IMPACT OF PATIENT CHARACTERISTICS ON PROGNOSIS OF INCIDENT DIALYSIS PATIENTS

Csaba P Kovesdy, MD
University of Tennessee Health Science Center
Memphis VA Medical Center
Memphis TN USA

Disclosure of Interests

Reseach grants: NIH, Shire

Research contracts: Abbvie, Amgen, Bayer, Janssen, OPKO

Consultant: Abbott Nutrition, Astra-Zeneca, Fresenius Medical Care, Keryx, Relypsa, Sanofi-aventis, ZS Pharma

Objectives

- Describe characteristics of incident ESRD patients

- Examine the effect of patient characteristics on outcomes in incident ESRD patients
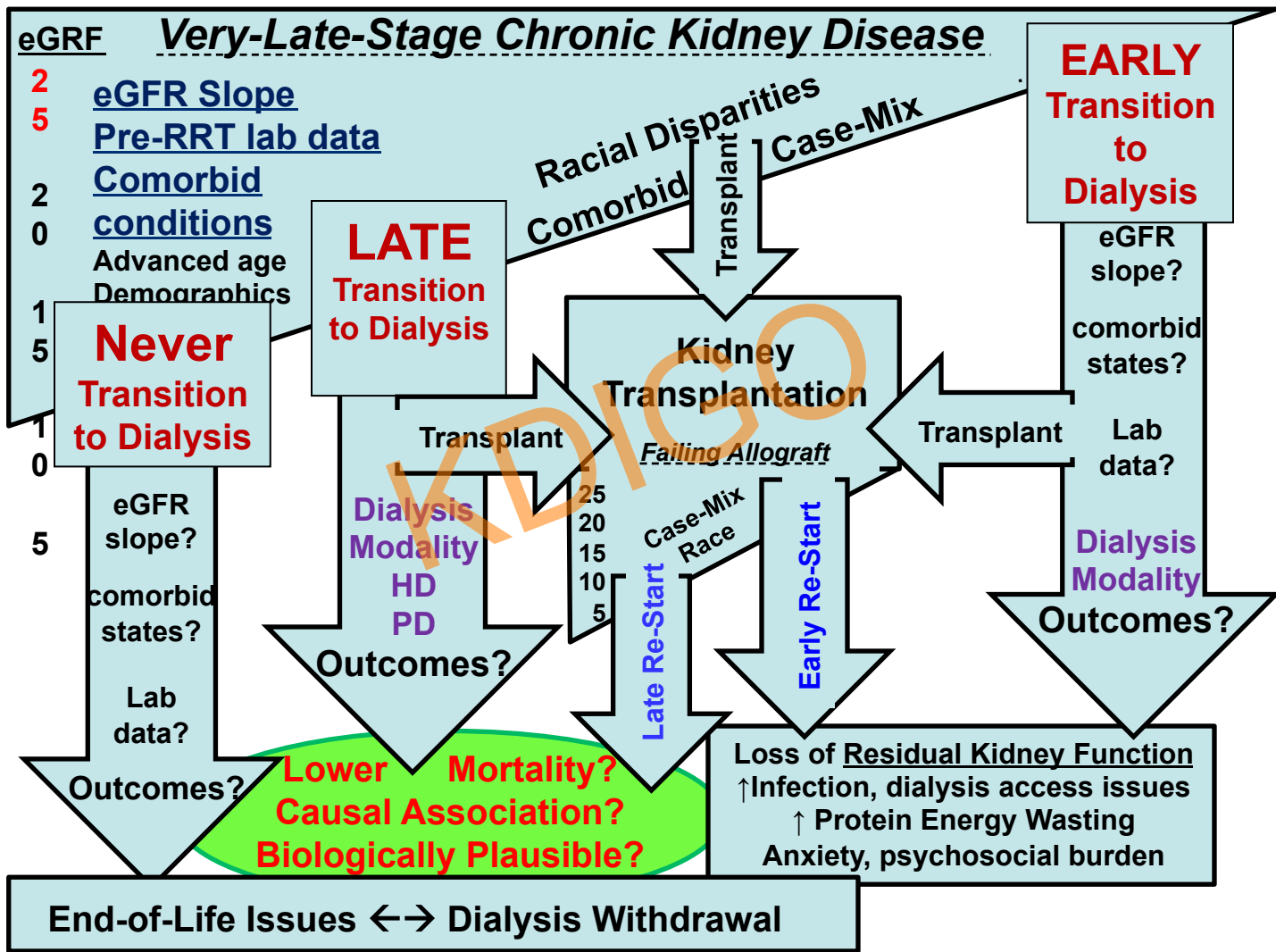
transition

- *[tran-zish-uh n, -sish-]*

- **noun 1. *movement, passage, or change from one position, state, stage, subject, concept, etc., to another;***

- **"the transition from adolescence to adulthood."**

  – **Dictionary.com**

start

- *[stahrt]*

- 1. to begin or set out, as on a journey or activity.
- 2. to appear or come <u>suddenly</u> into action, life, view, etc.; rise or issue <u>suddenly</u> forth.
- 3. to spring, move, or dart <u>suddenly</u> from a position or place: The rabbit started from the bush.
- 4. to be among the entrants in a race or the initial participants in a game or contest.
- 5. to give a <u>sudden</u>, <u>involuntary jerk, jump, or twitch, as from a shock of surprise</u>, alarm, or pain: The sudden clap of thunder caused everyone to start.

KDIGO

Kalantar-Zadeh et al, *NDT* 2017

Kalantar-Zadeh et al., Nephrol Dial Transplant 2017

The United States Renal Data System (USRDS)
## Special Study Center
Transition of Care in CKD (TC-CKD)

NIH/NIDDK

University of California Irvine School of Medicine
Harold Simmons Center for Kidney Disease Research & Epidemiology
UC Irvine Medical Center, Orange, CA; and
VA Long Beach Healthcare System, Long Beach, CA

University of Tennessee Health Sciences Center
Division of Nephrology
Clinical Outcomes and Clinical Trial Program; and
VA Memphis Healthcare System, Memphis, TN

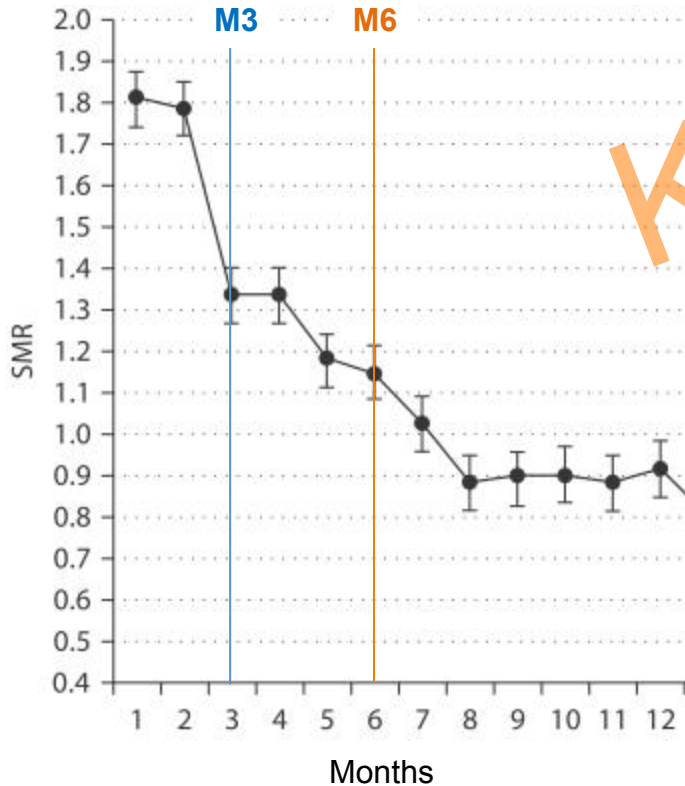**Dept. Research, Kaiser Permanente of Southern California,**
Pasadena, CA
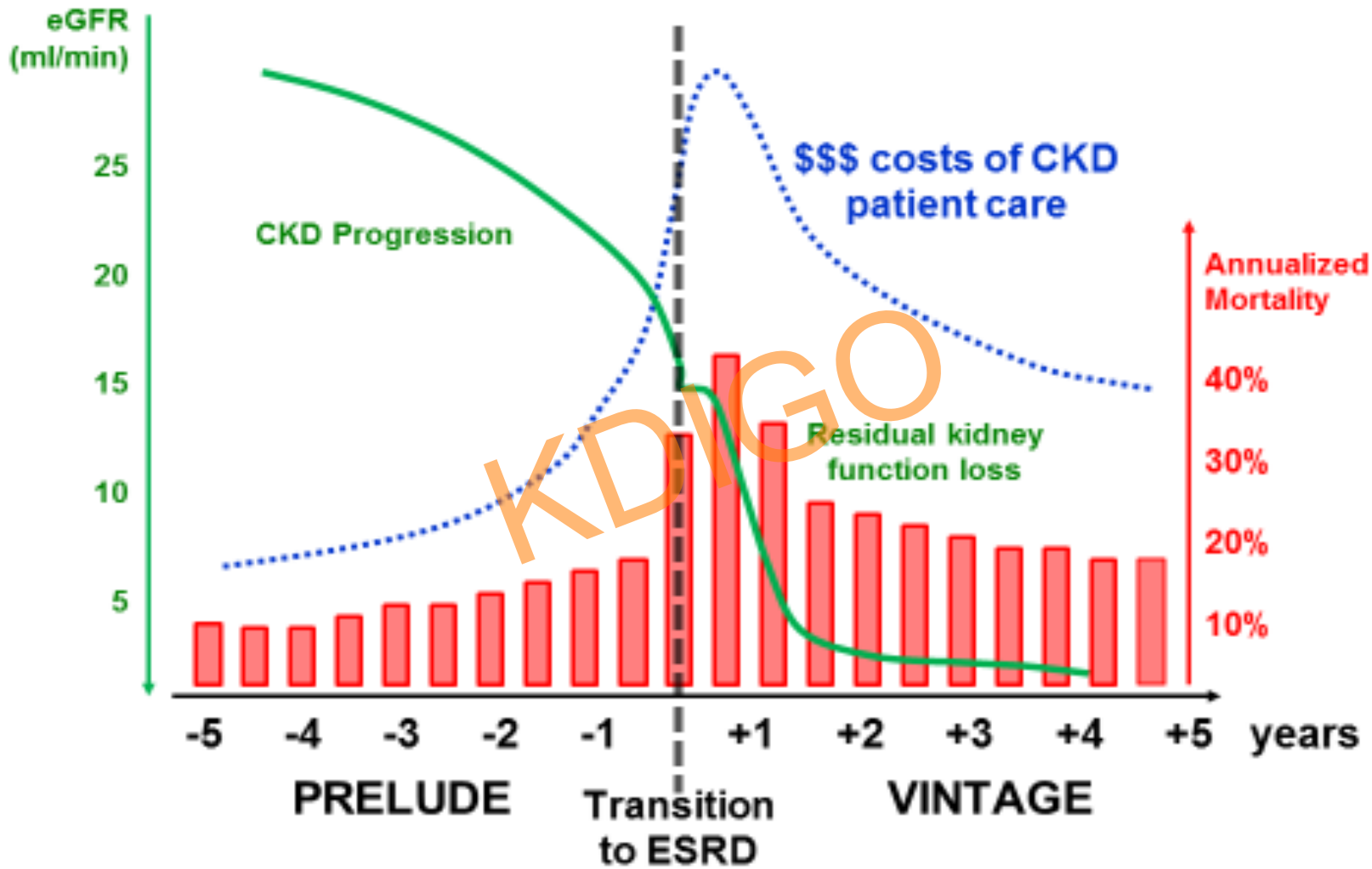
Kalantar-Zadeh et al., Nephrol Dial Transplant 2017

Patterns and Predictors of Early Mortality in Incident Hemodialysis Patients: New Insights (Am J Nephrol. 2012;35:548)

Lilia R. Lukowsky[a, b] Leeka Kheifets[b] Onyebuchi A. Arah[b, e]
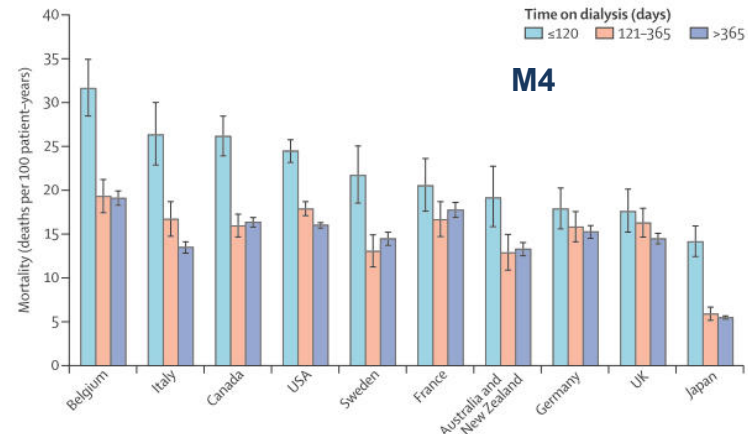Allen R. Nissenson[c, d] Kamyar Kalantar-Zadeh[a-c]

Early mortality in patients starting dialysis appears to go unregistered (Kidney Int. 2014;86:392)

Robert N. Foley[1,2], Shu-Cheng Chen[1], Craig A. Solid[1], David T. Gilbertson[1] and Allan J. Collins[1,2]
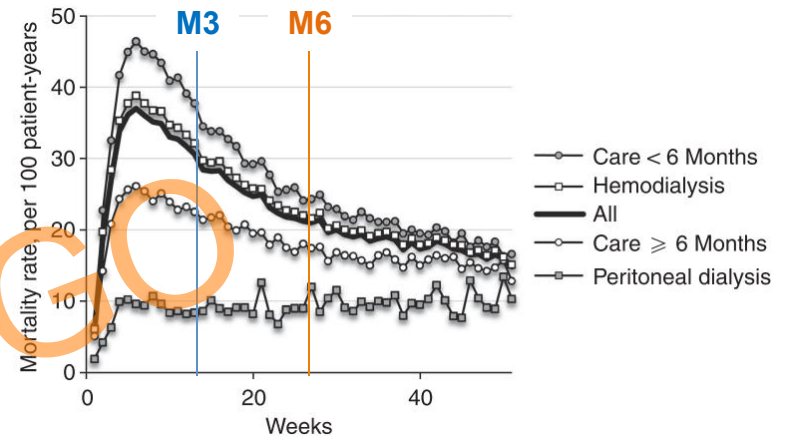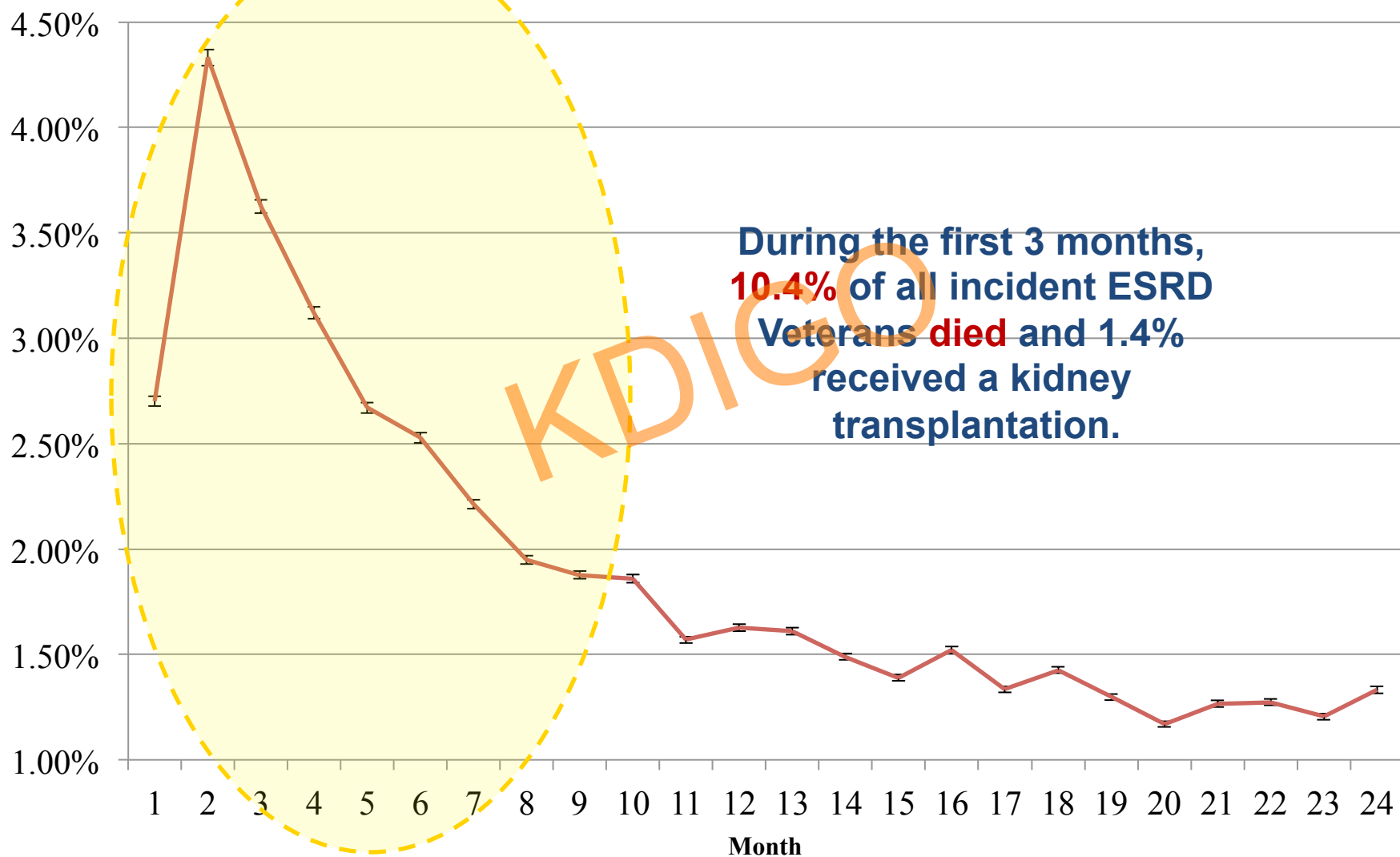
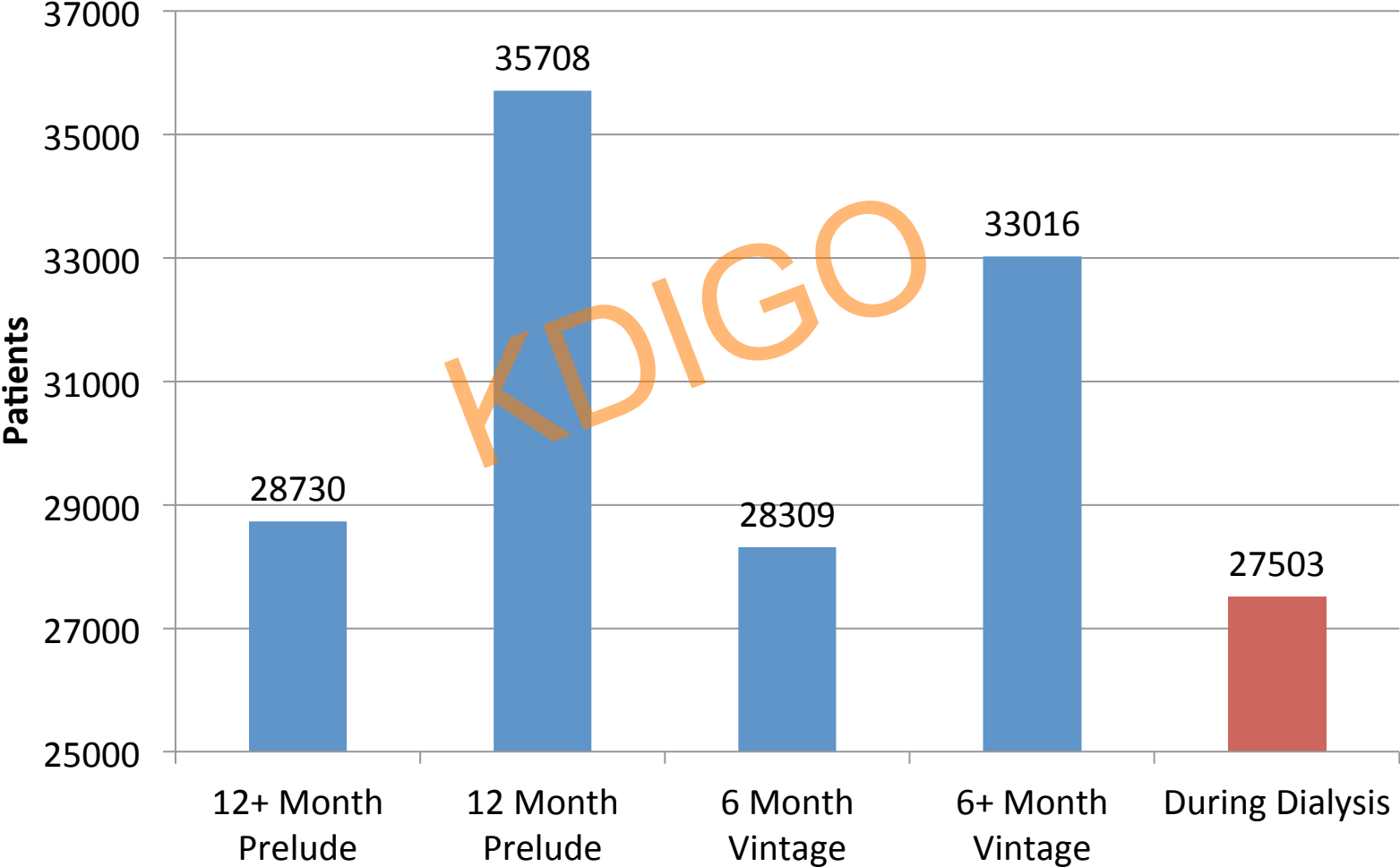**Worldwide, mortality risk is high soon after initiation of hemodialysis** (Kidney Int. 2014;85:158)

Bruce M. Robinson[1,2], Jinyao Zhang[1], Hal Morgenstern[1,3], Brian D. Bradbury[4,5], Leslie J. Ng[4], Keith P. McCullough[1], Brenda W. Gillespie[6], Raymond Hakim[7], Hugh Rayner[8], Joan Fort[9], Tadao Akizawa[10], Francesca Tentori[1,7] and Ronald L. Pisoni[1]

Crude Mortality Rates over First 24 Months in Incident Dialysis Patients

During the first 3 months, 10.4% of all incident ESRD Veterans died and 1.4% received a kidney transplantation.

Transition of Care in CKD, Veterans Data, www.USRDS.org

8/6/14

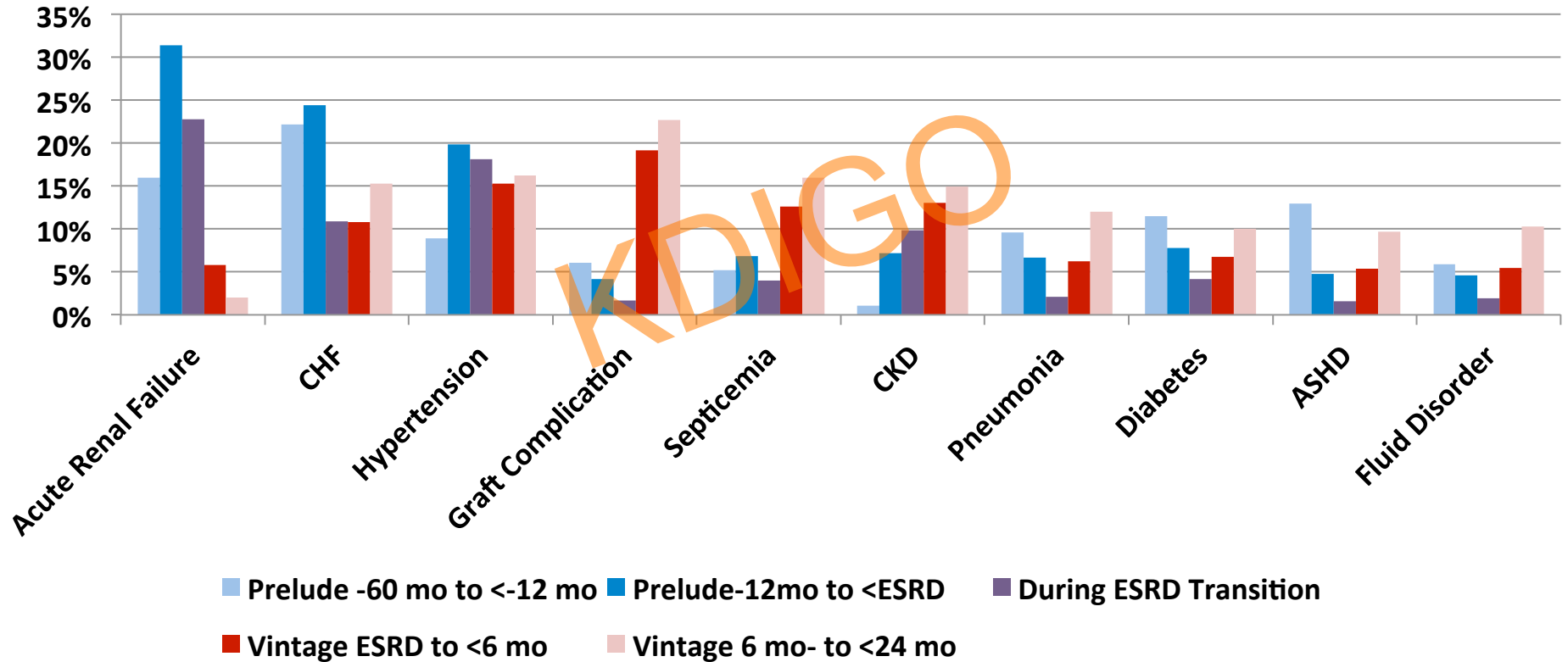# Hospitalization Patients by Prelude and Vintage

Top 20 Reasons for Hospitalizations
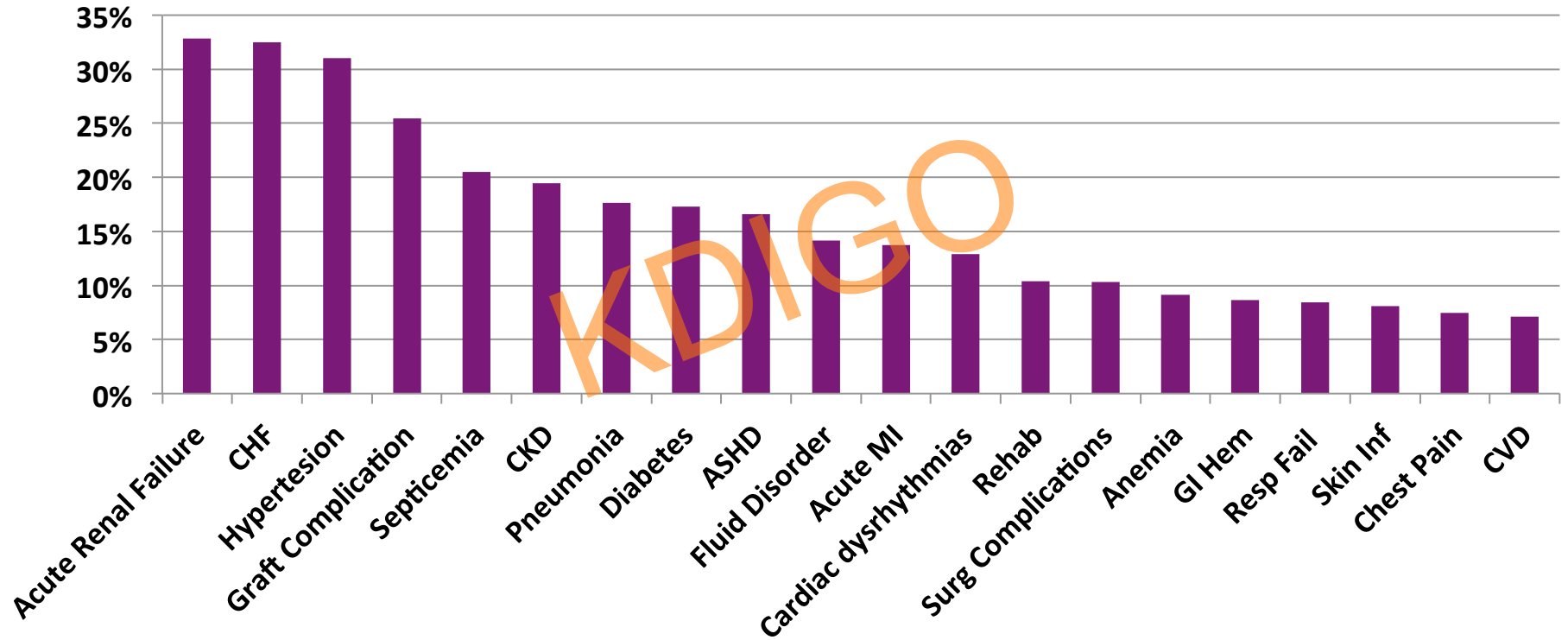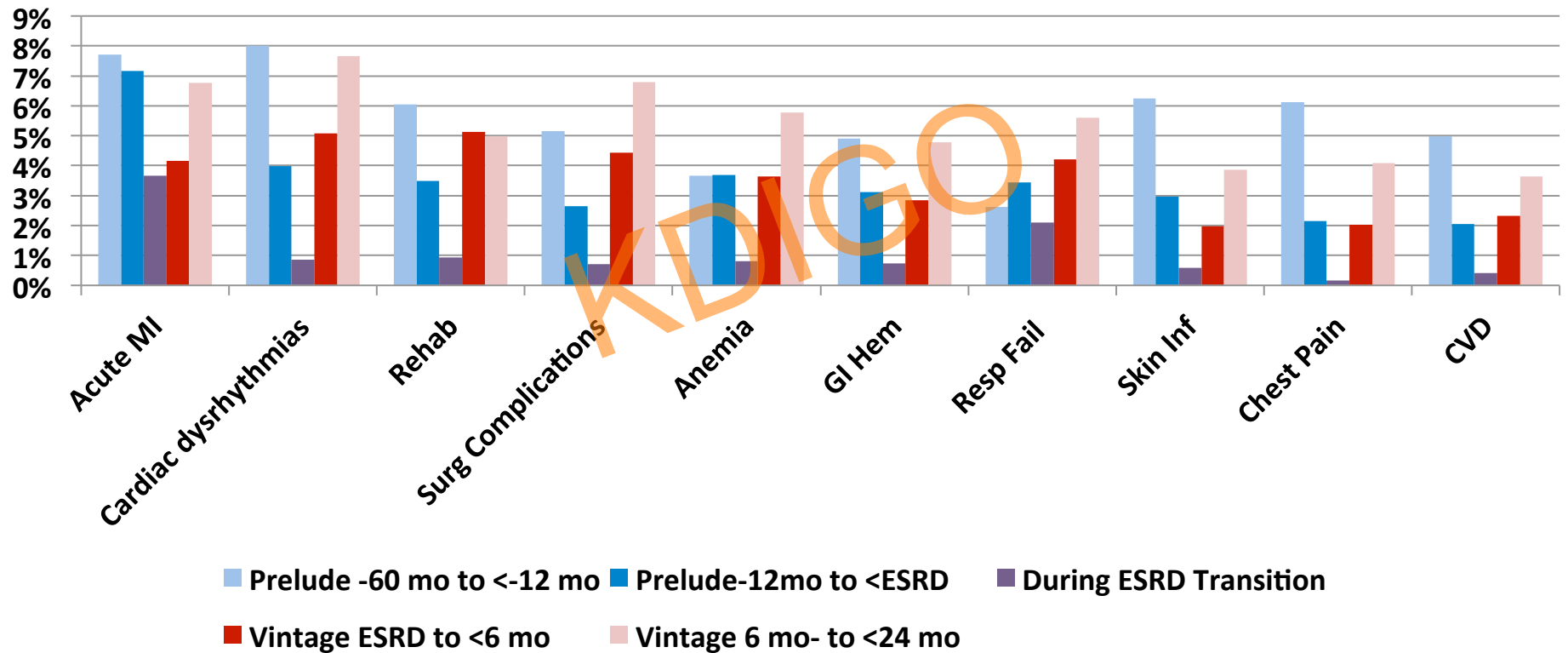

N=74382

Reasons # 1-10 for Hospitalization by time period

N=74382

Reasons # 11-20 for Hospitalization by time period

Legend:
- Prelude -60 mo to <-12 mo
- Prelude-12mo to <ESRD
- During ESRD Transition
- Vintage ESRD to <6 mo
- Vintage 6 mo- to <24 mo

Categories: Acute MI, Cardiac dysrhythmias, Rehab, Surg Complications, Anemia, GI Hem, Resp Fail, Skin Inf, Chest Pain, CVD

N=74382

Patient characteristics in incident ESRD

- Important as risk factors

    - Interventions in pre-ESRD period to improve outcomes

- Important for prediction

    - Help make decisions about best course of action

Key patient characteristics

- Demographic (age, gender, race)

- Socio-economic

- Comorbidities

- Biochemical

- Treatments/interventions

- Clinical events

Trends in adjusted* ESRD incidence rate (per million/year), by age group, in the U.S. population, 1996-2014
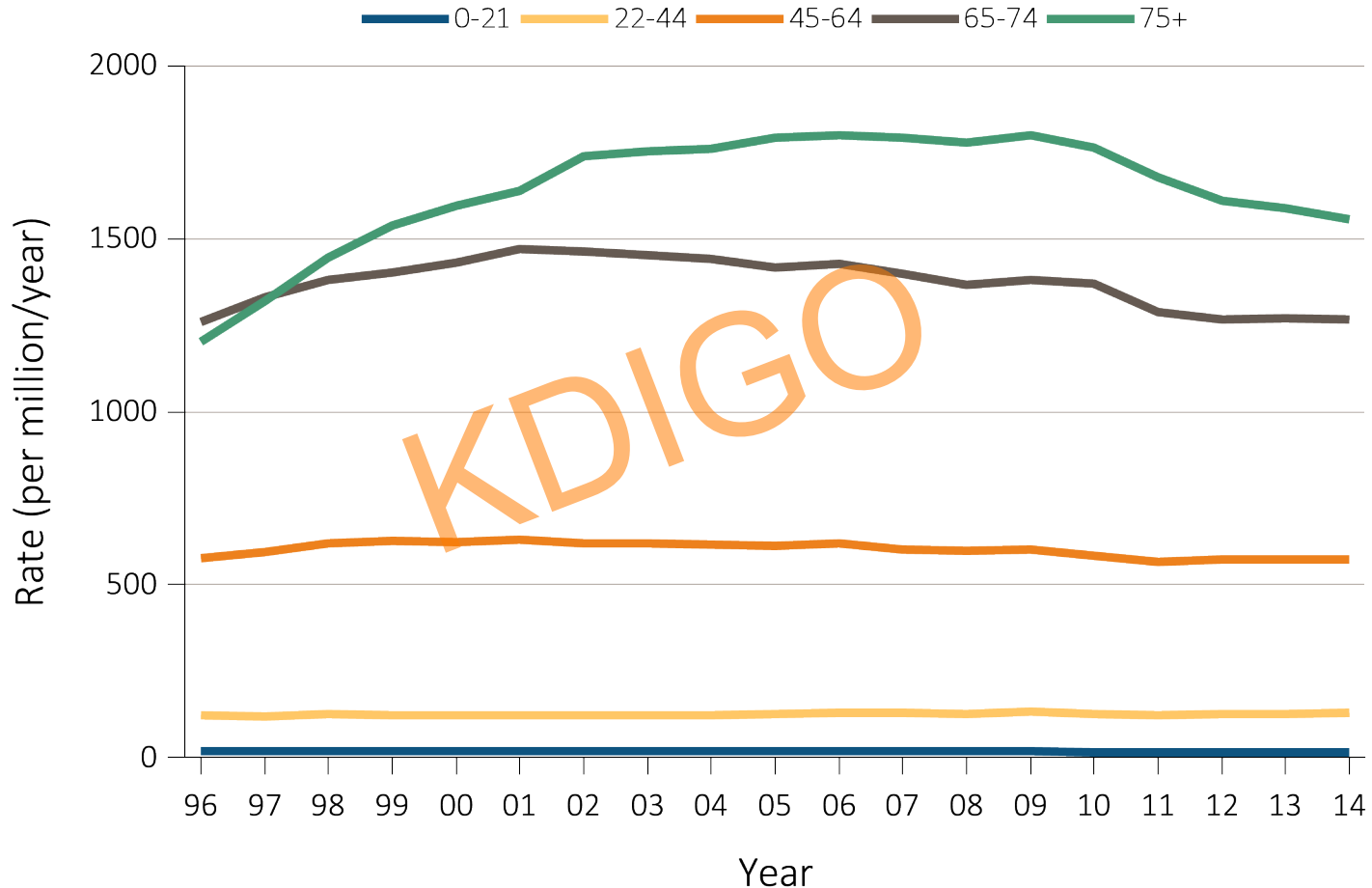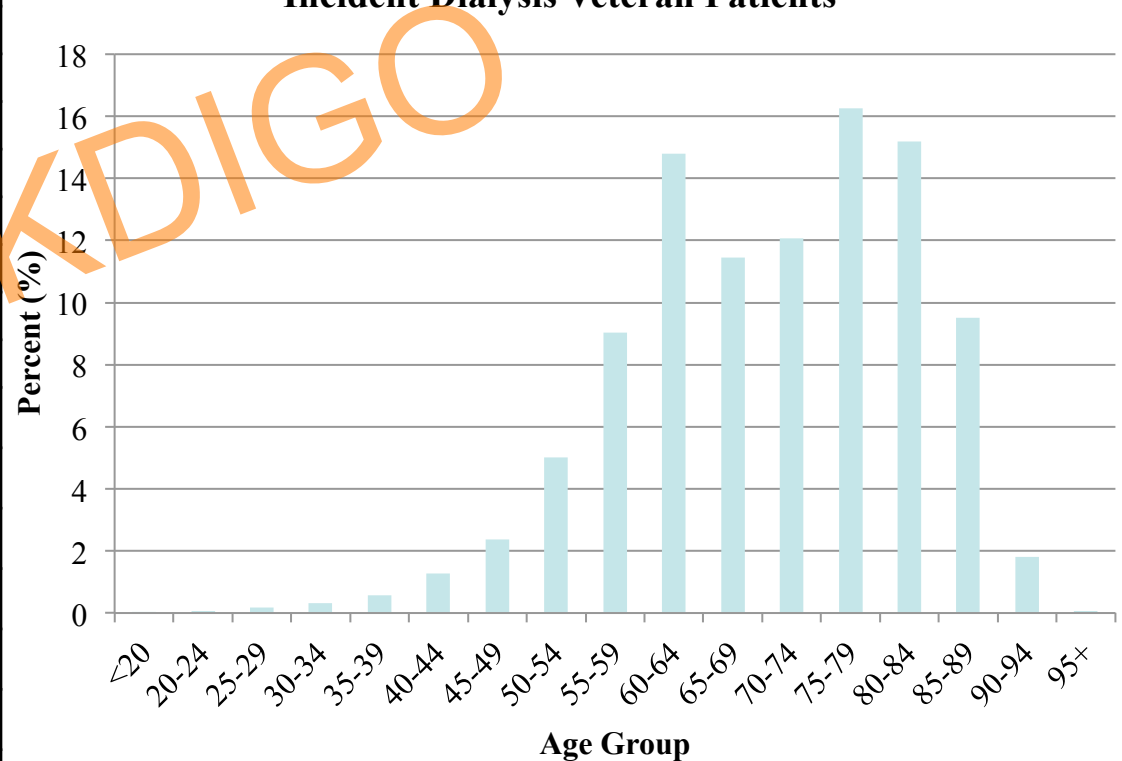

Data Source: Reference Table A.2(2) and special analyses, USRDS ESRD Database. *Adjusted for sex and race. The standard population was the U.S. population in 2011. Abbreviation: ESRD, end-stage renal disease.

# Age at first ESRD Service in 52,172 Incident ESRD Veterans

Age group	Frequency	Percent
<20	15	0.03
20-24	27	0.05
25-29	91	0.17
30-34	172	0.33
35-39	301	0.58
40-44	668	1.28
45-49	1236	2.37
50-54	2611	5.00
55-59	4718	9.04
60-64	7723	14.80
65-69	**5977**	**11.46**
70-74	**6296**	**12.07**
75-79	**8479**	**16.25**
80-84	**7923**	**15.19**
85-89	**4955**	**9.50**
90-94	**946**	**1.81**
95+	**34**	**0.07**

Age at First ESRD Service (5-year group) in 52,172 Incident Dialysis Veteran Patients
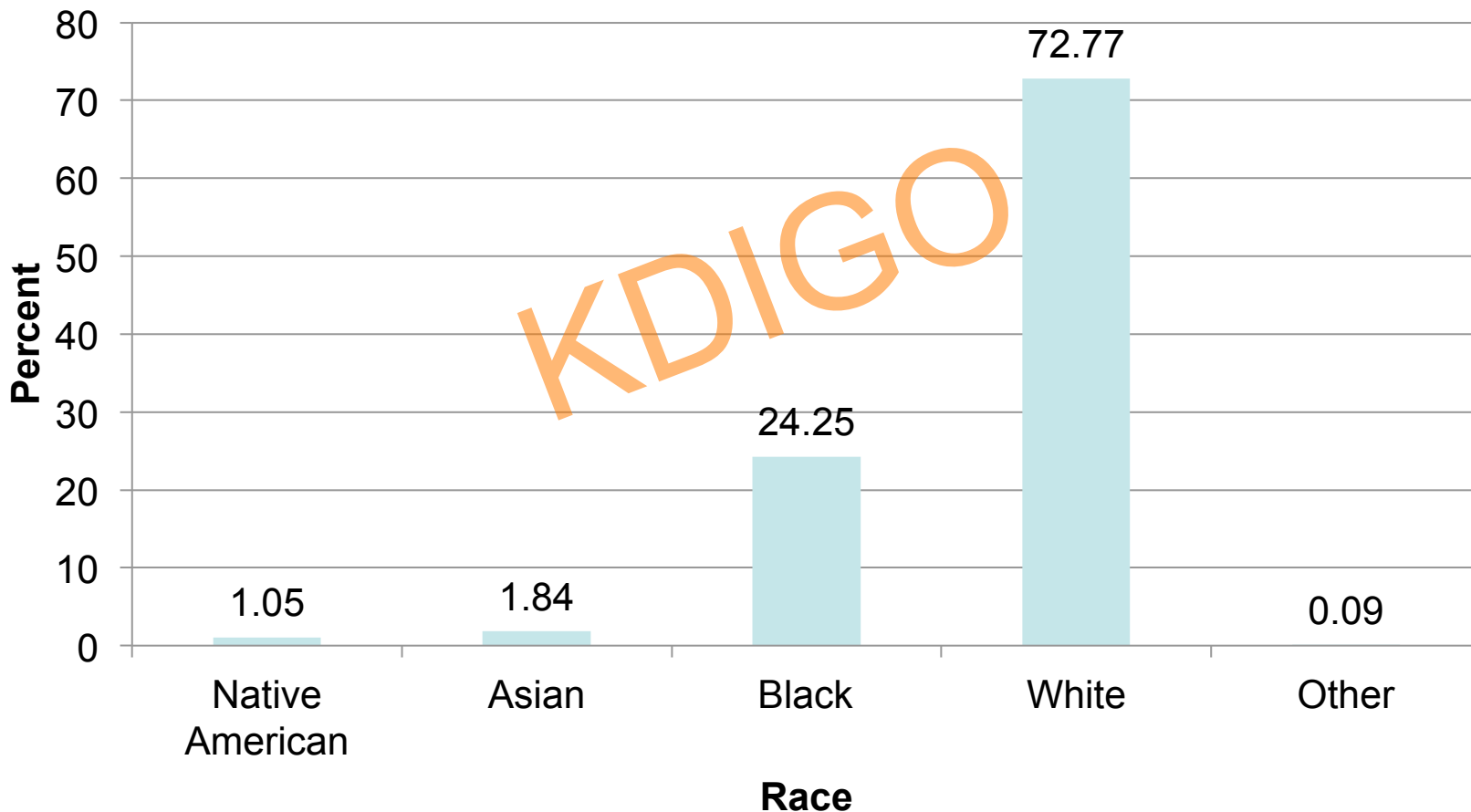

USRDS – TC-CKD: Data on file

Trends in adjusted* ESRD incidence rate (per million/year), by race, in the U.S. population, 1996-2014
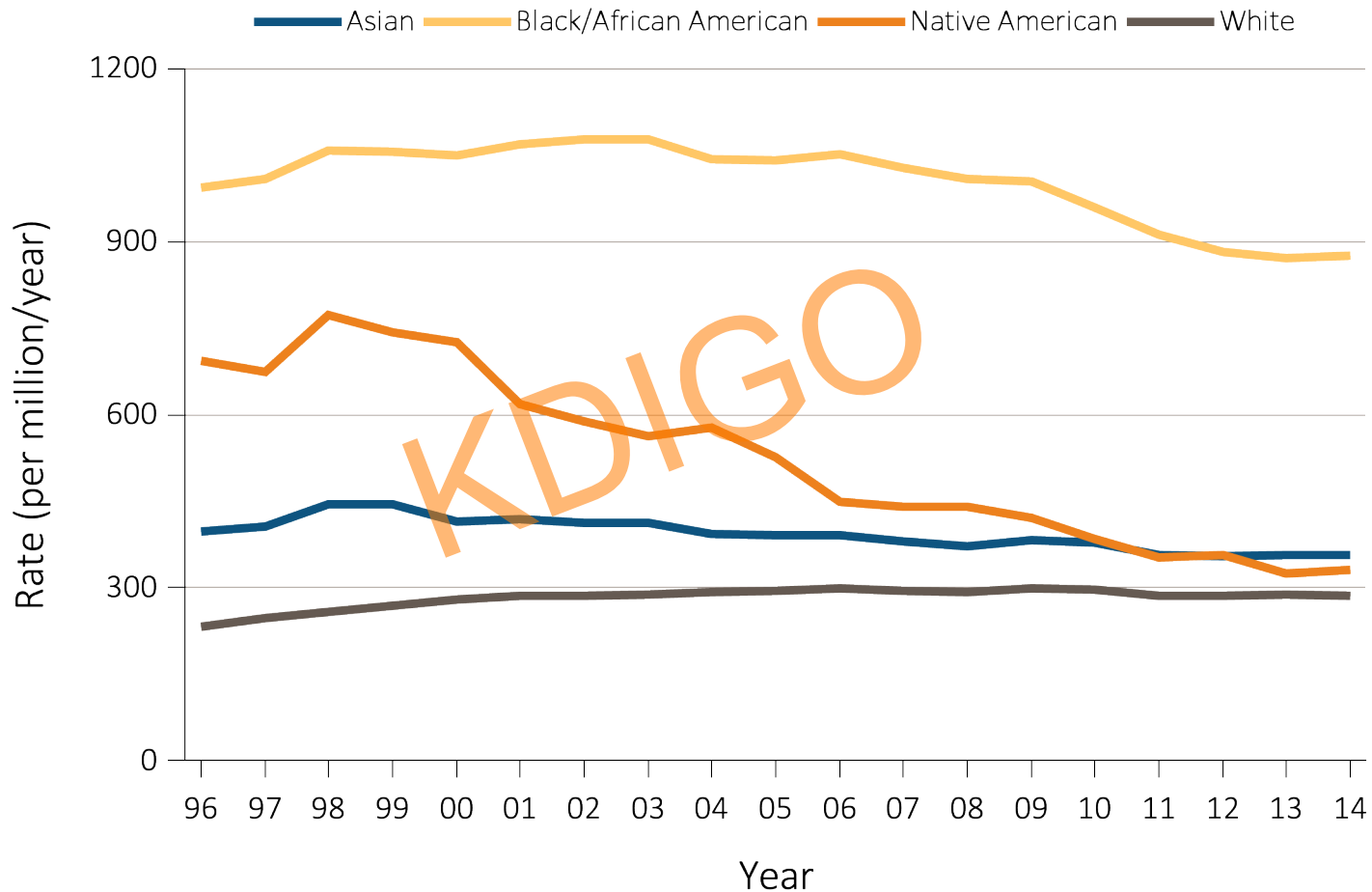
Data Source: Reference Table A.2(2) and special analyses, USRDS ESRD Database. *Adjusted for age and sex. The standard population was the U.S. population in 2011. Abbreviations: Af Am, African American; ESRD, end-stage renal disease.

Core Demographics from TCCKD

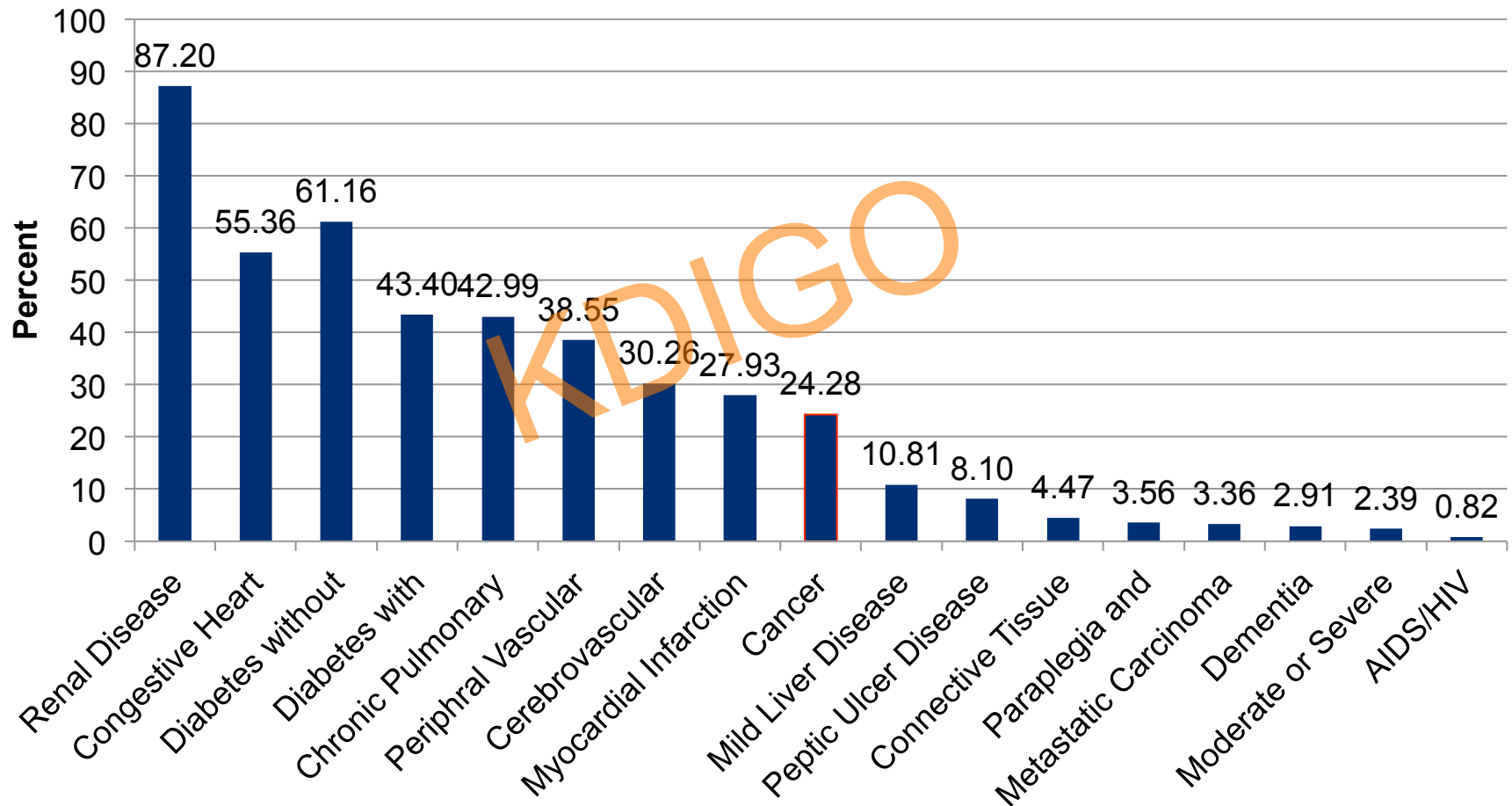**Race in 52,095 TCCKD Patients**

USRDS – TC-CKD: Data on file

Post-Transition Mortality: Age and Race

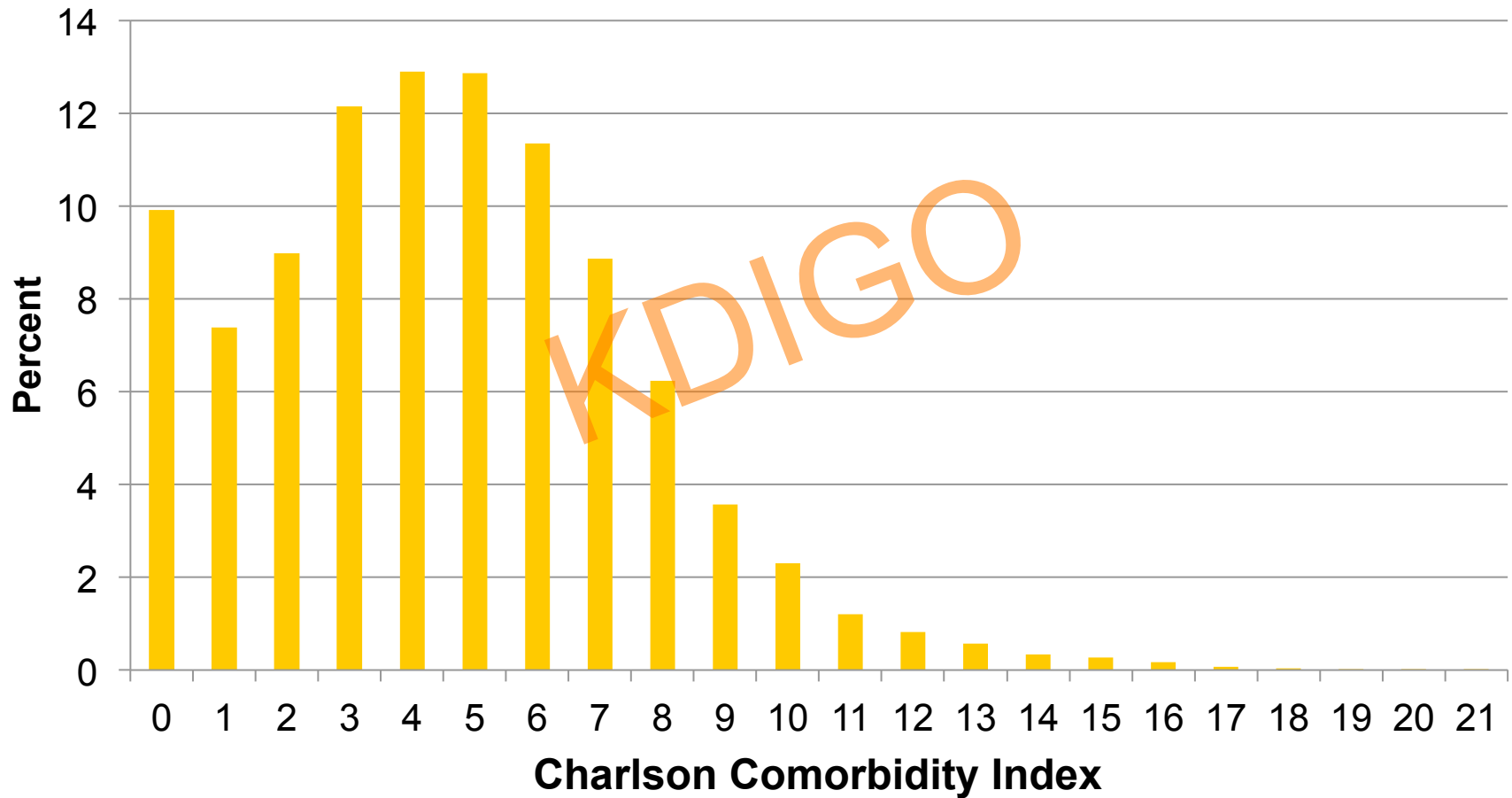| Mortality	Frequency	%	Age (yrs)	% Black
<3 mo	5489	11	76±10	15
3-<12 mo	8850	17	75±10	17
12 -<24 mo	7358	14	73±11	18
>=24 mo	12121	23	72±11	21
Alive after 2 years	18340	35	64±12	35

USRDS – TC-CKD: Data on file

Pre-existing Comorbidities

USRDS – TC-CKD: Data on file
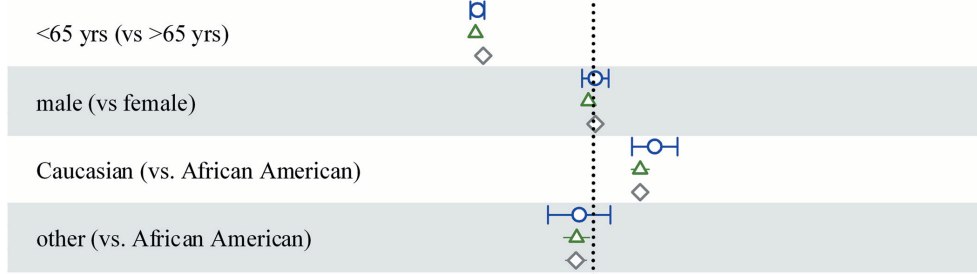
Charlson Comorbidity Index
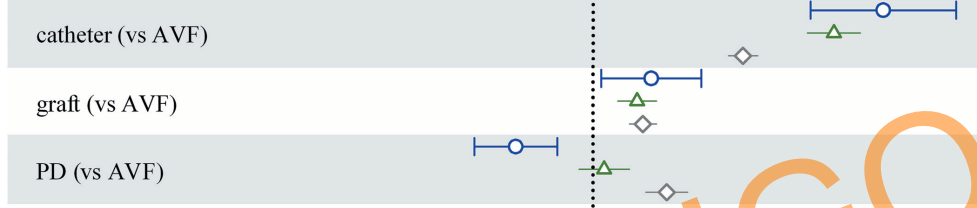

USRDS – TC-CKD: Data on file

A

DEMOGRAPHIC
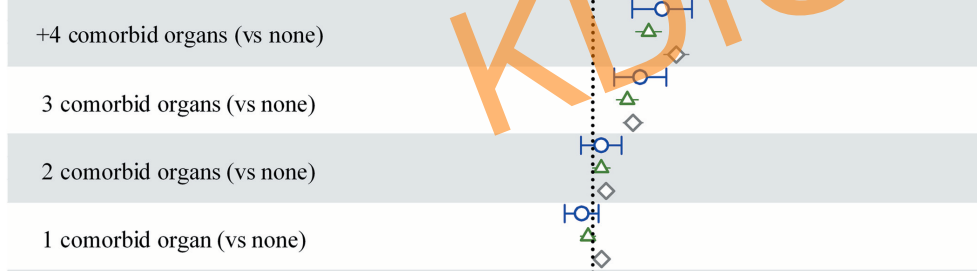
<65 yrs (vs >65 yrs)

male (vs female)

Caucasian (vs. African American)

other (vs. African American)

ACCESS

catheter (vs AVF)

graft (vs AVF)

PD (vs AVF)

COMORBIDITY

+4 comorbid organs (vs none)

3 comorbid organs (vs none)

2 comorbid organs (vs none)

1 comorbid organ (vs none)

PATIENT

BMI (kg/m^2)

previous inpt dialysis (vs outpt start)

BLOOD PRESSURE

systolic (10 mmHg)

diastolic (10 mmHg)

○ early patient death (<2 weeks)
△ incident patient death (<90 days)
◇ prevalent patient death (days 91-365)

0.5   1.0   1.5   2.0   2.5   3.0

decreased death risk   increased death risk

Chan KE et al.,
Clin J Am Soc Nephrol
6: 2642–2649, 2011

Comorbidity burden at dialysis initiation and mortality: A cohort study

Alwyn T Gomez[1], Bryce A Kiberd[2,3], J Patrick Royston[4], Talal Alfaadhel[2], Steven D Soroka[2,3], Brenda R Hemmelgarn[5,6] and Karthik K Tennankore[2,3*]

Table 2 Cox regression coefficients and c-index for precise and categorical CCI/ESRD-CI

Index	Regression coefficient [95 % CI]	c-index
Precise CCI	0.55 [0.38-0.71]	0.61
Categorical CCI	0.56 [0.39-0.72]	0.61
Precise ESRD-CI	0.52 [0.38-0.66]	0.63
Categorical ESRD-CI	0.52 [0.38-0.66]	0.62

B

LABORATORY

hemoglobin (per g/dl increase)

albumin (per 0.5 g/dl increase)

potassium (per meq/l increase)

SOCIOECONOMIC

employed (vs unemployed)
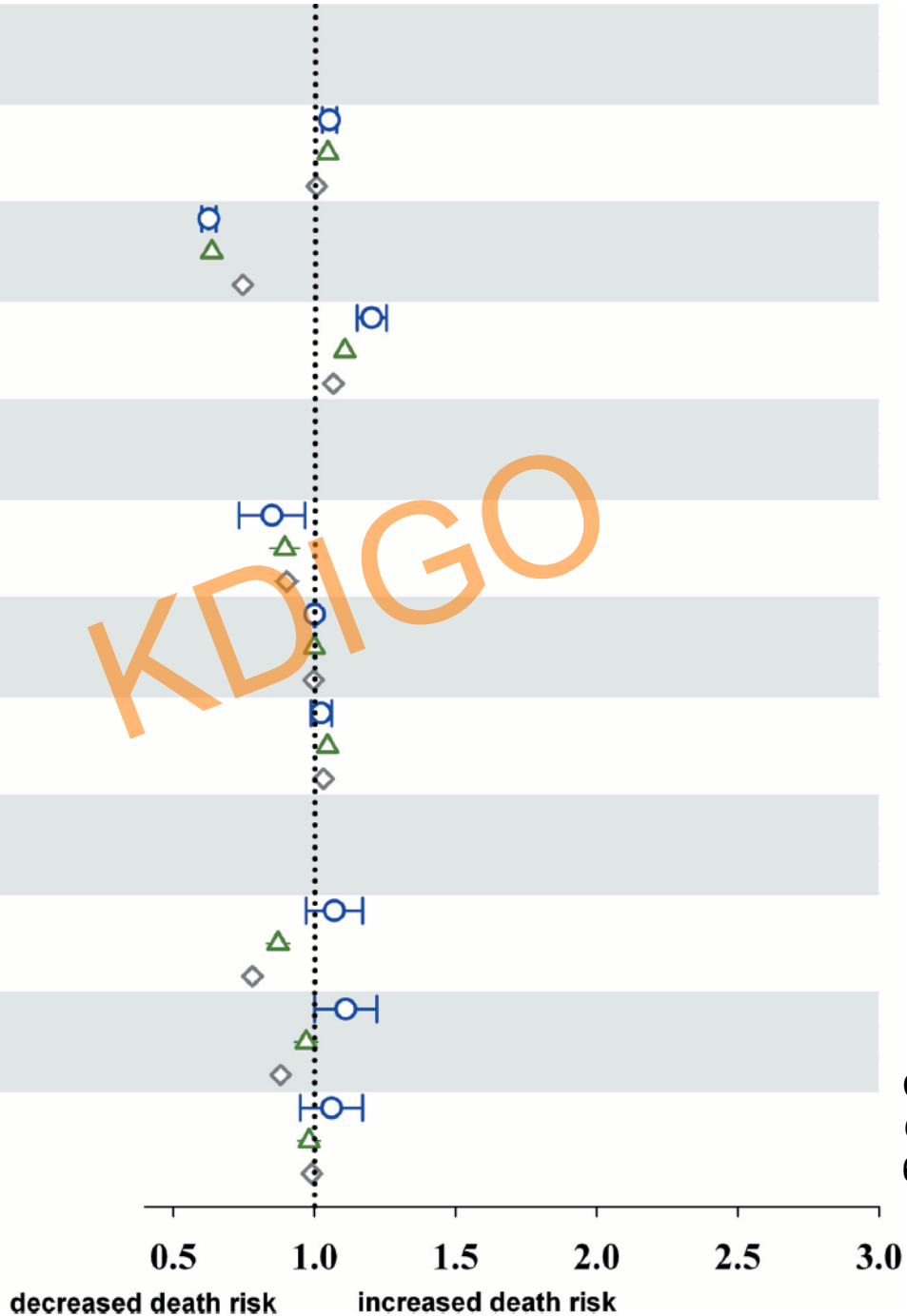
median annual income ($1000)

high school graduation rate (10%)

YEAR

2007-2009 (vs 1997-2000)

2004-2006 (vs 1997-2000)

2001-2003 (vs 1997-2000)

0.5   1.0   1.5   2.0   2.5   3.0

decreased death risk   increased death risk

KDIGO

A Need for Validated Prognostic Tools in CKD

Supportive Care: Time to Change Our Prognostic Tools and Their Use in CKD

(CJASN, *in press*)

Cécile Couchoud,* Brenda Hemmelgarn,[†‡] Peter Kotanko,[§‖] Michael J. Germain,[¶] Olivier Moranne,[**††] and Sara N. Davison[‡‡]

Valuable information on prognosis will spur the exchange between health professionals and patients, taking into account that many individual or cultural aspects will influence the shared decision–making process, in which <u>*practitioners and patients jointly consider best clinical evidence in light of a patient's specific health characteristics and values when choosing health care*</u>.

Although neither a clinician nor a prognostic score can predict with absolute certainty how well a patient will do or how long he/she will live, **validated prognostic scores** may improve the accuracy of the prognostic estimates that <u>*influence the clinical decisions and a patient-centered approach.*</u>

Prediction score for early mortality among ESRD patients transitioning to dialysis

Predicting Early Death Among Elderly Dialysis Patients: Development and Validation of a Risk Score to Assist Shared Decision Making for Dialysis Initiation

Mae Thamer, PhD,[1] James S. Kaufman, MD,[2] Yi Zhang, PhD,[1] Qian Zhang, MPH,[1] Dennis J. Cotter, MSE,[1] and Heejung Bang, PhD[3]
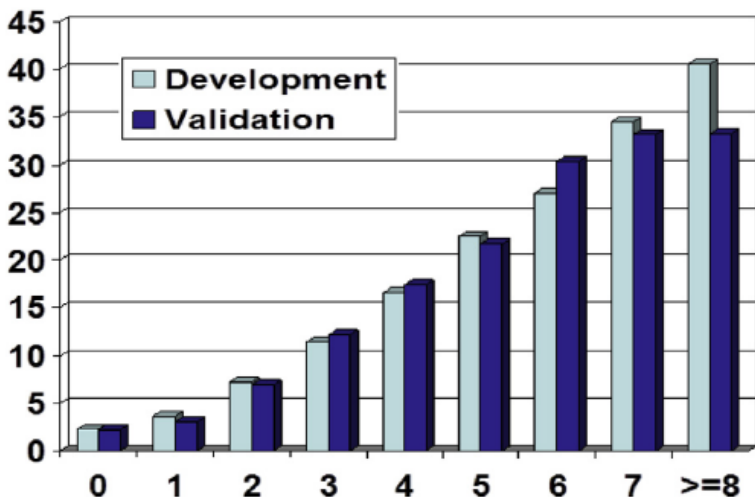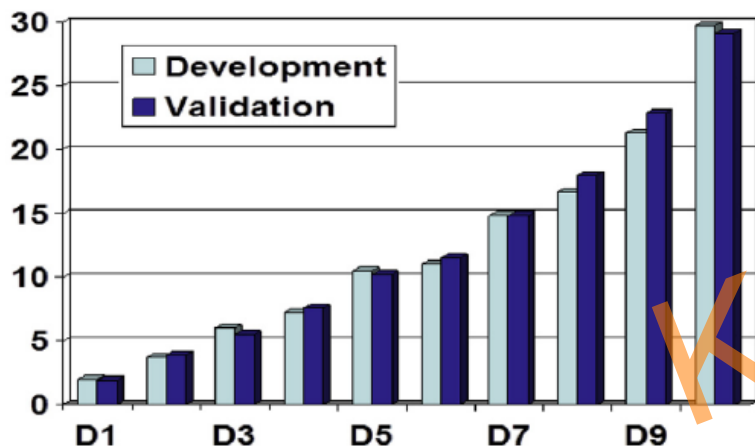
Total Score	Estimated Probability of Dying		Proportion of Patients With Same Score
	Within 3 mo	Within 6 mo	
0	2%	4%	2%
1	3%	7%	12%
2	7%	12%	25%
3	12%	20%	27%
4	17%	27%	19%
5	22%	35%	10%
6	28%	44%	4%
7	34%	49%	1%
≥8	39%	55%	0.2%

AUROC=0.69

A clinical score to predict 6-month prognosis in elderly patients starting dialysis for end-stage renal disease

Cécile Couchoud[1], Michel Labeeuw[2], Olivier Moranne[3,4,5], Vincent Allot[6], Vincent Esnault[5], Luc Frimat[7], Bénédicte Stengel[3,4], and for the French Renal Epidemiology and Information Network (REIN) registry
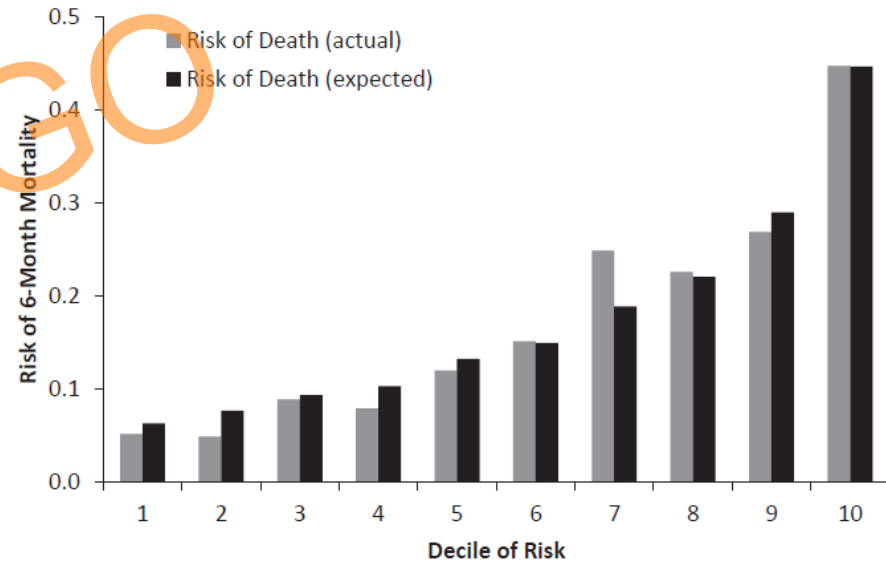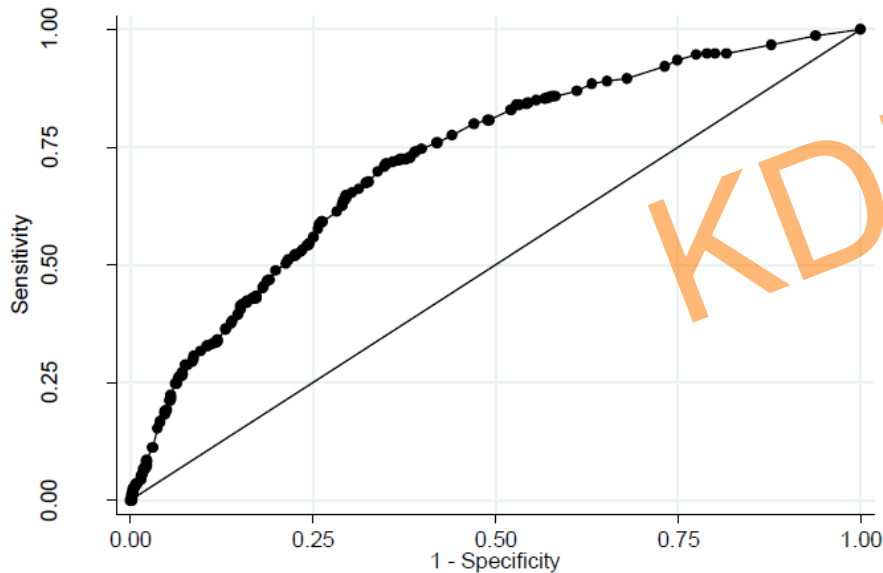
Table 4. Six-month mortality rates by risk score in the training and the validation samples

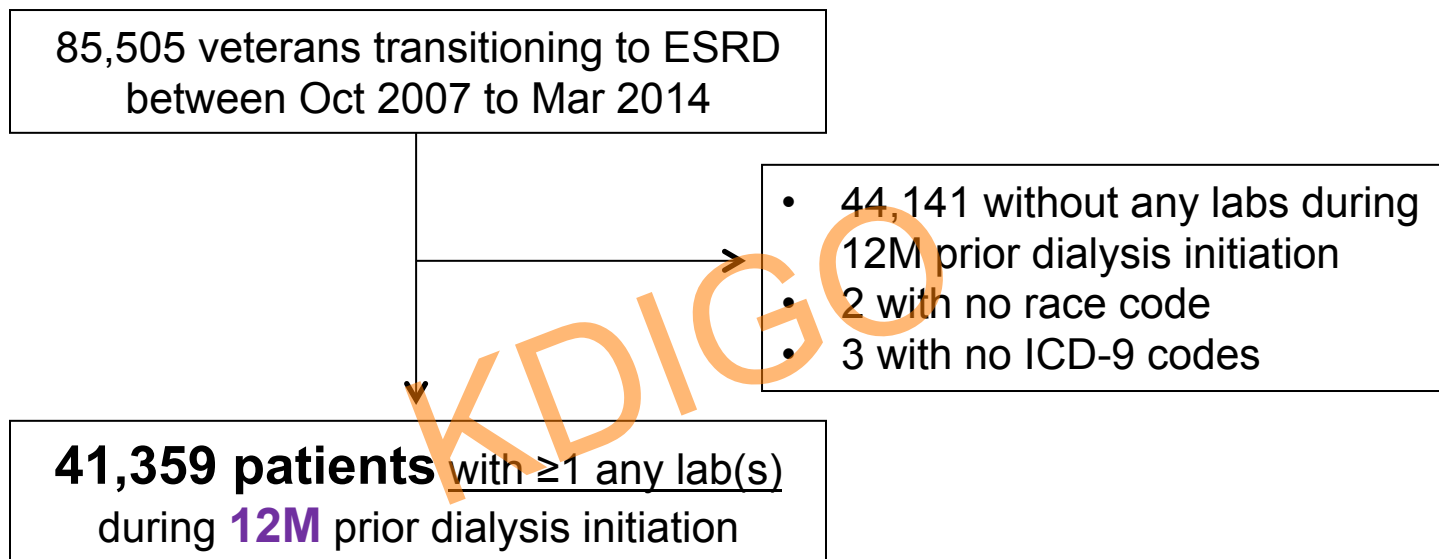| Risk score	Training sample			Validation sample		
	Number of deaths[a]	Number at risk[a]	Percentage	Number of deaths[a]	Number at risk[a]	Percentage
0 Point	41	511	8	26	330	8
1 Point	39	508	8	33	339	10
2 Points	64	453	14	49	294	17
3–4 Points	160	628	26	82	399	21
5–6 Points	93	266	35	59	178	33
7–8 Points	50	98	51	32	64	50
≥9 Points	22	36	62	25	35	70

AUROC=0.70

A Clinical Risk Prediction Tool for 6-Month Mortality After Dialysis Initiation Among Older Adults

James P. Wick, MSc,[1] Tanvir C. Turin, PhD, MBBS,[2] Peter D. Faris, PhD,[1]
Jennifer M. MacRae, MSc, MD,[1] Robert G. Weaver, MSc,[3] Marcello Tonelli, SM MD,[3]
Braden J. Manns, MSc, MD,[1,3] and Brenda R. Hemmelgarn, PhD, MD[1,3]

AUROC=0.72

Development and Validation of a New Prognostic Score for ESRD using Prelude Data

85,505 veterans transitioning to ESRD between Oct 2007 to Mar 2014

- 44,141 without any labs during 12M prior dialysis initiation
- 2 with no race code
- 3 with no ICD-9 codes

**41,359 patients** with ≥1 any lab(s) during **12M** prior dialysis initiation

Patients were **68±11 years old**, of which **98% were male**, 29% were black, and 7% were Hispanic; 47% and 28% had diabetes and hypertension as the cause of ESRD, respectively.

Median eGFR at dialysis initiation were **12 (IQR, 8-18) mL/min/ 1.73m^2**.
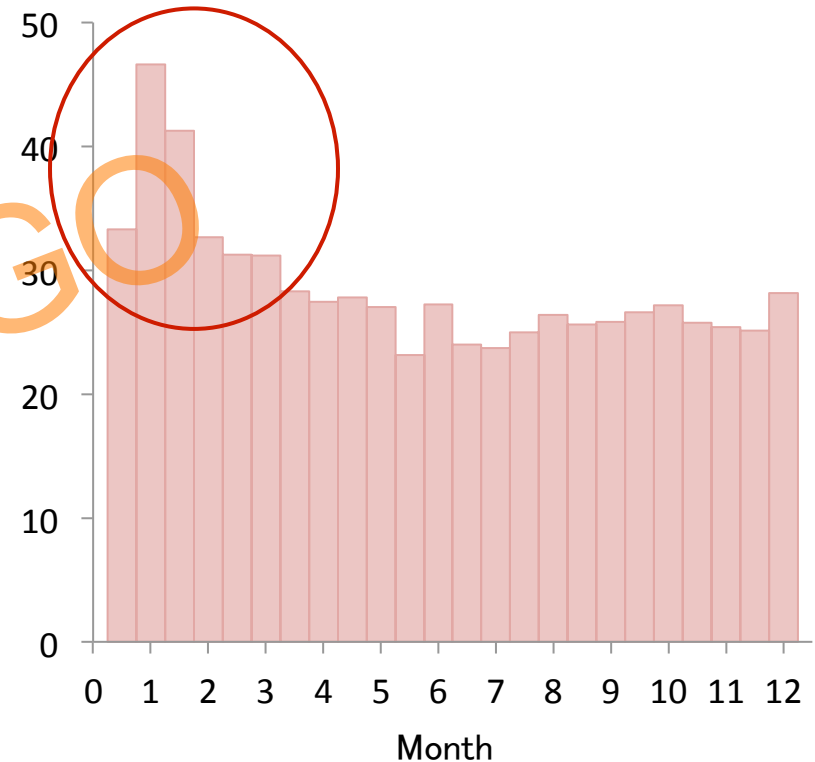
Estimated survival and change in mortality rate over 1 year following dialysis initiation among 41,359 veterans with ESRD

USRDS – TC-CKD: Data on file

Estimated survival
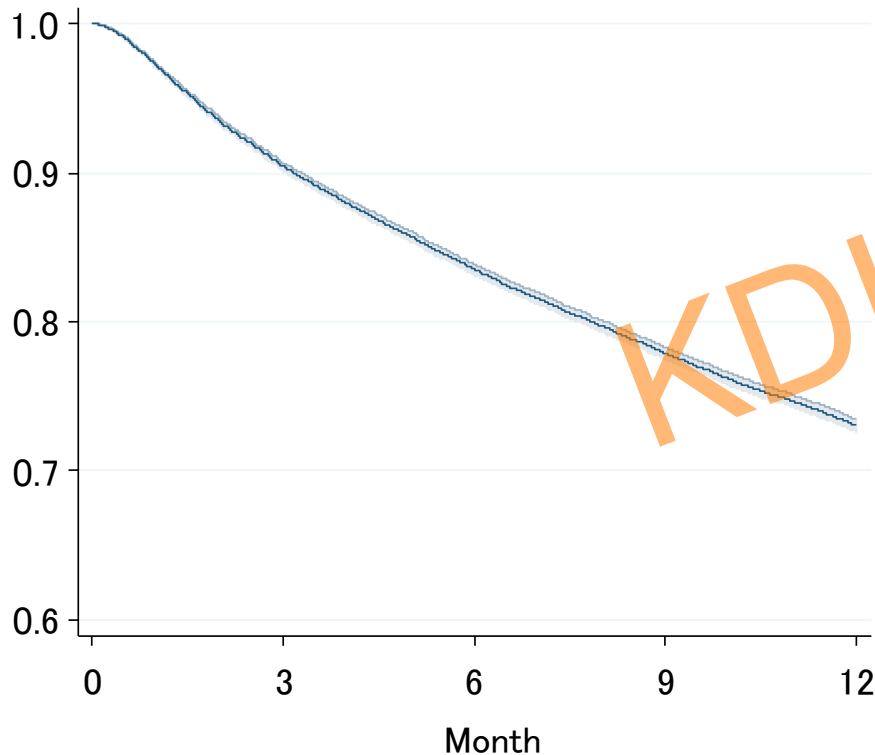
Mortality rate
(per 100 patient-years)

➤ By using the Cox PH model, **a new prognostic score** was <u>developed among randomly selected 27,710 patients</u> based on demographics, cause of ESRD, comorbid conditions, and less-modifiable laboratory variables (i.e., WBC, Albumin, BUN, eGFR, sodium), and then **validated among the remaining 13,469 patients**.

Potential models with and without labs

Multivariable logistic regression for 6M mortality

	Demo +16 Comorbids	+eGFR	+eGFR +Alb	+eGFR+Alb +1Y $\triangle$ eGFR
Base AUC*	0.7062	0.7103	0.7147	0.7238
AUC	0.7062	0.7167	0.7375	0.7529
$\triangle$ AUC	0	0.006	0.023	0.029

* Base AUC is based on the "Demo + 16 Comorbids" model

33

USRDS – TC-CKD: Data on file

Calibration plots
between predicted vs. observed mortality

Each group included 2,500 patients.
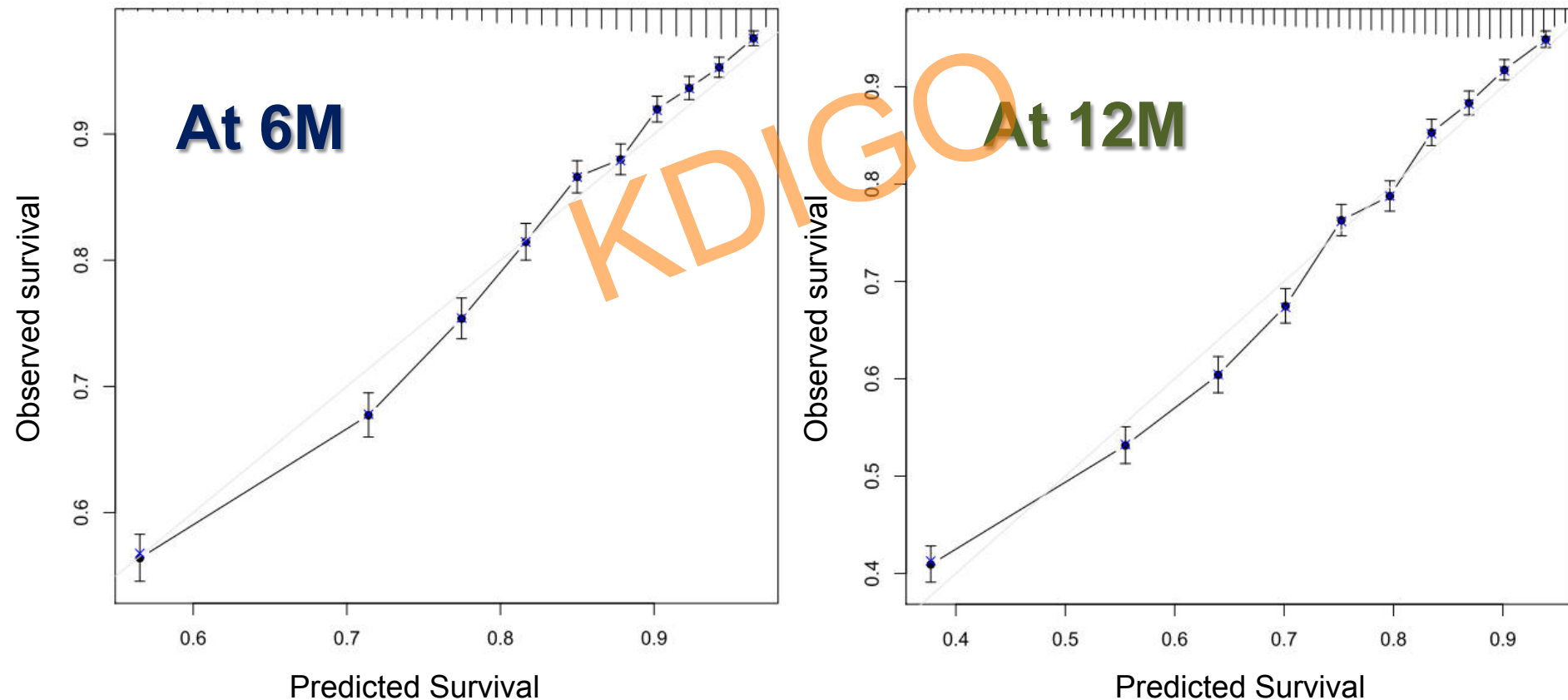
Dementia

- Dementia is more common in the elderly

  - Elderly patients now comprise a large proportion of the incident ESRD population

- Dementia represents a contraindication to RRT initiation

  - Decisions are often difficult in clinical practice

  - Many patients with dementia are started on RRT

- The associaiton of dementia with outcomes in incident ESRD are unclear

Dementia in Incident ESRD

- 45,076 US veterans who transitioned to ESRD between10/2007-09/2011
  - 1,336 (3%) patients with a dementia diagnosis
- Older age, black race and comorbid conditions (especially cerebrovascular disease) were associated with dementia

Molnar MZ et al., TC-CKD data on file

Dementia in Incident ESRD

- 8,476 patients died over the first 6 months post-transition
  - 8,080 non-demented (mortality rate 411/1000 patient-years)
  - 396 demented (mortality rate 708/1000 patient-years)
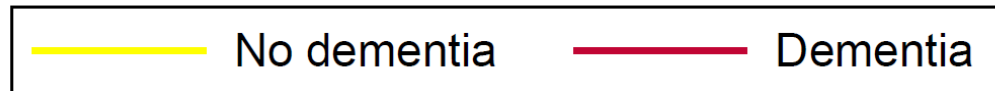- Crude hazard ratio: 1.71 (95%CI: 1.55-1.90)

Molnar MZ et al., TC-CKD data on file

Molnar MZ et al., TC-CKD data on file

HR 1.19, 95%CI: 1.03-1.37

Probability of Mortality

Follow-up time (months)
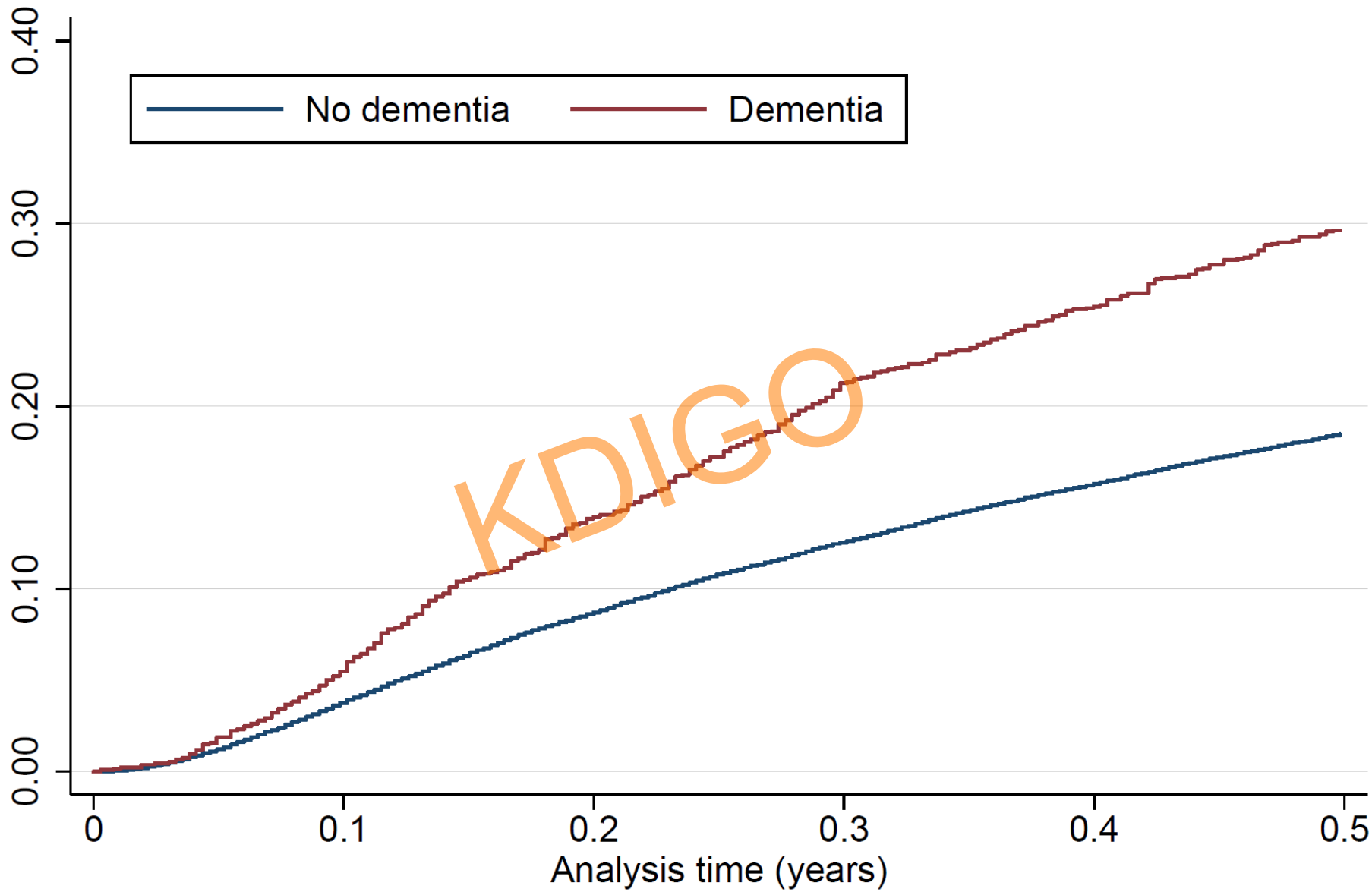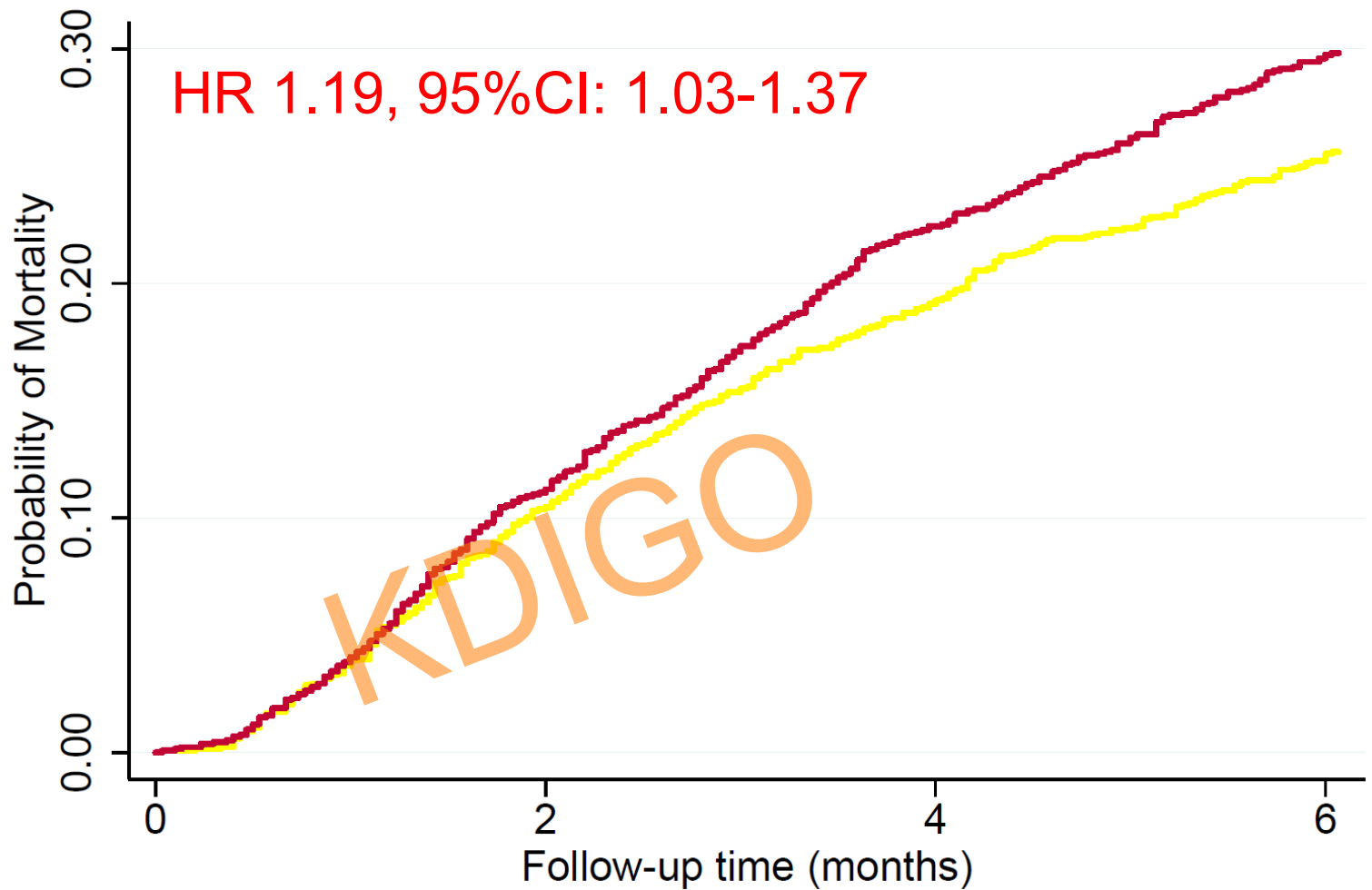
Number at risk

	0	2	4	6
Dementia absent	1328	1190	1074	993
Dementia present	1328	1181	1030	935

No dementia — Dementia

Molnar MZ et al., TC-CKD data on file

Using Patient Characteristics for Prognosis: Challenges

- ## Do we have the most relevant end points?

    - Mortality used ubiquitously
    - Other end points may be more relevant
        - E.g. hospitalization, QOL

- ## Do we have the most relevant characteristics?

    - Lots of data in cohorts with limited generalizability
    - Fewer data in generalizable cohorts

Conclusions

- Early mortality is extremely high in incident ESRD patients

  - Not all "mortality" is equal!!!

- Decisions about optimal ESRD transition (e.g. HD vs. PD vs. Tx vs. palliative care) should consider multiple outcomes and patient preferences

- More research needed for development of generalizable prognostic tools