 26% compared to those on corticosteroids. Our findings may underrepresent the true incidence of these side effects as only those who sought care and received a diagnosis for the mental health condition were included.

These data come from Cosmos, a dataset created in collaboration with a community of Epic health systems representing more than 243 million patient records from 1,400 hospitals and more than 32,500 clinics from all 50 states and Lebanon. This study was completed by two teams that worked independently, each composed of a clinician and research scientists. The two teams came to similar conclusions. Graphics by Brian Olson.

References

1. FDA requires Boxed Warning about serious mental health side effects for asthma and allergy drug montelukast (Singulair); advises restricting use for allergic rhinitis. U.S. Food and Drug Administration. Published March 13, 2020. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-requires-boxed-warning-about-serious-mental-health-side-effects-asthma-and-allergy-drug>. Accessed March 13, 2024.
2. Jewett C, Mueller B. The F.D.A. Warned an Asthma Drug Could Induce Despair. Many Were Never Told. The New York Times. <https://www.nytimes.com/2024/01/09/health/fda-singulair-asthma-drug-warning.html>. Published January 9, 2024. Accessed March 13, 2024.

Data Definitions

Term	Definition
Study period	1/1/2017 to 12/31/2022
Study population	<p>Patients with an initial prescription for montelukast or an inhaled corticosteroid.</p> <p>Patients were excluded if they were prescribed an exclusion medication or if they had a diagnosis for an outcome of interest in the 12 months preceding the medication order.</p>
Montelukast	An order with a simple generic name of montelukast sodium.
Inhaled corticosteroids	<p>An order with a simple generic name of one of the following and a route of respiratory (inhalation):</p> <ul style="list-style-type: none"> • Beclomethasone dipropionate • Budesonide • Ciclesonide • Flunisolide • Fluticasone furoate • Fluticasone propionate • Mometasone furoate • Triamcinolone acetonide
Exclusion medications	<p>An order with a simple generic name of one of the following:</p> <ul style="list-style-type: none"> • budesonide/formoterol fumarate • Flunisolide/menthol • Fluticasone furoate/vilanterol trifenate • Fluticasone propionate/salmeterol xinafoate • Mometasone furoate/formoterol fumarate • Arformoterol tartrate • Formoterol fumarate • Indacaterol maleate • Indacaterol maleate/glycopyrrolate • Olodaterol HCl • Salmeterol xinafoate • Tiotropium bromide/olodaterol HCl • Zafirlukast • Zileuton
Outcomes	<p>A diagnosis within 14 months of beginning montelukast or alternative medication:</p> <ul style="list-style-type: none"> • Agitation – ICD-10-CM code R45.1, R45.3, or R45.86 • Aggression - ICD-10-CM code R45.6 or R45.5 • Depression - ICD-10-CM code F32*, F33*, or F39* • Suicidal ideation/attempt – ICD-10-CM code R45.851, T14.91
Confounders	<p>Age, sex, race/ethnicity, history of condition</p> <p>History of:</p> <ul style="list-style-type: none"> • Anxiety - SNOMED-CT code 197480006 • Hallucinations – R44* • Mania – F30*

Table 1. Likelihood of Mental Health Diagnoses Following Montelukast Prescription by Age

Outcome	Age Range	OR	Low CI 95%	High CI 95%
Agitation/Aggression	6 - 11	1.15	1.00	1.33
Agitation/Aggression	12 - 17	1.09	0.92	1.29
Agitation/Aggression	18 - 30	0.91	0.76	1.08
Depression	6 - 11	1.08	0.92	1.27
Depression	12 - 17	1.01	0.93	1.10
Depression	18 - 30	0.91	0.86	0.96
Suicidal Ideation	6 - 11	0.95	0.72	1.25
Suicidal Ideation	12 - 17	0.96	0.83	1.11
Suicidal Ideation	18 - 30	0.74	0.66	0.85