Bracketology

AJKDblog.com

NephMadness 2017

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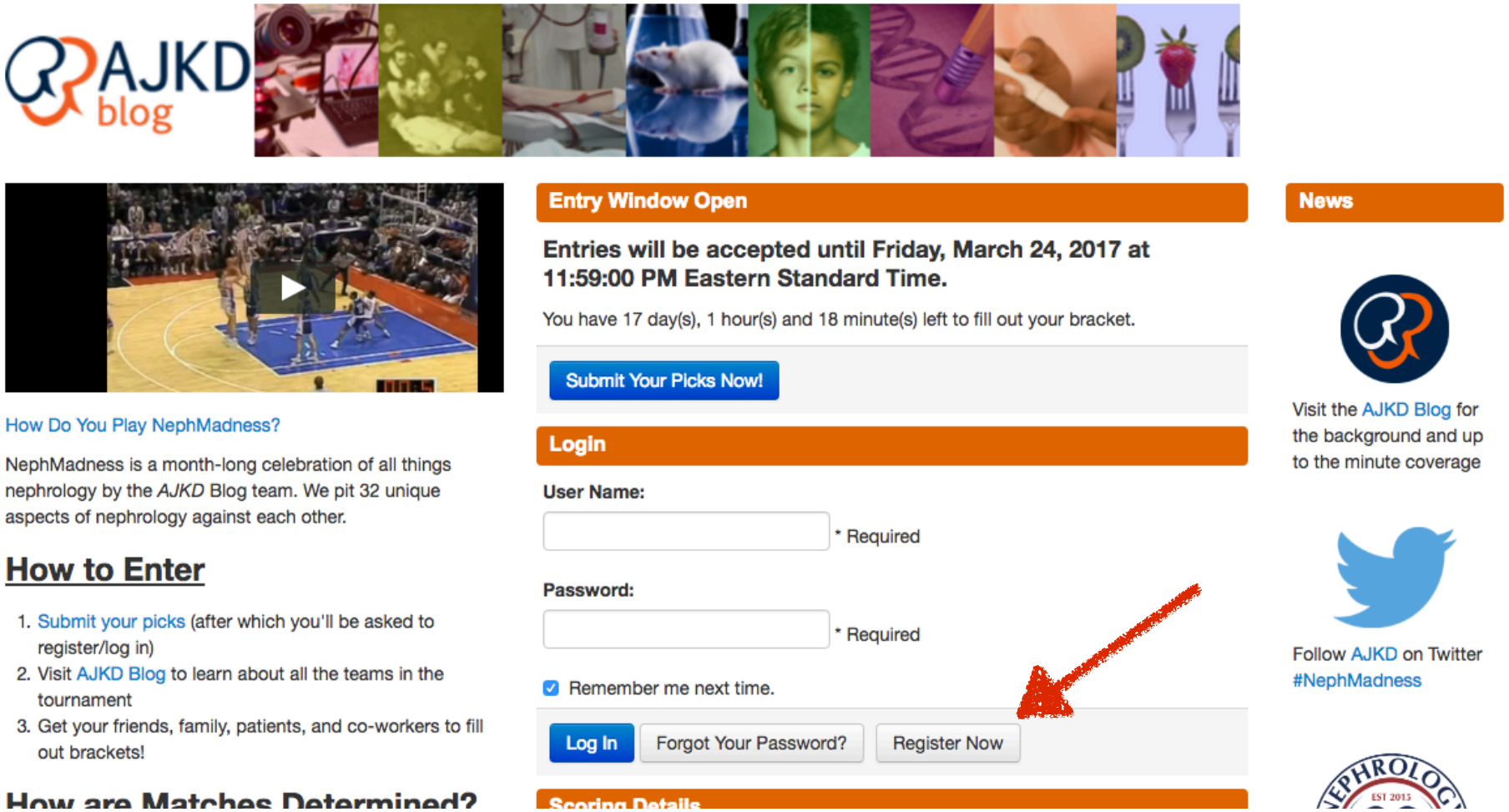
Register for the game



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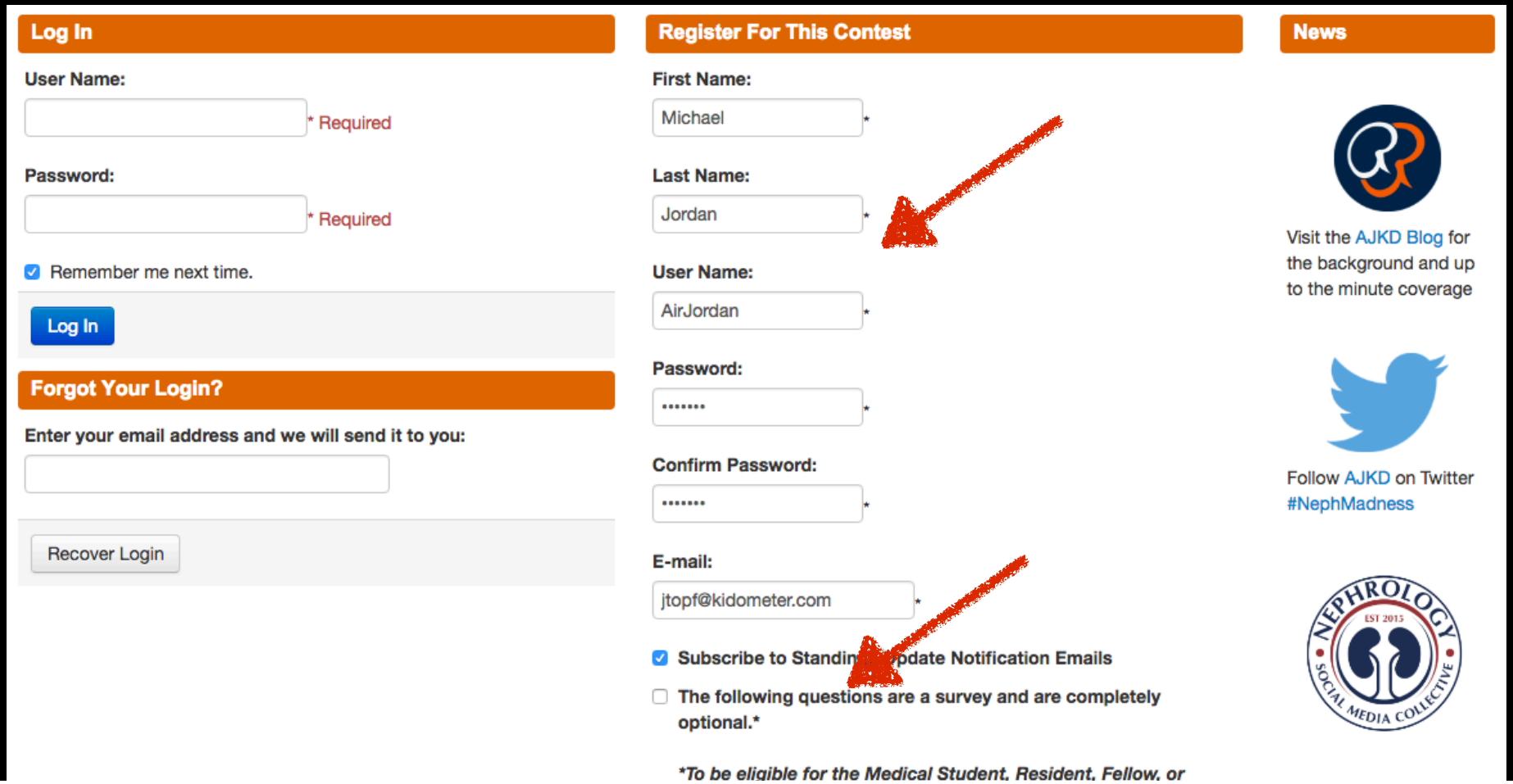


Submit your picks

Fill out your bracket

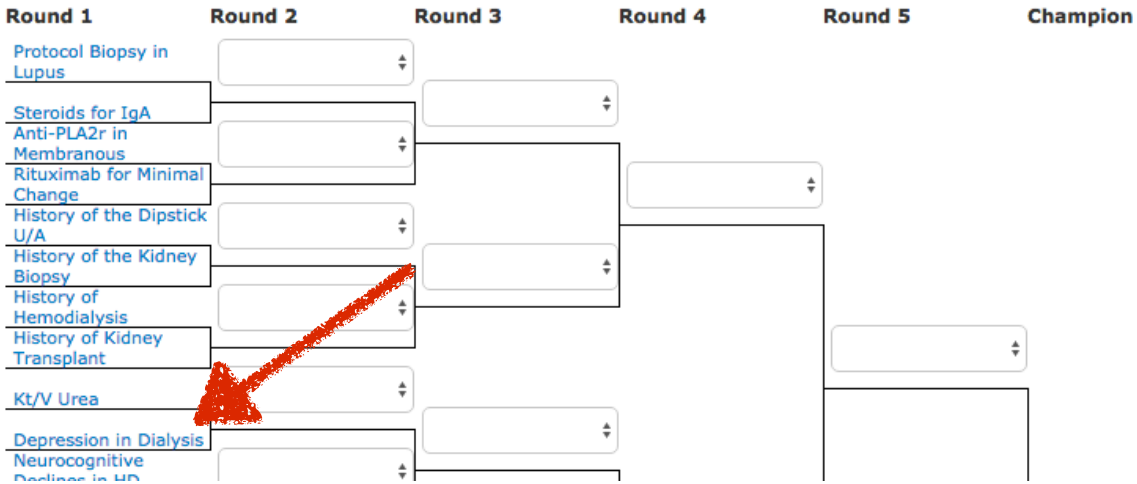
Submit Your Picks

Step 1: Understand the scoring rules

- Round 1 correct picks receive 1 point(s)
- Round 2 correct picks receive 2 point(s)
- Round 3 correct picks receive 3 point(s)
- Round 4 correct picks receive 4 point(s)
- Round 5 correct picks receive 5 point(s)

Step 2: Fill out your bracket

Try filling out the bracket from the right to speed up the process.



News

Visit the AJKD Blog for the background and up to the minute coverage

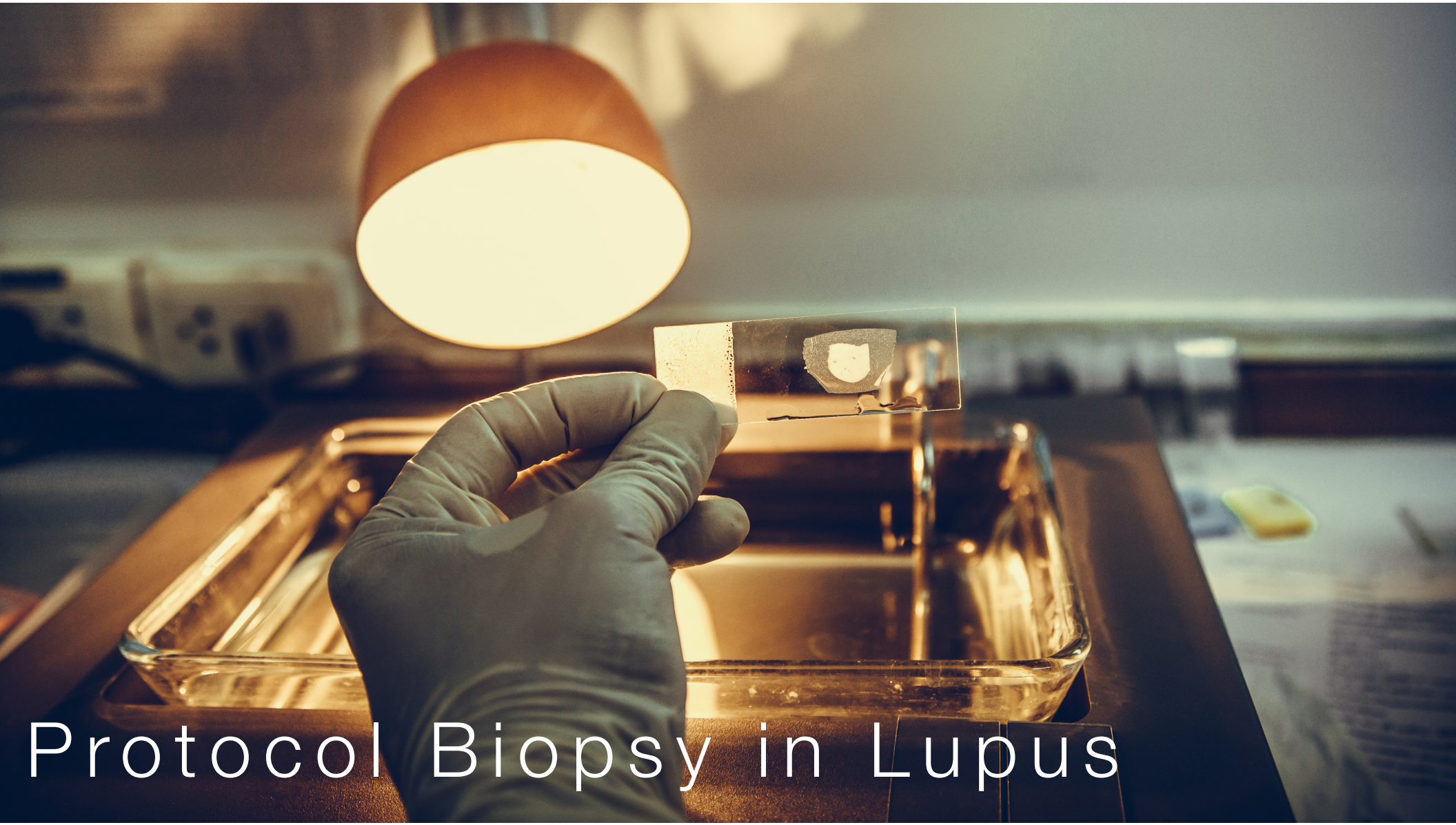
Follow AJKD on Twitter #NephMadness

Fill out your bracket

31 decisions

2,147,483,648 possible bracket combinations

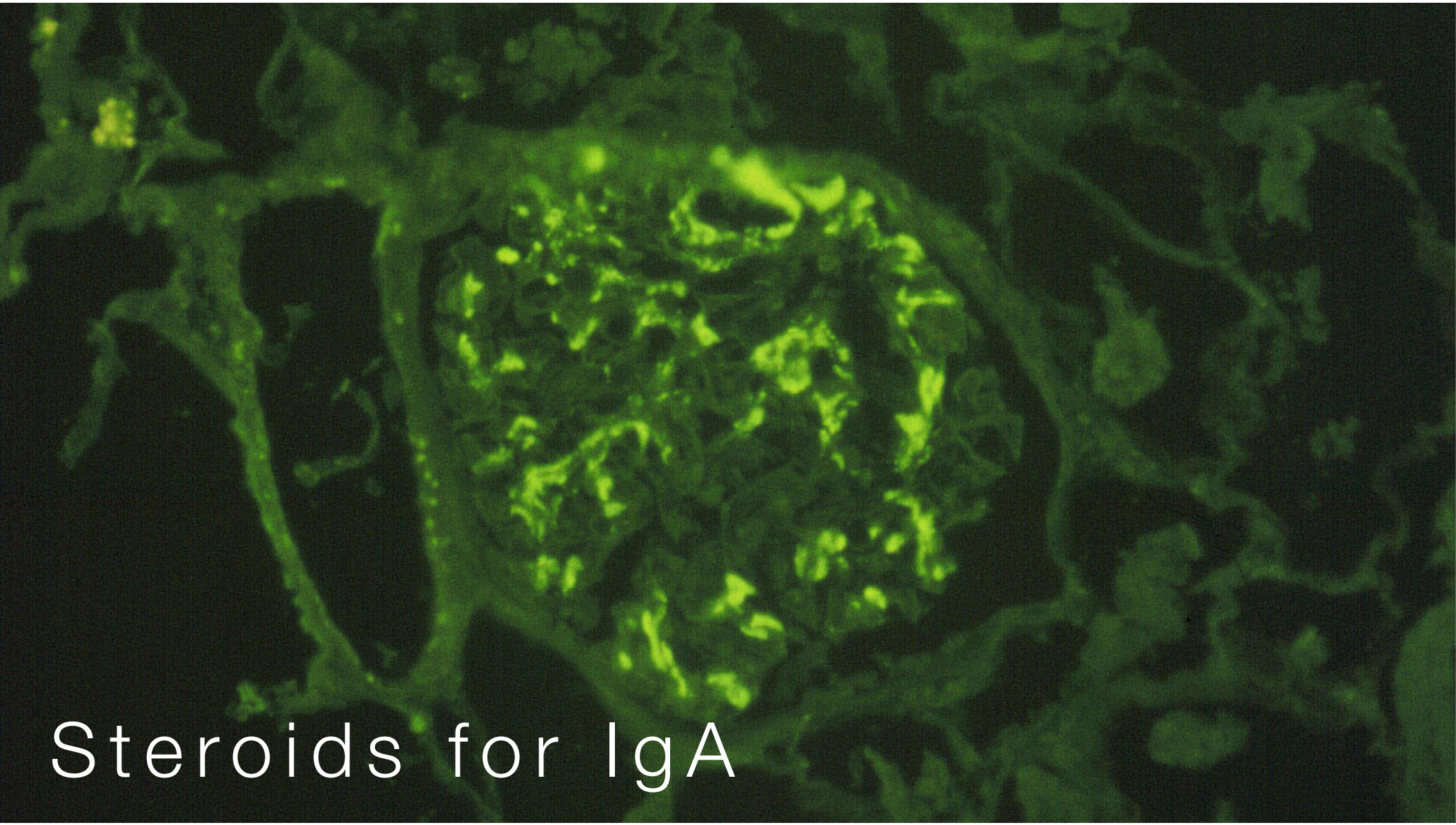
Glomerulonephritis Region



Protocol Biopsy in Lupus

Protocol Biopsy in Lupus

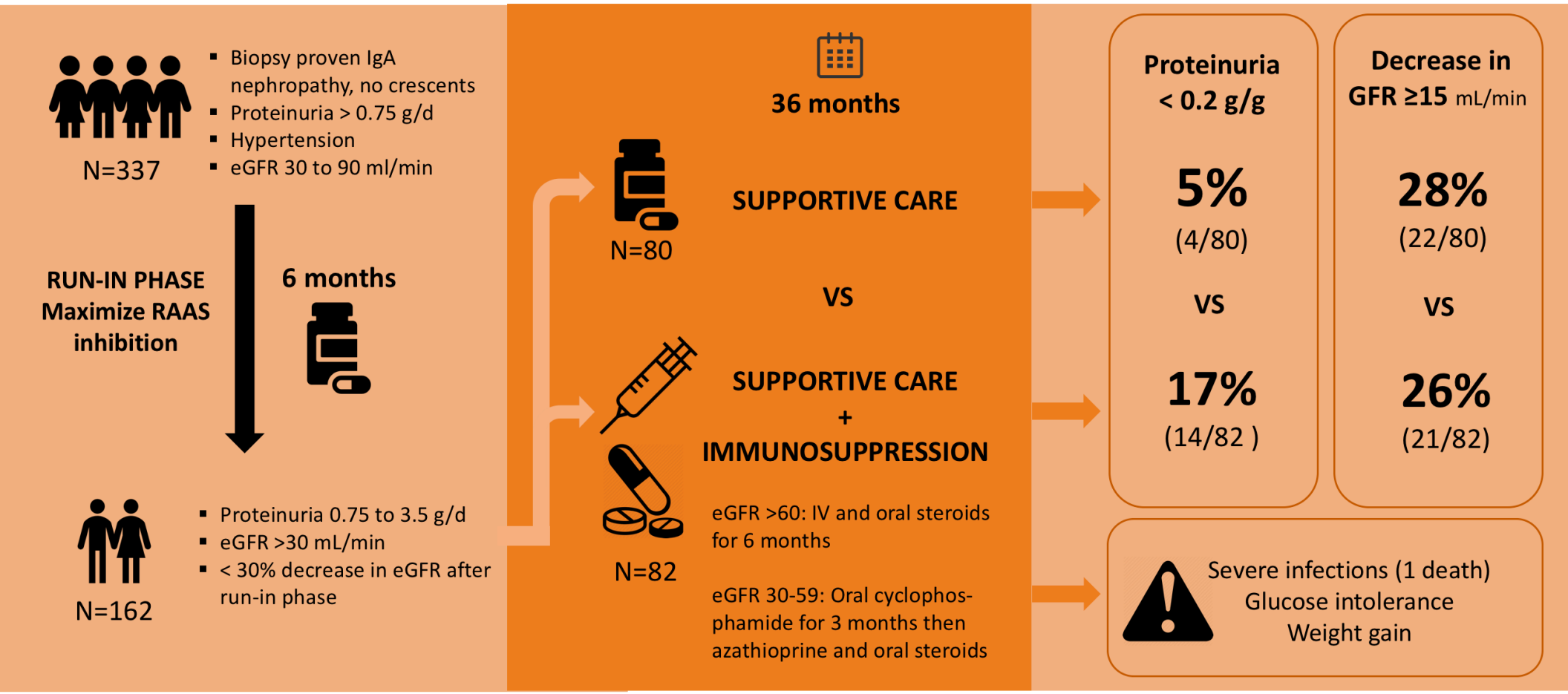
- Proteinuria, serologic markers and serum creatinine do not give a full picture of lupus nephritis
- Serial protocol biopsies can help inform decisions on discontinuing or intensifying maintenance immunosuppression
- Some clinical data shows progressive disease despite stable markers of disease. Other data shows stable histology despite progressive laboratory markers of disease.


Steroids for IgA

Steroids for IgA nephropathy

- Some patients do great and live their whole life without any renal deterioration
- Others progress to ESRD rapidly
- The Stop-IgA trial found increased clinical remission with steroids but no difference in GFR after 3 years.
- TESTING trial (not yet published) showed reduced loss of renal function and reduced proteinuria with steroids but a lot of adverse events, including 2 deaths.

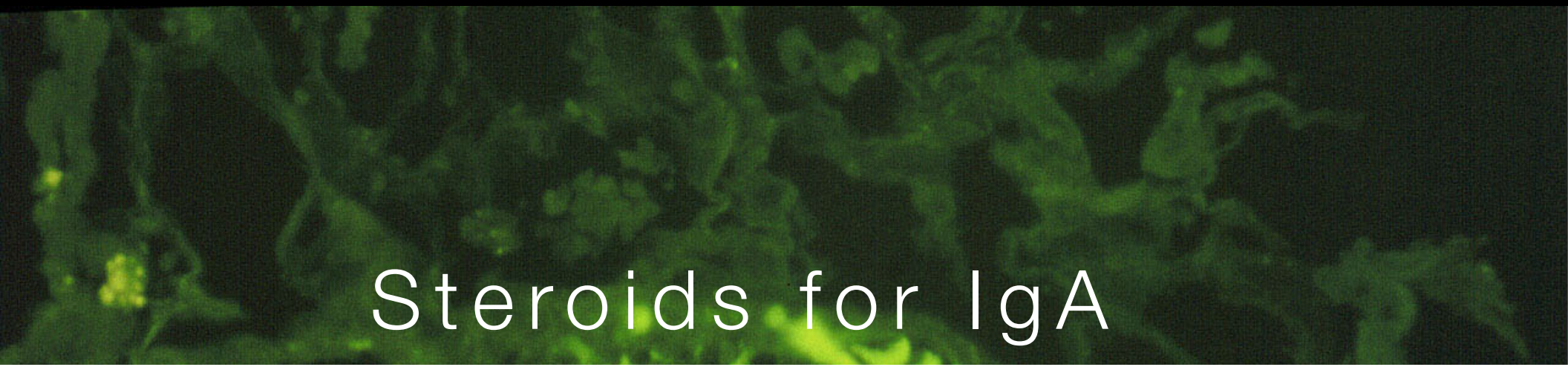
Intensive Supportive Care plus Immunosuppression in IgA Nephropathy: STOP-IgAN



#NephMadness
@KidneyBea_n

Rauen T, et al, N Engl J Med 2015; 373:2225-36

pick one



Anti-PLA2r in Membranous

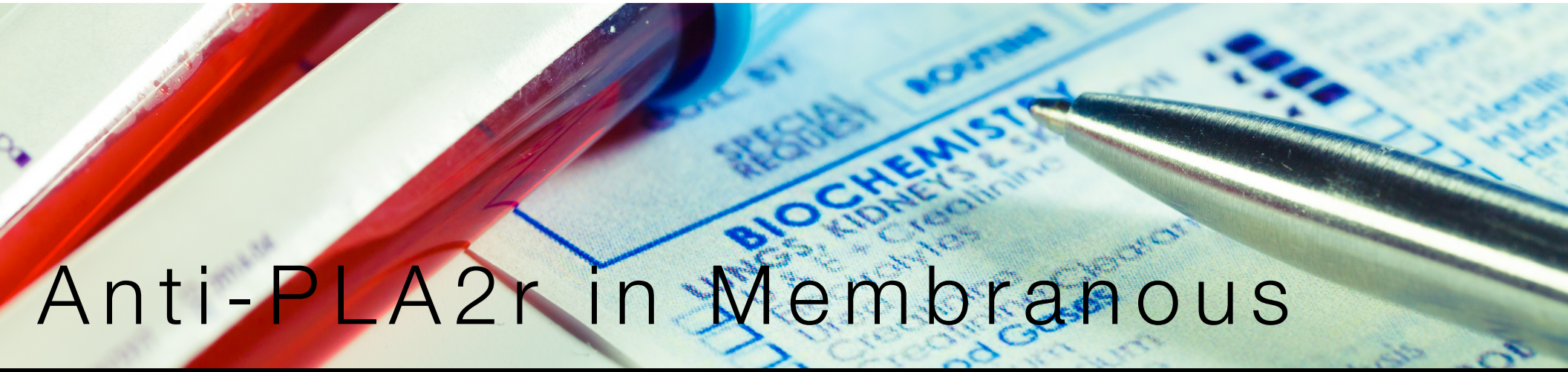
Anti-PLA2R antibodies in idiopathic membranous

- Discovered in 2009
- Positive in 80% of membranous patients
- 99% specific for membranous nephropathy
- Low titers are suggestive of spontaneous remission
- aPLA2R antibody titers predict disease course

Rituximab for Minimal Change

rituximab for minimal change disease

- MCD reliably responds to steroids
- However 50% will relapse and some become steroid dependent (respond to steroids, but relapse when the dose is tapered).
- Rituximab shown to be better than MMF, CNI, azathioprine in a number of studies world wide.

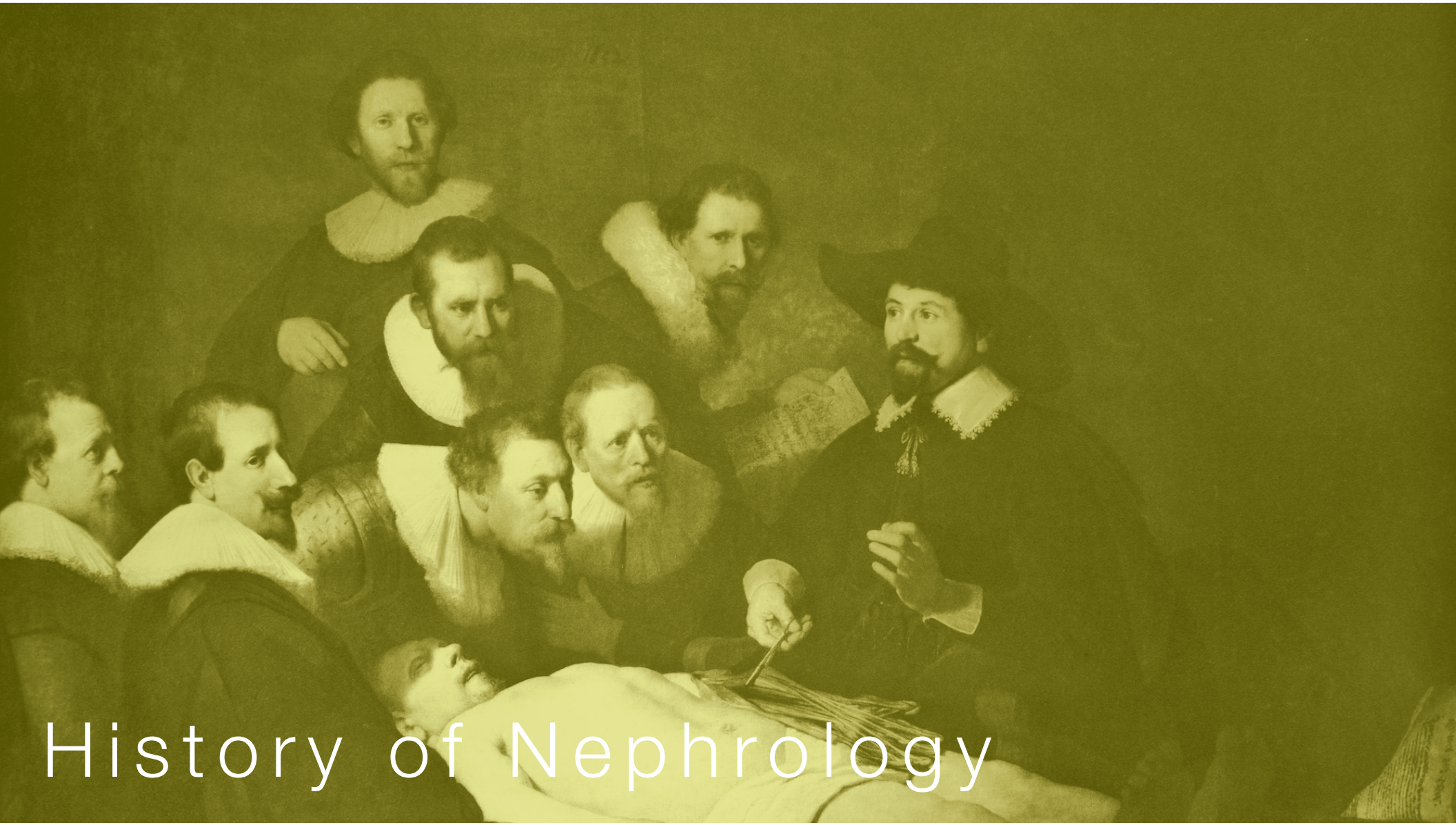


Anti-PLA2r in Membranous

pick one

Rituximab for Minimal Change

Protocol Biopsy in Lupus
Steroids for IgA
Now pick your glomerulonephritis Champion
Anti-PLA2r in Membranous
Rituximab for Minimal Change



History of Nephrology

History of the Dipstick U/A

History of the Dipstick U/A

- Before 1950s one had to add acid or heat the urine with a spirit lamp to precipitate protein
- Fritz Feigl discovered tetrabromophenol blue could detect protein, but he was Jewish and fleeing the Nazis from Austria to Brazil via Portugal curtailed his scientific career.
- Helen Murray and Alfred Free invented the modern dipstick in the 1950s

You can't detect glucose, blood, and protein with a single test.
Helen Murray and Alfred Free: Hold my beer
NEPH Madness 2017
AJKD

History of the Kidney Biopsy

History of the Kidney Biopsy

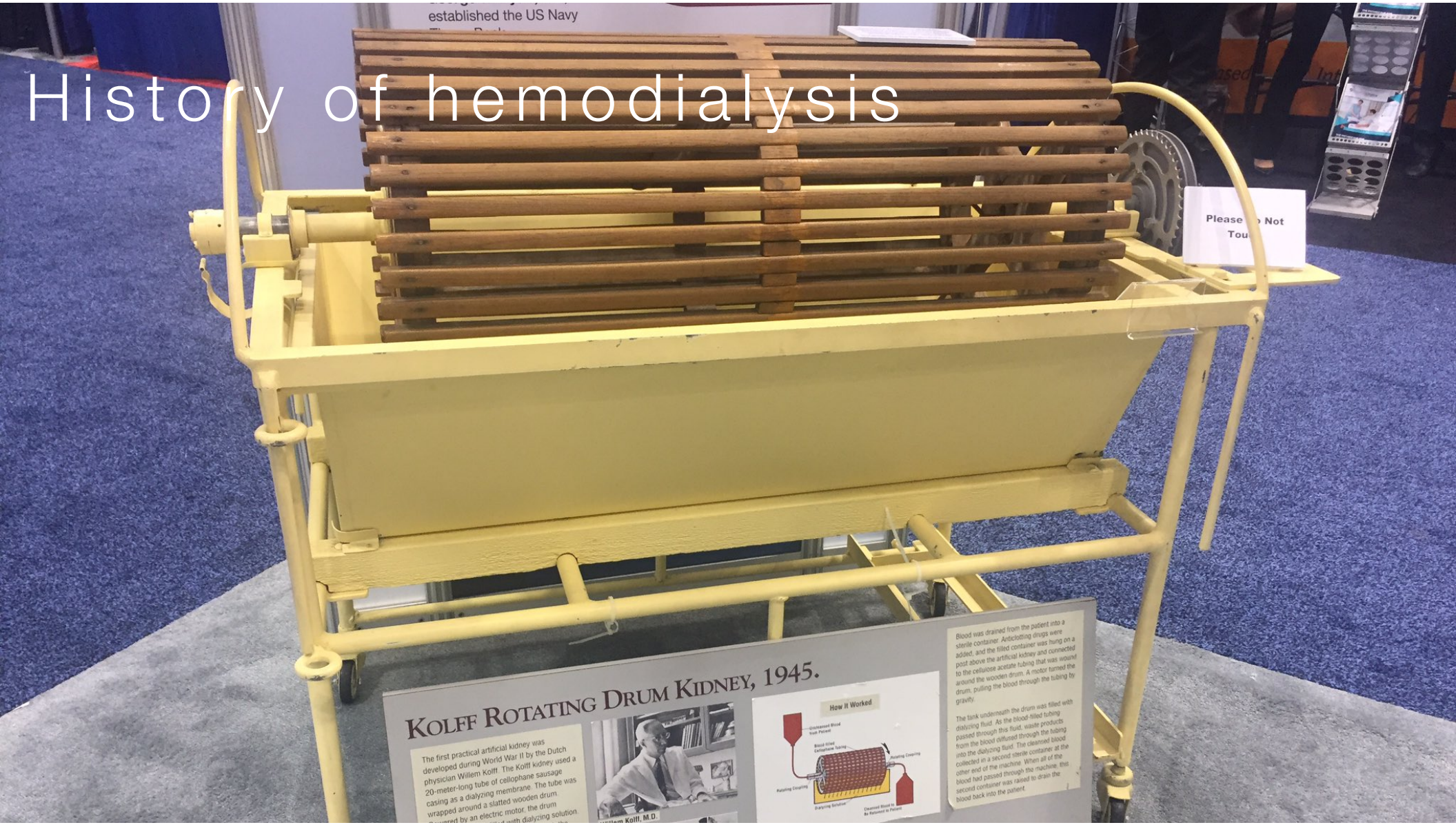
- Kidney biopsy was either an autopsy procedure or part of an open laparotomy until the 1940's
- Percutaneous biopsy was first developed for liver then applied to other organs, including the kidney.
- In the 1950's kidney biopsy was only 50% likely to get kidney tissue
- Immunoflorecence and the electron microscope were applied to the kidney biopsy in 1955-1957

History of the Dipstick U/A

pick one

History of the Kidney Biopsy

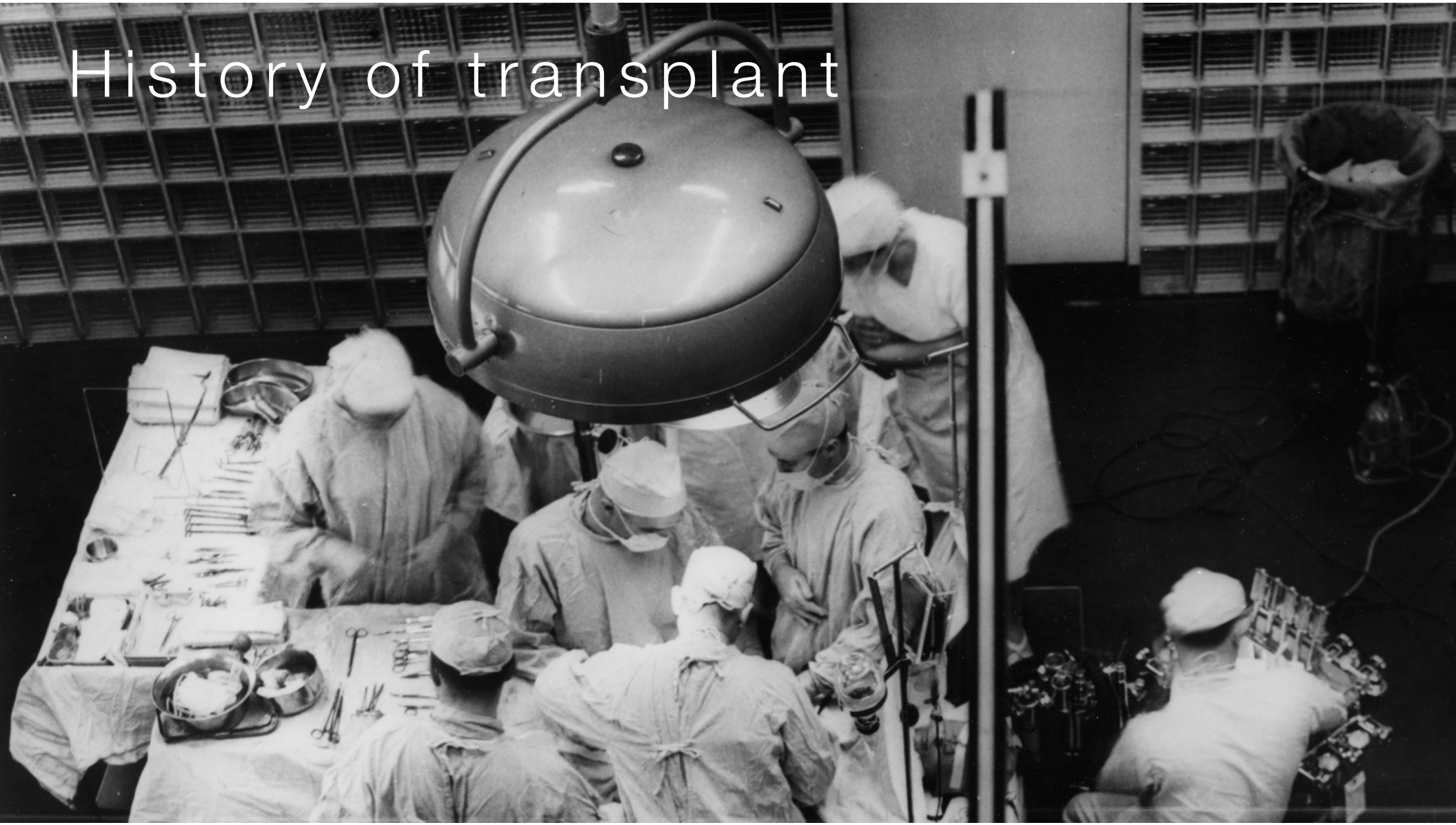
History of hemodialysis



History of hemodialysis

- First animal dialysis done at John Hopkins 1913
- First Human on dialysis was 1924. 15 minutes of dialysis.
- Willem Kolff performed the first successful dialysis while evading detection by Nazi sympathizers in Holland. Sixteen deaths before his first save.
- Nils Alwall invented ultrafiltration
- Kolff along with Watschinger invented the disposable dialyzer in 1956
- In 1960 Quinton and Scribner invented the AV shunt.
- In 1966 Brescia and Cimino invented the AV fistula. Both of these were the last peices of the puzzle to allow chronic dialysis.

History of transplant



History of Transplant

- First human kidney transplant was 1933, patient was dead in 2 days. ABO mismatch.
- Richard Lawler performed the first intra-abdominal kidney transplant on 44-year-old Ruth Tucker. The kidney lasted 10 months.
- Murray successfully transplanted a kidney between identical twin brothers in 1954.
- Immunosuppressants consisted of steroids, azathioprine and cyclophosphamide.
- Cyclosporine in the 1980's accelerated the field.

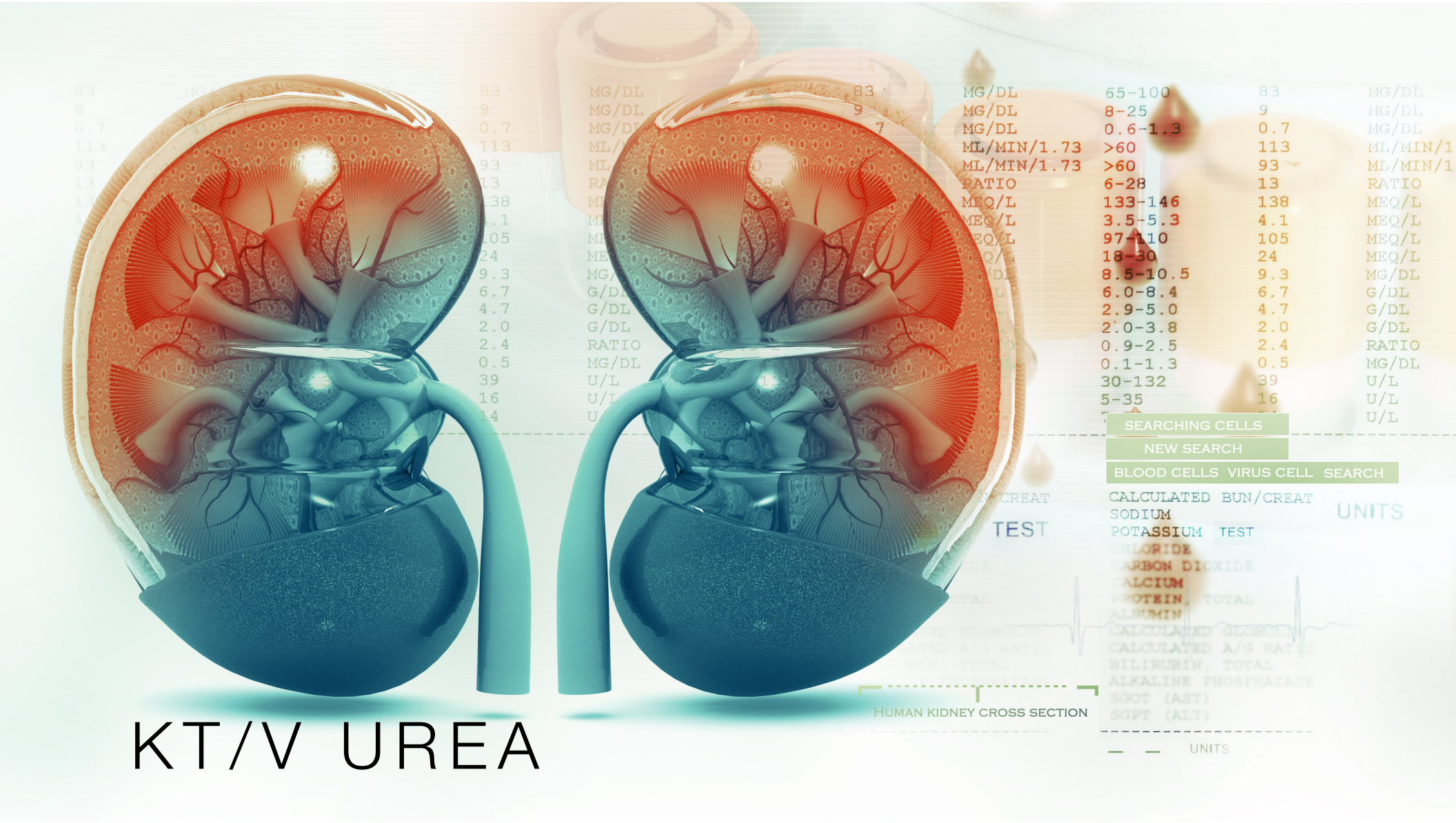
History of hemodialysis

pick one

History of transplant

History of the Dipstick U/A
History of the Kidney Biopsy
Now pick your History of Nephrology Champion
History of Hemodialysis
History of Transplant

Hemodialysis

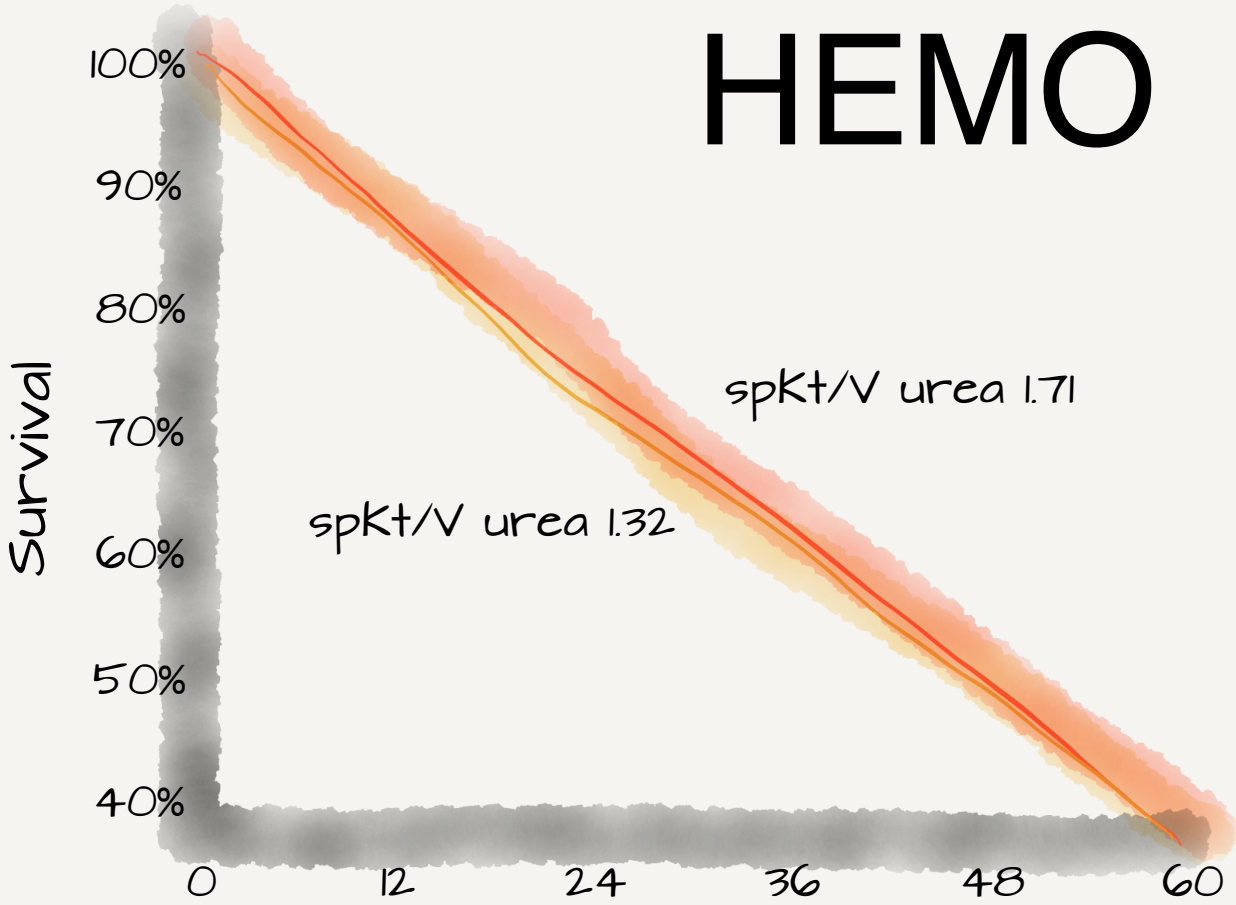

MG/DL 65-100
MG/DL 8-25
MG/DL 0.6-1.3
ML/MIN/1.73 >60
ML/MIN/1.73 >60
RATIO 6-28
MEQ/L 133-146
MEQ/L 3.5-5.3
97-110
18-30
8.5-10.5
6.0-8.4
2.9-5.0
2.0-3.8
0.9-2.5
0.1-1.3
30-132
5-35
SEARCHING CELLS
NEW SEARCH
BLOOD CELLS VIRUS CELL SEARCH
CALCULATED BUN/CREAT
SODIUM
POTASSIUM
TEST
UNITS
HUMAN KIDNEY CROSS SECTION
UNITS

KT/V UREA

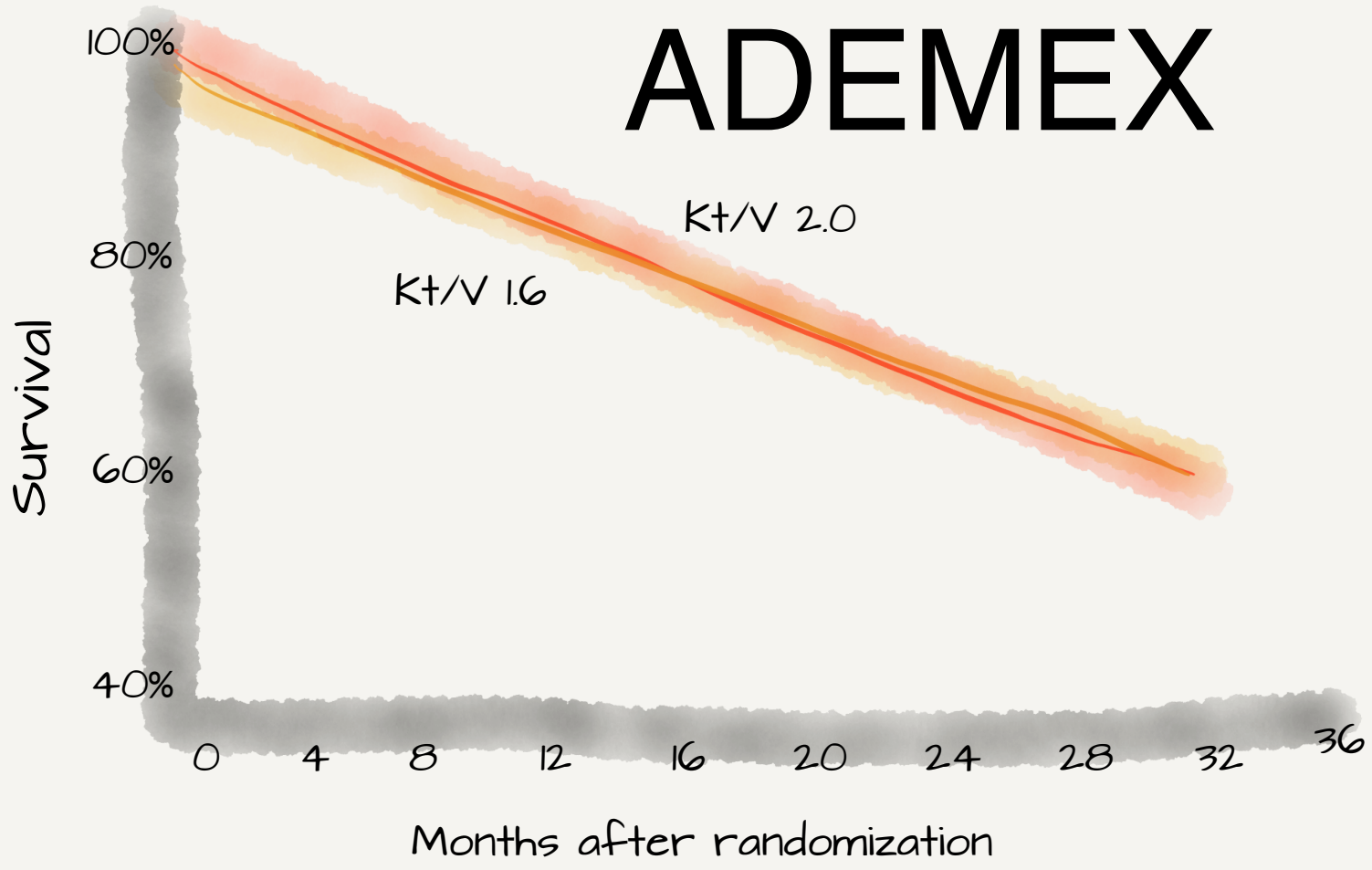
Kt/V urea

- This is a way to measure the amount of dialysis. It is the clearance provided by the dialyzer (K) times the time on dialysis (t) divided by the volume of distribution of urea (total body water).
- NCDS was a landmrk, but largely uninterpretable study of dialysis dose. Sargent and Gotch years later invented and used Kt/V to make sense of the data
- They found outcomes were worse below 0.8. Additional retrospective data brought the target up to 1.2.
- Three definitive studies explored higher Kt/V: HEMO, ADEMEX, ATN. All failed showed to improved outcomes with higher Kt/V.

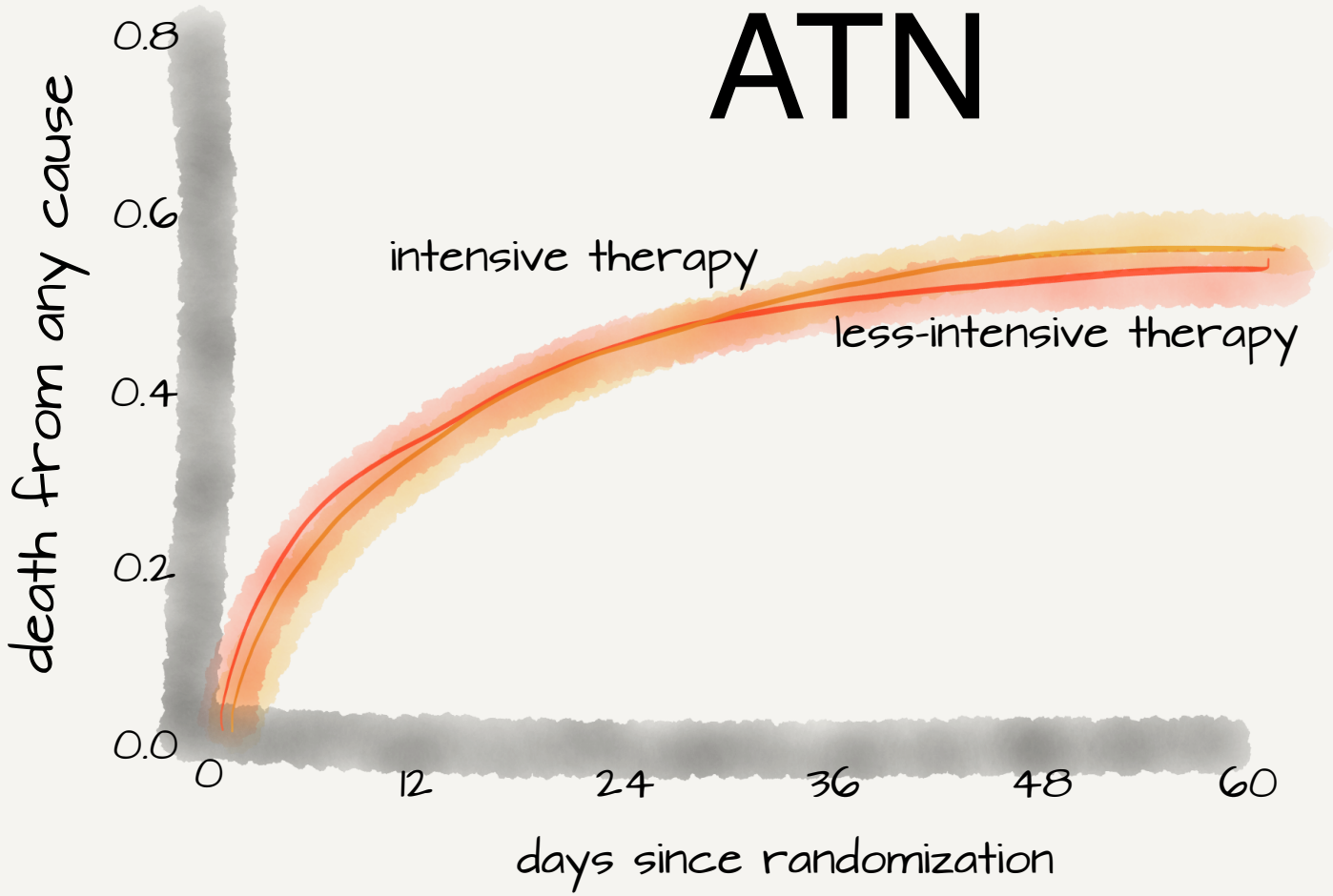
HEMO



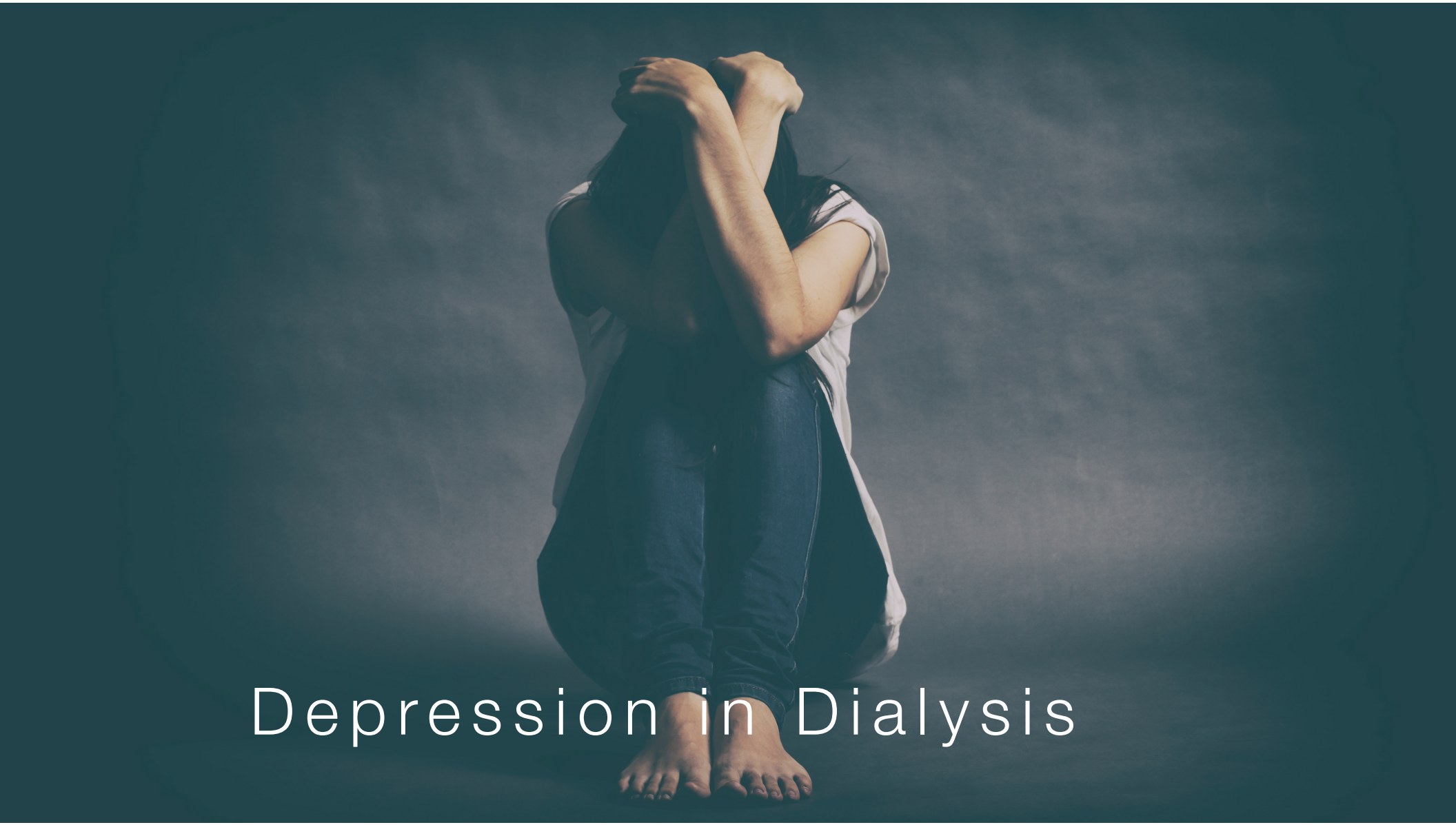
HEMO NEJM 2002;347:2010-9.



ADEMEX JASN 2002 Vol. 13(5) 1307-1320.

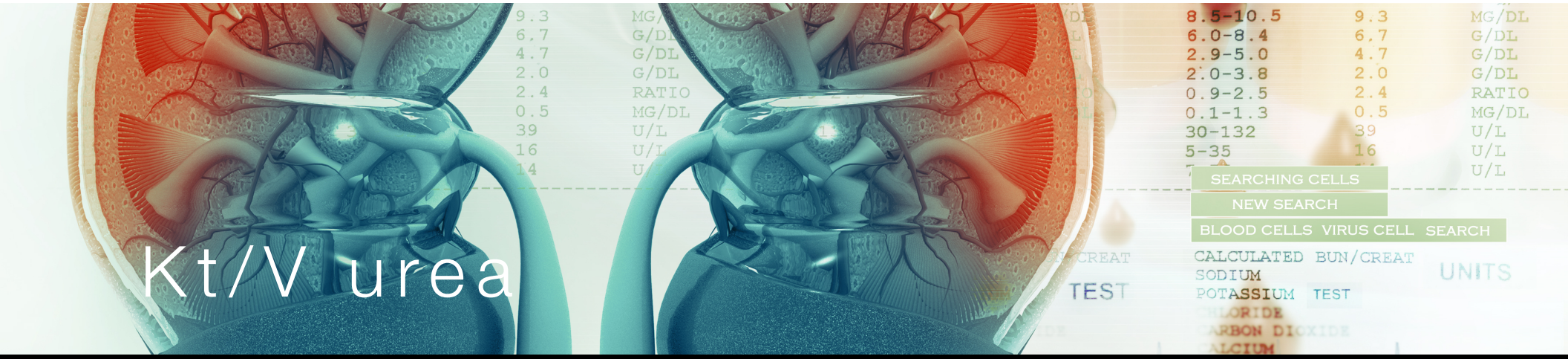


ATN NEJM 2008; 359:7-20.


Depression in Dialysis

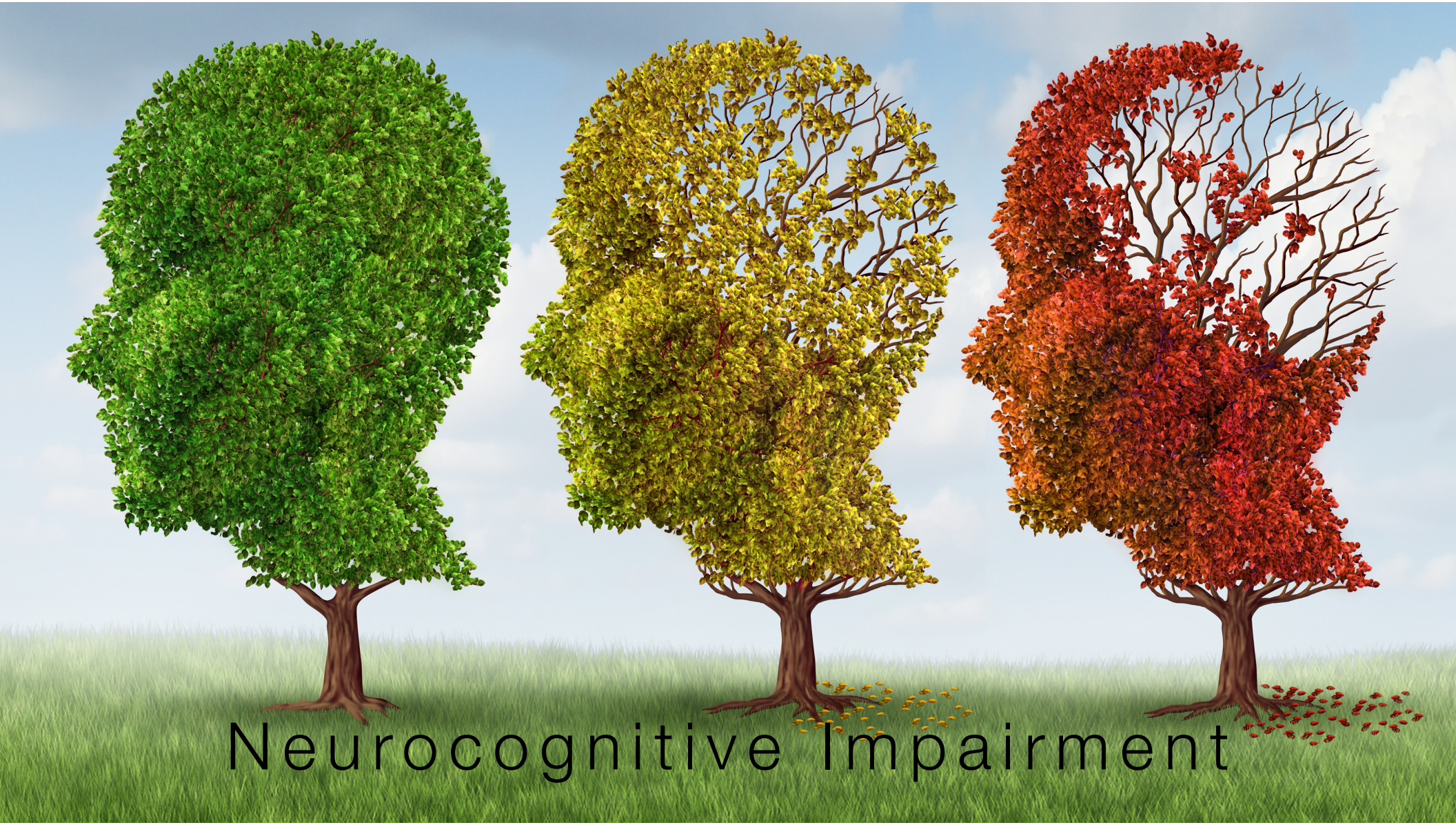
Depression in Dialysis

- 10-20% of dialysis patients have major depressive disorder
- Little data on how to treat it. The largest prospective RCT of pharmacologic therapy screened 709 patients and was only able to get 21 to complete 6 months of therapy.
- The SMILE Trial screened people for depression but most patients who screened positive refused initiation (91%) or intensification (73%) of therapy. If the patients agreed, in 60% of cases the physician refused.


Kt/V urea
SEARCHING CELLS
NEW SEARCH
BLOOD CELLS VIRUS CELL SEARCH
CALCULATED BUN/CREAT
SODIUM
POTASSIUM TEST
TEST
UNITS

pick one

Depression in Dialysis


Neurocognitive Impairment

Neurocognitive Declines in HD

- Cognitive impairment is equivalent to mild dementia
- 70% of dialysis patients have moderate to severe dementia
- Cognitive impairment is associated with decreased 2 year survival (24% vs 66%)
- Due to vascular causes and cerebral hypoperfusion and hypoxia associated with changes in fluid volume

Patient Reported Outcomes

Patient reported outcomes

- much of dialysis is focused on surrogate outcomes, many of which are not validated.
- Patients value outcomes that are not surrogate but affect how they and their family feel
- The SONG-HD is an initiative to create consensus outcomes to be shared among all studies of dialysis patients
- Vascular access, dialysis adequacy, fatigue CVD and mortality

Developing a set of patient oriented outcomes for hemodialysis studies. The SONG-HD initiative

patients/ caregivers

n=202

Round 1	Round 2	Round 3
1. dialysis adequacy*	1. dialysis adequacy*	1. dialysis adequacy*
2. ability to travel	2. ability to travel	2. ability to travel
3. dialysis-free time	3. dialysis-free time	3. vascular access problems

* From discussion it was apparent that patients and caregivers viewed "dialysis adequacy" as a broad quality-of-life outcome (ie, dialysis that is adequate for enabling patients to feel well) rather than quantification of urea kinetics.

Share comments and results

Share comments and results

health care professionals

n=979

1. vascular access	1. vascular access	1. vascular access
2. CVD	2. CVD	2. CVD
3. mortality	3. mortality	3. mortality

Five highest priority outcomes shared among patients/caregivers:

vascular access problems • dialysis adequacy • fatigue • CVD • mortality

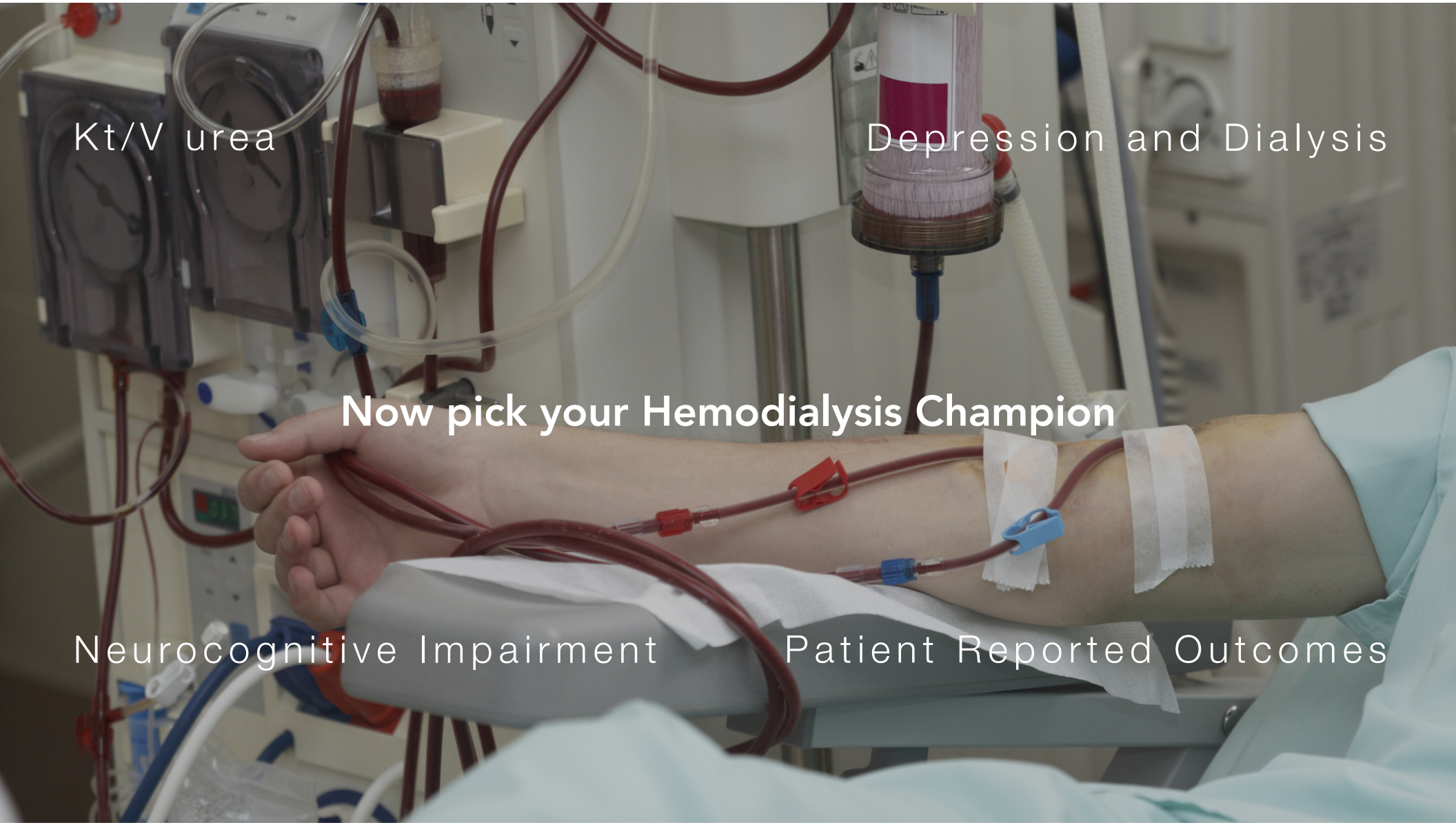
AJKD Official Journal of the National Kidney Foundation

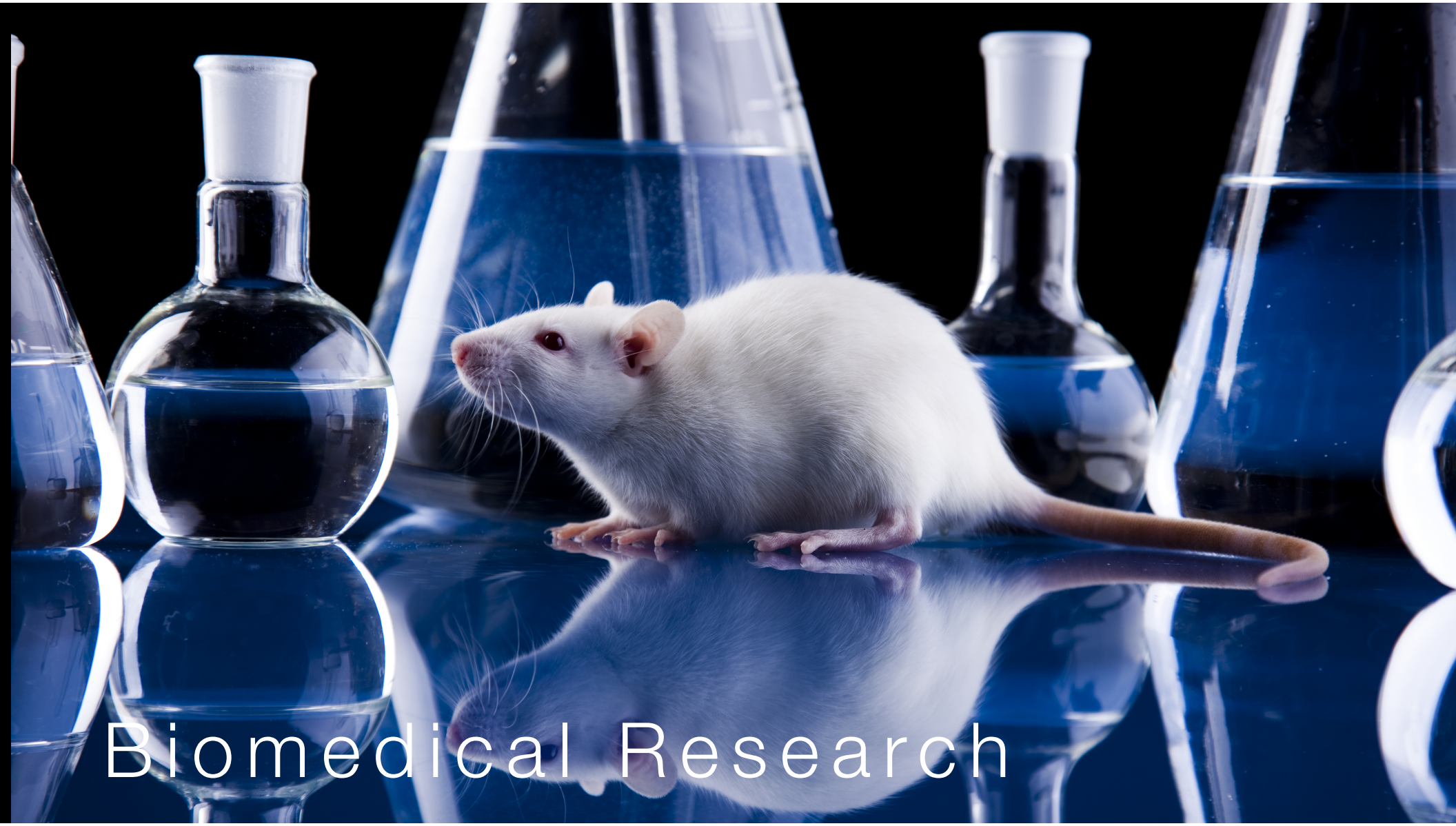
Developing a Set of Core Outcomes for Trials in Hemodialysis: An International Delphi SurveyAm J Kidney Dis. 2017 Feb 23

Neurocognitive Impairment

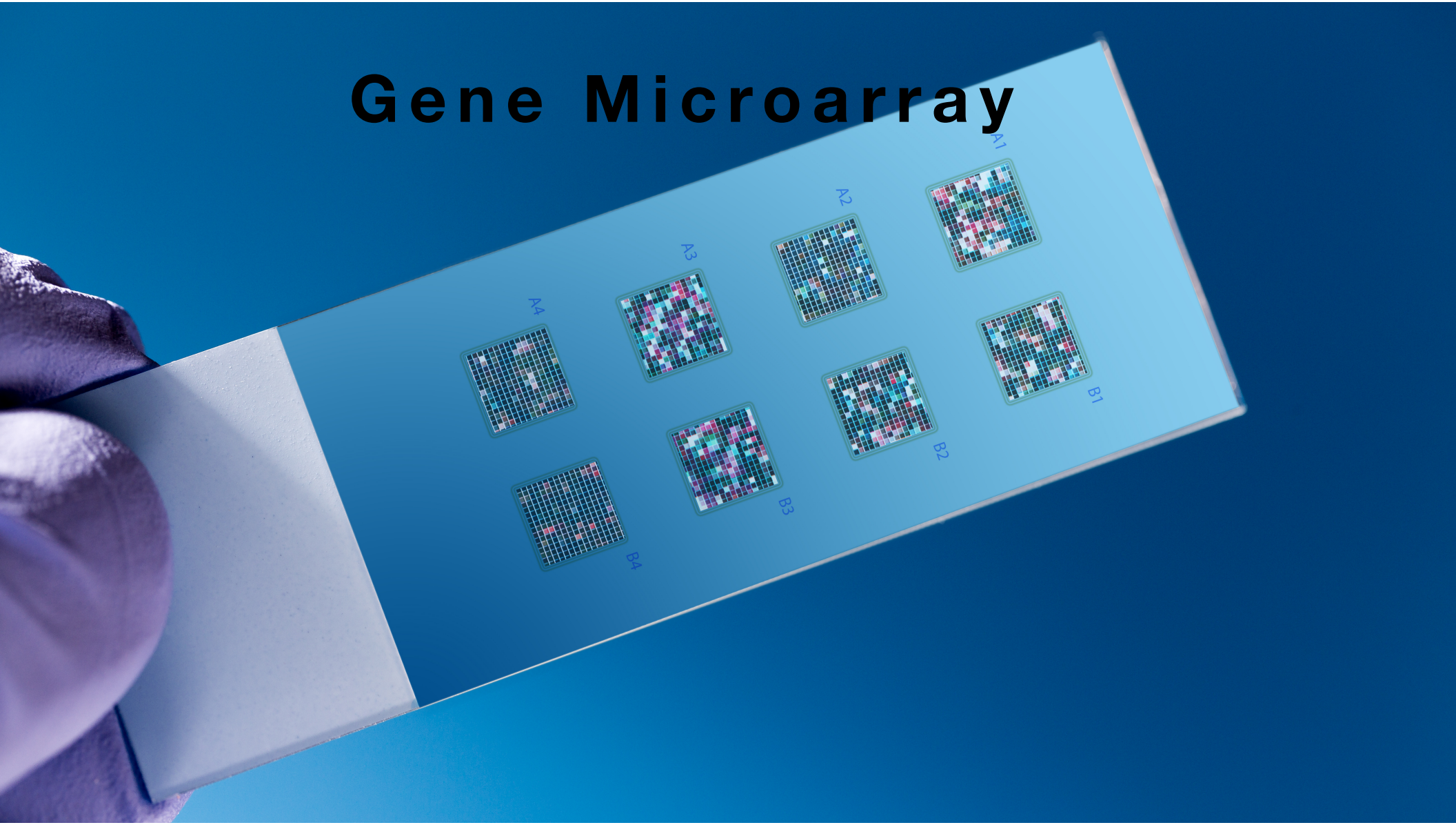
pick one

Patient Reported Outcomes


Kt/V urea
Depression and Dialysis
Now pick your Hemodialysis Champion
Neurocognitive Impairment
Patient Reported Outcomes


Biomedical Research

Gene Microarray



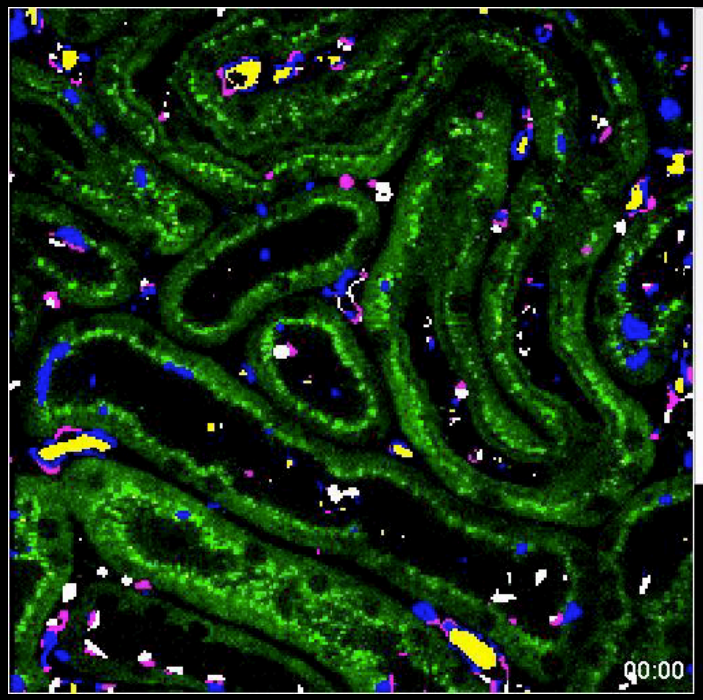
Gene microarrays

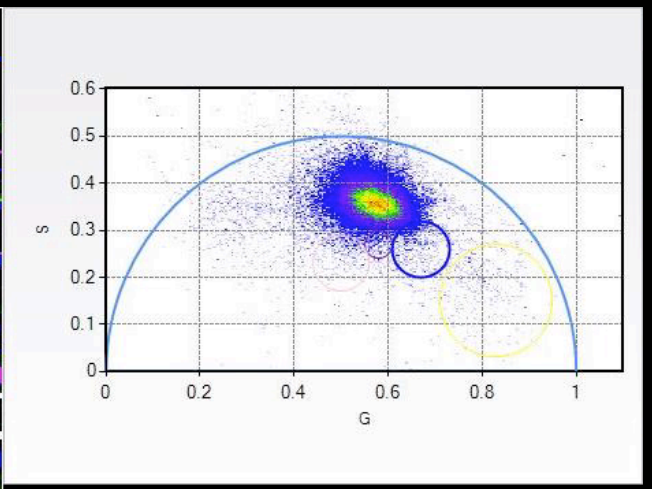
- Measures transcribed DNA in a tissue
- See what genes are turned on versus tuned off
- Can only see genes you know about, since complimentary probes must be created for each gene in advance.

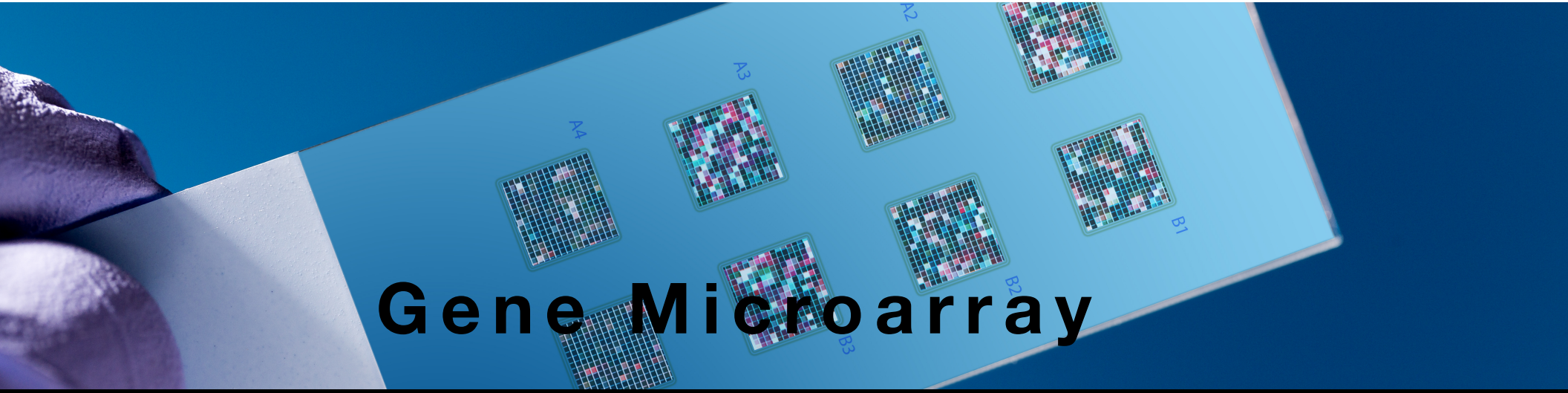
Two Photon Microscopy

two photon microscopy

- Allows real time 4-D microscopy of living tissue







Gene Microarray

pick one

Two Photon Microscopy

CRISPR-Cas9

CRISPR-Cas9

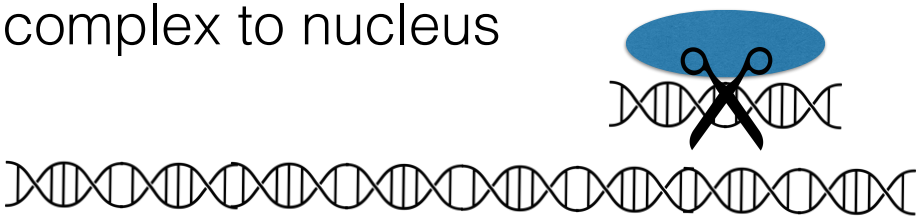
- Uses a a bacterial immune system to easily localize and edit segments of DNA
- CRSIPR is the DNA palindromeme that binds the target gene.
- Cas9 is the enzyme which snipe out a specific portion of DNA.
- Wide variety of applications
- Way easier than earlier versions of the same technology

CRISPR-Cas9

1 make complementary guide RNA

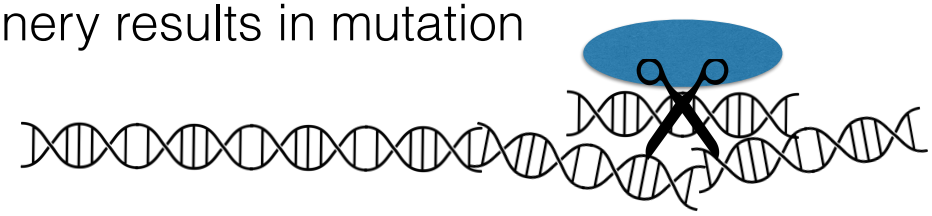
+ Cas9 enzyme

2 deploy Cas9 gRNA guided complex to nucleus



target DNA

3 Cas9 cuts target DNA & repair machinery results in mutation

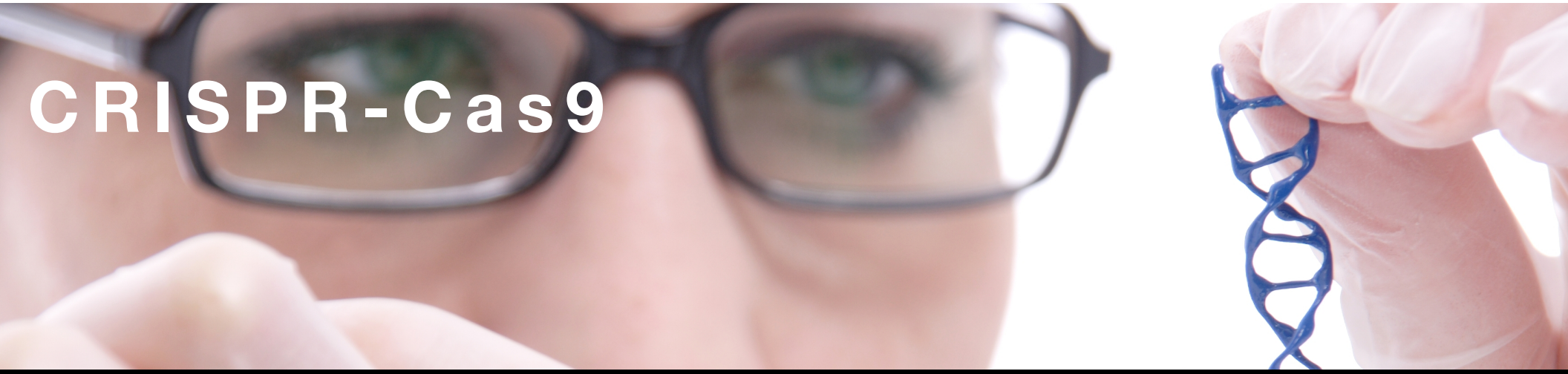


#NephMadness
#BioMedRegion
@Nephro_Sparks

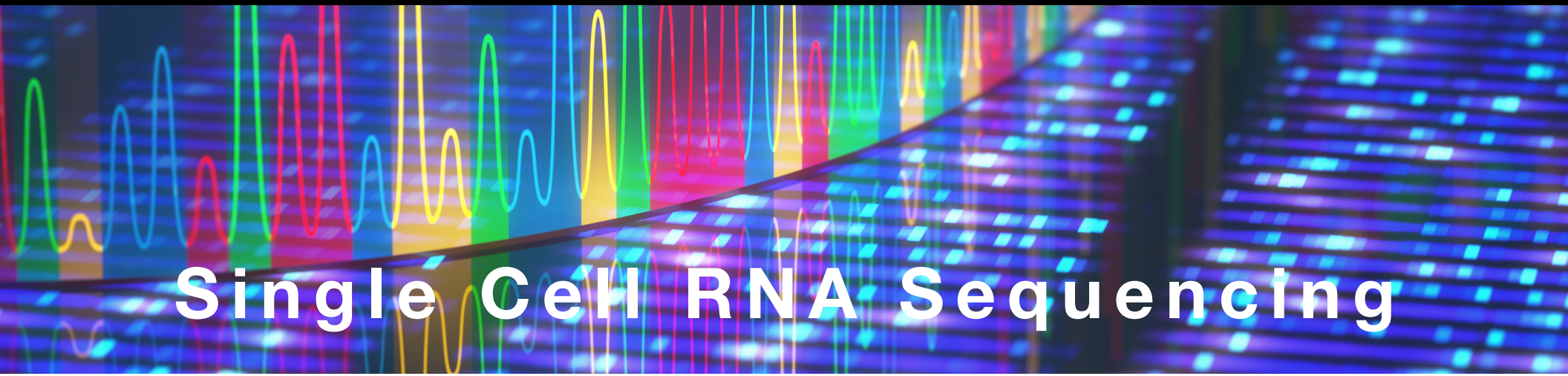
Single Cell RNA Sequencing

Single cell RNA Sequencing

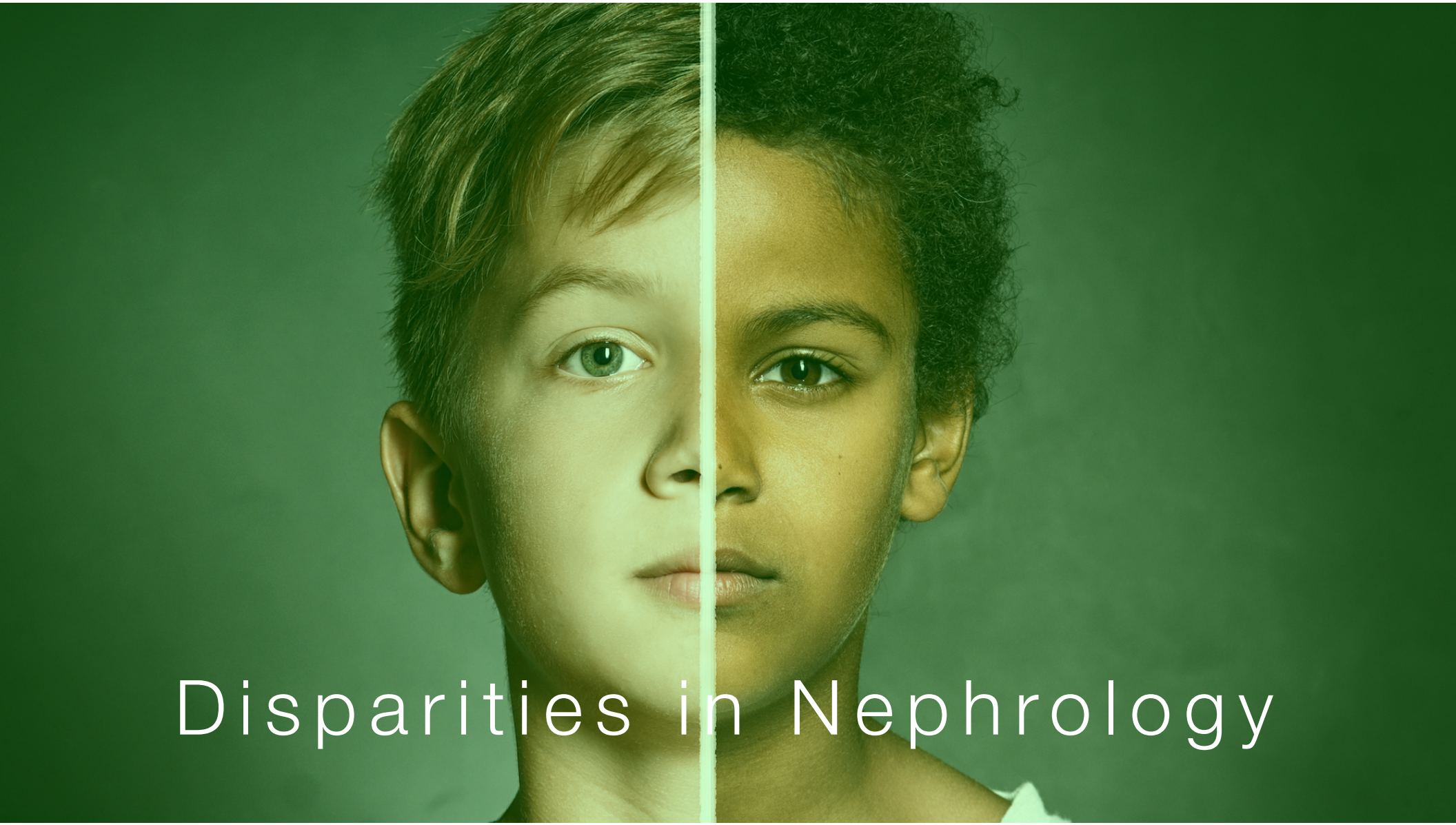
- allows measurement and quantification of all the RNA in a single cell. Powerful since tissues have many cell types, muddying signal.
- does not require you to know the genes prior to sequencing



pick one



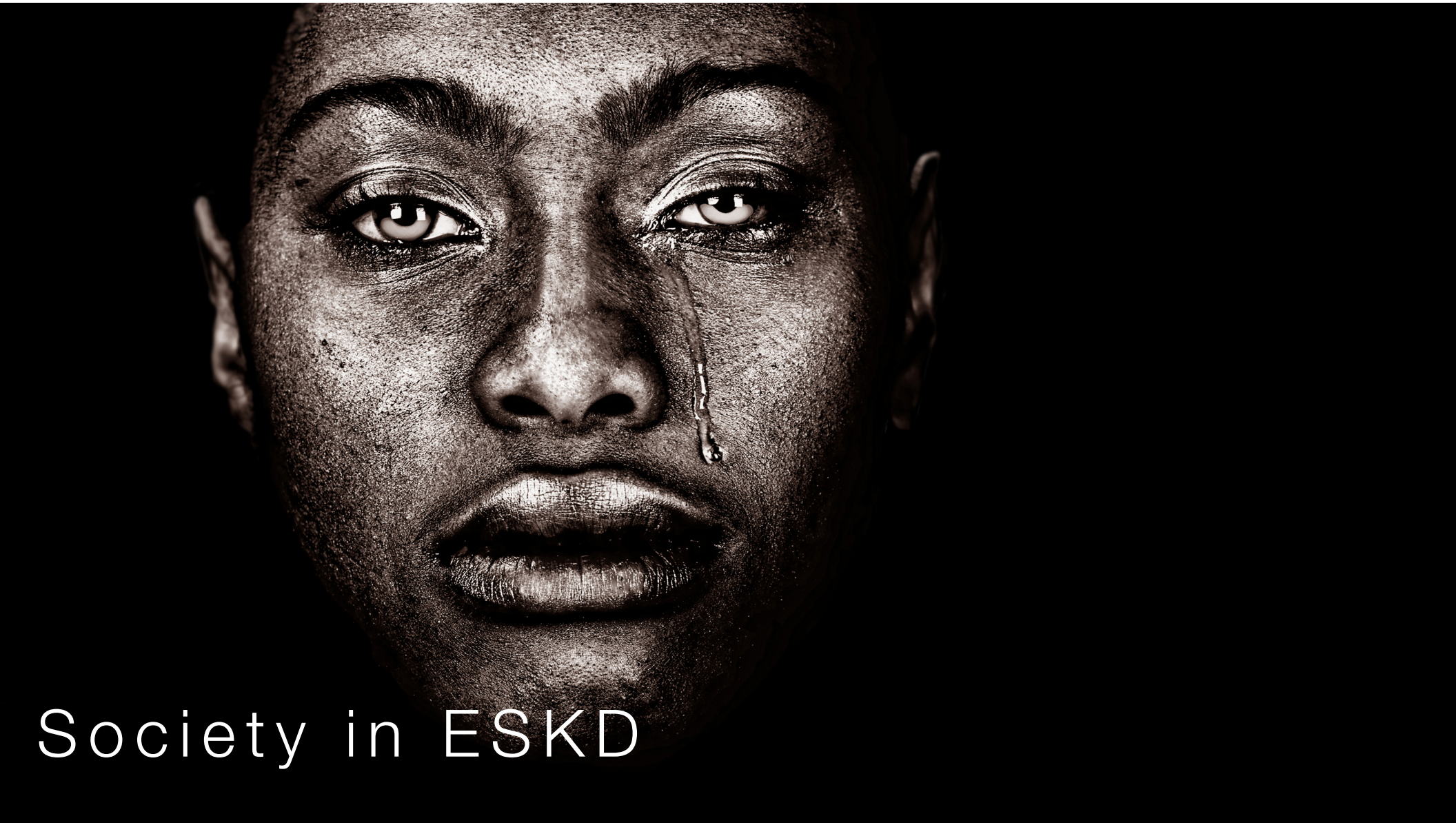
Gene Microarray
Two Photon Microscopy
Now pick your Biomedical Research Champion
CRISPR-Cas9
Single Cell RNA Sequencing


Disparities in Nephrology

Genes in ESRD

Genes in ESRD

- APOL1 is a powerful genetic risk factor. Commonin African Americans. Increases the risk of ESRD 2° to FSGS by 10x and increases the risk of ESKD 2° to hypertension by 7x.


Society in ESKD

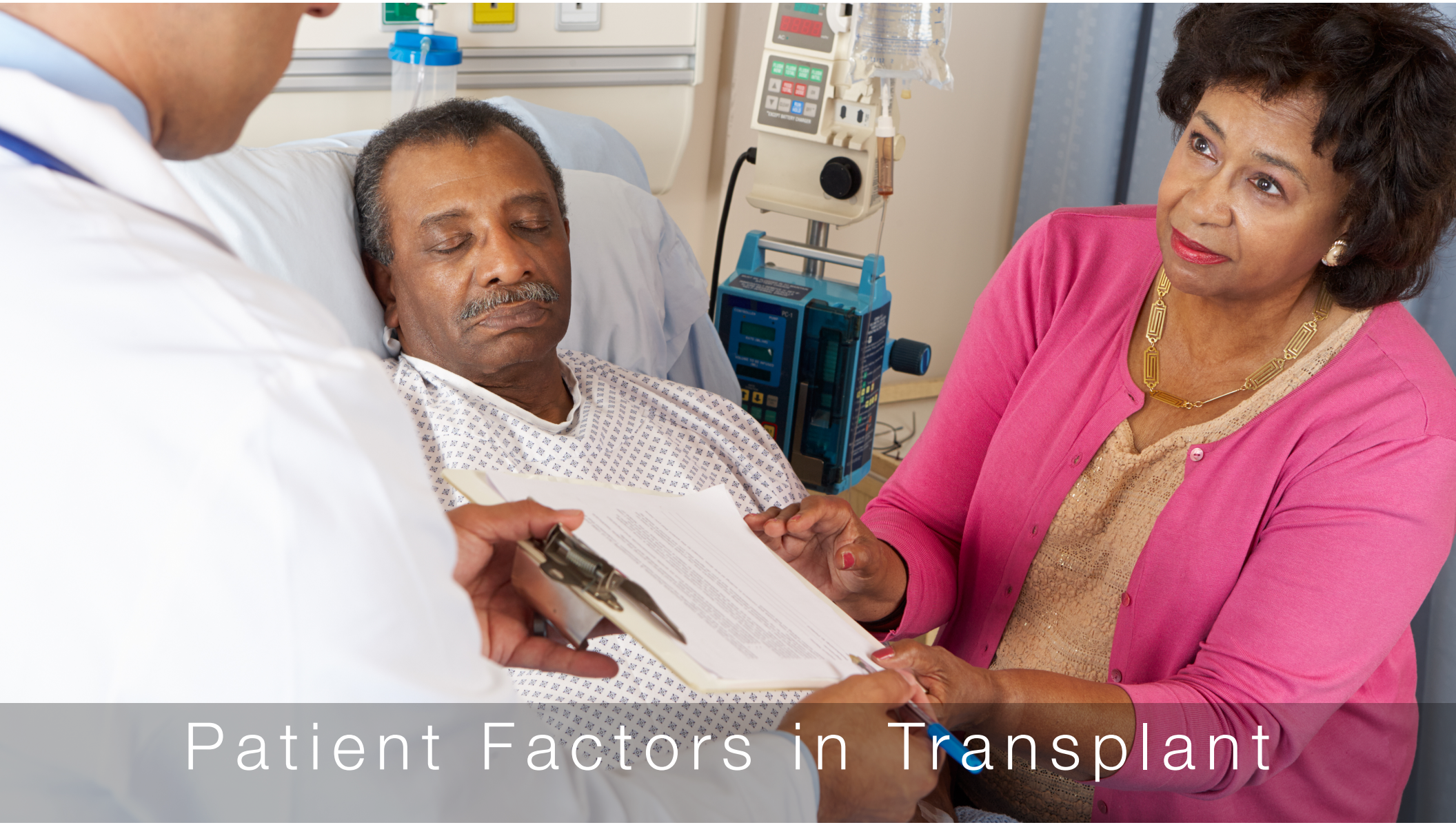
Society in ESKD

- Poverty is a risk factor for ESKD. HR is 2.74 for lowest quartile of income compared to the highest.
- Low education is a risk factor for ESKD HR is 1.78 from lowest educations quartile compared to highest
- Racial disparity in insurance rates with uninsured status highest among hispanics, then Blacks then Whites.
- Living in a highly segregated neighborhood is bad for African American survival on dialysis but not for Caucasian.
- Living in zip code with a lot of income inequality decreased Caucasian survival but not African American survival with ESKD.

Genes in ESRD

pick one

Society in ESKD



Patient Factors in Transplant

Patient Factors in Transplant

- Compared to Caucasians, African Americans are 3-5% less likely to want a transplant.
- African Americans are half as likely to complete the pre-transplant work-up
- Lack of understanding of transplant seems to be at the root of the disparity

System Factors in Transplant

System Factors in Transplant

- System factors include access to transplantation, variable insurance coverage, income, physician perception, location and health policies
- African Americans are less likely than whites to be rated as appropriate candidates for transplantation. More likely to have an incomplete evaluation and less likely likely to ultimately undergo transplant

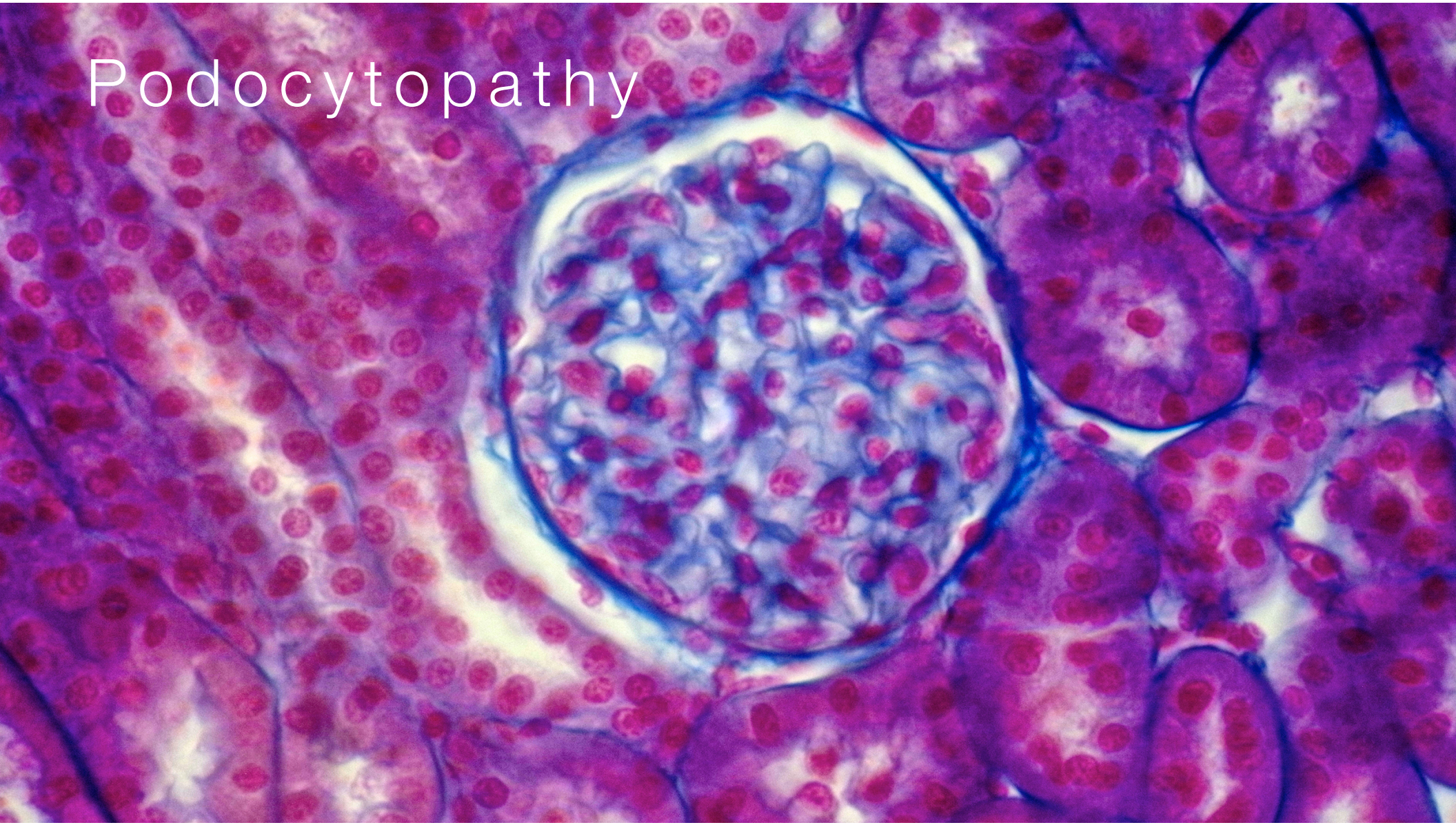
Patient Factors in Transplant

pick one

System Factors in Transplant

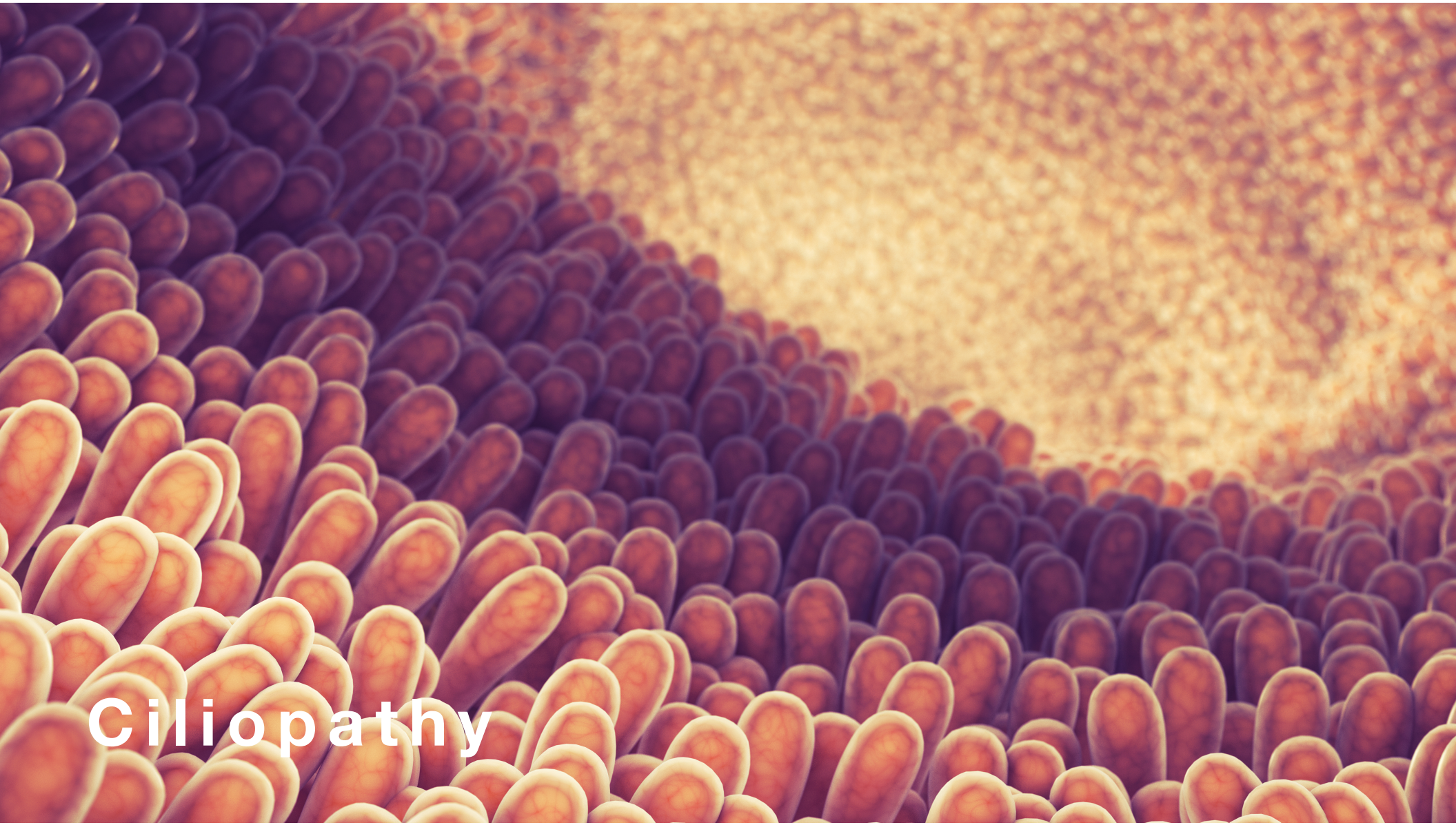
Genes in ESKD
Society in ESKD
Now pick your Disparities in Nephrology Champion
Patient Factors in Transplant
System Factors in Transplant

Genetics


Podocytopathy

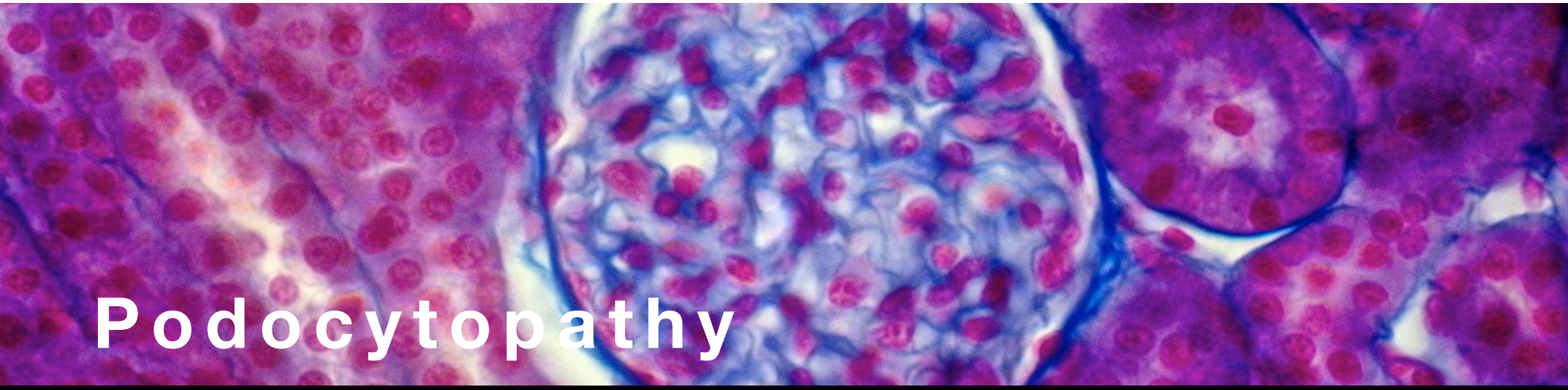
Podocytopathy

- Genetic causes of nephrotic system are usually due to podocytopathy.
- In some populations, developing nephrotic syndrome before the age of one has a 66% chance of having a mutation in one of four genes
  - NPHS1
  - NPHS2
  - WT1
  - LAMB2

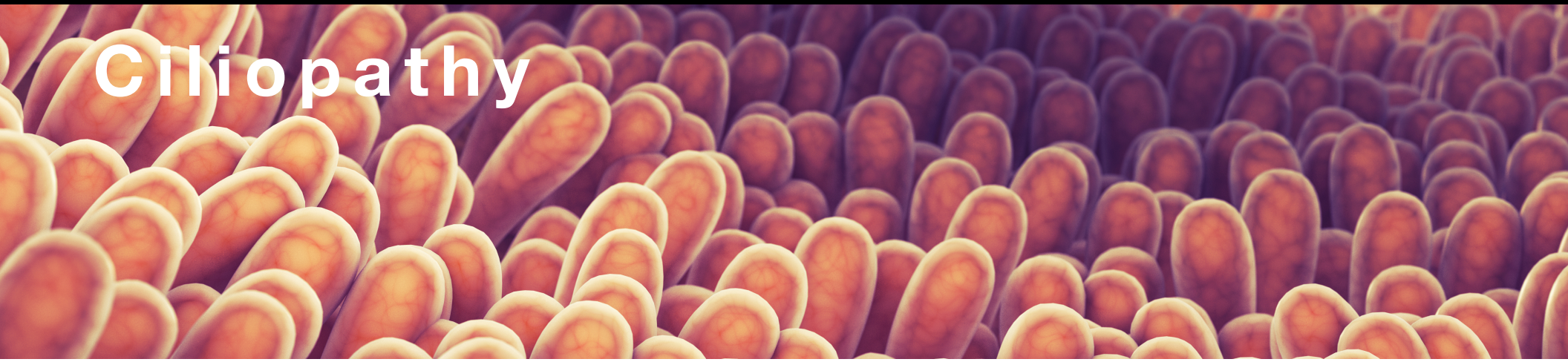

Ciliopathy

Ciliopathy

- Cilia are hair like organelles that act as mechano- and chemoreceptors
- In the tubules they probably detect urine flow and turn that into cell signals.
- Abnormalities of cilia genes result in cystic kidney disease



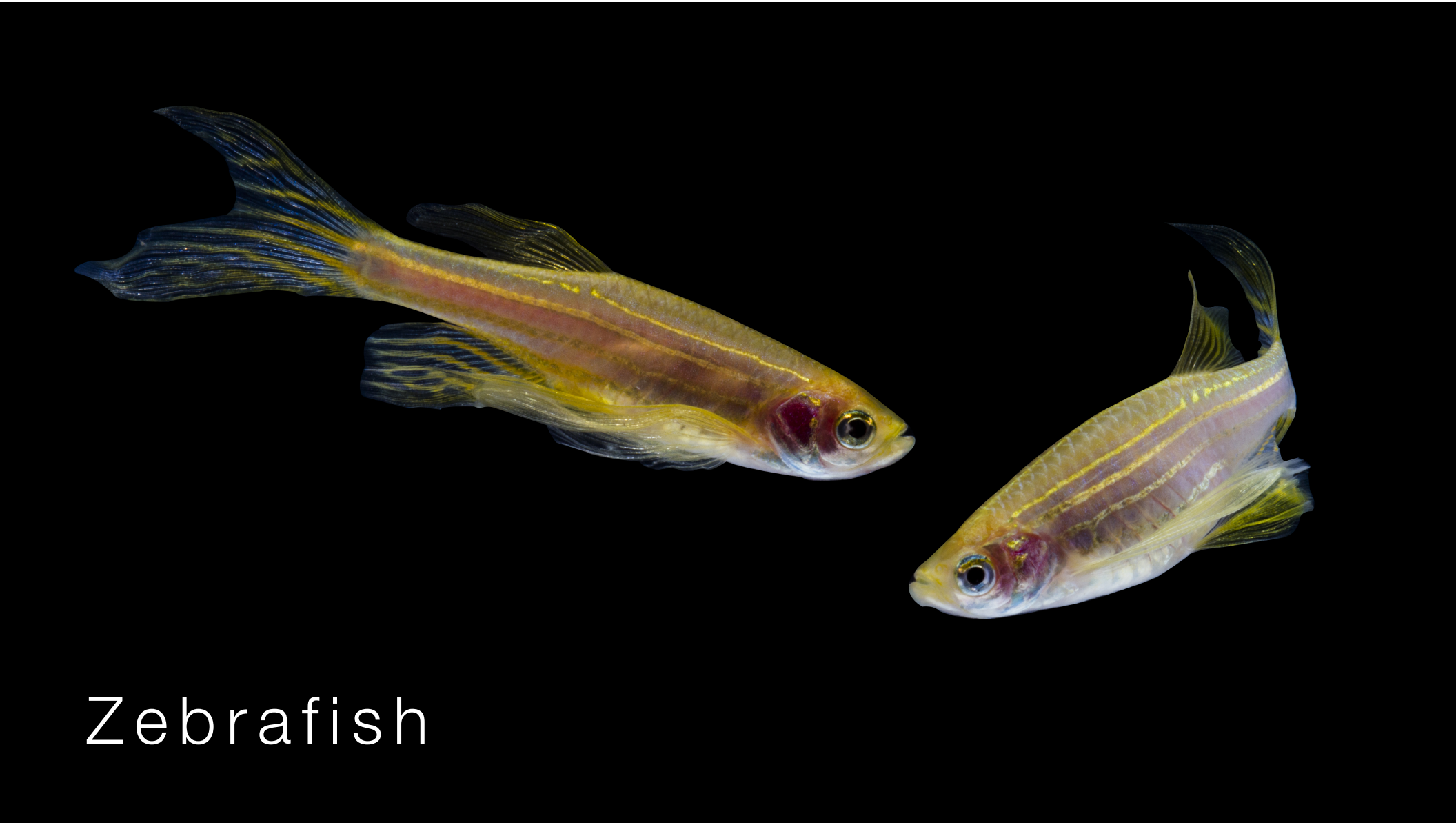
pick one



Drosophila

Drosophila

- These short lived flies do not have kidneys but do have nephrocytes that have a lot of the same roles as the kidneys including osmoregulation, transport and secretion.
- Nephrocyte slit diaphragms are being used to study APOL1.



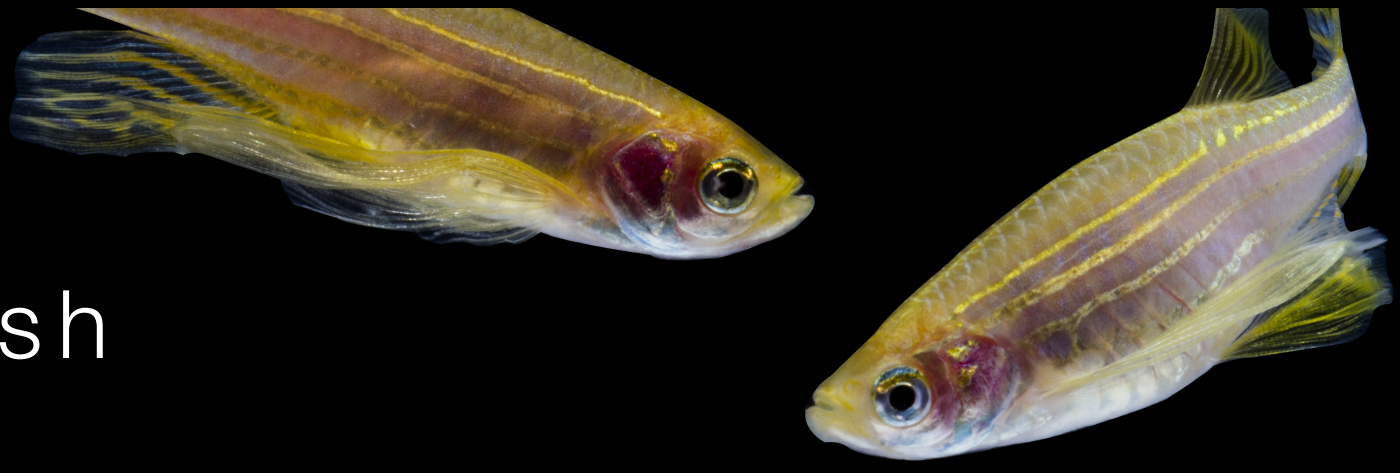
Zebrafish

Zebra Fish

- These small fast growing fish have 2 nephron kidneys that make it easy to study embryogenesis
- Also the fish are clear so you can literally see their tissues function in intact animals

Drosophila

pick one

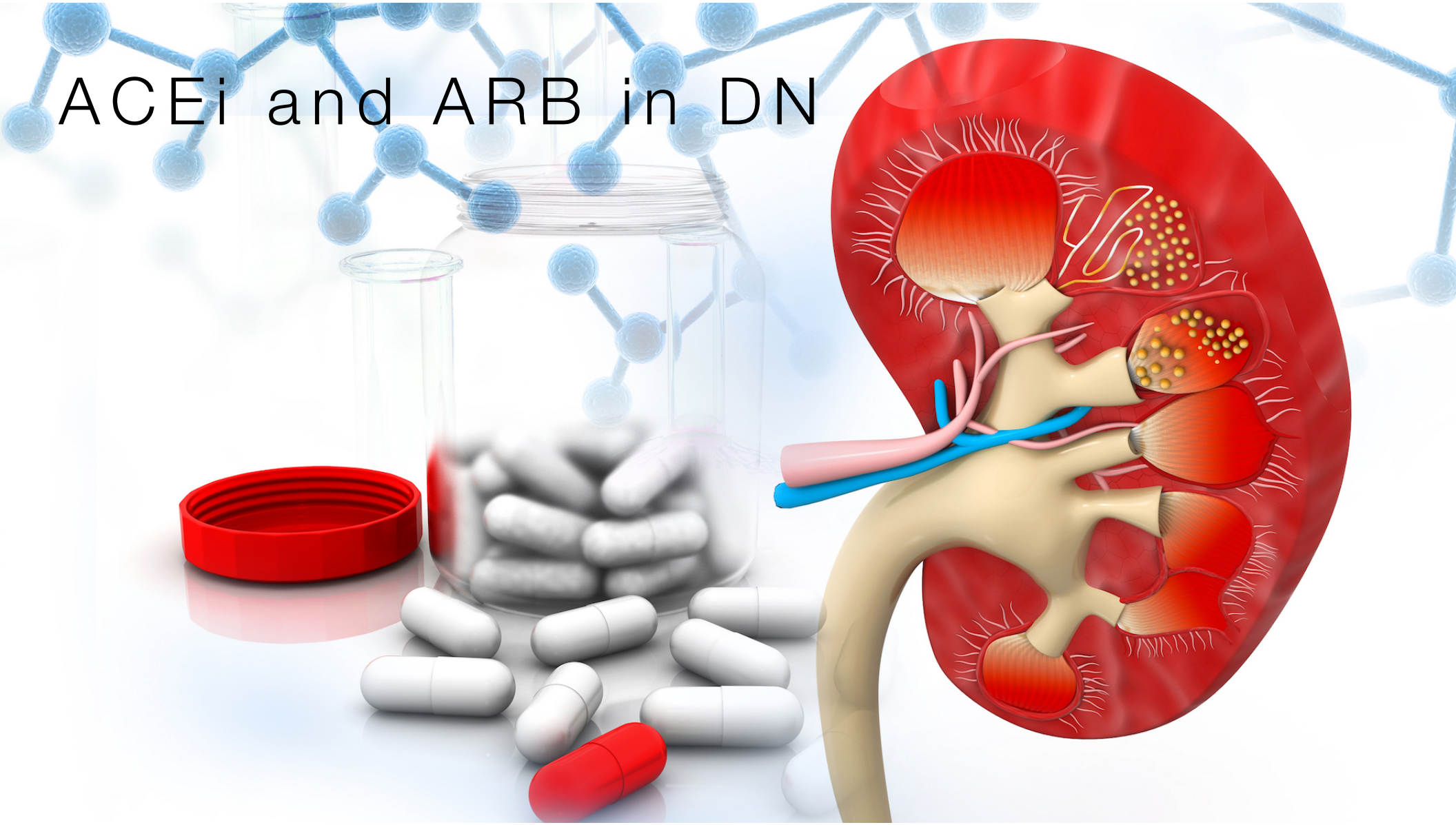


Zebrafish

Podocytopathy
Ciliopathy
Now pick your Genetics and the Kidney Champion
Drosophila
Zebrafish

Diabetes

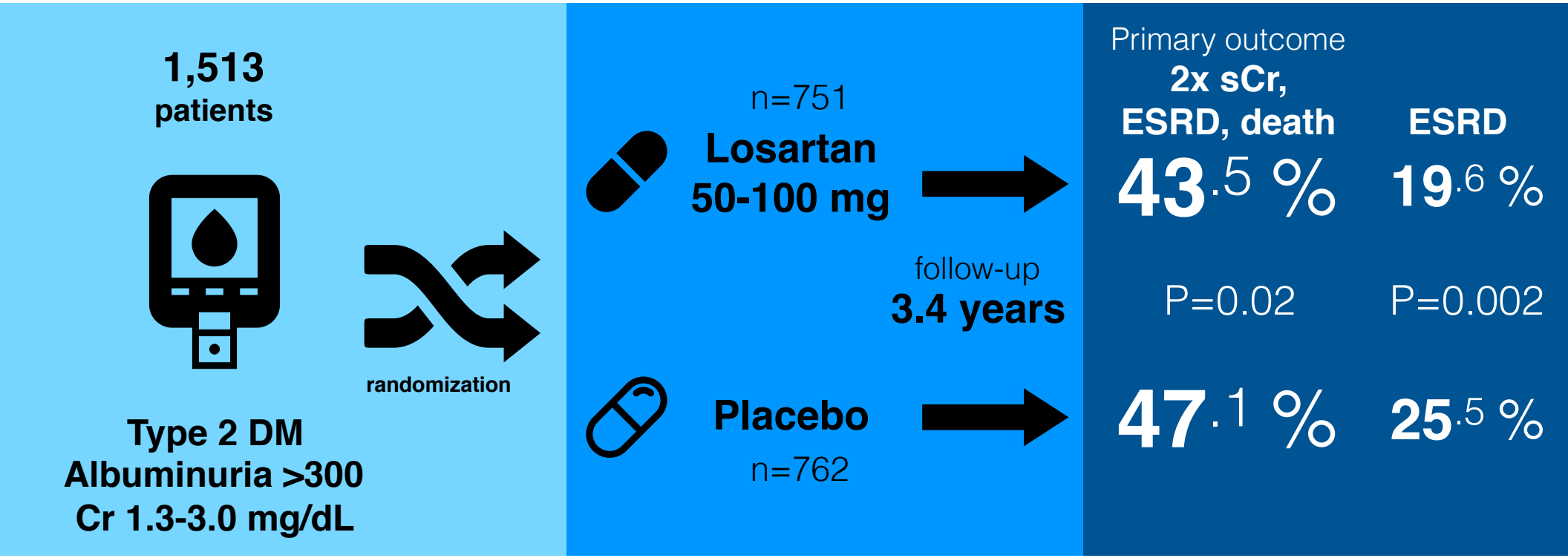
ACEi and ARB in DN



ACEi and ARB in DN

- In Type 1 DM the Collaborative Study Group showed slowed loss of GFR and ESRD with captopril
- In Type 2 DM RENAAL and IDNT decreased the composite outcome of doubling of serum Cr, dialysis or death
- Rates of diabetic nephropathy leading to ESRD have been falling recently, presumably due to RAAS inhibition.

Effects of Losartan on Renal and Cardiovascular Outcomes in Patients with Type 2 Diabetes and Nephropathy (RENAAL)

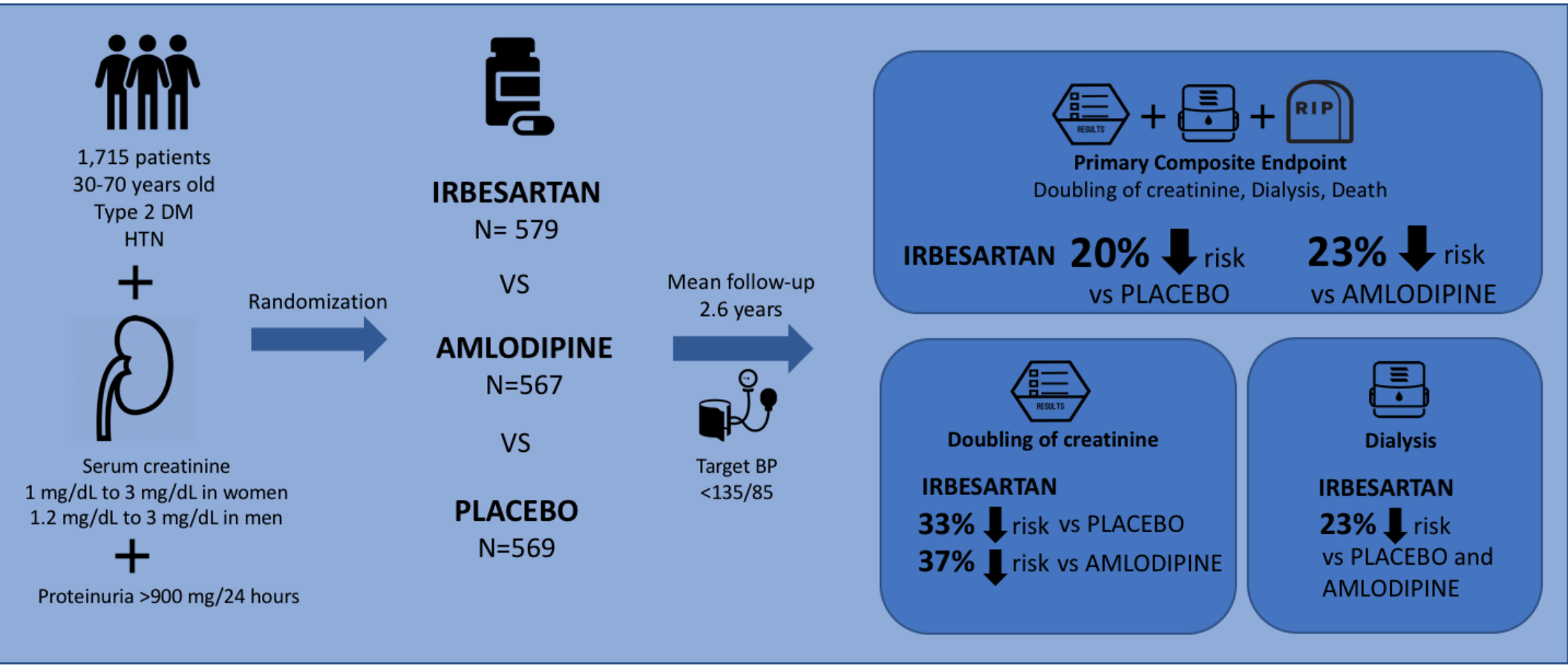


N Engl J Med, Vol. 345, No. 12 · September 20, 2001

The NEW ENGLAND JOURNAL of MEDICINE

Joel Topf @Kidney_Boy

Irbesartan Diabetic Nephropathy Trial (IDNT):
Renoprotective Effect of Irbesartan in Type 2 Diabetics with Nephropathy



#NephMadness
@KidneyBea_n

Lewis EJ et al, N Engl J Med, 2001

The NEW ENGLAND JOURNAL of MEDICINE

Glycemic Control in DN

Glycemic Control in DN

- In the reduction in the Diabetes Control and Complications Trial lowering A1c from 9% to 7% decreased the onset of albuminuria
- At 16 years this reduction of A1c resulted in decreased ESRD.
- ACCORD found increased mortality with patients randomized to A1c less than 6%
- A meta analysis of 28,000 patients found a reduced albuminuria but not a doubling of serum creatinine

pick one

SGLT2 inhibitors in DN

SGLT2 inhibitors in DN

- SGLT2 inhibitors block reabsorption of Na and glucose in the proximal convoluted tubule
- Rats with DM treated with dapagliflozin show tubuloglomerular feedback activation and decreased glomerular filtration
- EMPA-REG OUTCOME trial reduced the risk of the primary composite outcome of death from CVD, nonfatal MI, and nonfatal strokes
- EMPA-REG OUTCOME reduced the risk of progression to macroalbuminuria, risk of incident nephropathy, and doubling of serum creatinine

GLP1 Agonists in DN

GLP1 Agonists in DN

- GLP-1 is an incretin produced in the L-cells of the small intestine in response to ingestion of food
- GLP-1 receptors have been found in rodent and porcine proximal tubular cells
- The LEADER trial found a lower rate of the first occurrence of death from CVD, MI, or stroke with liraglutide
- Secondary renal outcomes showed decreased risk of new onset macroalbuminuria, but time to doubling of Cr, ESRD, and death due to renal disease were similar in both groups

SGLT2 inhibitors in DN

pick one

GLP1 Agonists in DN

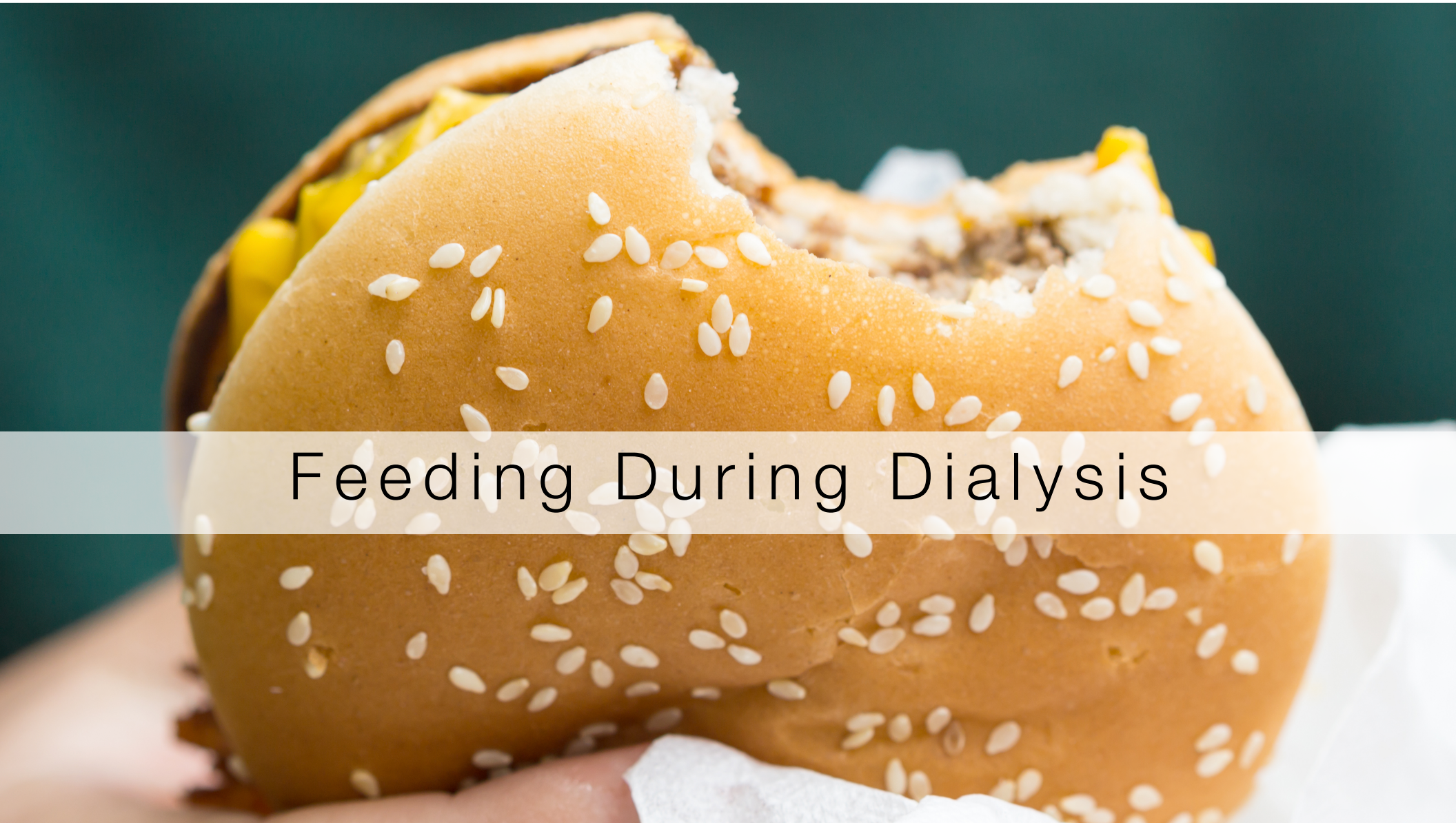
ACEi and ARB in DN
Glycemic Control in DN
Now pick your Diabetes Champion
SGLT2 Inhibitors in DN
GLP1 Agonists in DN

Nutrition

Protein Restriction in CKD

Protein Restriction in CKD

- Lowering protein intake was standard of care prior to the publication of the MDRD and Northern Italian Cooperative Trial.
- These two trials both failed to show any slowing of progression of GFR loss
- Post hoc analysis shows decreased uremic symptoms with low protein intake
- IDEAL trial showed that starting dialysis at a specific GFR prior to uremia was no better than starting due to uremic symptoms.This shifted standard of care shifted to starting dialysis based on symptoms. Maybe MDRD and Northern Italian Cooperative need reinterpretation.



Feeding During Dialysis

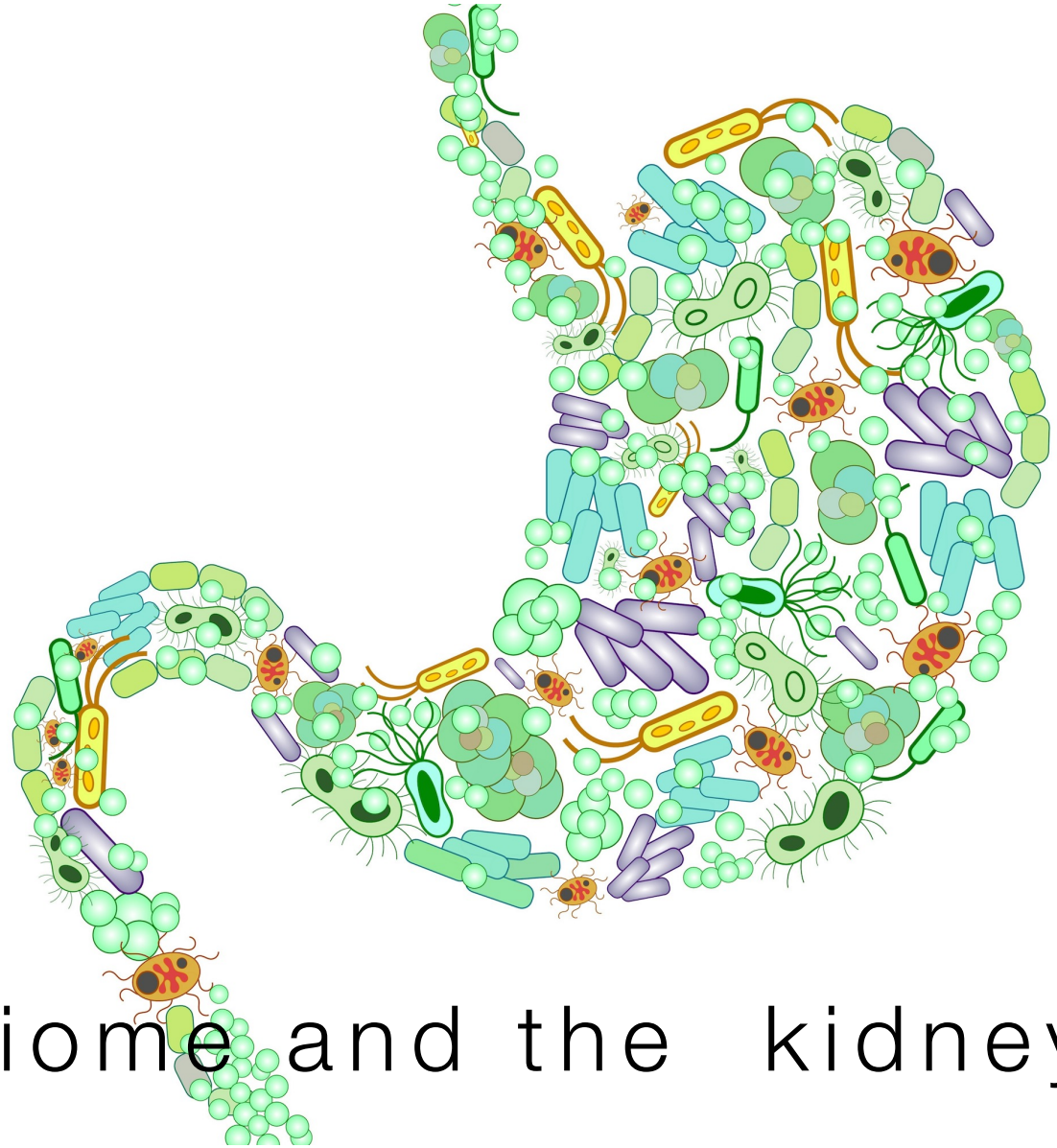
Feeding During Dialysis

- Eating during dialysis can cause dialytic hypotension, aspiration and choking
- A can of Nepro (237 mL) with each dialysis for 3 months improved albumin, pre-albumin, and subjective global assessment
- FINE Study was parenteral plus oral intradialytic nutrition vs oral supplemental nutrition. No difference in mortality, hospitalization rate, or reasons for hospitalizations
- FrEDI was a RCT of high-protein meals versus low-protein meals provided during dialysis. Primary outcome was an increase in albumin of ≥0.2 g/dL while maintaining a phosphorus of 3.5–<5.5 mg/dL. This was achieved by 27% in the high-protein group versus12% in the low-protein group.

Protein Restriction in CKD

pick one

Feeding During Dialysis



Microbiome and the kidney

Microbiome and the kidney

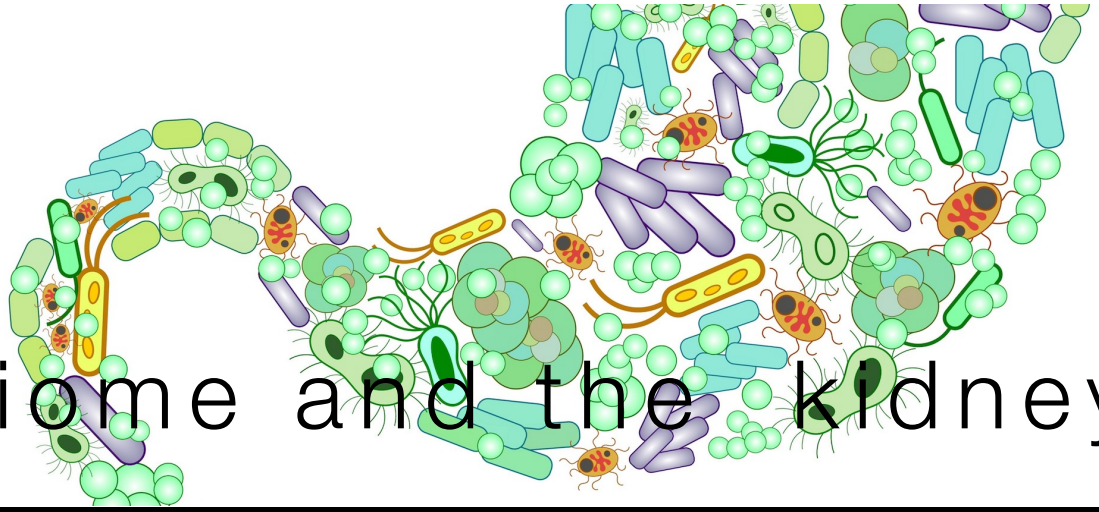
- uremic toxins, such as indoxyl sulfate, p-cresol sulfate and trimethylamine N-oxide, are generated by gut bacteria
- There is breakdown of colonic epithelial tight junctions in CKD, enabling translocation of endotoxins into intestinal walls and systemic circulation, potentially contributing to the inflammatory state of CKD
- Oxalobacter formigenes is an oxalate-degrading microbe and its presence is associated with lower rates of kidney stones

Do artificial sweeteners cause glucose intolerance?

Omega-3 Fatty Acids

Omega-3 Fatty Acids

- 1999 the GISSI-Prevenzione Trial 850 mg of omega-3 fatty acids qD reduced the composite of death, MI, and stroke in an unblinded RCT.
- Subsequent blinded trials could not reproduce this and then a meta-analysis of 20,485 patients from 14 RCT found no benefit of fish oil in secondary prevention of cardiovascular disease
- Fish oil for IgA and 1-3 g of proteinuria: 12 g of fish oil or placebo daily for 2-years. Significant reductions in disease progression (increased creatinine by 50%) and ESKD.
- Unable to be replicated
- Attempts to use fish oil for graft or fistula health have not been consistently successful



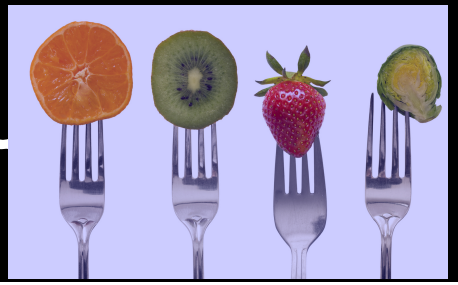
Microbiome and the kidney

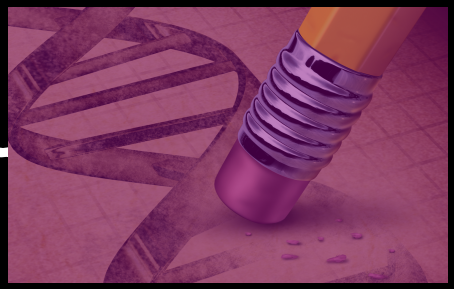
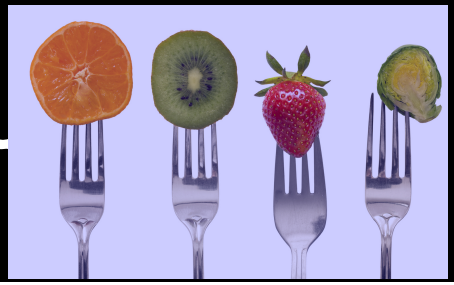
pick one

Omega-3 Fatty Acids

Protein Restriction in CKD
Feeding During Dialysis
Now pick your Nutrition in Nephrology Champion
Adaptive clinical trials
Omega 3 Fatty Acids in CKD

From your Effluent Eight
pick your Filtered Four



From your Filtered
Four pick your left
and right kidney…

…since you only
need 1 kidney,
your champion