

# Cognition in Organ Transplantation

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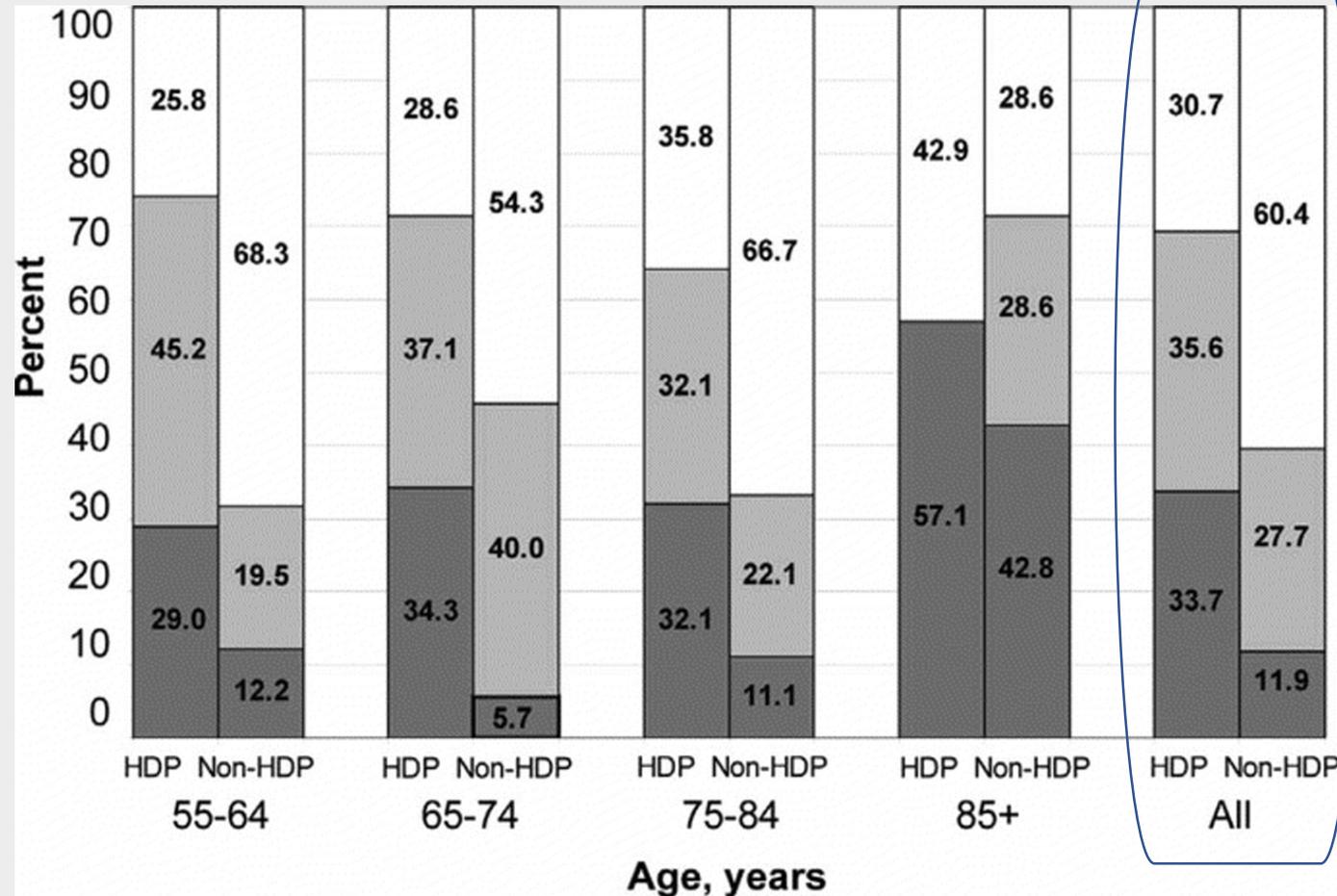
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# Up to 87% of patients on dialysis have cognitive impairment!!



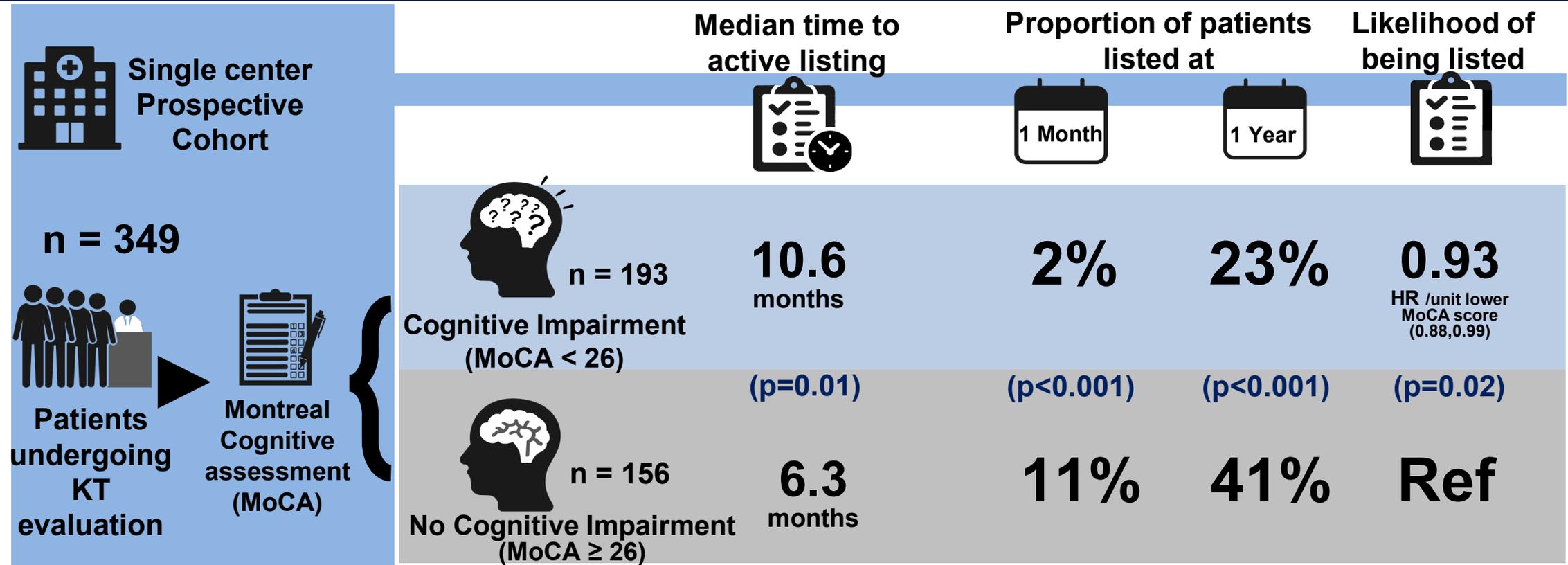
- Only 13% had normal cognition
- Adjusted odds ratio for severe cognitive impairment= 3.5

Normal to mild CI  
 Moderate CI  
 Severe CI

n = 338 for prevalence estimate  
 n = 101 for comparison with non-HDP

It is these dialysis patients who undergo KT

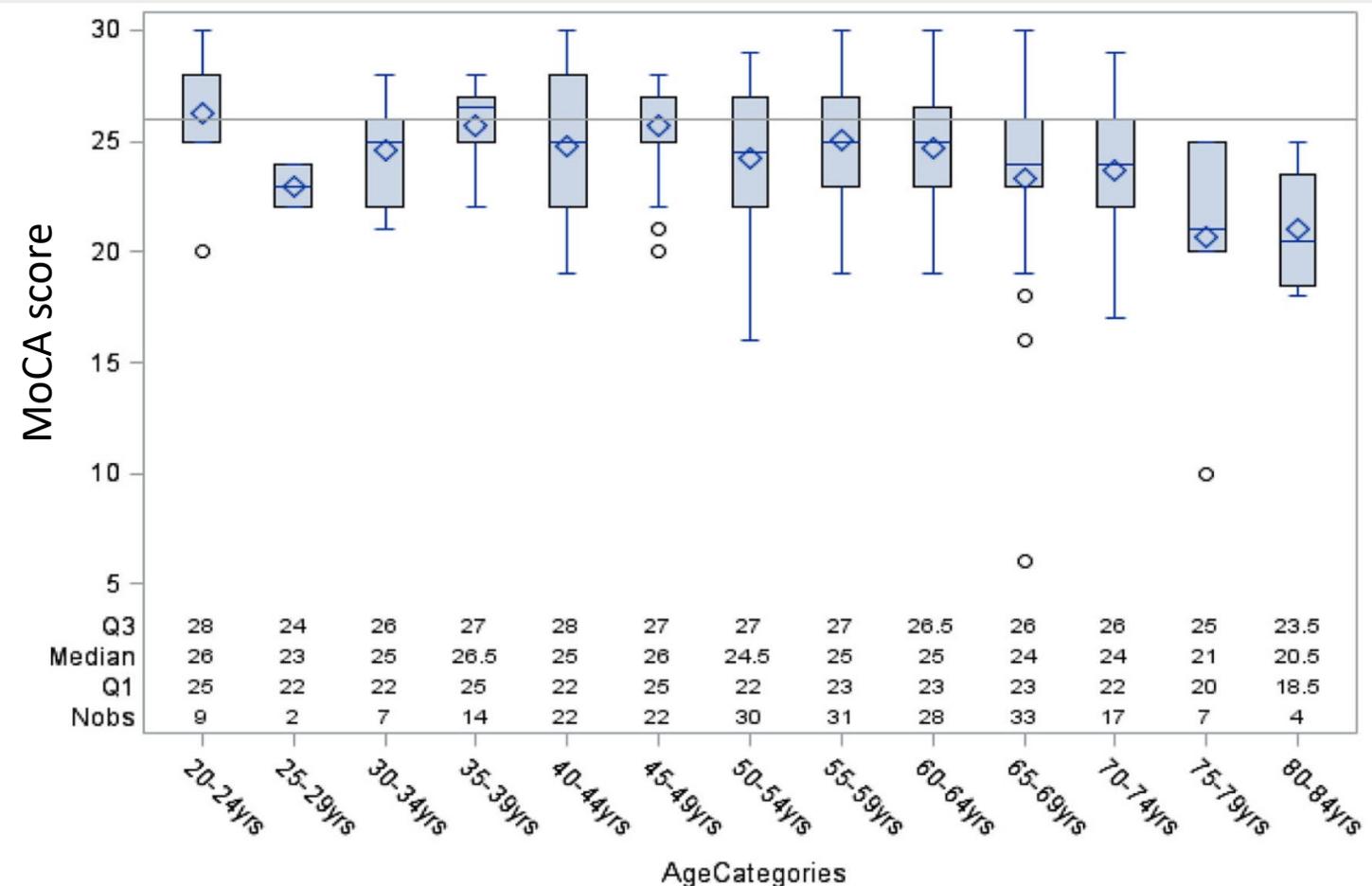
# Cognitive impairment influences KT eligibility- only the 'best' dialysis patients get transplanted



- Sub-clinical cognitive impairment is associated with a lower likelihood of being listed for KT and a longer time to transplant listing.
- KT recipients are a 'selected' group of patients with the 'best' cognition.

A Gupta, R Montgomery, V Bedros, et al. *Sub-clinical Cognitive Impairment and Listing for Kidney Transplantation*. CJASN doi: 10.2215/CJN.11010918.

# KT recipients have a high prevalence of cognitive impairment

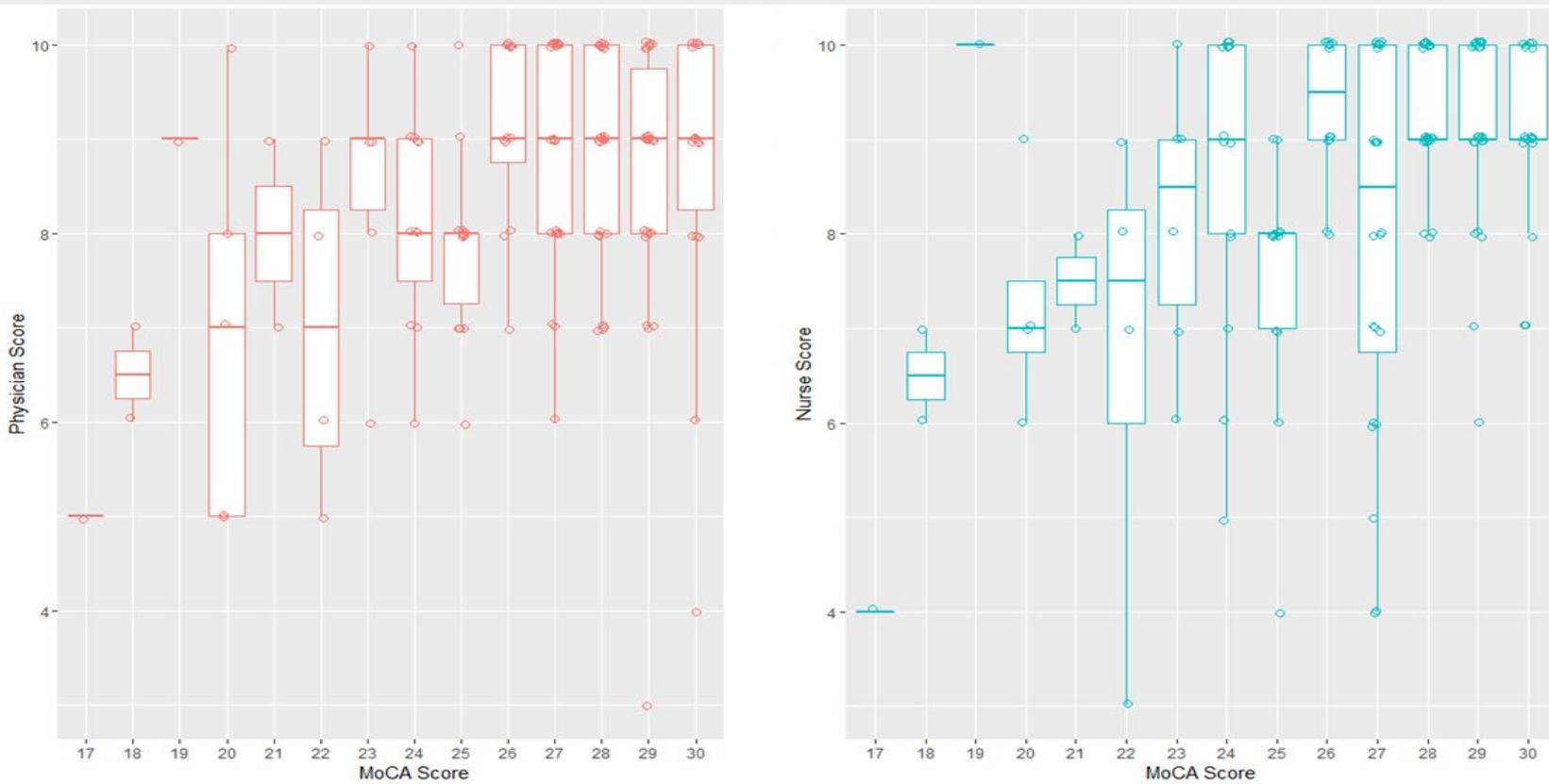


- N = 226, Prevalence = 58%
- Lower MoCA scores were associated with
  - Increasing age
  - AA or 'other' race
  - Male sex
  - Lower education
  - History of diabetes
- We used MoCA- Pros and Cons
- Pre-transplant MoCA scores were not known for these patients

- Despite these data, it is not standard of care to measure cognition in pre- or post- transplant care
- Most centers do not have the resources to measure cognition/screen for cognitive impairment

# How well can we Assess Cognitive Impairment in our Patients?

- The high prevalence is surprising to some
- We often feel that we know our patients well and will know if they are cognitively impaired



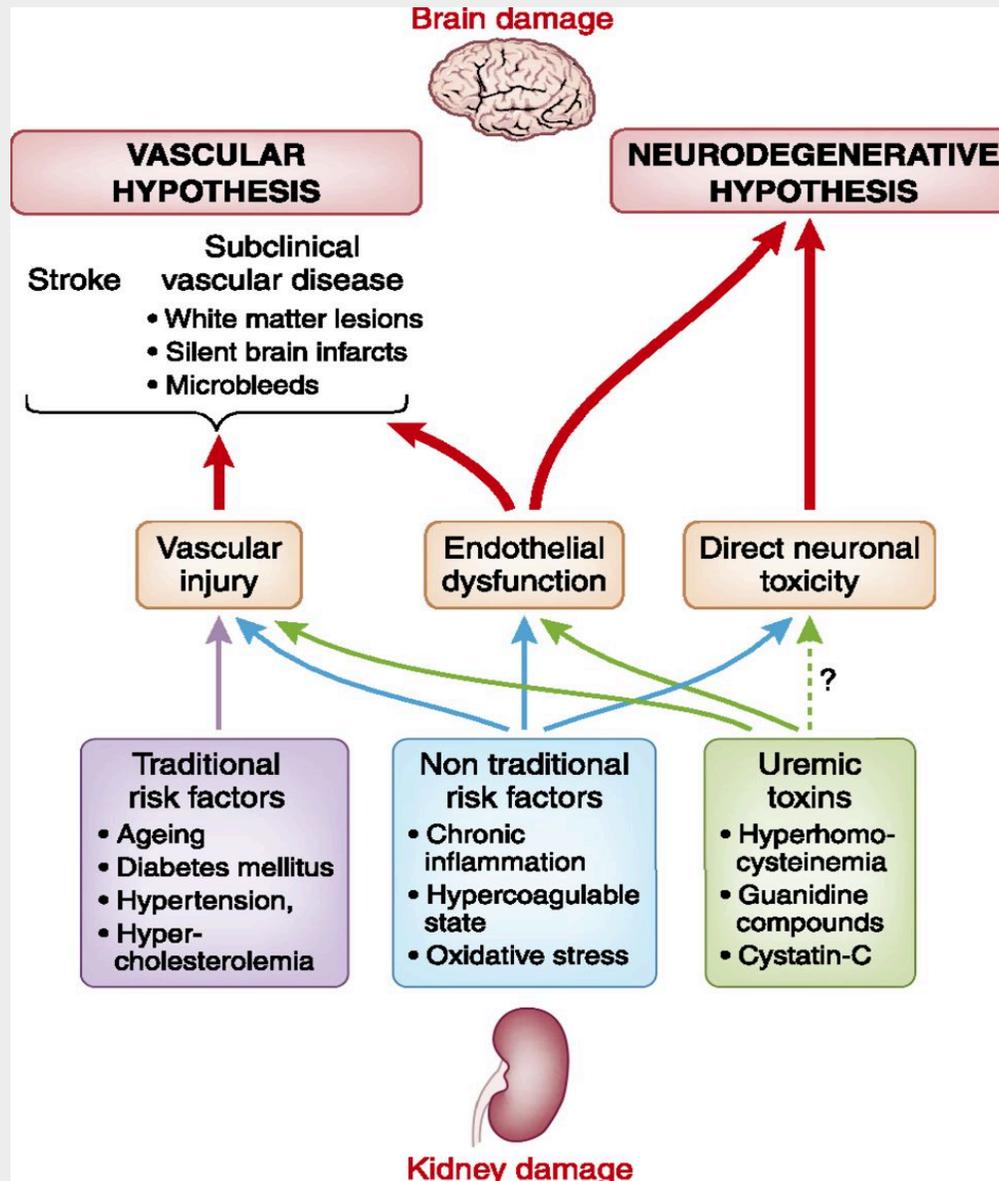
Boxplot of MoCA scores and perceived scores by

A) physicians ( $\gamma = 0.24$ )

B) nurses ( $\gamma = 0.33$ )

	Physician score	Nurse score
Sensitivity	65.9 %	65.2 %
Specificity	67.2 %	76.4 %
PPV	46.9 %	54.5 %
NPV	81.8 %	83.5 %

# Exact etiology unknown- multifactorial?



- Risk Factors Related to Hemodialysis Procedure-
  - Intradialytic hypotension/ hypovolemia,
  - Defective autoregulation of cerebral blood flow/ Disruption of blood brain barrier
  - Cognitive decline during HD
  - Chronic microembolization
  - Cerebral edema
- Effect of calcineurin inhibitors ?

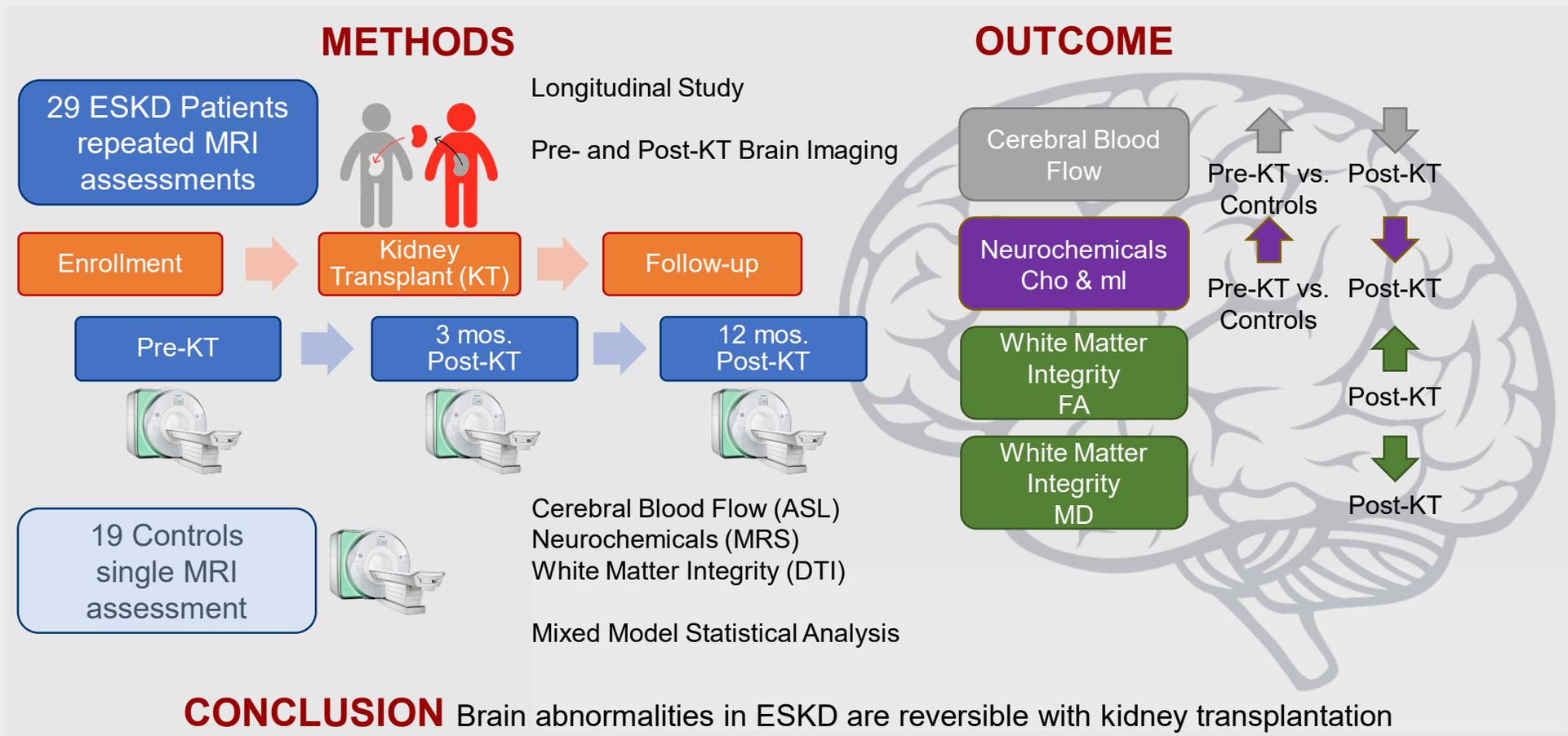
To understand the underlying mechanisms, it is important to understand what happens in the brain pre-to post-KT

# Brain Abnormalities in CKD

- Brain atrophy
- Silent infarcts
- Increased cerebral blood flow
- Altered brain neurochemical concentrations
- Decreased white matter integrity

Each of these abnormalities is associated with  
cognitive impairment

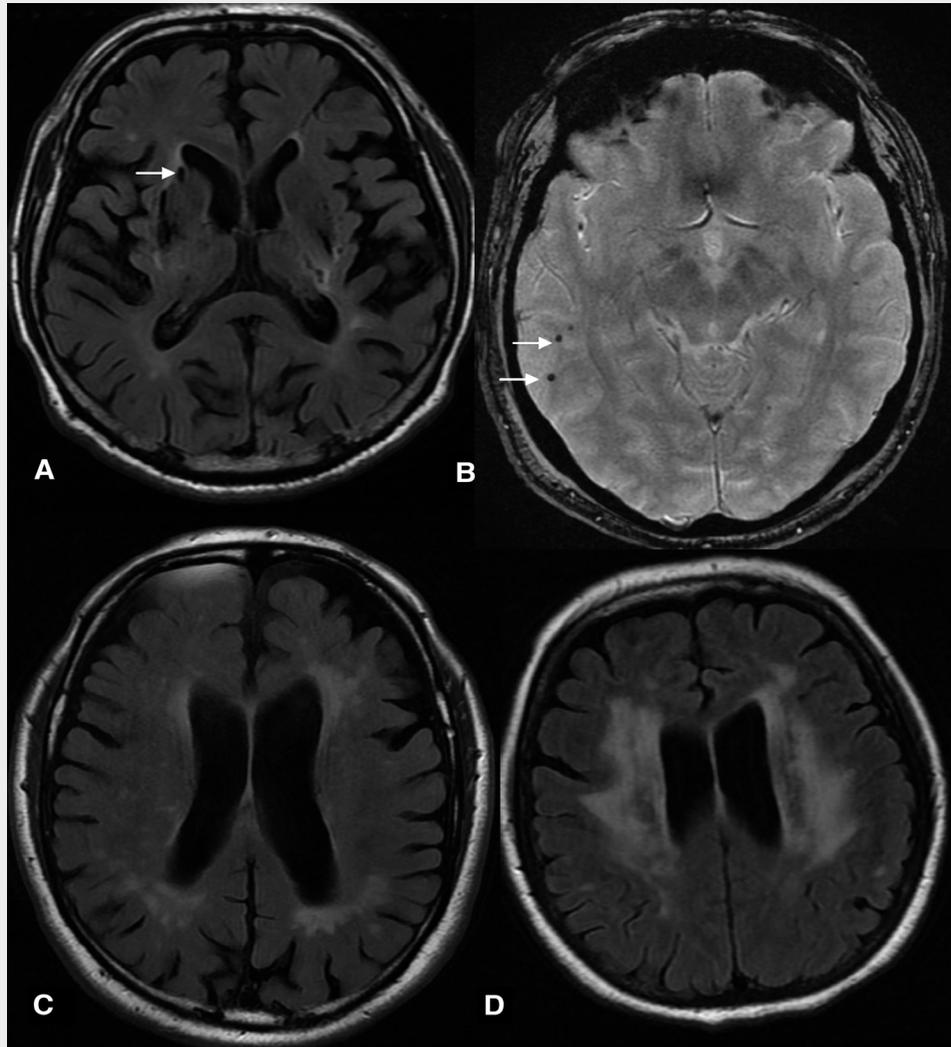
# Normalization of Cerebral Blood Flow, Neurochemicals, and White Matter Integrity After KT



doi: 10.1681/ASN.

Normalization of Cerebral Blood Flow, Neurochemicals, and White Matter Integrity after Kidney Transplantation. R J. Lepping... A Gupta, JASN Jan 2021, 32 (1) 177-187; DOI: 10.1681/ASN.2020050584

# Subclinical Vascular Brain Disease in CKD



(A) Silent brain infarct (arrow)

(B) Multiple microbleeds

(C) Moderate white- matter lesions

(D) Severe white- matter lesions

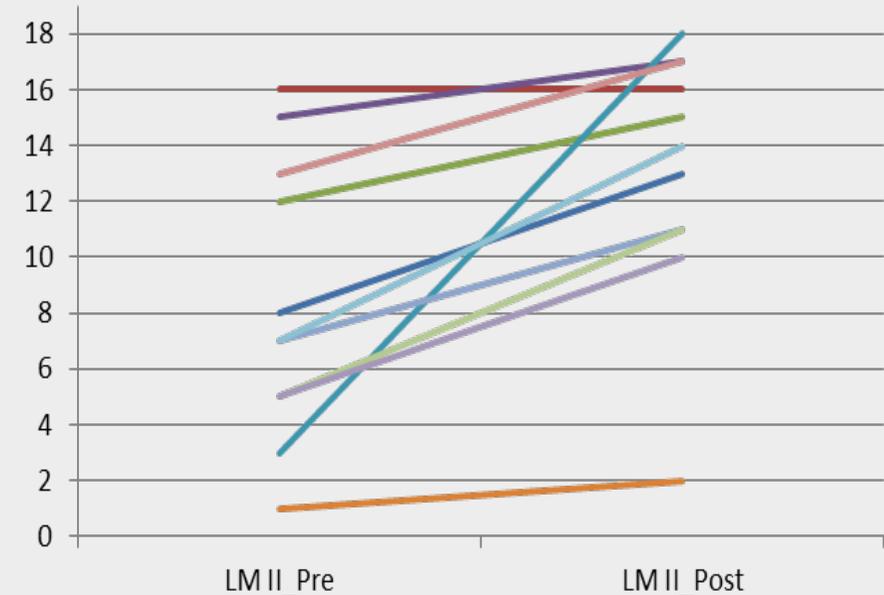
# Longitudinal studies assessing change in cognition pre- to post-KT

Author, yr	N	Results	NP test	Strong points	Limitations
Van Sandwijk, 2020	27	*Reaction time- improved *Executive visuomotor control- unchanged *Sustained action task- improvement (in donors & KT)	ANT & verbal fluency	*1 year f/u *Compared with donors	*Small N- Multiplicity *Only LD
Chu, 2019	665	*Low prevalence of CI pre-KT (7.2%) *3 MS score improved in 1st 3 months → stable	3 MS	*1.5 yrs (0.7-3.4) *Largest N	*Use of 3 MS *Assessment time *No controls
Gupta, 2016	11	*Logical memory, digit span backwards, category fluency (vegetables) and digit symbol improved. *MMSE, category fluency (animals), trailmaking A & B, block design, stroop test and free recall did not.	NP battery (2 hr)	*NP battery *3 mth & 1 yr f/u *Comparison with normative values	*Small N
Radic, 2011	21	*Improvement in processing speed, attention, short term memory, executive function	NP battery	*20 mths f/u	*Small N *No control
Griva, 2006	28	*Rey auditory verbal learning test, Benton visual retention test scores improved *Trailmaking A & B, digit symbol, grooved pegboard did not	NP battery	*NP battery *Comparison with normative values	*Small N
Kramer, 1996	15	*MMSE and trailmaking test results normalized	MMSE, Trailmaking	*Healthy controls	*Small N *Limited NP tests

# Cognition Improves after Kidney Transplantation

Comparison of pre- and post- KT NP test results with normative age adjusted data from the National Alzheimer's Coordination Center Uniform Data Set.

	Pre-transplant		Post-transplant	
	Z score	percentile	Z score	percentile
MMSE	-1.37	8.5	-0.91	18
Logical memory I	-1.1	13.6	-0.17	43.1
Logical memory II	-1.04	14.9	0.06	52.5
Digit span forward	-0.26	39.9	-0.49	31.1
Digit span backward	-0.77	22.1	-0.63	26.4
Category fluency: animals	-0.27	39.4	-0.2	42.2
Category fluency: vegetables	-0.92	17.9	-0.59	27.8
Trail making A	-0.11	45.5	-0.09	46.6
Trail making B	-0.5	30.9	-0.29	38.4
Digit symbol	-1.3	10.5	-0.81	20.9



# Unpublished Data

# Summary and conclusions

- Cognitive impairment is highly prevalent in KT recipients
- We need better ways to assess cognition in kidney disease
- Mechanisms for cognitive impairment vary among different solid organs
  - There might be some common mechanisms, such as effect of calcineurin inhibitors
  - But results from one solid organ transplant should not be extrapolated to other solid organ transplants
- Current data indicate that
  - Certain domains of cognition improve after KT
  - Improvement in cognition occurs relatively soon after KT (within 3 months)
- We do not have enough data to predict post-transplant cognition based on pre-transplant factors
  - Additional work is needed and is in progress

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