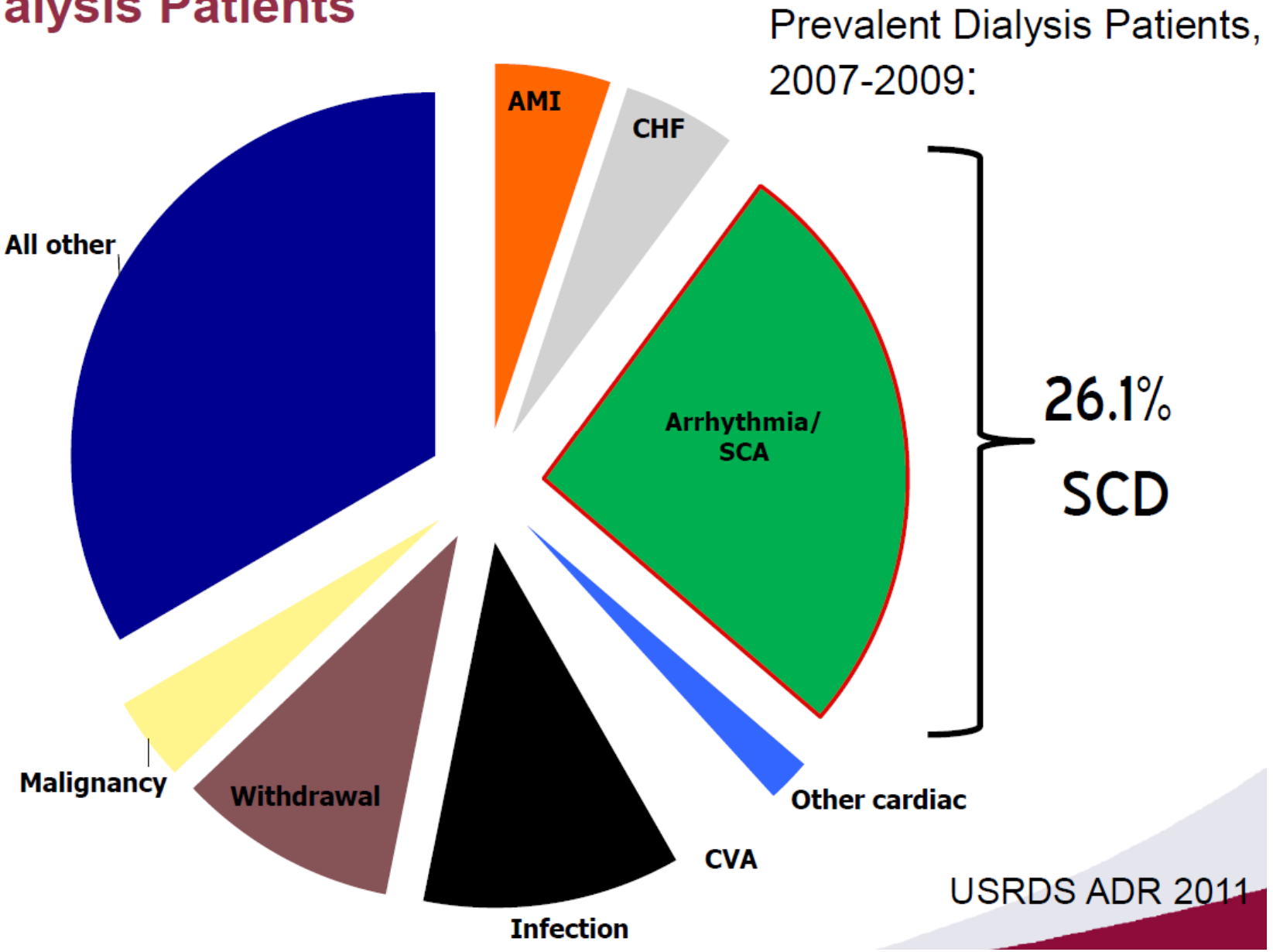
Sudden Cardiac Death in ESRD

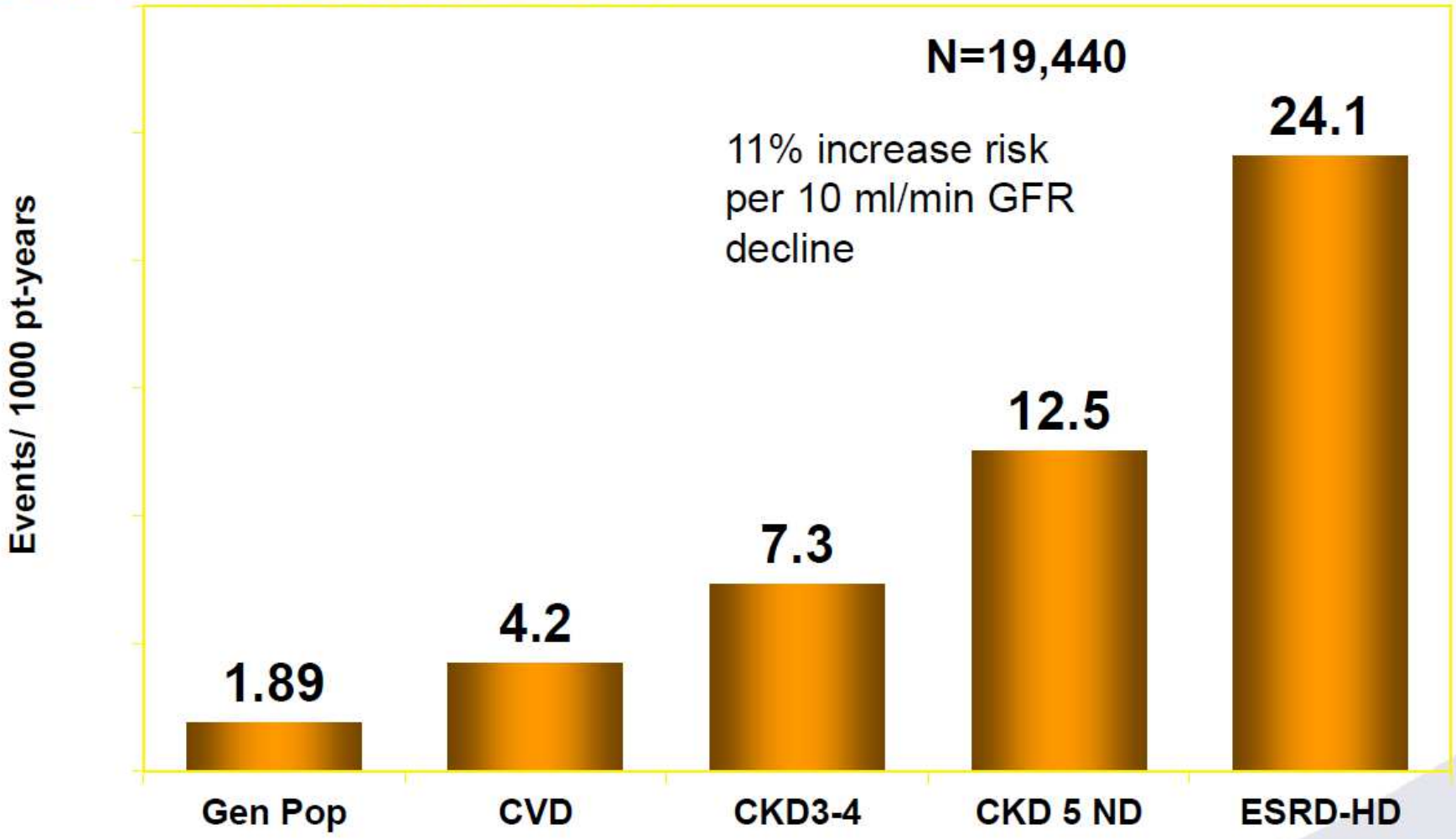
SKC In-service October 2015

Sudden Death is the Leading Cause of Death in Dialysis Patients



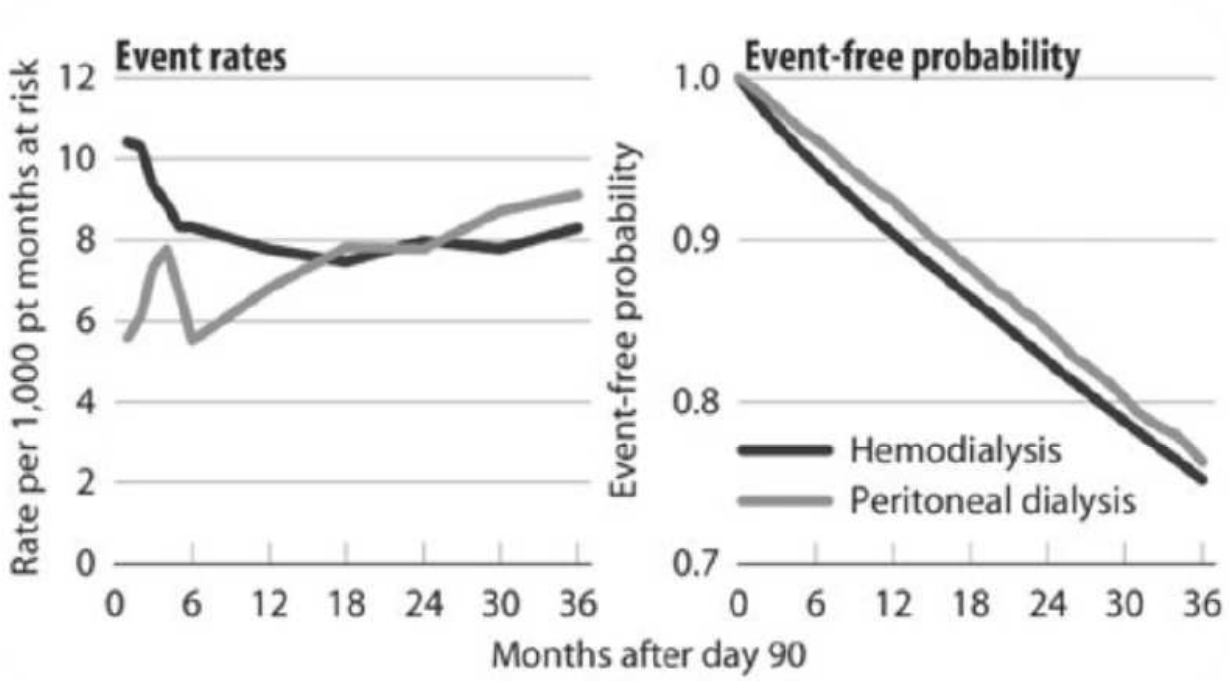
The risk of SCD in ESKD-HD is 20x greater than the general population

Duke catheterization database:



Pun et. al. Kidney Int. 2009 Sep;76(6):652-8

Risk of Sudden Cardiac Death after Dialysis Initiation: PD vs. HD



What is also clear is that the risk of SCD increases in relationship to the number of years on dialysis. Again data from the USRDS showing the increasing cumulative probability of SCD with each passing month on HD.

USRDS ADR 2011

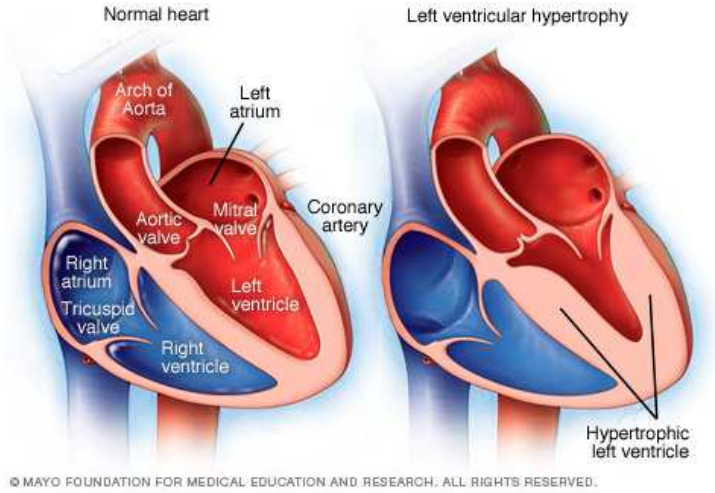
SCD Traditional Definitions

- **Witnessed cardiac arrest**
  - Within an hour of symptom onset
- **Unwitnessed death**
  - Unexpected
  - Patient known to be well in the last 24 hours
  - No other clear non-cardiac cause of death

- **Usually due to ventricular tachyarrhythmia**
- **Does this apply to dialysis patients?**

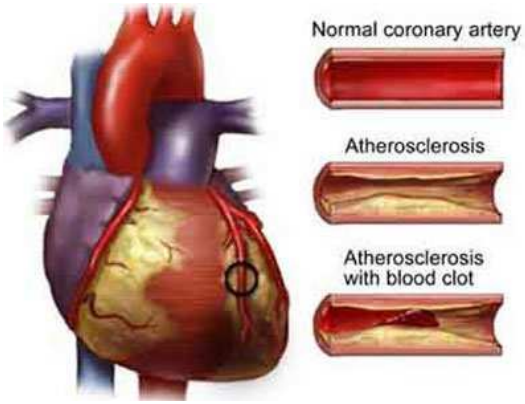
Differences in Structural Heart Disease

- **LVH and Diffuse Myocardial Scarring are more Common than ischemic heart disease or systolic dysfunction**
- **Left Ventricular Hypertrophy**
  - **56% of HD pts without CAD**
    - **Etiologic associations with**
      - Chronic ECFV excess/ vascular access
      - Pressure loading/ hypertension
      - Anemia
      - Mineral-bone-disease/ hyperphosphatemia
      - Aluminum

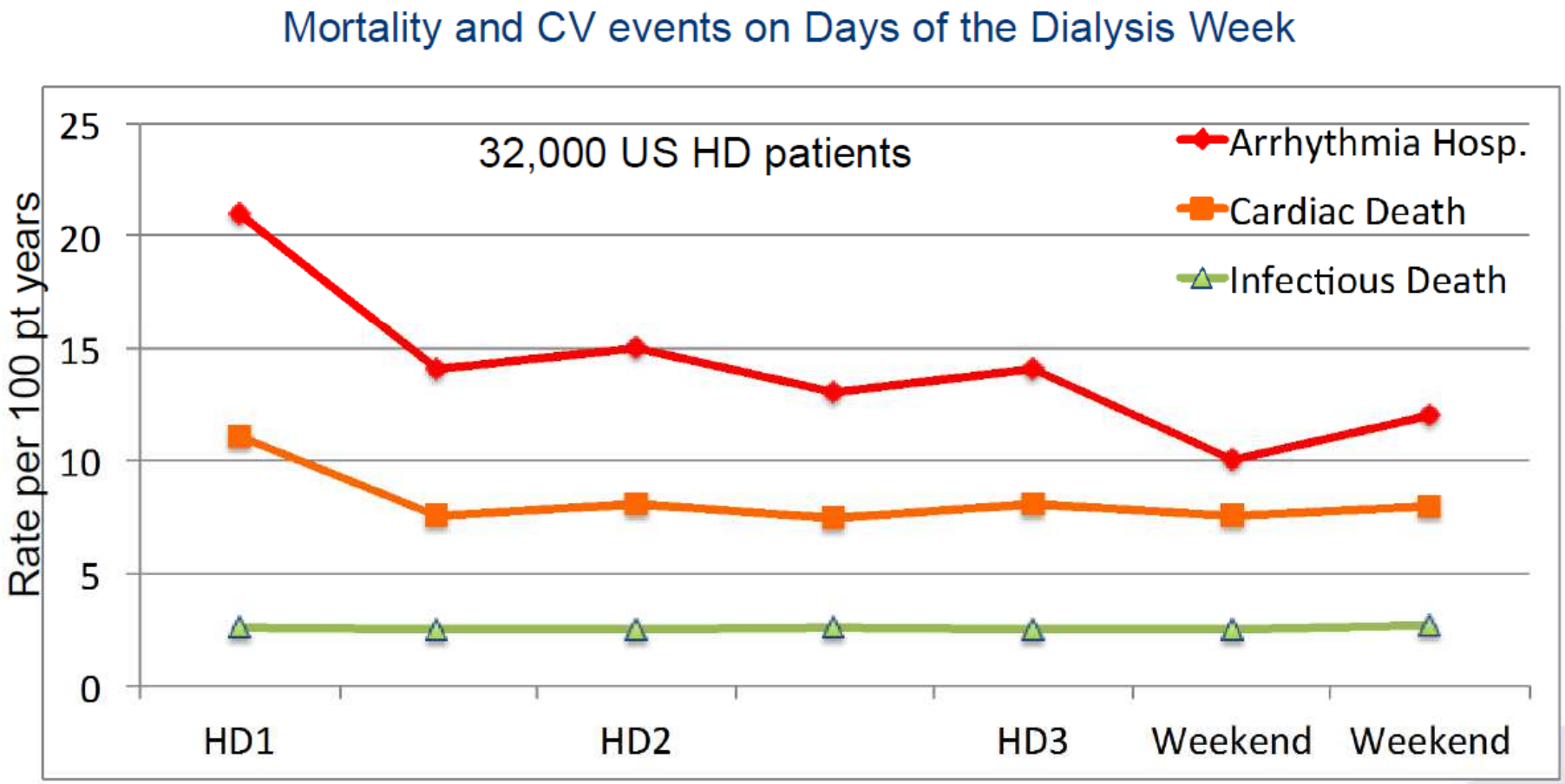


  - **LVMI > 125 g/m$_2$= 30% increased risk of death at 5 yrs**
  - **LVH = Increased rate of arrhythmias**
  - **Increased myocardial fibrosis with diffuse subendocardial enhancement**
    - Meier et. al. Nephron. 2001 Mar;87(3):199-214
    - Silverberg et. al. KI 1989
    - Ayuset. al. JASN 2005

Mark PB et al. *Kidney International*(2006) 69: 1839–1845



SCD Acute Triggers: SCD and Arrhythmias occur most frequently on the first hemodialysis day of the week.



Foley et. al. NEJM 2011: 365: 1099

Hemodialysis and SCD

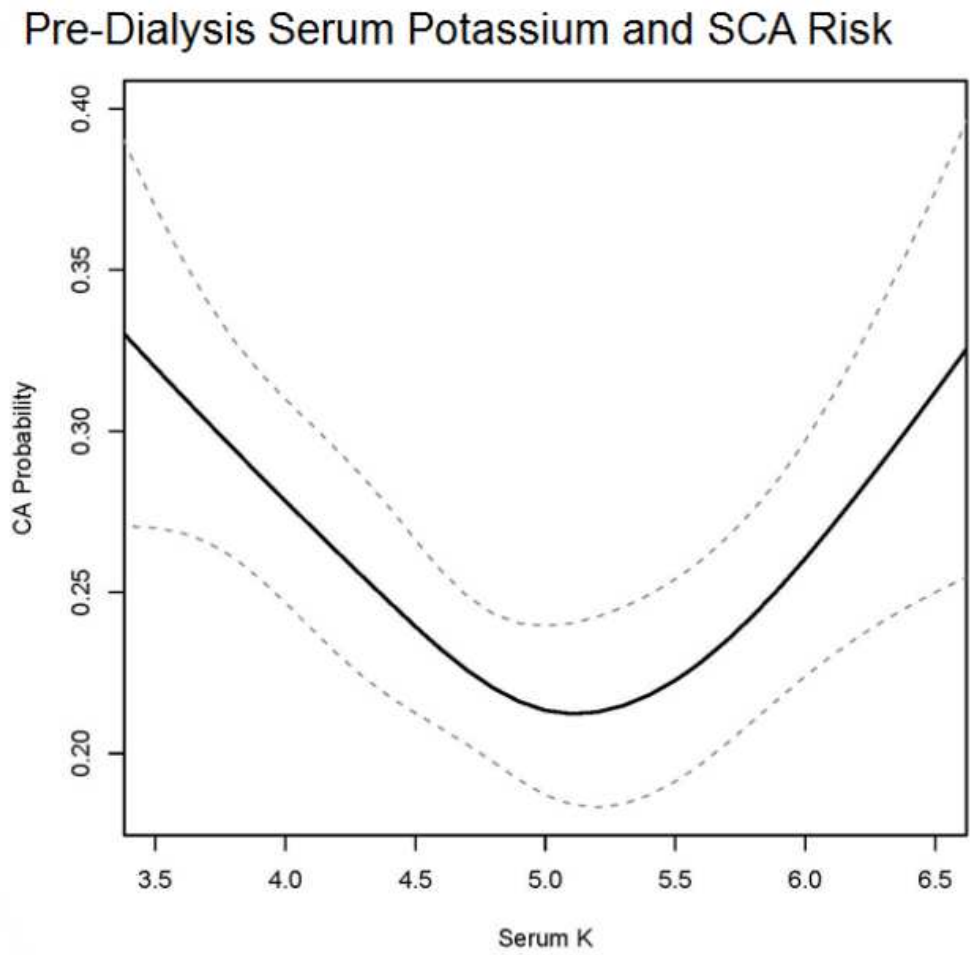
- Dialysis related triggers for SCD?
  - Potassium??
  - Calcium??
  - Fluid Shifts (Too much or too little UF)??

Role of Serum Potassium in SCA

Study of 500 witnessed peridialytic SCA vs. 1600 matched controls

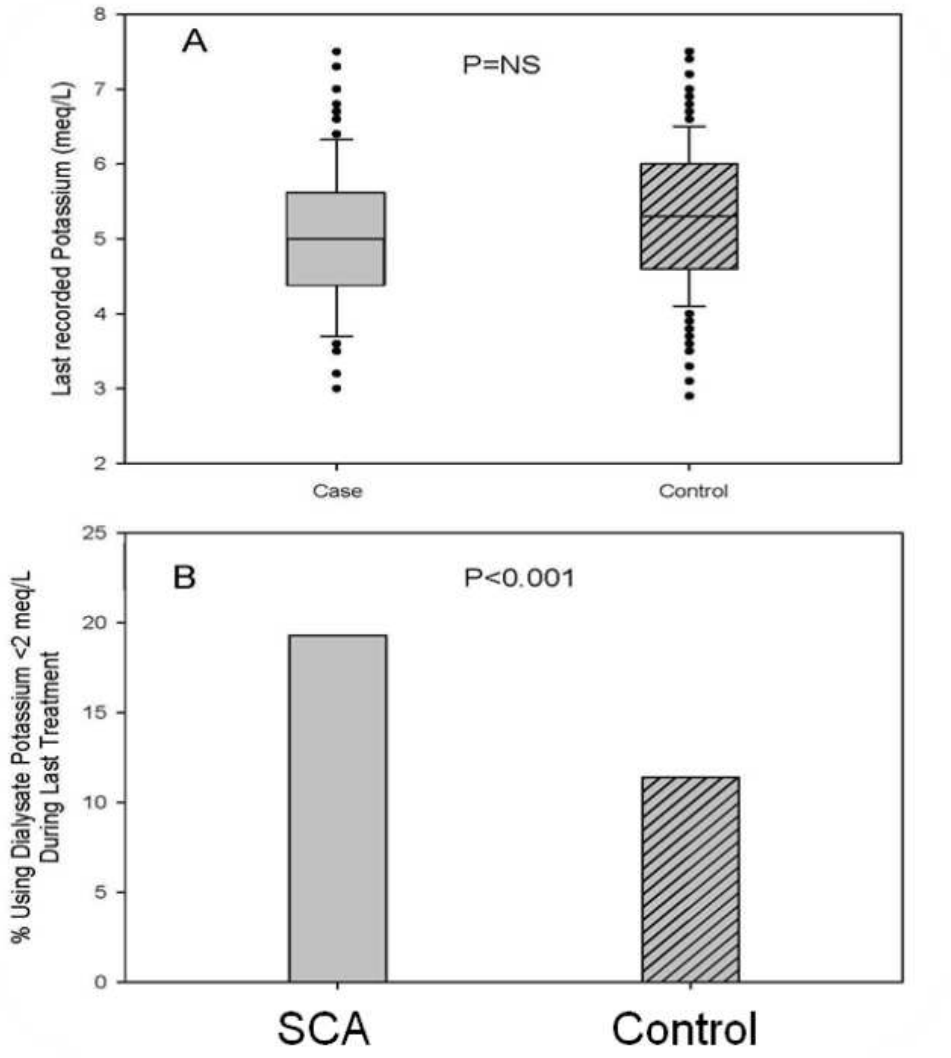
Risk linked to extremes of serum potassium (K)

Lowest risk at K ~ 5.0



Pun et. al. Kidney Int. 2011 Jan;79(2):218-27

Role of Dialysate Potassium in SCA



Use of low potassium diaysate (<2 meq/L) was associated with a two-fold increase in risk of SCA

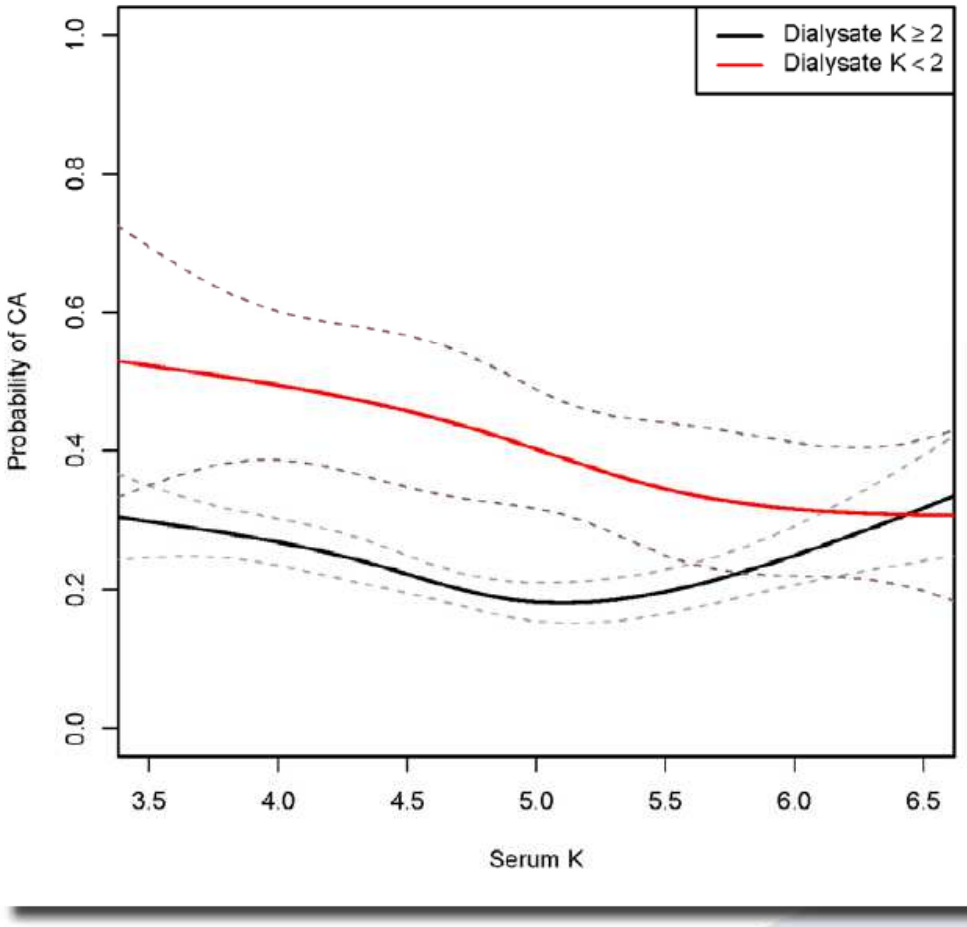
Mean Predialysis serum K was in the normal range (4.9 meq/L)

Pun et. al. Kidney Int. 2011 Jan;79(2):218-27

Potassium Homeostasis and Risk of SCA: Low [K] bath for High Pt [K]?

Difference in risk between low and high K dialysate decreases as serum K increases

No indication of benefit for low K dialysate at any level of serum K

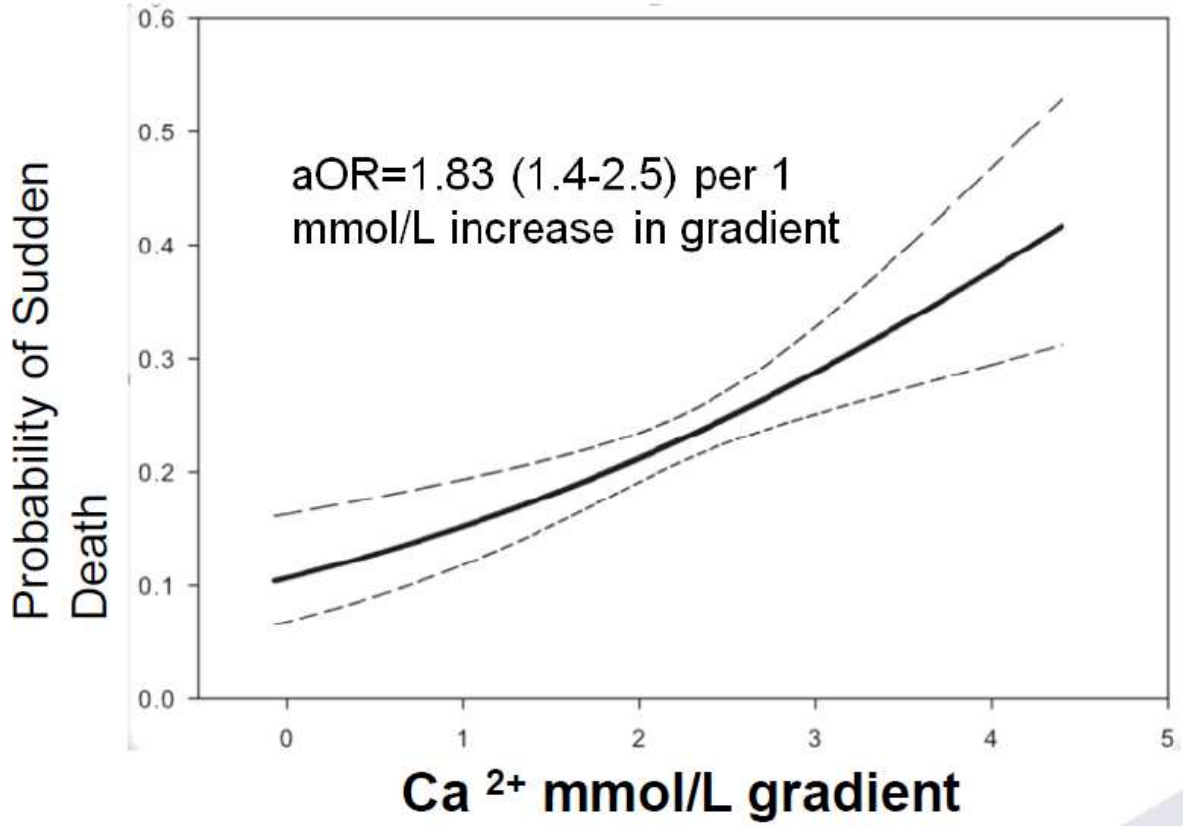


Pun et. al. Kidney Int. 2011 Jan;79(2):218-27

Calcium: Low Calcium Dialysate Associates With Increased risk of SCD

Matched Case Control Study of 2100 patients

- 50% Increase in SCA risk with dialysate calcium <2.5 meq/L
- Risk rises incrementally with increasing serum: dialysate gradient



Pun et. Al. Clin J Am Soc Nephrol. 2013 May;8(5):797-803

Amount and Rate of Fluid Removal During HD Associates With Myocardial "Stunning"

HD Exposure	Odds Ratio
1L Fluid Removal on HD	5.1
1.5L Fluid Removal on HD	11.6
2L Fluid Removal on HD	26.2

- Hemodialysis procedure can reduce myocardial blood flow, even in absence of significant CAD.
- A myocardial "stun" may be detected from echocardiogram regional wall motion abnormalities (RWMAs).
- RWMAs present in 50-64% of patients, and associated with poor outcomes.

Burton JO et al. *Clin J Am Soc Nephrol* (2009) 4: 914-920

Management of SCD

- **Prevent Sudden Cardiac Arrest**
  - Medical therapies to treat underlying cardiac disease
  - Reduce exposure to triggers
- **Improve survival following SCA**
  - Defibrillation

Beta Blockers

- Beta Blockers shown to be helpful for SCD prevention in pts with minimal or no CKD.
- Only 24% of dialysis patients with CAD or prior MI are on beta blockers
- Only one randomized trial of beta-blockers in ESRD
  - 114 pts with dilated CM randomized to Carvedilol or placebo
  - Significant survival advantage seen but non significant reduction in SCD

Cice: JACC 2003; 41:1438-44

Role of Phos and Secondary Hyperparathyroidism

Hyperphosphatemia can provoke vascular calcification, endothelial dysfunction and atherosclerosis.

- Observational study of 12,833 HD patients
- 6% increase in SCD per 1 mg/dl increase in Phos
- 7% increase in SCD per 10 mg/dl increase is Ca x Phos product
- 20% increase with Phos >6.5
- 6% increase with PTH > 495

Ganesh et. Al. JASN 2001

Other Medical Therapies?

- No clear benefit demonstrated for:
  - Statins
  - ACEI / ARB / Spironolactone
  - Antiplatelet agents
  - Vitamin D

Implantable Cardioverter Defibrillators in HD patients:

No ESRD patients included in any randomized trials

- **Secondary prevention ICD (ICD after cardiac arrest)**
  - Two retrospective studies show benefit ICD after cardiac arrest compared to patients with cardiac arrest and no ICD
    - HR 0.86 (95% CI 0.81-0.91)
    - Subject to indication bias

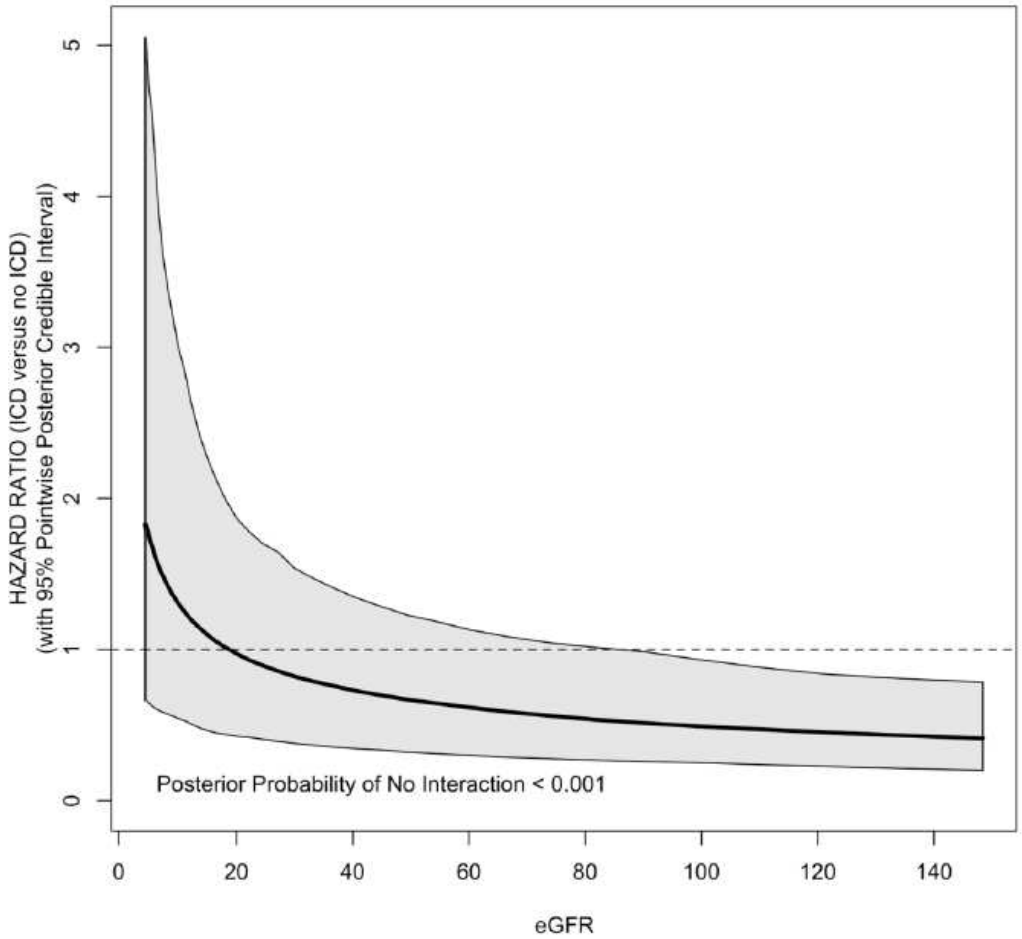
Charytan et. al. Am J Kidney Dis. 2011 Sep;58(3):409-17

Herzog et. al. Kidney Int. 2005 Aug;68(2):818-25

- **Primary prevention (prophylactic ICD)**
  - No data on mortality benefit in ESRD compared to controls
  - Increased mortality, risk of complications, in ESRD compared to non-ESRD ICD recipients

Agarwal et al. Heart Rhythm. 2009 Nov;6(11):1565-71

Diminishing Benefit of Primary ICD with CKD



Meta-analysis of 3 randomized controlled trials

- 2,867 patients
- 36.3% with eGFR<60; no HD patients
- Diminishing survival benefit of ICD vs. no ICD with lower eGFR

Pun Am J Kidney Dis. 2014 Jul;64(1):32-9

Why might primary ICDs not be beneficial?

- Increased defibrillation thresholds in CKD and ESRD pts compared to normal
- ESRD patients not having “shockable” events; 38% of ICD recipients on dialysis still die of arrhythmia!
- Competing risks may outweigh benefits:
  - Death: 45% annually
  - Bacteremia: 52%
  - Device infection: 4.2% (vs. 0.7%)
  - Generator replacement: 3.9% (vs <2%)
  - Vascular Access Complications

Wase J Interv Card Electrophysiol. 2004 Dec;11(3):199-204
Charytan et. al. Am J Kidney Dis. 2011 Sep;58(3):409-17
Drew et. al Am. J. Kidney Dis. 2011 Sep;58(3):494-496

Management of SCD Risk in ESRD

Treat Cardiomyopathy

- Assess at baseline and q3yrs (2005 K/DOQI guideline)
- Use beta-blocker for dilated cardiomyopathy EF <35%
- Control SHPT and phosphorus
- Unclear if other proven therapeutic interventions will also be beneficial in dialysis patients

Reduce and monitor triggers

- Avoid low potassium and low calcium dialysate
- Review and adjust prescription dialysis regularly in response to laboratory data
- Reduce IDWG/avoid large volume shifts
- More frequent/longer dialysis sessions?

No role for ICD placement in primary prevention, there may be a role in secondary prevention of SCD.