

Risiko für CKD nach Lebendspende

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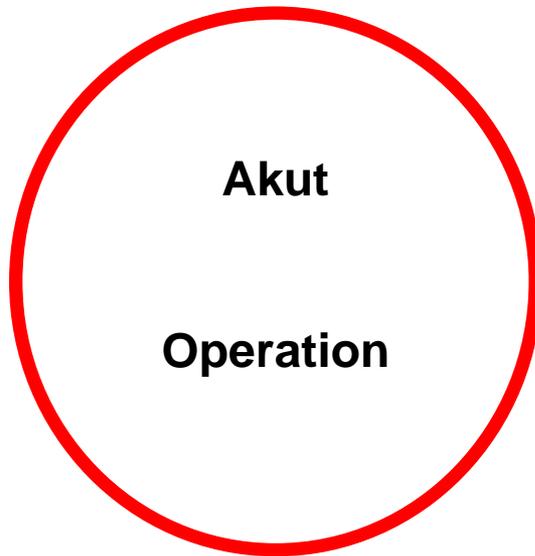
19. Transplantations-Workshop

Universitätsklinikum Freiburg

08. – 10. Dezember 2017



Risiko der Lebendspende



Operationsrisiko - Todesfälle

- 3.1 pro 10,000 Lebendniere spender



Operationsrisiko

Todesfälle pro 10'000 Eingriffen

- 3 Lebendnierenspende
- 18 Cholecystekomie
- 3-20 Liposuktion
- 3-10 Kaiserschnitt
- 1 normale Geburt

Operationsrisiko

Todesfälle pro 10'000 Eingriffen

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- 18 Cholecystektomie
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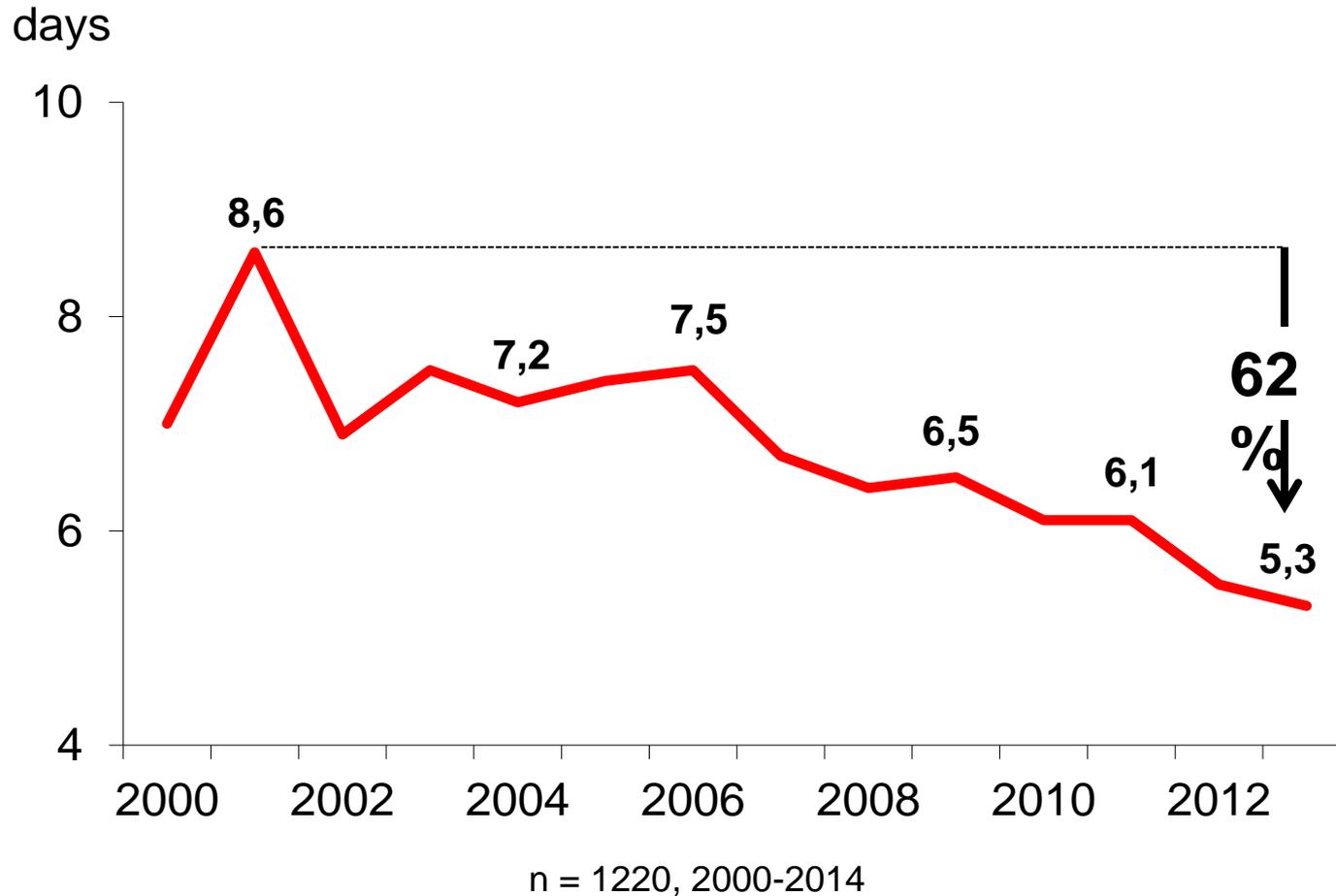
oder

74'000 km mit dem Auto fahren

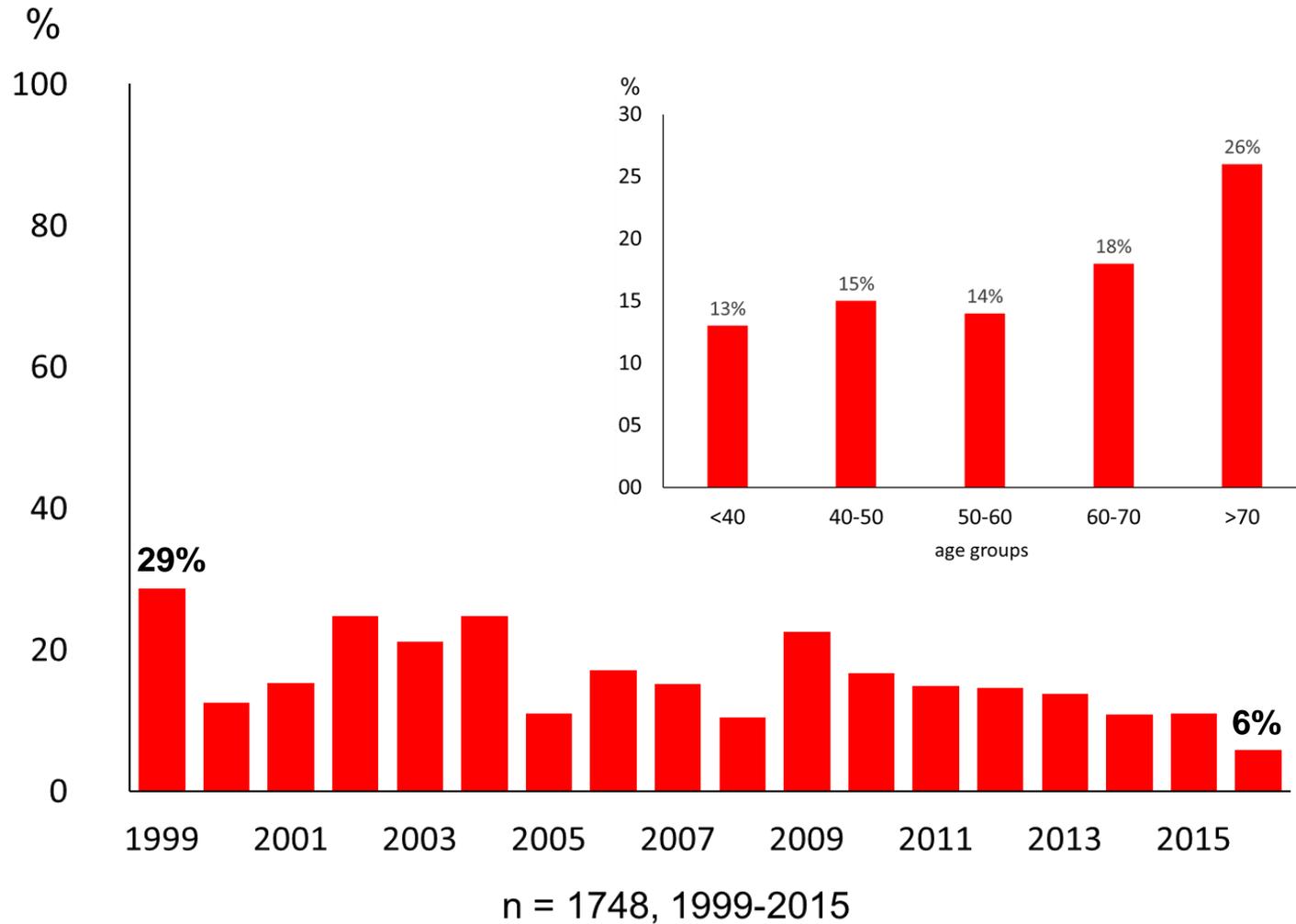
... oder 38 mal Gleitschirm fliegen



Länge des stationären Aufenthalts

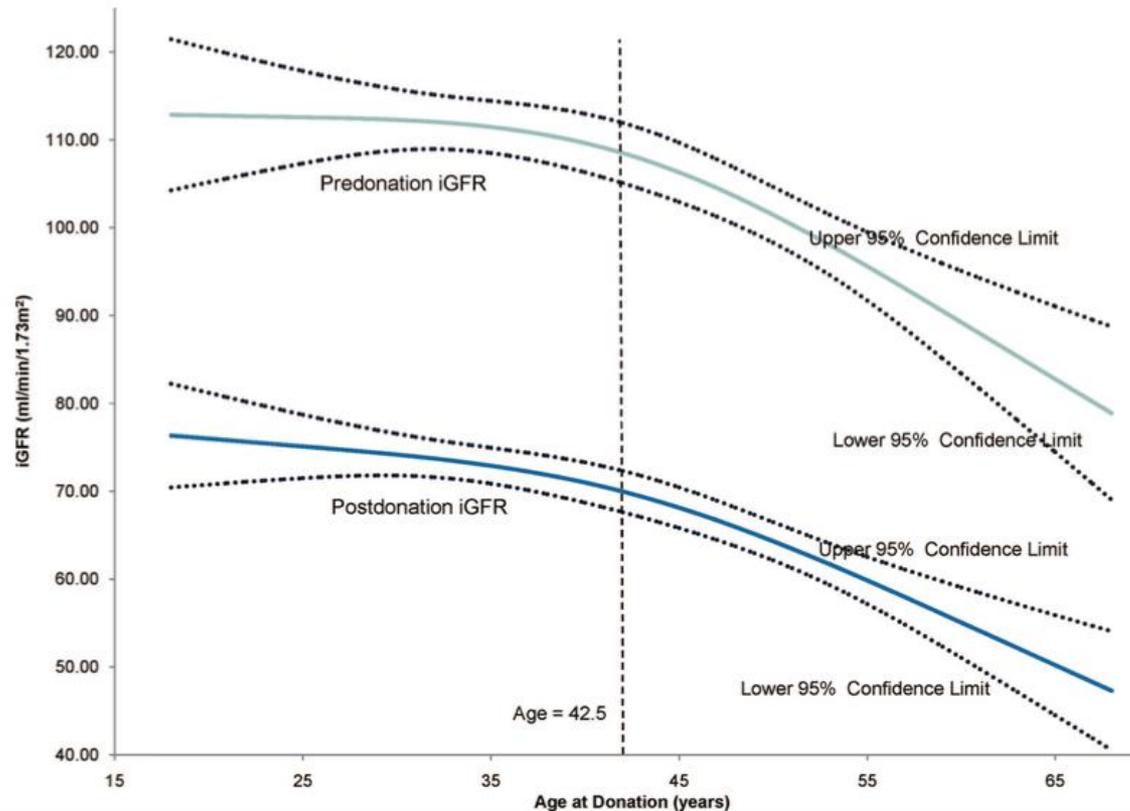


Rückgang früher Komplikationen



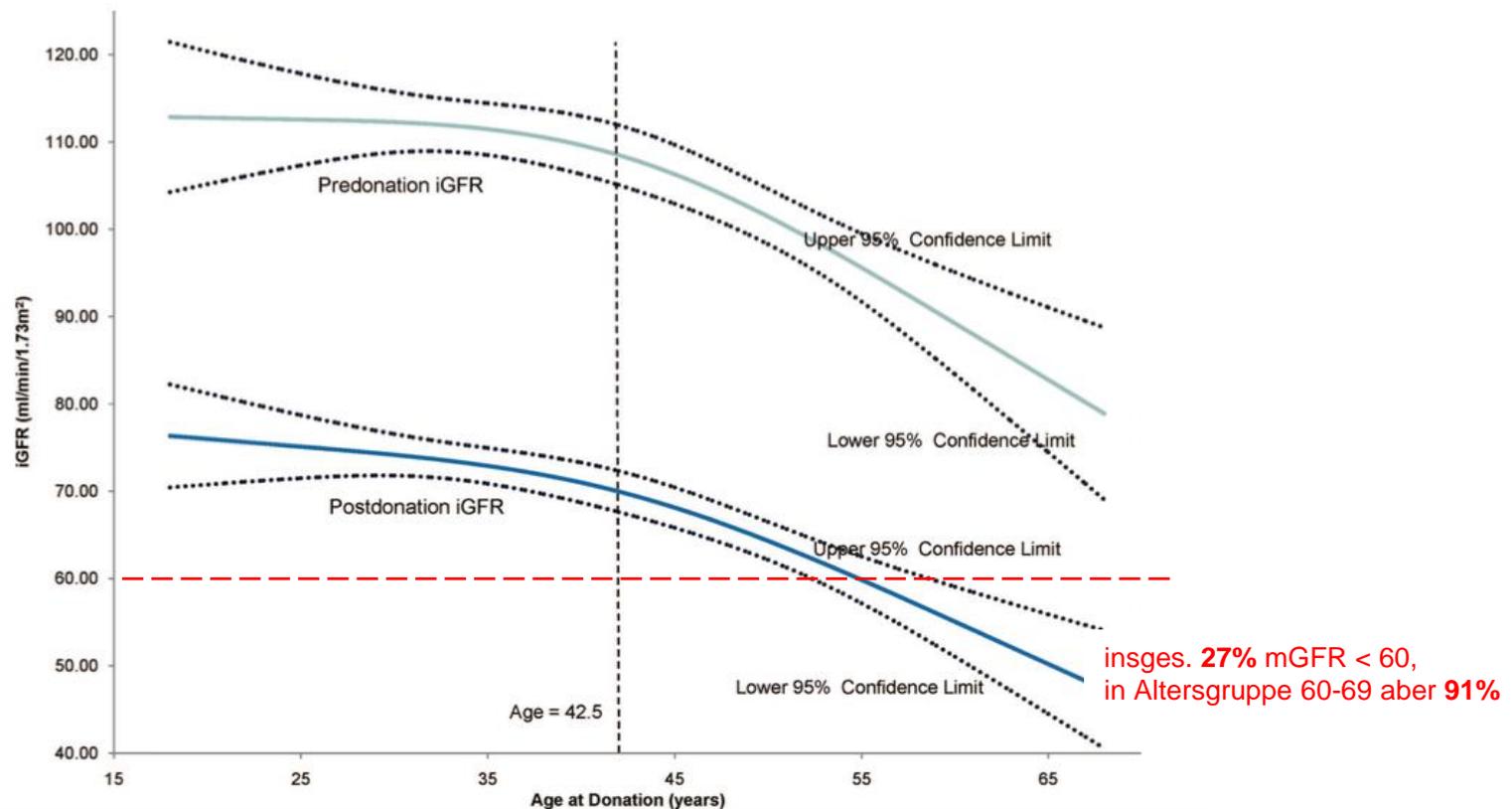
CKD3 nach Lebendspende?!

GFR < 60 ml/min/1.73m² nach Altersgruppen

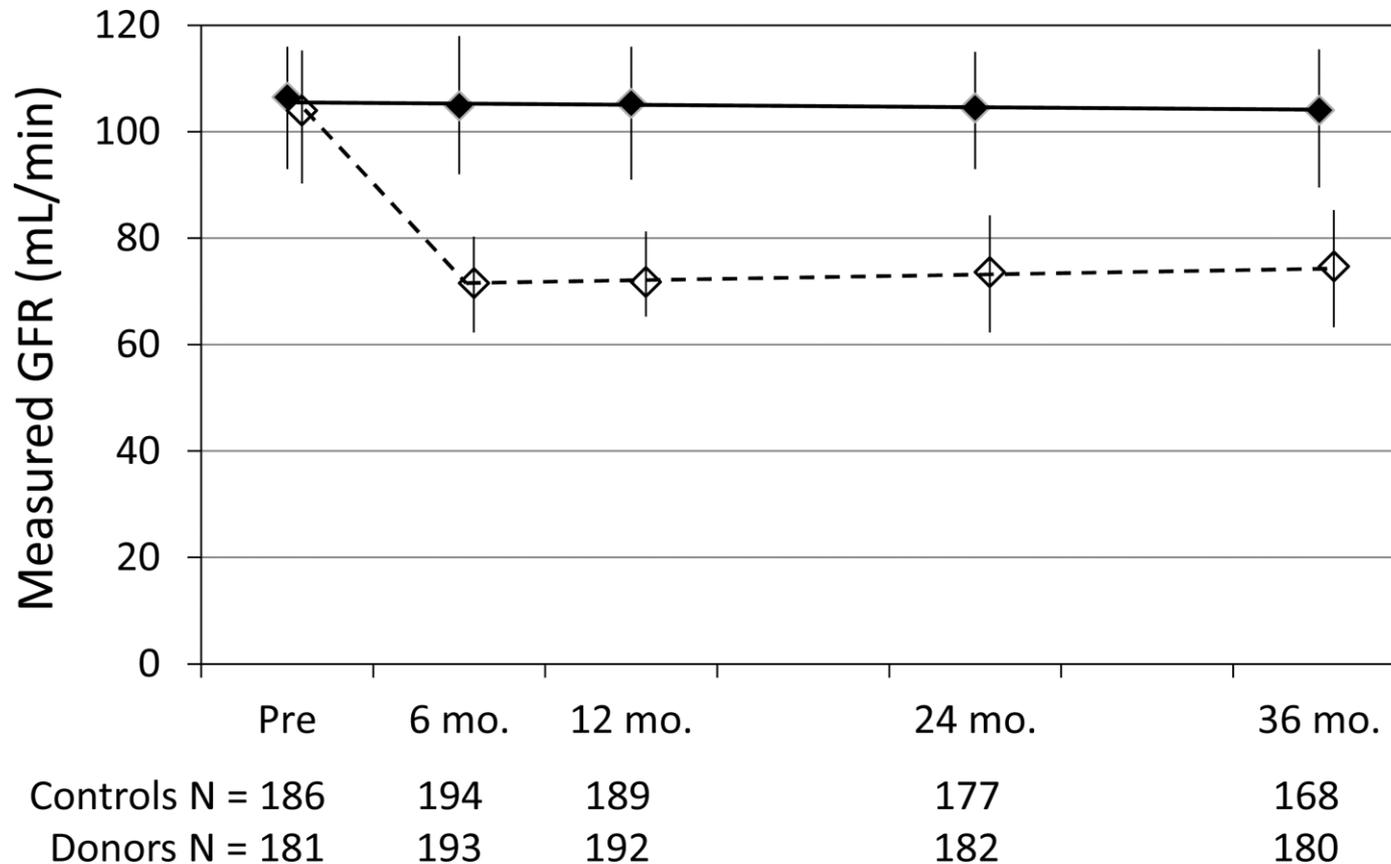


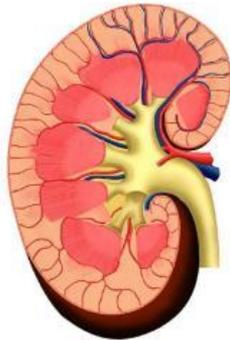
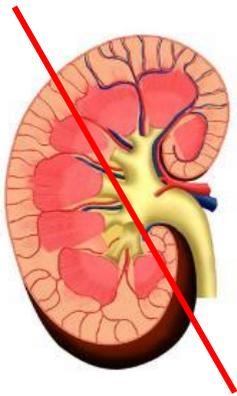
CKD3 nach Lebendspende?!

GFR < 60 ml/min/1.73m² nach Altersgruppen



Nierenfunktion in den ersten 3 Jahren nach Lebendspende

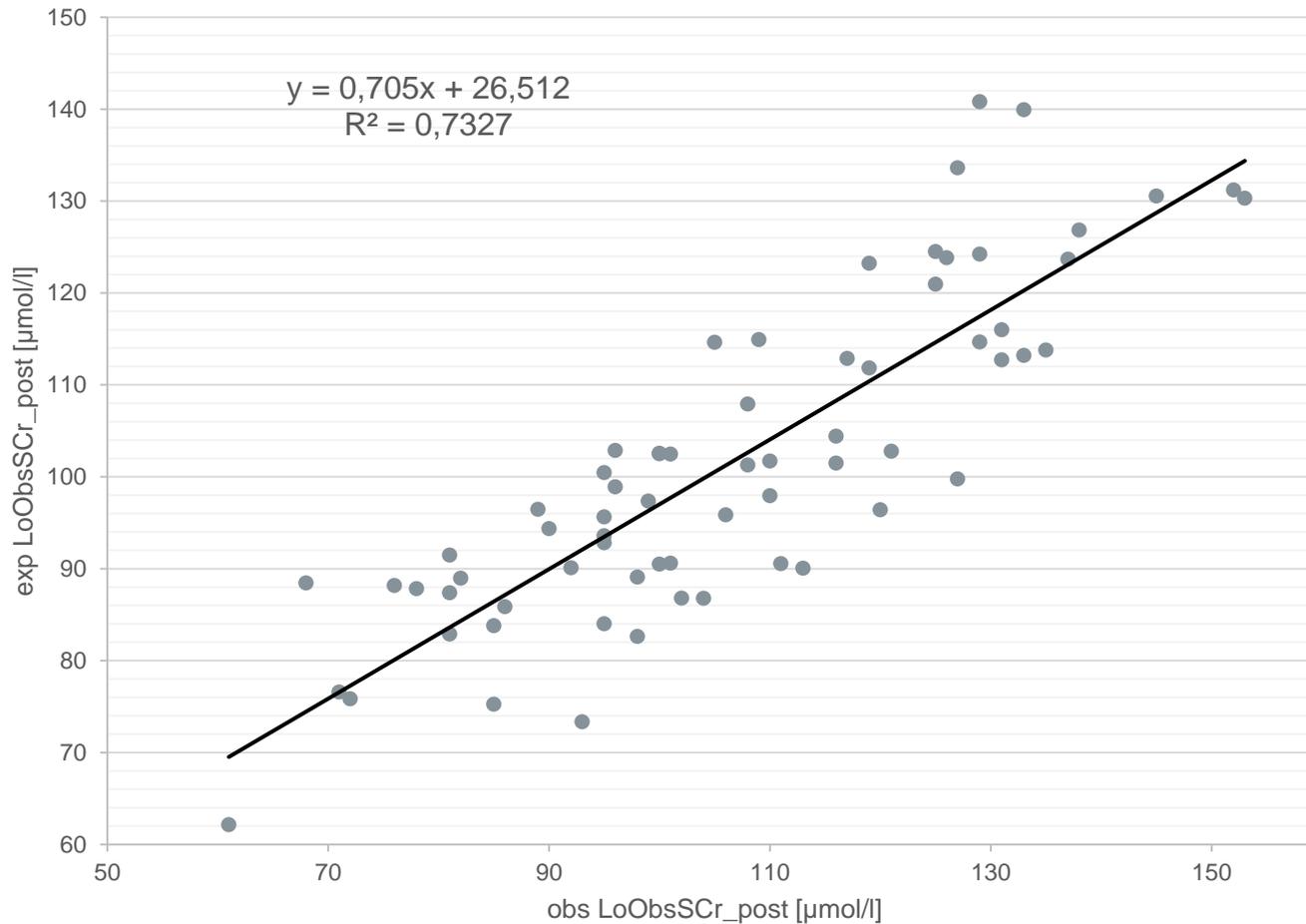




Adaptiver Anstieg um 35%

Vorhersage der erwarteten Nierenfunktion nach Spende

(LD n = 68, mean obs S-Cr 107, exp S-Cr 102 $\mu\text{mol/l}$)



Vorhersage der erwarteten Nierenfunktion nach Spende

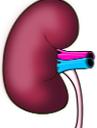
«Serum Kreatinin vor Spender x 1.49 = Serum Kreatinin nach Spende»

Calculation of the expected serum creatinine in the recipient

Post-transplant kidney function is based on...

1. ... the recipient's **metabolic demand**
2. ... the donor's nephron **supply**.

$$expSCr_R [\mu mol/l] = \frac{age_R * bwt_R * gender_R}{0.6 * GFR_{LD} + 8.7}$$

demand 
supply 

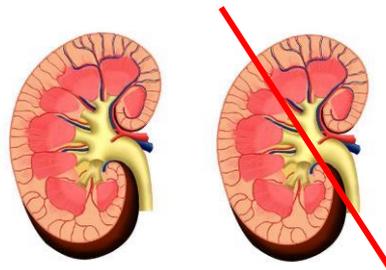
$$GFR_{LD} = \frac{age_{LD} * bwt_{LD} * gender_{LD}}{SCr_{LD}}$$

Al-Sehli et al, Transplantation 2015; 99: 1960

ABER



Risiko ein progredientes Nierenversagen zu entwickeln?

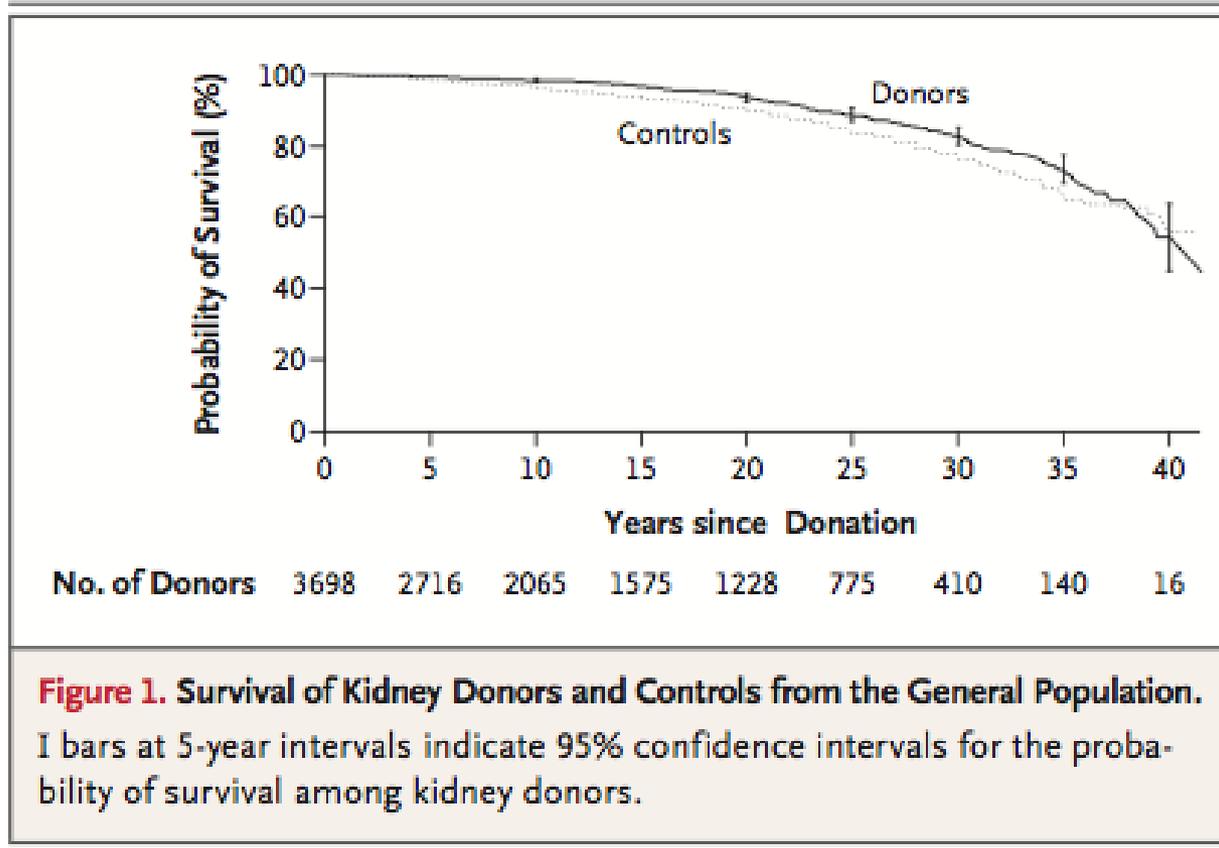


50 % Funktion Hyperfiltration → **75 % Funktion**

- Mehrarbeit
- Belastung Niere
- Eiweiss im Urin
- Hochdruck
- → → → Nierenverschlechterung

→ ? Lebenserwartung
? Nierenversagen

Vergleichbares Langzeitüberleben



Ibrahim, Matas et al, NEJM, 2009; 360: 459

Caveats

- inadäquate Kontrollgruppen
- hoher 'lost to follow up' und Positivauswahl
- zu kurze Beobachtungszeit
- ungenügende Nierenfunktionsmessung
- retrospektive Studien
- wenig Daten für Risikogruppen

Erhöhte Sterblichkeit bei 1'901 Nierenspendern verglichen mit 32'621 gesunden Kontrollen

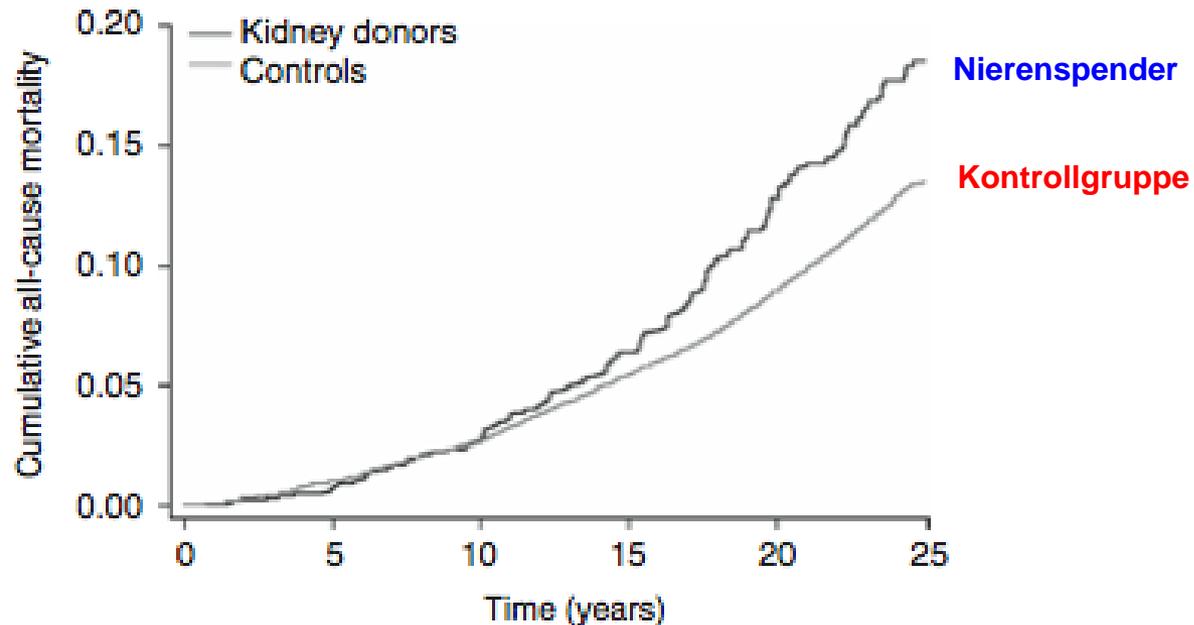
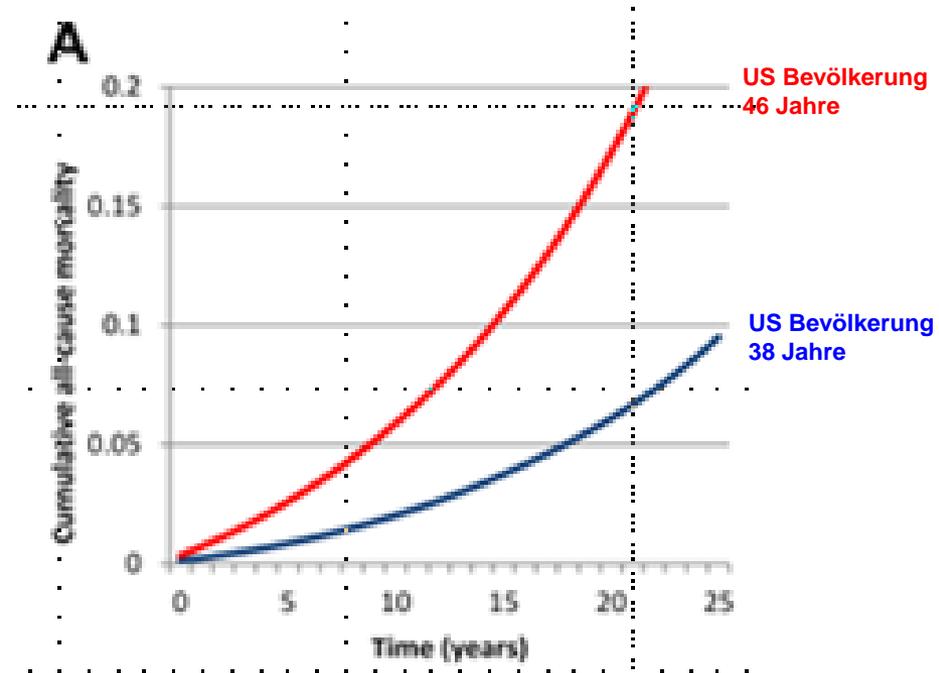
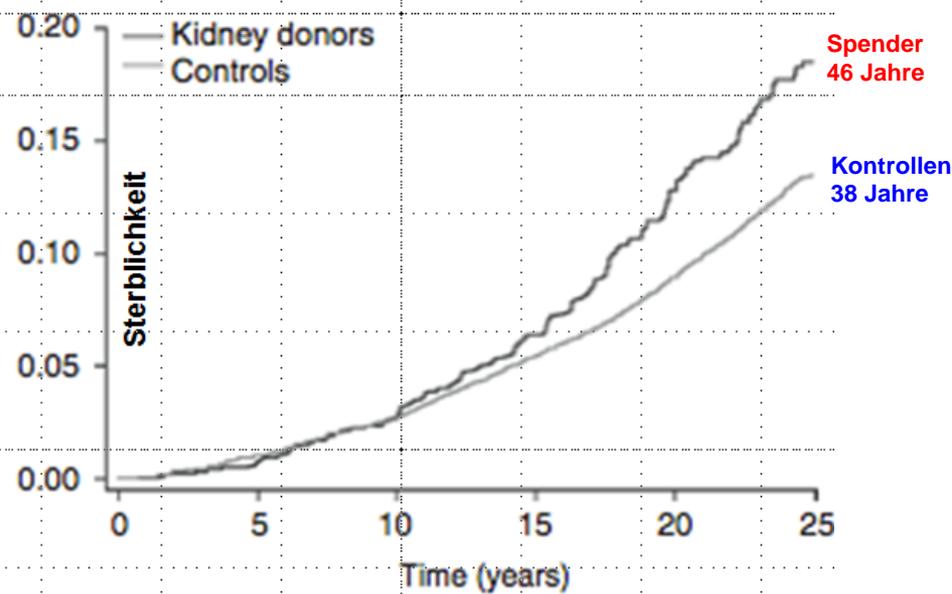


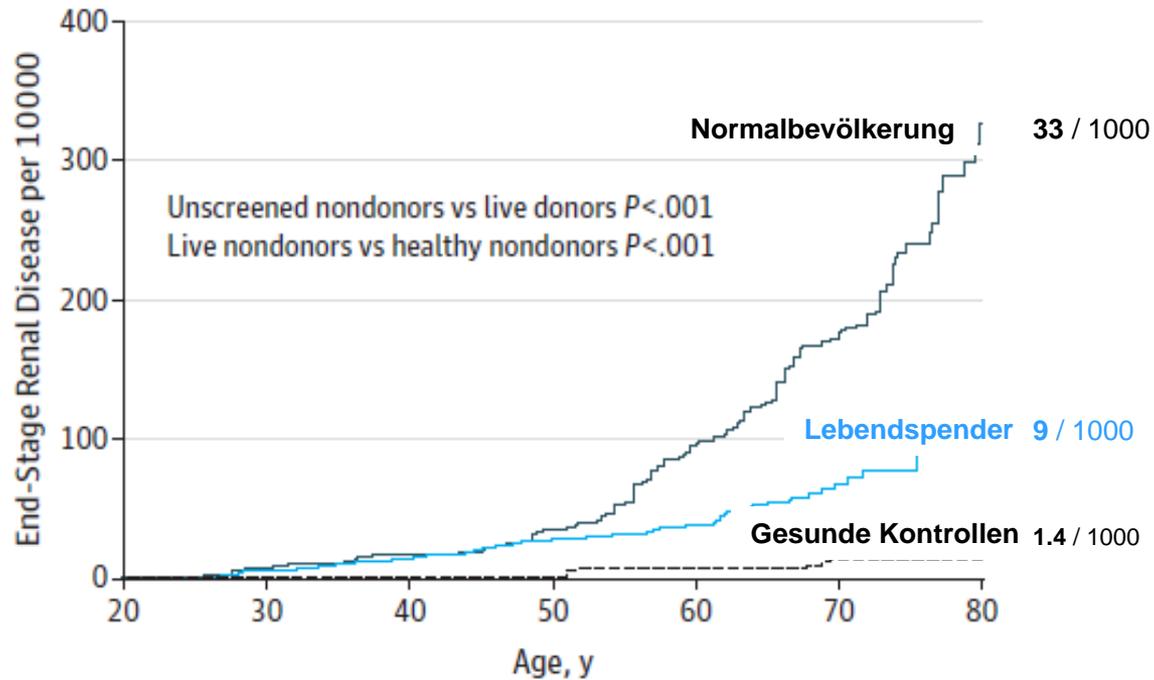
Figure 2 | Cumulative mortality risk in kidney donors and controls, adjusted for year of donation. Controls are matched to donors for age, sex, systolic blood pressure, body mass index, and smoking status.

Der Altersunterschied zwischen den Gruppen erklärt Unterschiede in der Sterblichkeit



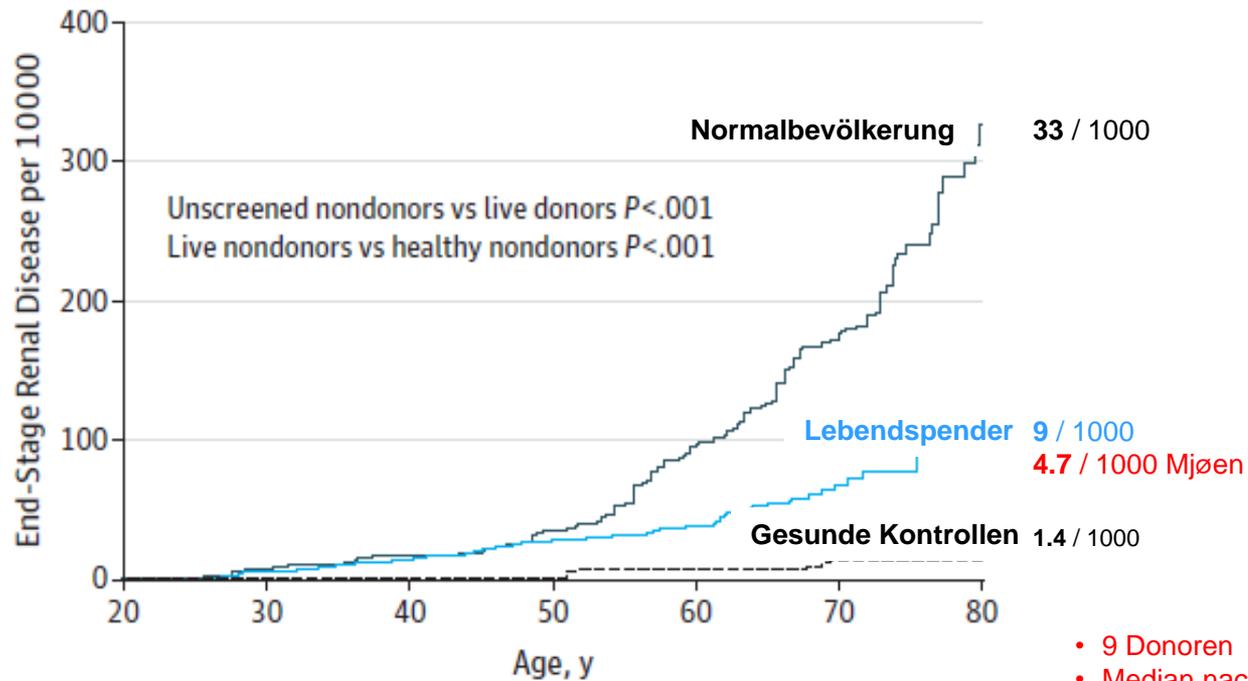
Mjøen et al, Kidney Int 2014; 86: 162

Dialyserisiko im Vergleich zu gematchten Kontrollgruppen



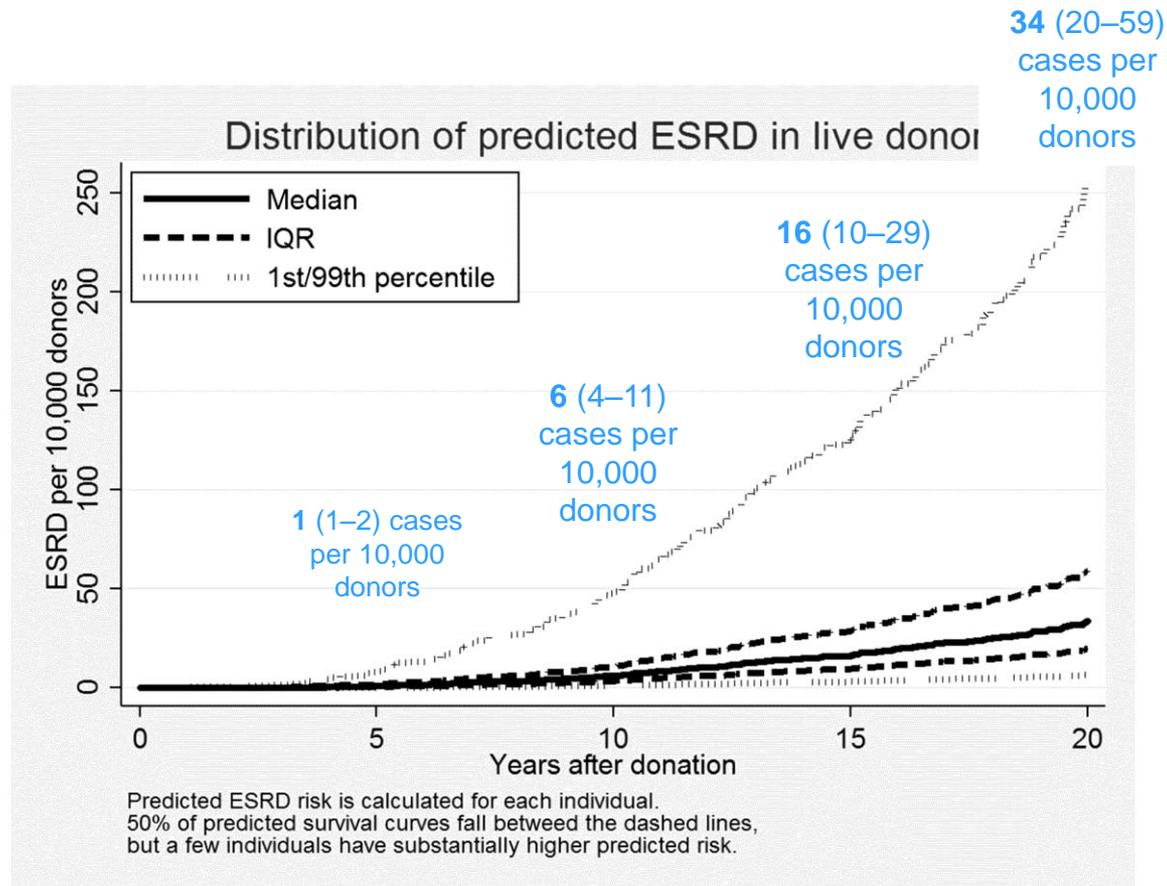
Muzzale et al, JAMA 2014; 311: 579

Dialyserisiko im Vergleich zu gematchten Kontrollgruppen

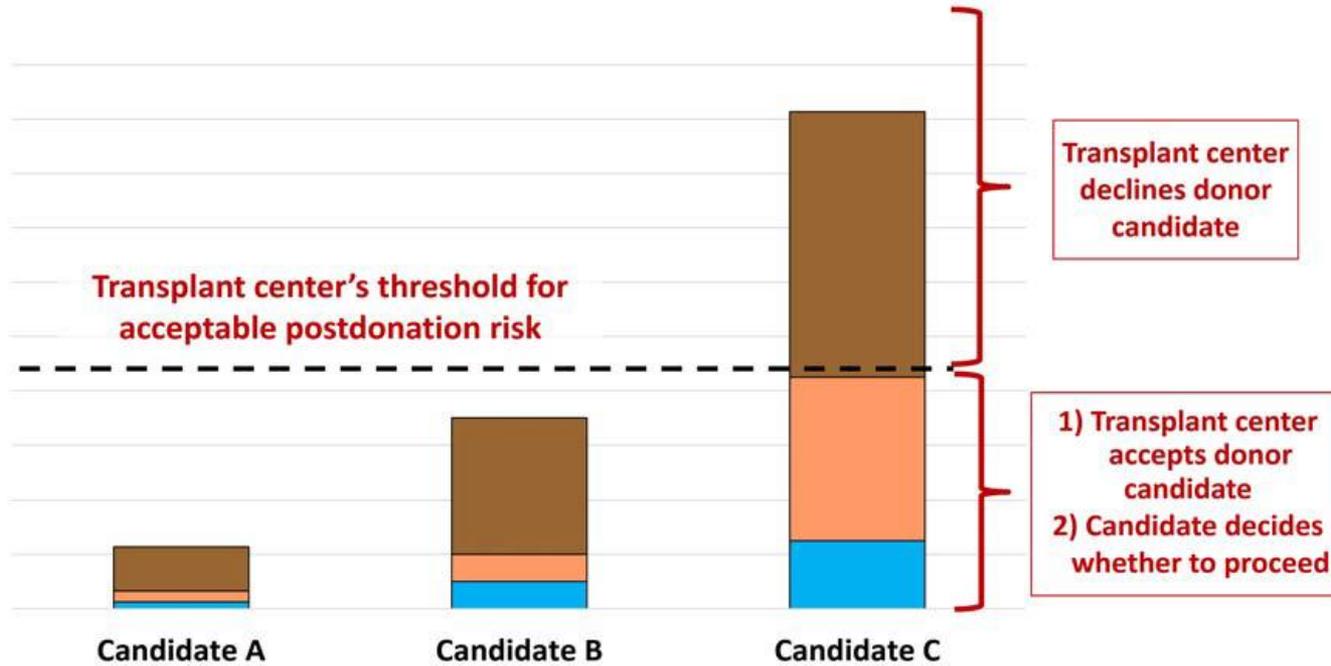


- 9 Donoren
- Median nach 18.7 Jahren
- alles Verwandte
- primäre Nierenerkrankungen

Vorhergesagtes Risiko für ESRD abhängig von den Jahren nach Spende



Projected Lifetime Risk of Kidney Failure, %



- Demographic-related risk in the absence of donation (age, sex, and race)
- Aggregate risk related to clinical characteristics in the absence of donation (e.g. GFR, blood pressure, BMI, smoking)
- Donation-attributable risk (may vary by demographic and clinical characteristics)

Risikokalkulation für terminale Niereninsuffizienz vor und nach der Spende

Risiko vor Spende

Risiko nach Spende

ESRD Risk Tool for Kidney Donor Candidates

Projected Incidence of End-Stage Renal Disease:	
0.07% Pre-Donation 15-Year*	0.08% Pre-Donation Lifetime*
?	?
Post-Donation 15-Year**	Post-Donation Lifetime**

blue: < 1%, green: 1-2%, yellow: 2-3%, orange: 3-5%, red: >5%

The pre-donation risks represent projections if a person does not donate a kidney. Details about estimating post-donation risk are provided below.

[reset](#) [print summary](#)

Patient Characteristics:

Age (18-80yrs)

Gender

Race (White or Black)

eGFR (mL/min/1.73m²)

Systolic Blood Pressure (mmHg)

Hypertension Medication

BMI (kg/m²)

Non-Insulin Dependent Diabetes

Urine Albumin to Creatinine (mg/g)
click on units to change between mg/g and mg/mmol

Smoking History

1. Grams ME, Sang Y, Levey AS, Matsushita K, Ballew S, Chang AR et al. Kidney-Failure Risk Projection for the Living Kidney-Donor Candidate. NEJM 2015 (epub ahead of print)
2. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk for end-stage renal disease. Ann Intern Med 2006;144:21-8.
3. Vivante A, Golan E, Tzur D, et al. Body mass index in 1.2 million adolescents and risk for end-stage renal disease. Arch Intern Med 2012;172:1644-50.
4. Mjøs G, Hallan S, Hartmann A, et al. Long-term risks for kidney donors. Kidney Int 2014;86:162-7.
5. Muzaale AD, Massie AB, Wang MC, et al. Risk of end-stage renal disease following live kidney donation. JAMA 2014;311:579-86.

transplantmodels.com



Studien (klein und kurz) zu Risikogruppen

Living donor group	Outcome	
African American versus white (United States)	Increased risk for hypertension (hazard ratio, 1.52) ^{24,31} Increased risk for macroalbuminuria (12% versus 0%) ³⁰ Greater decline in GFR after donation with higher BMI ³¹ Increased risk for CKD (hazard ratio, 2.32) ^{24, 30} Greater decline in estimated GFR in AA women at 273 days after donation ³² Highest risk for kidney failure among AA males donating before age 35 yr ²⁵ Greater proportion of AA donors listed for transplantation ²⁵	<ul style="list-style-type: none"> • ↑ CKD • ↑ Hypertonie • ↑ Albuminurie
Hispanic versus white (United States)	Increased risk for hypertension (hazard ratio, 1.36) ²⁴ Increased risk for CKD (hazard ratio, 1.90) ²⁴	<ul style="list-style-type: none"> • ↑ CKD & ↑ Hypertonie
Australian aboriginal versus white	Increased mortality (12% versus 0%) ²⁷ Increased prevalence of CKD and ESRD (81% versus 38%) ²⁷ Increased prevalence of hypertension (50% versus 6%) ²⁷ Increased prevalence of proteinuria (81% versus 6%) ²⁷	<ul style="list-style-type: none"> • ↑ CKD • ↑ Hypertonie • ↑ Alburie • ↑ Mortalität
Canadian aboriginal versus white	Increased prevalence of hypertension (100% versus 45% at 20 yr) ²⁶ Increased prevalence of proteinuria (21% versus 4%) ²⁶	<ul style="list-style-type: none"> • ↑ Hypertonie • ↑ Albuminurie
Older versus younger	Lower postdonation GFR in older donors ^{11,14, 32} Reduced renal functional reserve capacity with donor age > 54 yr ¹⁴	<ul style="list-style-type: none"> • ↓ GFR • ↓ RRC
Higher BMI	Lower postdonation GFR with increasing BMI ^{11,14,16} Reduced renal functional reserve capacity, especially with donor age < 49 yr ¹⁴	<ul style="list-style-type: none"> • ↓ GFR • ↓ RRC
 Low birth weight/low nephron number APOL1 variants Postdonation pregnancy	Unknown Unknown Unclear ¹⁷	

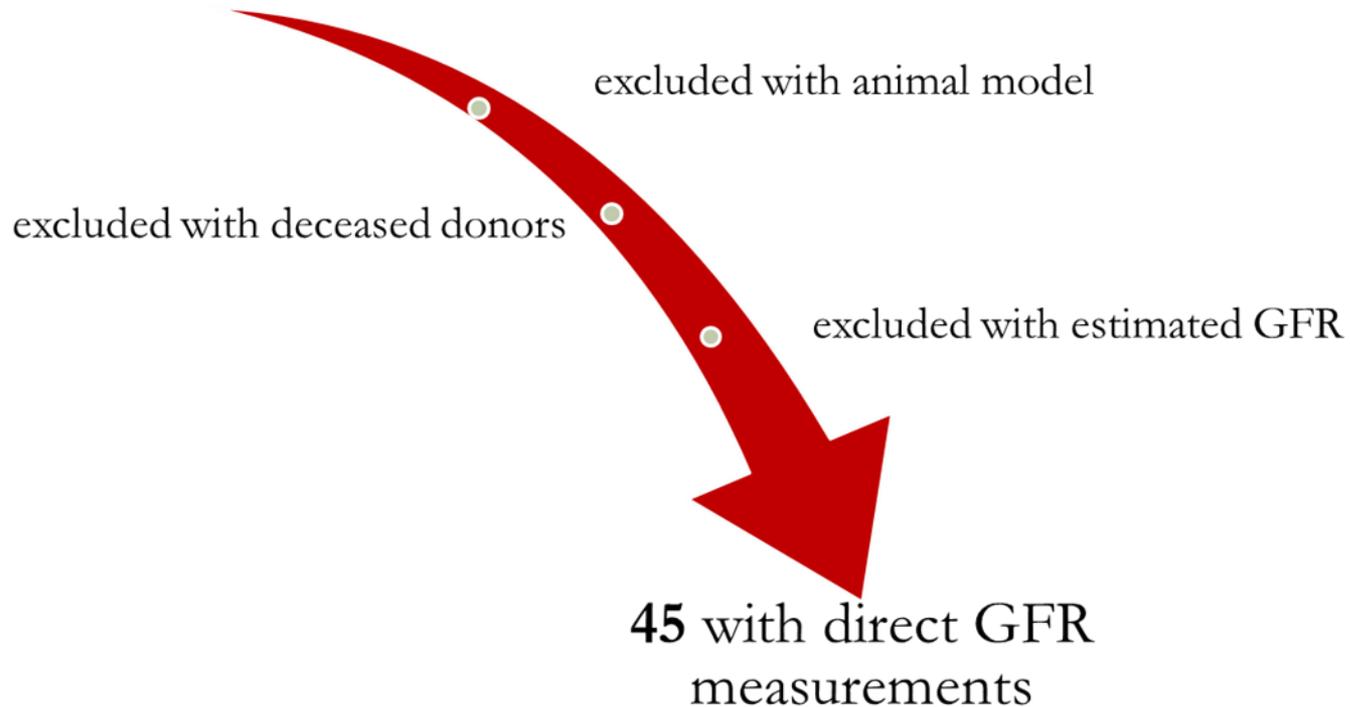
AA, African American.

Mueller, Luyckx, J Am Soc Nephrol 2012; 23: 1462

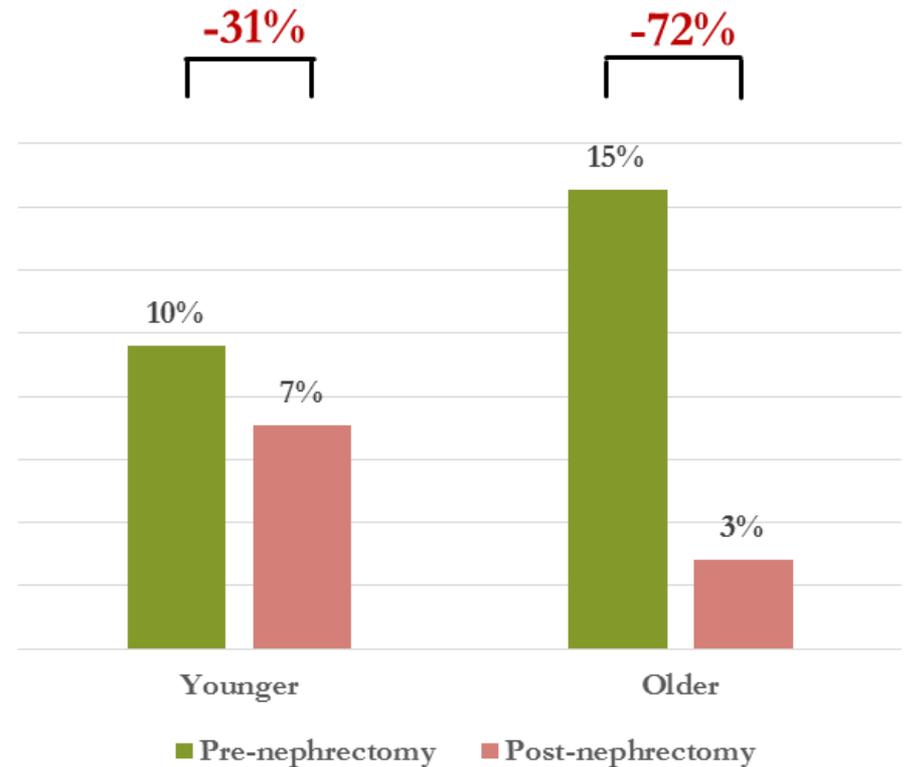
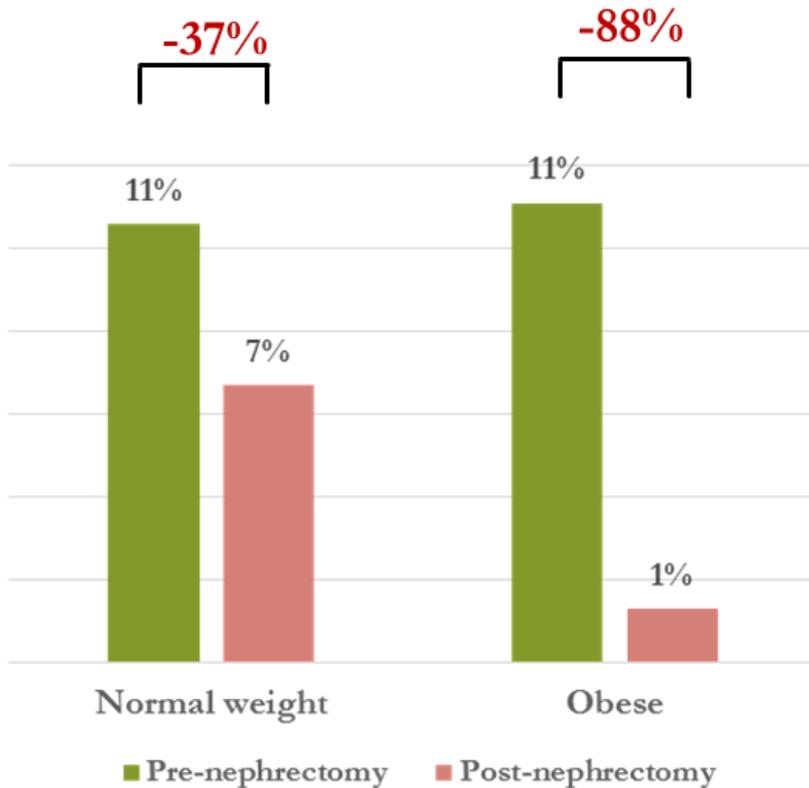
Review zu Studien zur Physiologie nach Lebendnierenspende

? GFR
? ERBF
? RFR

total of **3071**



Verlust der Reservekapazität bei 'marginalen' Donoren



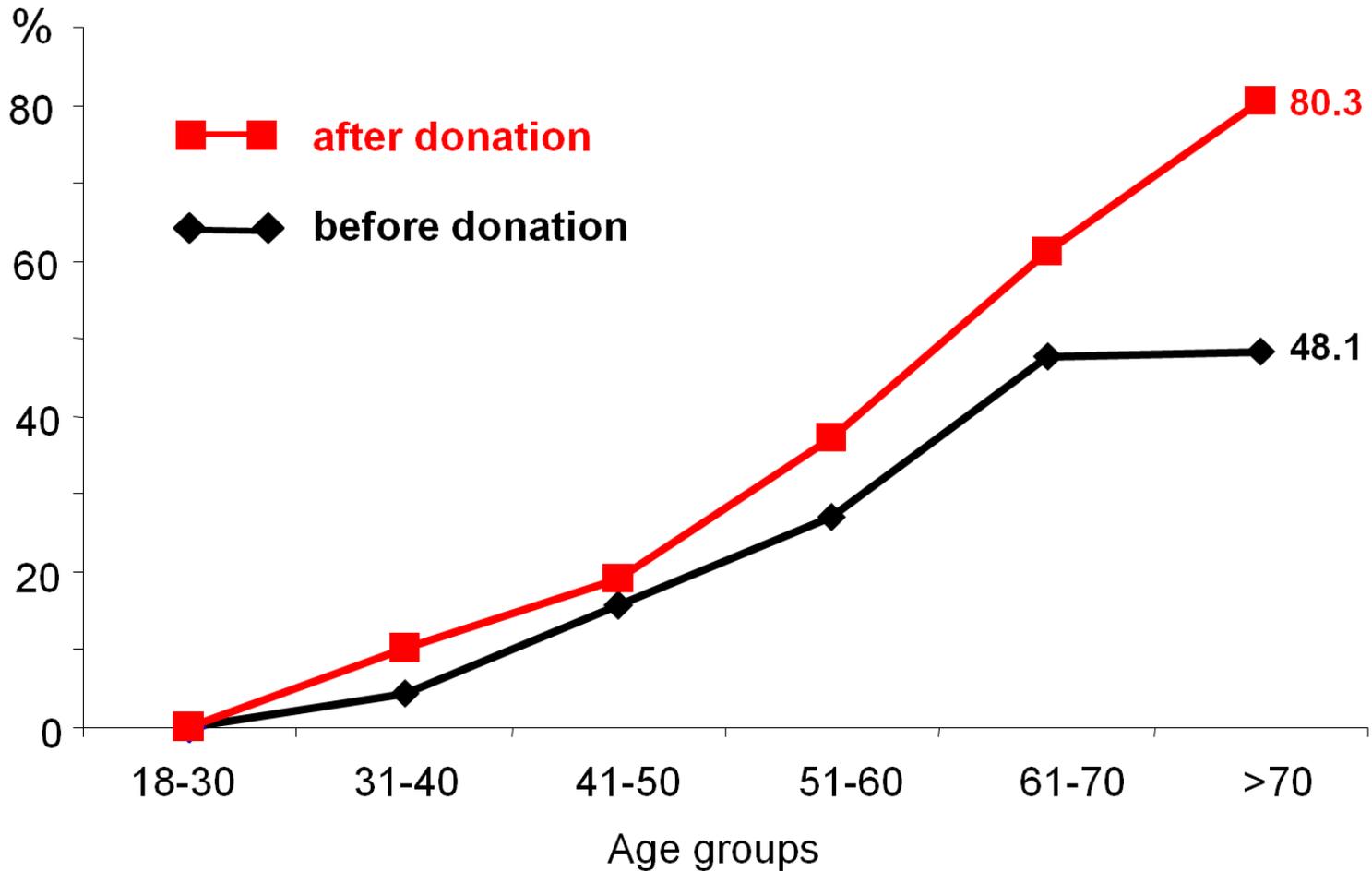
Schweizer Donorregister

- SOL-DHR = Swiss Living Kidney Donor Cohort Study
- 1993 von Prof. G. Thiel initiiert
- Prospektive und longitudinale Datensammlung:
 - 2014 Nierenspender von allen 6 Schweizer Transplantationszentren
 - 49 Leberlebendspener von 2 Zentren
- Follow up @ 1, 3, 5, 7, 10 Jahren, dann zwei-jährig

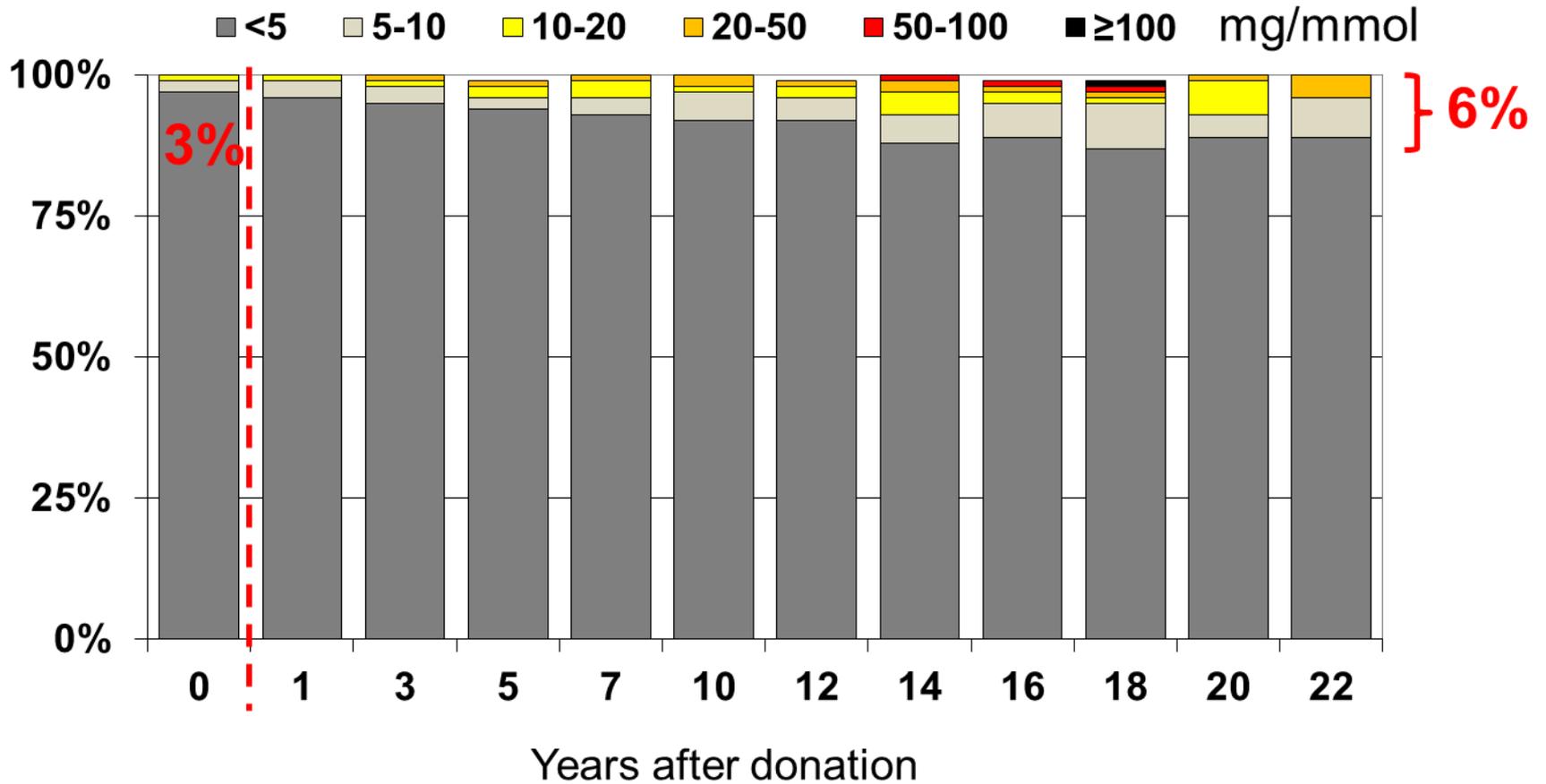
Bisher kein Spender mit Dialysepflichtigkeit



Hypertonie nach Spende

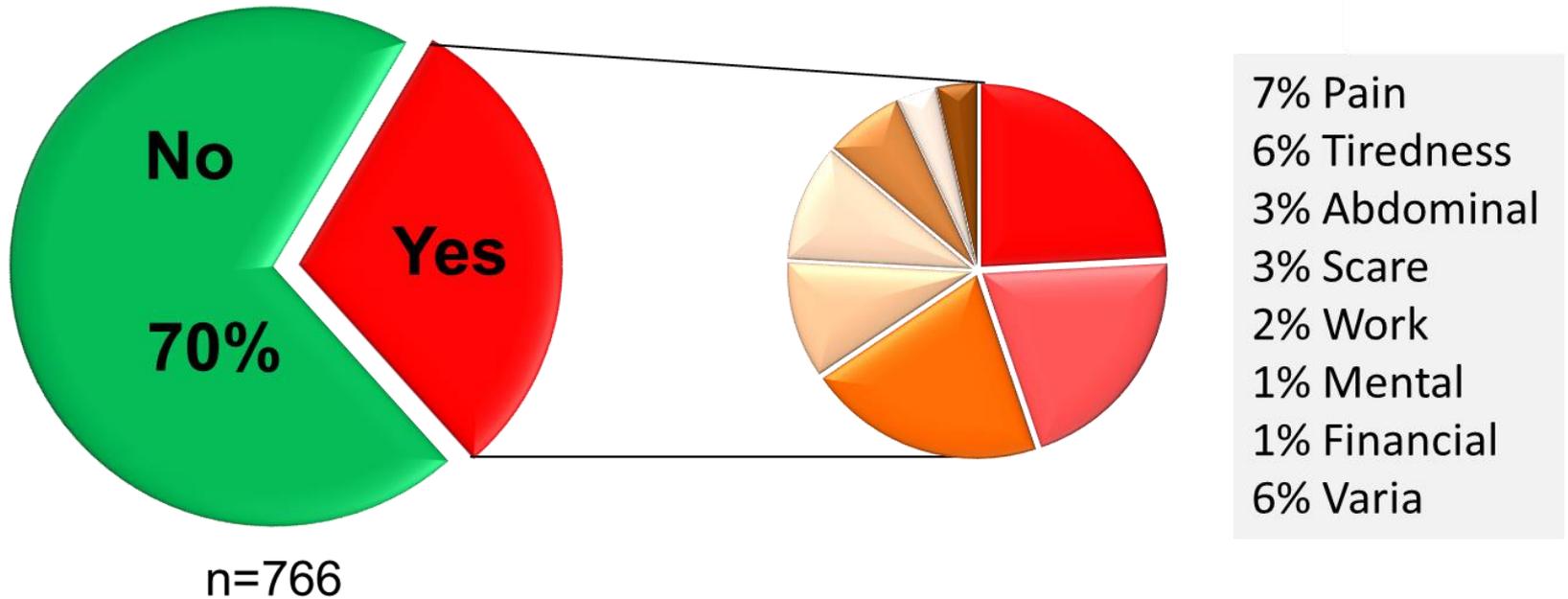


Albuminurie nach Spende



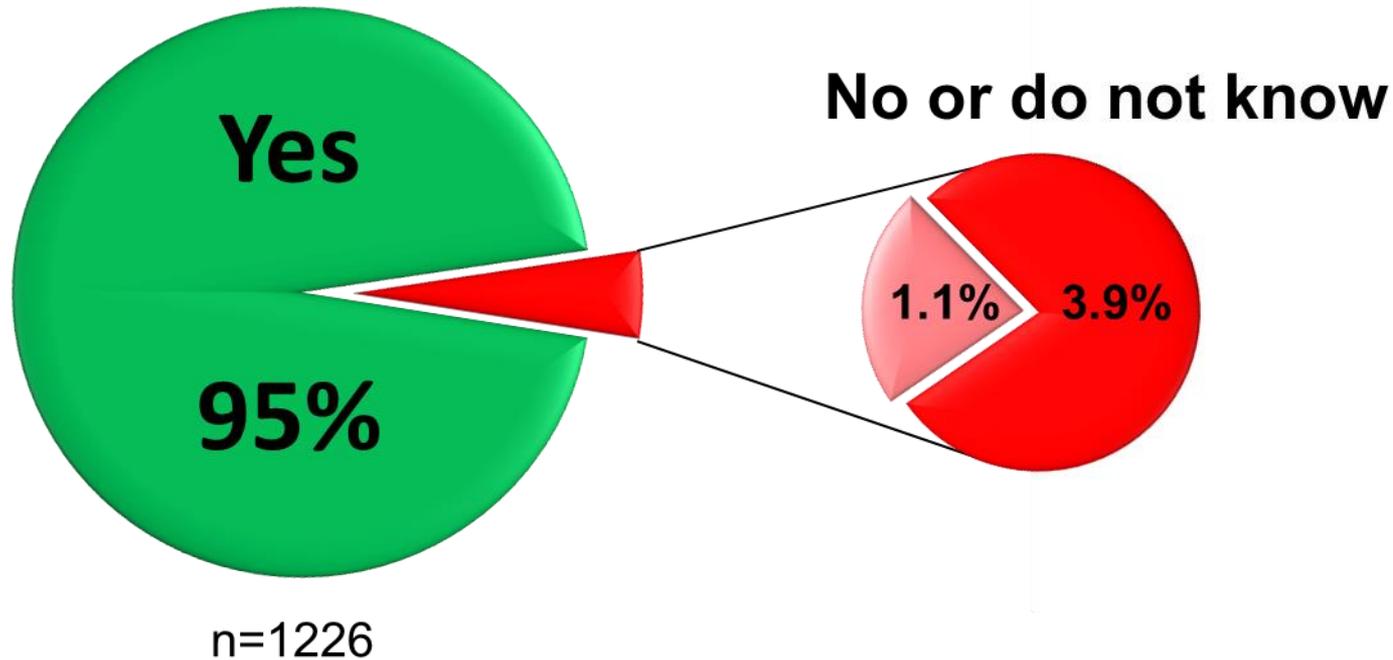
n = 1950, 1993-2015

Haben Sie Beschwerden nach der Spende?



By courtesy of Crista Nolte 2017

Würden Sie wieder spenden



By courtesy of Crista Nolte 2017

Zusammenfassung

- Lebendnierenspende ist nicht ohne Risiko
- das absolute Risiko für eine terminale Nierensinsuffizienz ist sehr klein
- gerade für Subgruppen wäre eine robuste Risikokalkulation sehr hilfreich
- prospektive Langzeitstudien mit adäquater Kontrollgruppe sind notwendig
- bis dahin ...

DANKE



ca
Ra
Kaa

$$2 + 2 = 7$$

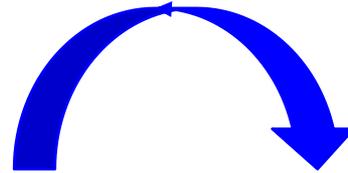
$$3 + 3 = 9$$

$$2 \times 2 =$$

Spenden?

Fall 1

25 ♀



65 ♂

ABO - O

A

Krea 80 $\mu\text{mol/l}$

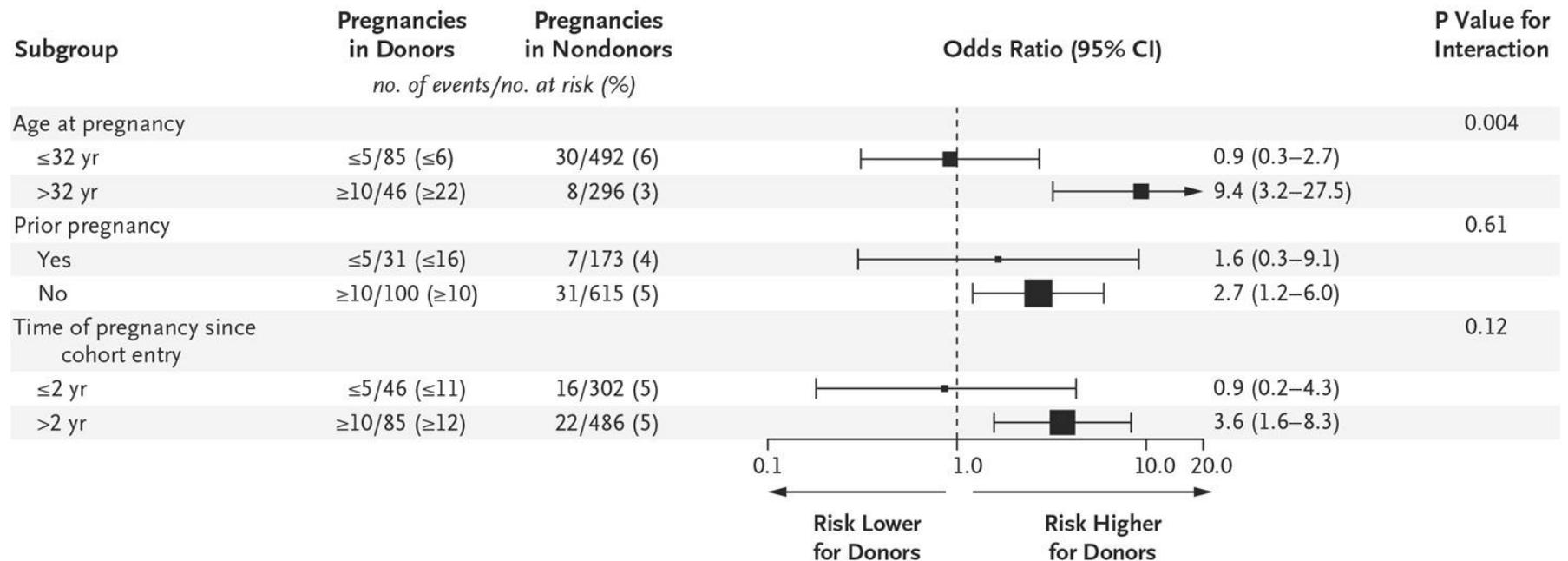
∅ DM

∅ HTN

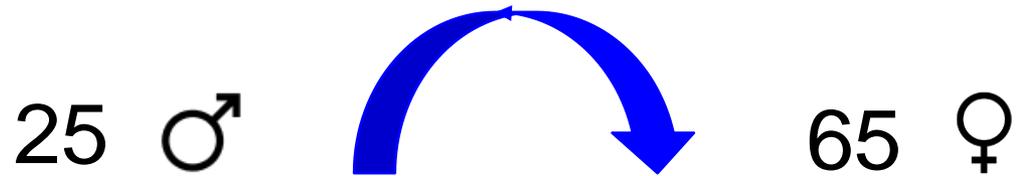
«gesund»

Gestational hypertension or preeclampsia is more common in living kidney donors compared with healthy controls

preterm birth, low birth weight, caesarean section and postpartum haemorrhage did not differ



Fall 2



ABO - O

A

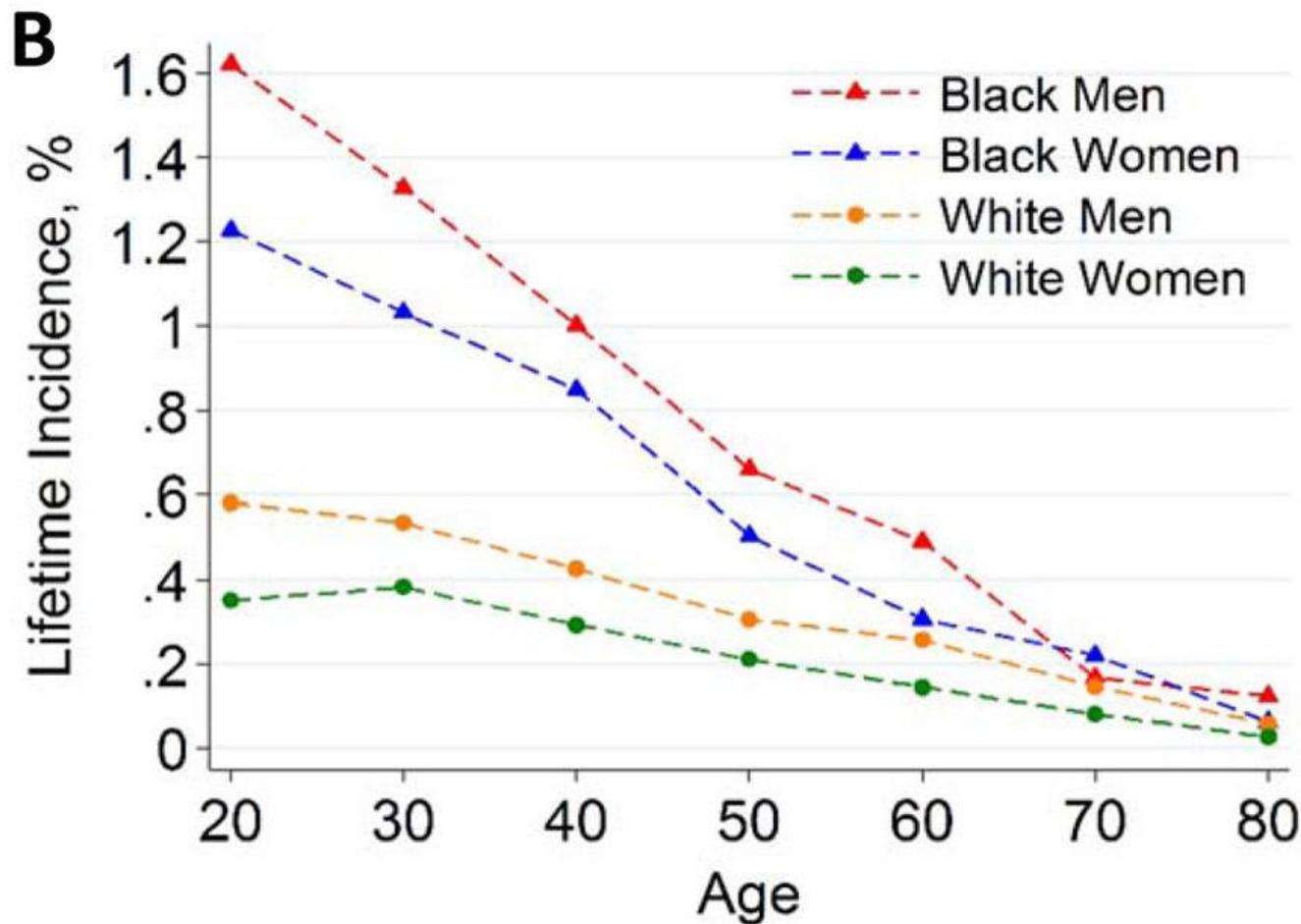
Krea 80 $\mu\text{mol/l}$

Ø DM

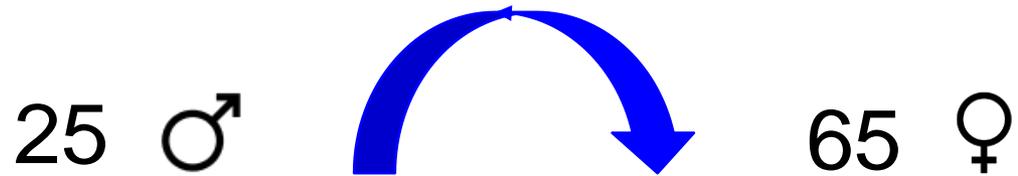
Ø HTN

«gesund»

Higher lifetime risk of ESRD for younger age, particularly among African Americans in the United States



Fall 3



ABO - O

A

Krea 80 $\mu\text{mol/l}$

∅ DM

∅ HTN

«gesund»

lebt in Indien

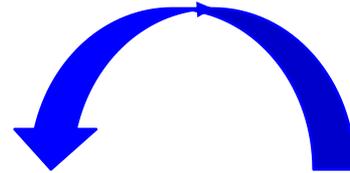
Transplantationsgesetz

Bedingungen für eine Lebendnierenspende:

- Urteilsfähigkeit und Mündigkeit des Spenders
- Freiwilligkeit und Unabhängigkeit
- Familiäre- oder emotionale Bindung nicht obligatorisch
- Kein finanzieller Gewinn
- Gesundheit und Leben des Spenders nicht gefährden

Fall 4

25 ♀



65 ♂

ABO - O

A

Krea 80 $\mu\text{mol/l}$

∅ DM

∅ HTN

«gesund»

Triple - Crossover Transplantation

Empfänger

WY
49 J
w
B pos
ZH

SS
44 J
w
A pos
ZH

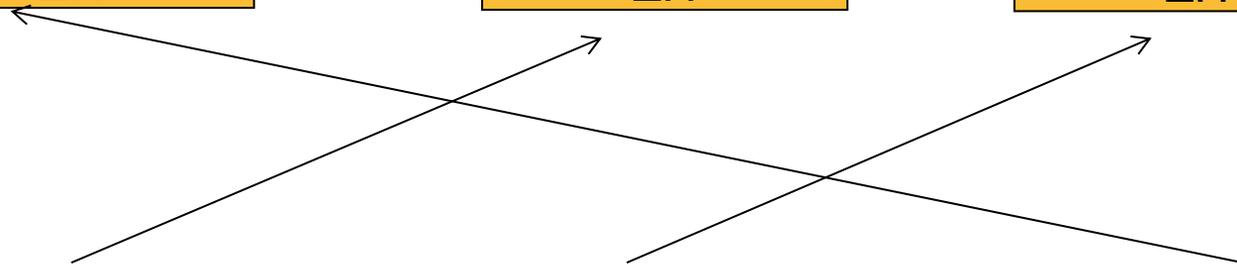
KJ
41 J
w
0 neg
ZH

Spender

LR
70 J
w
A pos
ZH

CS
40 J
w
0 pos
ZH

KR
59
w
0 neg
ZH



Kalkulatoren zur individualisierten Risikoeinschätzung

Quantifying Postdonation Risk of ESRD in Living Kidney Donors

Low Risk of ESRD
in the *average* donor



20-year risk of ESRD
34 Cases / 10,000 Donors

Up to *8x higher risk* of
ESRD in some donor groups



20-year risk of ESRD
256 Cases / 10,000 Donors

Calculate *personalized ESRD* risk using free calculator



doi: <https://doi.org/10.1052/ASB.2016.101084>

Tool available for clinicians at:
transplantmodels.com/donorsrd/

JASN
JOURNAL OF THE AMERICAN SOCIETY OF NEPHROLOGY

