Randomized Controlled Trials in Nephrology: Last Year and the Next 5 Years

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Disclosures

- Off label medication use:
 - prednisone / prednisolone / methylprednisolone for glomerular diseases
- Only time for sample of exciting, high quality work
 - Shameless plugs for some of my own work

• Why we need randomized controlled trials

- Some important RCTs from the last year
- Some potentially important trials underway

Does this treatment improve lives?

- Human health is complex
 - Genetics
 - Environment
 - Behaviour
- Need to isolate effects of treatment



27% of observational studies disagree with randomized studies (Ioannidis et al. JAMA. 2001)

Why Randomized?

Quantity of Randomized Controlled Trials in Nephrology and Other Specialties



Kyriakos et al. J Am Soc Neph. 2018; Konstantinidis et al. JAMA. 2016.

Chronic Kidney Disease is a Rapidly Increasing Cause of Death Globally



End-stage Kidney Disease is Increasing



ESRD incidence and prevalence per million population

McCullough et al. J Am Soc Neph. 2018.

Decreasing the Risk of Requiring Dialysis

- In 4200 patients with Type 2 DM and eGFR 30 to 60
- Canagliflozin 100 mg vs placebo



Primary Outcome: ESKD, Doubling of Serum Creatinine, or Renal or CV Death



Summary

Primary	Hazard ratio (95% CI)	P value	
1. ESKD, doubling of serum creatinine, or renal or CV death	0.70 (0.59-0.82)	0.00001	V
Secondary			
2. CV death or hospitalization for heart failure	0.69 (0.57-0.83)	<0.001	~
3. CV death, MI, or stroke	0.80 (0.67-0.95)	0.01	~
4. Hospitalization for heart failure	0.61 (0.47-0.80)	<0.001	V
5. ESKD, doubling of serum creatinine, or renal death	0.66 (0.53-0.81)	<0.001	~
6. CV death	0.78 (0.61-1.00)	0.0502	Not significant
7. All-cause mortality	0.83 (0.68-1.02)	-	Not formally

On the Horizon

Trial	Patients Included	Drug	New Knowledge
Dapa-CKD	4000 pts with CKD eGFR 25 to 75 or UACr 200-5000	Dapagliflozin	Extends to non-diabetic CKD, lower eGFR, lower ACR
EMPA-KIDNEY The study of heart and kidney protection with empagliflozin	5000 pts with CKD eGFR 20 to 45 or UACr >200	Empagliflozin	Extends to non-diabetic CKD, lower eGFR, lower ACR
SCORED	10,500 pts with diabetic CKD and high risk of CV disease eGFR 25 to 60	Sotagliflozin	New agent, lower eGFR, removes ACR

Glomerulonephritis and CKD



Steroids for moderate IgA Nephropathy: The TESTING Study

Effect of Oral Methylprednisolone on Clinical Outcomes in Patients With IgA Nephropathy Lv J, Zhang H, Wong MG, Jardine M, Et al. JAMA 318(5); 2017.



*Stopped early due to excessive SAE

#NephJC

Prednisone Exposure in ANCA Associated Vasculitis





Outcome	Reduced Dose	Standard Dose	Incidence Rate Ratio (95% Confidence Interval)	P-value
Year 1 Serious Infections, n (%)	96 (27)	116 (33)	0.70 (0.52 – 0.94)	0.02

Improving Heart Health for Patients that Require Dialysis



AMI and ASHD

CHF

- 🗆 CVA
- Arrhythmia/Cardiac ar
- Other cardiac
- Septicemia
- Other infection
- Malignancy
- Hyperkalemia
- Withdrawal
- All other causes

Heart Related Deaths ~50%







Cumulative Incidence of the Primary Efficacy End Point, of Death from Any Cause, and of Death from Any Cause and a Composite of Cardiovascular Events as Recurrent Events.



Mineralocorticoid Antagonists in Patients Receiving Dialysis







<u>At least</u> 2750 participants from 12 countries



What's the efficacy of cognitive behavioral therapy (CBT) Vs. Sertraline for treating depression in ESRD?



Conclusions: An engagement interview had no effect on patient acceptance of depression treatment. Patients who received sertraline had modestly better depression scores and other patient-reported outcomes than those in the CBT group.

Mehrotra R, et al. Comparative Efficacy of Therapies for Treatment of Depression for Patients Undergoing Maintenance Hemodialysis: A Randomized Clinical Trial. Ann Intern Med. doi: 10.7326/M18-2229

y @Errantnephron

Evaluation of routinely **M**easured **PAT**ient reported outcomes in **H**emodial**Y**sis care (**EMPATHY**): Implementing a cluster randomized controlled trial at the health system level

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Summary

- (Large) randomized controlled trials are the best way to determine if a treatment "works"
- Nephrology needs more RCTs to improve care
- In the last 12(ish) months we saw advances in treating patients with:
 - Diabetic kidney disease progressing to dialysis
 - Glomerulonephritis
 - Complications of dialysis
- Exciting next five years!
 - More trials
 - Larger trials
 - Treatments for problems most important to patients