

# Living Donor Evaluation, Unique Aspects of the Evaluation, and Management of ADPKD Transplant Recipients

**Presenter:**

**Klemens Budde**

**Charité Universitätsmedizin Berlin,  
Germany**



# Disclosure of Interests

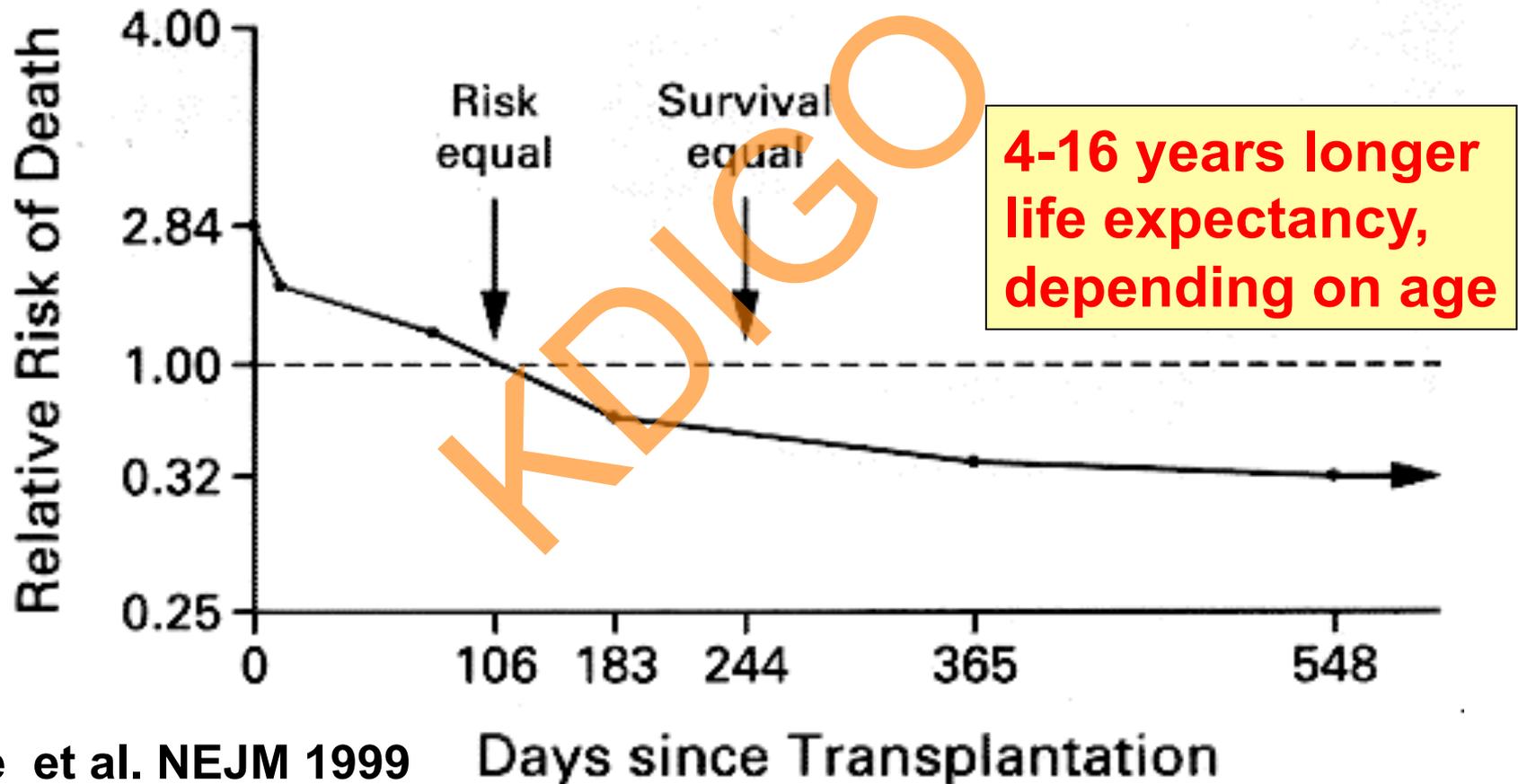
KB have/had consultancy agreements with  
Bristol-Myers Squibb, Chiesi, Effimune, Hexal, Novartis,  
Pfizer, and Veloxis

and has received research grants for clinical studies, speaker's  
fees, honoraria, travel expenses, and payment for development  
of educational presentations from

AiCuris, Astellas, BmT GmbH, Bristol-Myers Squibb,  
Chiesi, Hexal, Novartis, Otsuka, Roche, Pfizer, Siemens,  
and Veloxis

# 1. Optimal Choice of renal replacement therapy

Relative Risk of death after Transplantation in comparison to non-transplanted waitlisted patients



Wolfe et al. NEJM 1999

Days since Transplantation



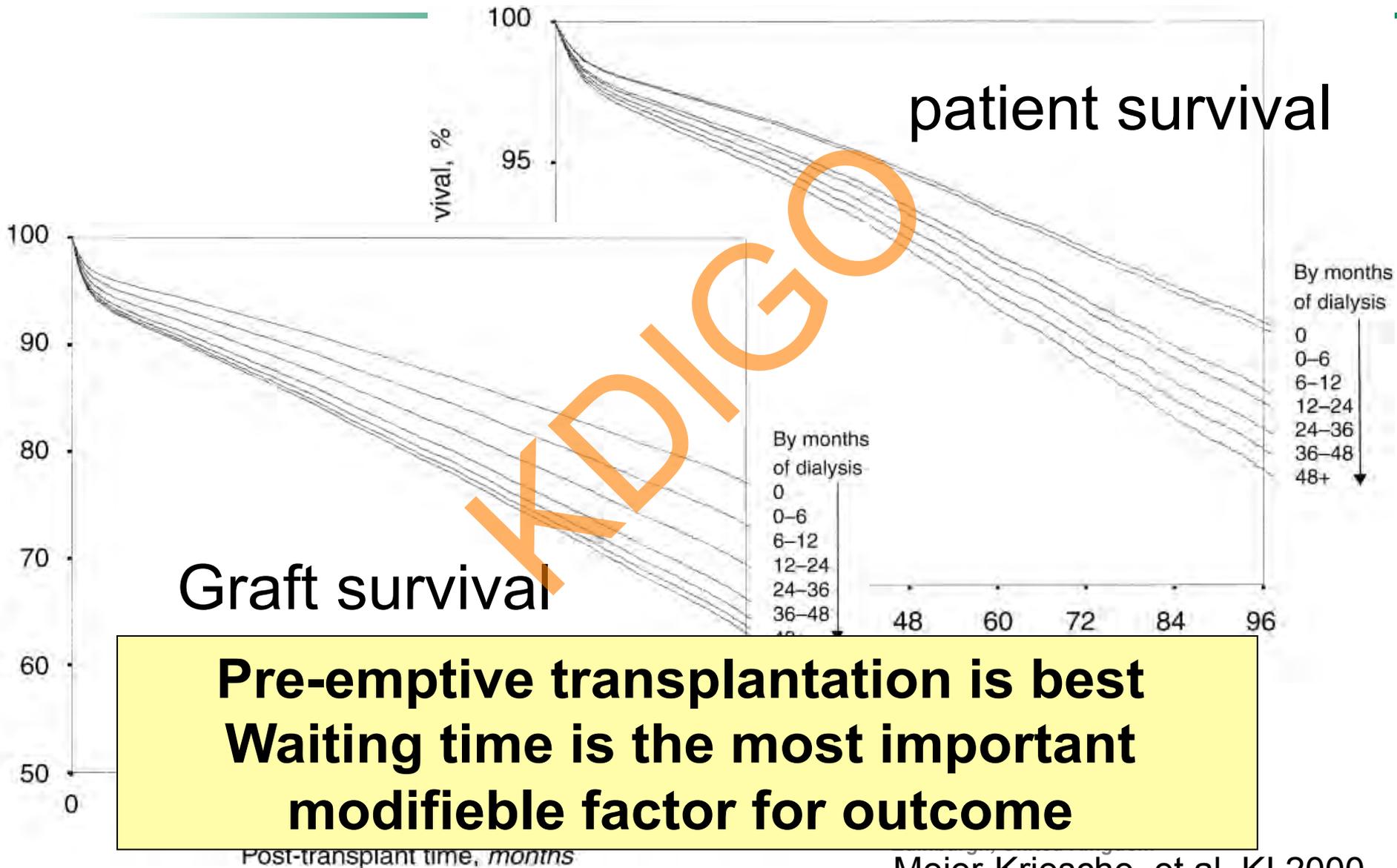
# kidney transplantation prolongs life in ADPKD patients

Multivariate Cox regression analysis in 693 Danish patients who had ADPKD and reached ESRD between 1990 and 2007. n= 330 events, mean follow-up 5.1 years

Comparisons	HR (95% CI)	P
Time periods		
1996 to 2001 <i>versus</i> 1990 to 1995	0.62 (0.49 to 0.80)	<0.001
2002 to 2007 <i>versus</i> 1996 to 2001	0.80 (0.56 to 1.15)	NS
Gender		
male <i>versus</i> female	1.34 (1.07 to 1.68)	<0.01
Treatment		
<b>transplantation <i>versus</i> dialysis</b>	<b>0.30 (0.22 to 0.42)</b>	<b>&lt;0.0001</b>
Age at onset of ESRD		
age per year	1.05 (1.04 to 1.07)	<0.0001



# Long Waiting time on dialysis is bad!

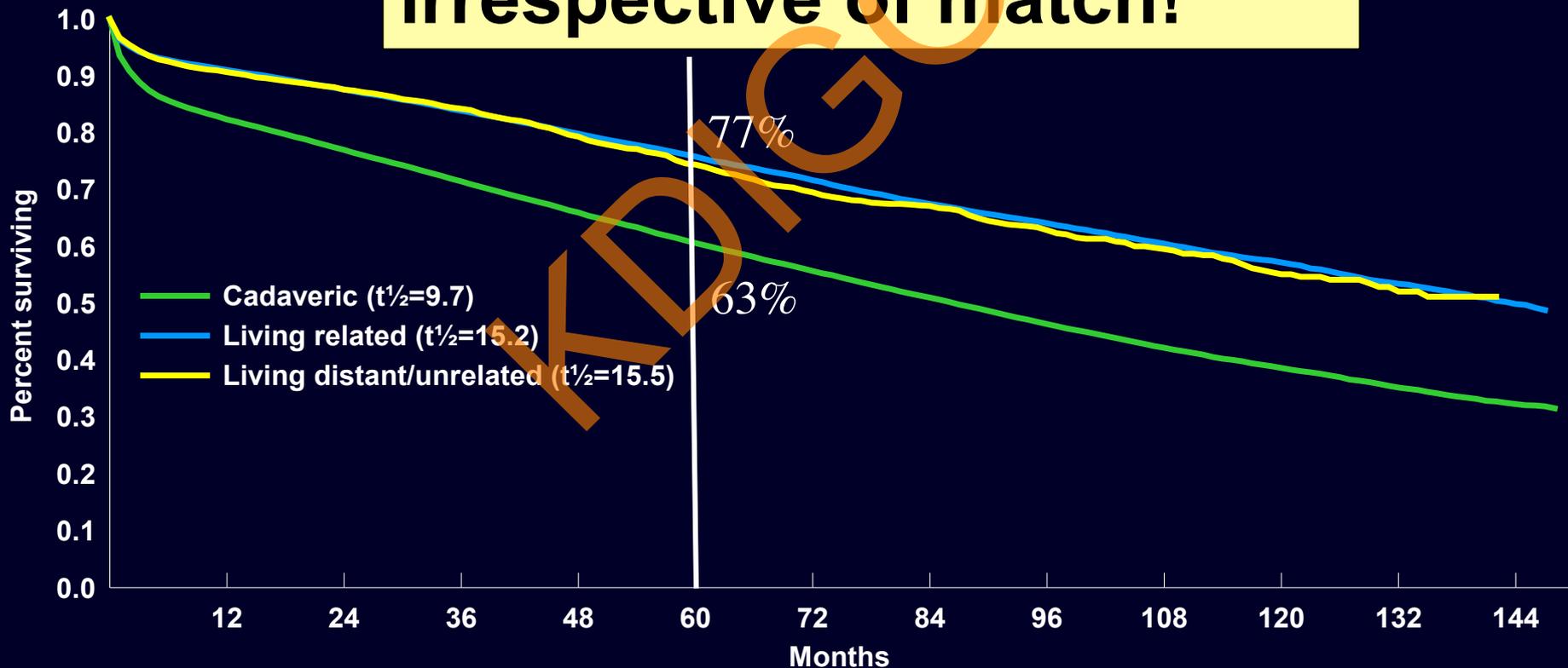


**Pre-emptive transplantation is best  
Waiting time is the most important  
modifiable factor for outcome**

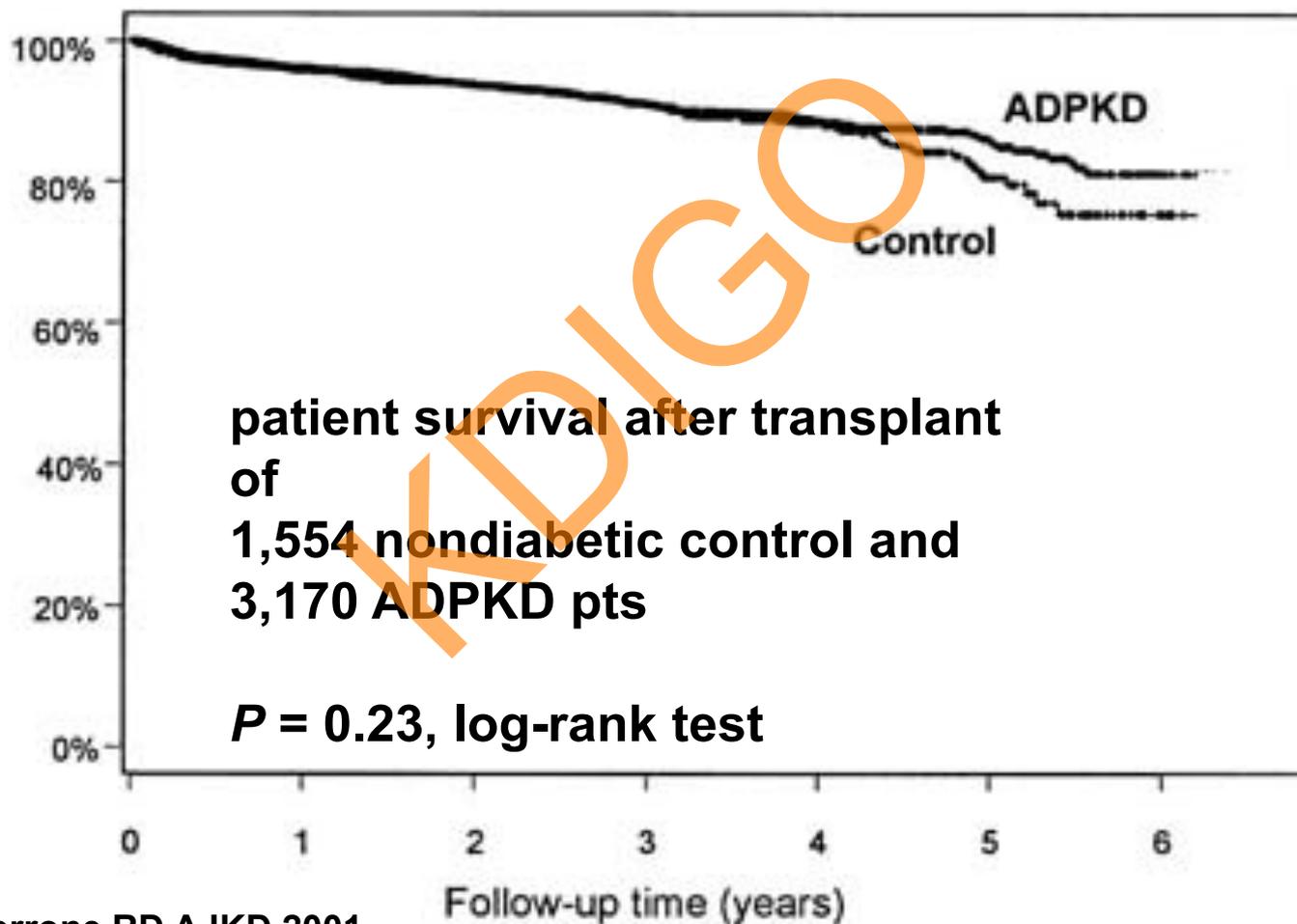
# Kaplan-Meier graft survival curves: donor type

figure 7.31, first transplant recipients, 1988–1998

Living donation ist better,  
irrespective of match!



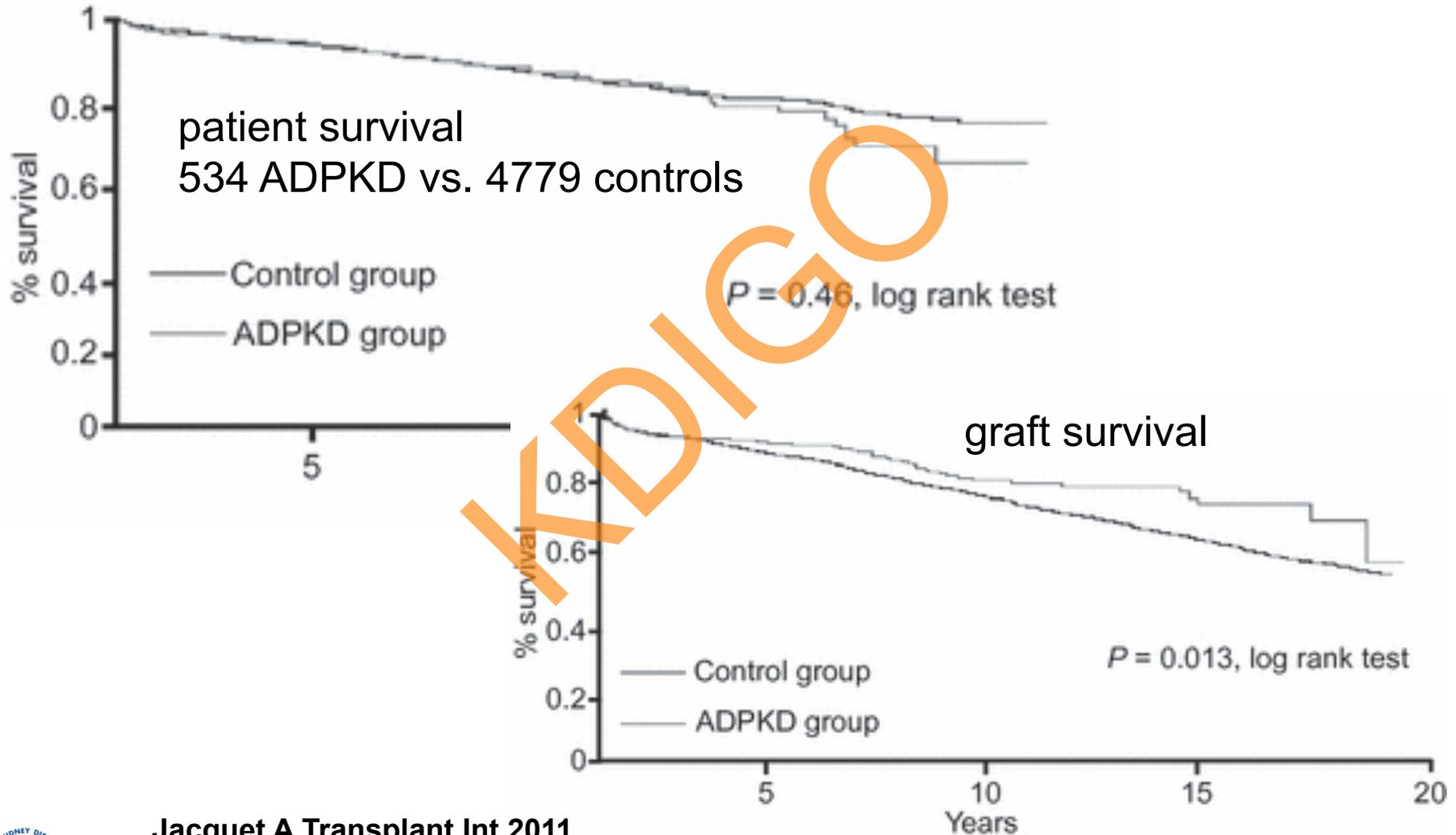
# ADPKD patients have at least similar outcomes after kidney transplantation



Perrone RD AJKD 2001



# ADPKD patients have at least similar outcomes after kidney transplantation



Jacquet A Transplant Int 2011

# 1. Optimal Choice of renal replacement therapy

Renal transplantation is the optimal RRT for ADPKD  
timely transplantation is crucial for outcome  
best results are obtained from preemptive  
transplantation from a living donor

## 2. what post-transplant complications occur more frequent in ADPKD than in non-PKD patients

potential risks discussed in the literature with partially controversial results  
(problems in retrospective study design and control groups)

related to polycystic kidney

size

infection (cysts, UTI)

bleeding

malignancy

related to extrarenal disease manifestation

cerebral aneurysm, stroke

diverticulosis

cardiac disease

liver cysts

related to other causes/associations

post-transplant diabetes

hypertension

erythrocytosis

malignancies (skin)

hyperlipidemia

coagulation disorder

# post-transplant complications in ADPKD compared to non-PKD patients

	ADPKD group (n = 534)	Control group (n = 4779)	P-value
Biopsy-proven acute rejection (%)	24.3	27.4	0.13
NODAT (%)	12.4	9.6	0.06
Hyperlipidemia (%)	49.7	39.3	<0.001
Lipid-lowering drug use (%)	48	37.5	<0.001
Hypertension (%)	49.7	42.3	0.001
Stroke (%)	1.1	1.7	0.31
Cutaneous cancer (%)	7.9	7.4	0.71
Kidney cancer (%)	0.4	0.6	0.5
Thromboembolic disease %	8.6	5.8	0.009

# post-transplant infections in ADPKD compared to non-PKD patients

	<b>ADPKD group (n = 534)</b>	<b>Control group (n = 4779)</b>	<b>P- value</b>
All types (%)	67.7	70.4	<0.18
Lower urinary tract infections (%)	48.4	44.9	0.12
Pyelonephritis (%)	6.2	7.6	0.22
Abdominal (%)	6.5	5.6	0.4
Pulmonary (%)	15.9	18	0.25
Bacteriemia (%)	7.5	5.6	0.07
Others (%)	15.5	18.3	0.3

### 3. What evaluations should ADPKD transplant candidates undergo to minimize the risk?

related to polycystic kidney

size

infection (cysts)

bleeding

malignancy

imaging

nephrectomy

related to extrarenal disease manifestation

cerebral aneurysm, stroke

diverticulosis

cardiac disease

liver cysts

imaging

intervention

related to other causes

post-transplant diabetes

hypertension

erythrocytosis

malignancies (skin)

hyperlipidemia

coagulation disorder

dermatology

lab investigation



# What evaluations are specifically recommended for ADPKD patients by current guidelines?

## **British guidelines 2008**

no specific recommendations for ADPKD patients

## **Canadian guidelines 2005**

not sufficient evidence to support screening for cerebral aneurysm of all patients or to deny access to KTX without screening  
no recommendation for routine screening for diverticular disease

## **KDIGO 2009 Transplant guidelines**

no evidence that the benefits of screening for RCC after Tx outweigh harm

## **Canadian guidelines 2005, ERBP 2013, and EAU 2009:**

nephrectomy (before transplantation) in case of severe recurrent symptomatic complications (e.g. bleeding, infection, stones)  
unilateral nephrectomy for space reasons

# What about nephrectomy?

**Data and procedures for nephrectomy are highly controversial**  
occurring in 10-100%

in Italy (1):

83% of centers before Tx, mainly for abdominal space

in France (2) 33% of pts with nephrectomy

prophylactic 71%

infection (cysts) 15%

bleeding 8%

malignancy 1.5%

**controversial issues:**

**imaging** (CT vs. MRI vs. ultrasound, no imaging = only clinical)

**indication** (prophylactic vs only for problems

(which problems? what severity?, what size? Iliac crest?)

**timing** (before vs. simultaneous vs. after Tx)

**uni- or bilateral**

**method** (open vs. laparoscopic (hand assistet vs. transperitoneal)  
vs. embolisation)

### 3. How should native kidneys be monitored after renal transplantation? increased risk of kidney cancer?

Risk of kidney cancer in ADPKD controversial  
depending on patient cohorts, and controls  
in some studies up to 8% in nephrectomy specimens  
clinical consequences of small (<1,5cm) incidental tumors unclear

Renal cancer is associated with acquired cystic kidneys

Screening modality unclear (ultrasound vs. MRI vs. CT)

no apparent higher mortality due to kidney cancer

#### **KDIGO post-Tx 2009**

Higher incidence of kidney tumors after Tx

no evidence that benefits of screening for kidney tumors  
outweigh harm



## 5. Can ADPKD kidneys be used as donor organs under specific circumstances?

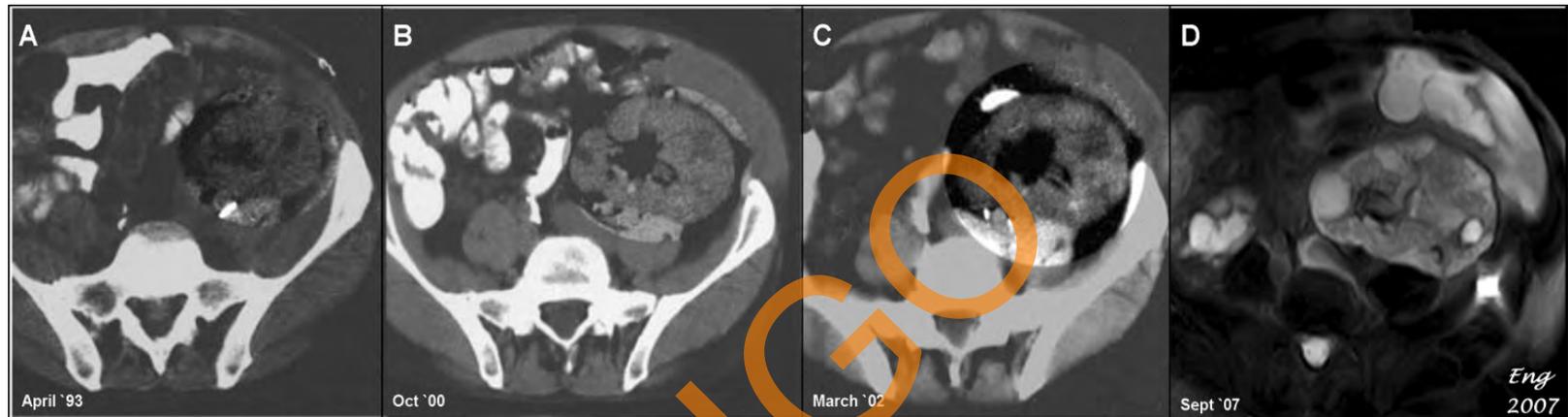


Fig 1 The slow progression of disease in the patient's ADPKD donor kidney is evident with serial imaging, which date from (A) April 1992, (B) October 2000, (C) March 2002, and (D) September 2007 (T2-weighted MRI). During this time, the largest cyst...  
Eng MK Transplant Proc 2008

so far around n=12 case reports of donors with ADPKD  
donor age 20-55 years (mean 30 years)  
normal renal function  
most kidneys < 15cm  
up to 15 years of follow-up with good results

informed consent of recipient?!

# ++ What is the work up for related living donors?

## British guidelines (2011)

...reasonable steps should be taken to exclude genetic disease in the potential donor.

record family history

routine work-up

screening for ADPKD by ultrasound

using revised ultrasound criteria (Pei Y et al JASN 2009)

proceed with donation

if donor >40 years of age and  $\leq 2$  cysts

20-40 years: additional CT or MRI (criteria?)

eventually additional genetic testing according to guidelines for genetic testing

linkage analysis

or DNA sequencing of recipient and donor for pathogenic variant

(Huang E. Transplantation 2009)

## 7. What is the optimal timing of preemptive renal transplantation in ADPKD?

Instead of dialysis  
or within 6 months after initiation of RRT

KDIGO

## 8. Should native nephrectomy be done and at what point related to transplantation: pre, concurrent, or post Tx?

Already discussed

KDIGO

## 9. What immunosuppressive therapies should be utilized in a transplanted ADPKD patient?

**Immunosuppressive treatment according to current guidelines, unless new data demonstrate specific benefits for ADPKD patients**

KDIGO

## 9. Should hepatic cystic disease impact on choice of immunosuppression?

**Immunosuppressive treatment according to current guidelines, unless new data demonstrate specific benefits for ADPKD patients**

KDIGO

**Thank you for your attention!**

**KDIGO**



# 10. What are the indications for combined kidney-liver transplantation?

## Combined kidney – liver transplantation is rare

Italy 40/1709 (0,023%) transplanted ADPKD pts

## Indications: severe clinical symptom burden

e.g. due compression syndrome,  
severe malnutrition

liver failure (e.g. HBV or HCV infection)

Budd-Chiari-like-Syndrome with hepato-venous outflow obstruction

Cyst infection?

## Eurotransplant waitlisting criteria:

Massive PLD (total Cysts/Parenchyma >1)

and complication(s), that can exclusively be treated by liver Tx

clinically apparent liver disease due to massive PLD,  
incl. weight loss, ascites, portal hypertension

Failure or contraindications of non-transplant related interventions

## 9. What immunosuppressive therapies should be utilized in a transplanted ADPKD patient?

mTOR inhibitors may have beneficial effects on kidney and liver cysts

mTOR inhibitors are approved immunosuppressants after kidney transplantation

however

mTOR inhibitors have several contraindications and side effects and are not considered standard of care according to KDIGO 2009

Excellent outcomes and quality of life with current standard of care

Cyst growth is not a major concern for the vast majority of patients, especially after nephrectomy

Potential benefits of mTOR inhibitor for ADPKD patients were not clearly demonstrated in large clinical trials

**Immunosuppressive treatment according to current guidelines, unless new data demonstrate specific benefits for ADPKD patients**



## 9. Should hepatic cystic disease impact on choice of immunosuppression?

mTOR inhibitors may have beneficial effects on liver cysts

mTOR inhibitors are approved immunosuppressants after kidney transplantation

however

mTOR inhibitors have several contraindications and side effects and are not considered standard of care according to KDIGO 2009

Excellent outcomes and quality of life with current standard of care

Cyst growth is not a major concern for the vast majority of patients,

Potential benefits of mTOR inhibitor for liver cysts were not clearly demonstrated

**Immunosuppressive treatment according to current guidelines, unless new data demonstrate specific benefits for ADPKD patients**