

# Disclosure of Interests: Ahsan Alam

- Investigator for TEMPO study and consultancy for Otsuka (Canada)

KDIGO



# Session Questions

## Prioritized:

**1. What is the optimal choice of dialysis modality? What are ADPKD specific issues associated with hemodialysis or peritoneal dialysis?**

2. How should native kidneys be monitored after initiation of dialysis or after renal transplantation? Is there an increased risk of kidney cancer?

3. What are the optimal hemoglobin, blood pressure and lipid targets in ADPKD patients on dialysis?

## Optional:

• How should anticoagulation be managed in ADPKD patients on hemodialysis (increased risk for bleeding in the kidney or elsewhere)?



# Choosing a Dialysis Modality

## Peritoneal Dialysis

- Preservation of residual kidney function
- Lifestyle and patient choice
- Cost

## Hemodialysis

- Prevalence of hernias (peritoneal leaks)
- Space occupied by enlarged kidneys
- Concern for peritonitis related to cyst infections
- Concern for colonic diverticular disease



***Are these concerns warranted?***

# PD Peritonitis

- US National CAPD registry: Median time to the first episode of peritonitis was 8.2 months in PKD vs 6.3-7.4 in other subgroups

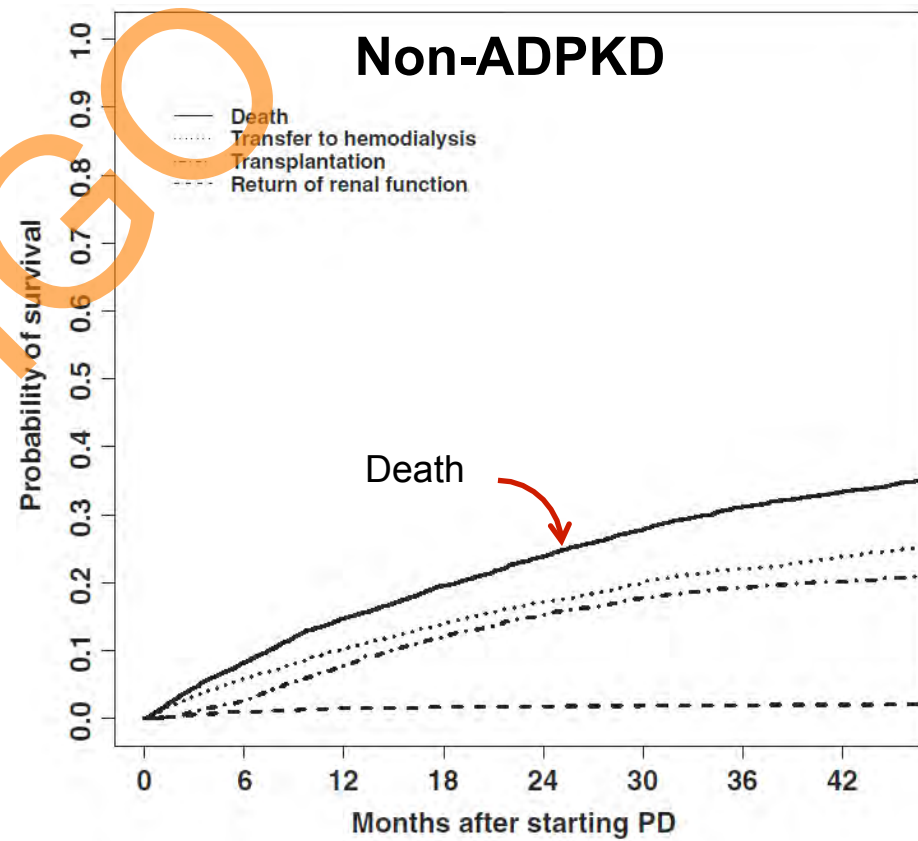
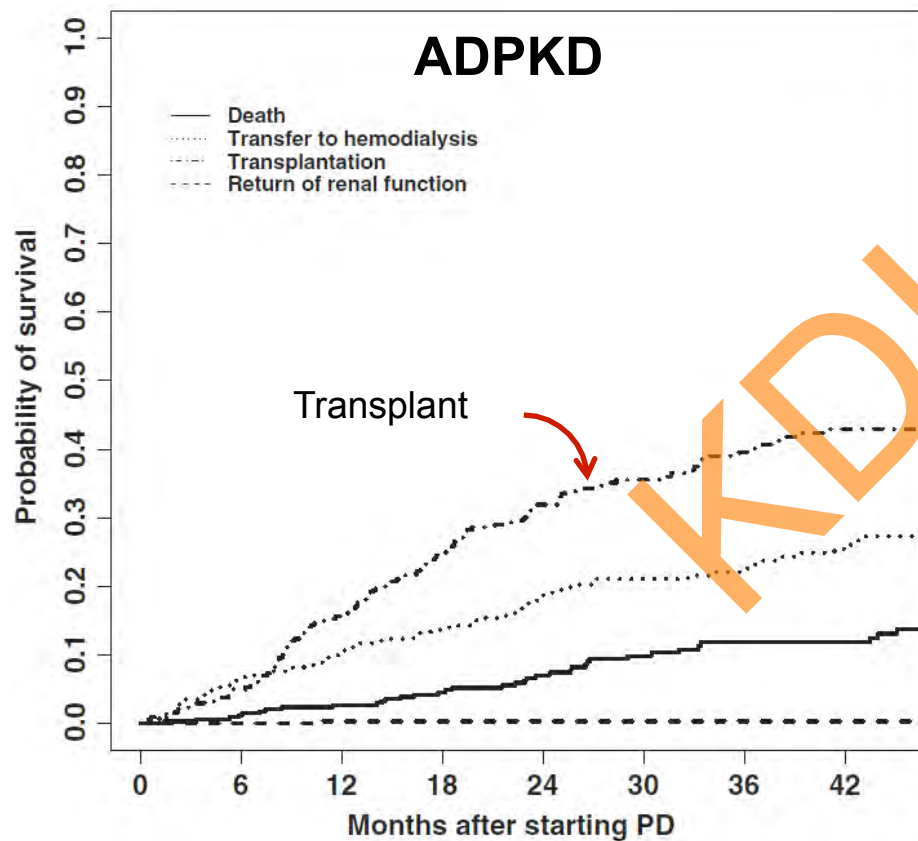
Study	Time (mo)	PKD			Control		
		N	Peritonitis	Tech. Failure	N	Peritonitis	Tech. Failure
Pandya (Perit Dial Int 2004)	17-19	30	1 per 21 months	-	505	1 per 20 months	-
Hadimeri (Perit Dial Int 1998)	10	26	1 per 20 months	0	26	1 per 27 months	8%
Kumar (Kidney Int 2008)	38	56	1 per 26 months	14%	56	1 per 31 months	16%
Lobbedez (NDT 2010)	84	344	2.7 per 100-pt-yrs	23%	3818	3.0 per 100-pt-yrs	23%
<b>Li (AJKD 2013)</b>	60	42	0.51 per pt-yr	48.4%	84	0.53 per pt-yr	62.7%

# *Selection Bias*

- When would PD not be considered suitable?
  - Very large kidneys
  - Presence of abdominal wall hernias
  - Recurrent cyst infections
  - Diverticulosis

# Competing Risks on PD

- 344 PKD and 3818 non-DM patients in France

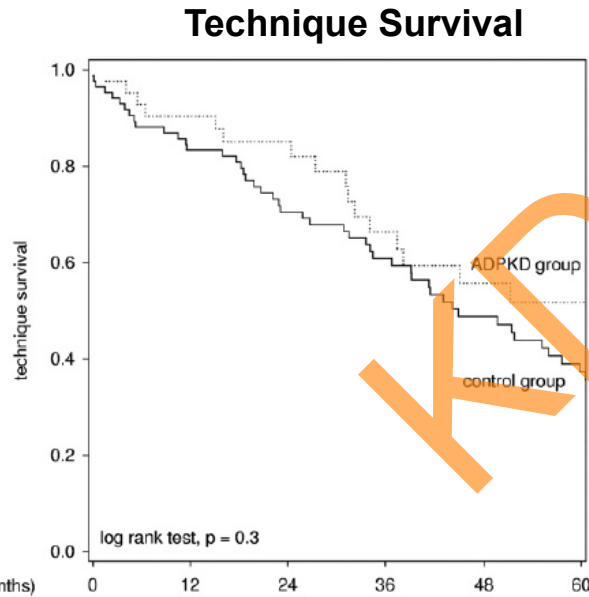


Lobbedez et al. NDT 2011; 26:2332

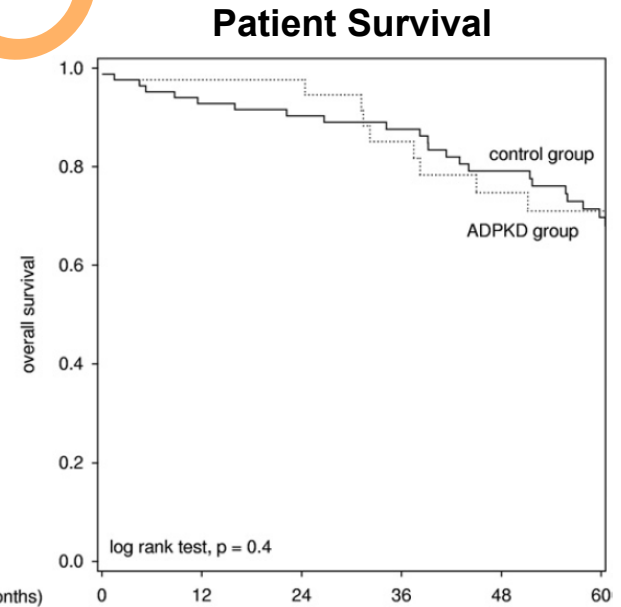


# First Line PD for ADPKD

- In Hong Kong all ESRD patients receive PD first
  - Transfer to HD for UF failure or peritoneal sclerosis
- Unselected population



follow up (months)	0	12	24	36	48	60
No. at risk						
ADPKD group	42	34	28	19	14	13
control group	84	69	53	43	31	22



follow up (months)	0	12	24	36	48	60
No. at risk						
ADPKD group	42	37	32	25	20	19
control group	84	77	69	64	53	42

# First Line PD - Outcomes

**Table 2. Summary of Clinical Outcomes**

	ADPKD Group (n = 42)	Control Group (n = 84)
Death	17	30
Coronary heart disease	6	12
Cerebrovascular accident <sup>a</sup>	2	1
Peritonitis	1	6
Nonperitonitis infection	1	4
Termination of dialysis	3	4
Malignancy	1	1
Liver failure	1	0
Other specific causes	2	2
Conversion to hemodialysis	4	10
Loss to follow-up	0	2
Transfer to other center	1	9
Transplant	4	10
Survival status censored	16	23

Abbreviation: ADPKD, autosomal dominant polycystic kidney disease.

<sup>a</sup>None of the patients had intracranial hemorrhage.

**Table 4. Position of Abdominal Wall Hernias**

	ADPKD Group	Control Group
Inguinal hernia	8	4
Paraumbilical hernia	6	1
Incision hernia	1	1
Total	14 <sup>a</sup>	6

Abbreviation: ADPKD, autosomal dominant polycystic kidney disease.

<sup>a</sup>One patient had both an inguinal and a paraumbilical hernia.

In 3 cases (2 PKD, 1 control) urgent surgical repair of hernia was required

All patients resumed PD after surgical repair, with no recurrent hernia



# Outcomes on PD

- No support for worse outcomes on PD (Hadimeri 1998; Kumar 2008; Abbott 2002)
  - pt survival, technique failure, peritonitis, etc.
- USRDS HD mortality (vs. PD) HR 1.40 (1.13-1.75) (Abbott 2002)

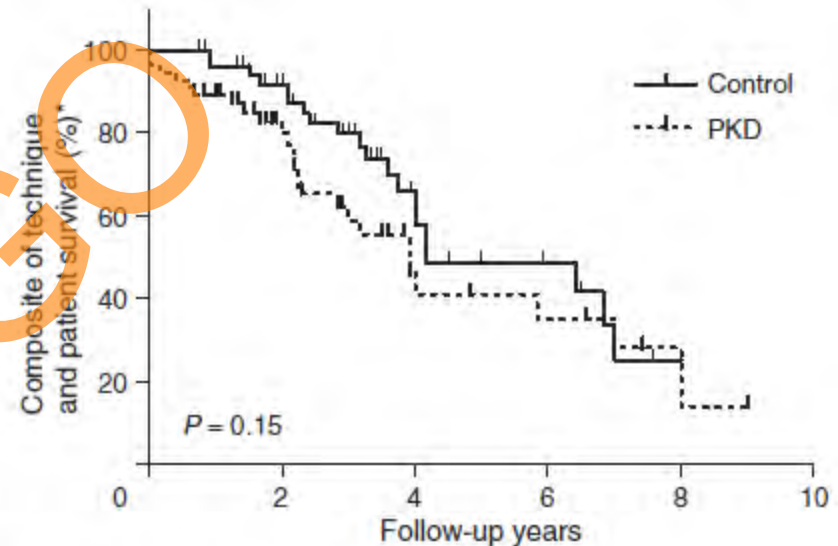


Figure 3 | Composite of technique and patient survival (transplant censored)\* in PKD patients and controls. Ticks represent censored observations. Logrank  $P = 0.15$  (not significant).

Kumar et al. *Kidney Int* 2008; 74:946

# Transcatheter Renal Artery Embolization

- Alternative to surgical nephrectomy for reducing kidney volume
  - 28 pts on HD with symptoms related to renal enlargement (Yamakoshi 2012)

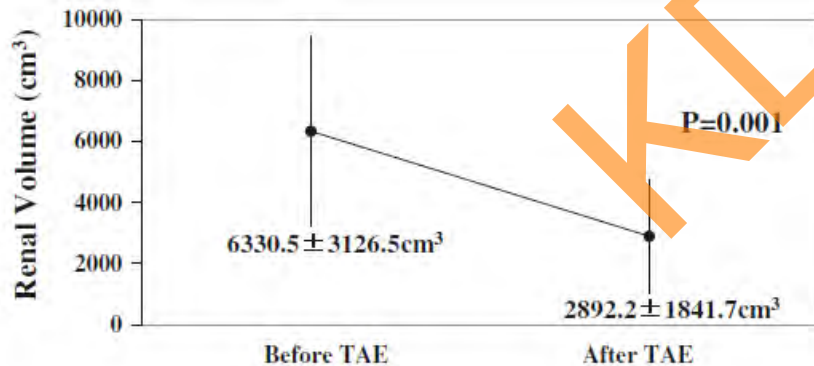


Fig. 2 Renal volume before and 12 months after TAE

- Reduction in renal volume correlated with improvement in FEV1 and VC
- Use of larger PD volumes, better Kt/V (Toyohara 2011)

# Session Questions

Prioritized:

1. What is the optimal choice of dialysis modality? What are ADPKD specific issues associated with hemodialysis or peritoneal dialysis?
- 2. How should native kidneys be monitored after initiation of dialysis or after renal transplantation? Is there an increased risk of kidney cancer?**
3. What are the optimal hemoglobin, blood pressure and lipid targets in ADPKD patients on dialysis?

Optional:

- How should anticoagulation be managed in ADPKD patients on hemodialysis (increased risk for bleeding in the kidney or elsewhere)?



# Renal Complications on HD

- Cohort of N=50 with ADPKD on HD

	Year 1	Year 3	Year 5	Ave. yearly incidence
Pain	14%	36%	57%	22%
Hematuria	18%	41%	51%	21%
Infection	9%	12%	12%	7%

Reported symptoms varied widely among patients

Christophe et al. NDT 1996; 11:1271



# Renal Cell Cancers

- Histopathologic prevalence of RCC (Jilg 2013)
  - 240 ADPKD pts with 301 surgical renal specimens
  - 5% of pts had malignant renal lesions, 66.7% were on dialysis
- No increased risk of RCC in ADPKD (Orskov 2012)
  - ESRD and acquired cystic disease increase risk for RCC (2-5% on dialysis)
- Gross hematuria should be evaluated, but CT/MRI is challenging due to distorted architecture

# Extra-renal complication on HD

- No consistent evidence for increased incidence of valvular disease, aneurysms, hepatic cystic disease, etc. on dialysis

	ADPKD N=50	Controls N=50
Acute MI/Infarction/Revascularization	12	19
CHF due to valve disease	0	1
Valve replacement	1	1
Endocarditis	1	0

Christophe et al. NDT. 1996; 11:1271

# Session Questions

Prioritized:

1. What is the optimal choice of dialysis modality? What are ADPKD specific issues associated with hemodialysis or peritoneal dialysis?
2. How should native kidneys be monitored after initiation of dialysis or after renal transplantation? Is there an increased risk of kidney cancer?
- 3. What are the optimal hemoglobin, blood pressure and lipid targets in ADPKD patients on dialysis?**

Optional:

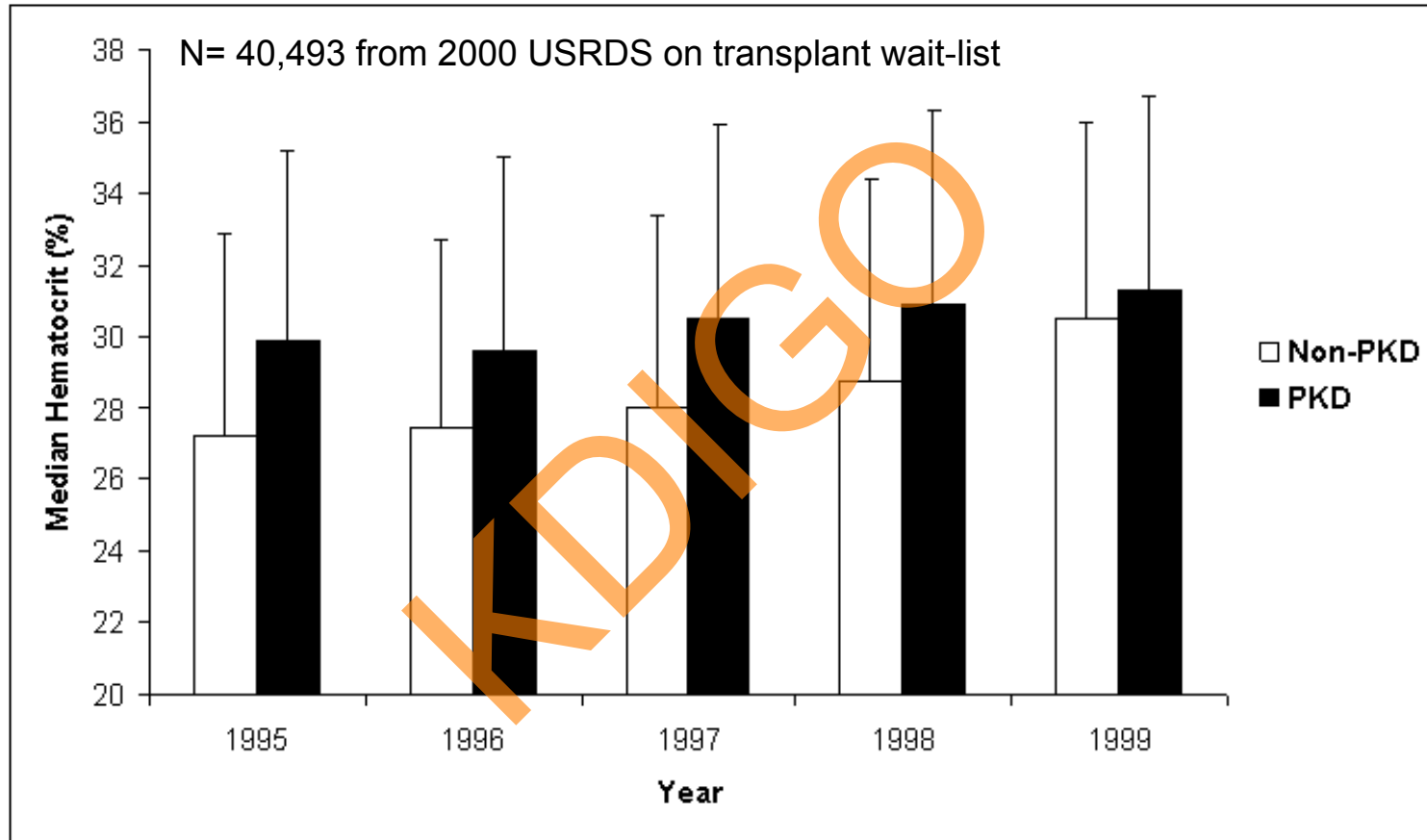
- How should anticoagulation be managed in ADPKD patients on hemodialysis (increased risk for bleeding in the kidney or elsewhere)?

# *Erythropoietin Levels in ADPKD*

- EPO levels in nephrectomized kidneys are elevated, independent of oxygen tension
- Likely related to higher EPO levels generated as a result of peri-cystic hypoxia from expanding cysts (HIF $\alpha$ )
- Preservation of residual kidney function and EPO production



# Hematocrit Levels on HD



PKD associated with higher HCT levels, independent of EPO use

Adapted from Abbott and Agodoa. BMC Nephrol, 2002



# ESA and Hemoglobin Level

- DOPPS II (N=11,041): difference in EPO 763 U/wk

**Table 2. Patient- and Facility-Level Characteristics Associated With Adjusted Odds of Patient Hgb Level of 11 g/dL or Greater, 2002 to 2003**

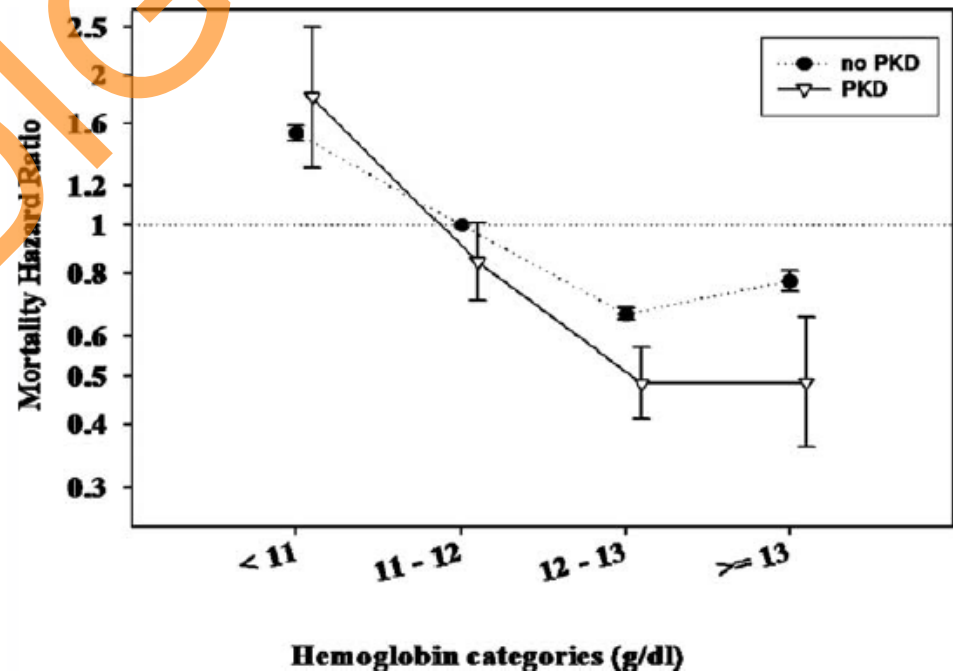
Covariate	AOR (Hgb $\geq$ 11 v <11 g/dL)	P
Patient-level characteristics* (n = 6,611)		
Polycystic kidney disease	1.62	0.0002
Serum albumin (per 0.3-g/dL higher)	1.29	<0.0001
TSAT (per 10% higher)	1.22	<0.0001
Male (v female)	1.21	0.001
Serum calcium (per 1-mg/dL higher)	1.15	<0.0001
Age (per 10 y older)	1.09	0.0002
Ferritin (per 100-ng/mL higher)	0.96	<0.0001
Catheter use for vascular access	0.73	0.0001
Gastrointestinal bleeding in previous year	0.63	<0.0001
Facility-level characteristics†		
Facility catheter use (per 10% higher use) (n = 6,389)	0.92	0.04
Percent of facility patients with TSAT < 20% (per 10% more patients) (n = 4,755)‡	0.82	0.07

Pisoni et al. AJKD 2004; 44:94

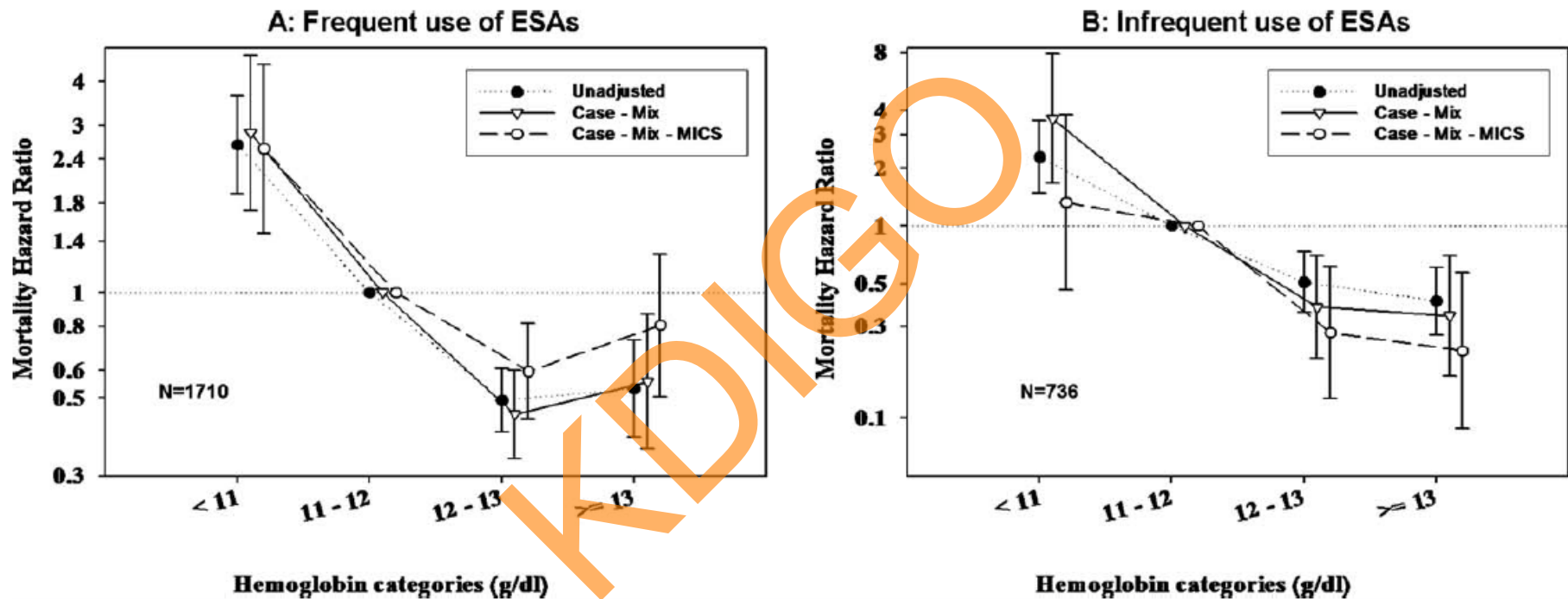


# Hemoglobin Level and Mortality

- To assess whether high-achieved Hgb in PKD is associated with poor outcomes (Shah 2012)
  - 6-year cohort study  
2,402 PKD and  
110,875 non-PKD
  - Compared frequent  
and infrequent ESA  
therapy



# Hemoglobin Level and Mortality



In pts with PKD who require infrequent ESA, incrementally higher achieved hemoglobin including >13.0 g/dL exhibit better survival

Shah et al. Am J Hematol 2012; 833



# *BP and Mortality*

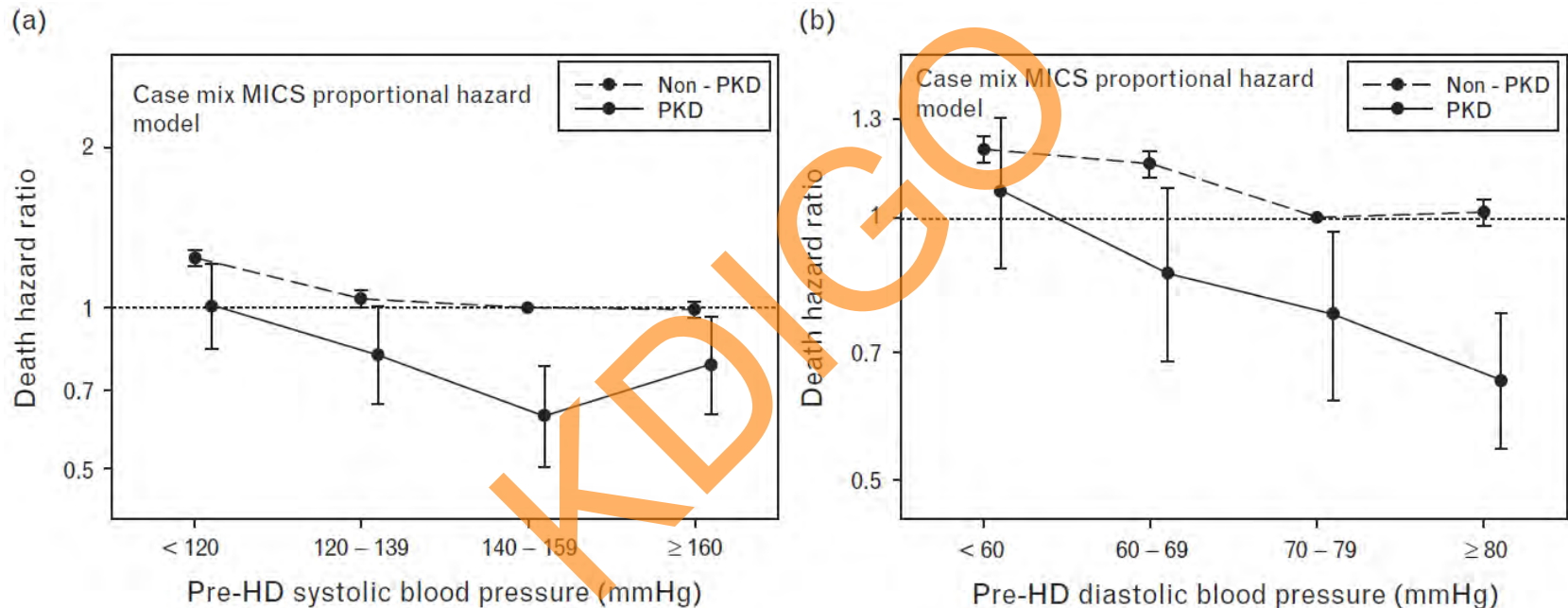
- U-shaped association with BP and mortality in patients on HD
- Does the “hypertension paradox” exist in those with PKD?

KIDIGO



# BP and Mortality on HD

5-year cohort of N=1,579 with and N=67,085 without ADPKD



- Within each BP category, higher survival in PKD vs. non-PKD
- Low BP assoc. with higher death rates compared to 'normal' and high BP
- Similar association using pre- or post-dilaysis BP

# Anticoagulation and HD

- No studies examining this specific question
- Persistent bleeding should prompt:
  - stopping anticoagulants
  - addressing any coagulopathy
  - consider embolization or nephrectomy