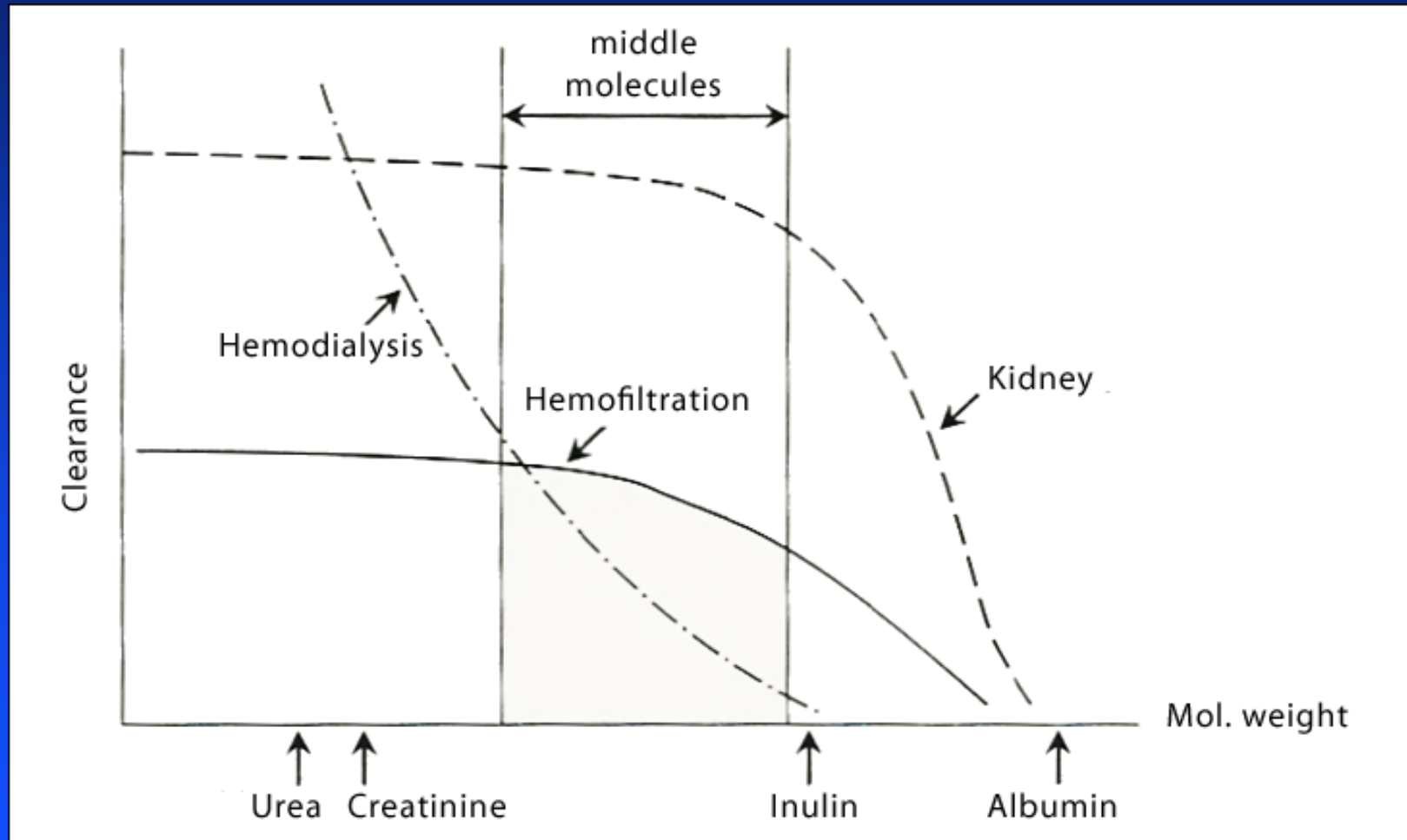


Hemodiafiltration: a new era?

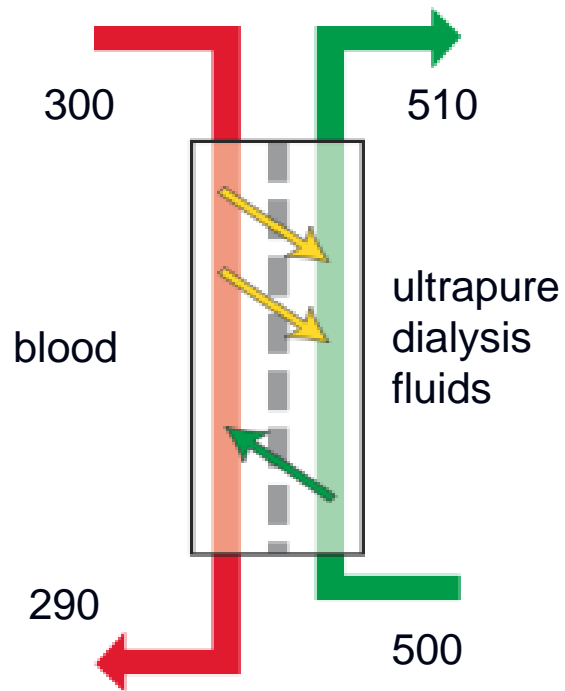
**Peter J. Blankestijn
Department of Nephrology
University Medical Center Utrecht
the Netherlands**

Solute fluxes in different treatment modalities

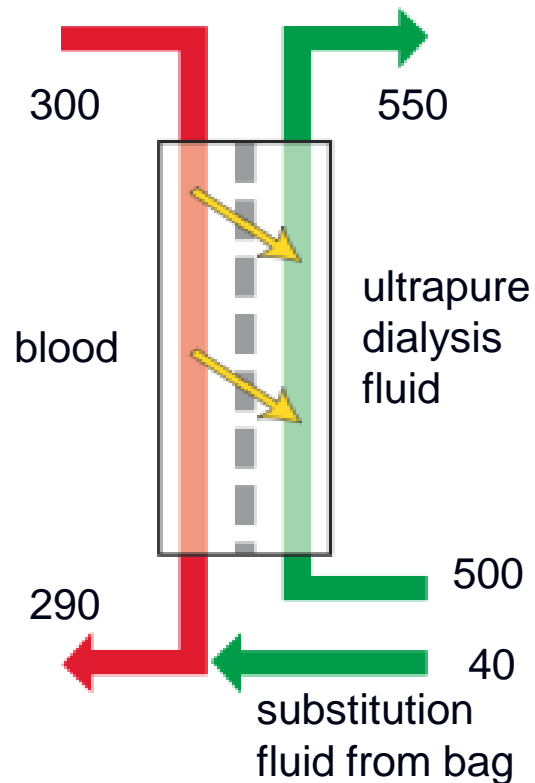


Different forms of HDF

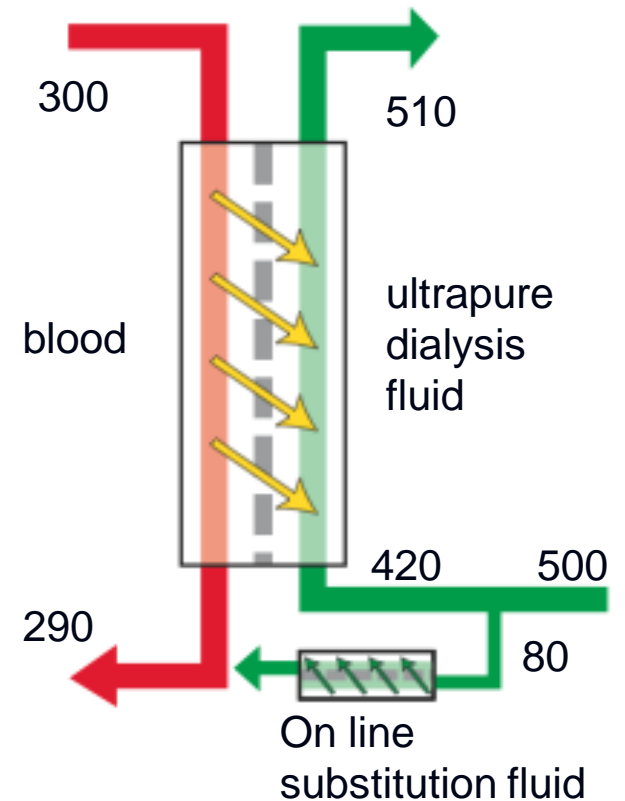
High-flux HD
with unknown
convective removal



Classical HDF
with 50 ml/min
convective removal



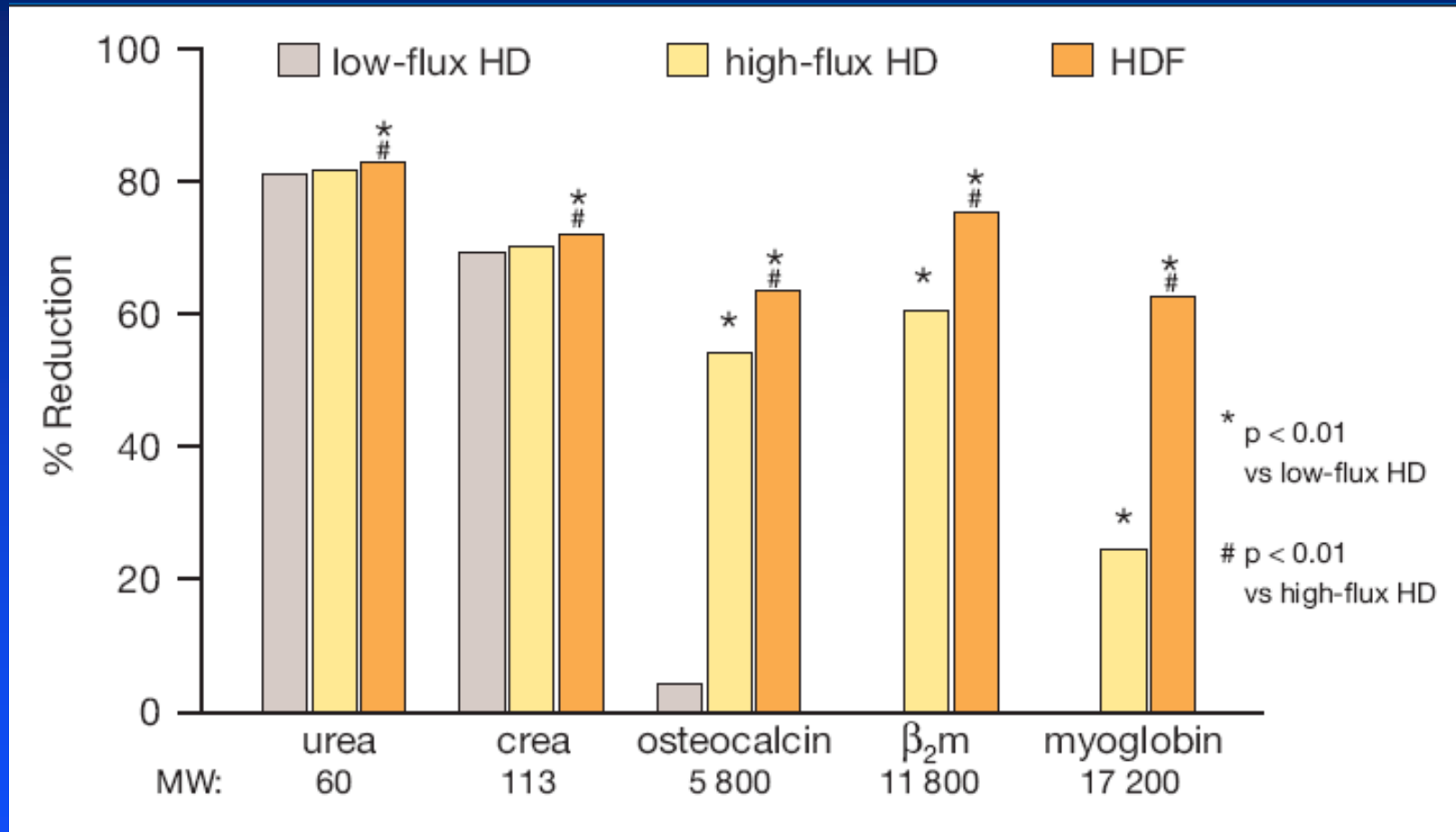
On-line HDF
with 90 ml/min
convective removal



Outline of presentation

- Biochemical data
- Morbidity / Mortality
- Safety
- Conclusions and perspectives

Solute removal with different therapies

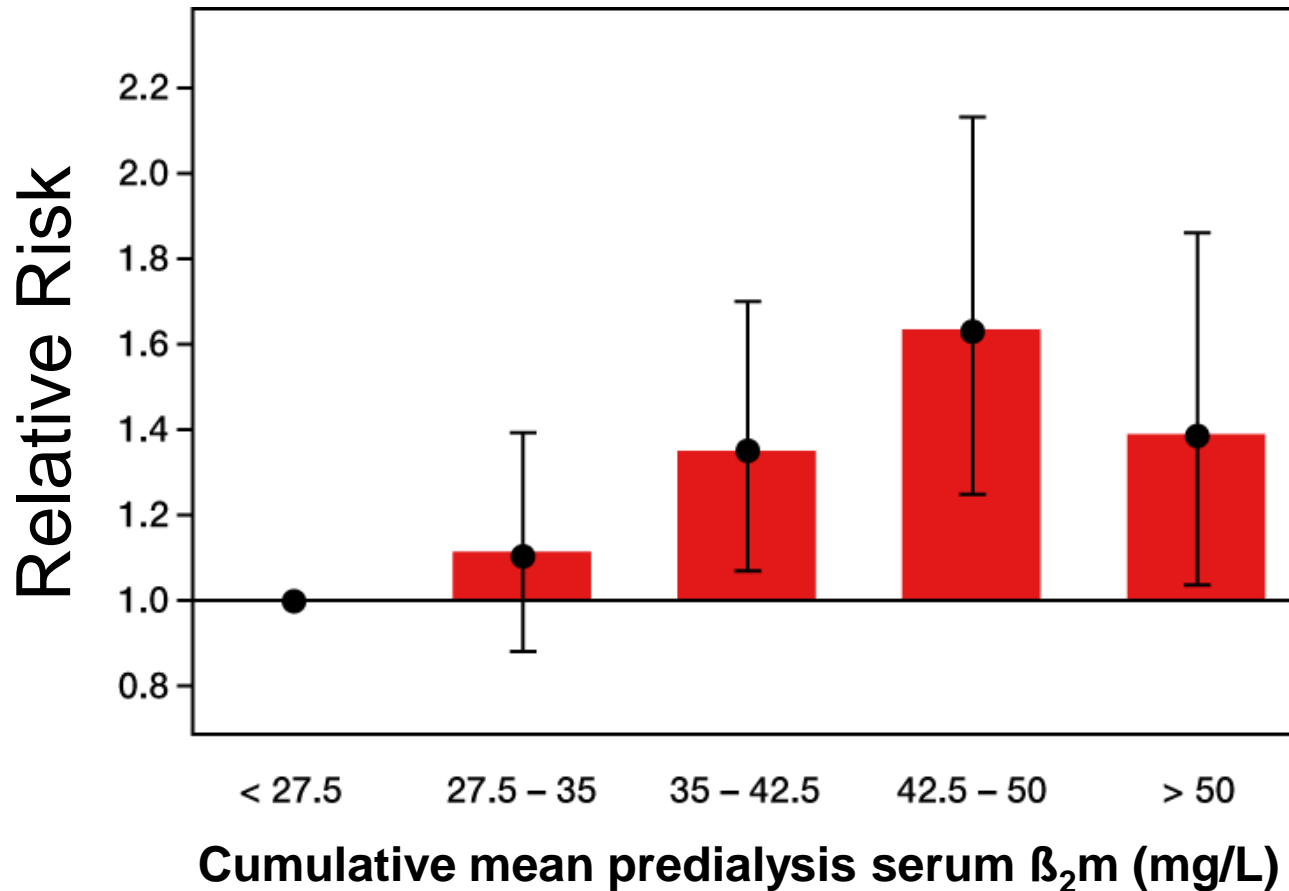


N=23, 3 treatment / mode

Same Q_B , Q_D , t, ΔBW and filter size

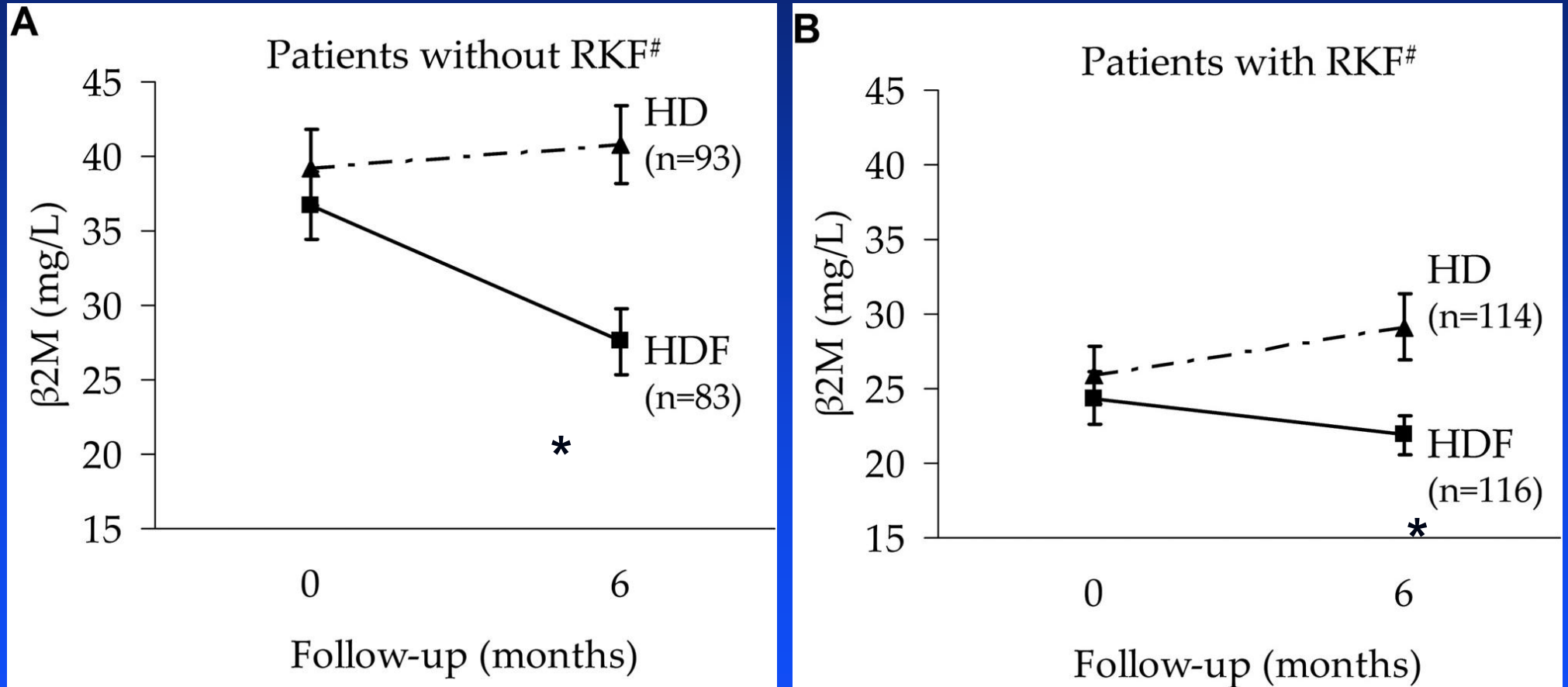
Am J Kidney Dis 2002; 40: 582

HEMO study: β_2m levels and mortality



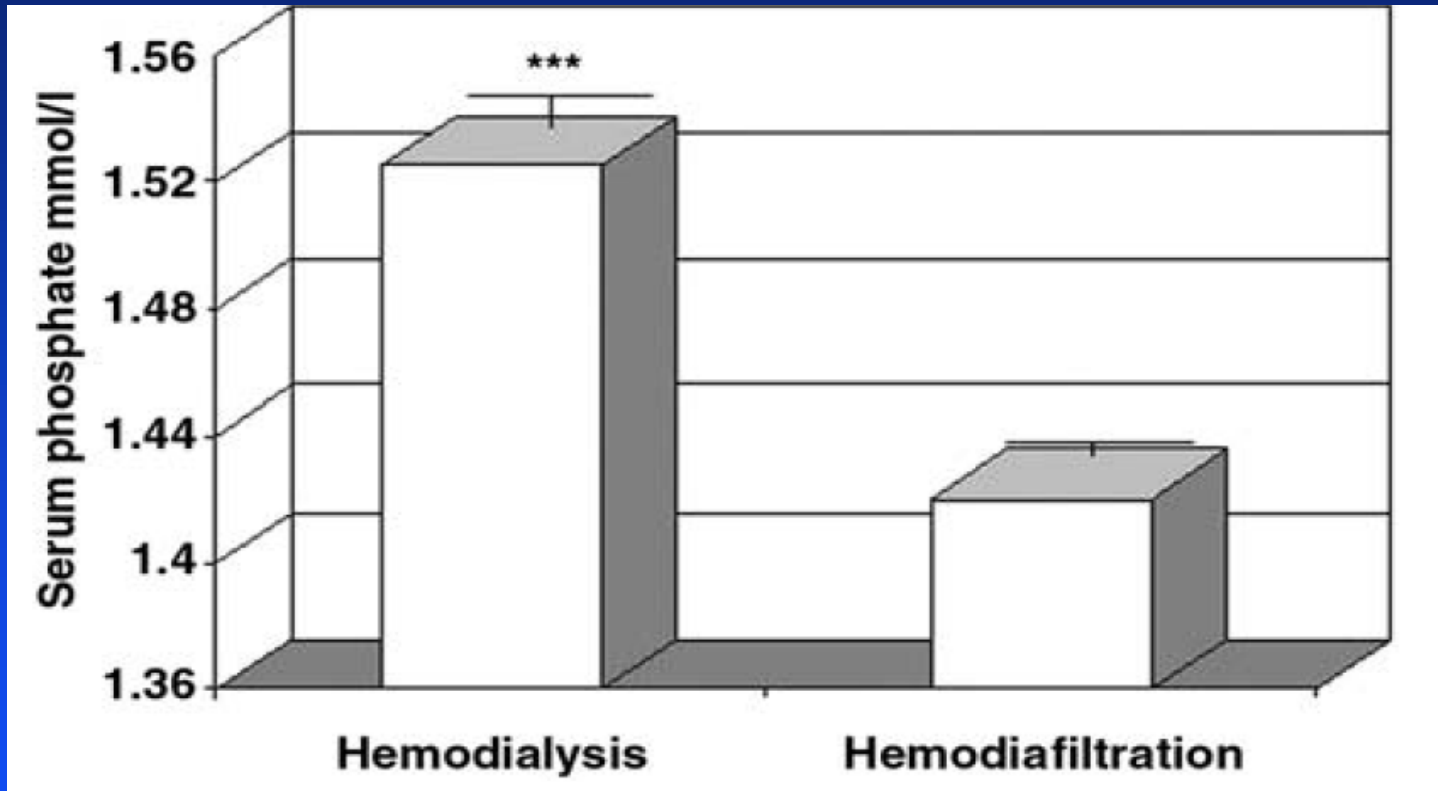
N=1704

Changes in predialysis β 2M



The effect of dialysis modality on phosphate control : haemodialysis compared to haemodiafiltration. The Pan Thames Renal Audit

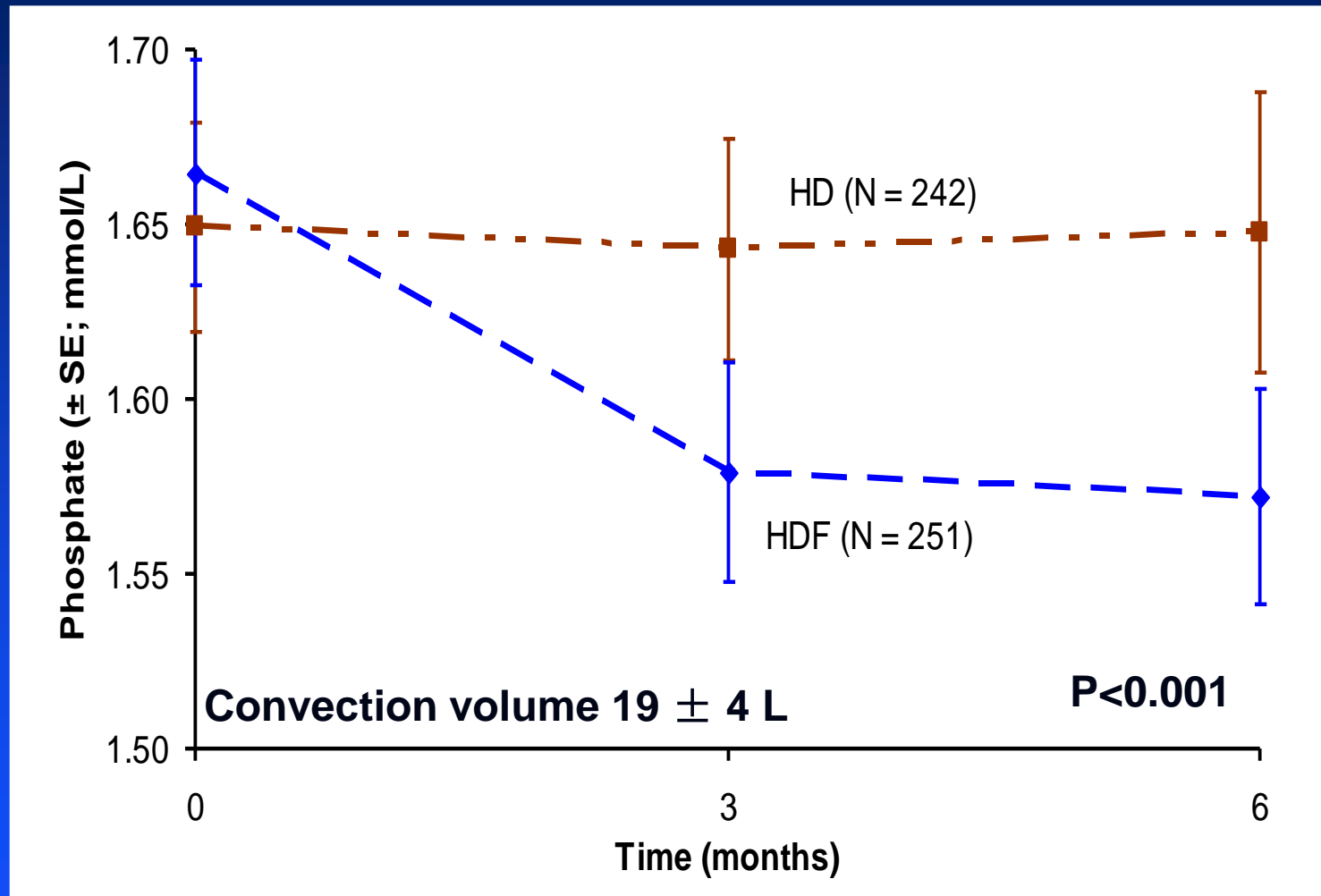
Andrew Davenport¹, Carrie Gardner², Michael Delaney³
and on behalf of the Pan Thames Renal Audit Group⁴



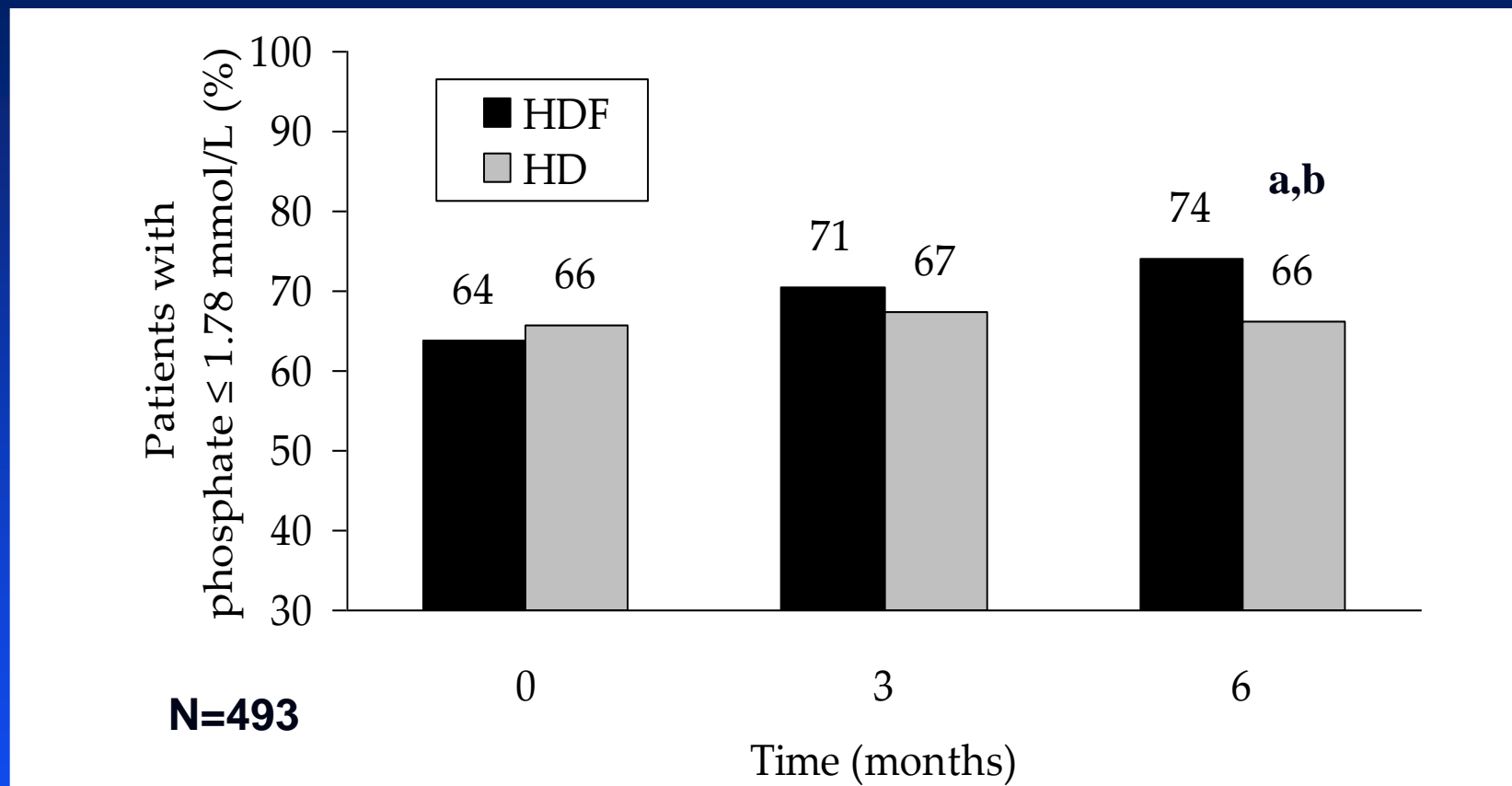
HD n=4515

HDF n=851

Short term effects of HDF on phosphate



Short term effects of online HDF on phosphate



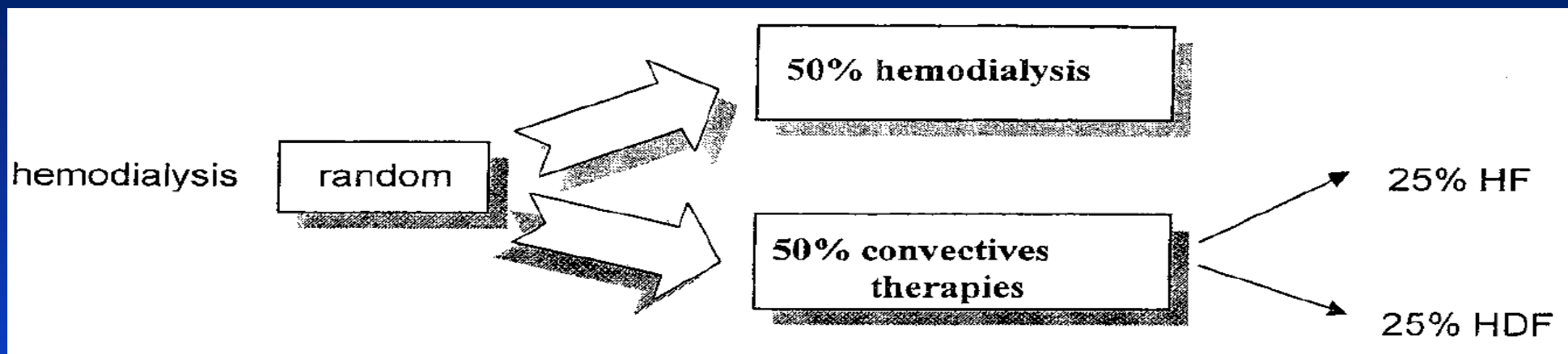
Proportion of patients achieving phosphate treatment targets (5.5 mg/dL = 1.78 mmol/L) at baseline and after 3 or 6 months of follow-up. Numbers above bars represent percentages.

a) $P < 0.05$ (vs baseline); b) $P < 0.05$ (difference in change between groups).

Outline of presentation

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Study design



Randomization



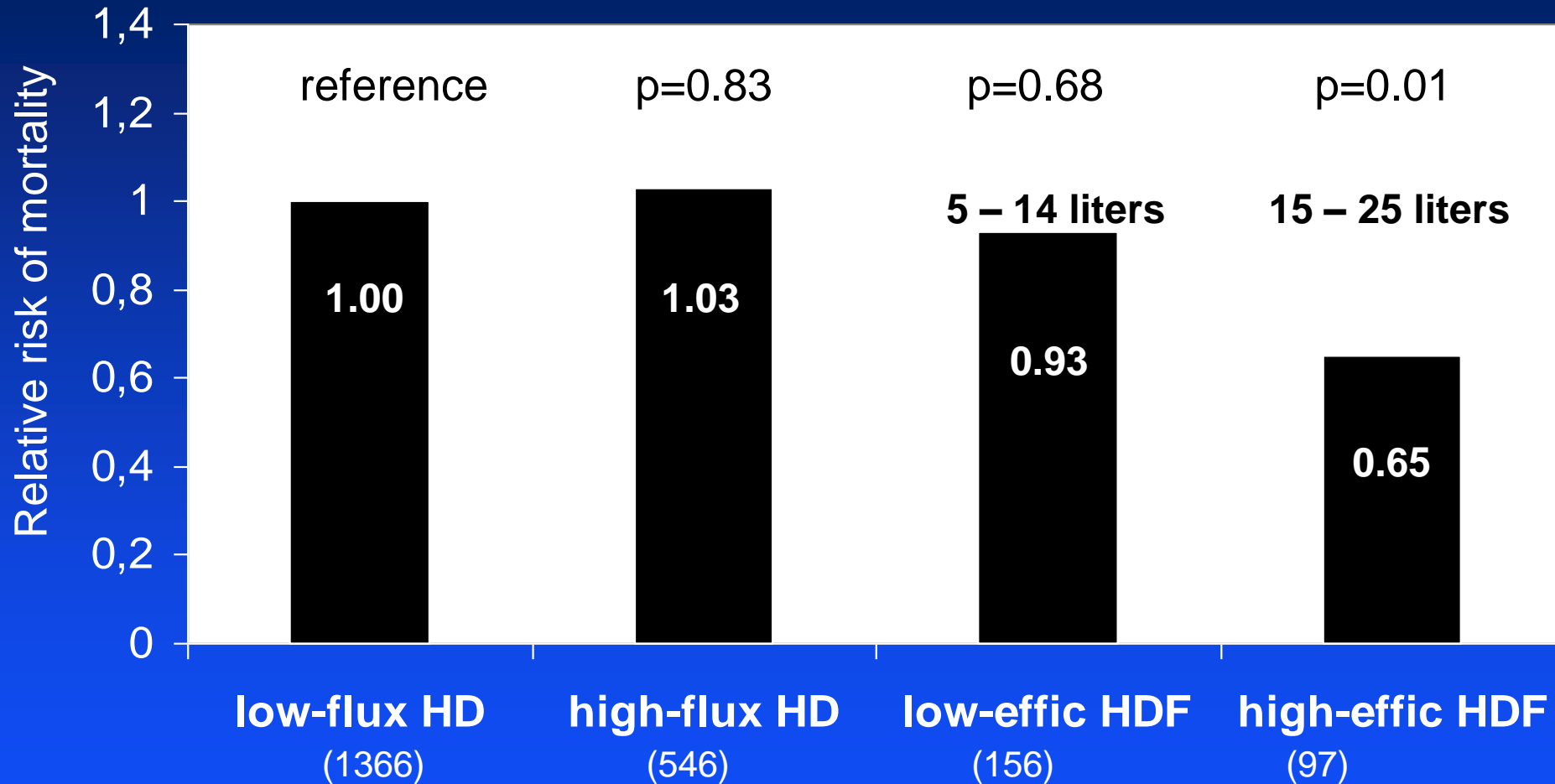
RCT showing decrease of intradialytic hypotension with convective therapies

% of dialysis sessions with symptomatic intradialytic hypotension

	at baseline	at 24 months
HD , n=70 low-flux	7.1	7.9
HDF , n=40 predilution, 40L	10.6	5.2 *
HF , n=36 predilution, 60L	9.8	8.0 *

* p<0.001

DOPPS: risk of mortality



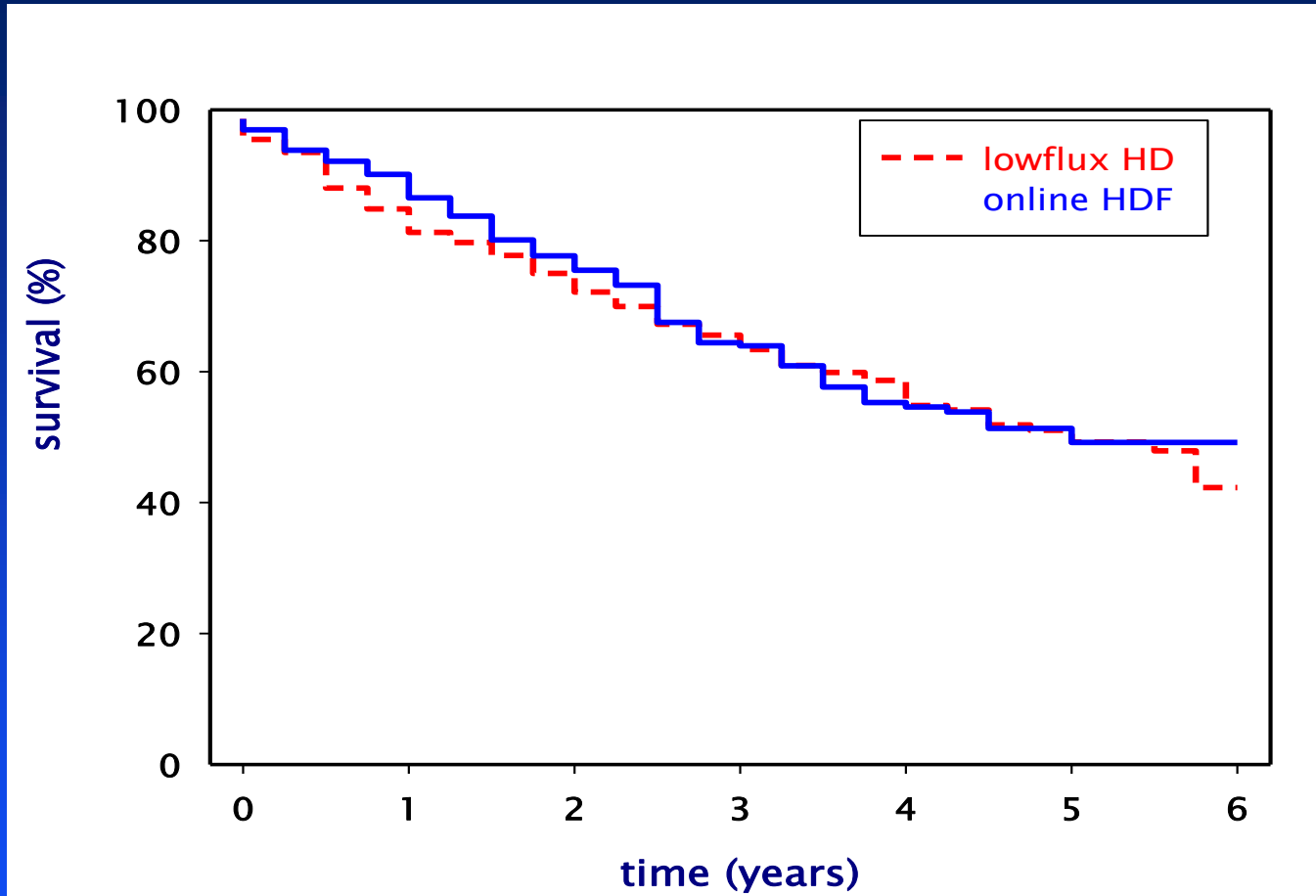
n = 2165, adjusted for age, sex, time on dialysis, comorbidity, weight, catheter, Hb, alb, nPCR, lipids, Kt/V, EPO, QoL

Kidney Int 2006; 69:2087-2093

CONTRAST Study Design

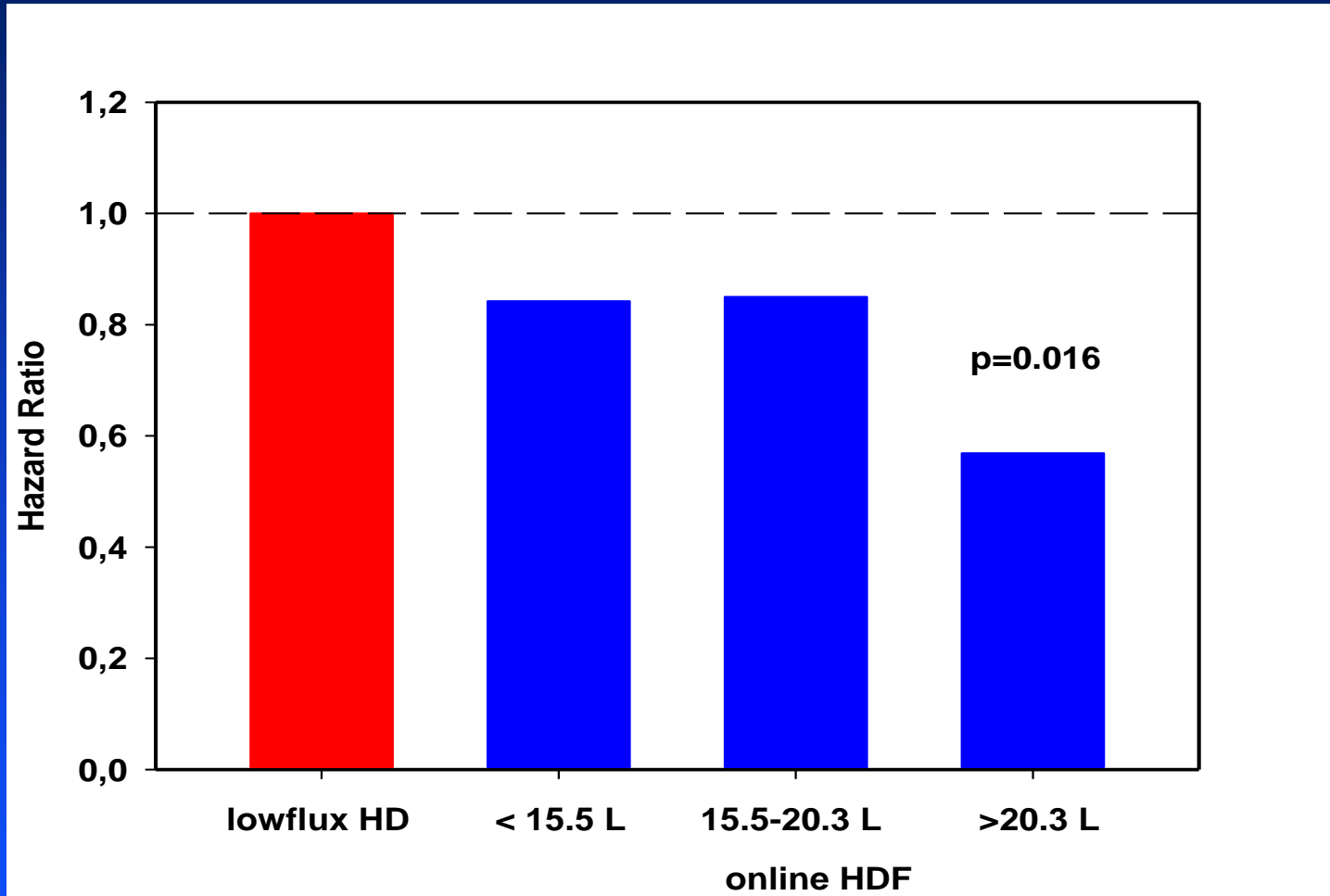
- Randomized prospective multi-center trial
- Continuation of low-flux HD ↔ switch to post-dilution online HDF
 - Ratio of randomization 1:1, stratified per center
 - Ultrapure dialysis fluid for both treatments
 - Online HDF: target convection volume 6L/hour
- Minimum follow up: 1 year

All cause mortality



HD	356	307	230	169	102	65	32
HDF	358	324	237	160	103	57	18

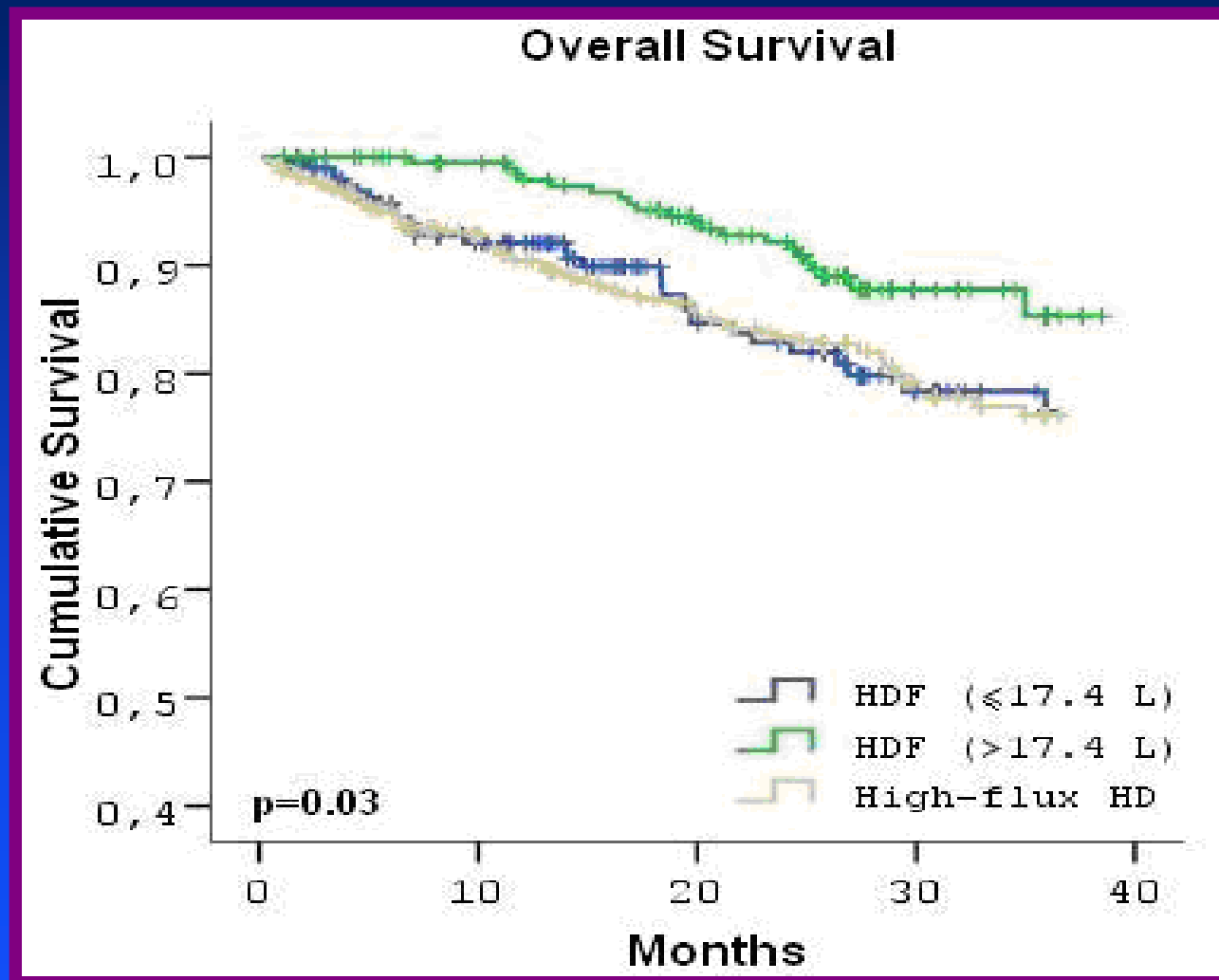
Risk of mortality and convection volume



Adjusted for confounders; p for trend 0.045

Turkish HDF study

HIGH EFFICIENCY vs LOW EFFICIENCY OL-HDF



N=782

Determinants of convective volume

Determinant	Univariable model		Multivariable model	
	B	95% CI	B	95% CI
Sex (Male)	1.8	0.7 to 2.8†	0.47	-0.16 to 1.1
Age (years)	0.0	-0.04 to 0.03		
BMI (kg/m ²)	0.14	0.03 to 0.25†	0.028	-0.04 to 0.09
History of CVD	-0.14	-1.2 to 0.90		
DM	0.67	-0.50 to 1.8		
Time on RRT (years)	0.01	-0.1 to 0.1		
SBP (mmHg)	0.0	-0.03 to 0.02		
DBP (mmHg)	0.01	-0.03 to 0.06		
Vascular access (Fistula)	-0.3	-1.5 to 1.0		
Hemoglobin (mmol/L)	-0.89	-1.5 to -0.28†		
Hematocrit (%)	-0.18	-0.30 to -0.06†	-0.14	-0.22 to -0.07†
Thrombocytes (x 10 ⁹ /L)	-0.003	-0.01 to 0.004		
Serum albumin (g/L)	0.19	0.07 to 0.3†	0.10	0.02 to 0.18†
Treatment time (min)	0.09	0.07 to 0.10†	0.09	0.07 to 0.10†
Blood flow rate (mL/min)	0.05	0.04 to 0.06†	0.04	0.03 to 0.05†

N = 256

Nephrol Dial Transplant 2009; 24: 3493-99

Interaction between bloodflow and filtration fraction in HDF

Blood flow (Q_B)	UF volume (FF 25%)	UF volume (FF 30%)
200 ml/min	3 L/h	3.6 L/h
300 ml/min	4.5 L/h	5.4 L/h
350 ml/min	5.25 L/h	6.3 L/h
400 ml/min	6 L/h	7.2 L/h

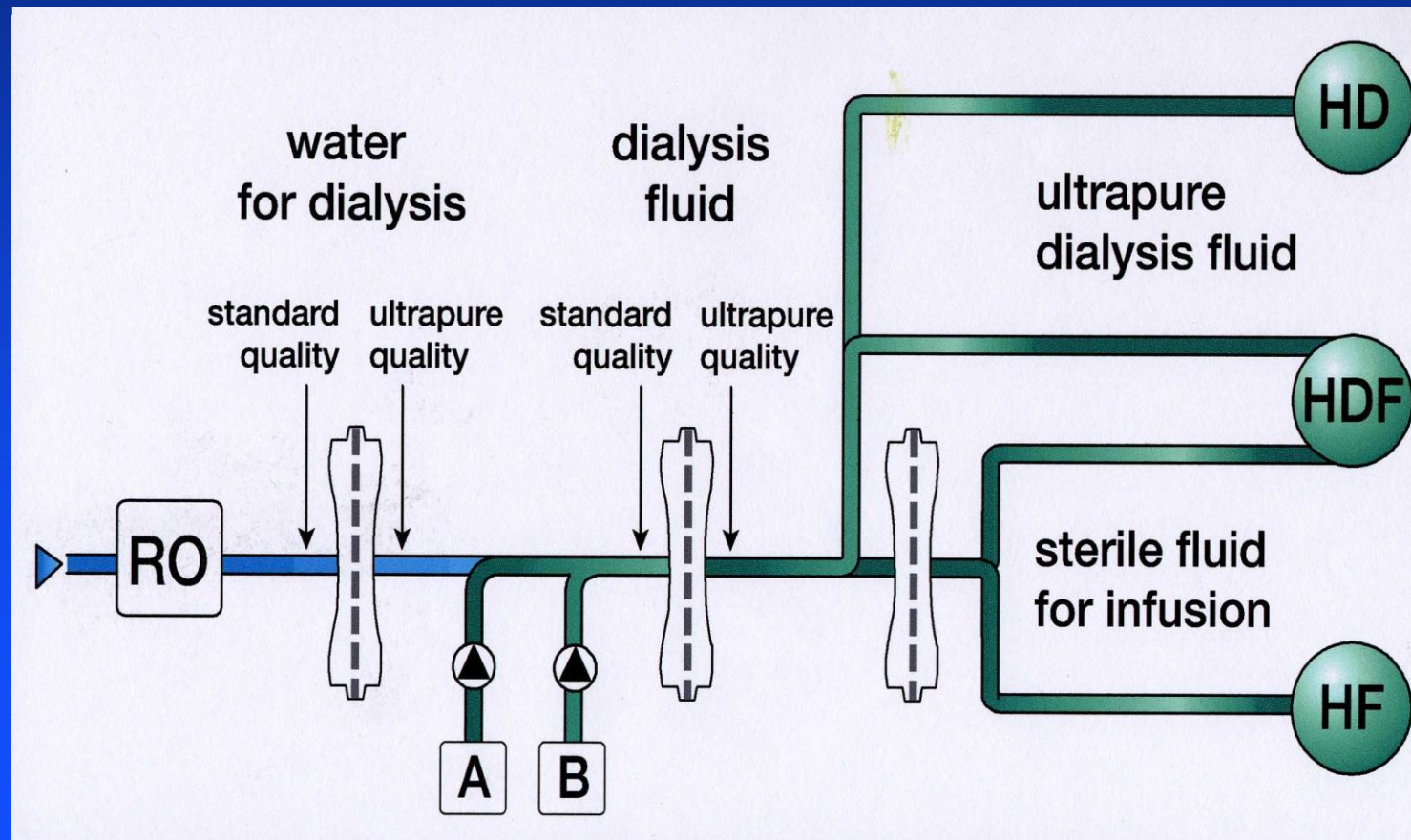
Filtration fraction = UF volume / bloodflow

Outline of presentation

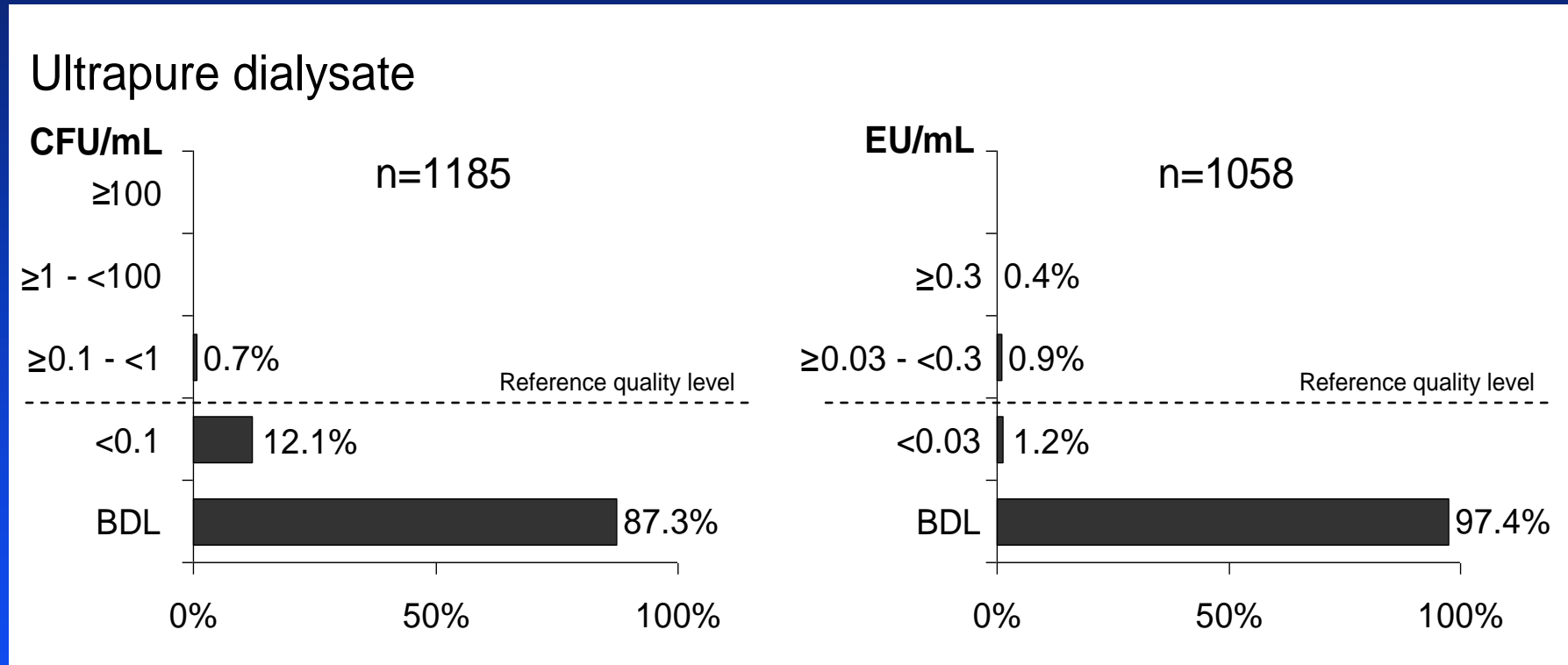
- Biochemical data
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Schematic representation of the production of substitution fluid

Quality level	Bacteria CFU/mL	Endotoxins EU/mL
standard	< 100 - 200	< 0.1 – 1.0
ultrapure	< 0.1	< 0.03
sterile	< 10 ⁻⁶	< 0.03



Results of CFU and endotoxin measurements



8 centers, 12 months

11258 HDF sessions in 97 patients

Kidney Int 2009; 76: 665-72



Outline of presentation

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Randomized clinical trials in Europe evaluating HDF vs HD

Italian Trial
LFHD vs HF/HDF
150/75/75
Tolerance
Morbidity
Mortality
24 months

Turkish Trial
HFHD vs HDF
300/300
CV events
Mortality
24 months

Dutch Trial
CONTRAST
LFHD vs HDF
350/350
CV events
Mortality
36 months

Catalonian Trial
ESHOL
HFHD vs HDF
400/400
CV events
Mortality
36 months

French Trial
HFHD vs HDF
> 65 y
300/300
Tolerance
CV events
Mortality
24 months

70 HD; 40 HDF
& 36 HF patients;
published
JASN 2010

~ 800
patients,
closed 2010

715 enrolled;
study closed
Dec 31, 2010

906 patients;
followed for 3
yrs;
Study ends
late 2011

420 patients;
enrollment
closed
Feb 2011

CONCLUSIONS

On line HDF as compared to standard HD:

- Short term results indicate that changes occur in potentially relevant substances / variables
- Better intra-dialytic hemodynamic stability
- Uncontrolled studies suggest (substantial) survival benefit
- Two RCTs:
 - On line HDF is safe
 - Intention to treat analysis: no survival benefit
 - On treatment analyses: a survival benefit when convection volume > 20 L/session is applied.

Perspectives

Hemodiafiltration: a new era?

- On line HDF can easily and safely be delivered with present day dialysis machines.
- Water of adequate quality can be produced on line with present day production systems.
- Present knowledge suggests that convection volume should be > 20 L/session.
- Treatment time and blood flow are the 2 most important modifiable factors in the effort to obtain these volumes.

Perspectives

Hemodiafiltration: a new era?

- Ideally this concept of minimum volume should be confirmed in properly designed trial(s). Presently running studies may provide new information.
- What is the most effective form of HDF?
- What is the best variable to guide convective therapy?
- Are there subgroups of patients especially benefiting from online HDF therapy?
- ERA-EDTA has instituted an official Working Group on convective therapies: EuDial. (www.era-edta.org/eudial)

