

# The Team



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The Wilson Disease Association (WDA) is a 501(c)(3), all-volunteer organization striving to promote the well being of patients with Wilson Disease and their families and friends. We rely on donations to achieve our mission.

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A DEEPER UNDERSTANDING  
OF THE PATIENT REGISTRY  
***A Wilson Disease Legacy Project***



in partnership with

**Yale SCHOOL OF MEDICINE**

## Creating our legacy

*The Patient Registry creates a framework for advances in diagnosis, treatment and potential cures for the disease. Not only will the current generation of Wilson Disease patients benefit, but this registry will serve as a roadmap for future generations to come.*

### FAST FACTS

- » It is the first of its kind in the world.
- » Patients will be followed at various study sites in the U.S, the U.K. and Europe.
- » A multi-center registry enables us to collect data and bio-specimens (blood, urine) from a diverse population of patients, both adult and pediatric.
- » It is a study that will require at least five years.
- » It has a cost of approximately \$3 million dollars as it is currently structured.
- » We receive no government funding for it.

### WHAT IS THE PATIENT REGISTRY & WHY IS IT SIGNIFICANT?

The Wilson Disease Patient Registry (WDPR) is a natural history study. Patients, medical practitioners and caregivers have waited years for this type of study in order to address unmet needs and unanswered questions about diagnosis, treatment, and monitoring. This type of study follows a group of people over a period of time who have a specific medical condition or disease. The study collects health information in order to better understand how the disease develops and how to treat it. The data collected will also be used to evaluate new therapies. In addition to data, the WDPR is also collecting and storing bio-specimens from each patient enrolled. All specimens are analyzed by the same laboratory in the UK. to ensure consistency and stored in a central facility at Yale University.



### AIM OF THE WDPR STUDY

By analyzing patient data and bio-specimens, the goal is to determine the ideal tests needed for diagnosis and the best monitoring practices. When compiled and analyzed by all study site investigators, this information will reveal the proper use of current treatments and guide the development of future therapies. These data may also help to define ideal patient outcomes.



### STUDY SITES

Study sites were chosen based on their expertise in adult and pediatric hepatology, neurology, psychiatry, nutrition as it relates to WD. Each site will have a study coordinator who will manage data, patient communications, and other important administrative tasks.



### STUDY POPULATION

Patients will be adults and children who are seeking a diagnosis of WD; relatives of patients who need to be screened for WD; newly diagnosed patients who are in their initial stage of treatment; and those who have been on treatment for many years.

## What we have accomplished so far

DATA FROM YEARS 1 & 2 HAVE ALREADY YIELDED INFORMATION THAT WAS PREVIOUSLY UNKNOWN.

We have a current enrollment of **75 patients; 52 adult and 19 pediatric**. They range in age from 2.5 to 74 years old with an average age of 36.

From this population we have learned that **50% of the adults have a major depressive disorder**.

This indicates that we need to evaluate depression and anxiety in the pediatric population as well.

*This illustrates the valuable progress that has been made in two short years with only a small cohort of patients at one center. Years 3 – 5, which will include a larger (+225 patients), a more diverse cohort of patients from other registry sites will yield information that is even more significant.*



- » Registry investigators have already published one scholarly paper in the Journal of Psychosomatic Research, Major depressive disorder in patients with Wilson disease.
- » Psychiatric assessments, to measure cognitive function, mood disorders, psychosis, personality changes and anxiety, will continue throughout the duration of the registry.
- » Another study was conducted using data from the registry. The aim was to determine quality of life (QOL) in Wilson disease patients. Both mental health and physical health are affected in WD. It was found that patients with WD have worse mental health QOL scores than physical health QOL scores. QOL assessments will continue throughout the duration of the registry.
- » These findings have been presented at professional meetings in the following countries: Denmark, Netherlands, United States, and United Kingdom in 2018 and 2019.
- » Standard tests used to determine copper status are being collected and tested at a central laboratory run by Dr. Chris Harrington in the UK. These are serum ceruloplasmin and copper, which aid in determining "free copper." Data from Years 1 and 2 have revealed that the calculation method of determining "free copper" is not a reliable indicator of copper status. To resolve these inconsistencies, Dr. Harrington has developed a test to measure "free copper" directly instead of using the calculation.

## Moving forward

YEARS 3 – 5 WILL BE CRITICAL IN EVALUATING THE FOLLOWING STANDARD TESTS USED TO MONITOR FOR GOOD COPPER CONTROL. They will be carefully studied and conclusions will be made about what is the best way to treat and monitor WD patients. Improved rating scales could be developed using this information. Clinical trials may also be designed to determine the best practices that will benefit current and future patients.



**GENETIC-** Molecular analysis of the ATP7B gene, will be done on each patient enrolled. The analyses will all be done by Dr. Sihoun Hahn at Seattle Children's Hospital in order to produce consistent results.



**HEPATIC EVALUATION-** Retrospective data on patients who have had a liver biopsy prior to entering the registry will be studied and categorized. New patients entering the registry who have not previously had a liver biopsy will have one and their results will be captured. Other laboratory testing, used to determine severity of liver disease, such as ALT, AST, albumin, INR, Bilirubin, GGT, alkaline phosphatase (ALP), creatinine and complete blood count (CBC) will be collected.



**NEUROLOGIC EVALUATION-** All enrollees will be evaluated for neurological symptoms using a testing instrument called the Unified Wilson Disease Rating Scale (UWDRS). They will also be videotaped (with consent) to capture subtle differences that may not be picked up by the UWDRS.



**COPPER METABOLISM-** As previously stated, ceruloplasmin and serum copper will continue to be tested and level of "free copper" determined. 24 hour urine copper for copper content will also be analyzed. Urine zinc levels for patients on zinc treatment will also be measured.

“Patients enrolled in the registry will likely have been on more than one treatment, or a combination of treatments. It will be important to understand why therapies were changed over the course of patients' treatment. Was it because of side effects or what was perceived to be treatment failure? To date we do not know exactly what constitutes treatment failure. It will be important to accurately define “treatment failure” in order to better design new clinical trials. It will also aid in learning how best to monitor patients who enter new clinical trials.”<sup>[1]</sup>

(1) Schilsky ML, FDA Office of Orphan Products Development (OOPD), Orphan Products Clinical Trials Grants, submitted, 2016.