Original Investigation

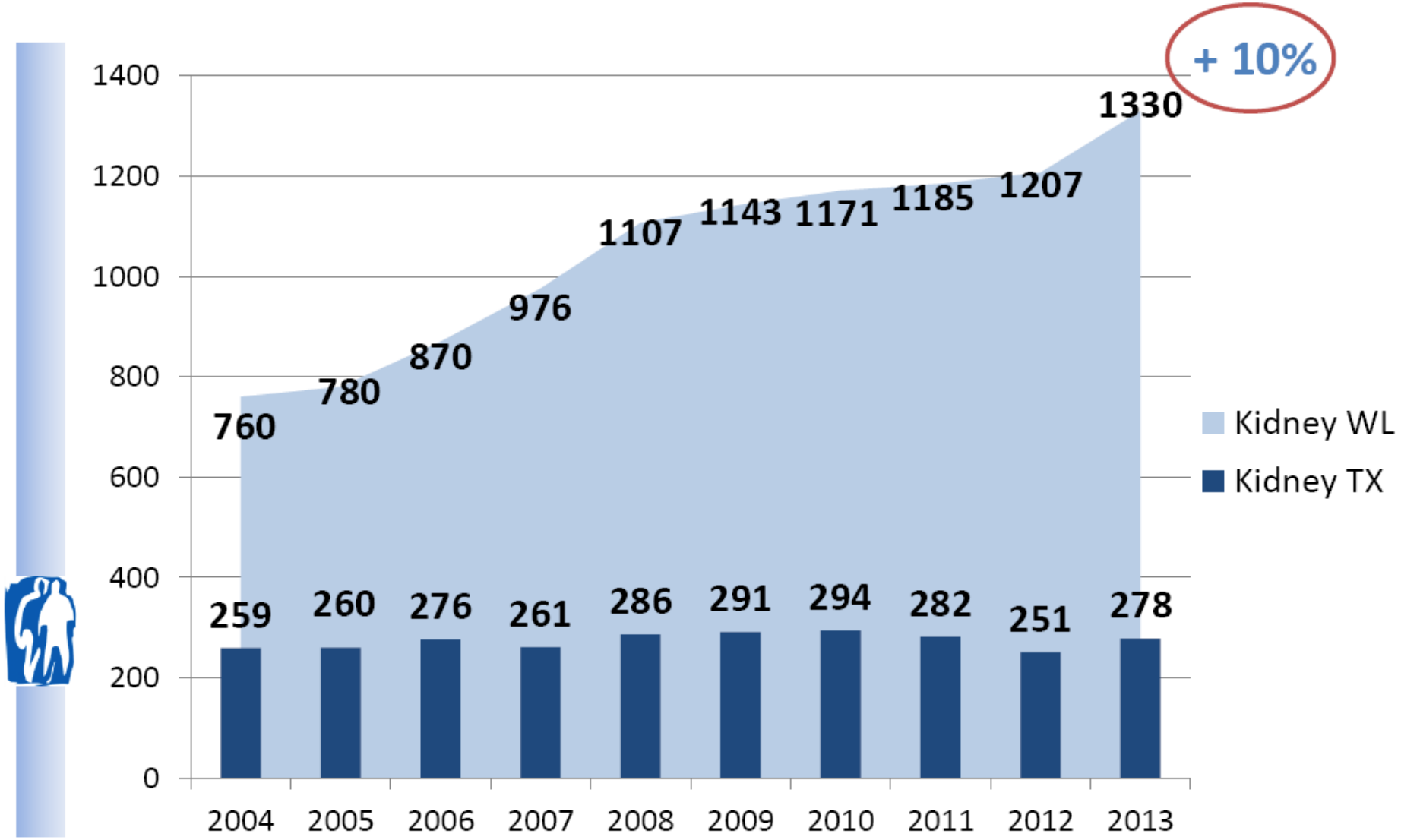
Risk of End-Stage Renal Disease Following Live Kidney Donation

Abimereki D. Muzaale, MD, MPH; Allan B. Massie, PhD; Mei-Cheng Wang, PhD; Robert A. Montgomery, MD, DPhil; Maureen A. McBride, PhD; Jennifer L. Wainright, PhD; Dorry L. Segev, MD, PhD

JAMA®
The Journal of the American Medical Association

Journal club 27 février 2014

Kidney Waiting List and Tx – SWTx 2004-2013



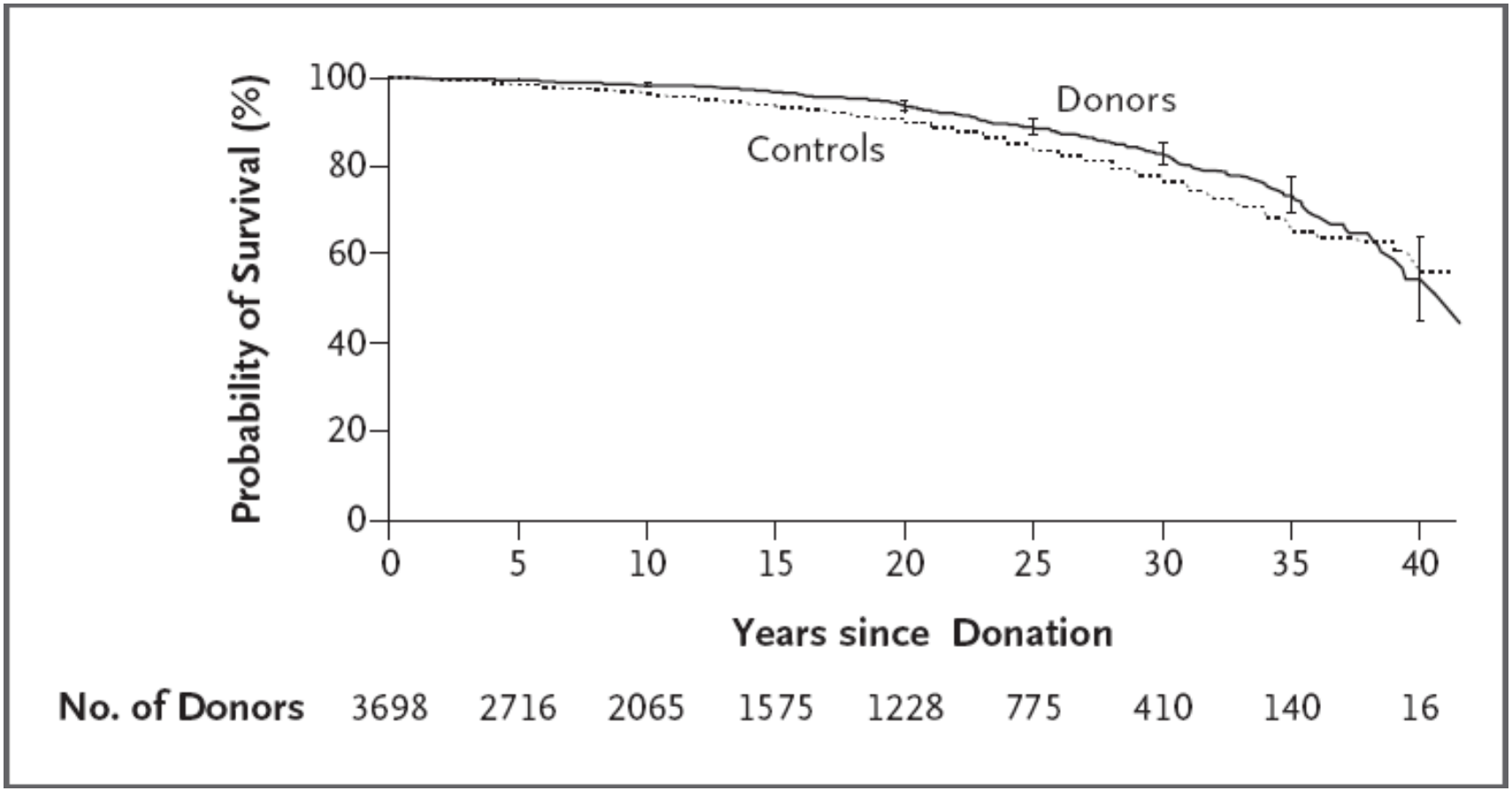
Background

Table 1. Results of Studies on Long-Term Follow-up (More Than Ten Years) in Kidney Donors*

	Vincenti	Hakim	Smith	Anderson	Total or Average
Patients, *n*	20	52	40	100	212
Men	7	29	20	48	104
Women	13	23	20	52	108
Mean duration of follow-up, *yrs*	15.8	12.9	11.8	12.6	12.8
With hypertension, † *%*	15	48	15	19	25
Men	NA	62	10	19	30
Women	NA	30	20	19	22
With proteinuria, *%*					
> 150 mg/24 h	20	25	20	13	17
Men	NA	31	NA	13	18
Women	NA	17	NA	13	15
500 to 999 mg/24 h	0	8	NA	2	4
Men	0	10	NA	2	5
Women	0	4	NA	2	3
> 1 g/24 h	0	2	NA	1	1
Men	0	3	NA	2	2
Women	0	0	NA	0	0
Mean serum creatinine level, *mg/dL*	1.16	1.25	1.29	1.20	1.23
Men	NA	1.30	NA	1.31	1.31
Women	NA	1.18	NA	1.09	1.12
With renal disease, ‡ *n*	1	1	0	2	4

WH Bay. Ann Intern Med 1987

Background

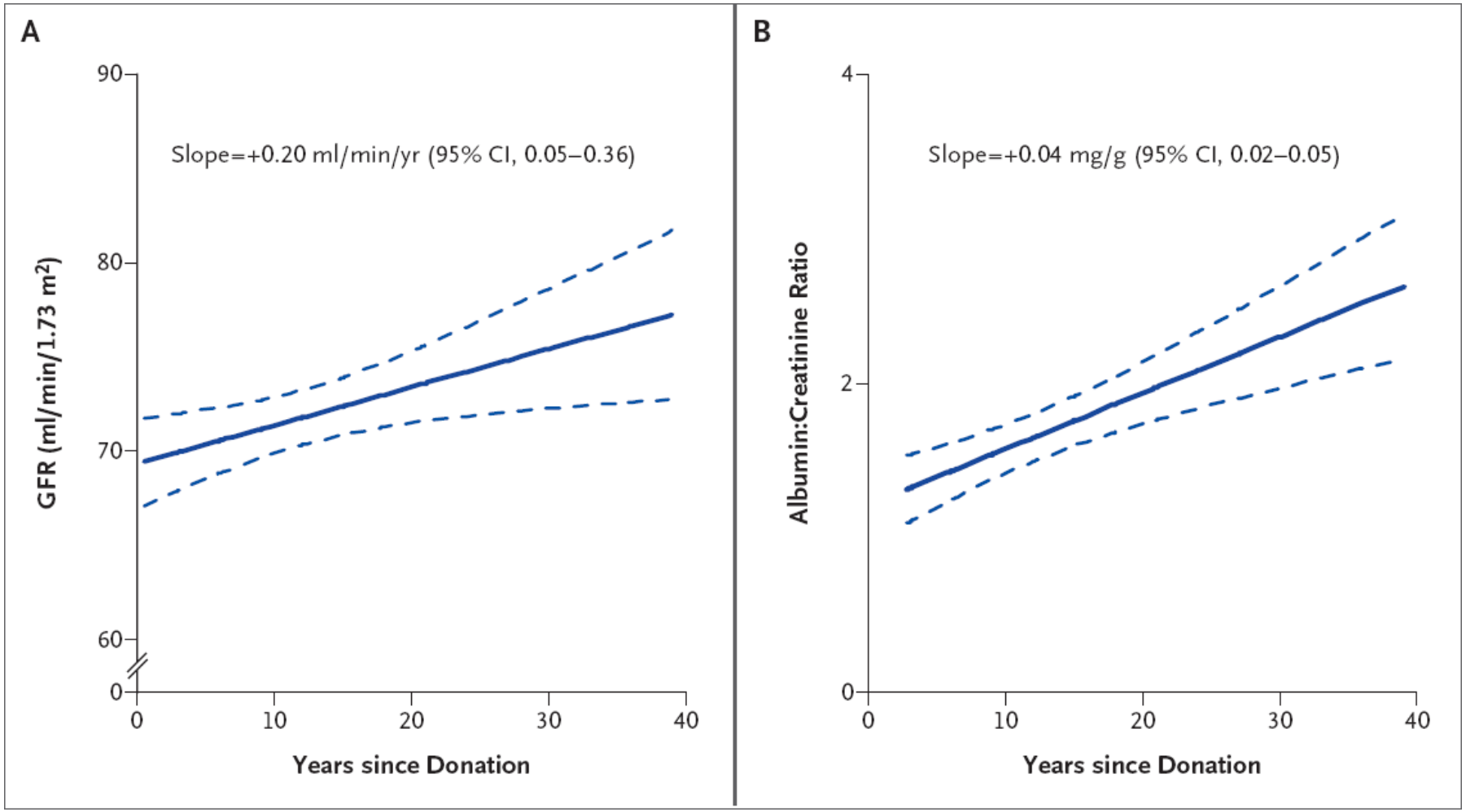


Controls= NHANES matched 1.1 for age, sex, ethnicity, BMI
Donors → 11 ESRD

Long-Term Consequences of Kidney Donation

Hassan N. Ibrahim, M.D., Robert Foley, M.B., B.S., LiPing Tan, M.D., Tyson Rogers, M.S., Robert F. Bailey, L.P.N., Hongfei Guo, Ph.D., Cynthia R. Gross, Ph.D., and Arthur J. Matas, M.D.

Background


A
90
80
70
60
0
GFR (ml/min/1.73 m²)
Slope=+0.20 ml/min/yr (95% CI, 0.05–0.36)
0
10
20
30
40
Years since Donation
B
4
2
0
Albumin:Creatinine Ratio
Slope=+0.04 mg/g (95% CI, 0.02–0.05)
0
10
20
30
40
Years since Donation

Background

Table 1. Multivariable Risk of Reduced Iohexol Glomerular Filtration Rate (GFR), Albuminuria, and Hypertension in 255 Kidney Donors.*

Variable	Odds Ratio (95% CI)	P Value
Iohexol GFR <60 ml/min/1.73m²	**14.5%**	
Age, per year	1.15 (1.08–1.21)	<0.001
Time since donation, per year	0.87 (0.79–0.95)	0.003
Body-mass index, per unit	1.12 (1.02–1.23)	0.02
Current smoker	0.42 (0.17–1.05)	0.06
Female sex	3.11 (1.11–8.67)	0.03
Albuminuria	**12.7%**	
Time since donation, per year	1.12 (1.05–1.20)	<0.001
Female sex	0.31 (0.12–0.79)	0.01
Hypertension requiring medication	**32.1%**	
Age, per year	1.09 (1.04–1.13)	<0.001
Body-mass index, per unit	1.12 (1.04–1.21)	0.003

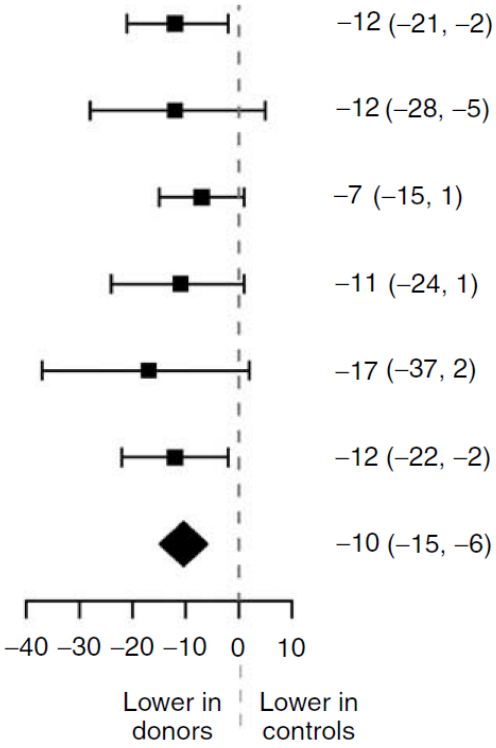
Background

Table 2. Current Health Status of Kidney Donors with Measured Glomerular Filtration Rate (GFR).*

Variable	Kidney Donors (N=255)	Controls† (N=255)	P Value
Age (yr)	52.9±9.9	52.9±9.9	
Female sex (%)	62.1	61.8	
White race (%)	99.2	99.2	
Body-mass index >30 (%)‡	29.3	29.3	
Blood pressure			
Systolic (mm Hg)	121.8±14.6	125.9±19.1	0.003
Diastolic (mm Hg)	73.0±8.9	71.0±16.5	0.07
Systolic ≥140 mm Hg or diastolic ≥90 mm Hg (%)	14.4	18.7	0.19
GFR (ml/min/1.73 m^2)§	63.7±11.3	81.6±18.5	<0.001
Urinary albumin-to-creatinine ratio			
Natural-log–transformed value	1.65±1.2	2.10±1.0	<0.001
>0.03 (%)	9.1	8.9	1.00
Hemoglobin (g/dl)	13.7±1.2	14.5±1.2	<0.001
Glucose (mg/dl)	90.9±11.9	102.8±33.1	<0.001
Cholesterol (mg/dl)	186.2±33.1	205.2±41.1	<0.001
Triglycerides (mg/dl)	124.5±95.6	174.3±182.5	<0.001
High-density lipoprotein cholesterol (mg/dl)	50.4±16.5	54.5±16.4	0.001
Clinical conditions (%)¶			
Diabetes	3.1	5.9	0.10
Cancer	8.2	14.5	0.01
Coronary heart disease	4.3	3.9	0.81
Cerebrovascular accident or transient ischemic attack	0.4	1.9	0.10
Use of antihypertensive drugs (%)¶	24.7	28.8	0.83
Current smoker (%)¶	14.5	21.5	0.03

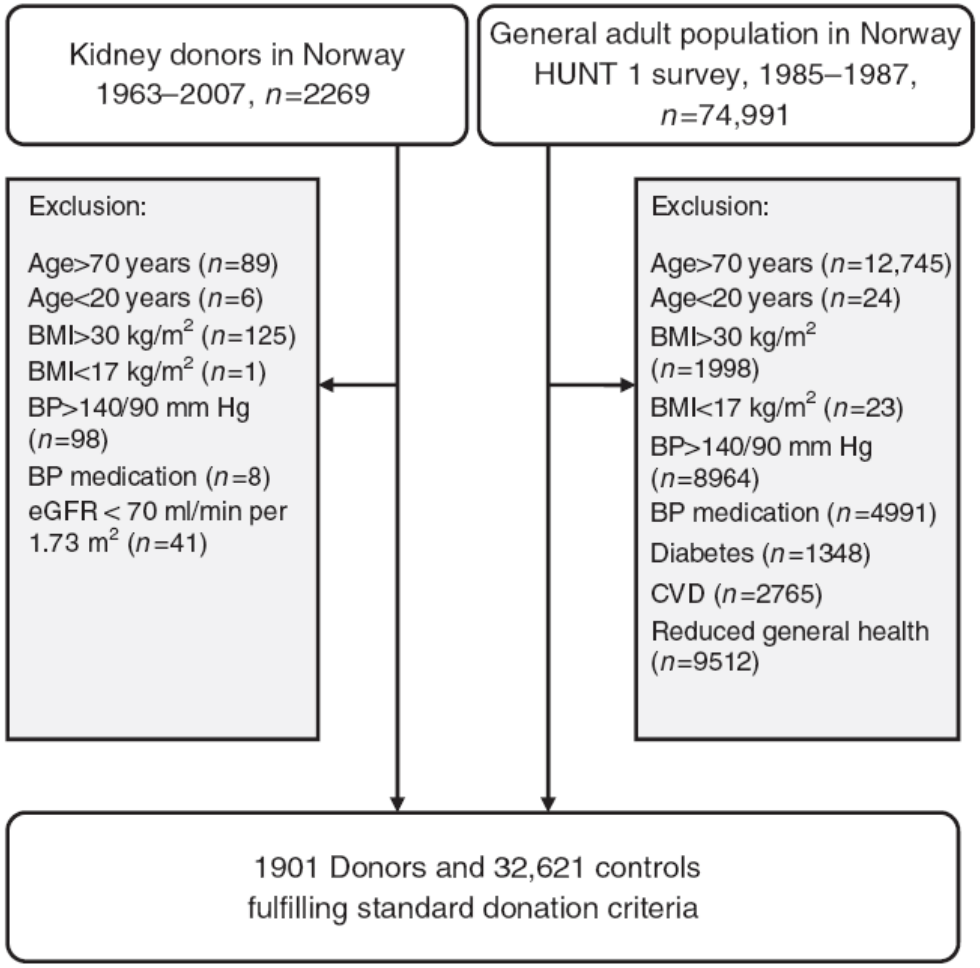
Background

Source*	GFR Assessment	Donors, post-donation: Years after Donation Mean (range)	Donors, post-donation: GFR (ml/min) (per 1.73 m²) *N* mean (s.d.)	Controls: GFR (ml/min) (per 1.73 m²) *N* mean (s.d.)	GFR mean difference, 95% CI ml/min (per 1.73 m²)
O'Donnell *et al.*[37]	24 h urine	6 (3–18)	33 100 (22)	33 111 (17)	−12 (−21, −2)
D'Almeida *et al.*[45]	24 h urine	7 (1–14)	59 86 (37)	28 98 (37)	−12 (−28, −5)
Najarian *et al.*[51]	24 h urine	8 (1–19)	57 82 (15)	50 89 (23)	−7 (−15, 1)
Undurraga *et al.*[54]	Cockroft-Gault	11 (1–21)	30 86 (22)	30 97 (27)	−11 (−24, 1)
Williams *et al.*[58]	24 h urine	13 (10–18)	38 86 (39)	17 103 (31)	−17 (−37, 2)
Watnick *et al.*[59]	Inulin	13 (9–18)	22 66 (14)	31 78 (22)	−12 (−22, −2)
Pooled estimate			239 84 (11)	189 96 (14)	−10 (−15, −6)



Garg. KI 2006

Background

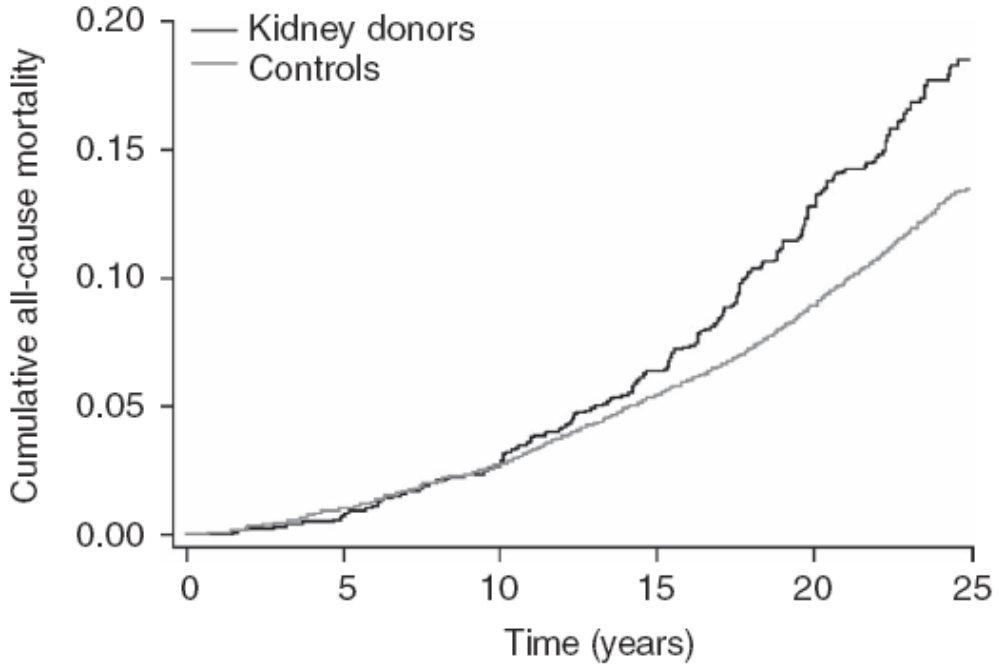


	Kidney donors	Controls
Age, years	46.0 ± 11.5	37.6 ± 11.7
	n = 1901	n = 32,621
Male gender, %	41.0	46.9
	n = 1901	n = 32,621
Current smoking, %	41.5	39.5
	n = 1375	n = 25,993
Systolic BP, mm Hg	123.3 ± 10.0	121.4 ± 10.4
	n = 1768	n = 31,398
Diastolic BP, mm Hg	77.4 ± 7.2	77.2 ± 7.9
	n = 1768	n = 31,394
BMI, kg/m^2	24.2 ± 2.8	23.5 ± 2.6
	n = 1558	n = 31,421

Long-term risks for kidney donors

Geir Mjøen[1], Stein Hallan[2,3], Anders Hartmann[1], Aksel Foss[1], Karsten Midtvedt[1], Ole Øyen[1], Anna Reisæter[1], Per Pfeffer[1], Trond Jenssen[1], Torbjørn Leivestad[4], Pål- Dag Line[1], Magnus Øvrehus[2], Dag Olav Dale[1], Hege Pihlstrøm[1], Ingar Holme[5], Friedo W. Dekker[6] and Hallvard Holdaas[1]

Background



HR 1.3 (95%CI: 1.11-1.52)

HR_{cv} 1.40 (95%CI 1.03-1.91)

N ESRD=9 vs 22
→302/1mio p-an
vs 100/1mio p-an

Table 2c | Cox regression analysis for risk of end-stage renal disease in kidney donors versus controls

	Unadjusted ($n = 25{,}063$–$35{,}222$)	Adjusted 1[a] ($n = 31/34{,}522$)	Adjusted 2[b] ($n = 31/34{,}522$)
Kidney donation	18.99 (8.63–41.76, $P<0.001$)	11.42 (4.43–29.40, $P<0.001$)	11.38 (4.37–29.63, $P<0.001$)
Inclusion year	0.76 (0.70–0.83, $P<0.001$)	0.91 (0.83–1.00, $P=0.04$)	0.90 (0.82–0.99, $P=0.03$)
Age, years	1.04 (1.01–1.07, $P=0.003$)	1.03 (1.00–1.06, $P=0.04$)	1.02 (0.99–1.05, $P=0.13$)
Male	0.94 (0.46–1.91, $P=0.86$)	1.04 (0.51–2.11, $P=0.10$)	0.90 (0.43–1.88, $P=0.77$)
Systolic BP	1.03 (1.00–1.07, $P=0.14$)	—	1.01 (1.00–1.06, $P=0.03$)
Smoking	1.09 (0.48–2.46, $P=0.83$)	—	1.19 (0.51–2.76, $P=0.68$)
BMI	1.19 (1.02–1.38, $P=0.03$)	—	1.13 (0.96–1.32, $P=0.14$)

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- Aim: Understand the risk of ESRD following live donation

  comparing incidence in donors and healthy non donors

- Population: 2 cohort studies

  all adult donors in USA from 1994-2011 (OPTN database)

  vs

  selected nondonors NHANES III from 1988-1994 (n= 9364 of 20'024)

  matched 1:1 per **gender, race, smoking**, age, education, bmi, sbp

- Outcome = ESRD defined as dialysis start or transplant

  use of census database

  - ESRD certificates from CMS's
  - Transplant network's kidney waiting list (for donors only!)
  - Profile and death certicication from CMS's (for controls only!)

Statistiques

- **Cumulative Incidence of ESRD**

  → Kaplan-Meier curves in years

- **Lifetime risk of ESRD** in donors, healthy and unscreened nondonors

  → Kaplan-Meier curves in age and years after donation or NHANES enrollment

- **Absolute risk increase o ESRD**

  = cumulative incidence donors – cumulative incidence nondonors

- **Bootstrap methods** = Resample - replicate healthy nondonors to obtain n

  Linear and logistic regression for population comparisons

  Log-rank test for ESRD risk within donors sub-groups

Résultats

Characteristics[a]	Live Kidney Donors, % (n = 96 217)	Matched Healthy Nondonors, % (n = 96 217)[b]	*P* Value
Age, mean (SD), y	40.2 (11.1)	40.2 (11.1)	.90
18-39	48.2	48.0	.70
40-49	30.1	29.8	
50-59	17.5	17.9	
≥60	4.2	4.3	
Women	59.0	59.0	>.99
Race/ethnicity[c]			
White/other	74.6	74.6	>.99
Black	12.9	12.9	
Hispanic	12.5	12.5	
Educational status[d]			
≤High school	36.3	42.5	<.001
Attended college	28.4	25.8	
College graduate	25.1	21.0	
Post college	10.2	10.7	
BMI[e]			
Mean (SD)	26.7 (7.5)	26.2 (4.8)	<.001
<24	33.0	40.1	<.001
25-29	41.8	38.6	
≥30	25.2	21.3	

Blood pressure, mm Hg[f]			
Systolic			
Mean (SD)	121.0 (16.3)	119.2 (12.5)	<.001
<120	44.3	51.1	<.001
120-139	46.7	43.0	
≥140	9.0	5.9	
Diastolic			
Mean (SD)	73.6 (11.5)	75.5 (10.2)	<.001
<80	69.0	62.1	<.001
80-89	26.6	30.3	
≥90	4.4	7.6	
Smoker[g]	24.2	10.4	<.001
Creatinine, mean (SD), mg/dL	0.9 (0.2)	1.0 (0.2)	<.001
eGFR, mL/min/1.73 m^{2},[h]			
Mean (SD)	100.7 (23.7)	86.4 (24.6)	<.001
<80	22.1	41.1	<.001
80-89	7.2	10.2	
≥90	70.7	48.7	
Urine albumin:creatinine ratio, mean (SD), µg/mg		0.04 (0.6)	

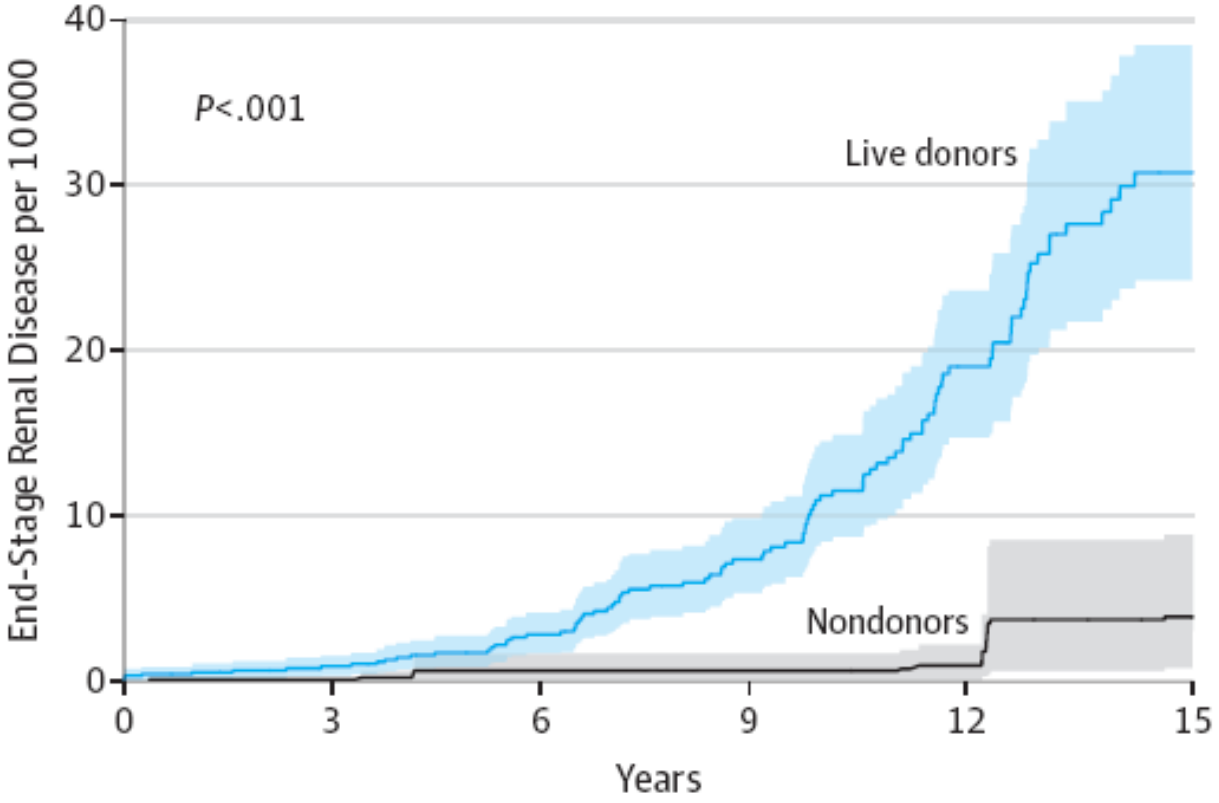
Median follow-up 7.5y , ESRD in a mean of 8.6y.

	No. of Donors	Cases of ESRD	Cumulative Incidence of ESRD at 15 Years per 10 000 (95% CI)
All donors[a]	96 217	99	30.8 (24.3-38.5)
Age at donation, y			
18-39	46 344	50	29.4 (21.4-40.2)
40-49	28 994	17	17.4 (10.1-30.0)
50-59	16 840	25	54.6 (34.8-85.4)
≥60	4039	7	70.2 (30.4-161.8)
Sex			
Women	56 775	42	21.1 (14.9-29.9)
Men	39 442	57	44.1 (32.9-59.1)
Race			
White/other	71 769	50	22.7 (15.6-30.1)
Black	12 387	36	74.7 (47.8-105.8)
Hispanic	12 061	13	32.6 (17.9-59.1)
Relationship to recipient[b]			
Biological	64 897	83	34.1 (26.9-43.3)
Nonbiological	31 081	16	15.1 (08.7-26.3)

Vs 36 ESRD in matched nondonors in 10.7y (but 17 in 9367 !)

Cumulative incidence ESRD - all

A Cumulative incidence of end-stage renal disease

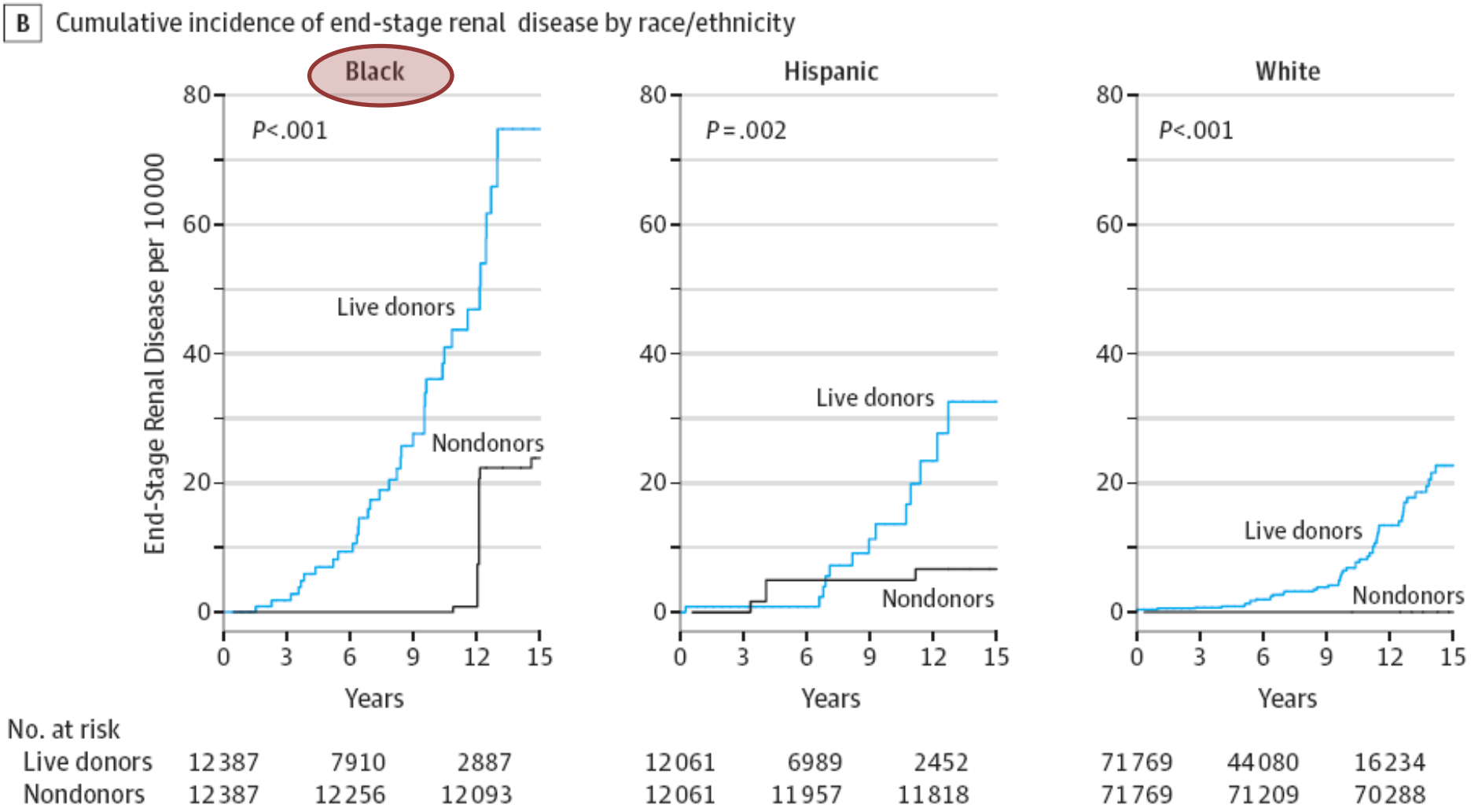


30.8(24.3-38.5)

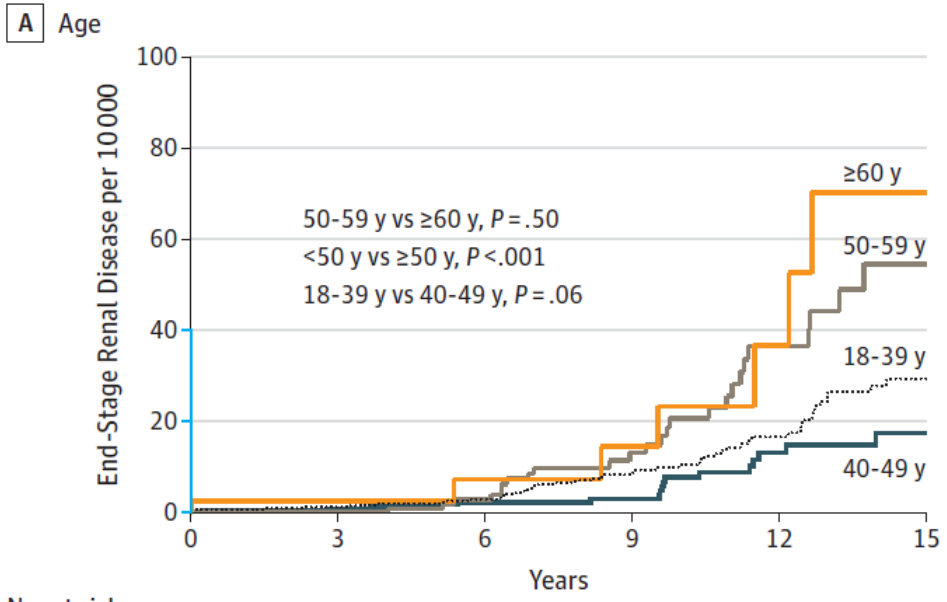
3.9(0.8-8.9)

No. at risk						
Live donors	96 217	77 587	58 979	39 231	21 573	8781
Nondonors	96 217	95 930	95 422	94 734	94 199	50 124

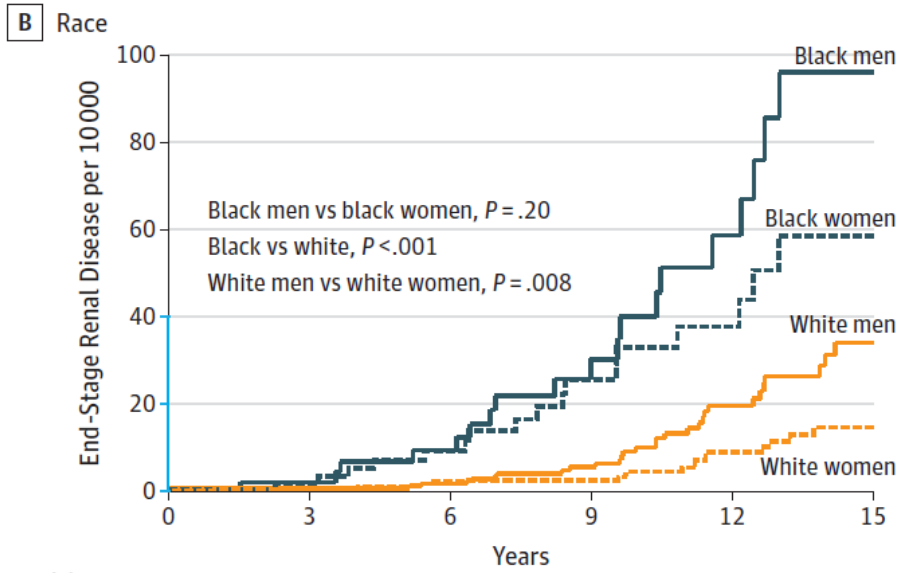
Cumulative incidence ESRD – by race



Cumulative incidence ESRD – by subgroups

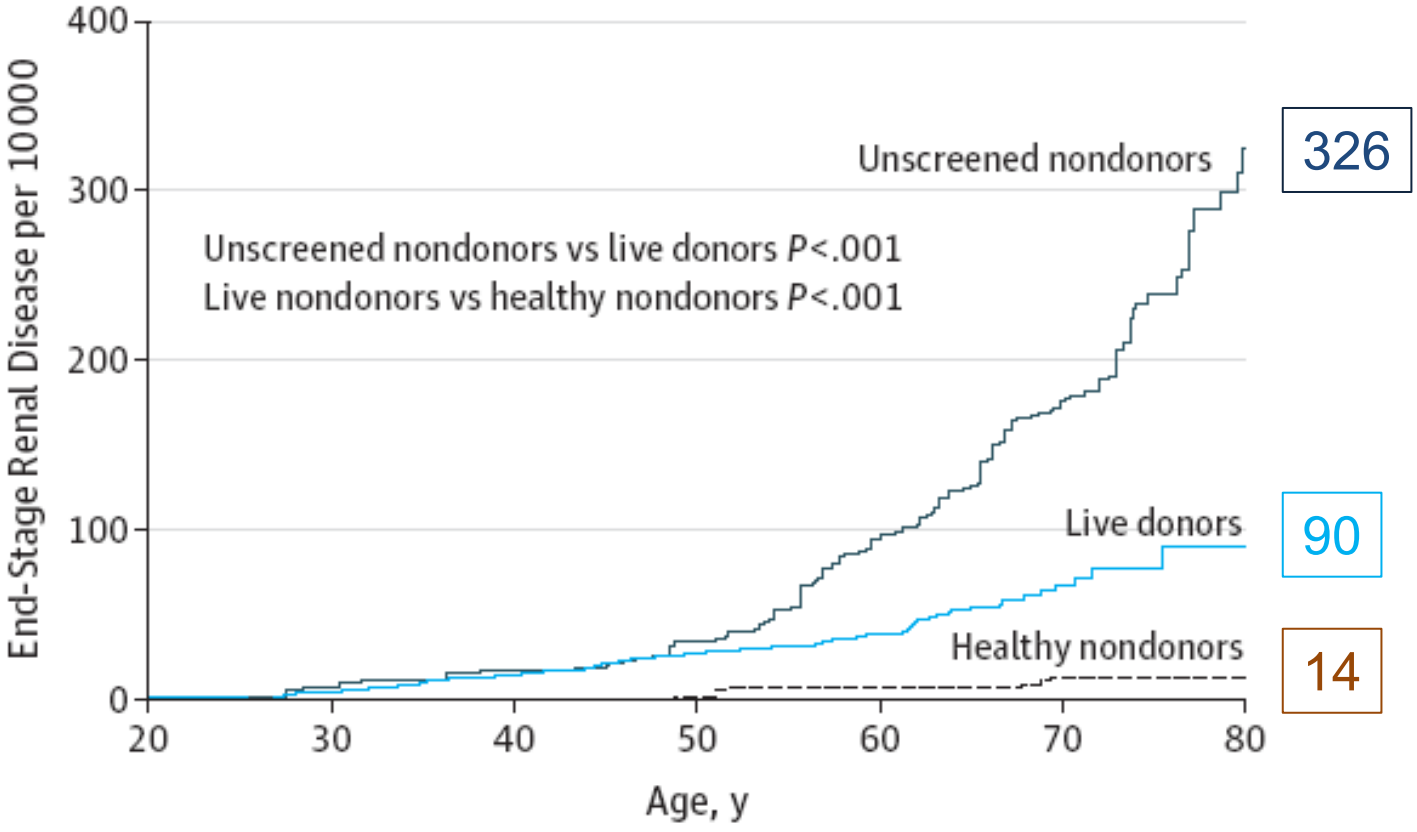


No. at risk Age, y						
≥60	4039	2858	1967	1223	656	244
50-59	16840	12881	9241	5887	3015	1101
40-49	28994	23621	17929	11728	6261	2549
18-39	46344	38227	29842	20393	11641	4887



No. at risk						
Black						
Men	5330	4409	3449	2247	1238	470
Women	7057	5773	4461	2968	1649	680
White						
Men	28941	23689	18120	12206	6744	2784
Women	42828	34266	25960	17278	9490	3886

Estimated lifetime Risk



No. at risk

Unscreened nondonor	1296	18436	36272	40863	26982	7990	647
Live donor	1143	13144	22647	22944	12151	2575	218
Healthy nondonor	1306	18487	36397	40961	28358	9011	870

Discussion - conclusions

In the US population, during 15 yeares follow-up:

- Donors have higher risk than healthy nondonors but lower than the general population
- Race is a risk factor

✓ Large sample
✓ Matched and selected healthy nondonors
- Healthy non donors not so healthy?
- Follow up not long enough?
- Different time frame between the 2 cohorts

Edito…

- Main problem: non donor group

  Ideal study : randomized patient to donate or not
- Undetected cases of ESRD in donors emigrating outside
- Low ESRD: inferences difficult in subgroups
- Sofisticated matching techniques to increase healthy nondonors number:

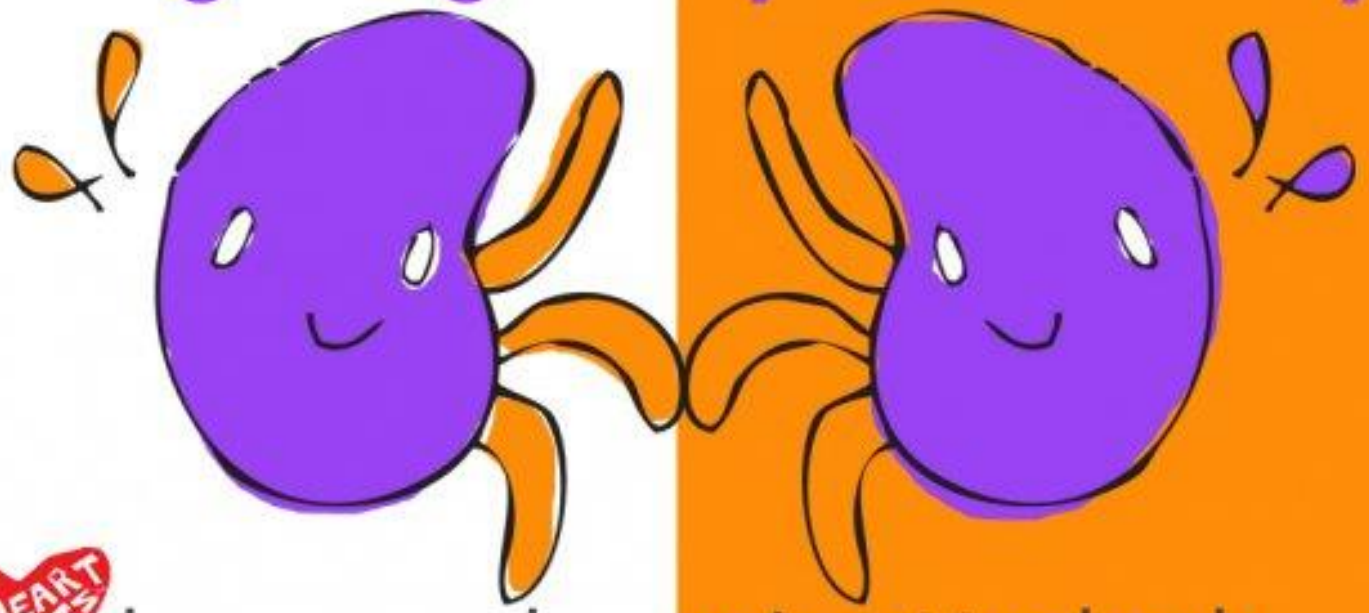
  →↓incidence in healthy (3.9 vs 18.2/10'000) but ↑ incidence in donors (30.8 vs10.3/10'000)
- Longer fup in controls:

  →many inclusions of those without event ↓ incidence
- Nondonors die before developing ESRD
- In controls those in the list not considered

But after all, risk of ESRD after donation remains low!!!

THANK YOU SO MUCH

for giving me your kidney



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