Perspectives on Research

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Disclosures

- Dr. Domoto-Reilly receives research funding from the National Institutes of Health as well as from Biogen.

Types of Research Studies

- Longitudinal
  - Follow participants over time

- Observational
  - Collect information
    - Daily activity questionnaires, family history, cognitive testing, neurologic examination
    - Biospecimen: blood, cerebrospinal fluid, skin biopsy, brain donation
- Interventional ("Clinical Trial")
  - Participants are given an investigational treatment
    - drug, cognitive training, transcranial magnetic stimulation
  - Typically a portion of participants are given placebo / sham treatment

Many studies require a co-participant

FTLD-specific measures are needed

- Cognitive and behavioral scales
- Biofluid measures
  - Blood, cerebrospinal fluid (CSF)
- Imaging measures
  - Structural (MRI), functional (FDG-PET, fMRI), molecular (PET)

- Biological marker ("biomarker"): a biologic characteristic that can be objectively measured. For example:
  - Blood pressure is measured to evaluate cardiovascular health/disease
  - Creatinine level is measured in blood to evaluate kidney health/disease

- Role of Biomarkers
  - Diagnostic
  - Prognostic
  - Monitor change over time and response to treatment

A·R·T·F·L

Advancing Research & Treatment for Frontotemporal Lobar Degeneration

Longitudinal Evaluation of Familial FrontoTemporal Dementia Subjects

LEFFTDS

Update on ARTFL / LEFFTDS

Brad Boeve MD

Mayo Clinic

Rochester, Minnesota

Howard Rosen MD and Adam Boxer MD PhD

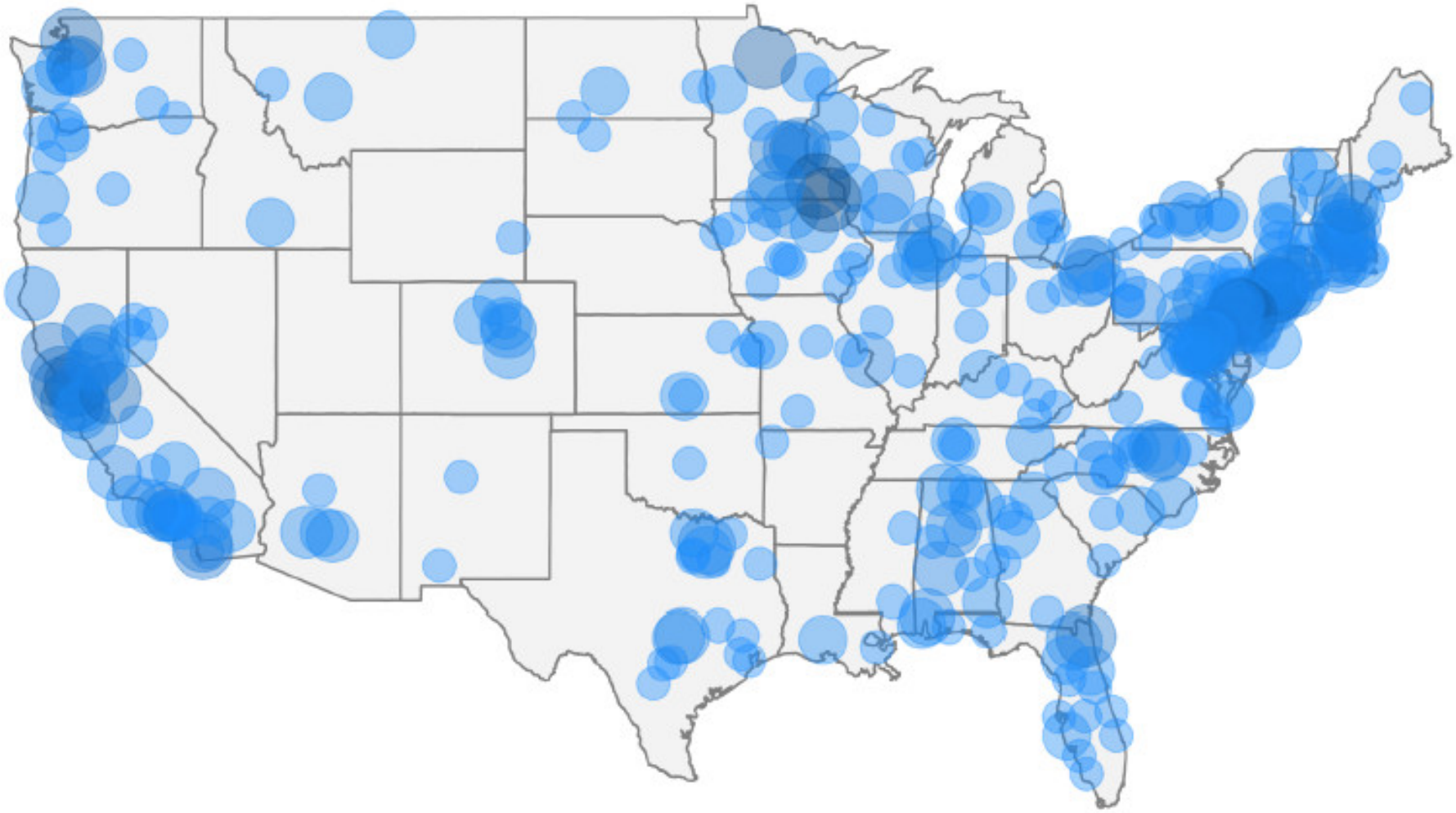
University of California - San Francisco

San Francisco, California

and the ARTFL/LEFFTDS Consortium

18 Clinical Sites

Participant distribution



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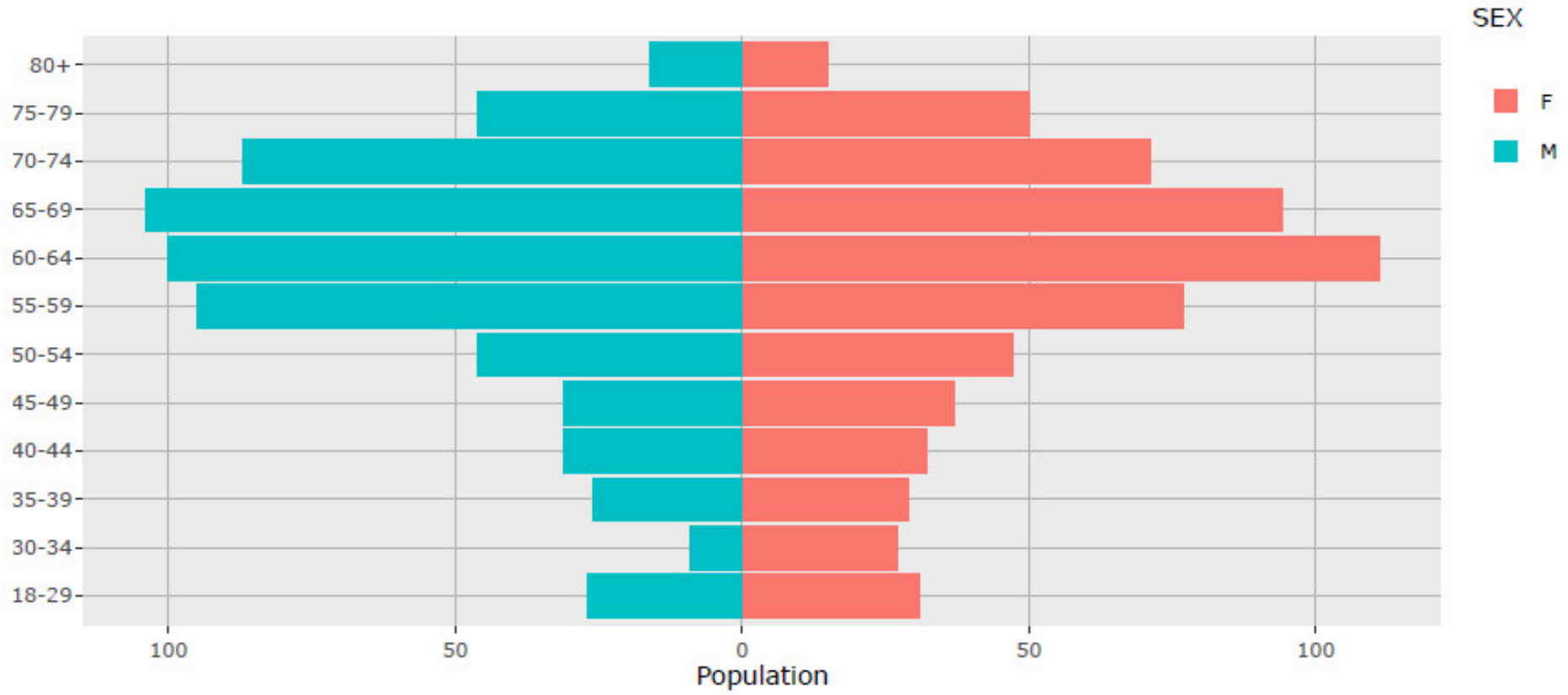
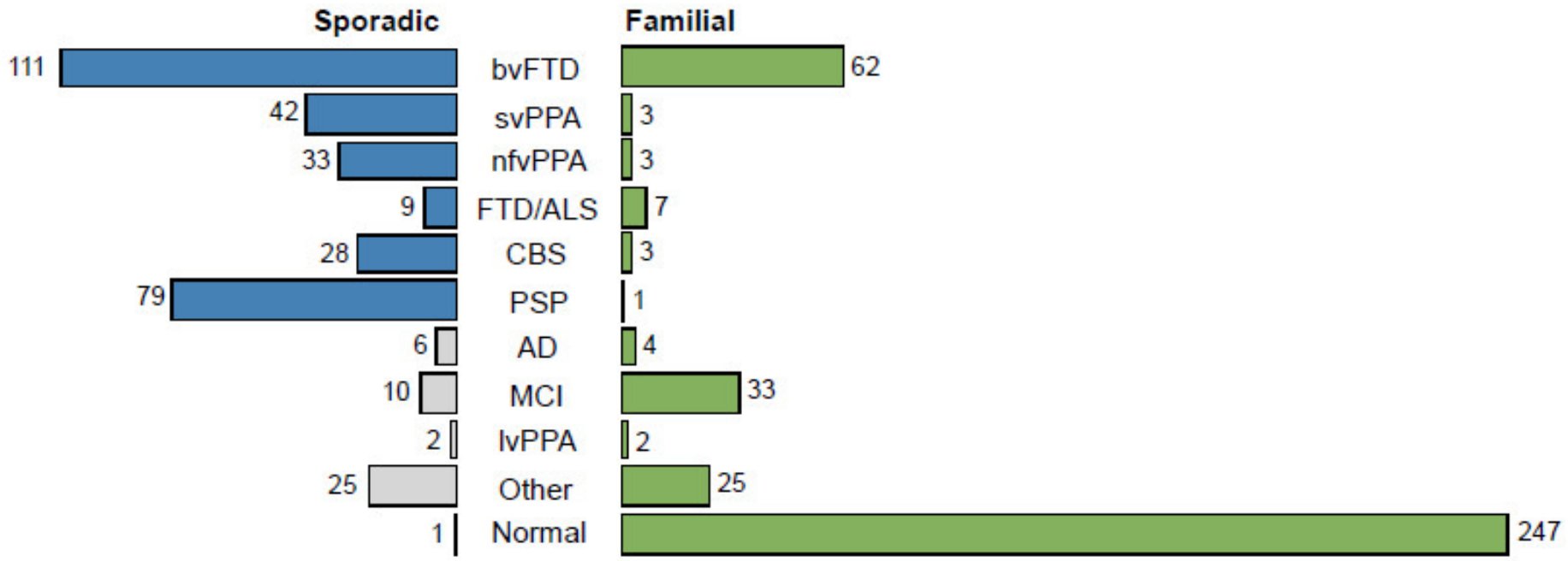
Age at Baseline



as of Jan 2019

Clinical Diagnoses: Sporadic vs Familial



Achievements

Enrollment

- >1200 participants, including ~400 in FTLD families
- >900 with cognitive data
- >1400 blood samples
- >1000 MRIs
- ~400 spinal fluid samples

Methodology and Infrastructure

- Collaborative infrastructure across 18 sites in the US and Canada for FTLD research
- Harmonized clinical / cognitive characterization, blood sampling procedures, MRI procedures
- Standardized normative scores for neuropsychological measures
- Created a new, reliable instrument for functional characterization of FTLD – the Multidomain Impairment Rating scale (“MIR”)

Discoveries

Cognitive Data

- Similarities between sporadic FTLD and familial FTLD suggest pooling participants for clinical trials is valid
- NIH-EXAMINER computer testing is a good tracker of disease burden in asymptomatic or mildly symptomatic familial FTLD

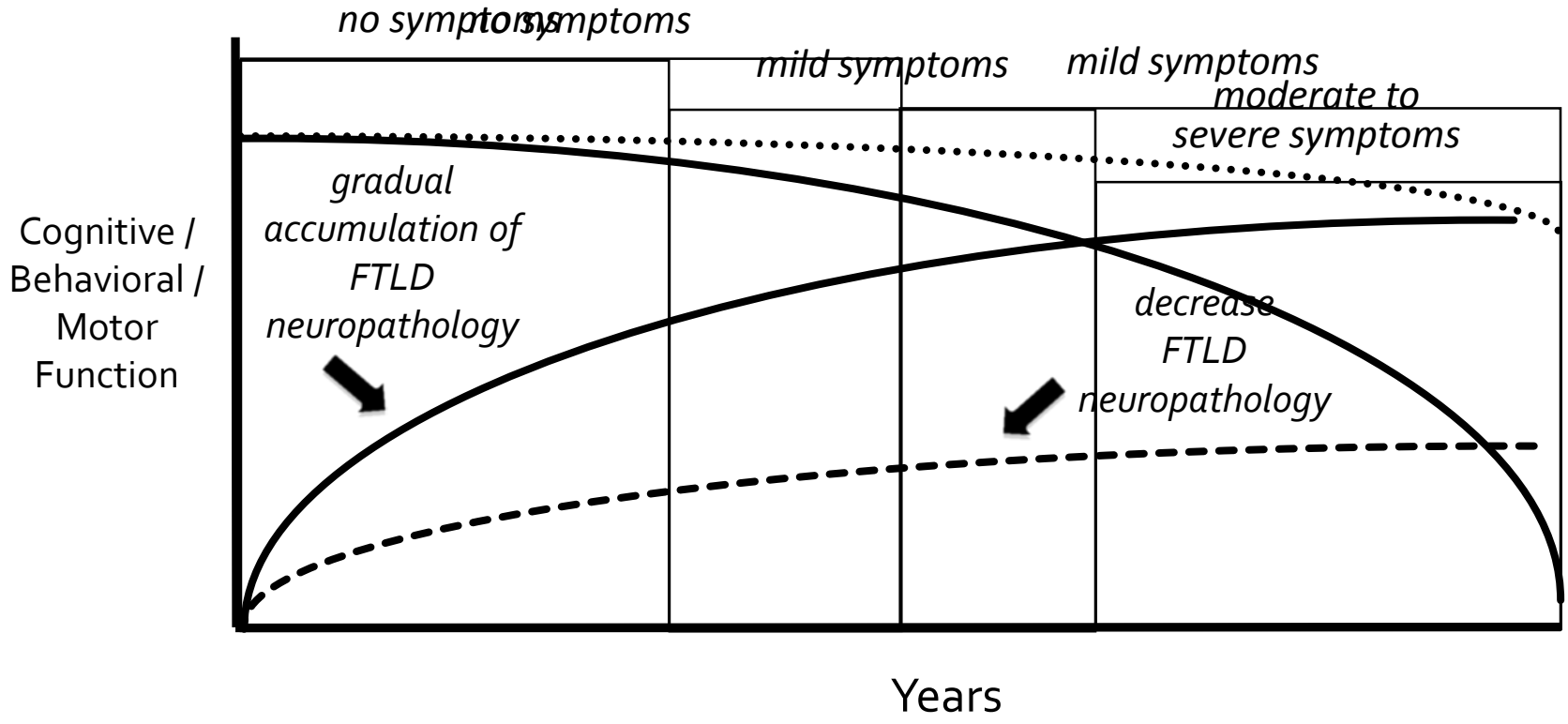
Genetic / Biofluid

- Several new genetic variants identified
- Neurofilament light chain (NfL) – blood and cerebrospinal fluid biomarker predictor of longitudinal change in both sporadic FTLD and familial FTLD

Neuroimaging (familial FTLD)

- Individualized maps of brain atrophy enhance prediction of conversion to dementia
- Rates of brain volume loss accelerate with transition from asymptomatic to symptomatic stage
- Volumetric MRI is a valid biomarker for clinical trials, including in the presymptomatic phase

Research Targets



- Understand natural history
  - "calibrate" tools for monitoring
- Risk/protective factors
  - Genetics
- Treatment
  - Disease modifying

Thank You to all research participants and co-participants!

ALLFTD

ARTFL LEFFTDS Longitudinal Frontotemporal Lobar Degeneration