WILSON DISEASE ASSOCIATION

# Wilson Disease

# Voice of the Patient Report

## Externally-Led Patient-Focused Drug Development Meeting

**Meeting date: January 29, 2026, Report date: July 29, 2026**

# Wilson Disease Voice of the Patient Report

This report has been published by Wilson Disease Association (WDA) as a summary of the input from people living with Wilson disease (WD), family members, and other caregivers during the Externally-Led Patient-Focused Drug Development (EL-PFDD) meeting. The meeting was conducted virtually on January 29, 2026. The WDA provides support and hope to people impacted by WD worldwide so they may lead the best quality of life possible.

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# Executive Summary: Wilson Disease

**Wilson disease (WD) is a lifelong condition caused by the body's absence of an enzyme for processing copper; accumulation of copper in the liver and brain leads to severe hepatic, neurologic and/or psychiatric symptoms and is generally fatal if not diagnosed and treated.**

**WD diagnosis occurs across the age spectrum, and misdiagnosis often occurs before the correct diagnosis is found**. Delayed diagnosis leads to delayed treatment.

**WD is a challenging and multifaceted condition, with liver disease, fatigue, tremors, muscle stiffness, gait/balance problems, anxiety or depression, speech difficulties, and behavioral challenges as the most troublesome health concerns**.

**WD symptoms can change with time.** Copper accumulation over time leads to the emergence of new symptoms or causes existing symptoms to become more severe; treatments for WD can make symptoms worse. Medical non-adherence also causes symptoms to intensify.

**Life with WD is characterized by uncertainty.** All aspects of daily living can be disrupted, including eating and drinking, sleep, work and school, exercise, and recreational activities. Symptoms can lead to psychosocial impacts on relationships. For some WD families, the care burden is heavy. Many of those living with WD feel stigmatized and isolated.

**Managing WD involves a complex and intensive treatment regimen**. Disease-modifying medications for WD are an unmet need. At present, copper chelators are the most frequently used, followed by zinc. A low-copper diet and laboratory or clinical monitoring are the most important non-medical approaches to WD treatment, but many other approaches are used. Stress, depression, cognitive symptoms, or psychiatric symptoms, as well as medication timing and side effects, can interfere with adherence to medications.

**Medication and treatment approaches for WD work for many but not all patients and have significant drawbacks.** These include strict medical timing away from meals**,** medication refrigeration and storage requirements, administration effort and/or time commitment, side effects including neurologic worsening, lack of efficacy, and limited availability.

**Those living with WD and their loved ones are fearful for the future.** They worry about uncertainties regarding disease progression, worsening symptoms, and losing their independence. Those living with WD — who depend on their medications for survival — expressed worries about medications no longer being tolerated or effective, symptoms worsening, running out of treatment options, and medications being inaccessible and unaffordable.

**The WD community needs therapeutic options to slow or stop disease progression, improve or reverse neurological symptoms, and have easier administration.** Other important treatment needs include more mental health support along the entire treatment journey, more research into treatment for children and pregnant patients, newborn screening, and screening psychiatric patients for WD. The WD community is eager to participate in clinical trials.

# Introduction

## Wilson Disease Clinical Summary

Wilson disease (WD) is a rare genetic disease that is inherited in an autosomal recessive fashion, affecting about one in 30,000 individuals globally. Symptoms can manifest for the first time in children, adolescents, or adults.

WD is caused by mutations in the *ATP7B* gene that impair the normal metabolism and excretion of dietary copper, leading to copper accumulation. While about 1,300 *ATP7B* gene mutations have been identified, specific mutations are not yet correlated with specific symptoms or disease severity.

Those living with WD can experience isolated hepatic, neurologic, or psychiatric manifestations. Some patients experience two types, and some all three types of symptoms, sometimes at the same time. Clinical symptoms can range from mild to very severe.

Very young patients are typically asymptomatic. With time, copper accumulation in the liver can lead to hepatic inflammation, cirrhosis, portal hypertension, liver failure, and death. Excess copper can also accumulate in the brain, resulting in neurological and psychiatric symptoms. Factors contributing to this variability are not completely known.

Diagnosis is complicated. A validated diagnostic scoring system exists that incorporates clinical findings, serum blood tests, urine copper, *ATP7B* gene mutation analysis, liver biopsy results, and family history. Although WD newborn screening is gradually being approved and implemented in different jurisdictions, newer and hopefully more accurate diagnostic methods are being tested.

## Wilson Disease EL-PFDD Meeting Summary

The WD Externally-Led Patient-Focused Drug Development (EL-PFDD) meeting was held virtually on January 29, 2026, and was accessible via livestream. Patient-focused drug development is a systematic approach to help ensure that patients' experiences, perspectives, needs, and priorities are captured and meaningfully incorporated into drug development and evaluation. This meeting was an important opportunity for the global WD community to share patient and caregiver perspectives regarding the symptoms and daily impact of WD, and to discuss current and future approaches to treatment. A total of 350 participants, including 40 FDA staff, attended the livestream. Those not able to attend participated in the survey, created video testimonies, and submitted comments before and following the live event.

The meeting was focused on two key topics: symptoms and their daily impacts, and current and future approaches to treatment. The meeting featured recorded video presentations, moderated discussions between individuals on live Zoom panels, and those who dialed in by phone. During the meeting, the WD community also contributed through live online polling, and by submitting comments through the online portal.

A recording of the EL-PFDD meeting, as well as other meeting materials, is available on the Wilson Disease EL-PFDD website.

## The Wilson Disease Voice of the Patient Report

This report is provided to all WD community supporters, including the FDA, other government agencies and regulatory authorities, medical product developers, academics, clinicians, and any other interested individuals. This report highlights the insights that emerged at the January 29, 2026, WD EL-PFDD Meeting, including the results of online polling. Each of the WD community members whose quotes are included in this report is listed with their age, age of diagnosis, and WD manifestations: hepatic (jaundice, fatigue, etc.), neurologic (tremors, difficulty speaking or swallowing, balance issues), and psychiatric (mood swings, depression, anxiety, cognitive impairment) when known.

Before the EL-PFDD meeting, the WDA surveyed the WD community. The survey results align very strongly with the EL-PFDD meeting outcomes. Additional comments from that survey are highlighted in this report.

The content of this report may help inform the development of WD treatments, including clinically meaningful endpoints for current and future clinical trials. The input received from the January 29, 2026, WD EL-PFDD Meeting reflects a wide range of experiences of individuals and family members living with WD, as well as bereaved caregivers and loved ones; however, not all symptoms and impacts may be captured in this report.

The final report is available through the Wilson Disease EL-PFDD website.

> *"My experience with Wilson disease would have been far less traumatic if the treatment hadn't worsened my neurological symptoms to the point where I was a shell of a human being, fully aware of my surroundings in a body that no longer worked. I had lost the ability to talk, walk, eat, and drink completely, relying on a feeding tube and a customized sign language only my parents could understand."* — Emma, 20-year-old diagnosed with WD at 17, neurologic and psychiatric

**Dedication:** ***This report is dedicated to the Wilson Warriors who lost their battle with Wilson disease, including Joe Scanlan (1996 – 2025).***

# TOPIC 1: Wilson Disease Symptoms and Daily Impacts

During the first EL-PFDD session, members of the Wilson disease (WD) community spoke candidly about WD-related health concerns, describing a broad range and severity of symptoms. Panelists and callers shared the impacts that WD has on daily life and their fears for a future living with WD. Insights and poll results from this first session are summarized and illustrated with quotes from those living with WD, as well as family members, close friends, and other direct caregivers. Poll results can be viewed on the Wilson Disease EL-PFDD website.

## Wilson Disease Insight

### Wilson disease diagnosis occurs across the age spectrum, and misdiagnosis often occurs before the correct diagnosis is found.

Delayed diagnosis leads to delayed treatment. Some living with WD described subtle symptoms that went undiagnosed for years, while others experienced a rapid and devastating decline. While liver symptoms can lead to a more rapid WD diagnosis, neurologic and psychiatric symptoms are often harder to recognize and were sometimes dismissed as dehydration, sleep deprivation, extreme stress, or anxiety. Some families have multiple affected members.

> *"My diagnosis was entirely coincidental; I had no visible symptoms at the time. It was discovered only because of an abnormal liver function detected in a routine blood work."* — Ade, 45-year-old diagnosed with WD at 14, hepatic

> *"I had exhibited many Wilson disease symptoms throughout my life, and it was always missed or misdiagnosed. … During my diagnosis, it was a very difficult and scary time. There was very little information out there, and the first doctors that I saw didn't seem to take it very seriously."* — RJ, 42-year-old diagnosed with WD at 40, neurologic and psychiatric

> *"I was 17 when Wilson disease nearly took my life. Looking back, I see that there were earlier signs — fatigue, nightmares, mood changes, dystonia, jaundice — that didn't really make sense at the time. I went into acute liver failure and was being prepared for a transplant."* — Raisa, 31-year-old diagnosed with WD at 17, hepatic, neurologic, and psychiatric

## Poll 1 & 2 Results

### Wilson disease is a challenging and multifaceted condition, with liver disease, fatigue, tremors, muscle stiffness, gait/balance problems, and anxiety or depression as the most troublesome health concerns.

Poll results indicated that, on average, individuals living with WD experience 6.3 different WD-related symptoms and health concerns. The four most frequent and troublesome health concerns selected in the polls aligned: liver disease, fatigue/low energy, tremors, muscle stiffness, gait/balance problems, and depression/anxiety. WD-related health concerns are listed in descending order of most troublesome below, illustrated with select quotes.

### *Liver disease including inflammation/hepatitis, fatty liver/steatosis, cirrhosis*

Liver-related conditions were the first WD symptom for many and ranged in severity from abnormal liver enzyme levels to acute liver failure. Those living with WD described jaundice, stomach pain, ascites, and vomiting, and several had such severe abdominal distention that they appeared pregnant.

> *"Wyatt was only four when diagnosed with Wilson disease. He never had neurological symptoms, just the elevated liver enzymes, ALT and AST. … His numbers were dangerously high, over 600 when they should've been below 60. We were told he couldn't go to preschool because his liver was so compromised that a common cold could be dangerous."* — Brett, parent of a nine-year-old diagnosed with WD at four, hepatic

> *"The very first symptoms I noticed were severe stomach aches almost every day. My liver was already cirrhotic, and copper was building up in my brain. Getting diagnosed so young probably saved my life."* — Nicole A., 41-year-old diagnosed with WD at 10, hepatic, neurologic, and psychiatric

> Lana's abdomen was so distended from her swollen liver that she appeared pregnant, although she was not. *"When I was diagnosed, I had severe fibrosis, severe cirrhosis. Immediately put on the transplant list, and they didn't know if I was going to survive a transplant. I was throwing up eight times a day. I was so emaciated. I started growing fine body hair all over my body. I was jaundiced, and I had to wear extra-small maternity clothes because my abdomen was so swollen. They'd come in and drain two liters from my stomach, and [it made no difference]."* — Lana, 42-year-old diagnosed with WD at 22, hepatic, with minor neurologic

### *Fatigue/low energy, weakness, and loss of physical strength*

Fatigue was repeatedly described as pervasive and life-limiting. Due to excessive fatigue, some must choose between essential daily tasks and other activities.

> *"For years [after my diagnosis], I would tell my doctor I always felt tired, and come home from work, and I would just sleep. And sometimes you don't know, is it due to a busy career, or is it the Wilson disease?"* — Rhonda, 63-year-old diagnosed with WD at 21, hepatic

> *"[My two siblings and I] feel fatigue because all the things that we do are conscious. For example, when we walk, we have to think all the time, 'right leg, left leg, right leg, left leg', and this is very tiring."* — Eugeni, 37-year-old diagnosed with WD at 11, hepatic and neurological

> *"Fatigue has always been an issue. I had a really hard time getting up for school in the morning as a kid. … I just have less energy to do stuff in general."* — Stuart, 27-year-old diagnosed with WD at 24, hepatic and psychiatric

### *Tremors, muscle stiffness, or gait/balance problems*

Those living with WD described a wide range of neurological symptoms, such as numbness and tingling, loss of fine motor control, mild tremors, muscle stiffness, loss of control of facial muscles, loss of balance, and difficulty walking. Some experience severe repetitive muscle

contractions, clenching, constant movement, and pain. Coordination and balance challenges can make it difficult to walk more than a short distance or to climb stairs independently. Symptoms can become more severe over time.

> *"I could just feel that I had a loss of control in my hand, and my handwriting got larger and not as precise. Then it was a balance issue. I went from wearing four-inch heels, and it was dropping inch by inch until I was only wearing flats. Then I started noticing tremors, and my eyes were unable to focus to read. … By the time that I was diagnosed, I was completely disabled. I was unable to speak. I could not walk. I could not take care of myself. I needed help 24 hours a day and seven days a week."* — Mary P., 49-year-old diagnosed with WD at 39, neurologic

> *"When he came home from college, he had what we called a wiggle. When he spoke, his head would move. At first, he could control it, until he couldn't."* Now, six years later, *"The dystonia shapes his whole body. His right arm is in constant motion, always moving while his left arm stays curled tightly, his fists clenched. His left leg curls too, while his right leg can extend. It's exhausting for him and for us."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

> *"I had hand-flapping (like I was trying to work a hand puppet's mouth), tremors, balance issues, slurred speech, drooling, and my handwriting became very small and illegible."* — Stacy, 58-year-old diagnosed with WD at 24, neurologic and psychiatric

### *Anxiety or depression*

Throughout the meeting, those living with WD and their families described cycles of uncontrollable anxiety and depression. The emotional burden of WD is significant; some experience grief from ongoing losses, medical trauma from invasive biopsies, and medication side effects.

> *"Throughout high school, I recognized I would go through bouts of depression where I wouldn't want to get out of bed, I wouldn't want to do any physical activity. … Today, I typically go through these depressions and think, 'Is it seasonal depression?' if it comes about during winter … Is it the Wilson disease? Is it me being lazy? What is it?"* — RJ, 42-year-old diagnosed with WD at 40, neurologic and psychiatric

> *"My anxiety and depression make it hard to get out of the house. Mood swings are crazy; I can go from happy to upset really fast. I'm in pain the majority of the time."* — Teri, 36-year-old diagnosed with WD at 24, hepatic and psychiatric

> *"I remember struggling with nightmares, mood changes, and heightened emotionality at the time of my diagnosis. I cried a lot and got angry very quickly, and this usually felt outside of my control. The unregulated emotions did not actually get addressed until 10 years after the fact, when I found that these symptoms were still impacting my work and daily function."* — Raisa, 31-year-old diagnosed with WD at 17, hepatic, neurologic, and psychiatric

### *Speech difficulties*

Those living with WD described their voices weakening, their words slurring, and how they have to speak very slowly and intentionally. Speech difficulties can be stigmatizing when others

assume that they are cognitively impaired. For some, speech declines throughout the day, and others have completely lost the ability to speak at all.

> *"Dysarthria or speech difficulties…. that's probably my biggest challenge. If I think about what I'm going to say, it comes up perfectly clear. During this interview, I'm thinking, 'Oh my gosh. Do I sound okay? Is my speech clear enough for people to understand?' People have assumed I was drunk or impaired, including someone that called my boss once, and a pharmacist who thought I was intoxicated. It was very embarrassing."* — Jean Marie, 62-year-old diagnosed with WD at 16, neurologic and psychiatric

> *"We have difficulties with speech that affects social interactions, for example, talking by phone."* — *Sergi, 37-year-old diagnosed with WD at 11, hepatic and neurological*

> *"About a year and a half ago, my speech was significantly impaired. I could no longer communicate correctly. … I could think properly, however, I could not articulate my words correctly. So, in social situations, people would look at me very awkwardly. And I was in a mentorship position. People would look at me as if I didn't know what I was talking about."* — RJ, 42-year-old diagnosed with WD at 40, neurologic and psychiatric

### *Behavioral changes (e.g., personality changes, impulsiveness)*

WD-related behavioral changes are thought to be caused by copper accumulation in the brain, which can impact decision-making, cause mood swings, impulsive behaviors, and personality changes. Some living with WD described psychiatric conditions, including extreme irritability and behavioral outbursts, obsessive compulsive disorder (OCD), psychosis (hallucinations, delusions), borderline personality disorder, bipolar disorder, and suicidal ideation. Behavioral changes can be among the most impactful symptoms on daily life, and among the most misunderstood and isolating aspects of the disease, leading many to experience stigma, isolation, and loss of confidence.

> Sometimes behavioral changes were not initially recognized as being due to WD. *"He always had been very easygoing as a person and really fun. And now he just was angry all the time and would lash out. And it was like being married to somebody who was completely different. And at the beginning, I thought, 'Oh, maybe this is age. I don't know. We've been married a long time."* — Tonya, wife of a 55-year-old diagnosed at 49, hepatic, neurologic, and psychiatric

> *"She's had a complete personality change from when she was younger with Wilson disease. She used to be very lighthearted, very fun-loving, very humorous, and now she's very low much of the time. … Her psychiatric issues really have become prominent. She has a lot of anxiety, depression, OCD. Her sleep has become very erratic. And of course, that affects her compliance with taking her zinc."* — Kathy, sister of a 66-year-old woman diagnosed with WD at 16, neurologic and psychiatric

> *"Joe was making irrational decisions that were not in line with his character. It's like he couldn't always make wise and sound decisions. He might lash out if he got agitated or frustrated, and that was not a normal behavior for him."* — Brock, friend of Joe who was diagnosed with WD at 24 and recently passed away at 29, neurologic and psychiatric

***The WD community selected additional health concerns in the polls***

These include **issues with memory, processing information, or the ability to focus (**such as cognitive overload, brain fog, and cognitive impairment), **nausea or vomiting (**often from medications), chronic or acute **pain** from tremors, arthritis or stomach conditions, and **difficulty swallowing or choking**. Note that the health concerns highlighted in bold (above) are poll responses.

> Ariana experiences constant pain from her tremors. *"At the beginning, my feet would continue to twitch. The pain was like I had shin splints, but it would be constant because I was constantly [moving my feet]. That was super painful. We actually went to a point where we put a 100-pound sandbag on my feet at the dinner table just to get them a little rest, a break from moving constantly. And then I have severe pain in my neck, but my neck constantly moving as well."* — Ariana, 34-year-old diagnosed with WD at 25, neurologic

> *"When he was first diagnosed, he was very fatigued, often vomited when he tried to eat, was very skinny, and had terrible nosebleeds."* — Hayley, parent of a 14-year-old diagnosed with WD at four, hepatic

> *"I have very little liver damage. Most of my symptoms that were noticeable had to do with... skin changes, behavioral issues, sleep problems. I had problems swallowing, arthritis, neck and muscle pain*." — Andy, 55-year-old diagnosed with WD at 49, hepatic, neurologic, and psychiatric

The WD community described other health concerns during the meeting and in the submitted comments. Many experience a range of different WD health concerns, medication side effects, or both. These include sleep issues, drooling, dry mouth, seizures, insomnia, skin changes (such as rashes, red patches, and deterioration of skin elasticity), weight loss, joint deterioration, osteoarthritis, rheumatoid arthritis, and kidney loss from copper overload. Kayser-Fleischer rings are a characteristic of WD and often help with making a diagnosis, however, do not cause discomfort or distress.

## Wilson Disease Insight

### Wilson disease symptoms can change with time.

Copper accumulation leads to the emergence of new symptoms or causes existing symptoms to become more severe. Medical non-adherence also causes symptoms to intensify. Stress, depression, cognitive symptoms, or psychiatric symptoms, as well as medication timing and side effects, interfere with medication compliance.

> *"Symptoms tend to worsen during periods of treatment interruption, stress, sleep disruption, or when laboratory monitoring is inconsistent. Even subtle changes in mental clarity can significantly impact academic performance and quality of life."* — Laura, 30-year-old diagnosed with WD at seven, neurological and psychiatric

> *"Fatigue sometimes forces me to choose between social activities or work, and then depression adds to the weight of the journey. Staying compliant on medications*

*becomes especially tough during these times*." — Raisa, 31-year-old diagnosed with WD at 17, hepatic, neurologic, and psychiatric

Rhonda met a young WD patient who was being evaluated for transplant. "*Later, the patient's father found me and, sobbing, told me never to stop taking my medicine. His son was diagnosed because of a sibling and had never had symptoms, so he had stopped taking his medication. Sadly, this young man did not make it. That experience — it's what's kept me adherent to my medication all these years."* — Rhonda, 63-year-old diagnosed with WD at 21, hepatic

## Poll 3 Results

Life with Wilson disease is characterized by uncertainty. All aspects of daily living can be disrupted, including eating and drinking, sleep, work and school, exercise, and recreational activities.

An important point made during the EL-PFDD meeting was that while those living with WD experience significant physical symptoms, the psychological and behavioral impacts often have the greatest effect on daily life, shaping relationships, employment, treatment adherence, and overall quality of life. The WD-related impacts on daily life are listed in descending order of most impactful as selected in the poll and illustrated with select quotes.

### *Eating and drinking*

Those living with WD need to strictly adhere to a low-copper diet, avoiding many foods, including chocolate, nuts, and shellfish. They must take their medications in a fasting state, long before or after meals, which makes shared mealtimes challenging, if not impossible. Neurological manifestations can make swallowing difficult, and some must eat slowly and mindfully so they don't choke. Some even require a feeding tube.

> *"Here's what I want people to know. Having Wilson disease sucks. I wake up every morning — the first thing I do is take medicine. Sometimes I forget, which means I have to wait even longer to eat. ... I get so hungry that my stomach hurts. I can't describe how bad it hurts, and then I get hangry. It's really hard because a lot of people don't understand my Wilson disease."* — Wyatt, nine-year-old diagnosed with WD at four, hepatic

> *"I had intention tremors, not able to pick up a spoon and eat."* — Arjun, 30-year-old diagnosed with WD at age 10, neurological and psychiatric

> *"Unfortunately, my middle son (16 years old) is severely affected with neurological symptoms. … He can NOT walk on his own, cannot eat (uses a gastric tube), and can NOT talk. He was previously an active 15-year-old who excelled academically and was on the tennis and water polo team."* — Khanh, parent of three children living with WD, neurological

### *Restful sleep*

Sleep disturbances can be both a symptom of WD and a medication side effect. The lack of sleep can impact the entire family.

*"His decline was so rapid that trientine was stopped and replaced with zinc, but things only worsened. He slept all day and was awake all night. This went on for weeks and affected everyone in our home."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

*"Minh had to take a lot of melatonin to try to sleep. And even then, he would stay up until 2:00 AM, a lot of times messaging me, just sharing his anxieties about everything."* — Joseph, cousin of a 26-year-old living with WD, hepatic, neurologic, and psychiatric

*"Early in my treatment, I had trouble with sleep, weight loss, and irritability that affected my relationships and my ability to work productively."* — Andy, 55-year-old diagnosed with WD at 49, hepatic, neurologic, and psychiatric

### *Managing work or school responsibilities*

Adhering to strict medication schedules disrupts the day. WD-related symptoms, such as fatigue, speech issues, muscle weakness, fine motor impairment, pain, nausea, cognitive challenges, medication side effects, and tremors, lead to missed classes, college withdrawals, leaves of absence, and lost jobs. Some individuals can only work part-time, while others have had to change careers or abandon career dreams entirely. Many cannot work at all, and the loss of employment leads to the devastating loss of health insurance.

*"He was unable to hold employment due to his WD symptoms. He could no longer drive within weeks of his diagnosis. The ability to participate in daily activities was severely hindered. He often needed assistance just to walk from A to B."* — Brock, friend of Joe who was diagnosed with WD at 24 and recently passed away at 29, neurologic and psychiatric

*"The stress of the diagnosis, paired with the tremors I used to have, led me to lose several jobs."* — Calvin, 24-year-old living with WD, neurologic and psychiatric

*"I bounce back a bit slower than my peers. I feel like I need more sleep [which is a severe handicap because I am/was a surgical resident]. I feel like some surgical residents really push themselves to superhuman boundaries, and a lot of times, I have to say, 'I can't do this anymore. I need to go home and sleep. The end of the 24-hour shift is done.' It is really hard to push through it sometimes."* — Mandy, 29-year-old diagnosed with WD at six, hepatic

*"I have severe osteoarthritis and rheumatoid arthritis as a result of the penicillamine, and that has limited my mobility to a great extent. In fact, I am a nurse and attorney, spent most of my career as an attorney working in Congress, and I had to retire from my job due to the inability to walk through the halls of Congress."* — Patricia, 70-year-old diagnosed with WD at age 14, hepatic with minor neurologic

*"As a NICU nurse, I was having trouble putting in IVs, which I had always been pretty good at, and it rattled me. … I decided to go into the case management side of nursing instead of clinical nursing, just because I didn't ever want the tremors to affect anything with patient care*." — Mary M., 36-year-old diagnosed with WD at nine, hepatic, neurologic, and psychiatric

### *Exercise, working out, and other recreational activities*

Strict WD medication schedules and disease-related symptoms make participation in exercise and other recreational activities difficult. Some have had to give up their hobbies and sports entirely.

> *"Speaking, writing, and performing music were most affected. I talk with kids for my work regularly in schools, and have to repeat myself to make sure I'm being understood. I also have to handwrite reports, which is challenging due to fine motor impairments. I also had to stop playing musical instruments recreationally because of the fine motor changes from WD."* — Ian, 29-year-old diagnosed with WD at 12, hepatic and neurologic

> *"[My 9-year-old son] has a special watch to track when he eats and takes his meds. He has to stop playing and run home to take meds, and he misses class time at school [to take meds on schedule]. The constant vigilance is exhausting for all of us. We are always calculating and thinking about what he needs to take, when he needs to take his medication to be able to eat at a party or before a swim meet to have energy to swim, but not get sick by eating too close to his heat, or when to eat before school starts, et cetera."* — Brett, parent of a nine-year-old diagnosed with WD at four, hepatic

> *"I played a lot of soccer and basketball. It became harder to manage the strict timings for eating, fasting, and medication with so many practices and games. When I was a college athlete playing soccer, it was nearly impossible. I couldn't get in a routine… Team meals at set times that didn't match my medication or fasting schedule, a stringent travel schedule."* — Mary M., 36-year-old diagnosed with WD at nine, hepatic, neurologic, and psychiatric

### *Communicating and social relationships*

For some patients, WD interferes with speaking clearly and social conversations, leading to lost social opportunities and isolation. Some also avoid social interactions because of tremors, fatigue, dietary restrictions, anxiety, or irritability.

> *"My son is 25, and the biggest challenges are socializing with other 20-somethings, given his alcohol and diet restrictions, GI issues with medication, and ongoing liver fibrosis issues."* — Alice, parent of a 25-year-old living with WD, hepatic

> Cognitive issues and pain interfere with making plans and keeping in touch with friends. *"Her ability to have a normal life, normal social interactions is gone. She just can't do it anymore. She can't think in a normal fashion anymore."* — Kathy, sister of a 66-year-old woman diagnosed with WD at 16, neurologic and psychiatric

> *"Wilson disease symptoms make it hard to keep up with work and social activities, especially on days when fatigue, nausea, or migraines hit. There have been times I've had to cancel plans last minute or push through work while feeling completely drained. It can be frustrating not being able to show up the way I want to, but I've learned to adjust and give myself some flexibility when I need it."* — Ginta, 33-year-old diagnosed with WD at 21, hepatic, neurologic, and psychiatric

### *The WD community selected additional WD impacts in the polls*

Other WD-related impacts necessary for independent life include problems with **walking/ mobility, fine motor tasks (e.g., writing, typing), driving or traveling independently,** and **self-care (e.g., bathing, dressing, toileting, eating)**. Some require assistance with all these activities.

During the meeting, three siblings living with WD spoke about how hard they worked to care for each other and to maintain their independence despite experiencing significant hepatic and neurologic symptoms.

> *"I have difficulties to walk and talk. It is very difficult to understand me talking, and I fall a lot of times. … For example, I am very nervous if I have to talk, and I walk very slow. I need a lot of concentration to do both."* — Eugeni, 37-year-old diagnosed with WD at 11, hepatic and neurological

> *"Traveling was always something that I knew would be difficult for me, seeing as how most of the chelating medications had to be refrigerated. So I knew that wouldn't be an easy option without sacrifice or side effects. Also, joining friends for meals has always been tricky to manage."* — Laura, 30-year-old diagnosed with WD at seven, neurological and psychiatric

> *"I also lost my driver's license after realizing I couldn't feel the bottom of my foot on the gas pedal. That crushed my independence."* — Nicole A., 41-year-old diagnosed with WD at 10, hepatic, neurologic, and psychiatric

The WD community described other WD-related impacts during the meeting or in the submitted comments. Some individuals described injuries from falling, which can lead to potential brain injuries and extensive hospital stays. They also described challenges in managing concomitant medical conditions, such as diabetes, ADHD, multiple sclerosis, or hypothyroidism, which can have conflicting medication or food restrictions.

## Wilson Disease Insight

## Many living with Wilson disease feel stigmatized.

Symptoms such as speech issues and tremors are visible, but many, such as fatigue or cognitive challenges, are not. Many living with WD described feeling judged and stigmatized and living with an "invisible disease".

> *"I don't feel safe going out in public by myself because of all the judgment that I get and all the stares ... I park in handicap spaces, and I get accused of not being handicapped. I didn't walk for a year. How am I not handicapped? But people don't see me, and it's just hard."* — Ariana, 34-year-old diagnosed with WD at 25, neurologic

> *"Difficulty speaking has caused others to perceive me as mentally challenged and to feel sorry for me and not taking my intelligence and abilities seriously; this caused me to severely limit both personal and professional contacts."* — Avonne, 57-year-old diagnosed with WD at 52, neurologic and psychiatric

*"I live in a very stigmatised state of life due to the debilitating psychiatric issues. I have been bullied for these psychiatric issues all my life."* — Sanaa, 27-year-old diagnosed with WD in early adulthood, hepatic and psychiatric

## Wilson Disease Insight

### For some Wilson disease families, the care burden is heavy.

WD can impact entire families, as caregiving responsibilities reshape family roles, finances, and long-term plans.

*"Our parents and grandparents had to stop their lives and take care of us."* — Eugeni, 37-year-old diagnosed with WD at 11, hepatic and neurological

*"Over the past six years, my son has gone from being in college to the inability to walk, talk, or perform any day-to-day personal duties. … My son is basically bedridden. Our small family's life revolves around James, and we are his only caregivers. … This has significantly impacted our lives — both emotionally and practically. These limitations have required full-time caregiving by his father and I, constant medical attention, and major lifestyle adjustments. ... Together, these challenges have altered our family dynamics, introduced financial and emotional strain, and required deep resilience and adaptation."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

*"As caregivers, we have to stay alert and be ready to provide both physical and emotional support. It's a constant responsibility, but one we carry out with love and determination."* — Tina, parent of a 20-year-old diagnosed with WD at 17, neurologic

## Poll 4 Results

### Those living with Wilson disease and their loved ones are fearful for the future.

When thinking about their future, fear and uncertainty are dominant themes of the WD community.

#### *Not knowing how WD will progress*

The worry of not knowing how WD will progress encompasses the other top selected worries in the polls, including **worsening symptoms (e.g., tremors, stiffness, pain, fatigue)**, **worsening liver disease and possibly a transplant, dying prematurely** from a catastrophic choking incident, or a fall, or liver tumor, and **losing the ability to walk or move independently**. Many experience waves of anxiety about whether and how their WD will progress.

*"There's just this constant fear that I'm going to go in, and my copper levels are going to be back, or I'm going to go to the eye doctor, and they're going to see KF rings for the first time. Or is this twitch I have because I'm nervous? Is it because I now have tremors? … And so, there's this constant fear and anxiety in the back of your mind that you're going to get sick again. … Any symptom that might be related to when I was first diagnosed, then my first thought is, 'Oh my gosh, is my liver failing? Am I going to be ill?'"* — Lana, 42-year-old diagnosed with WD at 22, hepatic, with minor neurologic

*"On a daily basis, I worry about choking. I have choked twice in the past, like I've been around people, I do it by myself. So, if I were to choke, I don't know what would happen to me. So that's a big concern. As well as slipping in the shower or something like that and banging my head. Since I do live by myself and I am independent, but I'm worried because my gait is a little off and I do fall easier."* — Ariana, 34-year-old diagnosed with WD at 25, neurologic

*"My sister had WD too. She sadly died last August at age 52 due to cholangiocarcinoma and a tumor in the liver. There were no symptoms at all, and WD was always stable."* — Helen, 55-year-old diagnosed with WD at age 11

### *Loss of independence/inability for self-care*

Worries about the loss of independence and the inability for self-care also include worries regarding what would happen as caregivers aged, who would care for their child with WD in the future.

*"As I get older, my residual neurological symptoms are limiting my mobility and activities more and more. My husband is a big help to me, but he is older than I am, and I worry that I might need more help than he can give, and my illness will be too much of a burden for him, but he won't tell me and would suffer or die because of it."* — Carol, 79-year-old living with WD, neurologic

*"What happens when we're gone? Who will care for him? And will they treat him with dignity? Will he be respected, loved, and not left alone? These questions haunt me."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

RJ worries about his children. "*Am I going to be there for them as a father, and how is this going to affect my ability to raise them as children essentially? … As my children grow up, am I going to be able to have the energy that they need for a father to be there? Am I going to have the strength to get out of bed in the morning? Are my tremors going to come back, and am I going to be able to do regular physical activities like throwing around the ball, picking them up, taking them to the park?"* — RJ, 42-year-old diagnosed with WD at 40, neurologic and psychiatric

### *Cognitive or behavioral changes affecting judgment or personality*

Although this was selected further down in the polls, many expressed their fear of WD-related cognitive and behavioral changes during the EL-PFDD meeting and in submitted comments. In particular, many worried that cognitive changes would affect social relationships and schoolwork.

*"From a symptom standpoint, I'm probably most worried about cognitive problems or psychological problems. …That definitely worries me more than the physical symptoms."* — Andy, 55-year-old diagnosed with WD at 49, hepatic, neurologic, and psychiatric

Nora worries about WD-related changes to her children's cognition, even with treatment. *"We didn't know if there would be lasting neurological effects. We still worry because there are hard days. We worry about the impact on schoolwork, academics, social relationships, and the future."* — Nora, parent of 14- and 10-year-olds diagnosed with WD three years ago, neurologic

### *Losing speech or ability to swallow and safely eat, and worsening depression, anxiety, or emotional distress*

Those who have already experienced an inability to communicate or speak clearly expressed a fear of this happening again. Some spoke of depression and suicidal ideation.

> *"I also worry if my symptoms get back to where they were before, … when I couldn't talk for two years. If I'm getting worse by the day, how much worse would I get? Will I go back to where I began? I don't know. I hope not, but at this rate, I don't know."* — Ariana, 34-year-old diagnosed with WD at 25, neurologic

> *"I also worry about the emotional toll accumulating over time. About two years ago, he started saying, 'I hate my life, and why do I have to be me?' So, we're keeping an eye on how that progresses."* — Lee, parent of a nine-year-old diagnosed with WD at four, hepatic

### *The WD community selected additional WD-related worries in the polls*

During the EL-PFDD meeting, many worried about the **inability to attend school or maintain employment**. They shared their worries about being unable to fulfill their employment responsibilities, being unable to attend graduate or professional school, and the uncertainty associated with a lack of employment. They also worry about the **inability to participate in social or family activities**.

> *"Tremendous impact on quality of life — cannot take any employment in spite of completing higher education, and long-term impact socially with little possibility to get married."* — Ashok, 37-year-old diagnosed with WD at seven, neurologic

> *"Everyone has a little bit of a tremor, and you kind of learn how to work through that as a surgeon. Every time I tremor in surgery, I think, 'Oh gosh, is this more than other people are tremoring? Is this a Wilson disease thing?' So, I think that's always in the back of my mind. …I'm just grateful for every day that I've come this far with having neurological control over my body, but that sounds really scary to have to deal with, and something I think about a lot."* — Mandy, 29-year-old diagnosed with WD at six, hepatic

> *"I can't hold a full-time job. I can't [obtain] insurance. How will I survive?"* — Ariana, 34-year-old diagnosed with WD at 25, neurologic

> *"I get scared when I have days with symptoms. I don't know how long they will last or why. I worry that I'm going to miss a lot more school. I like seeing my friends. I went two years without being able to see them every day. I worry that I won't keep up with my schoolwork or grades."* — Brinley, 14-year-old diagnosed with WD at age 11, neurologic

Additional WD-related impacts described during the meeting or in the submitted comments focused on medication-related fears. Those living with WD depend on their medications for survival. They expressed fears about medications no longer being tolerated or efficacious, running out of treatment options, and medications becoming inaccessible. This included worries about needing to fight hard for the medications that they need and potentially losing their insurance. Parents of children and adolescents specifically worried about medication adherence.

*“Psychologically, we feel vulnerability and sometimes fear because our lives depend on medication.”* — Aida, 40-year-old diagnosed with WD at 13, neurologic

*“I always worry about what happens if I can't tolerate the medication because there aren't many options. If that happens, what do you do after that? I tried zinc at one point and couldn't literally stomach that. So, there's not a lot of other options there*.” — Andy, 55-year-old diagnosed with WD at 49, hepatic, neurologic, and psychiatric

*“I am scared to retire and am concerned about Medicare coverage of penicillamine during retirement … Would a nursing home accept me because of high drug cost?”* — Karen, 63-year-old diagnosed with WD at 18, neurologic and psychiatric

*“As Wyatt gets older, my biggest fear is his medication compliance. He has such a strong, independent personality already, and I worry about what happens when he's a teenager, decides he doesn't want to deal with the restrictions anymore, or wants to experiment with alcohol, which would be terrible for his liver.”* — Lee, parent of a nine-year-old diagnosed with WD at four, hepatic

# TOPIC 2: Perspective on current and future approaches to Wilson disease treatment

During the second EL-PFDD session, members of the WD community described the different treatments and strategies they used to manage their WD-related symptoms and their hopes for the future. Their stories reflected decades of lived experience across many treatment options, highlighting both the progress made in the WD treatment landscape and the significant unmet need that remains. Poll results can be viewed on the Wilson Disease EL-PFDD website.

Wilson Disease Insight

## Managing Wilson disease involves a complex and intensive care regimen.

The WD community described treatment as a constant balancing act involving individualized medication dosing, medication timing, dietary restrictions, monitoring, and ongoing adjustments. For many, WD management feels like a second full-time job because of the medication alarms, timers, and meal planning. In addition, supportive medications and other therapies increase the complexity.

Those living with WD described experiencing very different responses to medications and different side effects. Many described having to cycle through the different available medications to try to manage symptoms and side effects.

> *"I've tried different therapies, but the side effects and physical constraints, keeping it cold while I'm traveling for business and things like that, always pushed me back to penicillamine. What has never changed is how hard it is to take the medicines exactly as directed, multiple times a day and separated from food. … And here I am. I've been on the regimen for half a century now. It's difficult."* — Erol, 65-year-old diagnosed with WD at 13, hepatic

> *"Managing Wilson disease requires constant vigilance — medication timing, dietary monitoring, hydration, and laboratory follow-up. When combined with cognitive fatigue, this can feel like managing a full-time responsibility in addition to work or school."* — Laura, 30-year-old diagnosed with WD at seven, neurological and psychiatric

> A mother of an adult patient said, "*Every day begins early with his first medication, penicillamine, which must be taken on an empty stomach. An hour later, we give him a mix of meds — baclofen, clonazepam, glycopyrrolate, and Ingrezza. An hour later, he gets breakfast, which is a carton of liquid food given through his PEG tube. At 11:00 AM, he gets zinc. At 12:00 PM, more food and medications (baclofen, clonazepam, glycopyrrolate, and escitalopram). At 3:00 PM, more penicillamine, and at 5:00, zinc. At 6:00 PM, food and baclofen, clonazepam, glycopyrrolate. At 8:30, baclofen, clonazepam, glycopyrrolate, risperidone, and a pill to alleviate stomach pain…then one more meal at 9:30."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

## Poll 5 Results

## Disease-modifying medications for Wilson disease are an unmet need. At present, copper chelators are the most frequently used, followed by zinc.

On average, those living with WD have used 3.4 different medications to manage copper accumulation or WD-related symptoms. Medical approaches for WD, including liver transplantation, are listed in descending order below, illustrated with select patient quotes.

### *Copper-chelating medications*

Lifelong copper-reduction therapies — to remove excess copper and prevent copper (re)accumulation — are the standard-of-care treatment for WD and the most commonly used medication. These include penicillamine [Cupramine], trientine [Syprine], and trientine tetrahydrochloride [Cuvrior]. Another chelating medication mentioned during the meeting was DMPS (2,3-dimercaptopropane-1-sulfonate).

**Penicillamine.** For many years, penicillamine was the only therapy available, and for many individuals with hepatic-only manifestations, it can be a successful long-term therapy. For others, penicillamine does not work at all or eventually loses efficacy. Penicillamine can be very toxic, inducing allergic reactions in some patients, worsening neurologic symptoms, and causing long-term joint problems and disfiguring skin effects and rashes. Penicillamine timing is difficult, particularly when combined with zinc.

> When first diagnosed: *"There was one treatment at the time, the drug penicillamine. My doctor said if I tolerated it and took it every day for the rest of my life, I'd live a normal life. ... I was lucky I tolerated the drug, and it worked. … While penicillamine saved my life and was effective in managing my disease, years later I developed troubling side effects."* — Rhonda, 63-year-old diagnosed with WD at 21, hepatic
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> *"[My siblings and I] took D-penicillamine, the only drug marketed for Wilson disease at the time. We took it for about two weeks, and the result was a disaster. Sergi and Eugeni spent almost two years in the hospital in a bed with spasms and cramps throughout their bodies, which they could not control. We no longer walked, talked and could only eat by a direct tube to the stomach."* — Eugeni, 37-year-old diagnosed with WD at 11, hepatic and neurological

**Trientine hydrochloride [Syprine] and trientine tetrahydrochloride [Cuvrior].** Again, these medications help to resolve symptoms for many patients but can have serious side effects such as increased tremors or sleep issues. They have many of the same drawbacks as penicillamine, including strict medication timing, and some of the formulations require refrigeration.

> Minh's gait issues improved with medication. *"At one point, he was wheelchair bound, but it's definitely improved since we got the Wilson disease diagnosis, and he started using trientine three years ago. A lot of his symptoms have improved. He's now able to go out for walks independently, and he boasts that he walks for miles a day now, which is great."* — Joseph, cousin of a 26-year-old living with WD, hepatic, neurologic, and psychiatric
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> *"Once I did take the FDA-approved medication trientine, within two days, my tremors increased to five times a second, which is actually faster than a helicopter — helicopter is only four times a second. I cannot walk, talk, or speak within two days of taking the*

*medication. I would just say 'I had an adverse reaction' is an understatement."* — Ariana, 34-year-old diagnosed with WD at 25, neurologic

### *Zinc*

In the online poll, zinc was the second most selected WD medication, administered to block the uptake of intestinal copper. Zinc can include prescription formulations [Galzin] and over-the-counter brands [Gluzin]. Zinc works well for many living with WD but requires careful timing with meals and other medications and can cause side effects, including severe gastric issues such as nausea, cramping, and gastric distress, which can interfere with compliance.

> *"I switched from penicillamine to Galzin, a prescription zinc therapy, because it's safer not to be on chelation therapy. I did great with Galzin and stayed on it for years through high school."* — Mary M., 36-year-old diagnosed with WD at nine, hepatic, neurologic, and psychiatric

> *"I was put on Galzin, couldn't tolerate the GI side effects, so I switched over to an over-the-counter preparation [a different salt of zinc], which I'm currently taking. … It's so difficult to take it separate from food. … But in spite of being a physician and knowing the importance of taking medication, I would often conveniently forget to take it because I wanted to live life."* — Alpana, 60-year-old diagnosed at 8, hepatic

### *Investigational medicine in a clinical trial*

Many of those in the WD community have participated in different clinical trials. People who participated in the tetrathiomolybdate trial described life-changing improvements in tremors, dystonia, cognition, and overall functioning. When this trial was discontinued, patients were devastated and had to resort to therapies they viewed as less effective or less tolerable. During the meeting, individuals spoke about having been excluded from clinical trials because of their age or because their specific ATP7B gene mutation would not be addressed by the gene therapy.

> *"Two to three months after I started taking the drug, slowly one symptom at a time vanished. It was both physical and mental changes that I noticed. … After discontinuation of the study drug, my tremors and dystonia returned. What I miss most is the sense of relief I had during the study — I could stop my constant search for solutions to manage my tremors and Wilson disease."* — Arjun, 30-year-old diagnosed with WD at age 10, neurological and psychiatric

> Enrolling in the TTM clinical study, "*Was one of the best decisions in my life. I remained on the study drug for more than five years, and I believe it completely reversed all my neurological symptoms, and I was able to return to working full-time as a nurse in the hospital, something I wasn't sure I would ever be able to do again. During that time, I felt healthy, capable. Most importantly, I felt normal. My body tolerated the medication extremely well."* — Ginta, 33-year-old diagnosed with WD at 21, hepatic, neurologic, and psychiatric

> *"I was fortunate to get into a double-blind clinical treatment study, which I believe saved my life. … TTM or the Alexion drug. For me, the time periods when I was on those drugs have been the best, I think, in my life. … That started in October of 2000. I was discharged from the hospital in December of 2000. I went back to college classes in*

> *January. And that's a miracle."* — Lana E., 42-year-old diagnosed with WD at 22, hepatic, with minor neurologic

***Liver transplantation***

A small proportion of people with WD go into acute liver failure or require a liver transplant at the time of initial diagnosis, because they already have hepatic failure. Other WD patients may need a liver transplant later in their course, if their liver deteriorates further, or because of chronic liver disease. Liver transplantation restores normal copper metabolism and can prevent further neurological damage, but it cannot reverse the existing neurological damage. A liver transplantation requires lifelong immunosuppressive medication to prevent rejection of the new liver.

> At the age of 27, *"My liver failed because of the cirrhosis, and I needed an urgent liver transplant. … Now I am liver transplanted, so I only take medication for the transplant. The transplant saved my life because my liver was very bad before."* — Sergi, 37-year-old diagnosed with WD at 11, hepatic and neurological

> Rhonda describes another patient she met shortly after her own diagnosis who required a liver transplant*. "My doctor said … they did not know why my liver hung on and hers did not. I met Darcy in the ICU as she waited for a donor liver — an image I'll never forget. That's when I knew just how serious my disease was … Amazingly, 42 years later, she's still living with that donor liver."* — Rhonda, 63-year-old diagnosed at 21, hepatic

### *The WD community selected additional medical approaches*

Additional medications mentioned in the polls include medications for **anxiety and depression** (clonazepam, escitalopram, propranolol), **gastrointestinal medications for vomiting or nausea** (ondansetron), and **pain management medications**. There were many comments about **Botox** injections and **seizure medications**.

> *"Botox has actually helped [my tremors and pain]. I get Botox injections in my neck, and it releases some of the pain, but not all of it, unfortunately."* — Ariana, 34-year-old diagnosed with WD at 25, neurologic

> *"I also take propranolol, which helps with anxiety and tremors and also helps with migraines."* — Ginta, 33-year-old diagnosed with WD at 21, hepatic, neurologic, and psychiatric

The WD community described other medical approaches during the meeting and in submitted patient comments. These other approaches include sleep medications (melatonin), migraine medications (fremanezumab-vfrm, ubrogepant), muscle relaxants (baclofen, glycopyrrolate), and antipsychotic medications (risperidone, clozapine, lithium). Some use off-label medications for involuntary movements (propranolol, deutetrabenazine [Austedo], valbenazine [Ingrezza]).

## Poll 6 Results

## A low-copper diet and laboratory or clinical monitoring are the most important non-medical approaches to WD treatment, but many other approaches are used.

Members of the WD community each use an average of three different non-medical approaches. These are listed in descending order below, illustrated with select patient quotes.

### *Low-copper diet*

A low-copper diet is the top approach to managing WD. The diet must be adhered to for a lifetime. Managing a restrictive diet and coordinating medication timings takes a great deal of time and effort and can be especially difficult during childhood and adolescence.

> *"Alongside medication, I've also followed low-copper diets since my teens. Giving up favorites like chocolate, nuts, shellfish, even mushrooms was painful, especially as a teenager, when my peers were free to eat whatever they wanted. … Now, as an adult, I recognize the risk more clearly and avoid those foods completely, but the longing for them never fully goes away."* — Ade, 45-year-old diagnosed with WD at 14, hepatic

> *"Emma reads the labels of every prepackaged product or dessert to make sure there are no high-copper ingredients. We have discussions with teachers and new friends about dietary restrictions and can't-haves. I have to adjust the meals we have in our routine and keep their diet in balance. The girls get nervous if they don't know what is in a dish."* — Nora, parent of 14- and 10-year-olds diagnosed with WD three years ago, neurologic

### *Routine laboratory or clinical monitoring*

Those living with WD require ongoing monitoring for copper excretion for medications, including penicillamine, trientine, and zinc, to be optimally dosed. A 24-hour urine collection is difficult for everyone, especially younger children, and impossible for those who are not yet toilet-trained.

> *"For me, monitoring is most important — diet and medication compliance secondarily."* — Cathleen, 65-year-old diagnosed with WD at the age of 11, hepatic, asymptomatic

> *"There were many more appointments figuring out the right dose of medication to treat my symptoms. We travel to see the experts two to three times a year. I see the cardiologist, neurologist, GI liver specialists at home, along with my regular doctor and now dermatology, allergy, and neurogenetics. I get blood draws and have to do 24-hour urine tests. I have to stay home for a full 24 hours to do the urine test, pee in a jug, and carry it down to the basement fridge."* — Brinley, 14-year-old diagnosed with WD at age 11, neurologic

> *"Zinc medication three times daily away from food, doctor check-up every four months, blood work every three months, ultrasound every six months, urine collection every year."* — Hayley, parent of a 14-year-old diagnosed with WD at four, hepatic

### *Physical therapy, exercise or structured physical activity, occupational therapy, and speech therapy*

Many have found that therapies have helped them to successfully regain and maintain their ability to stand, walk, write, and speak. These therapies are expensive and take a great deal of effort.

> *"With hard work, the three of us did rehabilitation, and we managed to walk again with difficulty. Sergi and Eugeni managed eating by mouth again. We did physiotherapy and speech therapy. …We all three started sailing, a sport that was great for our rehabilitation, helping with balance, strength, and coordination."* — Eugeni and Sergi, 37-year-olds diagnosed with WD at 11, hepatic and neurological

> *"I had to relearn how to write, swallow, walk, and talk. For two years, I did speech, occupational, and physical therapy while using a typing device to keep up with my classes. I stayed strong and graduated with a bachelor's degree in graphic design."* — Nicole A., 41-year-old diagnosed with WD at 10, hepatic, neurologic, and psychiatric

> *"I underwent intense physical, occupational, and speech therapy to regain all of my basic functions. I've been told that people can't tell I have a neurological condition, but now my symptoms are hidden: I deal with crippling anxiety, depression, and fatigue. But other than that, I worked immensely hard to regain what I lost."* — Emma, 20-year-old diagnosed with WD at 17, neurologic, and psychiatric

### *The WD community selected other treatment approaches selected in the polls*

These include **psychological therapy or counseling**, **mobility and positioning equipment**, **feeding therapy, or other nutritional support,** including feeding tubes.

> *"The presence of a stomach tube has further complicated daily routines, requiring specialized feeding and increasing vulnerability to infections."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

The WD community also described other treatment approaches during the meeting or in submitted patient comments. These include general good health practices, such as getting enough sleep and exercise and avoiding alcohol. Some avoid potential heavy metal exposure by using water and shower filters and only cooking with lower temperature, moisture-based methods. Some take different types of dietary supplements. Other approaches mentioned included electroshock therapy as well as medical-grade red-light therapy for pain relief.

## Poll 7 & 8 Results

## Medication and treatment approaches for Wilson disease work for many but not all patients and have significant drawbacks.

While 94% of polling respondents indicated that their treatment works "to a great extent" or "somewhat" to control the symptoms, a significant minority (6%) said that their treatment works "very little" or "not at all". The WD community identified many treatment drawbacks, including strict medication timing away from meals/fasting, side effects that interfere with medical compliance, and the inability of these medications to stop or slow disease progression.

Treatment-specific drawbacks are listed in descending order below, illustrated with select patient quotes.

### *Strict medication timing away from meals/fasting*

**Strict medication timing away from meals/fasting, medication refrigeration and storage requirements,** and medication **administration requiring too much effort and/or time commitment** were identified as related challenges by those attending the meeting. The WD community emphasized the difficulty of taking medications multiple times per day on an empty stomach, waking in the middle of the night to take doses, and managing refrigeration requirements, frequent lab testing, and constant scheduling that complicate work, school, travel, and social life. Patients and caregivers were candid about the impact of treatment burden on adherence. Several acknowledged missing doses, not intentionally, but because life interferes, particularly for children, adolescents, and young adults seeking independence.

> *"I've got zinc twice a day, penicillamine twice a day. That's four times a day with a three-hour fasting period for each one of those dosings. That's 12 hours of fasting. I'm asleep eight hours. That leaves me four hours to get the three meals in. The issue is just a complicated lifetime, and you end up skipping the normal life moments."* — Erol, 65-year-old diagnosed with WD at 13, hepatic

> *"Managing Wilson disease is a full-time job. My treatment includes around 10 pills a day, quarterly Botox injections, a low-copper diet, and constant planning. The side effects can be rough. Pills used to make me gag, arthritis makes my fingers swell painfully, and sometimes migraines land me in the ER, but I've learned how to cope."* — Nicole A., 41-year-old diagnosed with WD at 10, hepatic, neurologic, and psychiatric

### *Side effects, including neurologic worsening*

Individuals living with WD selected side effects as a top treatment drawback. Chelators and zinc are frequently associated with severe nausea, gastrointestinal distress, fatigue, and neurological worsening. The latter is particularly traumatic for many. For some, trientine causes sleep issues. Some experienced severe reactions to penicillamine, including autoimmune complications, joint degeneration, chronic pain, and skin changes.

> *"The biggest downside of my treatment is nausea. All the medication I've ever taken for Wilson disease makes me nauseated, and the complex dosing schedule is really challenging. Taking medication three times a day on an empty stomach is incredibly difficult for compliance."* — Jean Marie, 62-year-old diagnosed with WD at 16, neurologic, and psychiatric

> As a result of taking WD medications*, "I experienced severe head pain like someone was hammering a nail into the center of my head or crushing my bones. … I had drooling, tremors, dystonia, hallucinations, and insomnia. My shirt would get soaked within minutes from drooling, and even simple tasks like eating or putting on a shirt became almost impossible because of the tremors. I lost my independence completely."* — Anonymous, 30-year-old diagnosed with WD at 10, hepatic, neurologic, and psychiatric

> *"In the year and a half that I was on trientine, my symptoms worsened even further. So, it went from loss of balance to completely bedbound, could not move myself at all, slurred speech to completely nonverbal. I could not move my face muscles at all. I could not close my mouth at all, so I was drooling 24/7."* — Emma, 20-year-old diagnosed with WD at 17, neurologic and psychiatric

### *Lack of medication efficacy*

Even with treatment, outcomes are uncertain. During the meeting, those living with WD selected many poll response options related to lack of medication efficacy, including: **does not stop or slow disease progression**, **not very effective at treating target symptom(s)**, **only treats some, not all, symptom(s)**, **loses effectiveness with time**, and, in some cases, **makes symptoms worse**. The lack of efficacy is particularly a problem for those with neurological symptoms.

> *"At first, he was prescribed trientine, and we were told he had a good chance of recovery. But instead of improving, within three months, he went from being an independent young man to being bedridden. He lost his ability to walk unassisted, required a stomach tube for feeding, and struggled to speak. …His decline was so rapid that trientine was stopped and replaced with zinc, but things only worsened. ... Eventually, a local neurologist prescribed penicillamine, but the disease continued to progress."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

> Medication dosing adjustments or switching medication types are often necessary and complex, especially when multiple medications are required. *"You have to deal with mood stability from both anxiety and depression. He has some sleep deprivation, so he's got to take medication for that. So there's always this intermix, this whole cocktail of medicine. Then the sleep deprivation gets to be too much, or depression's not quite working out, the medication is not really addressing the issue. Then he's got to switch to something else."* — Dan, parent of a 27-year-old diagnosed with WD at 22, psychiatric

### *Limited availability or accessibility*

During the meeting, many in the WD community described difficulties accessing treatment, including challenges accessing medical care or regular monitoring, fragmented medical care, financial and insurance challenges, and the unexpected cancellation of a clinical trial for a medication that many patients say they benefited from. As a result, treatment can be delayed, inconsistent, or less effective. Some described how these situations resulted in symptom progression and feelings of trauma.

> Joe lost his job. "*He was not able to get his hands on the medications, and he deteriorated very rapidly, which eventually led to his hospitalization, where he fell into a vegetative state, and he remained in that state until his untimely passing, which was just in December."* — Brock, friend of Joe who was diagnosed with WD at 24 and recently passed away at 29, neurologic and psychiatric

> *"I was part of the clinical trial for a new oral medication. To me, it felt like a breakthrough. It worked so well that even at the half standard dose, I was flushing copper very effectively with minimal side effects. I thought this could be the answer I'd been waiting*

*for. But after several extensions, the company ended the trial and stopped developing the drug. The decision was devastating. It felt like the rug has been pulled from under me, like the dream solution had slipped away."* — Ade, 45-year-old diagnosed with WD at 14 years, hepatic

## Poll 9 Results

### The Wilson disease community needs therapeutic options to slow or stop disease progression, improve or reverse neurological symptoms, and have easier administration.

The WD community wants a medication to slow or stop disease progression, however, many still wish for a cure. The top wishes for a new WD treatment are listed in descending order below, illustrated with select patient quotes.

#### *Slow or stop disease progression*

This was identified as the top medication requirement in the polls, and some patients asked to combine this with treatment durability and quality-of-life outcomes.

> *"From those options, I kind of paired slowing/stopping the progression with the durable effectiveness over time, just as having peace of mind, knowing that the treatment that my daughter may be taking in the future is working and doesn't lose its effectiveness over time is important."* — Ed, parent of a three-year-old diagnosed with WD at six weeks, still asymptomatic

> *"For me, the most significant impact of Wilson disease has been neurological and psychiatric rather than visible physical symptoms. Effective treatment would ideally address both copper control and meaningful quality-of-life outcomes."* — Laura, 30-year-old diagnosed with WD at seven, neurological and psychiatric

> *"I would ideally like to have gene therapy so I could eliminate my symptoms. If that's not possible yet, it would be nice to have a one time a day dose or even an infusion every three months or less."* — Jean Marie, 62-year-old diagnosed with WD at 16, neurologic and psychiatric

#### *Easier medication administration*

The **ability to take medication without strict fasting**, **reduce treatment frequency (e.g., fewer doses per day),** and **eliminate the need for refrigeration or special storage** generated so many related comments during the meeting and in the submitted comments that they are grouped. The WD community wanted medication that is simpler to adhere to, with more flexible dosing, extended-release formulations, or once-daily, weekly, or long-acting therapies.

> *"If I could wish for one thing, it would be for simpler treatment. The idea of gene therapy excites me. I wouldn't have to take pills daily, worry about forgetting them, or plan around meals. Just living. That's what I hope for myself, and for every other person with Wilson disease."* — Nicole A., 41-year-old diagnosed with WD at 10, hepatic, neurologic and psychiatric

> *"The most challenging aspect of my medications is having to take them 4 x day, one hour before I eat or two hours after I eat. For me, with an active lifestyle, this is difficult. My ideal treatment would be the ability to take the medication...regardless of timing of distance before/after meals; faster action would be wonderful."* — Janet, 77-year-old diagnosed with WD at 15, hepatic

> *"If I could describe an ideal treatment, it would be something simple to take once a day, well-tolerated, and effective at keeping copper levels stable. It wouldn't require refrigeration, which can be especially challenging for people who travel or work irregular hours*." — Ginta, 33-year-old diagnosed with WD at 21, hepatic, neurologic, and psychiatric

### *Improve or reverse neurological symptoms*

A huge unmet need in the WD community is for treatments that address neurological symptoms, including pain, fatigue, and tremors.

> *"My hope and prayer is that new treatments will be developed specifically for neurological Wilson disease, something that will allow James and others like him to have a better quality of life. Because right now, this disease has taken over not just his life, but ours as well."* — Kim, parent of a 26-year-old diagnosed with WD at 20, neurologic with minor hepatic

> *"I think neurological patients really need a more substantial drug that doesn't leave patients with this lifelong dealing with pain and fatigue."* — Emma, 20-year-old diagnosed with WD at 17, neurologic and psychiatric

> *"Improve neurological symptoms, not require refrigeration, and be cost-affordable and straightforward to obtain without logistical hurdles (e.g., insurance, needing to use a location-specific pharmacy)."* — Ian, 29-year-old diagnosed with WD at 12, hepatic and neurologic

### *The WD community selected other treatment goals in the polls*

Other specific things that the WD community needs in an ideal new treatment for WD, selected in the polls, included: **more durable effectiveness over time,** for example, with gene therapy; **improve tolerability** and reduce side effects; **improve specific activities of daily functioning,** including quality of life; and **reduce monitoring and emergency interventions**. Some voiced the wish for personal copper monitoring systems similar to how diabetics measure blood glucose.

> *"I am excited about the gene therapy. To be saved from a lifetime of side effects from pharmaceutical treatments and complications of WD, including kidney and liver disease would be incredible."* — Patricia V., 70-year-old diagnosed with WD at the age of 14, hepatic with minor neurologic

> *"What I really want is something that gives me quality of life. I'm about quality of life, not longevity without quality. And that means being able to participate in normal activities, like sharing meals with friends without having to worry about medication timing every single time."* — Jean Marie, 62-year-old diagnosed with WD at 16, neurologic and psychiatric

The WD community identified other important treatment needs during the EL-PFDD meeting or in the submitted comments. These needs include **more mental health support along the entire WD treatment journey; more research into WD treatments for pregnancy**, including more information about safe dosages during pregnancy and breastfeeding; **newborn screening for WD; more research into pediatric treatment and copper monitoring; and WD screening for psychiatric patients**.

Wilson Disease Insight

### The WD community is eager to participate in clinical trials.

Many who attended the EL-PFDD meeting spoke with enthusiasm about participating in clinical trials. During the meeting, in submitted comments, and in the pre-meeting survey, the WD community shared the factors important in deciding whether to participate in a new research trial. These include strong neurological safety data, inclusion of cognitive and psychiatric endpoints, a regimen that reduces daily burden, low risk of regression or worsening of neurological symptoms, no significant side effects, distance and frequency of traveling to the trial site, a clear communication of risks, and a realistic and affordable pathway to continued medication access if effective.

## Closing voices

*"Making WD meds, diet, and testing a priority in my life has helped me become a healthier and better person. This process has taught me that the healing I've experienced far outweighs the cost of being inconvenienced by diet, testing, or side effects."* — Andy, 55-year-old diagnosed with WD at 49, hepatic, neurologic, and psychiatric

*"For me, Wilson disease is not just about copper levels. It's about navigating a multifaceted condition, which is physical, mental, emotional, while still building a meaningful, joyful life*." — Raisa, 31-year-old diagnosed with WD at 17, hepatic, neurologic, and psychiatric

*"Consistent access to affordable medication and healthcare for monitoring is crucial for long-term management and care of Wilson disease…to live healthy, successful lives."* — Ian, 29-year-old diagnosed with WD at 12, hepatic and neurologic

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