DOPPS
Dialysis Outcomes and Practice Patterns Study

CKDOPPS
Chronic Kidney Disease Outcomes and Practice Patterns Study

CKD rein
Préserver la santé rénale

Aligning care to improve management of CKD complications: from before to after the transition to dialysis

Christian Combe

Service de Néphrologie Transplantation Dialyse Aphérèses

Centre Hospitalier Universitaire & Université, Bordeaux, France

université de BORDEAUX

CHU BDX CENTRE HOSPITALIER UNIVERSITAIRE BORDEAUX

Arbor Research Collaborative for Health

Disclosure Information

Category	Disclosure Information
Employer	Université de Bordeaux and CHU de Bordeaux
Consultancy	Travere ; Rhythm

DOPPS
Dialysis Outcomes and Practice Patterns Study

CKDOPPS
Chronic Kidney Disease Outcomes and Practice Patterns Study

CKD REIN

Since 1996 in the US, 1998 elswhere
>10,000 patients on line
➔ Several dozens of thousands patients
➔ >300 clinics

>12,000 pts
Brazil, France, Germany, Japan, US
140 clinics
Follow-up ≥ 3 years

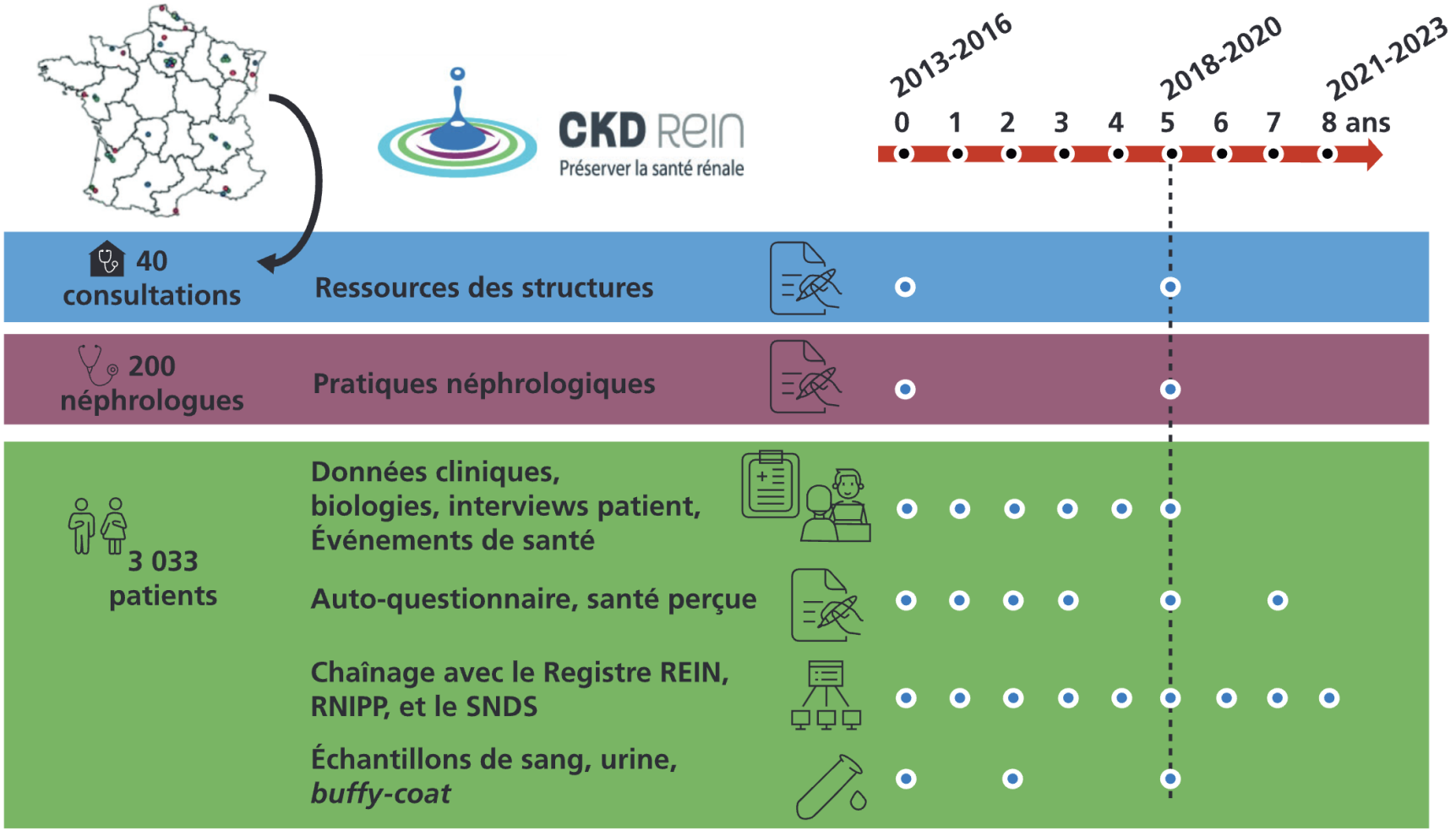
CKDopps France
40 clinics, 3,033 pts
Follow-up 5 years.
Complete
Biosamples and specific questionnaires

Young et al.The Dialysis Outcomes and Practice Patterns Study: An international hemodialysis study. Kidney Int Suppl 2000;74:S74-S81

Mariani et al. The CKD Outcomes and Practice Patterns Study (CKDopps): Rationale and Methods. Am J Kidney Dis 2016;68:402–13

Stengel, Combe et al. The French Chronic Kidney Disease-Renal Epidemiology and Information Network (CKD-REIN) cohort study. Nephrol Dial Transplant 2014;29:1500-7

The CKD REIN cohort (N = 3 033)



CKD REIN

Alencar de Pinho et al. Nephrol Ther 2023;19:233-250

From advanced CKD to…

- **Transplantation**
- **Dialysis**
- **Conservative care**

➔ Information of patients: a complex process

Preparation of ESRD care

Data collected at inclusion by CRAs from patients files

eGFR	Total N=3,033 (%)	<20 N=470 (%)	20-30 N=893 (%)	≥30 N=1670 (%)
Education on therapeutic options for ESRD in the 6-mo interval before inclusion	14.1	38.3	13.1	4.1
Patient informed on hemodialysis	14.6	42.1	19.5	4.3
Patient informed on peritoneal dialysis	11.5	33.4	16.2	2.8
Patient informed on renal transplantation	11.0	31.3	15.7	2.8
First modality of ESRD treatment chosen	7.0	19.9	5.2	0.6
Conservative treatment without HD or Tx	4.9	9.4	4.3	2.6

Preparation of Kidney Replacement Therapy (KRT)

*Data collected at inclusion by **CRAs** from patients files*

eGFR	Total N=3,033 (%)	<20 N=470 (%)	20-30 N=893 (%)	≥30 N=1670 (%)
Vascular access created	2.3	8.7	2.6	0.4
Evaluation of vessels for creation of AV access	1.3	5.5	1.3	0.1
Patient on waiting list	1.6	8.1	0.7	0.2
Planned living-donor transplantation	1.7	7.7	1.6	0.1

Planning of Kidney Replacement Therapy (or not)

Data collected from nephrologists (n=137)

- "Which KRT options are typically discussed with patients by you and your team? Tick all that apply"

Modality	*N*	%
In center HD	*108*	96%
Nocturnal HD	*52*	46%
Home HD	*69*	62%
Peritoneal Dialysis	*107*	96%
Living Donor Transplantation	*109*	97%
Deceased Donor Transplantation	*108*	96%
Conservative Treatment (including palliative care)	*104*	93%

Discussion and planning of KRT (or not)

Data collected from patients

- Analysis restricted to pts with eGFR < 30 at inclusion

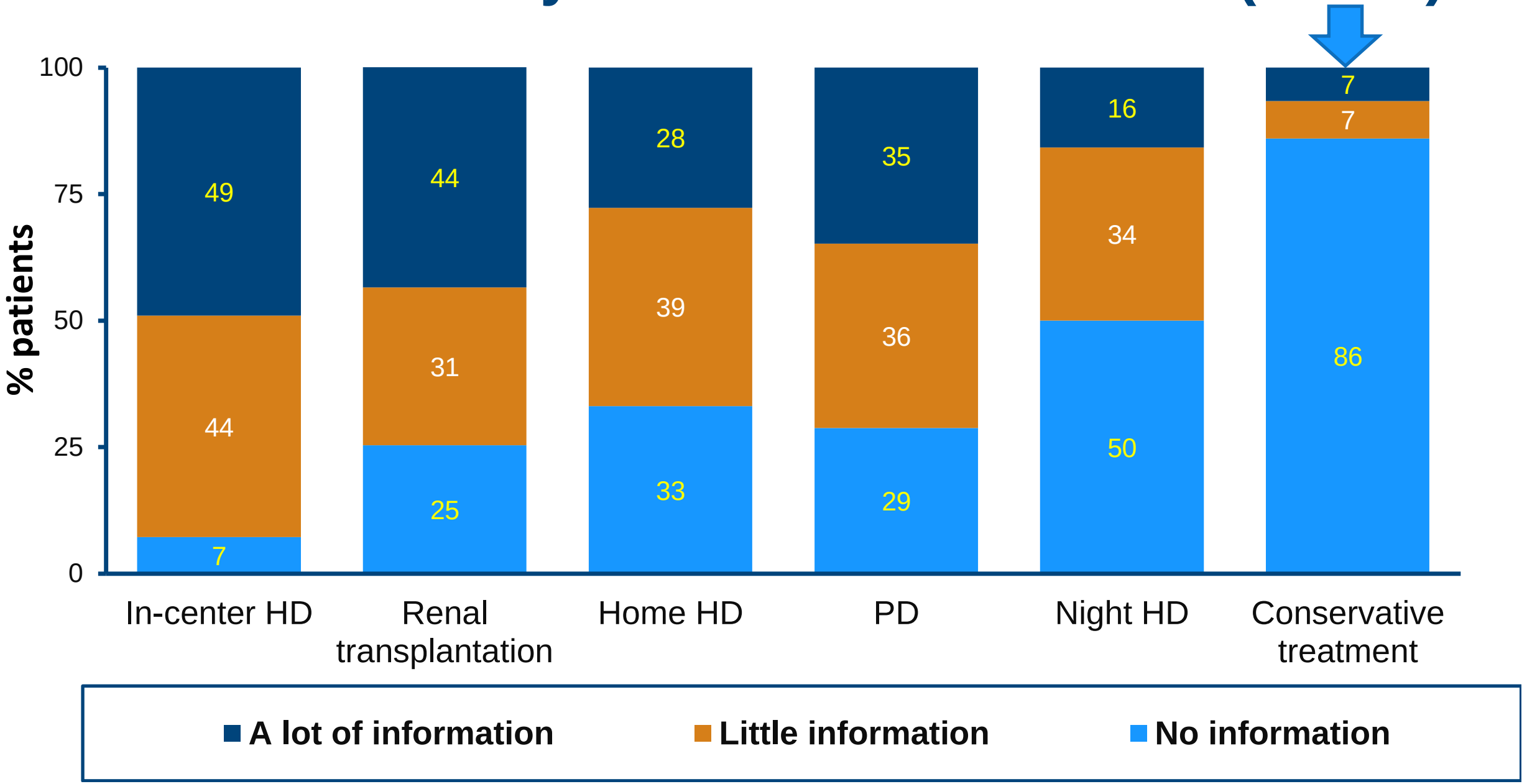
	Total N=1,204		eGFR <20 N=413		eGFR ≥20 N=791	
	N	%	*N*	%	*N*	%
Option(s) discussed between patient and physician (several possible answers)						
In-center or satellite HD	*285*	23.7	*139*	33.7	*146*	18.5
Home HD	*121*	10.0	*72*	17.4	*49*	6.2
Peritoneal Dialysis	*166*	13.8	*94*	22.8	*72*	9.1
Kidney Transplantation	*217*	18.0	*111*	26.9	*106*	13.4
Living-donor Transplantation	*128*	10.6	*80*	19.4	*48*	6.1
None of these options	*56*	4.7	*13*	3.1	*43*	5.4

62%

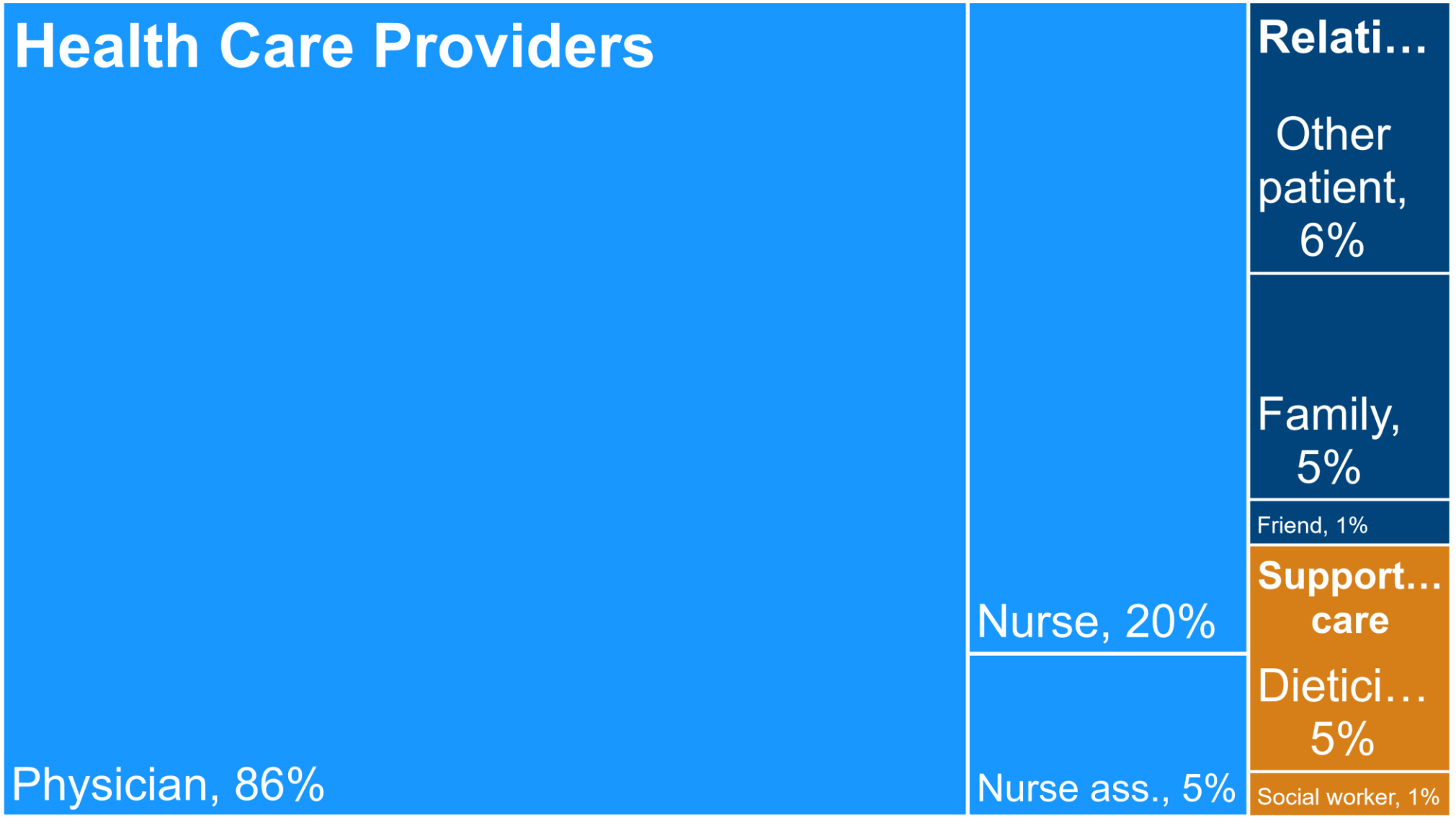
97%

Nephrologists answers

Patients: summary of information on KRT (or not)



Who gave information on KRT options?

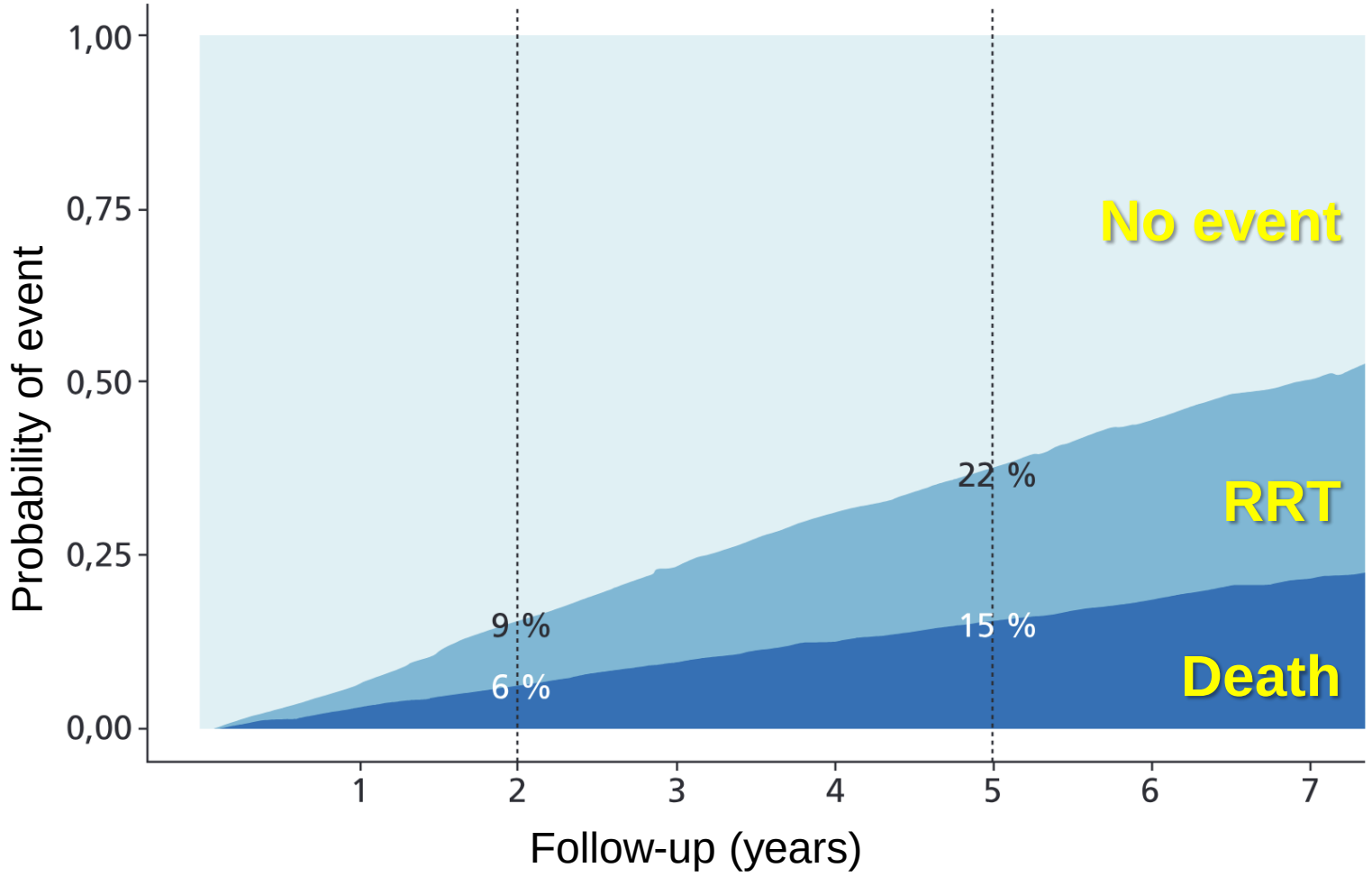


CKD Rein

Advanced Chronic Kidney Disease: competing risks between death and end-stage renal failure

CKDOPPS

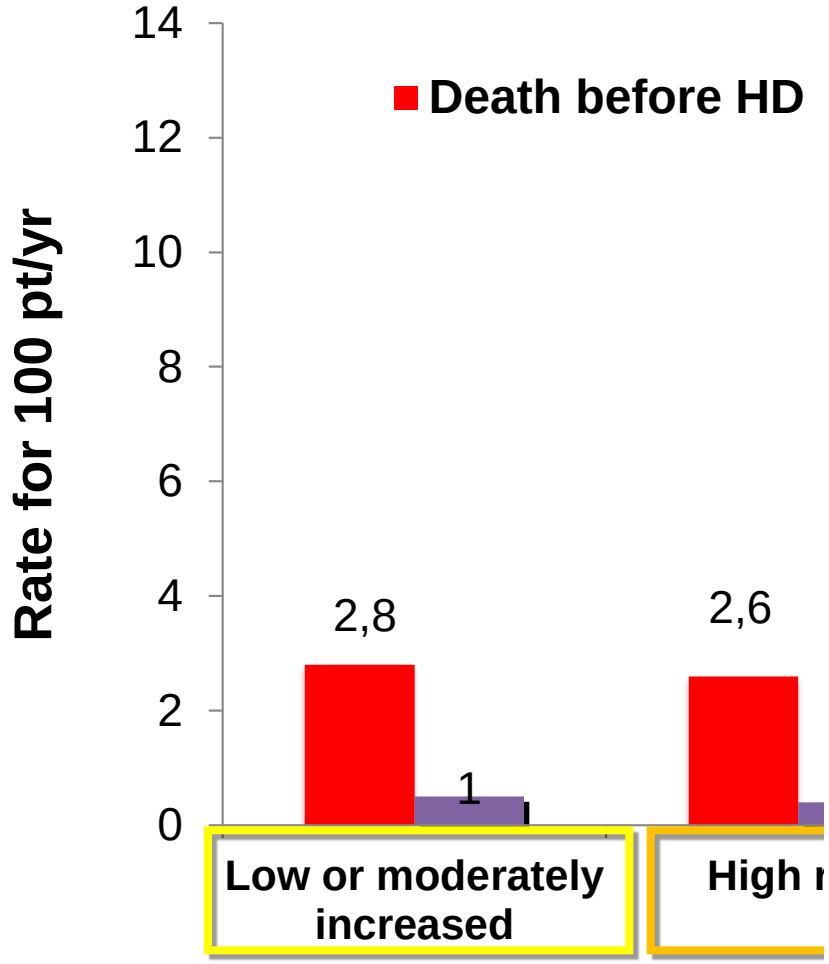
Cumulatice incidence of kidney failure with RRT and death in CKD REIN (N = 3 033)



CKD REIN

Alencar de Pinho et al. Nephrol Ther 2023;19:233-250

2-year risk of ESRD and Death, by KDIGO risk category



KDIGO 2(

Prognosis of CKD by GFR and Albuminuria Categories: KDIGO 2012

GFR categories (ml/min/ 1.73 m²) Description and range				Persistent albuminuria categories Description and range		
				A1	A2	A3
				Normal to mildly increased	Moderately increased	Severely increased
				< 30 mg/g < 3 mg/mmol	30-300 mg/g 3-30 mg/mmol	> 300 mg/g > 30 mg/mmol
	G1	Normal or high	≥ 90			
	G2	Mildly decreased	60-89			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	< 15			

Green: low risk (if no other markers of kidney disease, no CKD); Yellow: moderately increased risk; Orange: high risk; Red, very high risk.

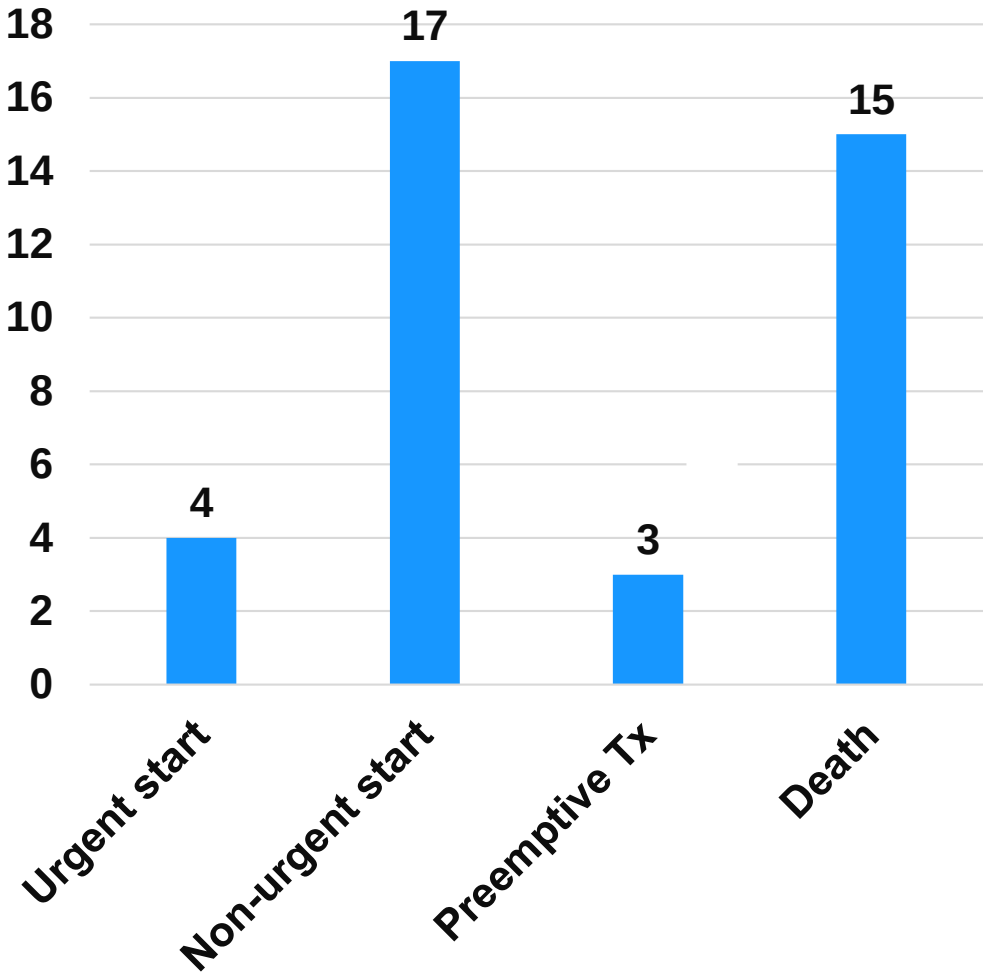
CKD REIN

CKD-REIN data 2018

Urgent-start dialysis:
to be avoided… but not that simple

CKD Rein

Urgent-start dialysis in patients referred early to a nephrologist in CKD-REIN



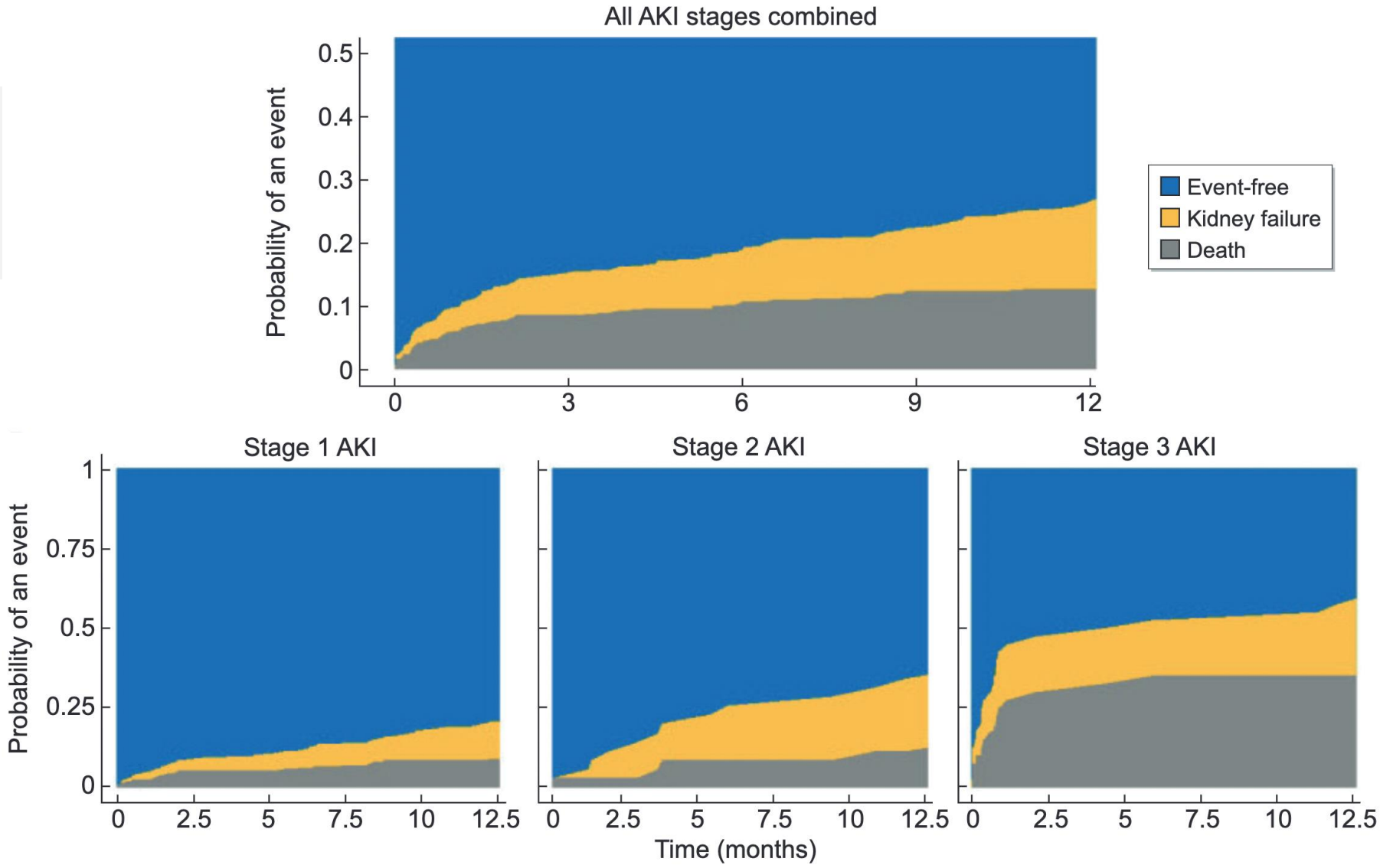
Odds ratio for urgent start dialysis

Variable	HR	95%CI
Patients living alone	2.14	1.08–4.25
Low health literacy	2.22	1.28–3.84
Heart failure	2.60	1.47–4.57
Hyperpolypharmacy taking >10 drugs	2.14	1.17–3.90
Age	NS	
Lower eGFR at initiation	NS	
Planned dialysis modality	0.46	0.19–1.10
Each nephrologist visit in the 12 mo before dialysis	0.81	0.70–0.94

Fages et al. Nephrol Dial Transpl 2021;36:1500-1510

Cumulative incidence of kidney failure and death after a first Acute on CKD event in all AKI stages combined and according to AKI severity (KDIGO stages)

CKD-REIN study
3033 pts stages 3 to 5
Follow-up 2013–2020

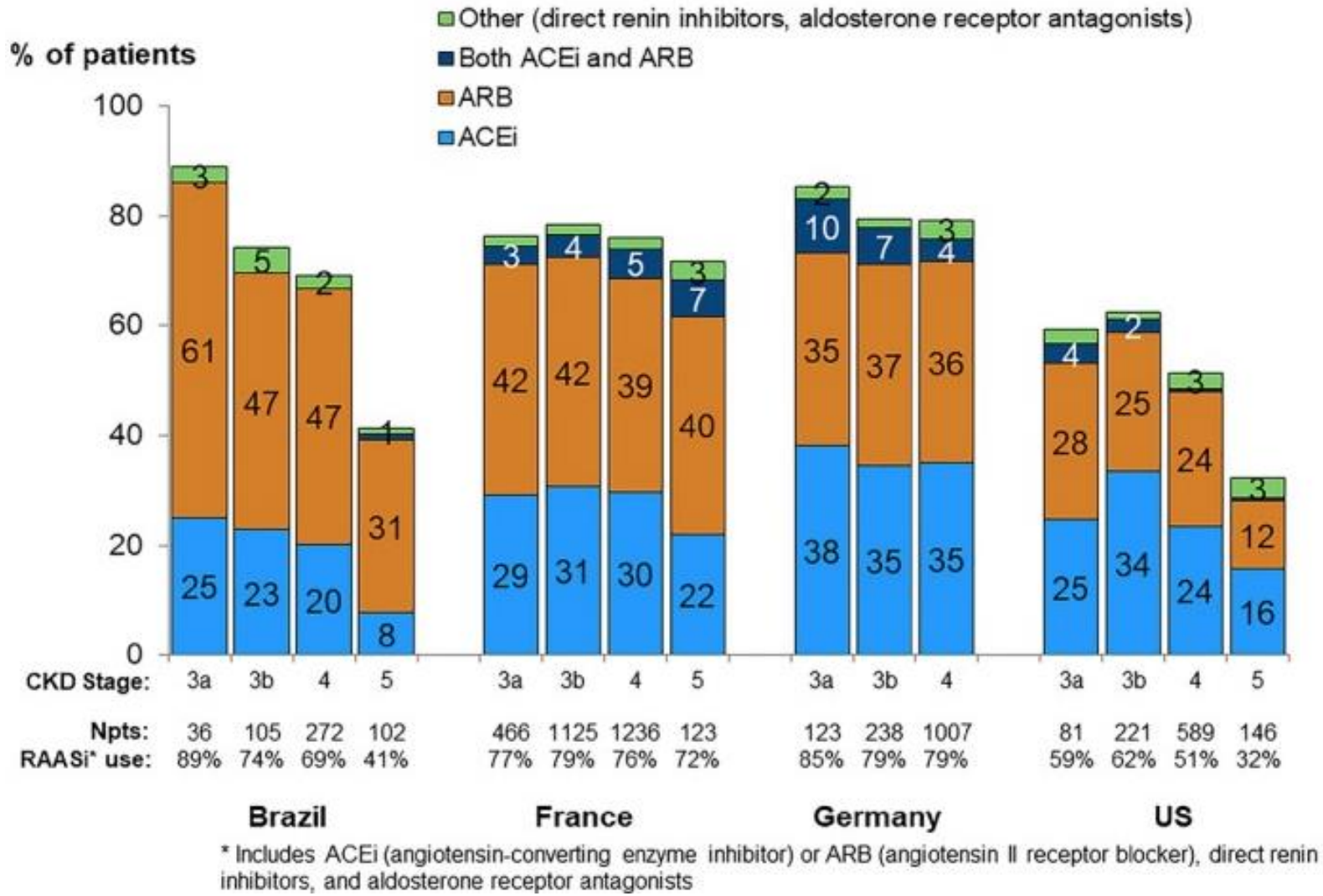


Hamroun et al. Nephrol Dial Transpl 2021;37:1700-9

CKD REIN

Medications used in advanced Chronic Kidney Disease might be useful when patients are on hemodialysis

Prevalence of RAASi prescription by CKD stage and country



* Includes ACEi (angiotensin-converting enzyme inhibitor) or ARB (angiotensin II receptor blocker), direct renin inhibitors, and aldosterone receptor antagonists

CKDOPPS

Pecoits-Filho R et al. J Clin Hyperten 2019

DOPPS: possible survival benefit of RAAS inhibitors for hemodialysis patients

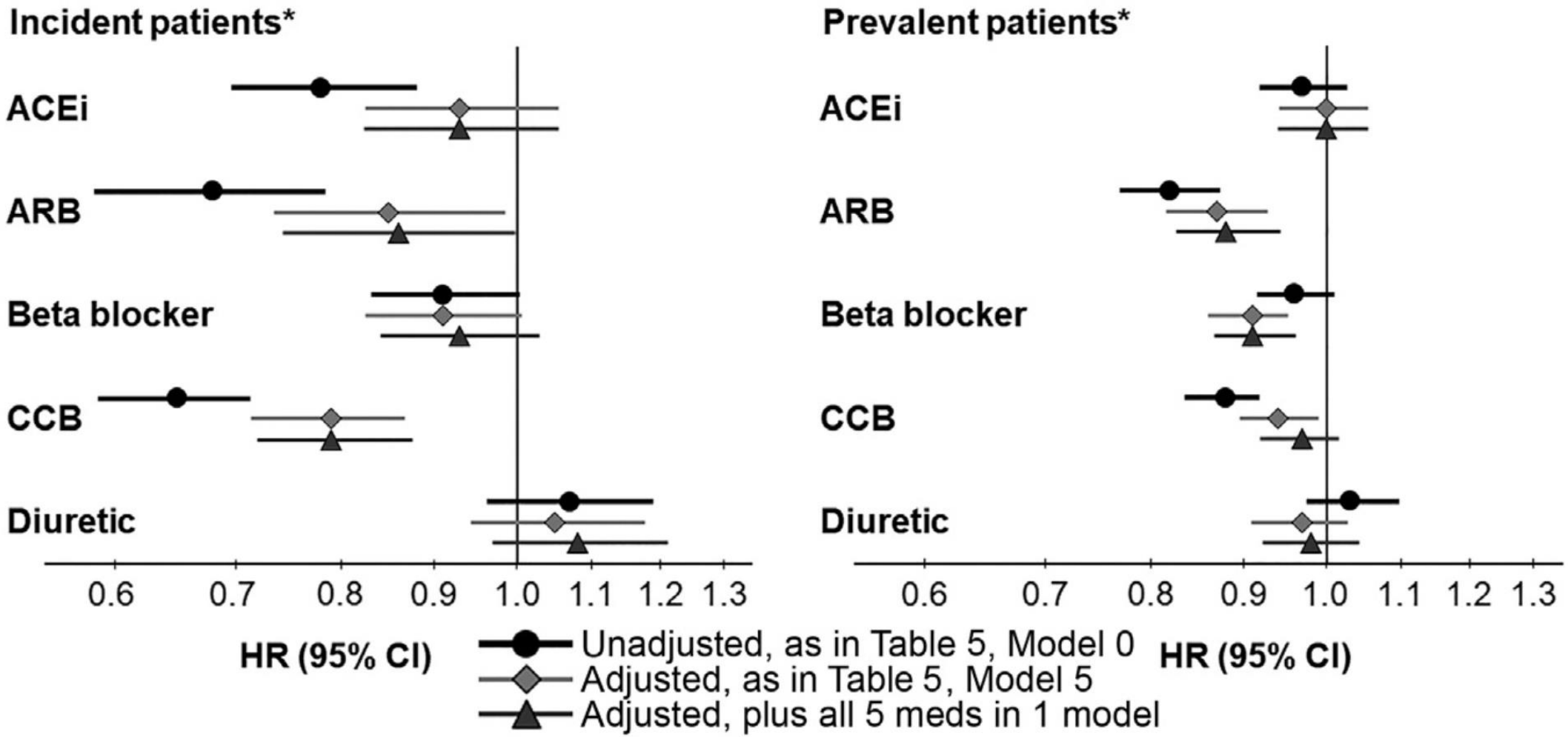
Association between RAASi and all-cause mortality by level of adjustment

Model	Covariate adjustment	Incident HD patients[a] (*N* = 11,421; 1906 events)	Prevalent HD patients[a] (*N* = 37,124; 8217 events)
0	Stratified by DOPPS phase, country	0.71 (0.64–0.78)	0.89 (0.85–0.94)
1	M0 + age	0.82 (0.74–0.90)	0.95 (0.91–1.00)
2	M1 + sex, black race, vintage	0.82 (0.74–0.90)	0.95 (0.91–1.00)
3	M2 + 13 comorbidities[b]	0.86 (0.78–0.95)	0.95 (0.90–0.99)
4	M3 + HD treatments[c]	0.89 (0.80–0.98)	0.94 (0.89–0.99)
5	M4 + BMI, albumin, calcium, phosphorus, hemoglobin	0.88 (0.80–0.98)	0.93 (0.88–0.97)
6	M5 + beta-blocker, CCB, diuretic	0.89 (0.80–0.99)	0.94 (0.90–0.99)

DOPPS

Karaboyas et al. Kidney Int. 2018;94:589-98

DOPPS: possible survival benefit of RAAS inhibitors and other antihypertensive drugs for HD patients

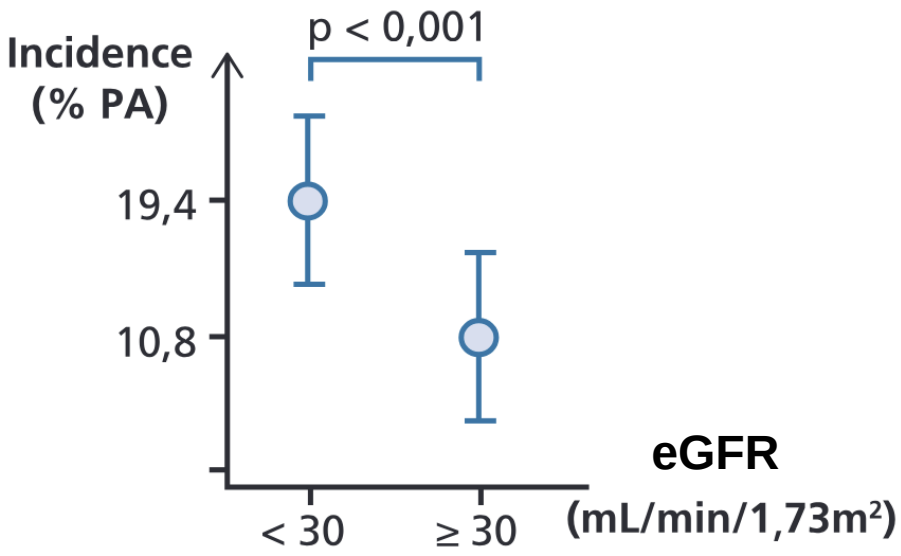


DOPPS

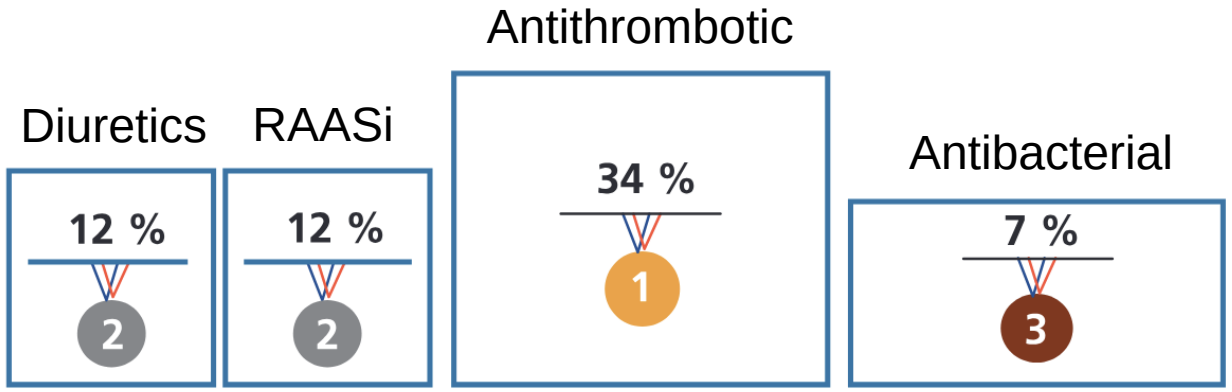
Karaboyas et al. Kidney Int. 2018;94:589-98

Adverse drug reactions in CKD REIN (N = 3 033)

Incidence of adverse effects of all severity according to baseline eGFR



Pharmacological classes most often responsible for serious adverse effects



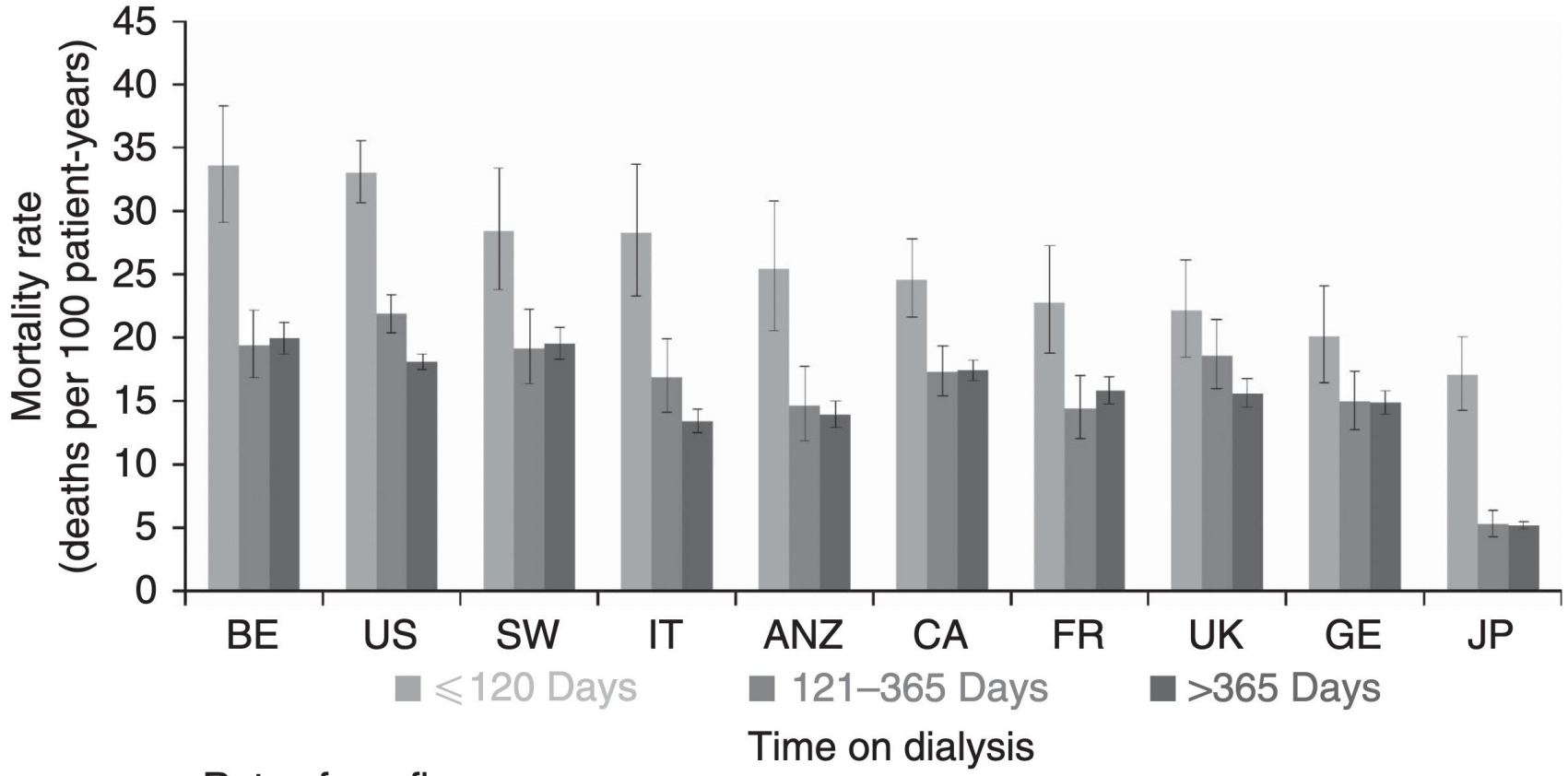
CKD REIN

Alencar de Pinho et al. Nephrol Ther 2023;19:233-250

Hemodialysis start: a high-risk period!

Worldwide, mortality risk is high soon after initiation of hemodialysis in the Dialysis Outcomes and Practice Patterns Study

86,886 pts
11 countries
Early HD period



Rates from figure

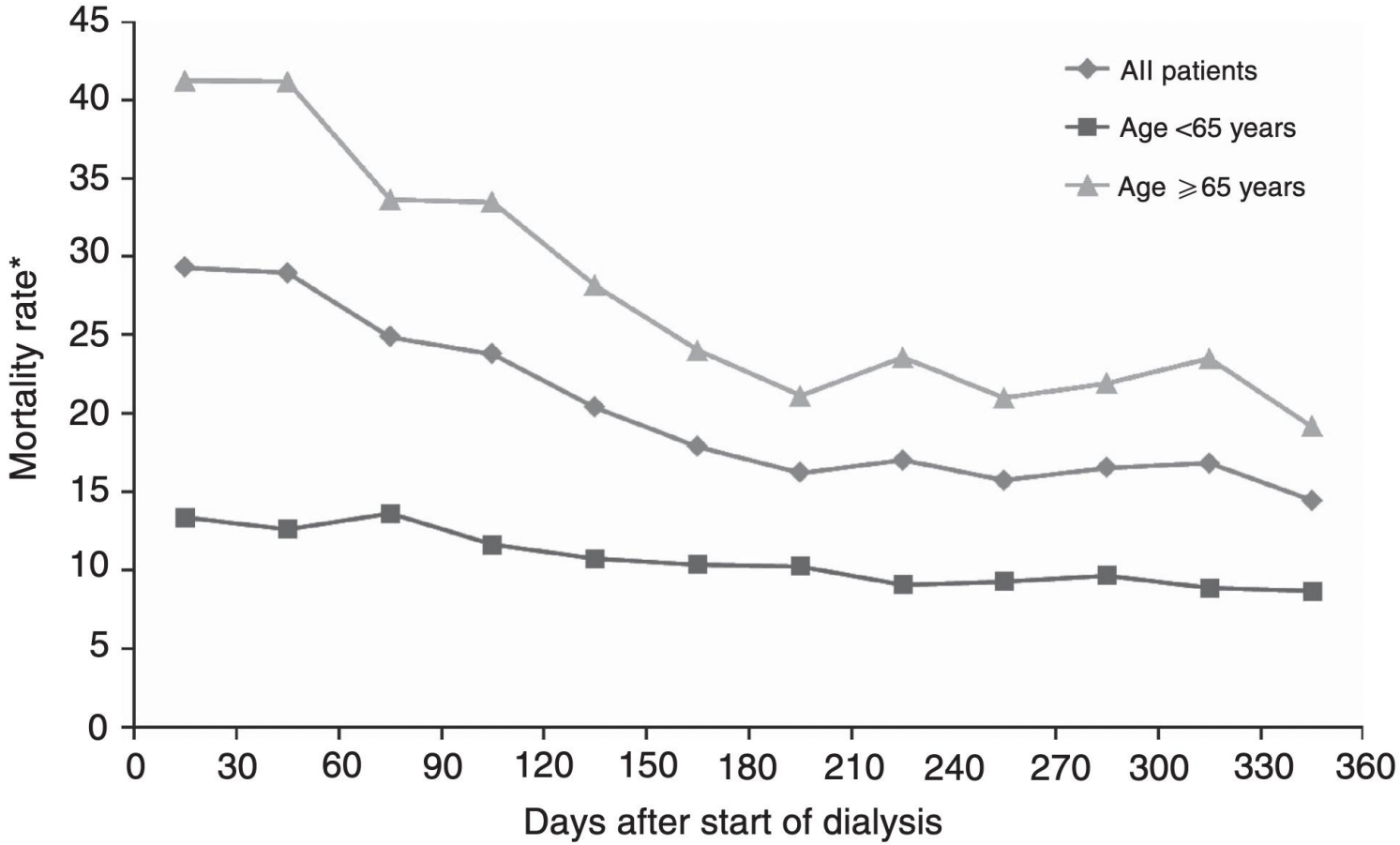
DOPPS country	BE	US	SW	IT	ANZ	CA	FR	UK	GE	JP
⩽120 Days	33.5	33.0	28.4	28.3	25.4	24.6	22.8	22.1	20.1	17.0
121–365 Days	19.4	21.8	19.2	16.9	14.6	17.3	14.4	18.6	14.9	5.3
>365 Days	19.9	18.1	19.5	13.4	13.9	17.4	15.8	15.6	14.8	5.2

Robinson et al. Kidney Int 2014;85:158–65

DOPPS

Worldwide, mortality risk is higher in elderly patients soon after initiation of hemodialysis in the DOPPS

86,886 pts
11 countries
Early HD period



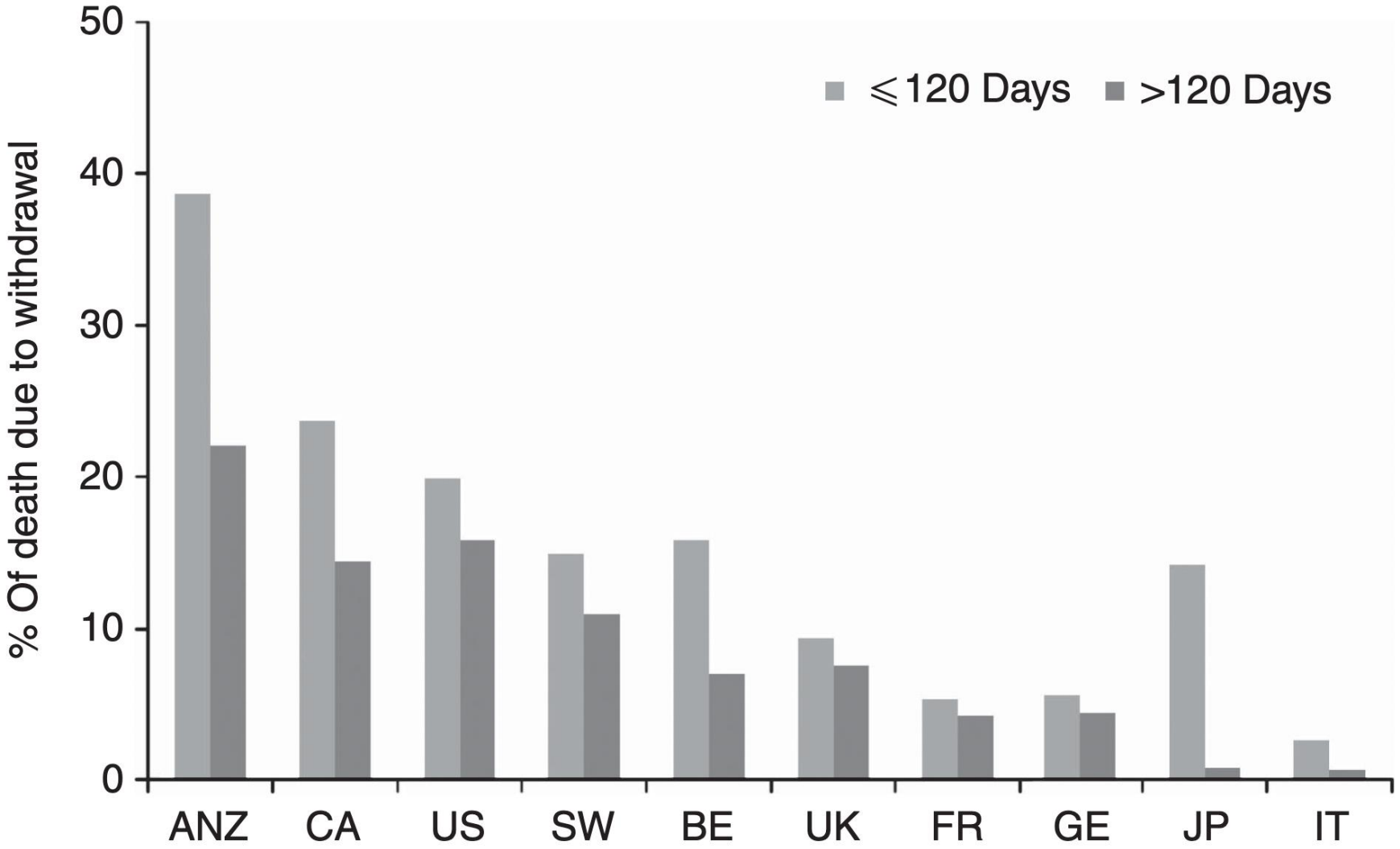
	Mortality rate during the first 360 days of HD treatment											
	0–30	31–60	61–90	91–120	121–150	151–180	181–210	211–240	241–270	271–300	301–330	331–360
All patients	29.3	28.9	24.9	23.8	20.4	17.9	16.2	17.0	15.7	16.5	16.8	14.4
Age <65 years	13.3	12.6	13.6	11.6	10.7	10.4	10.2	9.1	9.3	9.7	8.9	8.7
Age ⩾65 years	41.2	41.2	33.7	33.5	28.2	24.0	21.1	23.6	21.0	21.9	23.5	19.2

Robinson et al. Kidney Int 2014;85:158–65

DOPPS

Withdrawal from dialysis soon after initiation of hemodialysis in the DOPPS

86,886 pts
11 countries
Early HD period



Robinson et al. Kidney Int 2014;85:158–65

DOPPS

First-Year Hemodialysis Deaths Attributable to Potentially Modifiable Risk Factors in the DOPPS

15,891 incident pts Vintage <60 days

Attributable Fractions for Mortality Risk-Factors Among Incident (<60 Days Vintage) Patients, by Region

Risk Factor	North America (N=8972)			Europe/ANZ (N=5278)		
	% pts	HR (95% CI)	AF (95% CI)	% pts	HR (95% CI)	AF (95% CI)
Catheter use	71%	1.46 (1.27–1.69)	22% (14–29%)	45%	1.50 (1.22–1.83)	18% (9–26%)
Albumin <3.5 g/dL	54%	1.54 (1.32–1.78)	20% (13–26%)	46%	1.45 (1.16–1.82)	17% (7–26%)
Creatinine <6 mg/dL	49%	1.33 (1.15–1.52)	13% (6–18%)	39%	1.30 (1.05–1.64)	10% (2–19%)
Lack of pre-ESRD care	30%	1.34 (1.18–1.57)	8% (5–13%)	21%	1.39 (1.10–1.74)	8% (2–13%)
No reported RUV	41%	1.37 (1.19–1.59)	11% (6–17%)	18%	1.22 (0.94–1.53)	3% (0–8%)
SBP >160 mm Hg	28%	0.88 (0.76–1.03)	9% (3–14%)	23%	0.84 (0.66–1.09)	6% (0–13%)
SBP <130 mm Hg	24%	1.56 (1.35–1.77)		23%	1.44 (1.16–1.79)	
Phosphorus >5.5 mg/dL	37%	1.22 (1.05–1.42)	7% (1–12%)	42%	1.12 (0.90–1.38)	5% (0–14%)
Phosphorus <3.5 mg/dL	14%	1.09 (0.90–1.31)		13%	1.14 (0.84–1.50)	
Hemoglobin >12 g/dL	10%	1.05 (0.84–1.28)	3% (0–9%)	11%	1.06 (0.75–1.44)	14% (5–23%)
Hemoglobin <10 g/dL	48%	1.07 (0.93–1.23)		46%	1.39 (1.15–1.73)	
WBC count >10,000/μL	22%	1.23 (1.07–1.40)	4% (1–7%)	17%	1.42 (1.12–1.78)	6% (2–10%)
Ferritin >800 ng/mL	9%	1.27 (1.02–1.58)	2% (0–4%)	7%	1.50 (1.09–2.03)	3% (1–6%)
Calcium >9.5 mg/dL	10%	1.12 (0.89–1.37)	0% (0–5%)	20%	1.04 (0.78–1.37)	0% (0–9%)
Calcium <8.4 mg/dL	38%	0.97 (0.84–1.11)		31%	0.98 (0.78–1.25)	
PTH >300 pg/mL	43%	0.87 (0.74–1.03)	0% (0–3%)	35%	0.88 (0.69–1.14)	0% (0–5%)
PTH <150 pg/mL	30%	0.92 (0.77–1.10)		35%	0.90 (0.71–1.16)	

Karaboyas et al. Clinical Epidemiology 2020:12;51-60

DOPPS

First-Year Hemodialysis Deaths Attributable to Potentially Modifiable Risk Factors in the DOPPS

15,891 incident pts Vintage <60 days

Risk Factor	North America (N=8972)			Europe/ANZ (N=5278)		
	% pts	HR (95% CI)	AF (95% CI)	% pts	HR (95% CI)	AF (95% CI)
Catheter use	71%	1.46 (1.27–1.69)	22% (14–29%)	45%	1.50 (1.22–1.83)	18% (9–26%)
Combined AF						
Malnutrition*	–	–	31% (23–38%)	–	–	26% (15–35%)
Inflammation*	–	–	6% (3–10%)	–	–	9% (4–14%)
MBD abnormality*	–	–	0% (0–11%)	–	–	0% (0–16%)
All risk factors	–	–	66% (58–73%)	–	–	62% (49–72%)

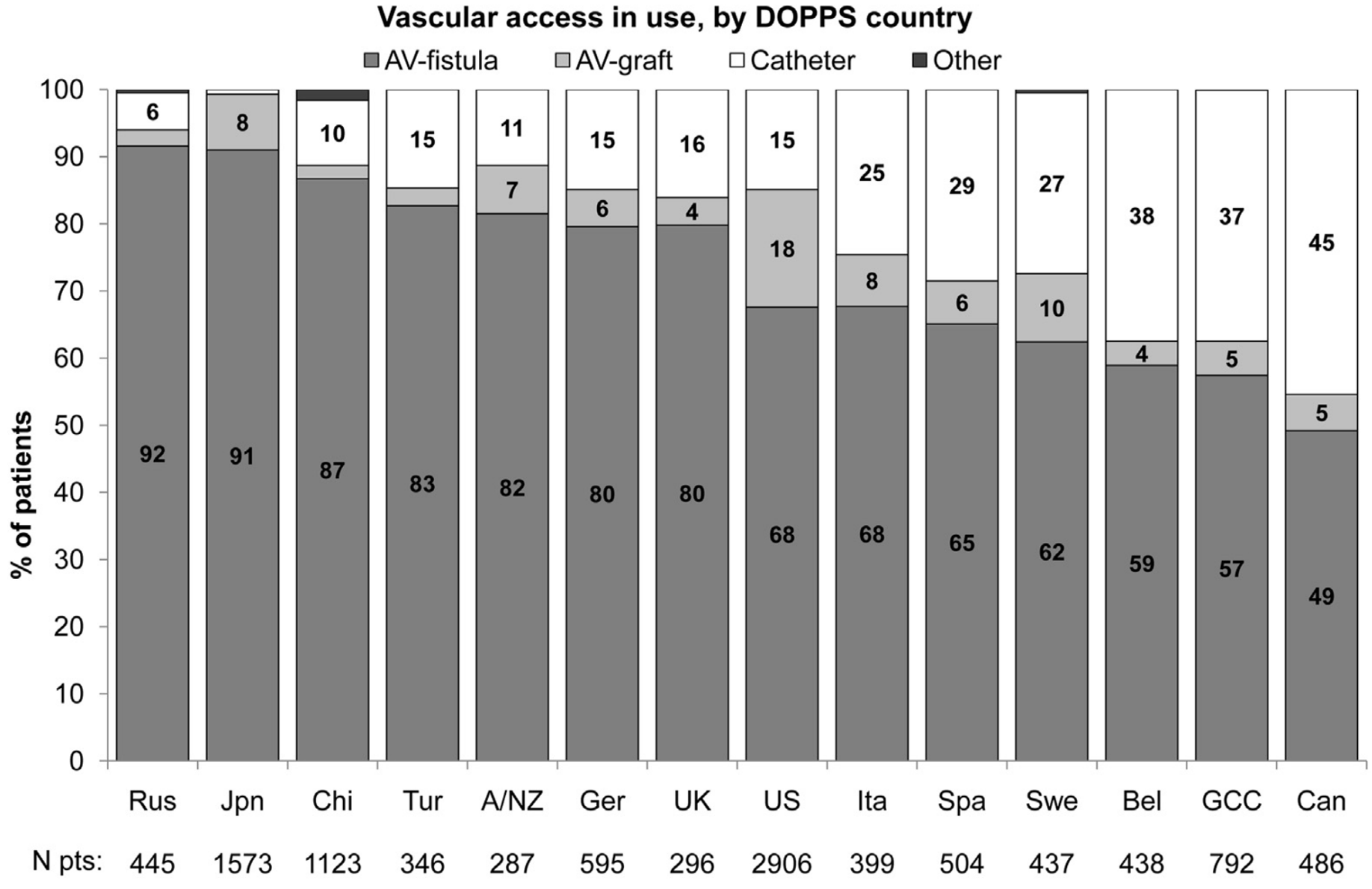
DOPPS

Karaboyas et al. Clinical Epidemiology 2020:12;51-60

Vascular access: a key factor in HD initiation

DOPPS: Vascular accesses differences in prevalent patients. 2013

United States
3,442 patients
19 other nations
8,478 patients

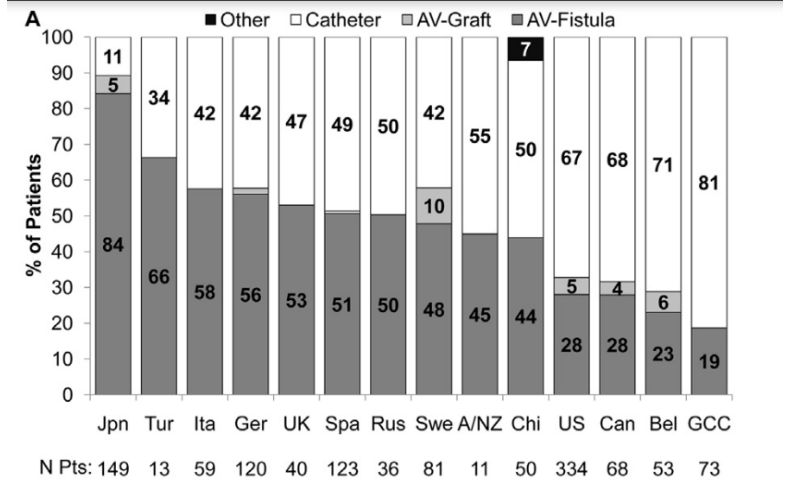


Pisoni et al.
Am J Kidney Dis 2015;65:905–15

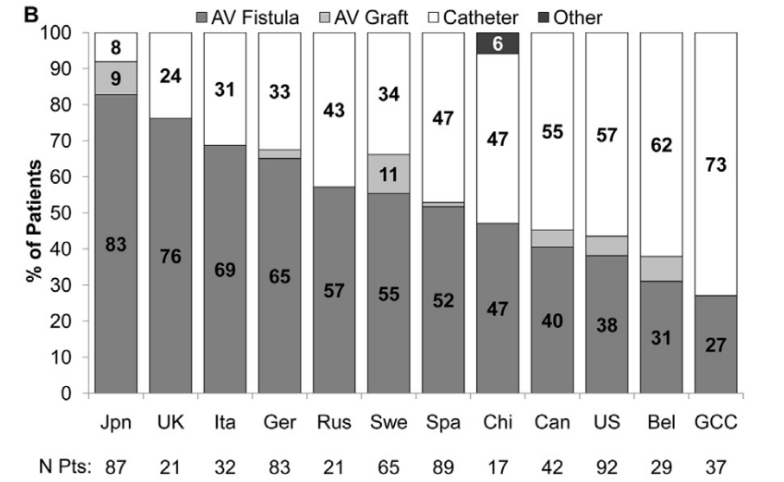
DOPPS

DOPPS: Pre-HD nephrology visits and VA type in incident patients

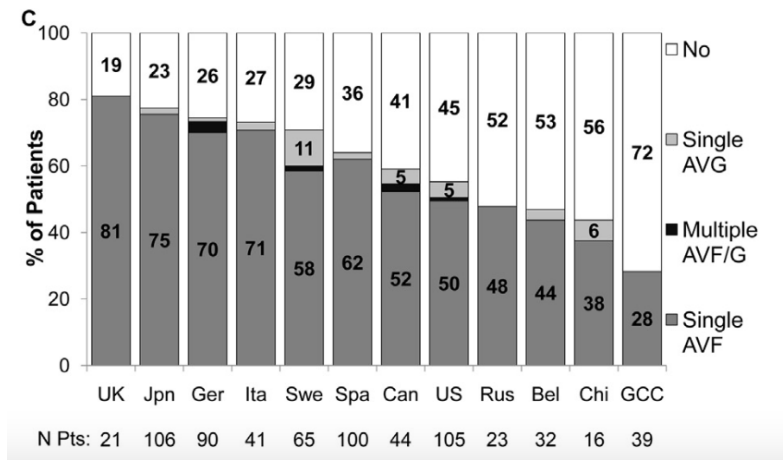
All incident patients
US: 28% AV-Fistula



Incident pts
Nephro visit < 4 months
US: 38% AV-Fistula



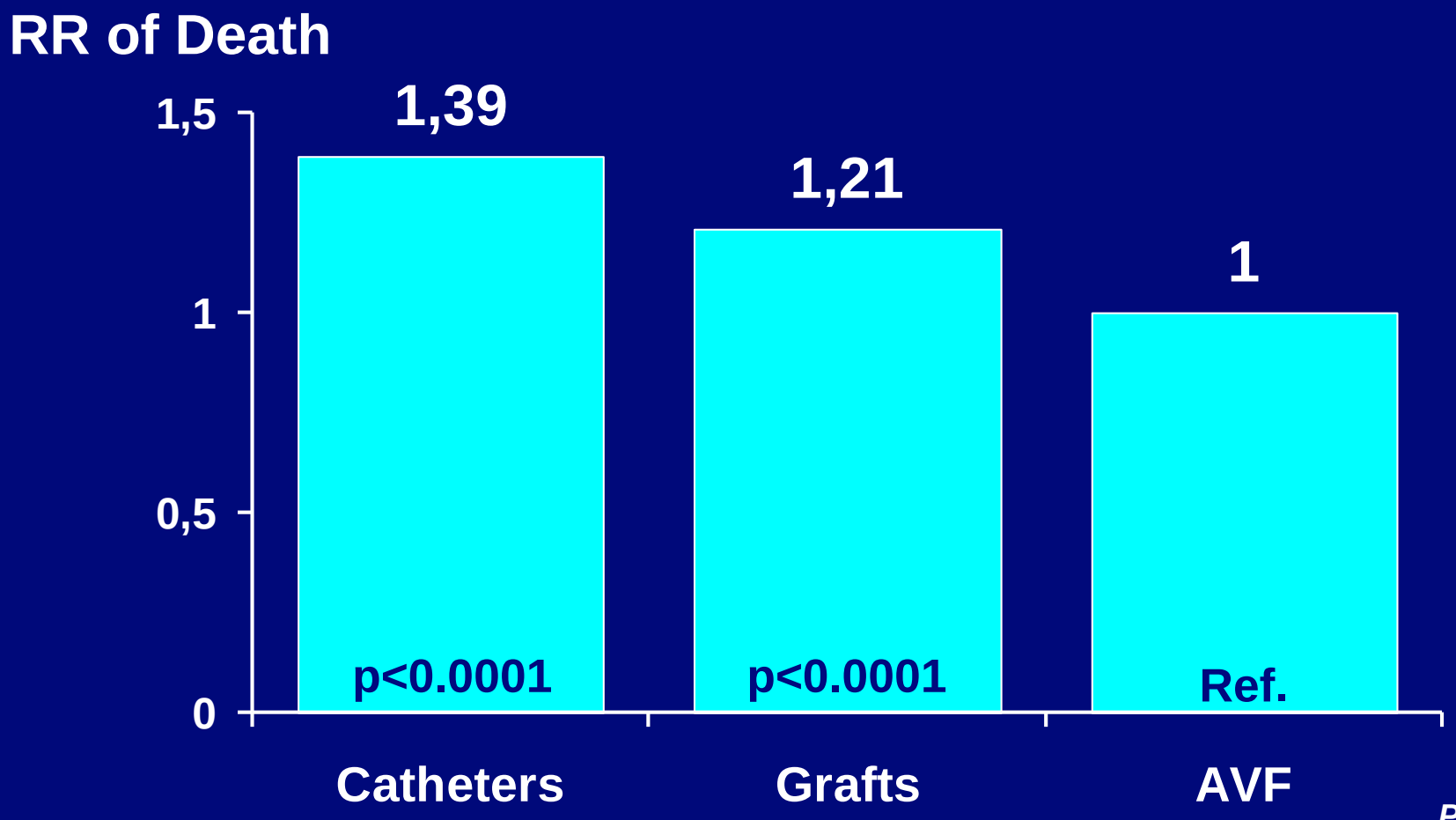
Incident pts
Nephro visit ≥ 4 months
US: 50% AV-Fistula



Pisoni et al.
Am J Kidney Dis 2015;65:905–15

DOPPS

Vascular Access: Mortality Risk
Patient Based Model



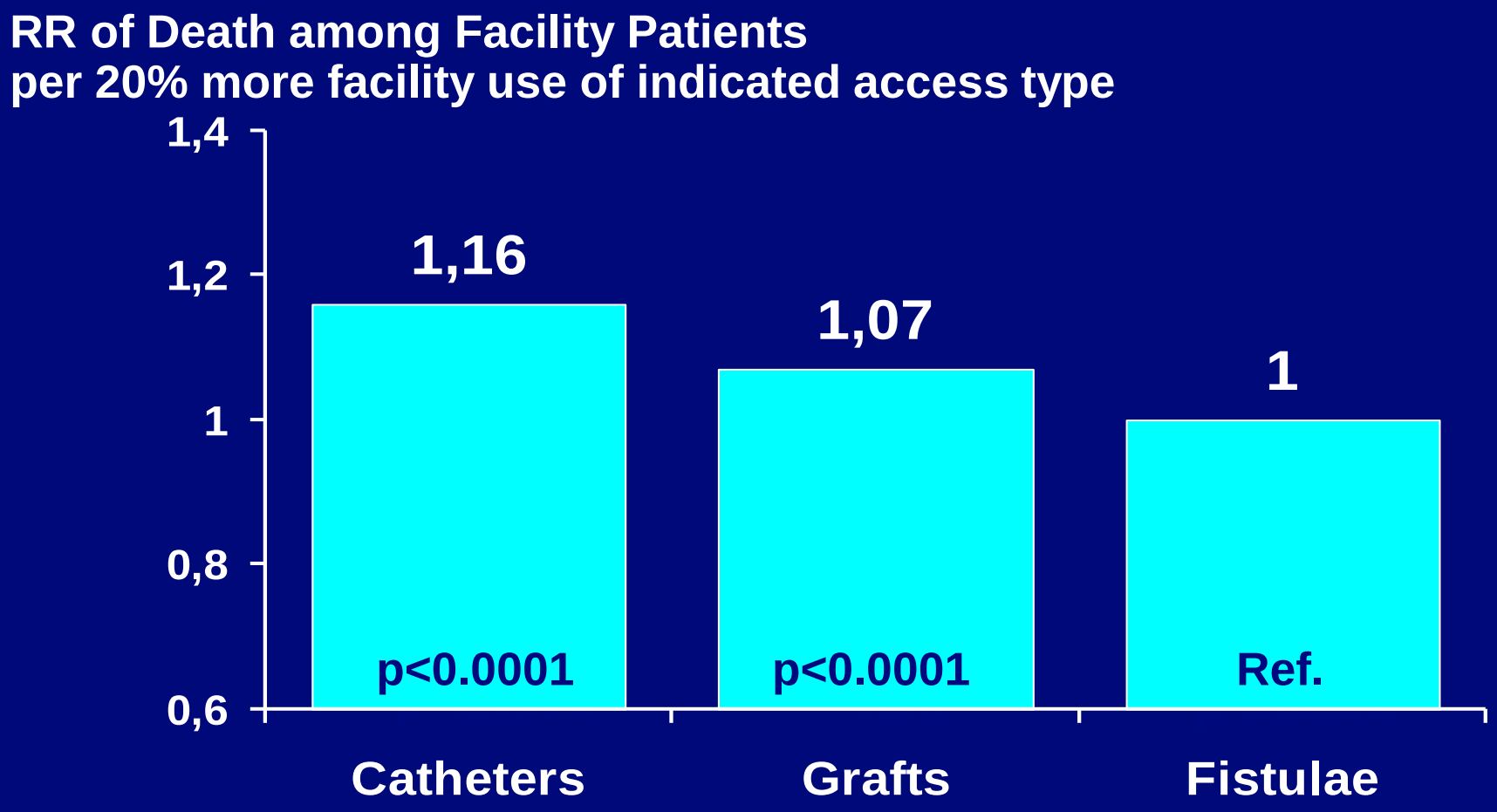
Pisoni et al ASN, 2005

*DOPPS I+II, 1996-2004; n=25,806; adjusted for age, gender, black race, yrs with ESRD, 14 comorbidity classes, baseline Hgb, Kt/V, serum albumin, calcium, PO_4, accounted for facility clustering effects; stratified by continent [Japan, US, EUR (Fr,Ge,It,Sp,UK]; RR based upon access in use at study entry.

Catheters often are given to sicker patients and so outcomes, even with adjustments, are expected to be worse for patients using a catheter (Bias by indication).

What do facility-based analyses show for catheter use and outcomes?

Vascular Access: Mortality Risk
Facility Based Model

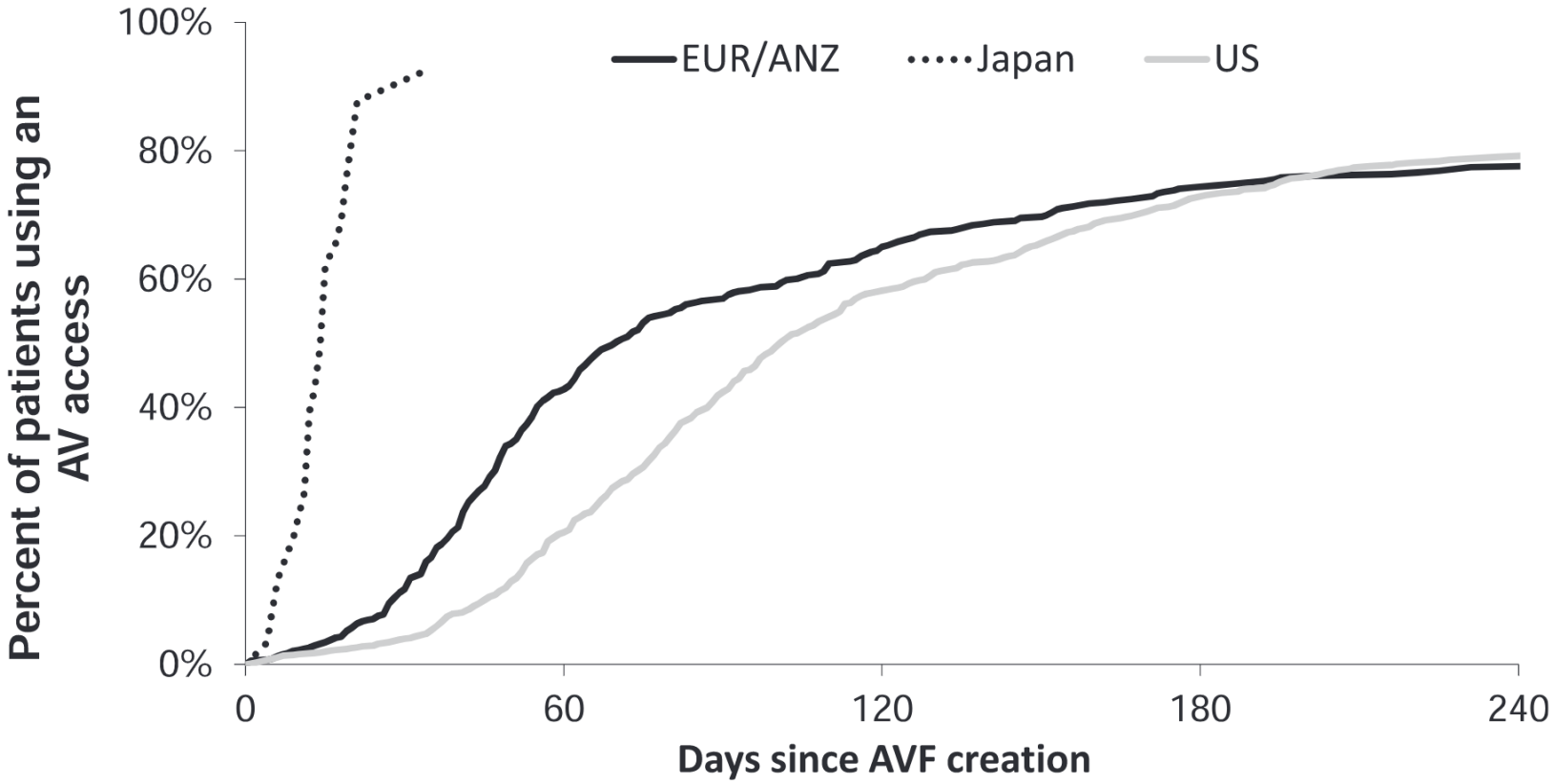


*DOPPS I+II, 1996-2004; n=25,709; adjusted for age, gender, black race, yrs with ESRD, 14 comorbidity classes, baseline Hgb, Kt/V, serum albumin, calcium, PO_4, accounted for facility clustering effects; stratified by continent [Japan, US, EUR (Fr,Ge,It,Sp,UK]; RR based upon access in use at study entry.

Pisoni et al, ASN 2005

Arteriovenous fistula (AVF) use after creation in pts with CVC on HD

Cumulative incidence until successful AVF use from the date of AVF creation, by region, among patients using a central venous catheter at time of AVF creation. DOPPS phases 4 and 5 data (2009-2015)



N (AVFs) at day 0 were: EUR/ANZ (579), Japan (29), and US (755)

Pisoni et al.
Am J Kidney Dis. 2021;77:245-254

DOPPS

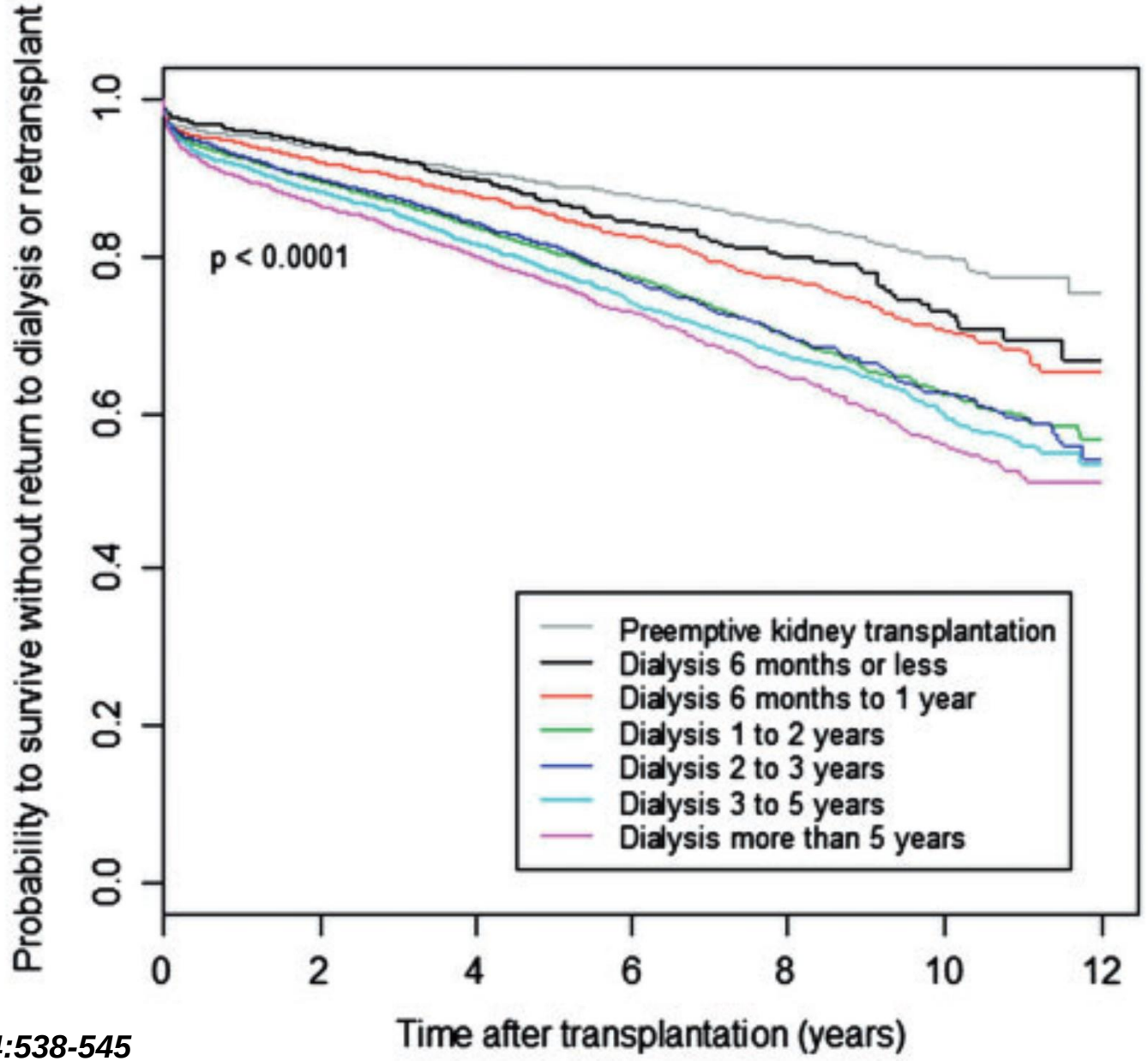
Kidney transplantation should be a priority, before and after initiation of dialysis

Preemptive transplantation is best. Less dialysis before transplantation is better

1st kidney-only Tx in adults
France 2002-2012

Association of PKT and of pre-Tx dialysis time with graft failure HR
Death, return to dialysis or reTx

22,345 pts, 50.5±13.4 yrs at Tx
61.9% men
3112 (14.0%) received a PKT
Median time of FU 4.7 yrs



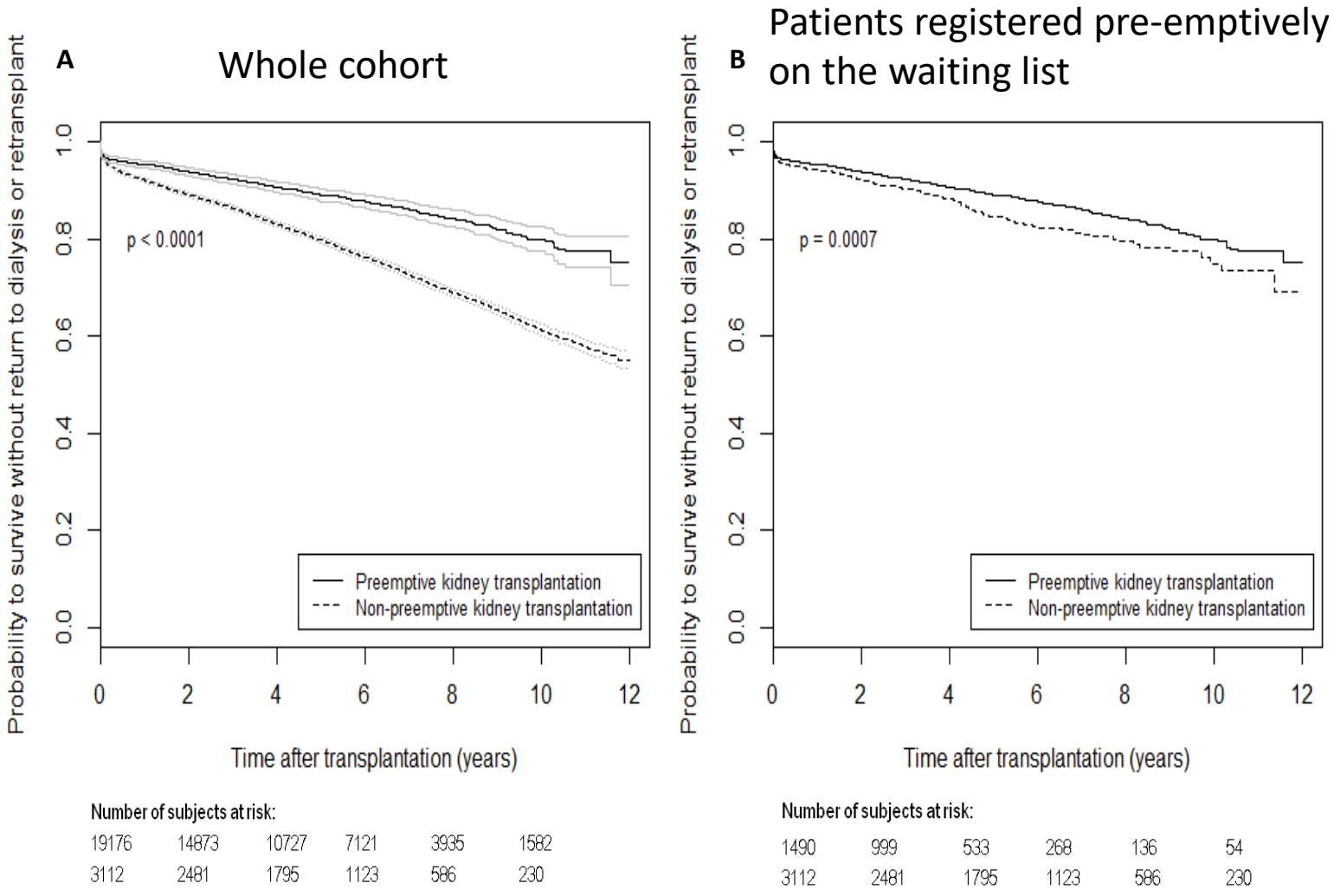
Réseau Epidémiologie, Information, Néphrologie

Prezelin-Reydit, Combe et al. Nephrol Dial Transplant 2019;34:538-545

Preemptive Tx vs Tx after dialysis: Tx survival
(A) All cohort
(B) Pts on the waiting list before dialysis

All first kidney-only transplants performed in adults in France between 2002 and 2012:
22 345 patients

Cox multivariable model: association of PKT and of pretransplant dialysis time with the hazard of graft failure defined as death, return to dialysis or retransplant, whichever occurred first



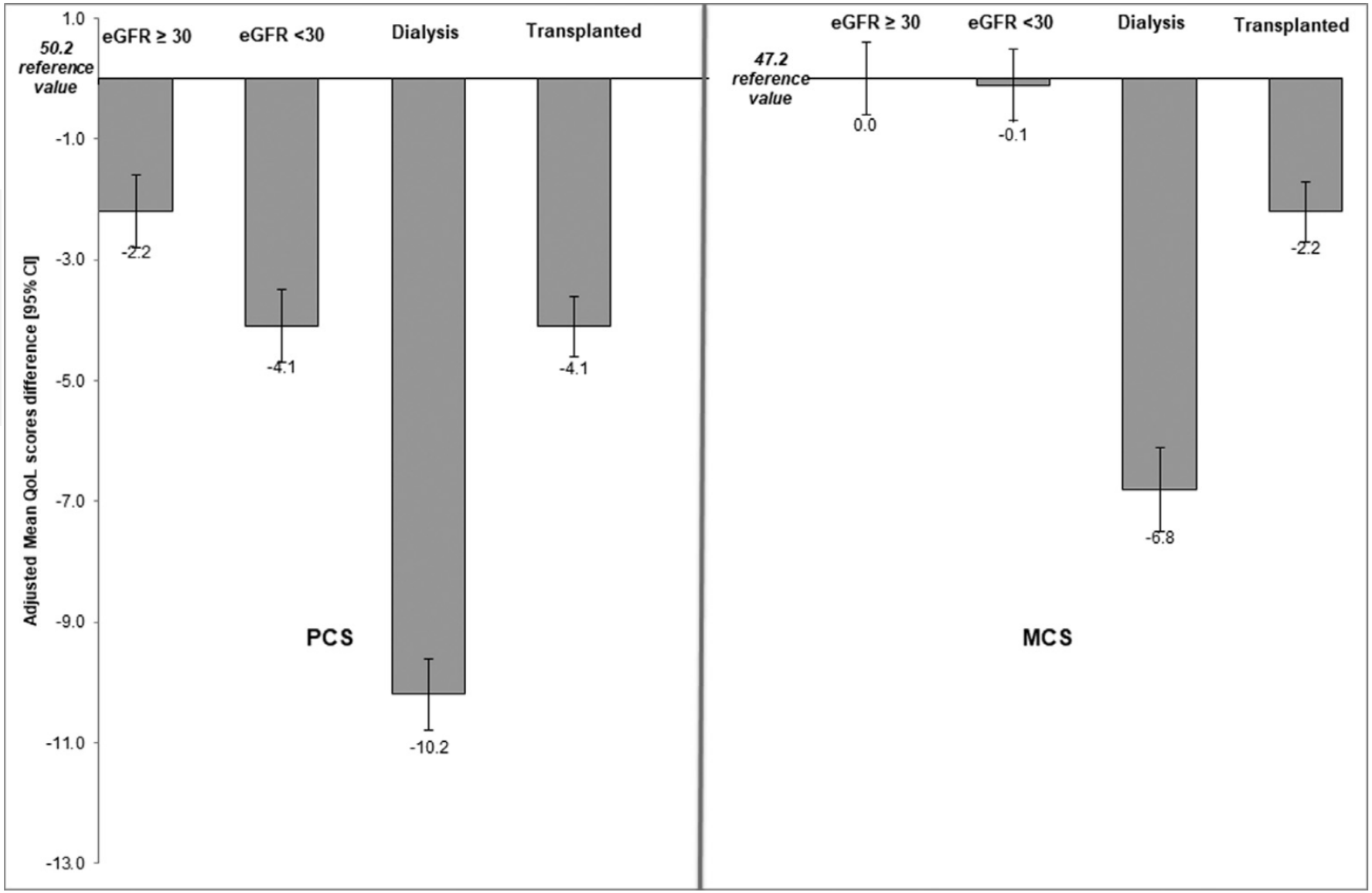
Prezelin-Reydit M, Combe C, et al. Nephrol Dial Transplant. 2019;34:538-545

CKD stages: Quality of Life SF-36

2,693 pts CKD-REIN

1,658 pts Tx

20,574 normal subjects



CKD REIN

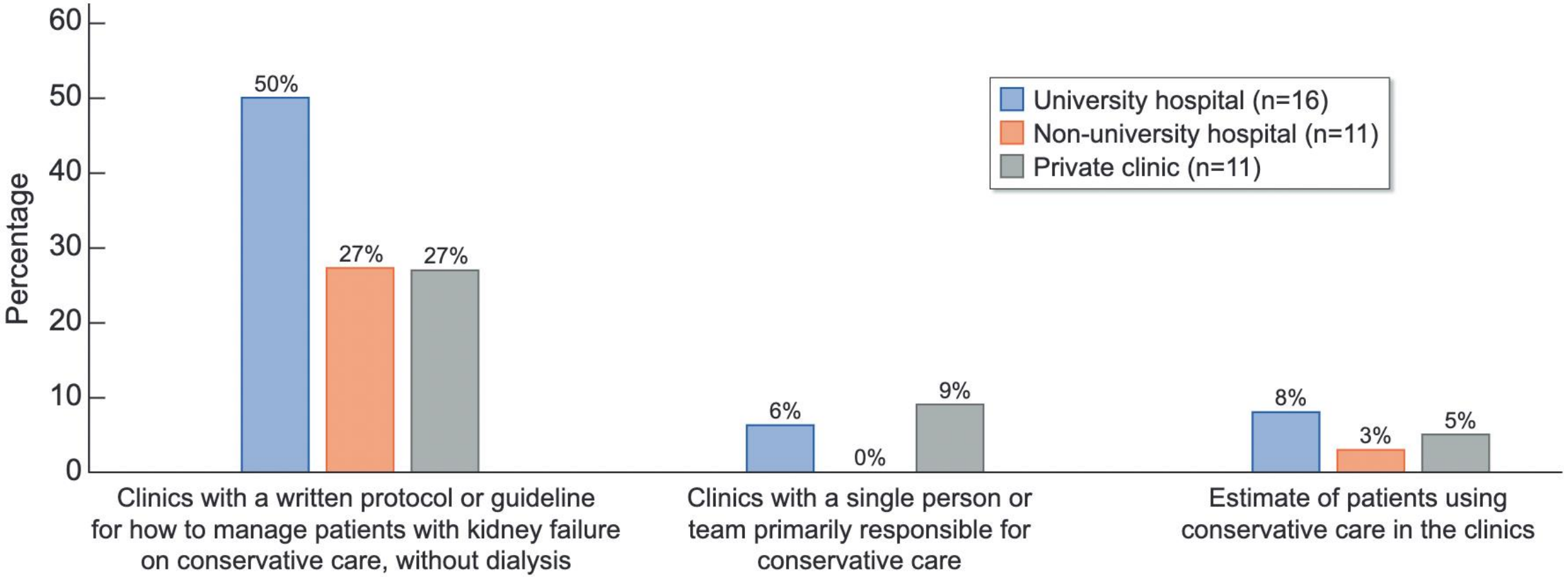
Réseau Epidémiologie, Information, Néphrologie

Legrand et al. Am J Kidney Dis 2019;75:868-878

Conservative care
Barriers for nephrologists… in France

CKD Rein

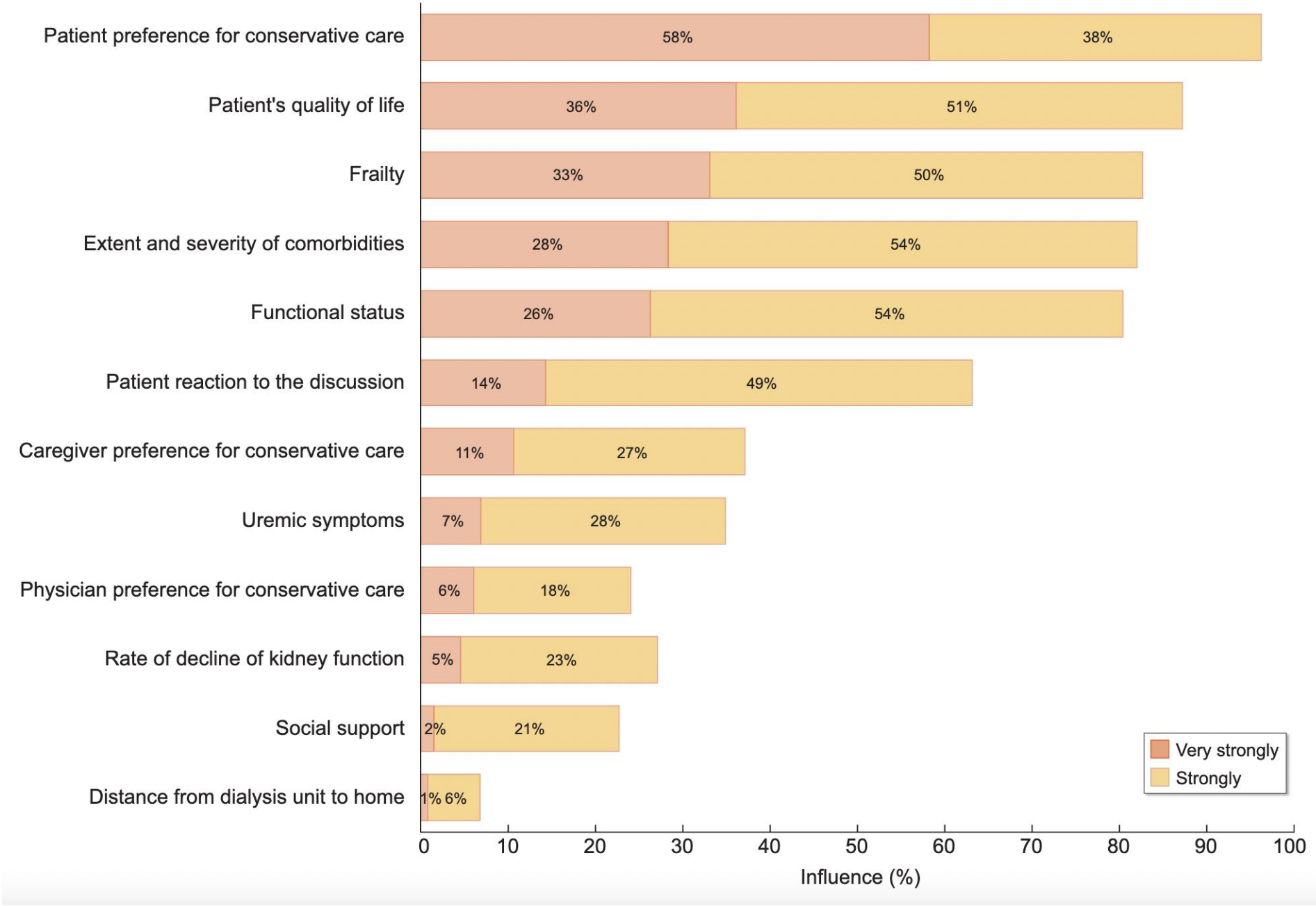
Nephrology clinic resources for conservative care and proportion of patients using this treatment option



CKD REIN

Hamroun et al. Nephrol Dial Transpl 2022

Factors likely to influence nephrologists when evaluating the suitability of conservative care for a patient



CKD REIN

Hamroun et al. Nephrol Dial Transpl 2022

Transition from CKD to RRT. Summary

- Patient education ➔ shared decision process between caregivers and patient
- Consider competing risks between ESRD and death
- Kidney transplantation ➔ priority, even when dialysis has begun
- Discuss all options, including conservative care (≠ palliative care)
- Prepare vascular access for hemodialysis
  - Forearm AVF > arm AVF > AV graft >> CVCath
- Beware of HD initiation: very high risk period
  - Special attention to older patients
  - Early withdrawal ➔ social and cultural context
- Right eGFR to begin dialysis ➔ KDIGO!

If I had kidney disease, I would…

Going Upstream: Coordination to Improve CKD Care

If I had kidney disease, I would want to avoid dialysis. If I could not avoid dialysis, I would want to delay it as much as possible.

If I had kidney failure, I would choose to receive a kidney transplant.

If I needed to start dialysis, I would like to discuss the possibility of medical management without dialysis before choosing a dialysis modality.

If I chose to start dialysis, I would choose to start at home.

If I needed to start dialysis in center, I would choose to start dialysis with a fistula instead of a catheter.

If I needed to start dialysis, I would prefer to start in an outpatient setting.

At all stages of my kidney disease, I would want to continue to work or to go to school.

Johnson et al. Seminars in Dialysis. 2016;29:125-134

If I had kidney disease, I would…

Going Upstream: Coordination to Improve CKD Care

If I had kidney disease, I would want to avoid dialysis. If I could not avoid dialysis, I would want to delay it as much as possible.

If I had kidney failure, I would choose to receive a kidney transplant.

If I needed to start dialysis, I would like to discuss the possibility of medical management without dialysis before choosing a dialysis modality.

If I chose to start dialysis, I would choose to start at home.

If I needed to start dialysis in center, I would choose to start dialysis with a fistula instead of a catheter.

If I needed to start dialysis, I would prefer to start in an outpatient setting.

At all stages of my kidney disease, I would want to continue to work or to go to school.

Johnson et al. Seminars in Dialysis. 2016;29:125-134