

## Lybalvi: Second Chance at a First Impression

**Wouldn't you love a second chance?** Everyone has a story about the one that got away or some other tale of regret that they wish they could do over. Meta-analyses and expert consensus generally agree that some of the older atypical antipsychotics (specifically clozapine and olanzapine) have greater efficacy but more side effects than newer agents. In comparison, newer antipsychotics tend to have fewer side effects but less efficacy on average. While having a better side effect profile may be an advantage in most cases, some people with Severe Mental Illness (SMI) require the kind of efficacy that newer treatments may not be able to offer.

But could there be a way to harness the efficacy of older antipsychotics with a lower risk of side effects? Over five decades of research has not found the means to reduce clozapine's risk for potentially deadly white blood cell reductions while retaining its superior efficacy. Olanzapine's Achilles heel is its high potential for weight gain and other metabolic disturbances. However, there are ways to moderate this, like adding the medication metformin at the start of treatment. Still, it can be challenging to get a person with SMI to accept a second medication when they often don't want to take any medication. And while it may play second fiddle to clozapine, olanzapine's efficacy is no consolation prize. My psychiatry residency training was in the mid to late 2000s when large, real-world effectiveness studies in the US and Europe showed that olanzapine had the lowest all-cause discontinuation rate of any antipsychotic studied. But olanzapine was so vilified within my program for its metabolic side effects that I felt ashamed to use it except as a last resort. However,



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when I left training for my first real job in the community, and I was the sole clinician responsible for some extremely sick patients, I found that sometimes it was the only medication that got people healthy.

Some people are susceptible to considerable weight gain with olanzapine, but not all. Unfortunately, there's no good way to tell someone's potential for weight gain in advance. Often the fear that someone could end up with significant weight gain prevents clinicians from trying olanzapine at all. Shared Decision-Making would say that by assuming that people with SMI won't tolerate weight

gain no matter how beneficial the medication otherwise is, clinicians deny them the chance to make that decision for themselves. To that point, several of my patients who have developed substantial weight gain or type 2 diabetes attributed to olanzapine have expressed sentiments to the effect of, "you can pry it out of my cold, dead hands!"

*In May of 2021, the FDA approved Lybalvi for adults with schizophrenia and bipolar I disorder, and it may be able to provide a measure of redemption to the olanzapine story.*

Lybalvi is a single tablet that combines olanzapine with a second medication called samidorphan, which significantly reduces the potential for weight gain and makes it more predictable. The odds of gaining a clinically significant amount of weight with Lybalvi were half that of olanzapine alone in a 6-month trial, and 73% of those who took Lybalvi did not gain a clinically significant amount of weight. Historical data shows that weight gain from olanzapine tends to continue throughout up to 4 years of treatment. However, with Lybalvi, it appears to plateau within the first 6 weeks of treatment and generally remains stable over a total of 18 months. A 4-year safety trial is also ongoing to assess longer-term effects.

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Tyson McGuire

## Overcoming Schizoaffective Disorder



**Tyson McGuire** is a student at the University of Cincinnati working toward a bachelor's degree in physics and a joint master's degree in mechanical engineering. Following his high school graduation, he won a full ride to attend UC starting in fall of 2016. Prior to college, he knew very little about schizophrenia, let alone ever expected it would dramatically affect his life.

Tyson enjoyed a happy childhood with his younger sister and two half-sisters. When he was eight years old, his father left the United States to live in New Zealand. His mother, a school principal, remained a positive driving force in his life. Tyson excelled at piano, performing works by Liszt and Chopin, though he was primarily self-taught. He also learned musical composition independently.

During high school, he occasionally heard someone calling his name, although no one was there. When he shared this with friends, they didn't understand, so he kept it to himself.

From the start of his University of Cincinnati experience, Tyson became depressed, missing his high school friends. In 2018, he climbed to the top of a parking garage on the campus, intending to jump. One of his friends recognized that Tyson was in danger, left class early to find him on top of the parking garage, and convinced him to return to the dorm. Another friend who heard about his situation called the police. Tyson was arrested and taken to a psychiatric hospital, but managed to convince the staff that he was apprehended by mistake. He was released only hours later.

From 2016 to 2018, despite depression, Tyson maintained high grades in his physics major. In summer of 2018, he did an internship at Fermi Labs in Chicago, and despite the stress, he enjoyed working forty-hour weeks. Tyson had always maintained an internal dialogue with himself, but during that time, a new distant voice appeared inside his mind.

The hallucinations would only get worse. In 2019, Tyson saw the form of a person in his peripheral vision. This new voice in his mind began to speak to him. As the hallucinations became increasingly frequent, his grades began to drop, although sometimes the hallucinations were positive, and the person he hallucinated felt like a companion. With the passing months, he began to believe that people were out to get him and even try to kill him at every street corner. Afraid of going outside, and scared of his professors, he began to skip classes.

One morning in 2019, Tyson woke up with a sharp pain in his chest which he believed was a heart attack. He hadn't slept for two days and had been pacing around his dorm room. The shadowy figure was present in his peripheral vision. Later that day, he took an exam in Chinese and did well. When he confided about

the heart pain to a friend studying medicine, she convinced him to see a family doctor. He consented to see a doctor with his mom.

At the appointment, Tyson recalls being introduced to a "new vocabulary." The doctor suggested he may have schizophrenia, and could be suffering from hallucinations, paranoia and panic attacks. Nonetheless, believing that nothing was wrong with his mind, Tyson refused medication.

A few months following the appointment, as his symptoms were worsening, Tyson visited a psychiatrist recommended by the family physician. He was diagnosed with bipolar disorder with psychotic features and was put on a medication which made him drowsy, aloof and catatonic. He later tried another medication with little success. He was later diagnosed with major depression and psychosis.

In late 2019, he tried cariprazine which brought him to partial recovery and enabled him to continue classes. Finally, in late 2021, he tried clozapine, which cleared his mind and brought him to full recovery. His diagnosis was changed one more time, to schizoaffective disorder.

Today, Tyson is studying full time at the University of Cincinnati in his fifth year. He hopes to complete his joint physics major and engineering master's degree in 2023. He also still plays the piano at a high level, studies Chinese with plans of becoming fluent, and in the future, hopes to study Russian.

*On clozapine, all his hallucinations have disappeared. He now lives without paranoia, enjoying meaningful relationships with family and friends.*

In an effort to learn more and give back, Tyson joined the University of Cincinnati's CURESZ on Campus in 2021 and became president for the 2021-2022 academic year. Through sharing his story, he hopes to encourage other students to know that recovery is possible.

Following his graduation from UC, he hopes to pursue his PhD in science.



# MY HOMELESS CHRISTMAS



This December, I celebrate thirteen years of recovery from schizophrenia. As I decorate my apartment for Christmas, send off cards, and buy gifts, I think back to my life outside, homeless in Los Angeles. In 2006, I spent Christmas wandering parks nearby my former university, looking for any food that had been discarded by healthy and normal people who walked the area. It was an improvement over my Thanksgiving, as I had spent five days in jail for trespassing at the university where I had once excelled as a student. During this time, I was totally unaware that I was suffering from a brain disorder which had plunged me into a state paranoia and estrangement and caused me to have delusions and hallucinations.

Today, for me, holidays are a special time to spend with family and friends. Throughout the year, I have the pleasure of seeing my parents often, as they live half an hour away. I enjoy living a block from the university campus where I graduated ten years ago. I play violin every week at my church and teach piano lessons at my apartment. I look forward to seeing people from every facet of my life over the holidays. It's such a contrast from years back, when my psychosis led me to avoid everyone I loved and cared about.

When I look back at my life, one of the biggest surprises was my inability to seek help, even after being incarcerated over a major holiday. All through my childhood, I had so many friends, a great relationship with my parents, a love for piano and violin, and a dream to become a scientist in the future. My life was filled with love and excitement.

So how did I end up homeless and in jail and still refuse all help from my parents and from so many other families that would have been happy to help me rebuild my life? The only thing that could have caused me to fall so far was a brain that was "broken" by my illness and failing me.

Isolation and a lack of interest in spending time with others are common symptoms of schizophrenia. In hindsight, my behavior went far beyond normal, as I survived for days and even weeks without seeing any friends. Today I realize that my lack of contact with others was more than a choice. It was a serious symptom, indicating a problem with normal brain function.

In 2007, a year later, my Thanksgiving and Christmas were difficult for very different reasons. I had been diagnosed with schizo-

phrenia, and for about ten months, had been taking a partially effective medication. I was able to live outside the hospital, but struggled to get through every day, as the side effects of my medication were severe, and the voices in my mind were still present. Over the holidays, I wanted to have one single day off my medication, but I knew better, and remained medication compliant. In 2007, with my illness in partial remission, my biggest wish was for a quiet mind and normal relationships. But my medication left me with a flat affect and a drugged appearance, and I was too exhausted to enjoy spending time with anyone.

Today, over the holidays, I pray for those who are struggling either on a partially effective medication or untreated, unaware that they are sick. It is my hope that patients in these situations will continue trying other medications and treatments and not give up, reaching the highest level of recovery possible.

In 2008, I had much to be grateful for. For months, my medication had been working. In less than a year, my miracle would happen. I would be at a university again, scoring A's in molecular biology classes.

Today, in 2021, as president of the CURESZ Foundation, I enjoy reaching out to families who are torn apart by a loved one's schizophrenia. I find comfort in volunteering to serve the homeless over Christmas and Thanksgiving. My church supports a program that helps the most mentally ill and desperate people, many who live under bridges, find housing in local hotels. I wish I had been able to accept this kind of help in 2006 while living in the churchyard.

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*My mom and dad were so committed to my recovery, as well as my psychiatrist who was committed to press forward until an effective medication was found that would clear my mind. Because of these people, I got a new chance at life.*

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**Bethany Yeiser,**  
President of the  
CURESZ Foundation

*There is hope, even for those of us who reject all friends and family over the holidays as I did, because of an illness affecting their brain. I resolve to always look deeper and see the mentally ill for who they really are underneath their illness, and encourage them toward treatment, which may include medication. I feel I owe a debt to those who have helped me most. I endeavor to always give back, and never give up on those who have not recovered and struggle the most over the holidays.*

## Lybalvi: Second Chance at a First Impression

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As with all medications, Lybalvi has some risks and limitations. Besides the weight and metabolic risks already discussed, Lybalvi has a similar risk of other side effects associated with olanzapine. These may include sedation, motor side effects, dry mouth, and others. Samidorphan blocks the effect of opioids, so Lybalvi is contraindicated for anyone taking opioid medication. If someone taking Lybalvi needs opioids for a planned surgery, it can be switched to standard olanzapine tablets a few days before the procedure and switched back to Lybalvi 1-2 weeks after the opioids are stopped. And trained anesthesiologists can still provide adequate pain relief without a planned washout of Lybalvi if urgent opioid treatment is needed. Finally, Lybalvi has not been shown to produce weight loss in people already taking olanzapine. Still, open-label data suggest that there could be prevention of further weight gain in this scenario.

Based on efficacy alone, one would expect olanzapine to be used early and often in the treatment of SMI. However, the long-term weight and metabolic consequences have relegated it to near the last resort. I think Lybalvi could change the calculus of this sequencing for clinicians. With more confidence that someone could reap the benefits of olanzapine with less likelihood of having runaway weight gain, it might move the option up on the list for appropriate patients. Side effects can be mitigated or managed, but there's no way to increase the efficacy of an antipsychotic that doesn't let people live their lives and achieve their goals, which is what every person with schizophrenia deserves.

### VIDEO HIGHLIGHT

**Schizophrenia:**  
Science-Based Facts



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TO VIEW VIDEO

Schizophrenia, commonly referred to as a mental illness, is in fact a neurological disorder. It can be compared to Alzheimer's Disease and Parkinson's Disease, as well as to other medical illnesses such as diabetes, cancer and arthritis.

It is not an emotional disease, nor a sign of personal weakness, or a personality flaw. Persons with schizophrenia cannot simply choose to avoid having their psychotic symptoms any more than an Alzheimer's patient can choose to avoid losing her memory. The vast majority of people suffering from schizophrenia will definitely need an antipsychotic medication. Generally, this antipsychotic medication must be taken indefinitely, just as a person with type-1 diabetes will always need insulin or a person with hypertension must remain on the medication permanently.

There are additional strategies to treat symptoms of various brain disorders (such as schizophrenia, bipolar disorder, anxiety and depression) in addition to medication. Psychotherapy as well as diet and exercise can help improve physical health as well as the quality of life. Certain supplements such as Omega-3 fatty acids as well as NAC (N-Acetyl Cysteine) can also help reduce the inflammation and free radicals in the brain during acute psychotic episodes. Vitamin D is also important to take if the blood level is low.

In this video, various fallacies and myths of schizophrenia are debunked. Symptoms of schizophrenia are explained. Dysfunction in certain brain regions, such as the frontal lobe where planning and decision making originate, is discussed along with disruption in neurochemistry and neurotransmitters in the limbic system.

### Please consider making a donation to the CURESZ Foundation online at CURESZ.org

Your contribution will help provide education and referrals to persons with schizophrenia, their families, and those who work with the seriously mentally ill. CURESZ informs the general public to better understand this serious brain disorder, and to provide scientific advances showing that there is hope for recovery, and a return to a fulfilling and normal life. The CURESZ Foundation is a 501(c)(3) nonprofit organization. All contributions are tax deductible.

***"We are committed to helping individuals to cope with and recover from schizophrenia."***

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