Predicting Mortality in Hemodialysis Patients

How good are we?

September 19, 2015

Dan Martinusen PharmD

Declaration

- I have no conflict of interest to declare for this topic

Objectives

- Describe why prognostication is useful for both the patient and organization
- Describe some patient factors that may be helpful in predicting mortality
- Be able to prognosticate death using existing tools
- Engage in conversation regarding some other patient factors that may improve the precision (sensitivity and specificity) of a prognostication equation.
- Describe to how to use the prediction in actual clinical care

What is Prognostication?

- Making a prediction about the future.
- With respect to end of life, it is the estimation of length of life left.

Why prognosticate?

- To make us feel good (or bad – depending)
- To plan for timely referral to palliative care
- To consider conservative management where appropriate
- To monitor more frequently to provide pain and symptom management
- To plan the program's needs and growth
- To plan for home supports / social infrastructure
- To engage in conversations around the end of life with the patient and family

What is the % chance of predicted death that should trigger a conversation or action?

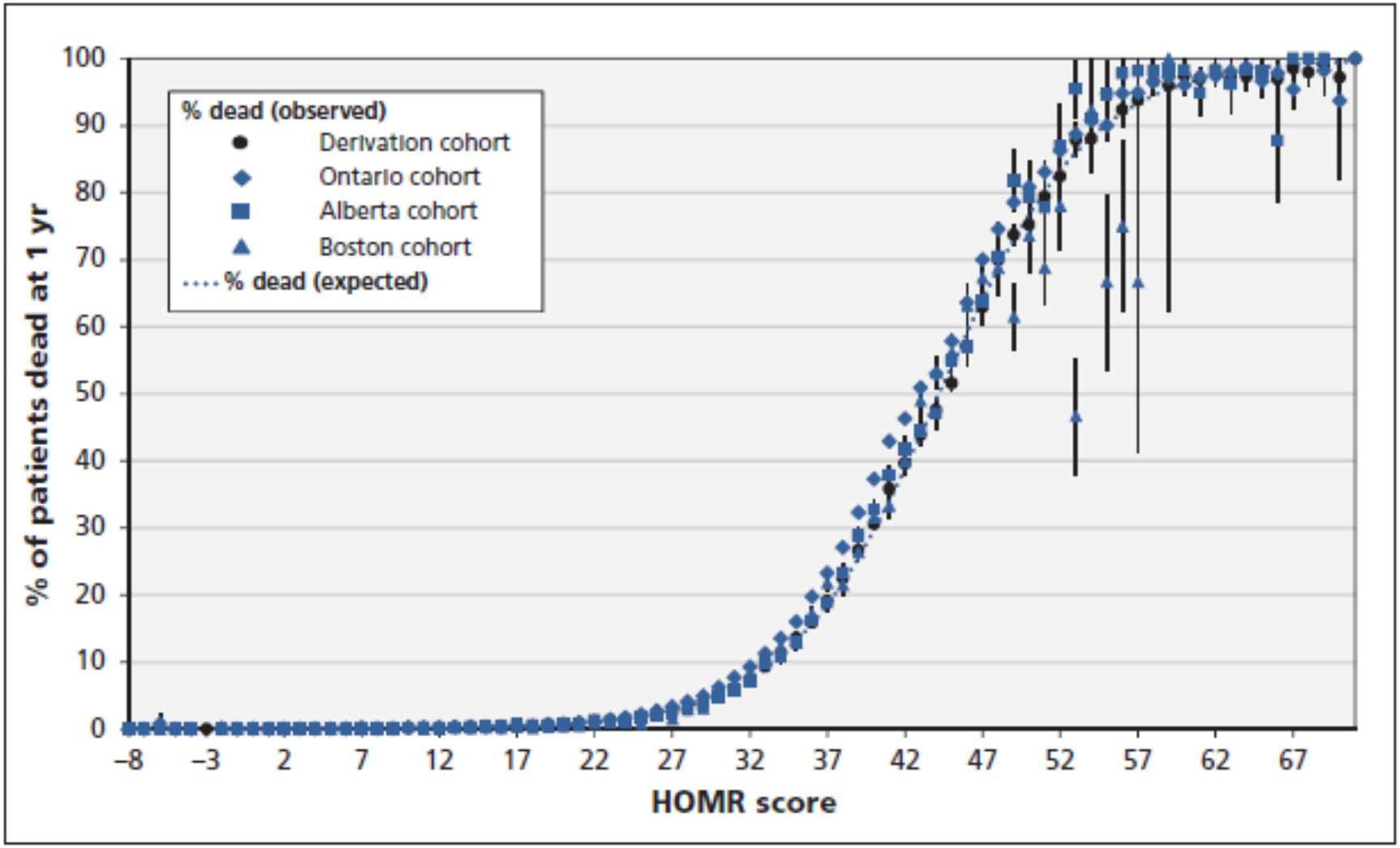


Figure 2: Observed and expected risks of death within 1 year after admission to hospital in the 3 validation cohorts (Ontario, Alberta and Boston) and the derivation cohort,[1] as calculated by the Hospital-patient One-year Mortality Risk (HOMR) model. Error bars indicate 95% confidence intervals. A summary of the calibration of each cohort to the expected risk of death is given in Table 2.

Van Walraven CMAJ June 2015

Admission urgency				
Elective	0	0	0	0
ED, no ambulance	3	1	0	0
ED, ambulance	5	2	1	0

Prognostication trials in renal care

- Couchoud C, Labeeuw M, Moranne O et al. A clinical score to predict 6-month prognosis in elderly patients starting dialysis for endstage renal disease. Nephrol Dial Transplant 2009; 24: 1553–1561

- Cohen L, Ruthazer R, Moss A, Germain M. Predicting Six-Month Mortality for Patients Who Are on Maintenance Hemodialysis. Clin J Am Soc Neph 2010 Jan;5(1): 72-29

- Liu J, Huang Z, Gilbertson DT, Foley RN, CollinsAJ. An improved comorbidity index for outcome analyses among dialysis patients. Kidney international 2010; 77: 141–151

- Weiss J, Platt R, Thorp M, Yang X et al. Predicting mortality in older adults with kidney disease: a pragmatic prediction model. J Am Geriat Soc 63 (2015): 508-515 (not dialysis)

- Floege J, Gillespie I, Kronenberg F et al.Development and Validation of a Predictive Mortality Risk Score from a European hemodialysis Cohort. Kidney Int 2015; 87: 996–1008

What “things” would be good to measure to predict death in a dialysis patient?

Current prognostic efforts

- Purely using clinical features (>74yo) (Couchoud model)
- The Surprise Question: "Would you be surprised if this patient died in the next 12 months?"
- Surprise question + predictive features (Cohen model)
- Purely using comorbid conditions (Liu model)
- Comorbidities & health status markers (Weiss)
- Purely using objective measures (Floege model)

Using Just Clinical Features

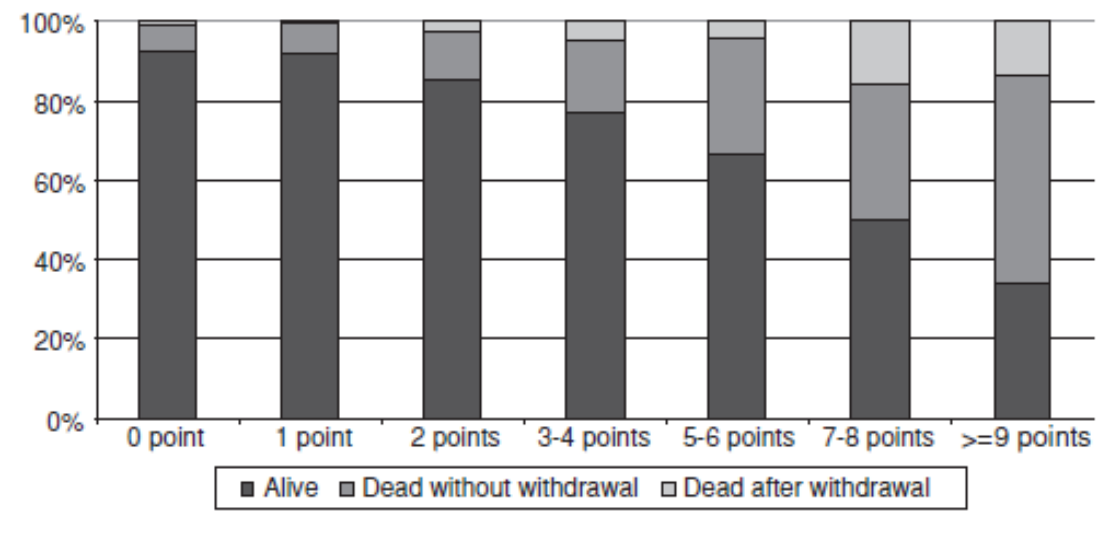
Couchoud 2009

Predicting **6 month mortality** in elderly (over 74) French patients initiating dialysis using 9 clinical features

Risk factors	Adjusted OR[a] (95% CI)	β-coefficient	Points[b]
Body mass index (kg/m^2)			
≥18.5	1		
<18.5	1.3 (1.1–1.6)	0.283	2
Diabetes			
Absence	1		
Presence	1.2 (1.1–1.3)	0.180	1
Congestive heart failure stage III or IV			
Absence	1		
Presence	1.3 (1.2–1.5)	0.289	2
Peripheral vascular disease stage III or IV			
Absence	1		
Presence	1.3 (1.1–1.5)	0.269	2
Dysrhythmia			
Absence	1		
Presence	1.2 (1.1–1.3)	0.170	1
Active malignancy			
Absence	1		
Presence	1.3 (1.1–1.5)	0.250	1
Severe behavioural disorder			
Absence	1		
Presence	1.5 (1.2–1.8)	0.391	2
Totally dependent for transfers			
Absence	1		
Presence	1.7 (1.4–2.0)	0.519	3
Initial context			
Planned	1		
Unplanned	1.5 (1.3–1.7)	0.395	2

Nephrol Dial Transplant (2009) 24: 1553–1561

Can be used to facilitate discussion with families/patients but not to withhold dialysis

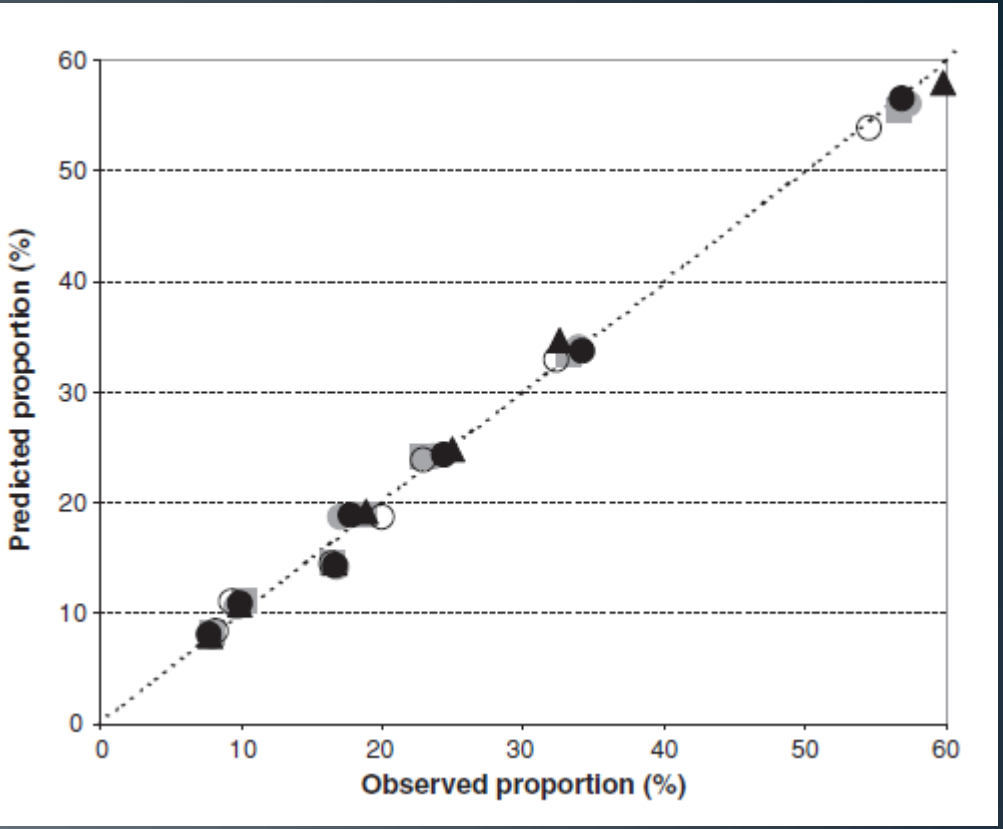


Risk score	Number of deaths[a]	Number at risk[a]	Percentage
0 Point	41	511	8
1 Point	39	508	8
2 Points	64	453	14
3–4 Points	160	628	26
5–6 Points	93	266	35
7–8 Points	50	98	51
≥9 Points	22	36	62
All	470	2500	19

Kidney International (2010) **77**, 141–151

Couchoud model fits very well with validation sample but "missing data imputed"

What risk score should trigger a conversation or action?



	Training sample			Validation sample		
Risk score	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
All	470	2500	19	306	1640	19

Kidney International (2010) **77**, 141–151

Clinical features PLUS surprise question

Cohen 2010

This 6 month equation is <u>not</u> perfect

- Originally developed in a single-centre (N= 449) by Cohen
- Uses surprise question, serum albumin, age, presence of dementia and peripheral vascular disease as predictive factors.

- Specificity = $\frac{\text{\# of individuals predicted to die}}{\text{\# of individuals who actually died}}$

- Sensitivity = $\frac{\text{\# of individuals predicted to live}}{\text{\# of individuals who actually lived}}$

100% in both sensitivity and specificity would be ideal

Clin J Am Soc Nephrol 5: 72–79, 2010

The Cohen Equation (hemodialysis)

- Survival probability at 6mo = $0.58^{\exp\{PI\}}$

where PI (prognostic index) = log(2.71)*SQ + log(0.27)*Albumin + log(1.36)*Age + log(1.88)*PVD + log(2.24)*Dementia

  - SQ: 1=not surprised, 0=surprised
  - Age: increment of 10 years, range: 16 – 92 years old
  - Albumin: range 1.7 – 5.0 g/dL
  - Estimates given in Table 3 of Cohen's paper
- Mortality probability at 6mo = 1 - Survival probability at 6mo
- (but you could just use the app)

Clin J Am Soc Nephrol 5: 72–79, 2010

The "Cohen equation"

- First – download "Qx Calculate" from the appstore on your Iphone / Android
- Search for "6-month mortality on HD"
- Answer questions, get prediction

Accessed apple app store Sept 10, 2015

Clin J Am Soc Nephrol 5: 72–79, 2010

ROGERS 3:15 PM 63%

By Name

PE Clinical Probability
Determine Pretest Probability of PE
Featured Content

6-Month Mortality on HD

A-a Gradient

ABCD² Score

ACC/AHA CV Risk Calculator (2013)

Access Care and Complications Management

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ROGERS 3:16 PM 63%

Cancel **Question 1/5**

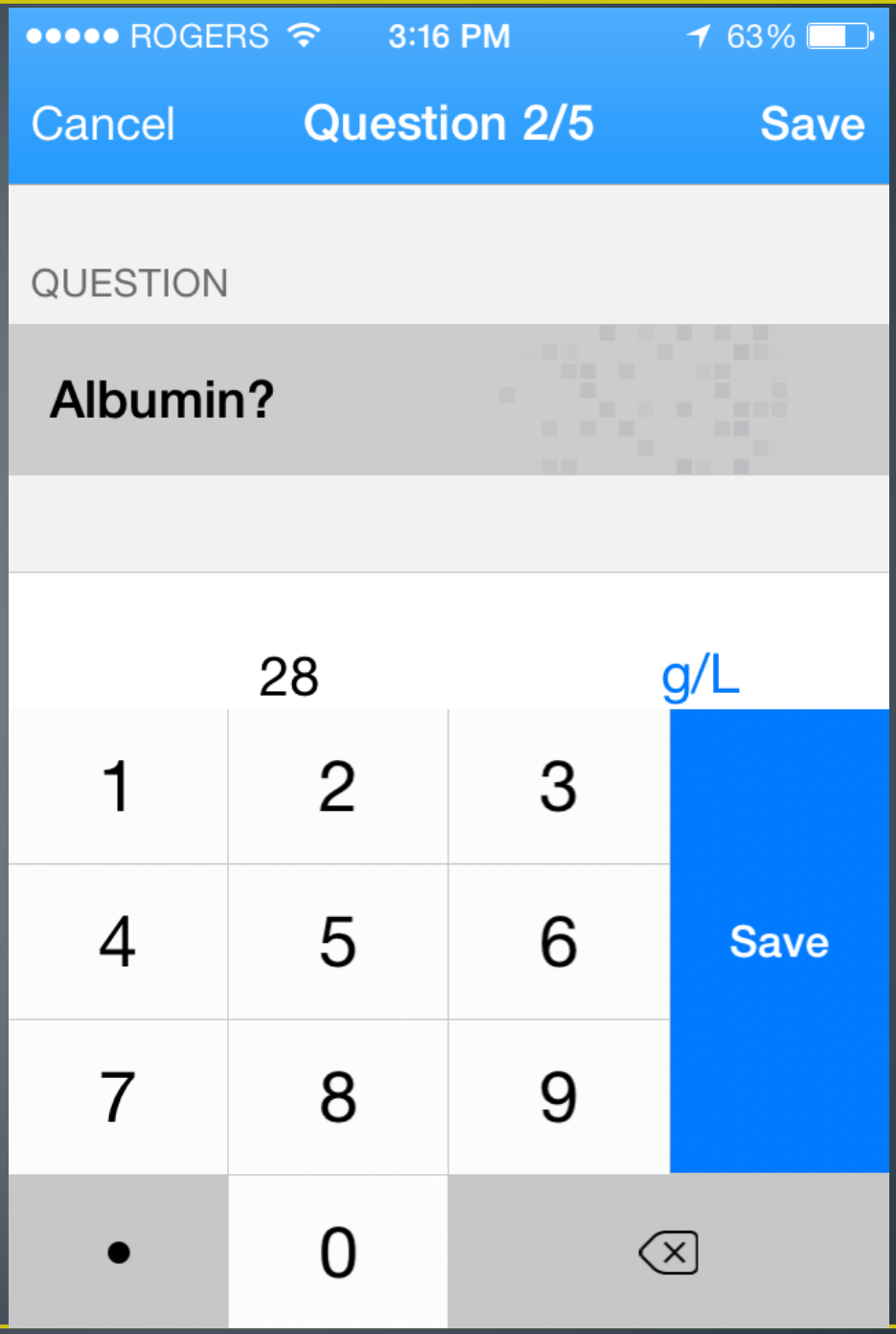
QUESTION

Would I be surprised if this patient died in the next year?

ANSWER CHOICES

No

Yes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QUESTION
Albumin?
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g/L
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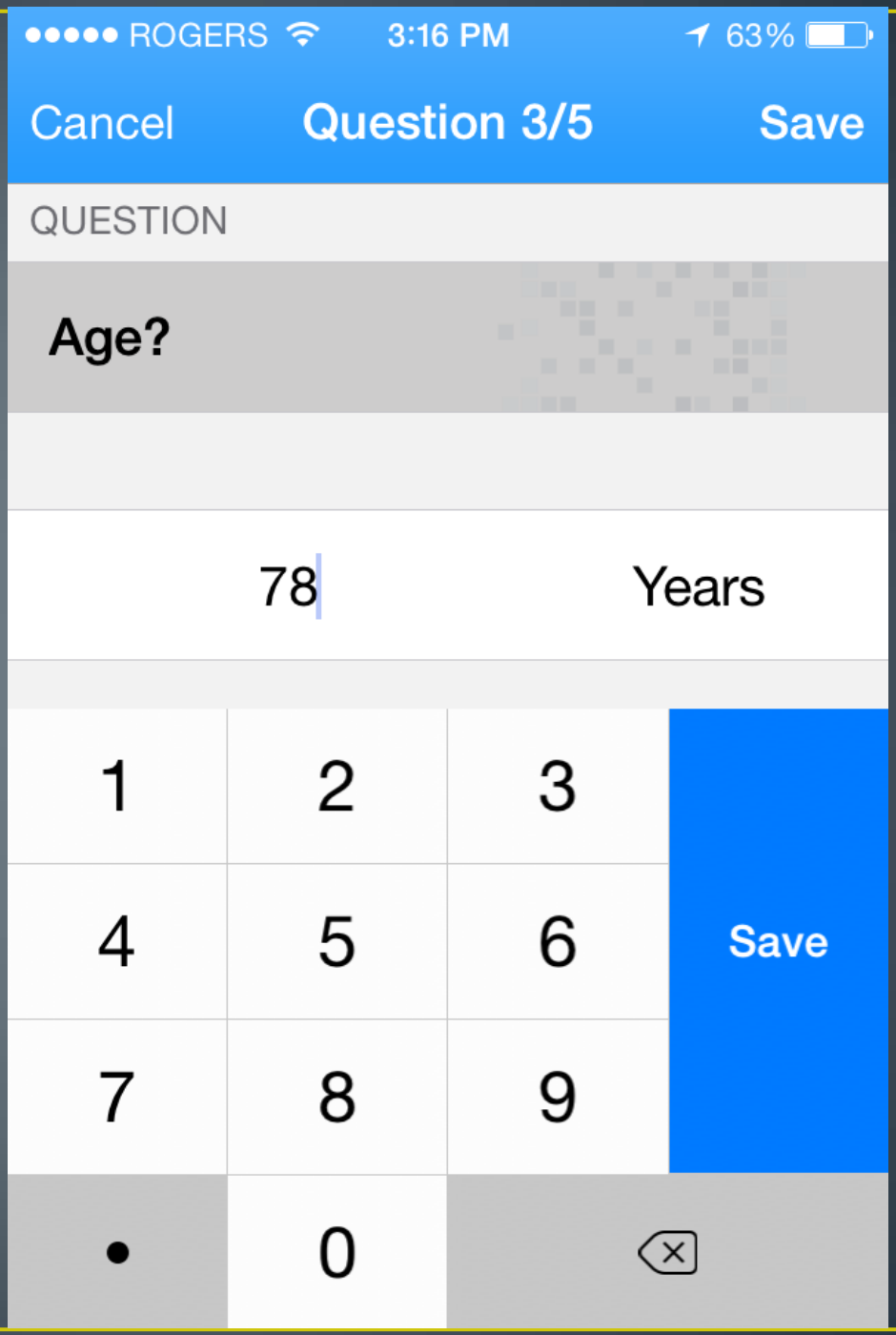
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QUESTION
Age?
78
Years
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•
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ROGERS 3:16 PM 63%

Cancel **Question 4/5**

QUESTION

Dementia?

ANSWER CHOICES

No

Yes

ROGERS 3:16 PM 63%

Cancel **Question 5/5**

QUESTION

Peripheral Vascular Disease?

ANSWER CHOICES

No

Yes

ROGERS 3:16 PM 63%

Back **6-Month Mortality on HD** Info

Would I be surprised if this patient died in the next year?	Yes
Albumin?	28 g/L
Age?	78 Years
Dementia?	Yes
Peripheral Vascular Disease?	No

ROGERS 3:16 PM 63%

Back **6-Month Mortality on HD** Info

Vascular Disease? No

RESULTS

Estimated Survival on Hemodialysis at 6 months

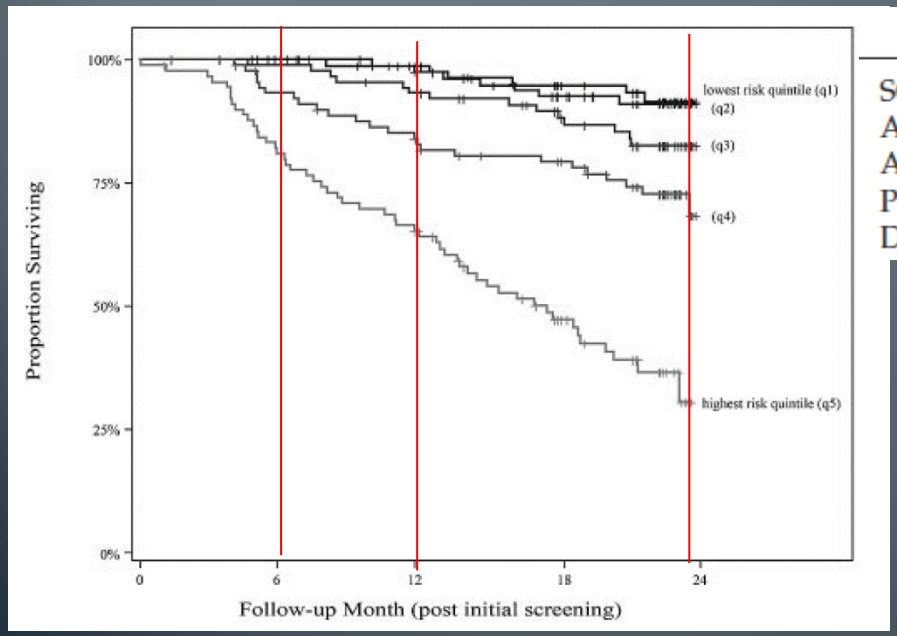
70.1 %

Estimated Risk of Death on Hemodialysis at 6 months

29.9 %

How predictive is the Cohen equation?

- Based on subjective parameters of dementia, peripheral vascular disease (harder to define in a dialysis patient?).
- Includes "surprise question" – highly subjective & variable based on physician background/training & knowledge of patient



Variable[a]	HR
SQ, not surprised *versus* surprised	2.71
Albumin (HR expressed for a 1-U increase)	0.27
Age (yr; HR expressed for a 10-yr increase)	1.36
PVD, yes *versus* no	1.88
Dementia, yes *versus* no	2.24

HR = hazard ratio

What is the % chance of predicted death that should trigger a conversation or action?

Clin J Am Soc Nephrol 5: 72–79, 2010

Using co-morbidities only

Liu 2010

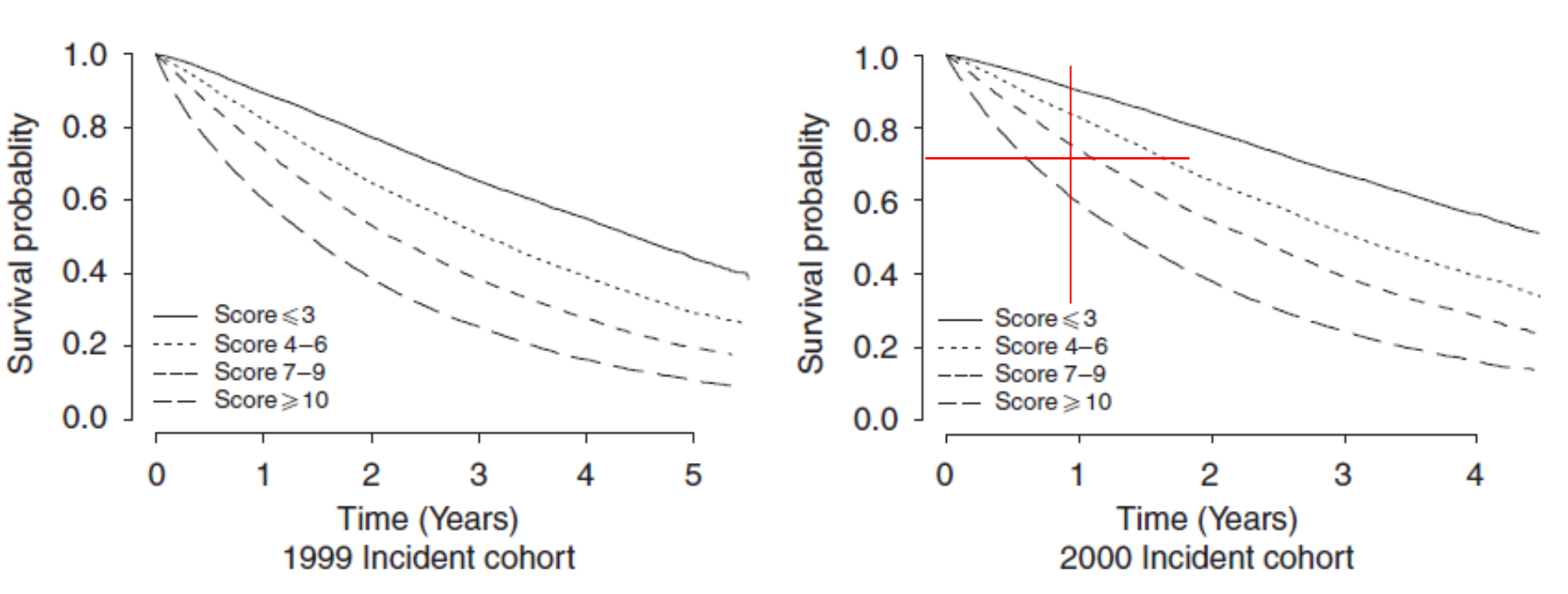
Kidney International (2010) **77**, 141–151

An improved comorbidity index for outcome analyses among dialysis patients

Jiannong Liu[1], Zhi Huang[1,2], David T. Gilbertson[1], Robert N. Foley[1,3] and Allan J. Collins[1,3]

Variable	Coefficient estimates	s.e.	Relative risk (95% CI)	*P*-value	Weight[a]
Age group, years					
0–19	−1.1560	0.2248	0.315 (0.203–0.489)	<0.0001	
20–29	−1.5569	0.0979	0.211 (0.174–0.255)	<0.0001	
30–39	−1.1940	0.0535	0.303 (0.273–0.336)	<0.0001	
40–49	−0.9646	0.0352	0.381 (0.356–0.408)	<0.0001	
50–59	−0.8238	0.0280	0.439 (0.415–0.464)	<0.0001	
60–64	−0.6663	0.0303	0.514 (0.484–0.545)	<0.0001	
65–69	−0.5770	0.0248	0.562 (0.535–0.590)	<0.0001	
70–79	−0.3712	0.0196	0.690 (0.664–0.717)	<0.0001	
⩾80[b]	0.0000	0.0000	1.000	NA	
Sex					
Men[b]	0.0000	0.0000	1.000	NA	
Women	−0.0137	0.0144	0.986 (0.959–1.015)	0.3421	
Race					
White[b]	0.0000	0.0000	1.000	NA	
Asian/Pacific Islander	−0.3242	0.0482	0.723 (0.658–0.795)	<0.0001	
African American	−0.2141	0.0170	0.807 (0.781–0.835)	<0.0001	
Native American	−0.2098	0.0616	0.811 (0.719–0.915)	0.0007	
Other	−0.1945	0.0778	0.823 (0.707–0.959)	0.0124	
ESRD primary cause					
Diabetes	0.2900	0.0322	1.336 (1.255–1.423)	<0.0001	3
Hypertension	0.1862	0.0303	1.205 (1.135–1.278)	<0.0001	2
GN/cystic kidney disease[b]	0.0000	0.0000	1.000	NA	0
Other	0.3463	0.0334	1.414 (1.324–1.510)	<0.0001	3
Comorbid conditions					
ASHD	0.0616	0.0165	1.064 (1.030–1.098)	0.0002	1
CHF	0.2950	0.0164	1.343 (1.301–1.387)	<0.0001	3
CVA/TIA	0.1881	0.0159	1.207 (1.170–1.245)	<0.0001	2
PVD	0.1990	0.0149	1.220 (1.185–1.256)	<0.0001	2
Other cardiac	0.1559	0.0154	1.169 (1.134–1.205)	<0.0001	2
COPD	0.2333	0.0167	1.263 (1.222–1.305)	<0.0001	2
GI	0.1794	0.0216	1.196 (1.147–1.248)	<0.0001	2
Liver disease	0.1885	0.0270	1.207 (1.145–1.273)	<0.0001	2
Dysrhythmia	0.2090	0.0158	1.232 (1.195–1.271)	<0.0001	2
Cancer	0.2020	0.0205	1.224 (1.176–1.274)	<0.0001	2
Diabetes	0.1250	0.0205	1.133 (1.088–1.180)	<0.0001	1

Using just comorbidities (Liu method)



comorbid conditions of atherosclerotic heart disease, congestive heart failure, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, dysrhythmia, other cardiac diseases, chronic obstructive pulmonary disease, gastrointestinal bleeding, liver disease, cancer, and diabetes.

What is the % chance of predicted death that should trigger a conversation or action?

Kidney International (2010) **77**, 141–151

Comorbidities and health status markers

Weiss 2015 (> 65 years old NON-dialysis patients)

Characteristic	65–79	≥80
Glomerular filtration rate, mL/min per 1.73 m^2		
Index		
30	0	0
20	41	32
10	74	63
2	100	89
Second		
30	30	2
20	12	2
10	6	1
2	3	0
Baseline systolic blood pressure, mmHg		
240	0	0
180	19	1
140	30	2
120	33	12
80	35	45
Age		
65	0	
70	17	
75	18	
79	22	
80		0
86		14
92		52
98		60
Body mass index, kg/m^2		
60	2	0
40	0	14
30	7	21
25	26	32
15	73	54
10	96	100
Sex		
Male	24	30
Female	0	0
History of heart failure	46	24
History of cardiovascular disease	25	11
Tobacco use	14	11
No history of hypertension	12	7
No statin use	23	15
Number of antihypertensive medications used		
1–2		5
≥3		9
Number of nondisease-specific measures		
1–2	44	46
≥3	51	62

Risk Score	Mortality Risk, %
Aged 65–79	
66	5
118	10
149	15
173	20
191	25
207	30
220	35
233	40
244	45
255	50
265	55
275	60
285	65
295	70
305	75
316	80
328	85
342	90
361	95
Aged ≥80	
45	10
75	15
97	20
115	25
129	30
143	35
155	40
165	45
176	50
186	55
195	60
205	65
214	70
224	75
234	80
246	85
259	90
278	95

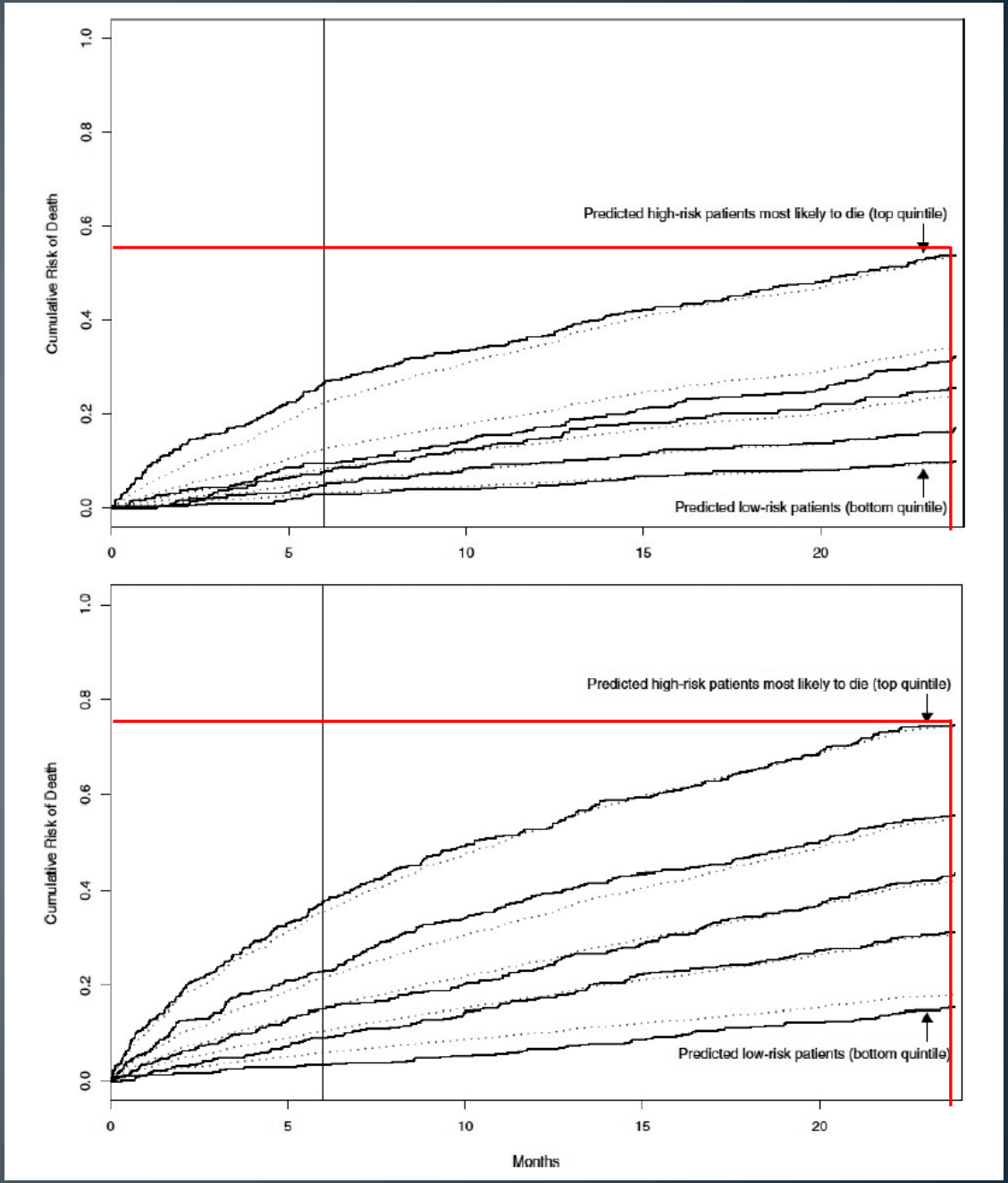
At 2 yrs

Age 65-79

Highest risk = 55% at 2 yr

Age >80

Highest risk = 75% at 2 yr



Using objective data only

Floege 2015

The 2015 AROii Study: A better prognostication tool??

clinical investigation

http://www.kidney-international.org

OPEN

see commentary on page 879

Development and validation of a predictive mortality risk score from a European hemodialysis cohort

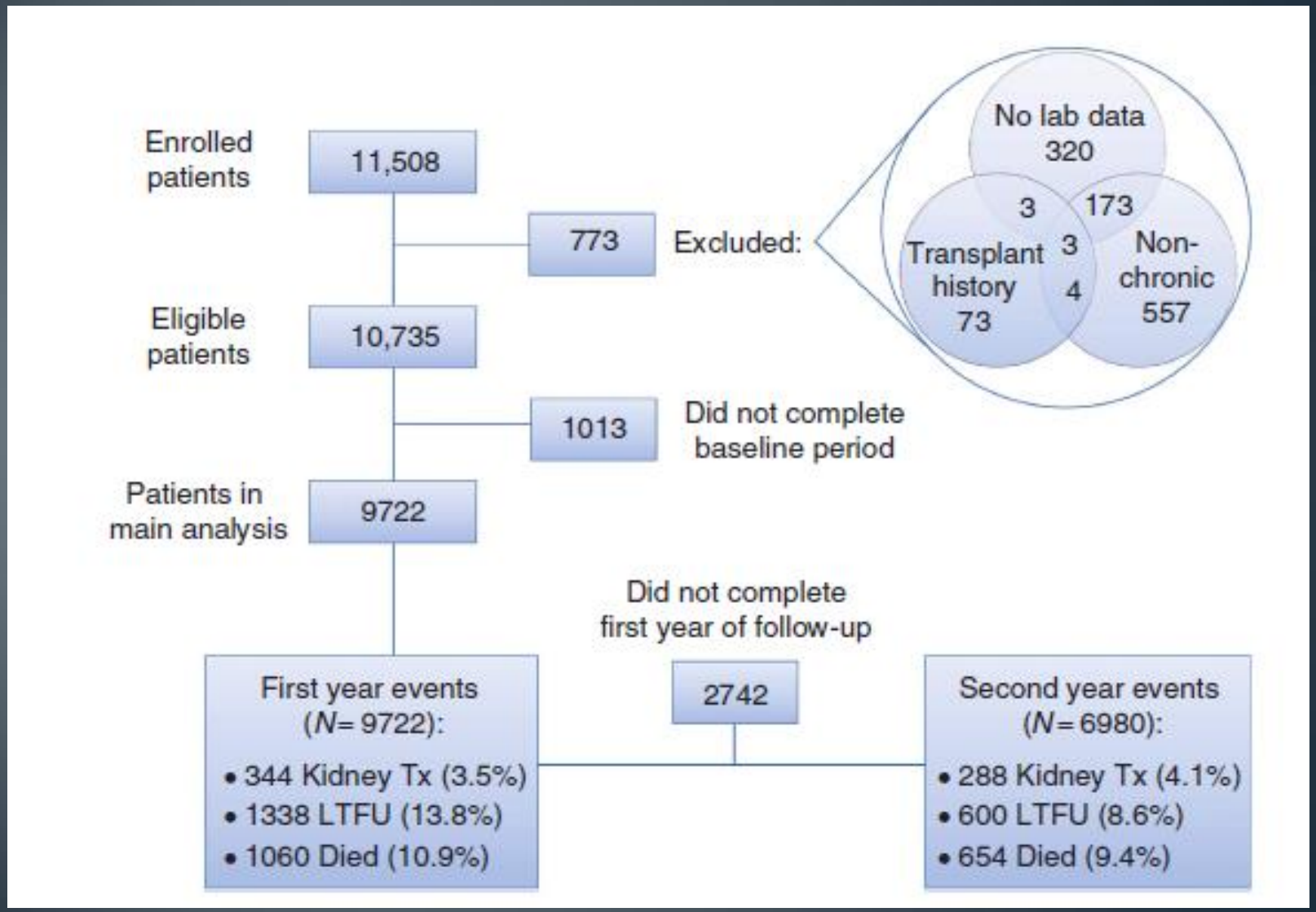
Jürgen Floege[1], Iain A. Gillespie[2], Florian Kronenberg[3], Stefan D. Anker[4], Ioanna Gioni[5], Sharon Richards[6], Ronald L. Pisoni[7], Bruce M. Robinson[7], Daniele Marcelli[8], Marc Froissart[9], Kai-Uwe Eckardt[10] on behalf of the ARO Steering Committee (collaborators)[11]

9722 Incident dialysis patients followed for 1 and 2 years

Objective measurements only (ie. no surprise question or dementia)

Kidney International (2015) **87**, 996–1008

Who was enrolled in the AROii trial?



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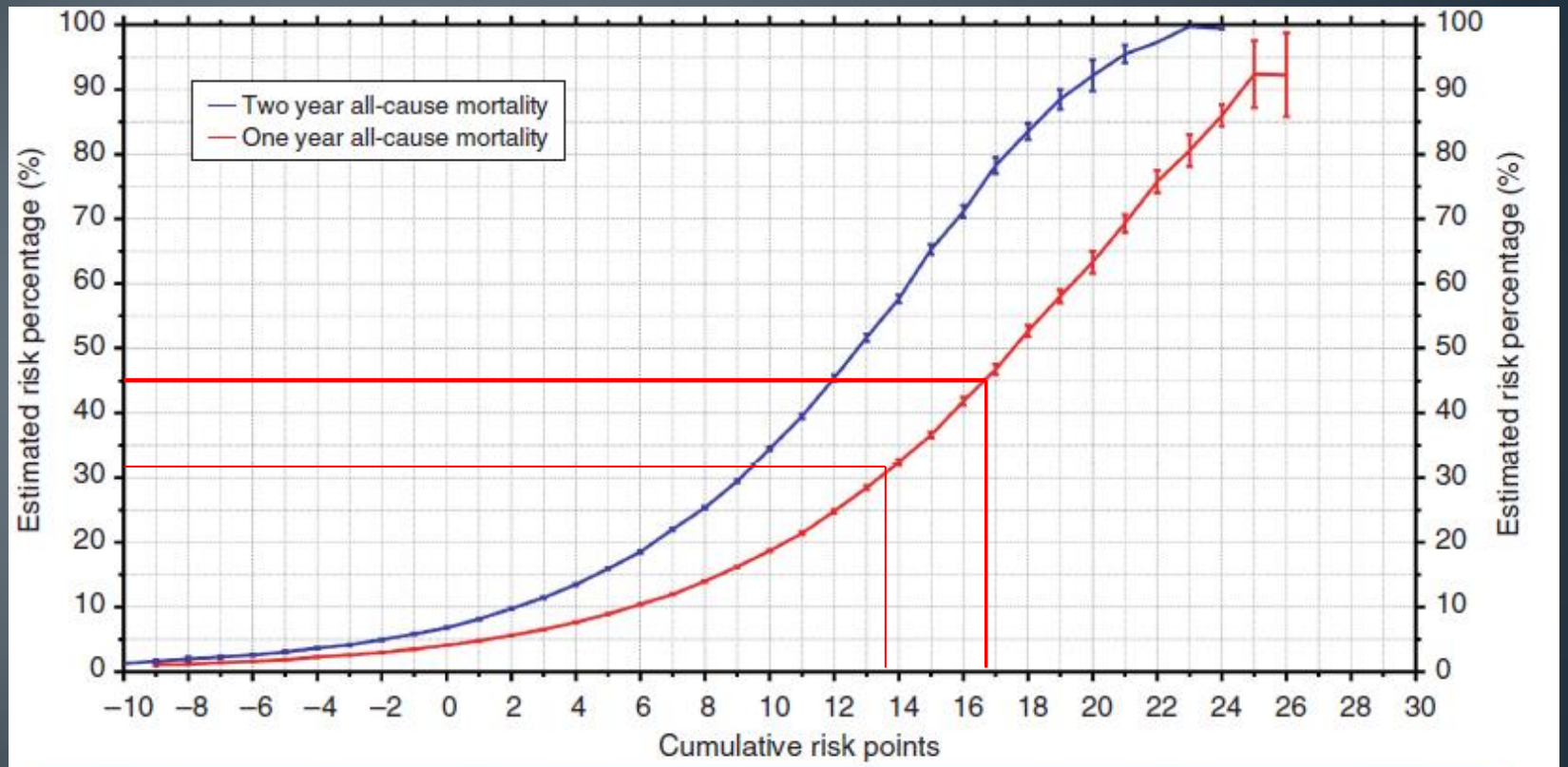
Convenient risk calculator

ARO All-cause mortality risk score for patients on chronic hemodialysis					
Parameter (unit) and values	1-Year risk points	2-Year risk points	Parameter (unit) and values	1-Year risk points	2-Year risk points
Age [years]			Actual blood flow [ml/min]		
≤39	–5	–5	< 267	0	0
40 to 49	–2	–2	267 to < 299	–1	–1
50 to 59	0	0	299 to < 332	–1	–1
60 to 69	2	2	≥ 332	–1	–1
70 to 79	4	4	Hemoglobin [g/dl]		
≥80	6	6	<10	2	1
Smoking status:			10 to < 12	0	0
Current	–	1	≥ 12	–1	–1
Former	–	1	Serum ferritin [µ/l]		
Non smoker	–	0	< 500	–1	–1
CVD history			≥ 500	0	0
Yes	2	1	C-reactive protein [mg/l]		
No	0	0	< 2.6	0	0
Cancer history			2.6 to < 7.0	1	2
Yes	4	3	7.0 to < 18.2	3	3
No	0	0	≥ 18.2	5	4
CKD Etiology:			Serum albumin [g/l]		
Hypertension/vascular	–	0	<35	3	2
Glomerulonephritis	–	0	≥35	0	0
Diabetes	–	2	Serum creatinine [µmo/l]		
Tubulo-interstitial	–	1	< 431	2	2
Polycystic kidney disease	–	–1	431 to < 539	1	1
Unknown renal diagnosis	–	1	539 to < 673	0	0
BMI [kg/m^2]			≥ 673	0	0
< 18.5	2	3	Serum total calcium [mmo/l]		
18.5 to < 25.0	0	0	<2.1	1	–
25.0 to < 30	0	–1	2.1 to <2.6	0	–
≥ 30	–1	–1	≥ 2.6	3	–
Vascular access					
No change: Fistula/Graft	0	0			
No change: Catheter	2	2	Total cumulated risk points		
Change: Fistula/Graft to Catheter	2	2			
Change: Catheter to Fistula/graft	1	0			

Kidney International (2015) **87**, 996–1008

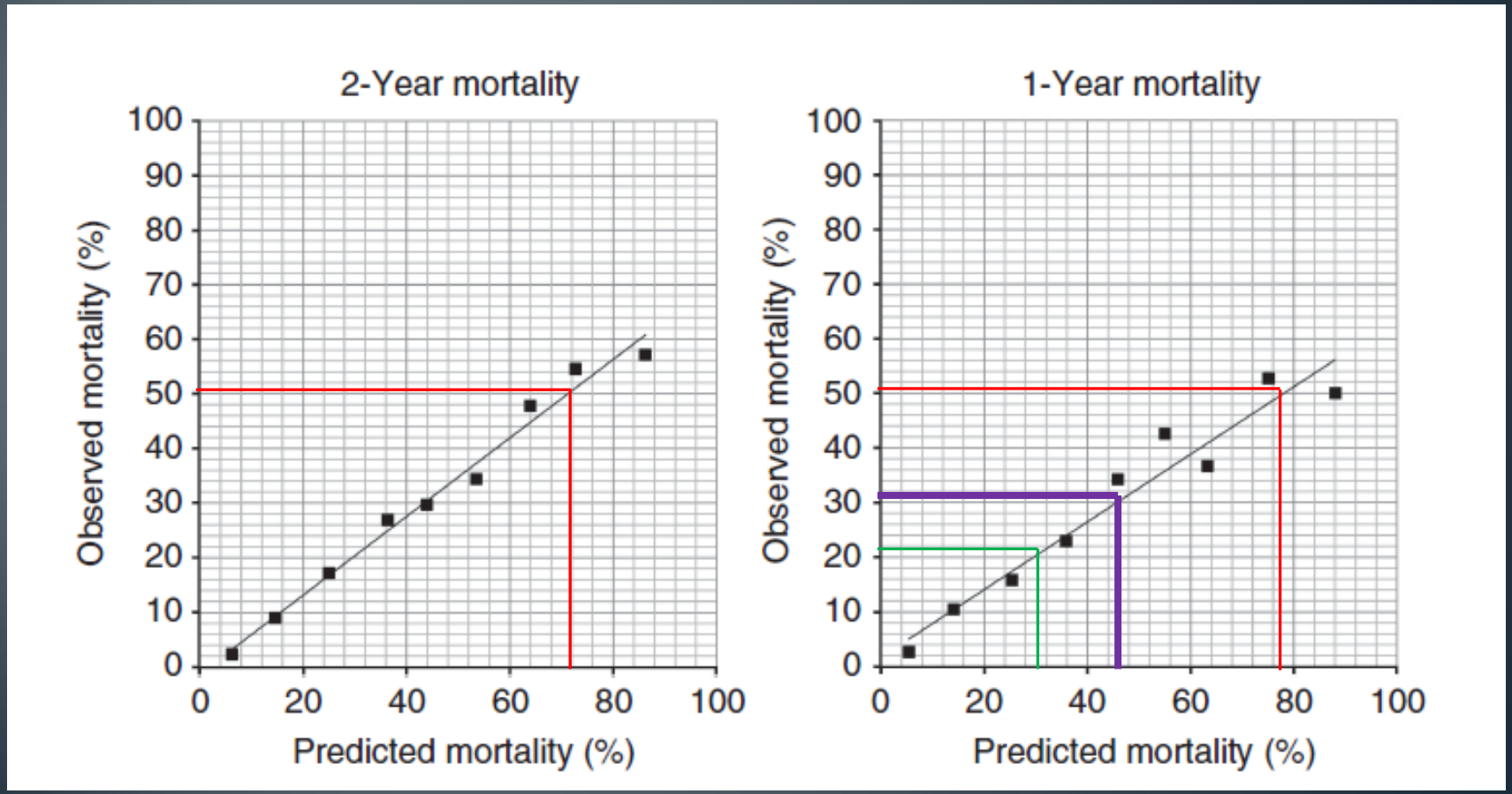
Add up the points, see risk of death



Risk stratification	Low risk	Intermediate risk	High risk
1-Year	< 9%	9 to <19%	≥19%
2-Year	< 15%	15 to <29%	≥29%

Kidney International (2015) **87**, 996–1008

Observed vs. predicted mortality: Overpredictive and variable at high %



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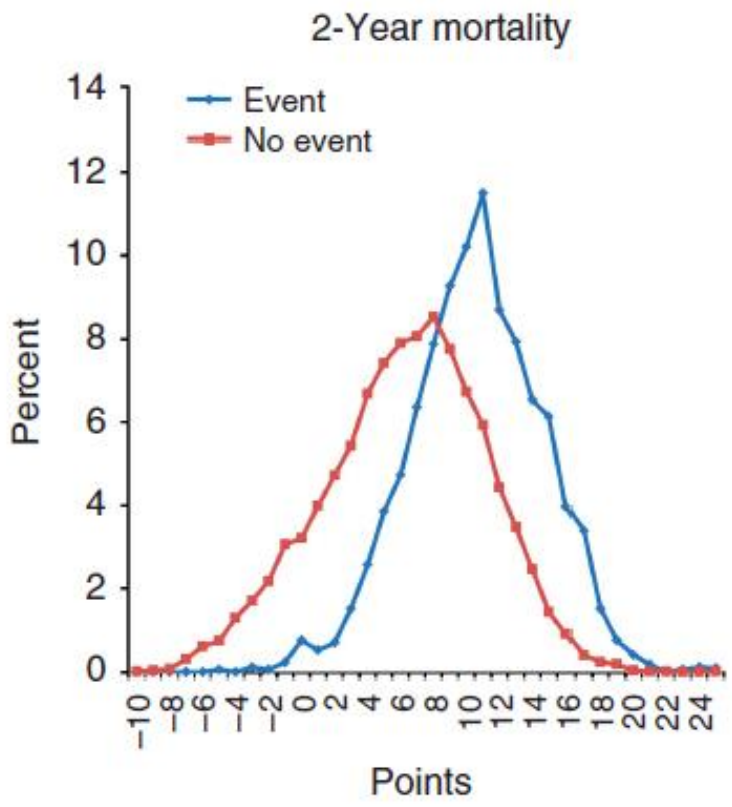
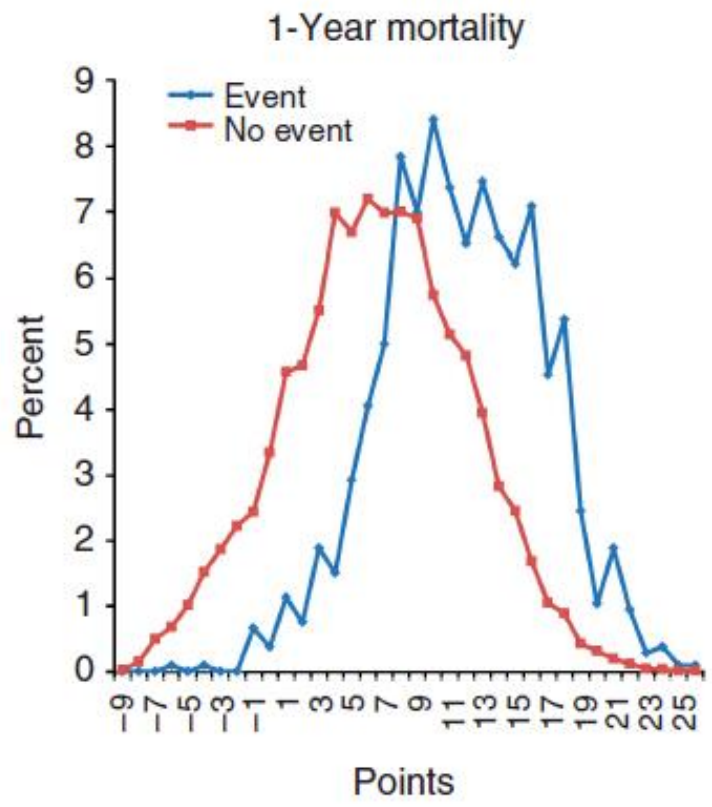
Specificity = # of individuals predicted to die / # of individuals who actually died

Sensitivity = # of individuals predicted to live / # of individuals who actually lived

Sensitivity: 70.7% [95% CI 68.5–72.8%]
Specificity: 66.0% [95% CI 65.0–67.0%]



Sensitivity: 81.5% [95% CI 79.2–83.9%]
Specificity: 56.4% [95% CI 55.3–57.4%]



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Compares well to 2010 North American study by Liu et al

Table 6 | Additional 2-year all-cause mortality discriminatory ability, conferred by different risk predictors, in a European incident hemodialysis cohort

Analysis	Original model	New model	AUC	Δ AUC	Abs IDI	NRI_{Events}	$NRI_{Non\text{-}events}$
Cumulative addition of variables							
	Liu	—	0.601	—	—	—	—
	Liu	+ age	0.696	0.094	0.046	0.35	0.11
	Liu + age	+ medical history	0.700	0.004	0.003	−0.62	0.60
	Liu + age + medical history	+ clinical	0.709	0.009	0.007	0.05	0.16
	Liu + age + medical history + clinical	+ dialysis	0.721	0.012	0.010	0.32	−0.04
	Liu + age + medical history + clinical + dialysis	+ labs	0.750	0.029	0.030	0.17	0.23
All vs. Liu alone							
	Liu	+ age + medical history + clinical + dialysis + labs	0.750	0.149	0.096	0.35	0.31

comorbid conditions of atherosclerotic heart disease, congestive heart failure, cerebrovascular accident/transient ischemic attack, peripheral vascular disease, dysrhythmia, other cardiac diseases, chronic obstructive pulmonary disease, gastrointestinal bleeding, liver disease, cancer, and diabetes.

Kidney International (2015) **87**, 996–1008

Liu J, Huang Z, Gilbertson DT *et al.* An improved comorbidity index for outcome analyses among dialysis patients. *Kidney Int* 2010; **77**: 141–151.

Still not a perfect risk predictor

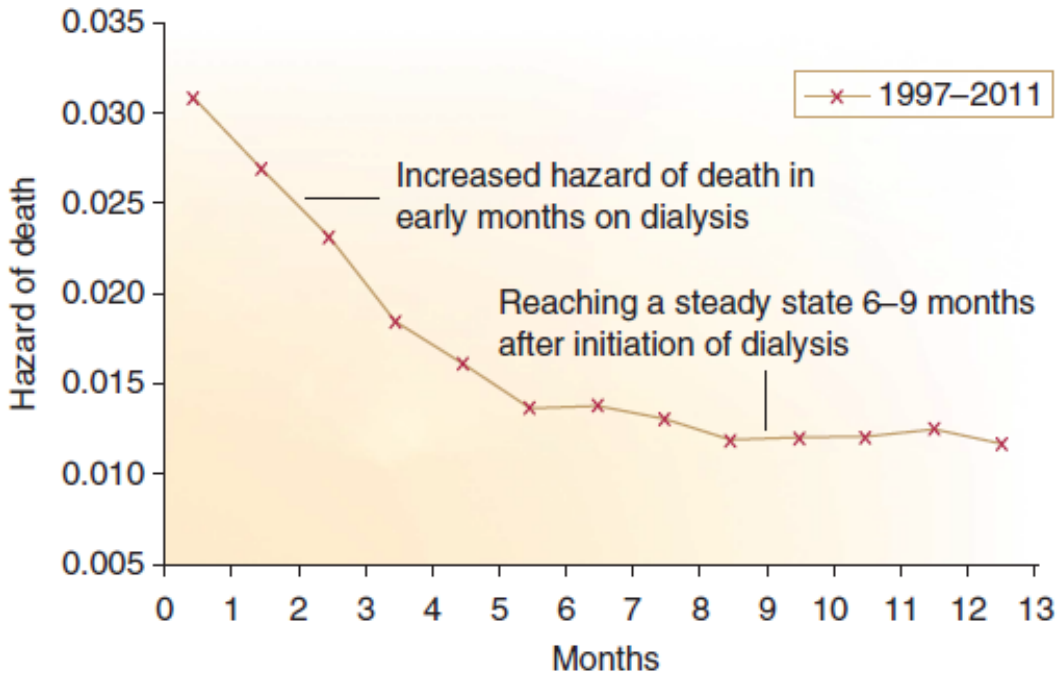


Figure 1 | Monthly hazard of death in the first year of starting dialysis: all incident patients between 1997 and 2011 reported to the UK Renal Registry. The higher early hazard of death is at odds with the comparable mortality rates reported in incident AROii patients and prevalent DOPPS patients in the accompanying paper by Floege and colleagues.

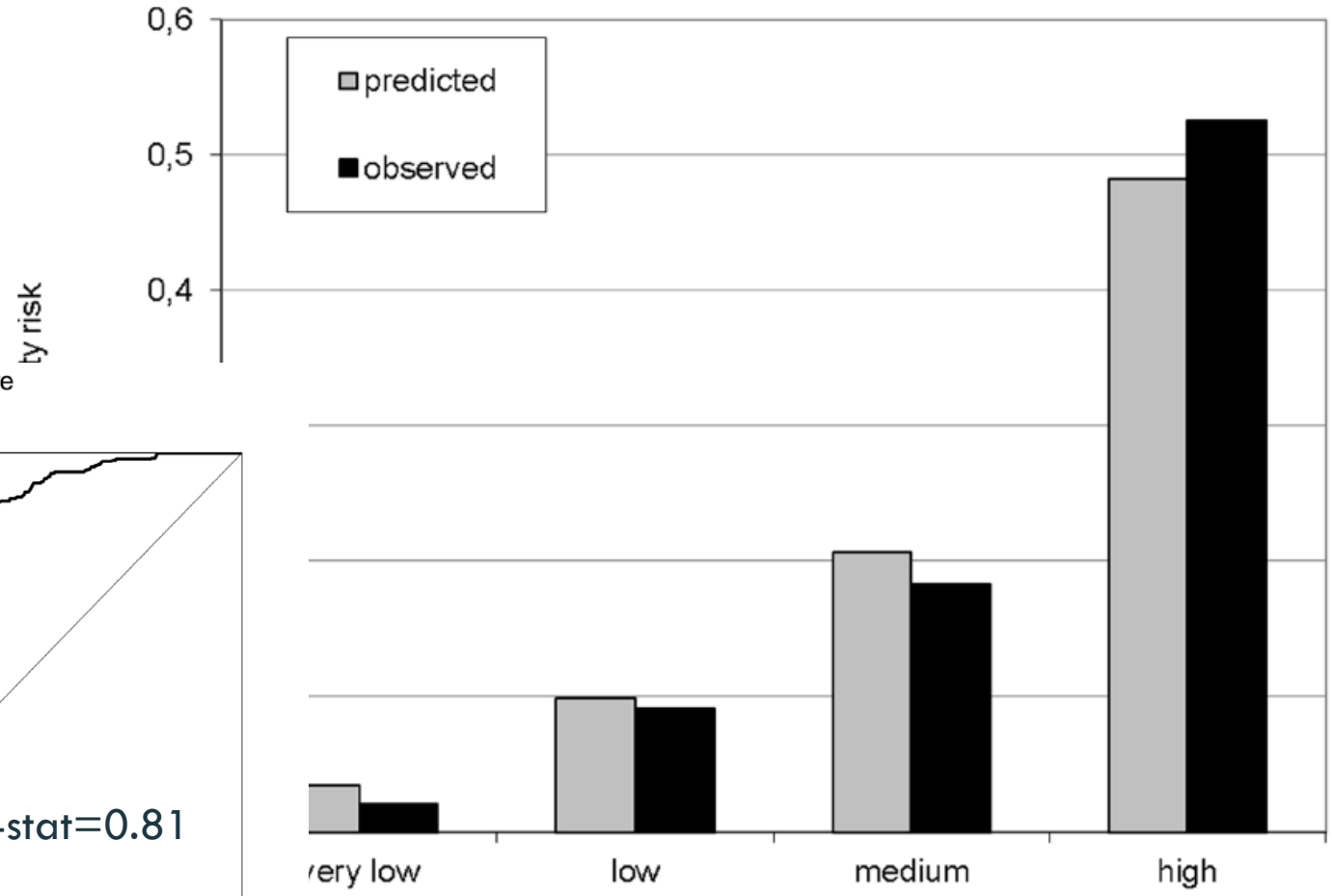
Kidney International (2015) **87,** 879–882

What about 1 yr mortality in diabetic patients starting dialysis specifically?

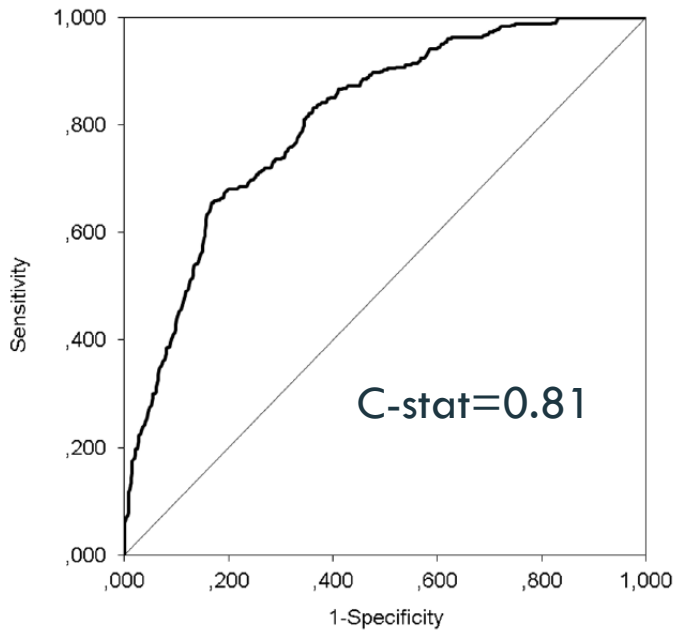
Van Diepen et al (2014) (external validation needed)

Table 2. Predictive variables for 1-year mortality based on multivariate regression analysis.

Predictor
Age (years)
Smoking
Macrovascular complications
Duration of DM (years)
Karnofsky scale
Hemoglobin level (g/dl)
Albumin level (g/l)



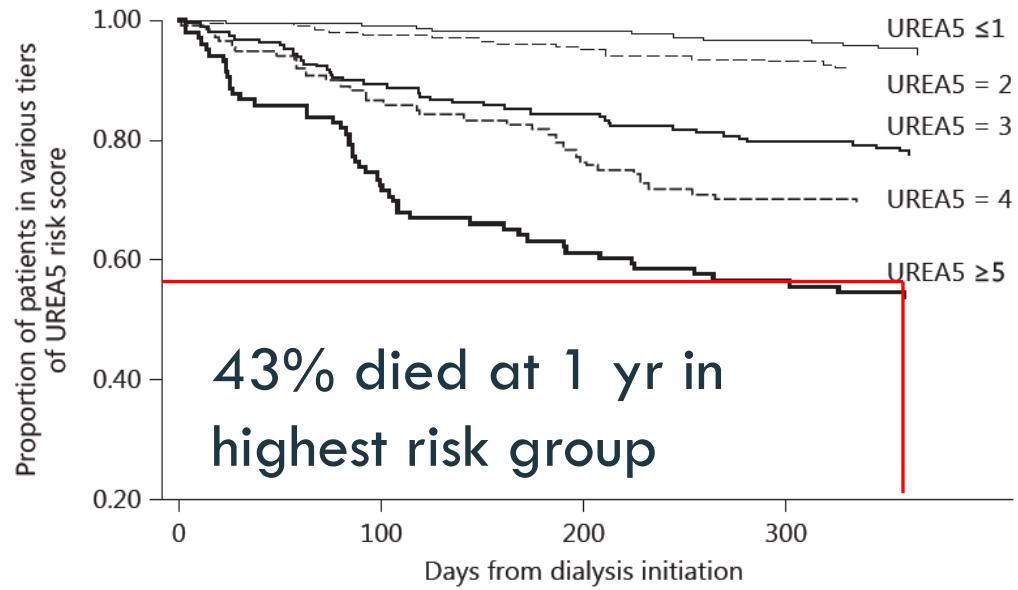
ROC curve



Citation: van Diepen M, Schroijen MA, Dekkers OM, Rotmans JI, Krediet RT, et al. (2014) Predicting Mortality in Patients with Diabetes Starting Dialysis. PLoS ONE 9(3): e89744. doi:10.1371/journal.pone.0089744

Should dialysis be initiated? Predicting first year mortality for incident patients

Chua 2014 (Asian population) (external validation needed)



Number of survivors

UREA5 score				
≤1	219	217	215	212
2	206	201	196	192
3	198	177	167	158
4	121	105	92	85
≥5	106	77	65	60

Score: (UREA5 score)
(age >70 years) × 2 + (LVEF 30–44%) × 1 + (LVEF <30%) × 3 + (CVA) × 1 + (PVD) × 1 + (Alb <30) × 1 + (ALP >80) × 1 + (urate <500 or >600) × 1
(weightages in formula 2 are rounded off to 1, 2, and 3)

Blood Purif 2014;37:85–92

So, what are we to do in BC??

What our research tells us…

At what predicted 1 or 2 yr mortality do we initiate interventions?

Our national survey says….

Conclusion

- Being able to prognosticate death is important to renal care
- Current models are less than perfect
- Creation of an "app" may give rise to false security in the result
- Models tend to overpredict mortality generally
- Significant life limiting events not represented in the models need to be considered (eg. Hip fracture, prolonged ICU stay)
- A high probability of 6 month, 1yr or 2 yr mortality should prompt the team to
  - Monitor more frequently for pain and symptoms
  - Engage the patient/family: conservative care, goals of care, paperwork
  - Make timely referrals after considering the whole patient (comorbidities)

Thank you

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