



What do Selena Gomez, Demi Lovato, and Mariah Carey have in common? These famous singers have all publicly disclosed they live with bipolar disorder, a challenging yet treatable mental illness.

While we all experience ups and downs, people with bipolar disorder experience mood swings known as manic and depressive episodes that significantly affect their ability to function in everyday activities and their relationships with others.

Bipolar disorder affects approximately 1% of people, typically begins in early adulthood, and has a chronic and relapsing course. But is it different in women compared with men?

Mind Over Matter® spoke with leading experts and reviewed studies to learn whether there are differences in bipolar disorder between the sexes in terms of prevalence, symptoms, diagnosis, associations with other conditions, and treatment responses.

Bipolar Disorder

IS IT DIFFERENT IN WOMEN?

BIPOLAR DISORDER DEFINED

Bipolar disorder, formerly called manic-depressive illness, is caused by an imbalance of chemical messengers in the brain. It is characterized by mood swings that may last for days, weeks, or months. It's certainly not a modern mental illness: the Greek physician and philosopher Hippocrates first described mania and melancholia in ancient times.

People experiencing a **manic episode** have an elevated or expansive mood and may have some of the following symptoms: more physical energy, less need for sleep, increased talking and moving, racing thoughts, anxiety, irritability, excessive anger, hallucinations and delusions, and an elevated sense of self-esteem. They may also engage in reckless or inappropriate behaviours.

A **depressive episode** is different from normal sadness. It involves intense, persistent, and pervasive feelings of hopelessness, despair, and frustration. The person affected can feel angry and irritable, have trouble sleeping, and experience a loss of energy and enthusiasm for usual activities.

They may also have consuming thoughts about worthlessness or attempting suicide, according to the Mood Disorders Society of Canada. In the Apple TV+ documentary *Selena Gomez: My Mind and Me*, Selena Gomez shared her struggles with negative voices in her head telling her she's not worthy and being hospitalized for a psychotic episode due to bipolar disorder. Bipolar disorders include a spectrum of conditions diagnosed by a psychiatrist.

Symptoms are highly individual and many overlap with other psychiatric disorders, especially major depressive disorder and schizophrenia.

The American Psychiatric Association's Diagnostic and Statistical Manual of Mental Disorders-5 defines the most common types of bipolar disorder as follows:

- **BIPOLAR I DISORDER:** individuals experience at least one manic episode and may also experience major depressive episodes that may exist with or without psychotic episodes; and
- **BIPOLAR II DISORDER:** individuals experience hypomanic and major depressive episodes that alternate in cycles and are typically less severe than bipolar I disorder.

BIPOLAR DISORDER CAUSES

Bipolar disorder is a complex and highly heritable psychiatric condition. Researchers have estimated the heritability of bipolar disorder to be more than 70%, meaning that inherited genetic factors are largely responsible for its development.

INHERITED GENES CONFER AN ELEVATED RISK OF DEVELOPING BIPOLAR DISORDER, BUT THEY ARE NOT DESTINY.

Non-genetic factors may also play a role. Physician and cancer researcher Dr. Siddhartha Mukherjee revealed his family's history of schizophrenia and bipolar disorder in his bestselling book *The Gene: An Intimate History*.

"Bipolar disorder is a complex disorder involving multiple genes, gene-environment interaction and chance," Mukherjee said in an interview with *Elle* magazine in 2016. "Although there is a hereditary component to it, it's not like there's one gene governing a certain type of mental illness."

Scientists have conducted genome-wide association studies and found thousands of genomic variants affecting bipolar disorder risk, including some overlapping with other severe mental illnesses.

For example, a study published in *Nature Genetics* in 2019 by the multinational Psychiatric Genomics Consortium Bipolar Disorder Working Group found 30 genetic variations affecting neurotransmitter function that were associated with the development of bipolar disorder. The researchers also found bipolar disorder I was strongly associated genetically with schizophrenia, driven by psychosis, and bipolar disorder II was strongly correlated with major depressive disorder.

MOST PEOPLE DIAGNOSED WITH BIPOLAR DISORDER HAVE A FAMILY HISTORY OF SEVERE MENTAL ILLNESS.

Dr. Louisa Sylvia, Associate Director of the Dauten Family Center for Bipolar Treatment Innovation at Massachusetts General Hospital and Associate Professor in the Department of Psychiatry at Harvard Medical School and colleagues found that 85% of 757 patients diagnosed with bipolar disorder reported having at least one first-degree relative with a history of bipolar disorder, major depressive disorder, psychotic disorder, substance abuse, or suicide.

Their research, published in the *Journal of Affective Disorders* in 2020, also found that people with a family history of mental illness tended to have more severe bipolar disorder and require more medications for treatment.

Most recently, a team of international researchers co-led by Dr. Duncan Palmer and Dr. Benjamin Neale at the Stanley Center →

for Psychiatric Research at the Broad Institute of Harvard and MIT identified the gene AKAP11 as a strong risk factor for both bipolar disorder and schizophrenia.

Their findings were published in *Nature Genetics* in 2022. While previous gene discoveries have played small roles in bipolar disorder risk, AKAP11 is the first gene that appears to have a more considerable impact.

Dr. Neale explained in a Broad Institute press release that while this variant doesn't contribute much to risk on its own, the discovery provides valuable insights into the roots of the disorder, how current treatments like lithium work, and holds potential for spurring research into new treatment targets.

SEX DIFFERENCES?

PREVALENCE

"Many people assume bipolar disorder is more common in women than men, but there's no appreciable difference in prevalence by sex or gender," said Dr. Abigail Ortiz, a clinician-scientist in the Campbell Family Mental Health Research Institute and Lead for the Bipolar Disorder Integrated Care Pathways at the Centre for Addiction and Mental Health in Toronto.



Major depression, which is different from bipolar disorder, is much more prevalent in women. That's likely where the misconception arises.

Dr. Bernardo Dell'Osso, Director of the Psychiatric Clinic of the Ospedale Luigi Sacco-Polo Universitario of Milan and colleagues recently found that bipolar disorder affects a higher proportion of women, 57 to 65%, based on their analysis of ten large studies conducted between 2011 and 2020.

IF YOU OR SOMEONE YOU KNOW IS IN CRISIS, GET HELP IMMEDIATELY:

CANADA:

Call 911 or text or call
Talk Suicide Canada at
833-456-4566

UNITED STATES:

Text or call 988 to reach
the 988 Suicide & Crisis
Lifeline

a rising trend for the disorder in women. However, Dr. Ortiz put this suggestion into perspective: "Study results are always going to be a bit biased because a disproportionate number of women participate in bipolar disorder studies."

SYMPTOMS & DIAGNOSES

There are some distinctions between women and men in bipolar disorder onset and symptoms, which in turn may affect diagnosis. "Women with bipolar disorder tend to have a depressive onset, experience more depressive episodes, and we tend to see them earlier and more frequently than men, making it trickier to diagnose," said Dr. Sylvia.



MEN TEND TO HAVE AN ELEVATED MOOD AT ONSET AND PRESENT FOR TREATMENT WHEN EXPERIENCING MANIA OR HYPOMANIA, WHICH OFTEN MAKES THEIR ILLNESS EASIER TO DIAGNOSE.

While bipolar I disorder affects men and women equally, women with bipolar II disorder are much more likely to experience more rapid cycling of episodes than men, according to the Depression and Bipolar Support Alliance.

COMORBIDITIES

"Women with bipolar disorder are more likely than men to be diagnosed with additional physical and psychiatric conditions, including thyroid disease, migraine, obesity, and anxiety disorders," said Dr. Sylvia. "But identifying these comorbidities showing up more often in women may trace to the fact that they seek care earlier and we follow them for a longer period than men."

Hormonal changes associated with menstrual cycles, postpartum, and menopause do not cause bipolar disorder but may exacerbate mood disorder symptoms, according to the U.S. Department of Health and Human Services' Office on Women's Health. For example, studies have found an association between bipolar disorder and premenstrual dysphoric disorder, a more severe form of premenstrual syndrome. "Understanding these associations is an area of ongoing research," said Dr. Sylvia.



WE KNOW THAT HAVING HORMONAL CHALLENGES CAN AFFECT THE COURSE OF A MOOD DISORDER, DEPRESSION, OR BIPOLAR DISORDER, BUT WHETHER YOU ARE MORE LIKELY TO HAVE HORMONAL ISSUES IF YOU HAVE A MOOD DISORDER IS UNCLEAR.

Bipolar disorder was linked with earlier and more severe cardiovascular disease more than a century ago. However, the connection has not been well understood, partly because the

onset of bipolar disorder typically occurs in adolescence or early adulthood and cardiovascular issues tend to develop much later.

Recently, investigators have been researching this connection to find insights that may lead to new treatment options and better outcomes for people with bipolar disorder. As a member of the Vascular Task Force of the International Society for Bipolar Disorders, Dr. Sylvia collaborated with investigators from Canada, the United States, and other countries on a literature review published in *Bipolar Disorders* in May 2020.

AMONG THEIR KEY FINDINGS WAS THAT INDIVIDUALS WITH BIPOLAR DISORDER WERE UNDER-TREATED FOR CARDIOVASCULAR DISEASE RISK FACTORS, INCLUDING OBESITY, HIGH BLOOD PRESSURE, AND DIABETES, AND THESE FACTORS WERE ASSOCIATED WITH INCREASED MORTALITY AND REDUCED COGNITIVE FUNCTION.

Their paper served as a call to action, shedding light on the increased cardiovascular mortality among individuals living with bipolar disorder in an era when deaths due to cardiovascular disease have decreased in the general population.

Dr. Ortiz recently published research into sex-specific relationships between bipolar disorder and cardiovascular disease risk. She and her Canadian research colleagues found a two- to three-fold stronger association in women versus men between bipolar disorder and cardiovascular disease risk factors, including rates of coronary artery disease, heart failure, and high blood pressure not caused by other conditions using data from a large U.K. biobank.

The association remained significant after adjusting for self-reported race, education, income, and smoking status. The findings appeared in the *Journal of Affective Disorders* in 2022.

"Seeing the higher risk rates for women was shocking and made me angry because many of my patients are young, economically disadvantaged, and are already dealing with bipolar disorder," said Dr. Ortiz.

"I hope our paper adds to increasing awareness that cardiovascular disease risk is a serious concern for women with bipolar disorder and that they are screened and followed more frequently for cardiovascular risk factors."

TREATMENT RESPONSES

Standard treatment for bipolar disorder is a combination of medications and psychotherapy. Medications may include mood stabilizers, antipsychotics, antidepressants, anti-anxiety medications, and anticonvulsants.

FINDING THE RIGHT DOSE AND COMBINATION OF MEDICATIONS CAN TAKE TIME BECAUSE SYMPTOMS VARY FROM PERSON TO PERSON.

"Treatment response does not depend on sex or gender; it's based on clinical characteristics and family history," Dr. Ortiz said. "For example, if someone has a well-defined episodic illness and a family history of bipolar disorder in a related parent who responded well to lithium, they will likely respond to lithium. Similarly, people experiencing psychotic symptoms during episodes with a family history of schizophrenia will likely respond to antipsychotics. Those who abuse substances and have a higher frequency of anxiety and depression will likely respond to anticonvulsants."

Dr. Sylvia and colleagues explored the relationship between a family history of bipolar disorder and disease severity and response to four frequently used treatment approaches in a study published in 2020 in the *Journal of Affective Disorders*.

They found that patients with a greater family psychiatric history required more intense treatment yet achieved similar responses to treatment compared with patients without a family history of psychiatric illness.

Dr. Sylvia also co-authored a study published in the *Journal of Affective Disorders* in 2022 that evaluated data from two comparative effectiveness trials of different treatments for bipolar disorder. She and her colleagues at leading U.S. health institutions looked for potential links with cardiovascular risk markers, including glucose, lipids, and vital signs before and after 24 weeks of treatment.

They discovered that treatment with the antipsychotic quetiapine was associated with an increase in cardiovascular risk markers, highlighting the importance of monitoring patients. While the research did not examine sex differences, 58% of 770 study participants were female.

THE PREVALENCE OF BIPOLAR DISORDER IS SIMILAR FOR WOMEN AND MEN, AND TREATMENT RESPONSES LARGELY DEPEND ON FACTORS UNRELATED TO SEX.

However, differences in symptoms, diagnosis, and associations with other conditions, such as cardiovascular disease, indicate that more research is needed to tease out sex-specific differences that may improve understandings of bipolar disorder and pave the way for targeted treatment strategies in the future.

What else do Selena Gomez, Mariah Carey, and Demi Lovato have in common? By speaking out about their challenges with bipolar disorder, they have raised awareness that it is a treatable condition and those affected by it can live successful, rewarding lives with the right support. 🌍