



Mark Guttman, MD, FRCPC – Center for Movement Disorders

Individuals at risk for HD are given a clinical diagnosis of the disease only after they have developed motor abnormalities. Clinicians, families and patients are aware that changes occur in many nonmotor domains, including cognition and behaviour, years before the motor-dependent clinical diagnosis is made in some individuals.

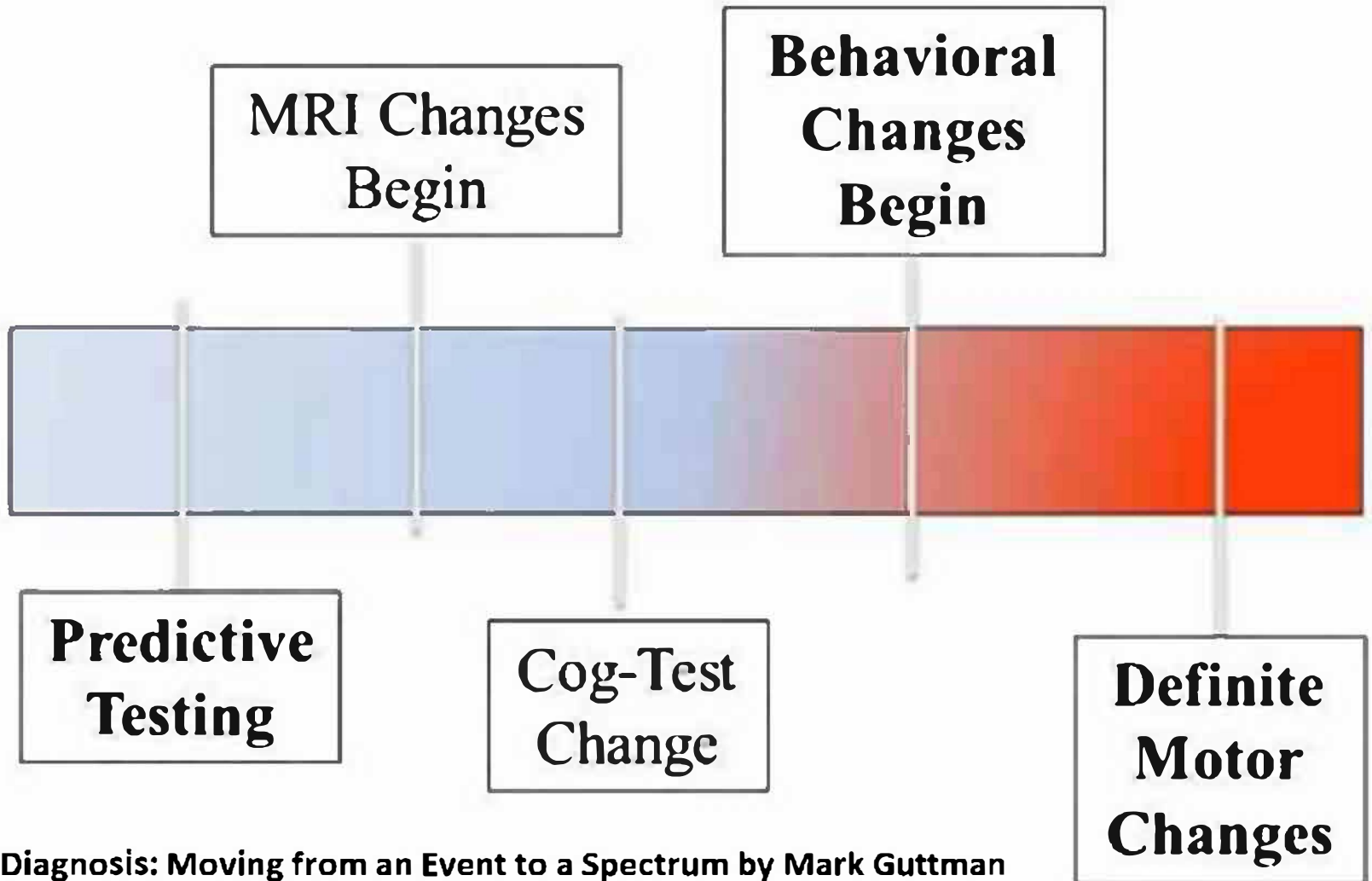
Longitudinal observational studies have identified that there are many changes that occur before the clinical diagnosis of HD. Researchers postulate that these changes should be considered part of the pathological process of HD. Since these changes have occurred before clinical diagnosis using motor criteria, to date it has been difficult to categorize them and to determine their relevance when planning clinical trials and dealing with regulatory agencies. Using the concept of a patient converting from a presymptomatic state to being diagnosed with HD as an endpoint of clinical trials creates considerable methodological problems. Furthermore, if this is to be the only focus of disease modifying research in HD, we will lose the opportunity to modify the underlying disease process in the earliest stages of the condition.

We propose a different conception of HD as the spectrum of clinical manifestations that includes the earliest symptoms as part of HD even before diagnosis by current diagnostic criteria. The paradigm shift is to change the focus of clinical research from the concept of preventing the transition of subjects from a “preclinical” to “diagnosed with HD” state to altering the progression of HD throughout the entire spectrum of the disease.

Top

Changing Prevalence of HD: Altered Demographics and its Implications

Spectrum of HD Symptoms



Onset Type

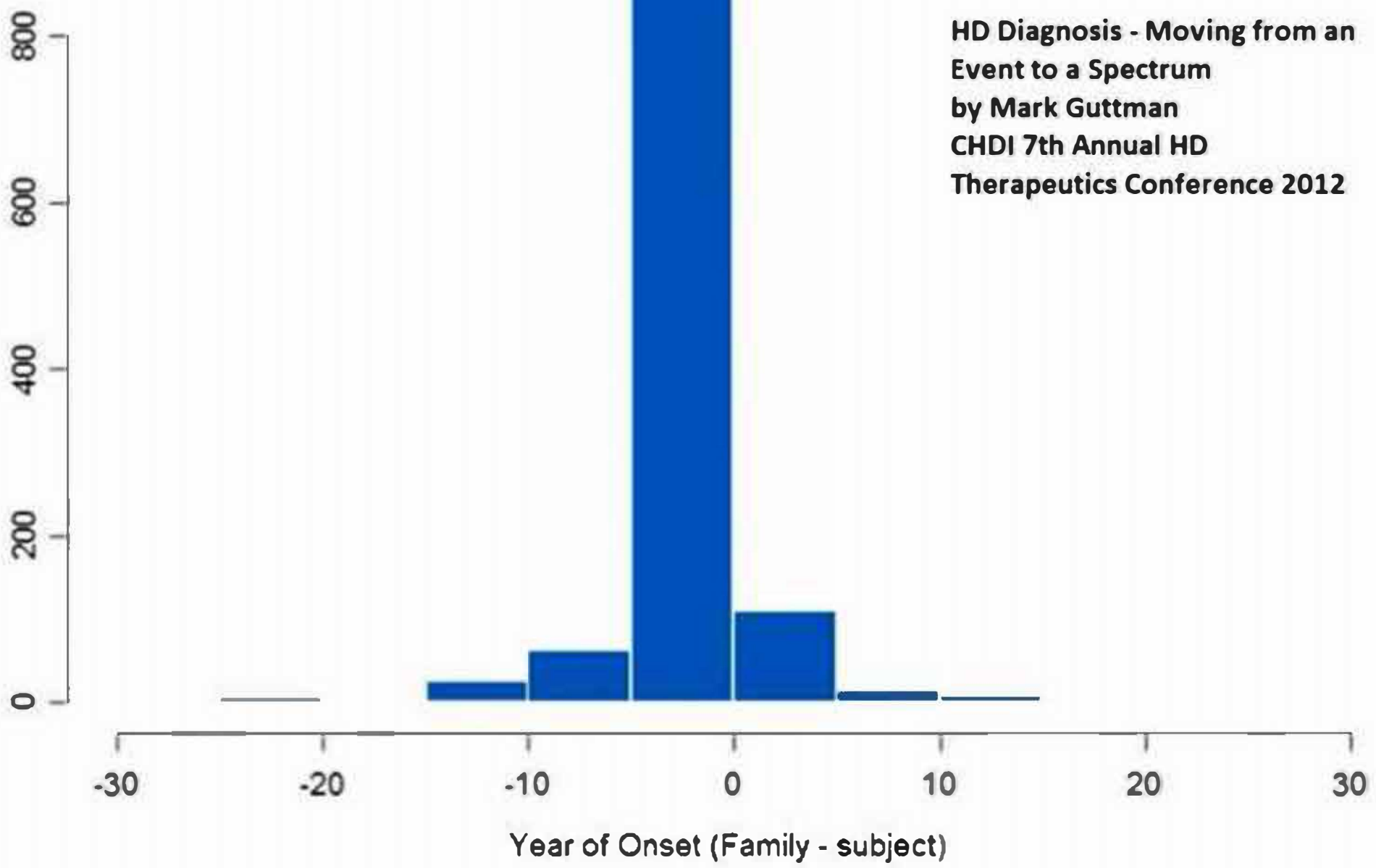
- The COHORT study collected data on the class of first symptoms observed by subject, an objective rater, and the family.
- First symptoms were classified as “motor”, “cognitive”, “psychiatric” and “other”. A total of 1443 subjects recorded answers to at least one of these questions.

	Motor	Cognitive	Psych.	Other	Not Given
Family	777	180	262	17	207
Rater	792	175	217	16	243
Subject	883 (63%)	259 (19%)	216 (15%)	37 (3%)	48

Diagnosis: Moving from an Event to a Spectrum by Mark Guttman

CHDI's 7th Annual HD Therapeutics Conference 2012

**HD Diagnosis - Moving from an
Event to a Spectrum
by Mark Guttman
CHDI 7th Annual HD
Therapeutics Conference 2012**



Proposed Paradigm Shift: Spectrum Versus Onset

- Need to move away from “Event” based concept that disease onset occurs after sufficient motor symptoms
- Move towards “Process” based concept that HD symptoms are a spectrum that can be measured from the earliest symptoms
- The paradigm shift is data based upon evidence that biological alterations are taking place at least 15 years before motor diagnosis
- Acknowledges what patients and their families have been reporting to clinicians