

How is the dialysis patient different?

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How is the dialysis patient different?

- Dialysis patients are different because their needs are different, they have *different risk factors* and the experience gained in non-dialysis patients may not apply.
- Survival of the dialysis patients is determined by different factors than the non-dialysis patients.

Dialysis patients have different risk factors

- One of the most important indicators of survival is nutrition: albumin
- Nutrition is more important in dialysis patients than dialysis efficiency, dialysis modality, treatment of anemia etc...

Adjusted* Relative Risk (RR) of Mortality and Percent of Patients Outside Guideline Target by Practice Pattern

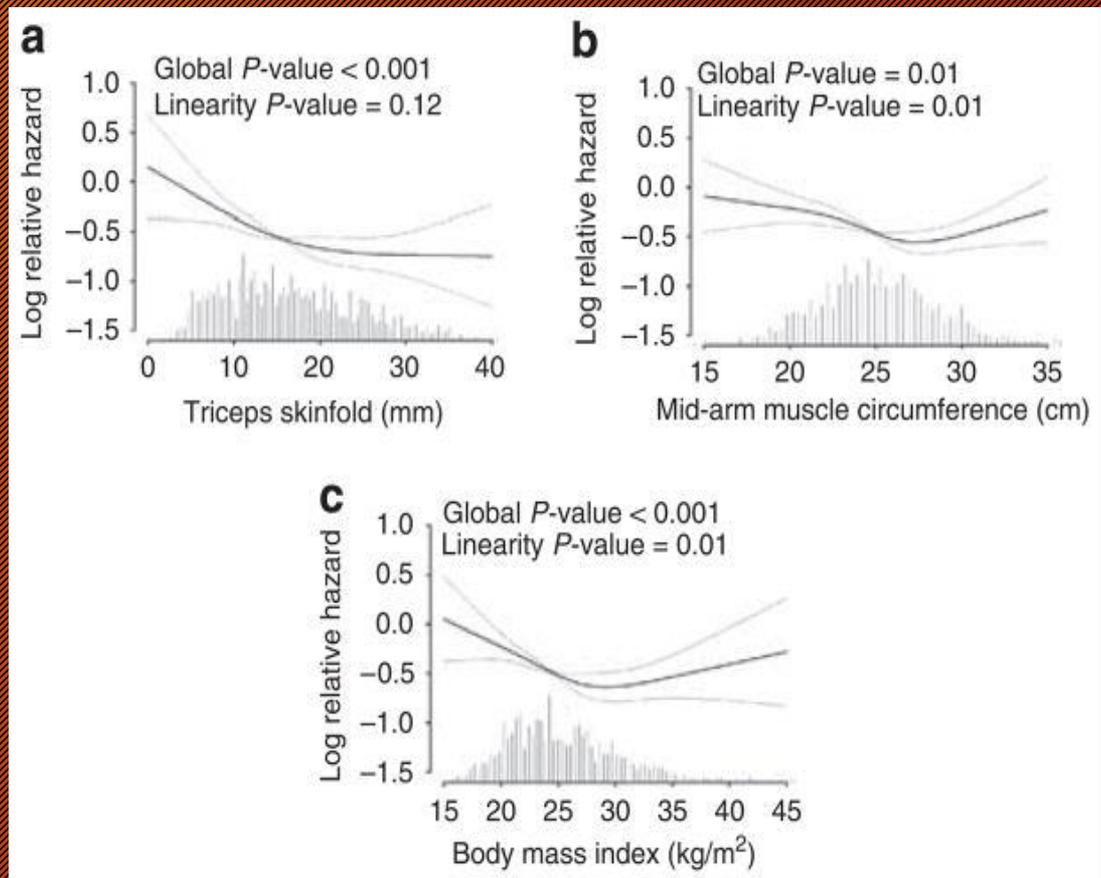
Selected Modifiable Practice Patterns	Out of Target Value	Percent of Patients Outside of Range from DOPPS II (US)	Mortality RR* from DOPPS I	
			RR	P value
Dialysis Dose				
SpKt/V	< 1.2	12.1%	1.16	0.025
Mineral Metabolism				
PO ₄	> 5.5 mg/dl	49.2%	1.11	0.005
Anemia Management				
Hemoglobin	< 11 g/dl	27.2%	1.14	<0.0001
Nutrition				
IDWG	> 5.7%	12.5%	1.22	0.002
Albumin	< 3.5 g/dl	20.5%	1.38	<0.0001
Vascular Access				
Facility Catheter Use	>28% vs. < 7%	50.0%	1.23	0.01

*Adjusted mortality risk analyses are based on Cox models while considering case mix and comorbidities through statistical adjustment. Additional adjustments include stratification by country and facility clustering effects.



Nutrition is one of the major determinants of survival

- Nutrition is a determinant of survival even if it means obesity; i.e.: obesity is better than malnutrition



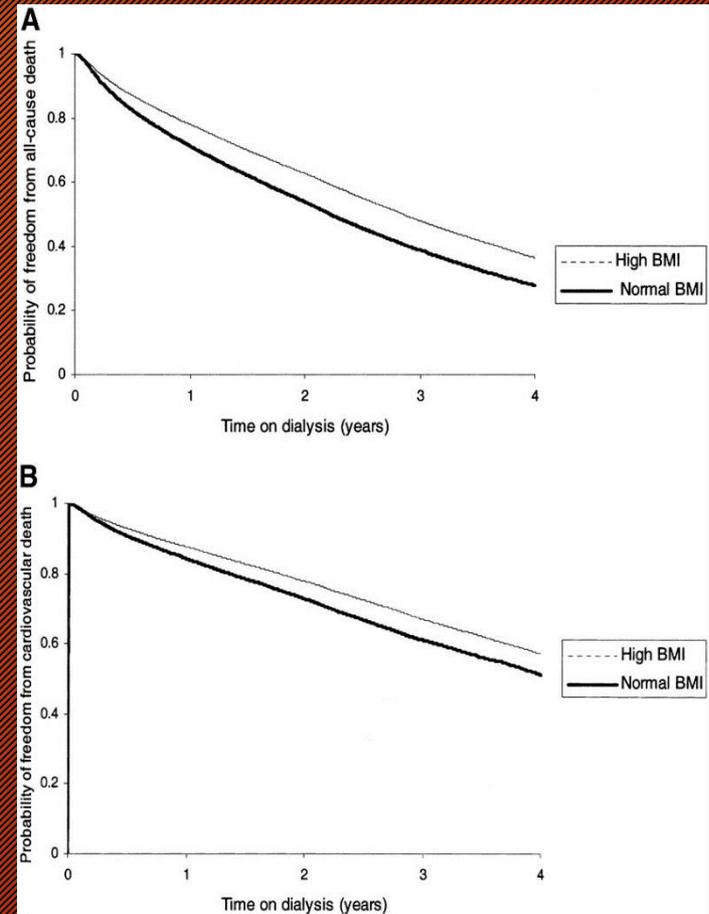
The effect of obesity in ESRD

- Does obesity decrease survival of dialysis patients?
- In a retrospective study of 74,167 Medicare patients:
 - The effect of BMI was examined on mortality using Cox proportional hazard ratios:

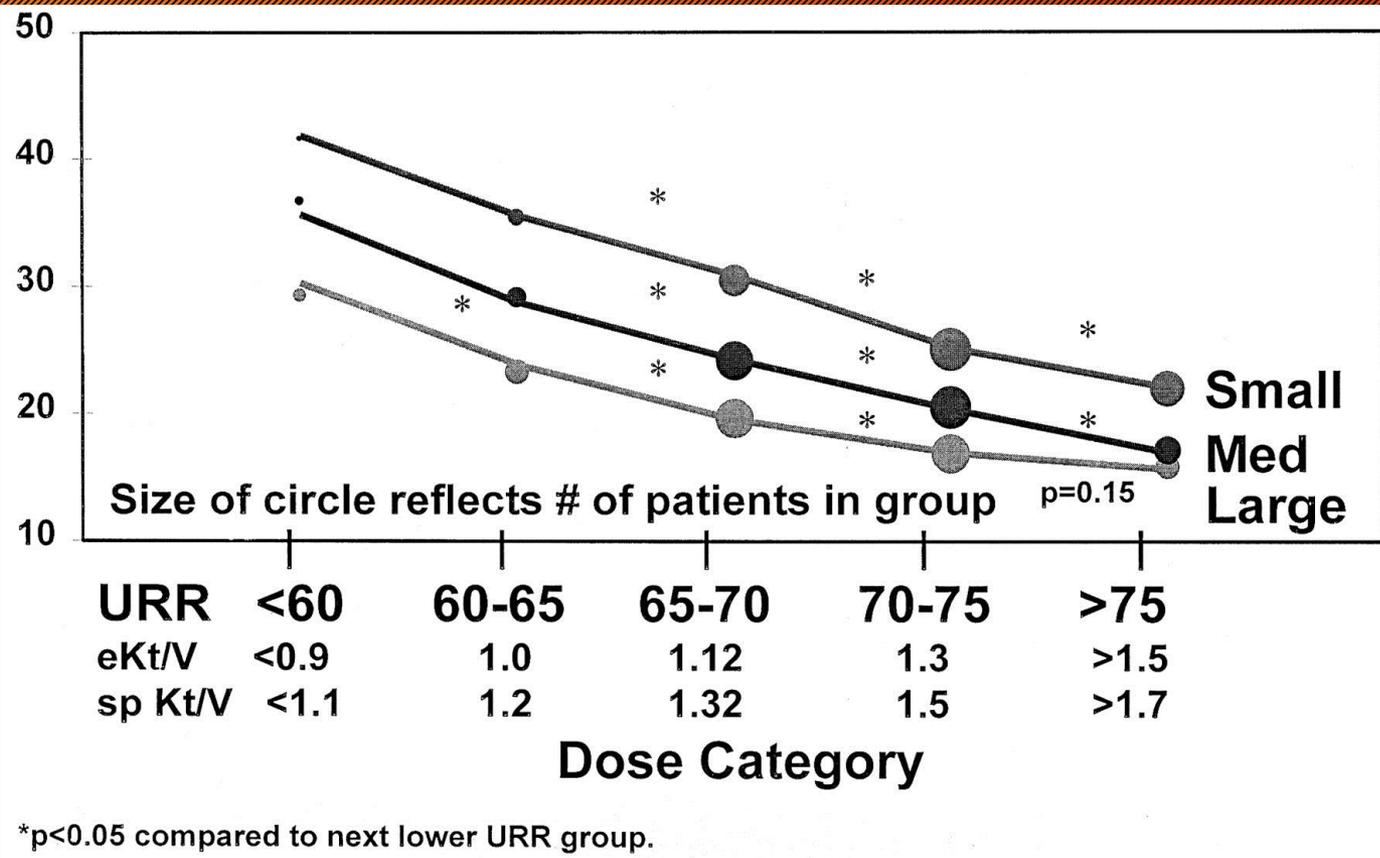
Obese dialysis patients had better survival chances than those with “normal” body weight

Obesity improves survival chances

- There are numerous studies showing a survival advantage of the obese dialysis patient.



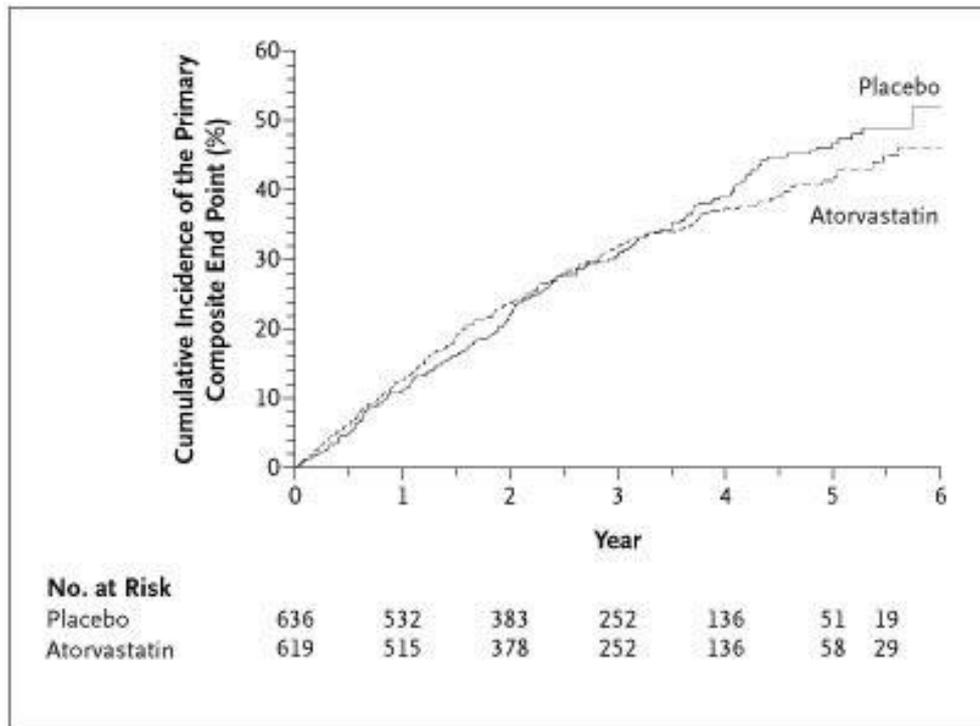
Mortality according to Urea Reduction Rates (URR) and Body Mass index (BMI)



Port, F. K. et al. J Am Soc Nephrol 2002;13:1061-1066

Those factors that improve the survival of the general population do not have the same effect on the dialysis population

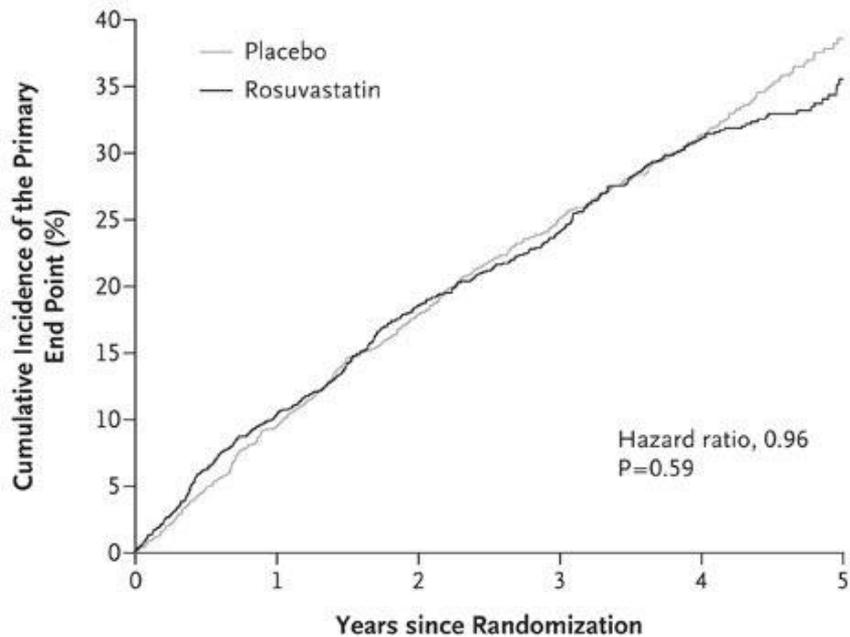
Mortality is not improved by cholesterol lowering



Treatment of cholesterol with statins does not improve survival:

DDDD study

Cholesterol lowering: no difference in hard end-points

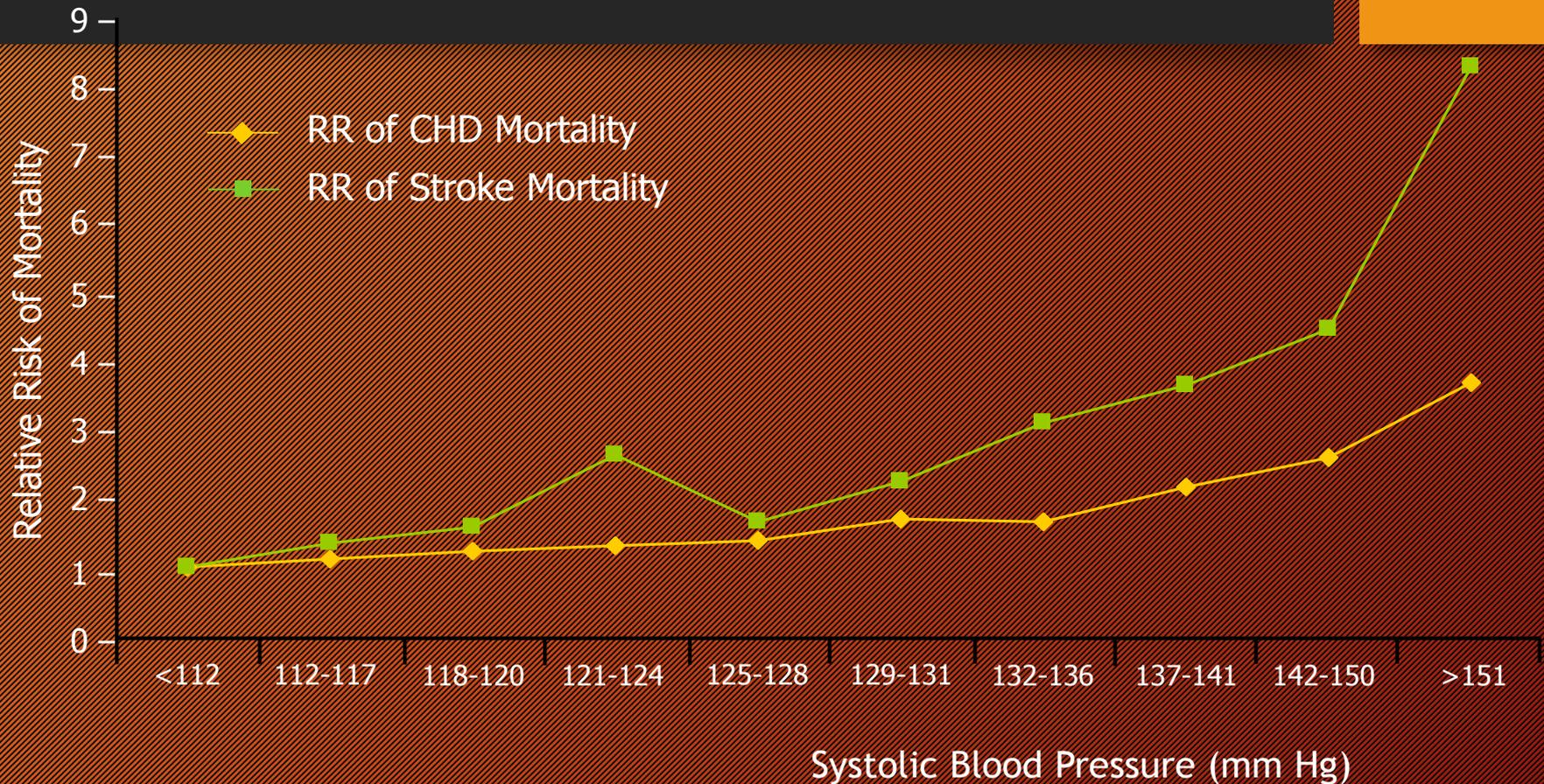


No. at Risk						
Placebo	1384	1163	952	809	534	153
Rosuvastatin	1390	1152	962	826	551	148

Cholesterol treatment does not improve outcome:

AURORA study

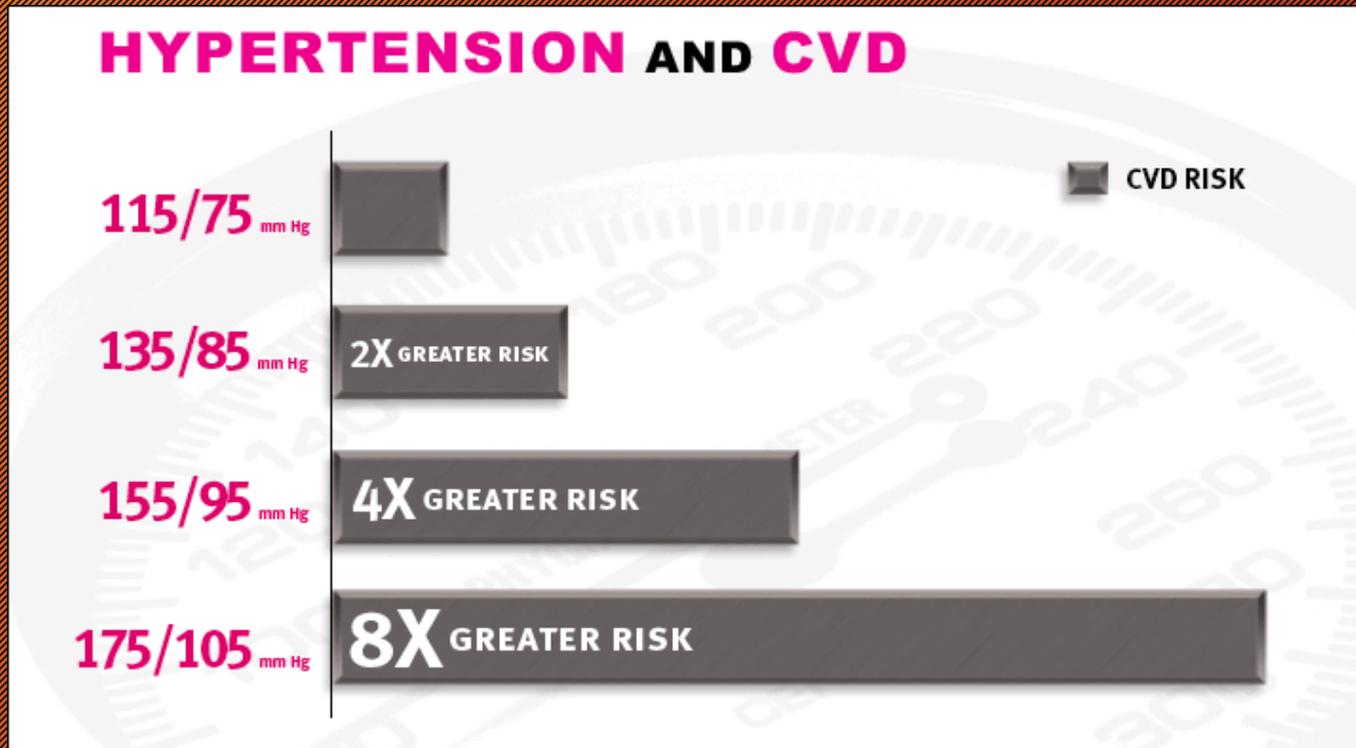
In the general populaion mortality rises as does blood pressure



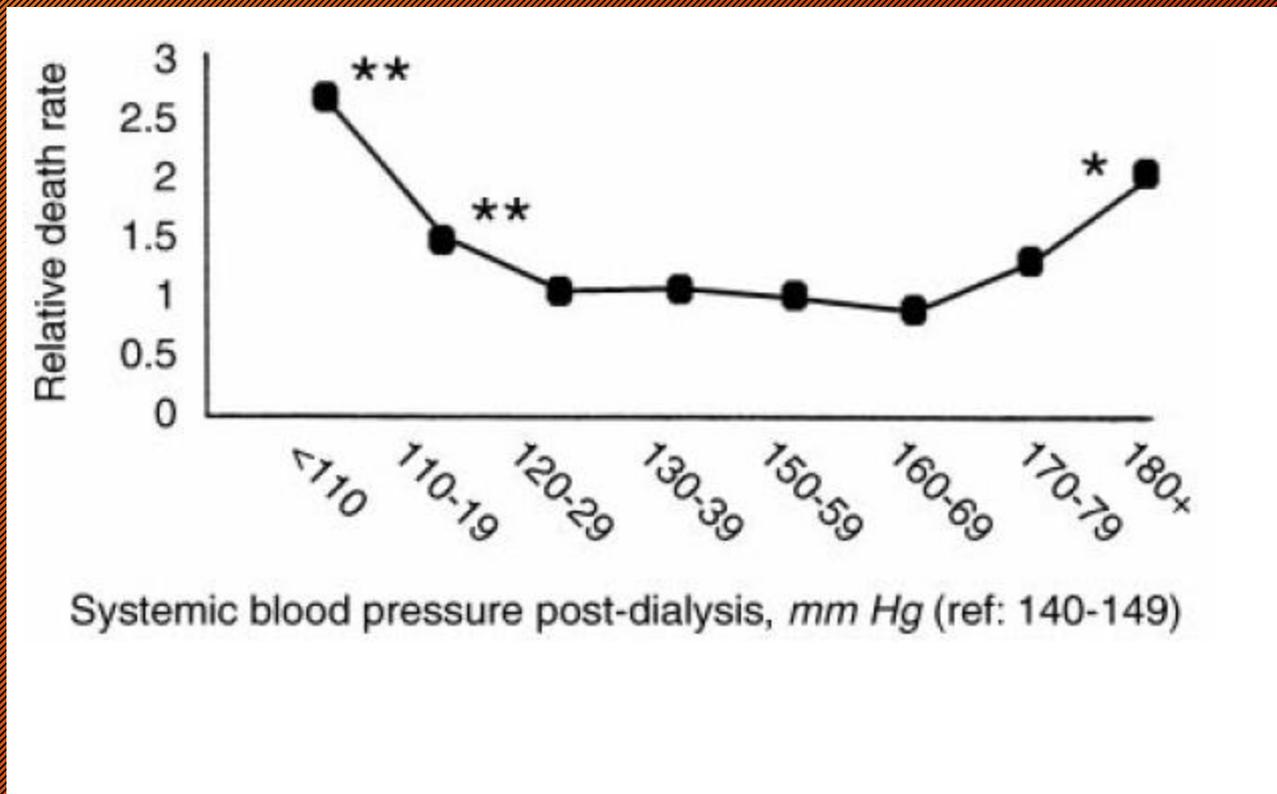
RR = relative risk.

Adapted from Stamler J, et al. *Arch Intern Med.* 1993;153:598-615.

In the general population blood pressure raises the risk of cardiovascular morbidity



However, **blood pressure lowering in the ESRD population does not seem to lower mortality**



Zager: *Kidney International* 54; 1998; 561-569

Treatment of HD patients with medications for 2 years does not improve their **mortality** but raises it

Table 3. Relative risk of death according to the level of blood pressure at baseline (univariate analysis)

	Regression coefficient	Relative risk	<i>P</i>
Normotensive	0.95	2.59	0.02
High normal	0.90	2.46	0.002
Mild hypertensives	0.54	1.71	0.04
Moderate hypertensives	0.41	1.52	0.13
Severe hypertension		1.0 (reference group)	

M Salem Hypertension in the haemodialysis population: any relationship to 2-years survival? Nephrol. Dial. Transplant., Jan 1999; 14: 125 - 128.

NECOSAD study

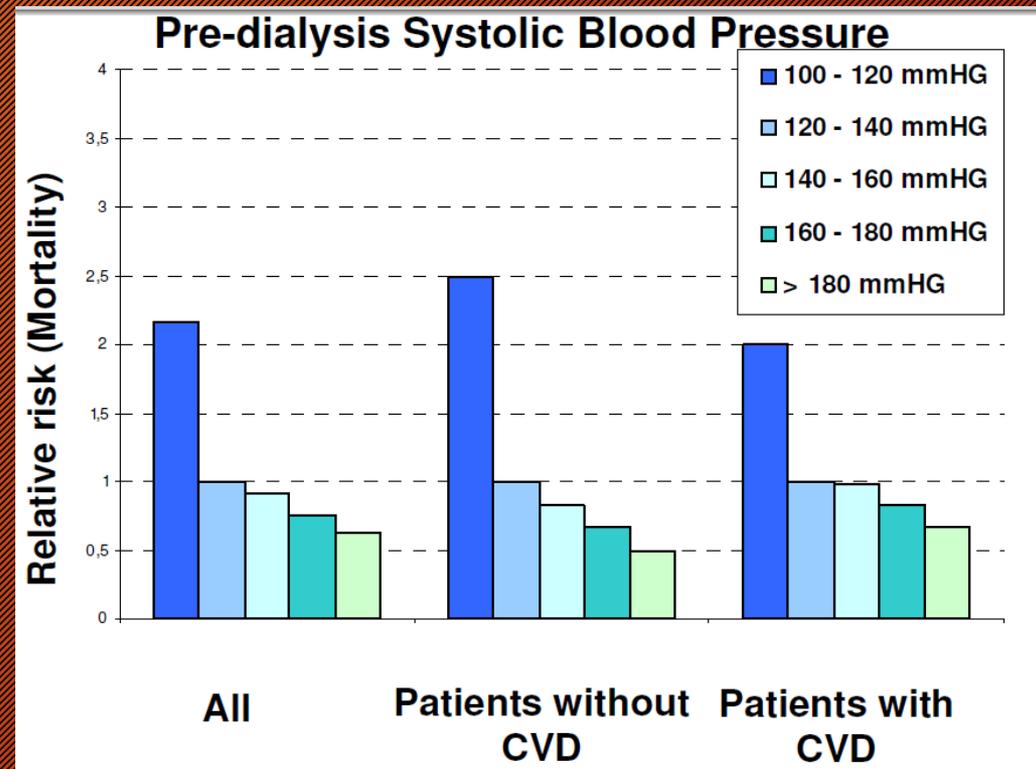
1111 incident HD patient

- 452 patients with preexisting CV illness
- 659 patients with NO preexisting CV disease
- 7.5 year follow-up

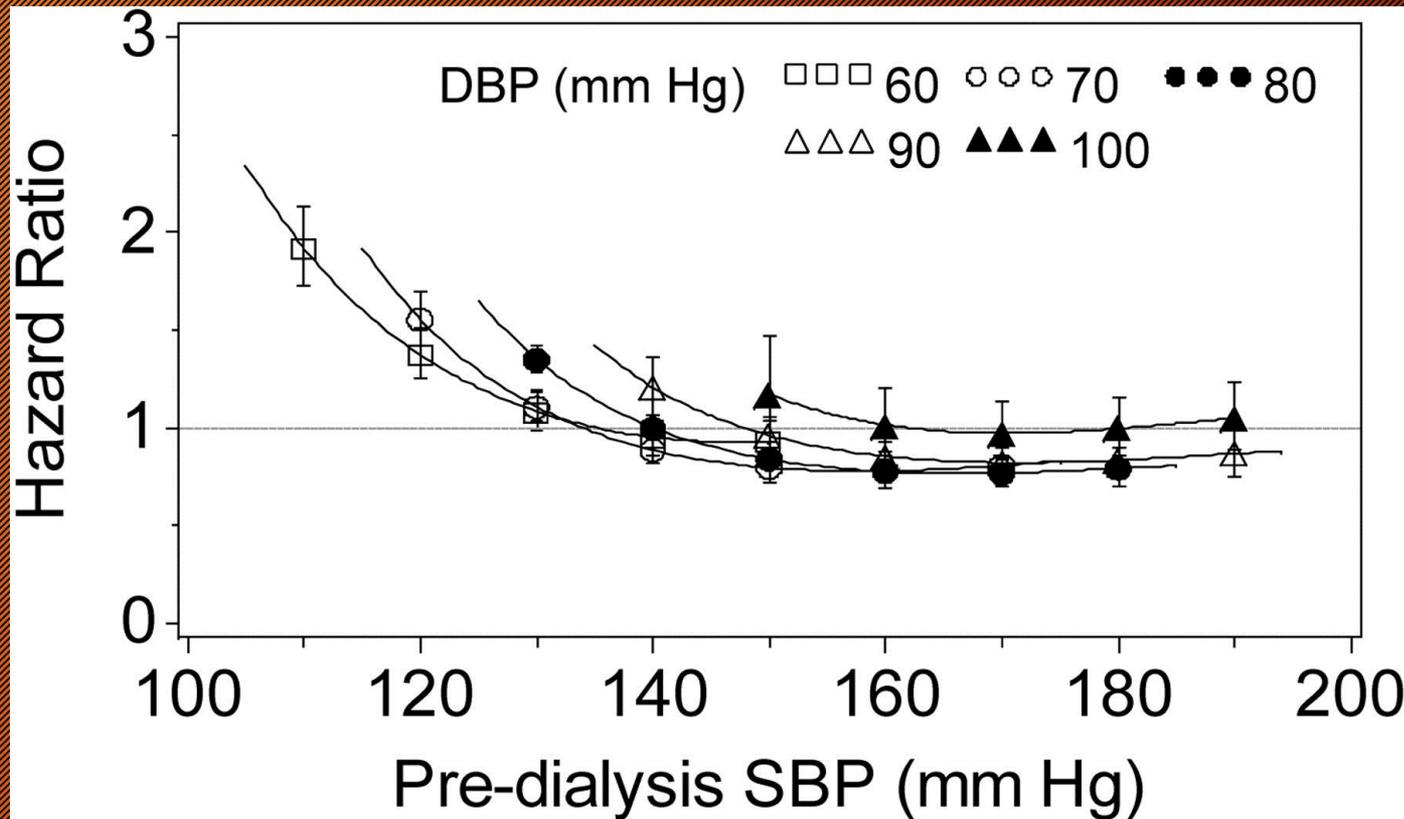
2-year mortality with 44% vs 20% without preexisting CV disease

Higher BP's afforded better survival whether they had CVD or not...

A “normalized blood pressure” is one risk factor!

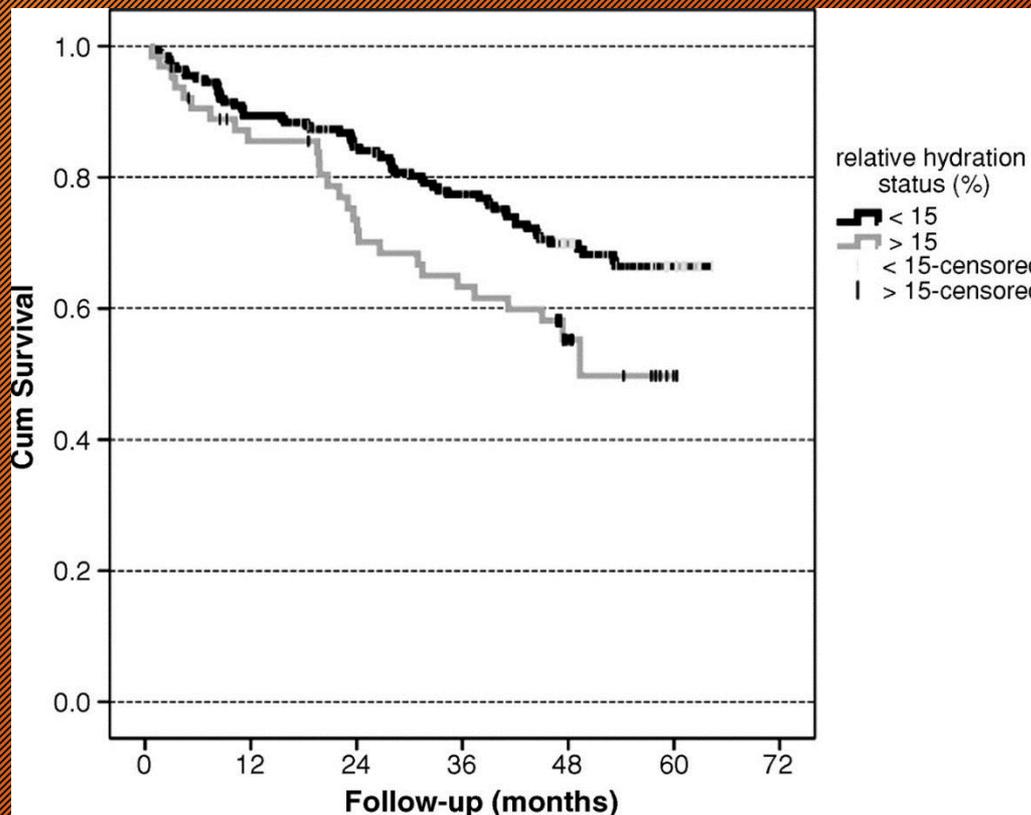


Mortality risk according to pre-dialysis blood pressures



Myers, O. B. et al. J Am Soc Nephrol 2010;21:1970-1978

The effect of fluid overload on survival



Wizemann, V. et al. *Nephrol. Dial. Transplant.* 2009 24:1574-1579;
doi:10.1093/ndt/gfn707

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❖ Bioimpedence measurement study

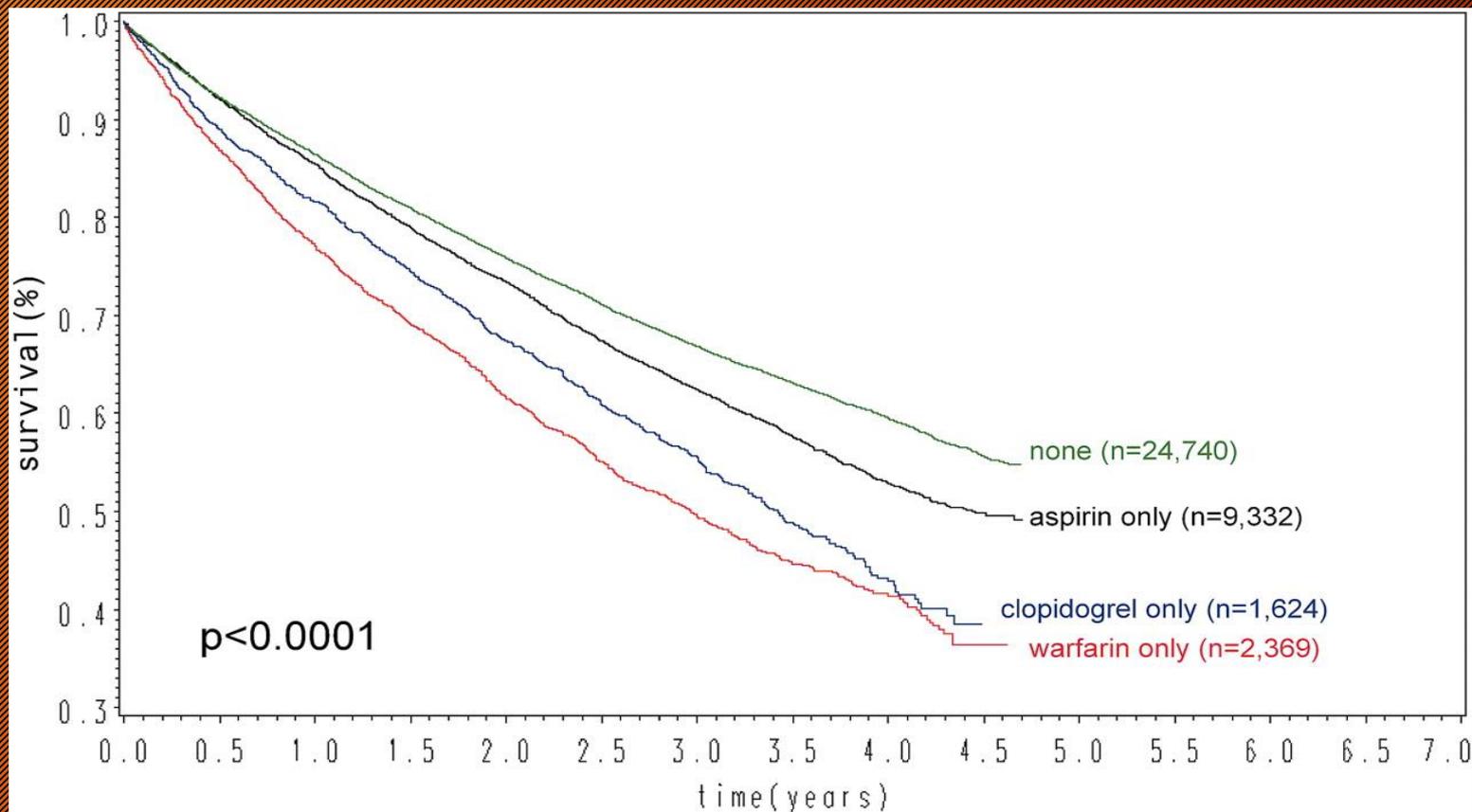
❖ Hyperhydration: if >15% excess in extracellular water (ECW), that translates to ~about 2.5L ECW

❖ It is the overhydrated state that is dangerous not the hypertensive status

Atrial fibrillation and the risk of stroke in dialysis patients

- In a retrospective study of 443 chronic HD patients (1111.16 patient-year)
 - The prevalence of stroke: 1.0/100 patient-year if not anticoagulated
 - diabetic nephropathy (6.46, p = 0.0036)
 - age >65 year (5.90, p = 0.0001)
 - Severe hypertension (6.8, p = 0.0017)
 - Interdialytic weight gain >2 L as an indicator of non-compliance (6.47, p = 0.0433)
 - Antithrombotic therapy with salicylate or warfar (8.33, p = 0.0002)
- The greatest risk factor is anticoagulation!

Treatment of dialysis patients with warfarin, clopidogrel or aspirin in atrial fibrillation

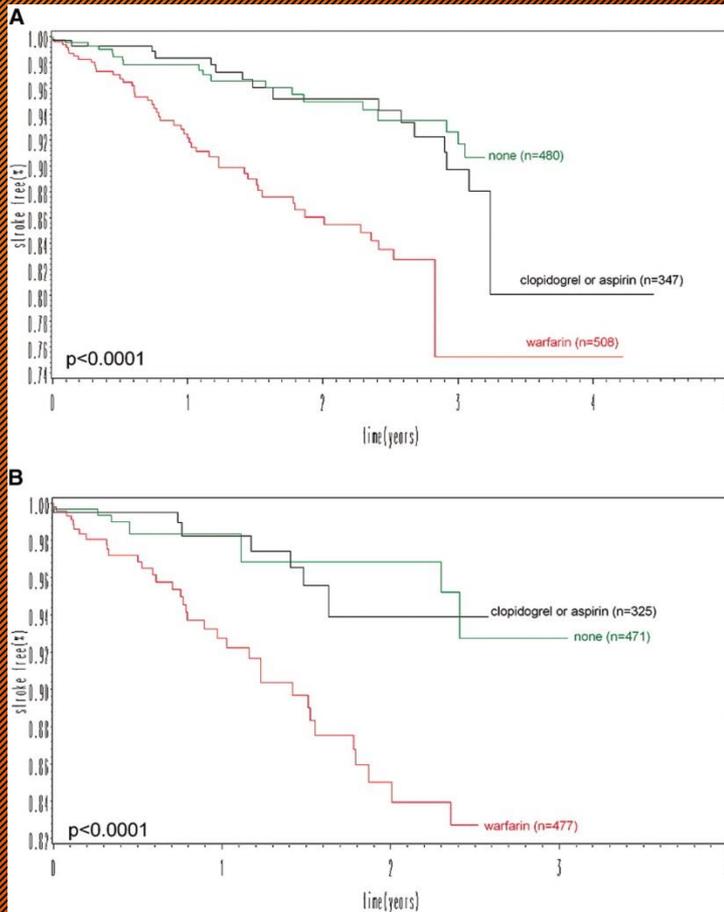


Chan, K. E. et al. J Am Soc Nephrol 2009;20:872-881

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JASN

Crude stroke curves by drug exposure.



- (A) intention-to-treat assumption
- (B) patients censored when they changed their Rx after study enrollment.

Anticoagulation increases strokes too...

The **risk of anticoagulation** in dialysis patients

- Anticoagulation of dialysis patients increases the risk of mortality and stroke
- The mechanism of this phenomenon is no known
- One of the potential mechanisms is that ESRD patients have a high fall risk.

FALL RISK INDICATORS

- Fall risk assessment:
 - Morse Fall Risk scale
 - Conley scale
 - Fall risk score by the American Heart Association
- These indicators assess the risk of life threatening falls and the risk of life threatening bleed

FALL RISK INDICATORS BY THE AMERICAN HEART ASSOCIATION

■ Risk factors:

- Anemia → 3 points
- Severe kidney disease → 3 points
- Age >75 years → 2 points
- Bleeding history → 1 point
- HTN → 1 point

■ Life threatening bleeds:

- 0-3: 0,8% low risk
- 4: 2,6% medium risk
- 5-10: 5,8% high risk

■ ...almost all dialysis patients are high risk

Morse Fall Risk

Morse Fall Scale

(Adapted with permission, SAGE Publications)

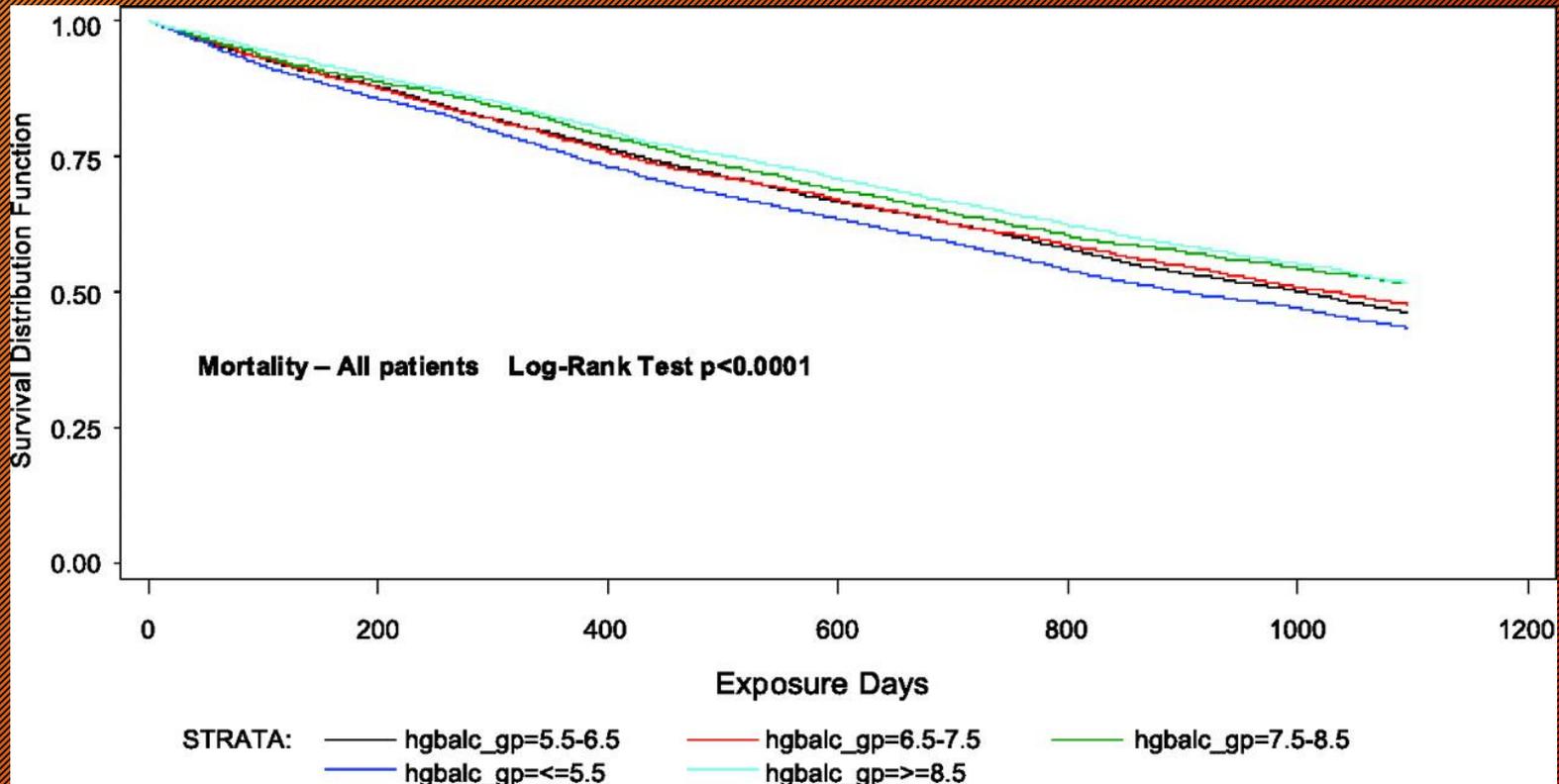
The Morse Fall Scale (MFS) is a rapid and simple method of assessing a patient's likelihood of falling. A large majority of nurses (82.9%) rate the scale as "quick and easy to use," and 54% estimated that it took less than 3 minutes to rate a patient. It consists of six variables that are quick and easy to score, and it has been shown to have predictive validity and interrater reliability. The MFS is used widely in acute care settings, both in the hospital and long term care inpatient settings.

Item	Scale	Scoring
1. History of falling; immediate or within 3 months	No 0 Yes 25	_____
2. Secondary diagnosis	No 0 Yes 15	_____
3. Ambulatory aid Bed rest/nurse assist Crutches/cane/walker Furniture	0 15 30	_____
4. IV/Heparin Lock	No 0 Yes 20	_____
5. Gait/Transferring Normal/bedrest/immobile Weak Impaired	0 10 20	_____
6. Mental status Oriented to own ability Forgets limitations	0 15	_____

Sample Risk Level

Risk Level	MFS Score	Action
No Risk	0 - 24	Good Basic Nursing Care
Low Risk	25 - 50	Implement Standard Fall Prevention Interventions
High Risk	≥ 51	Implement High Risk Fall Prevention Interventions

Glycemic indicators and the chance of survival in ESRD dialysis patients: a tighter control does not mean a better survival



Williams, M. E. et al. Clin J Am Soc Nephrol 2010;5:1595-1601

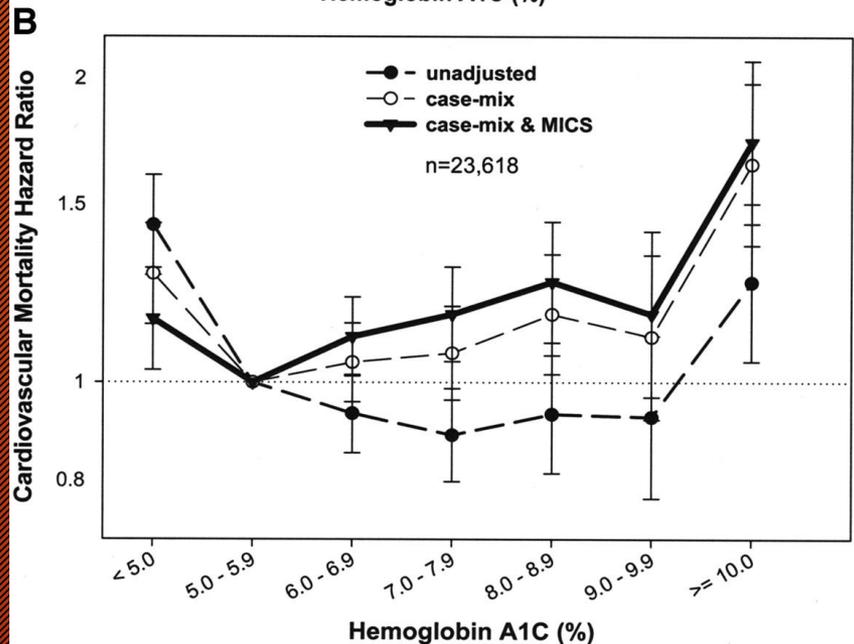
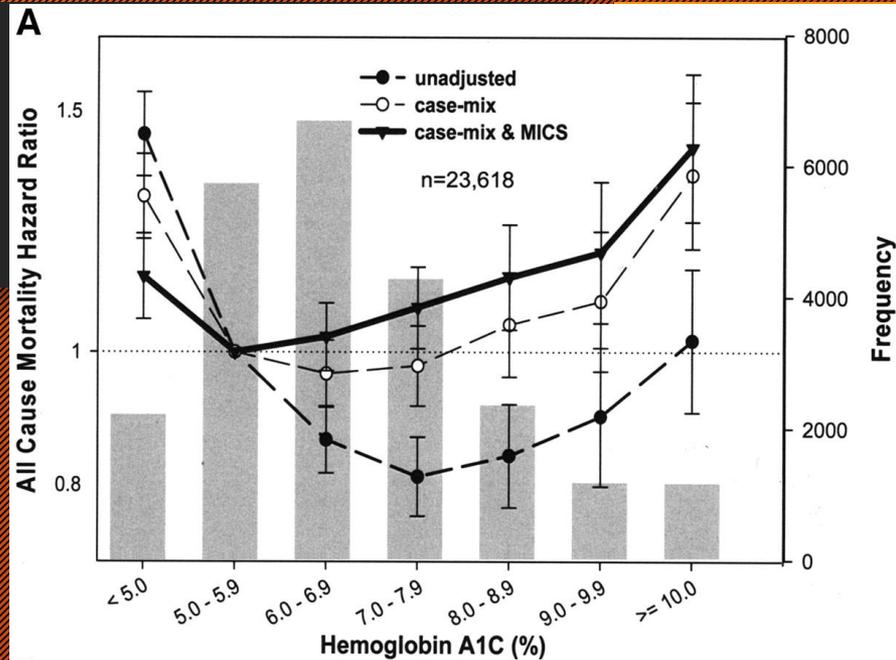
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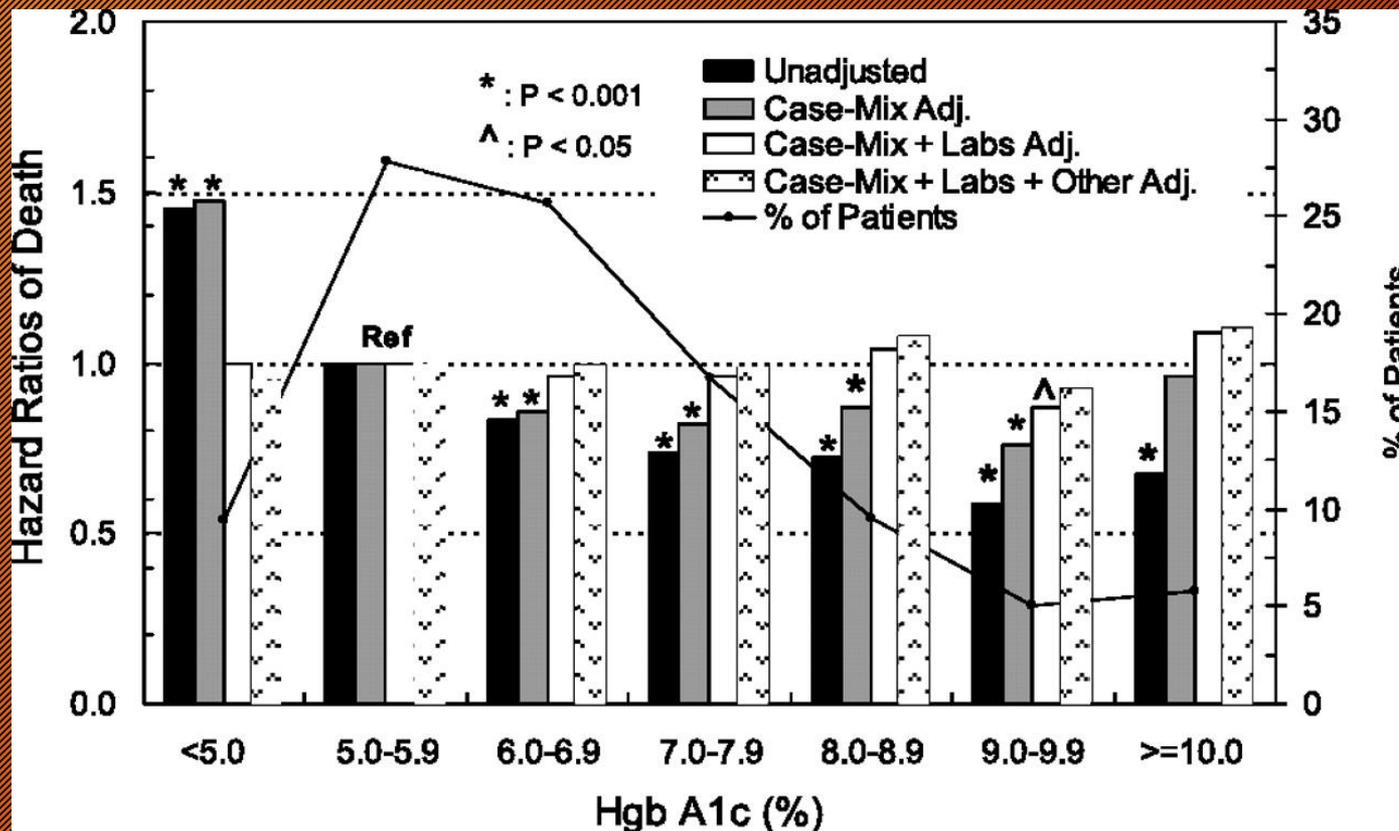
HgbA_{1c} and Survival in Maintenance Hemodialysis Patients

HRs of all-cause (A) and cardiovascular (B) mortality for the entire range of HgbA_{1c} in 23,618 diabetic MHD patients over 3 years (July 2001 through June 2004). Case-mix model is adjusted

KAMYAR KALANTAR-ZADEH *Diabetes Care* 30:1049-1055, 2007



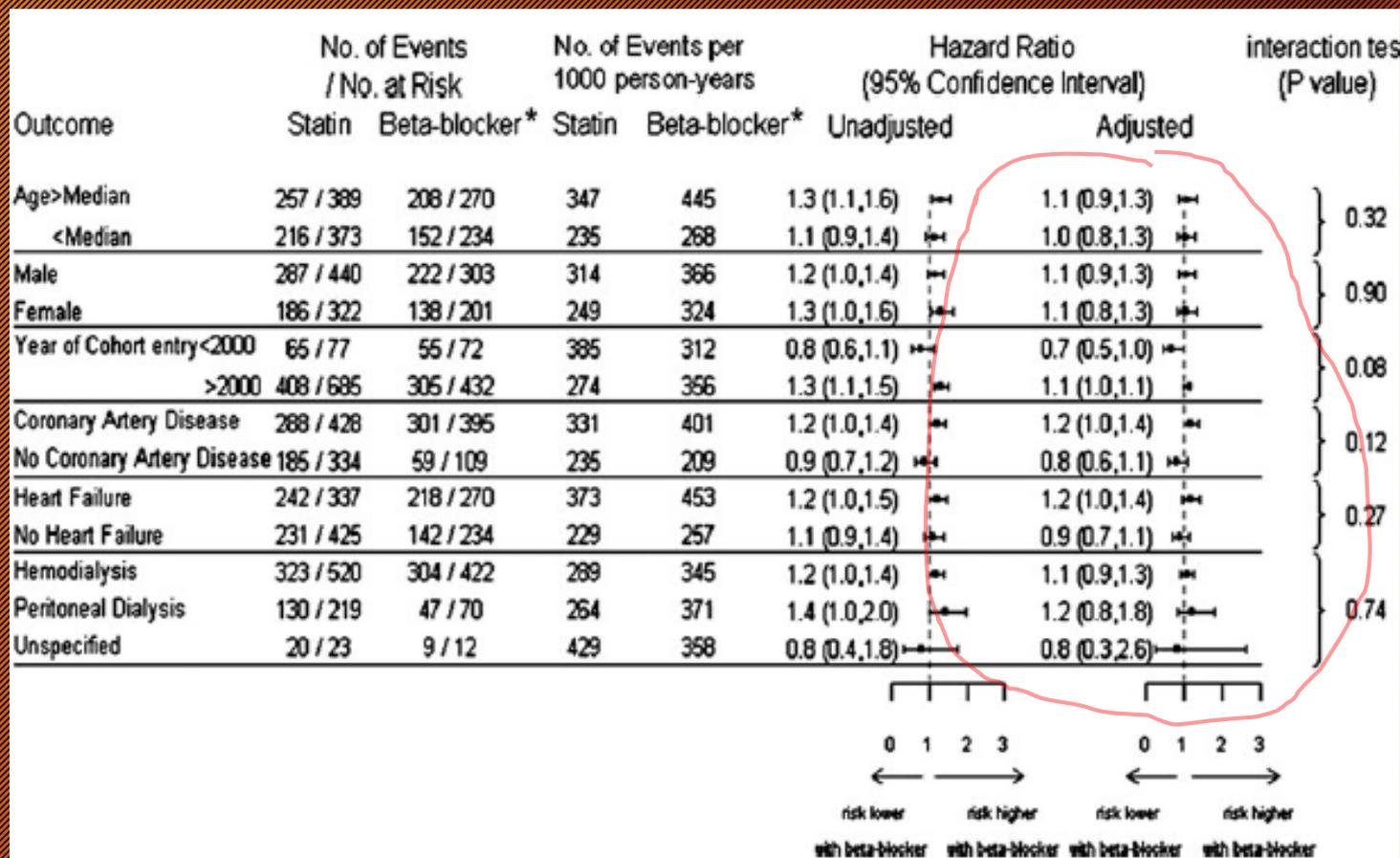
Time-dependent Cox analysis with HgbA1c categories to match previous publication by Kalantar-Zadeh et al



Williams, M. E. et al. Clin J Am Soc Nephrol 2010;5:1595-1601

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The effect of **beta blockers** in HD patients



Vitamin-taking for the general population

- The 2015-2020 Dietary Guidelines for Americans by the NIH **does not recommend** taking vitamin except for special populations:
 - Pregnant women
 - Strict vegetarians/ vegans
 - Alcoholics
- There is no benefit of taking multivitamins for the general population

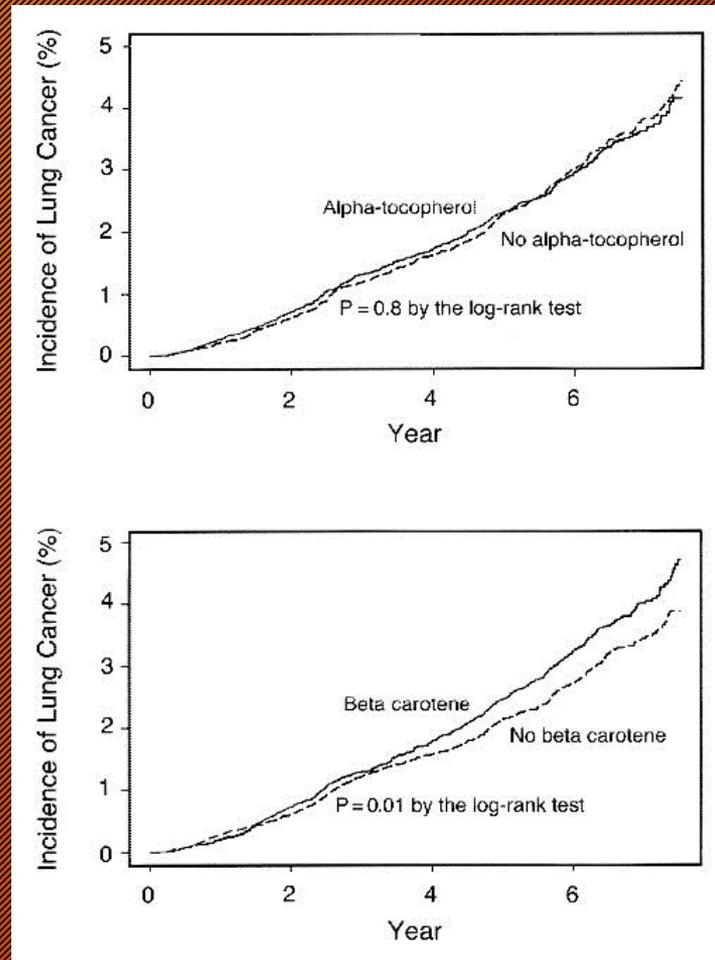
<https://www.nutrition.gov/dietary-supplements>

Sesso HD et al. JAMA 2012;308:1751-60.
Gaziano JM et al. JAMA 2012;308:1871-80.

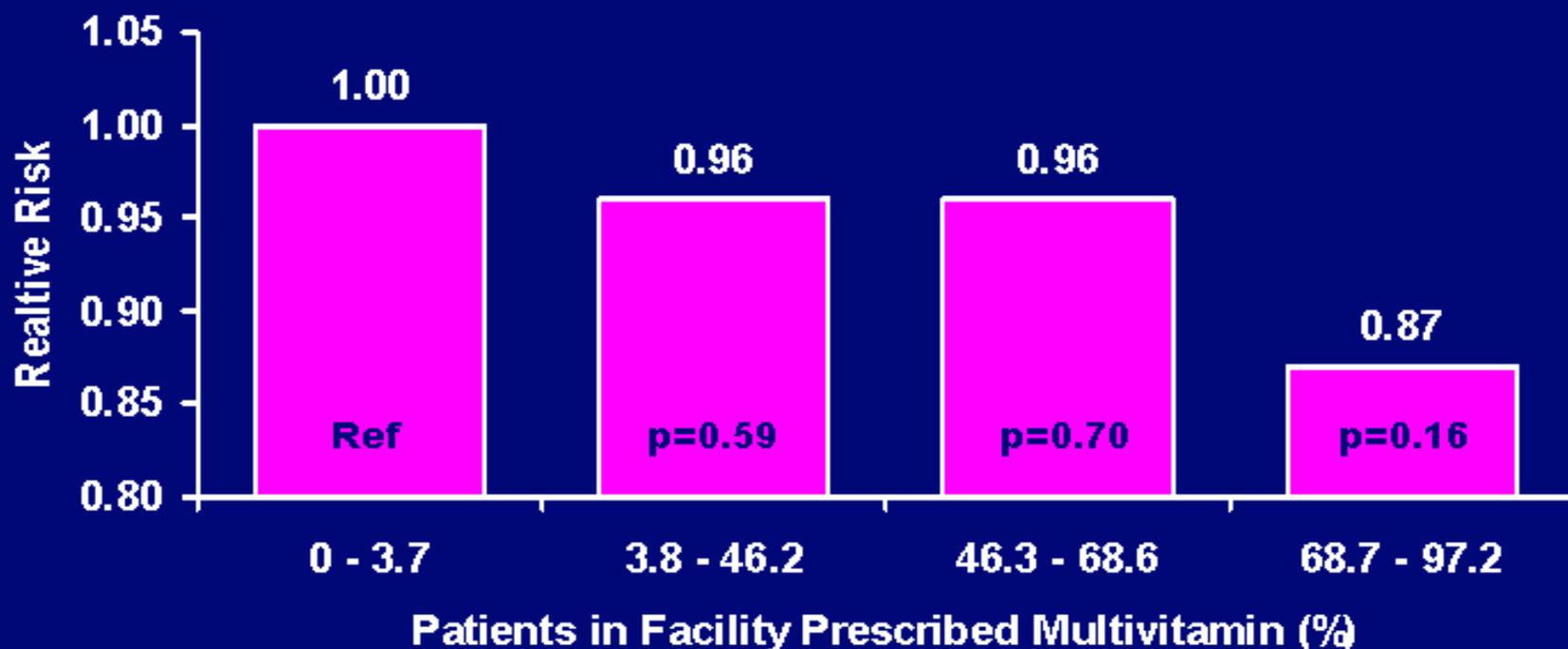
GENERAL POPULATION:

Cumulative Incidence of Lung Cancer Who Received Alpha-Tocopherol Supplements and Those Who Did Not (Upper Panel)

and among Participants Who Received Beta Carotene and Those Who Did Not (Lower Panel).



Dose-Response Relationship Between Relative Risk of Mortality, by Facility Quartiles of Water-Soluble Vitamin Use



Patient and Facility Associations Between Water-Soluble Vitamin Use and Relative Risk (RR) of Mortality and Hospitalization*

Water Soluble Vitamin Use	RR	95% Confidence Interval	P-value
Patient level (water-soluble vitamins vs. no water-soluble vitamins) [†]	-	-	-
Mortality	0.84	0.76 – 0.94	0.001
Hospitalization	0.94	0.85 – 1.04	0.24
Facility level (per 10% patient use of water-soluble vitamins)	-	-	-
Mortality	0.98	0.95 – 1.00	0.05
Hospitalization	1.00	0.99 – 1.01	0.59

*Adjusted for age, sex, race, comorbid conditions, albumin, time on end-stage renal disease, average facility dialysis dose (single-pool Kt/V), body mass index, average facility normalized protein catabolic rate, and average facility hemoglobin. Accounts for facility clustering. Stratified by country.



[†]Time-dependent Cox model; considers changes in multivitamin status over time in the study.

Fissell RB et al. *Am J Kidney Dis* 44(2):293-299, 2004

Summary

- Dialysis patients' survival is not determined by the same indicators that we are used to knowing in the non-dialysis population:
 - Nutrition is one of the most important indicator of survival
 - Obesity is not a risk but an advantage in ESRD
 - HTN is a risk factor as long as it means underdialysis
 - Cholesterol lowering has no benefit
 - Anticoagulation in atrial fibrillation is a risk factor not protection
 - HgbA1c lowering in HD patients does not translate to better survival
 - Beta blockers do not afford the extra survival advantage
 - Dialysis vitamins may be beneficial for HD patients
- Dialysis patients have different life or death indicators than non-dialysis patients; e.g.:
 - Fall risk

Caution!

- 1. most of these studies are RETROSPECTIVE studies, not controlled trials (except for the cholesterol trials)
- 2. absence of evidence is not evidence for absence!

Maybe... Einstein was wrong...

