Is the Superiority of Haemodiafiltration Evidence Based?

Francesco Locatelli

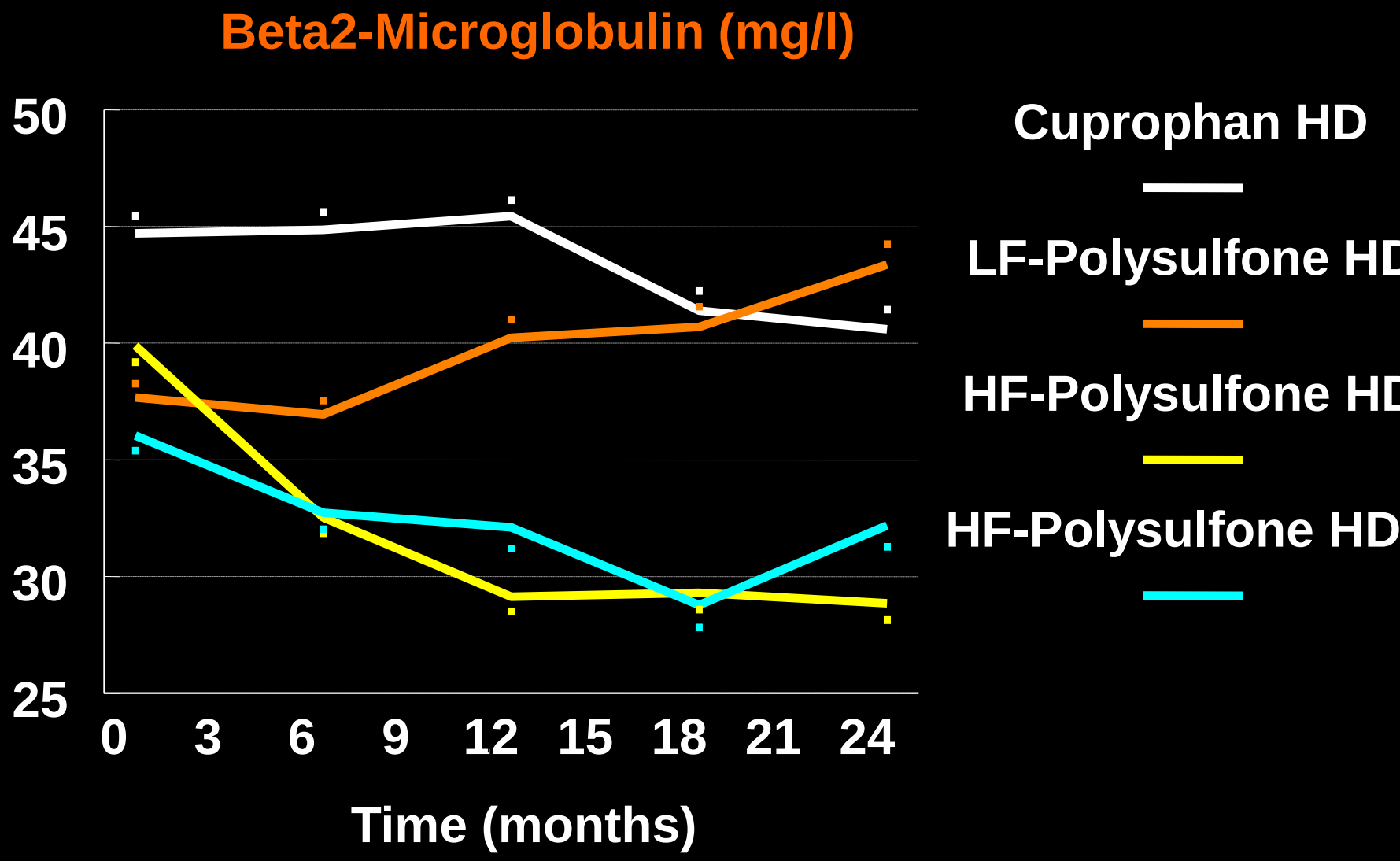
MD, Dr.h.c., FRCP(C)London, FNKF, FERA

Department of Nephrology, Dialysis and Renal Transplant

“Alessandro Manzoni” Hospital – ASST - Lecco - Italy

Prof Locatelli is or was a member of an advisory board of Akebia, Amgen, Astellas,GSK,Roche and Vifor Fresenius Medical Care Pharma and speaker at meetings supported by unrestricted grants from Abbvie,Amgen, Astra Zeneca, Roche and Vifor-Fresenius Medical Care Pharma.

β 2-Microglobulin plasma levels

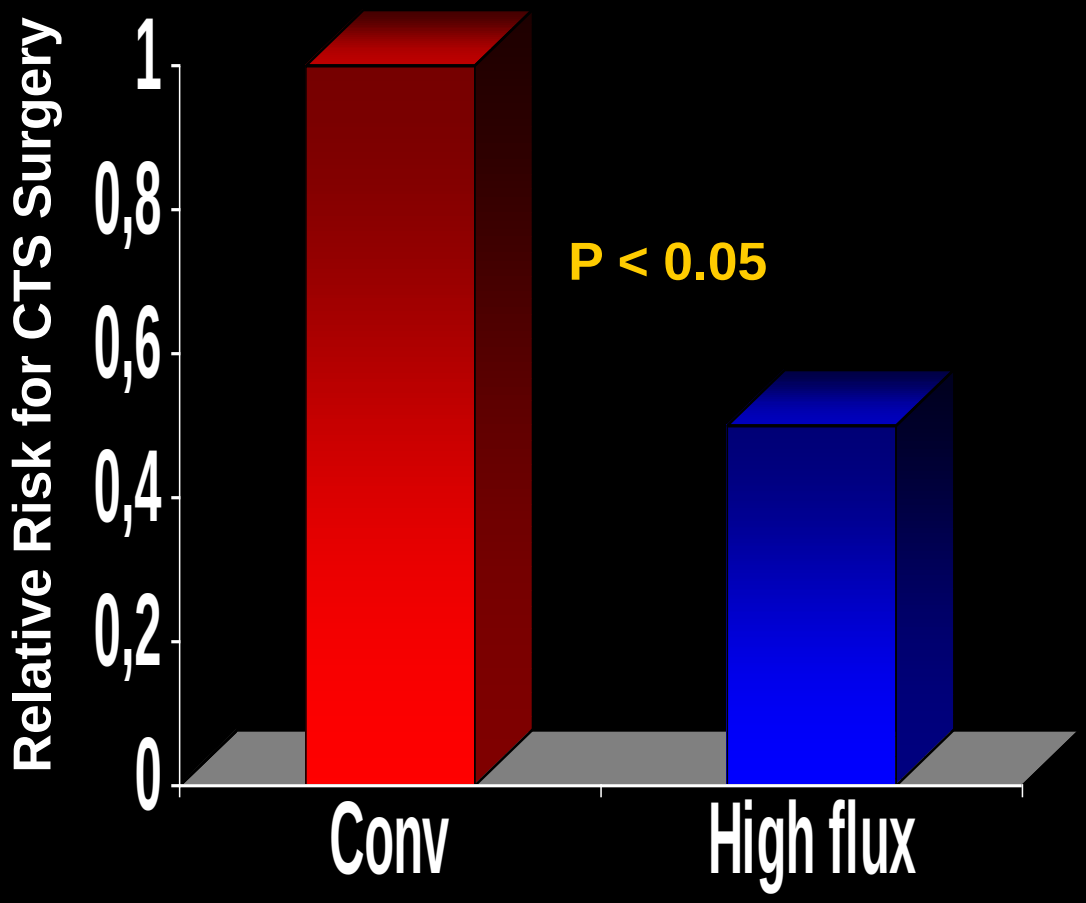


Locatelli F et al. Kidney Int 1996; 50: 1293-1302

Is the β2-Microglobulin plasma level reduction of clinical importance for improving patient comorbidity?

Dialysis membrane and the risk of carpal tunnel syndrome

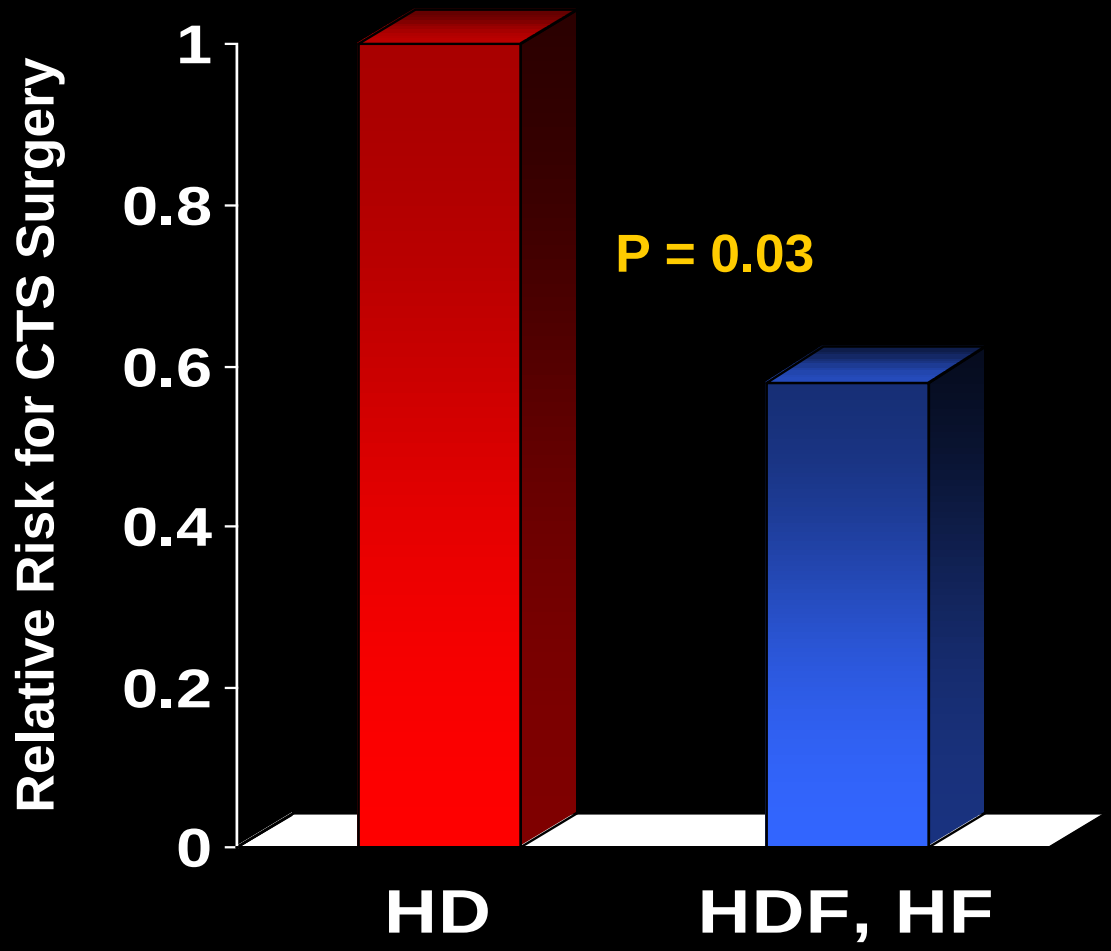
single centre observational study



Koda Y et al. Kidney Int 1997; 52: 1096-1011

Dialysis membrane and the risk of carpal tunnel syndrome

Data from the Lombardy Registry



RLDT

Locatelli F et al. Kidney Int 1999 ; 55 : 286 - 293

Is this β2-Microglobulin plasma level reduction of clinical importance for patient survival?

Volume 17, Issue 2, February 2006

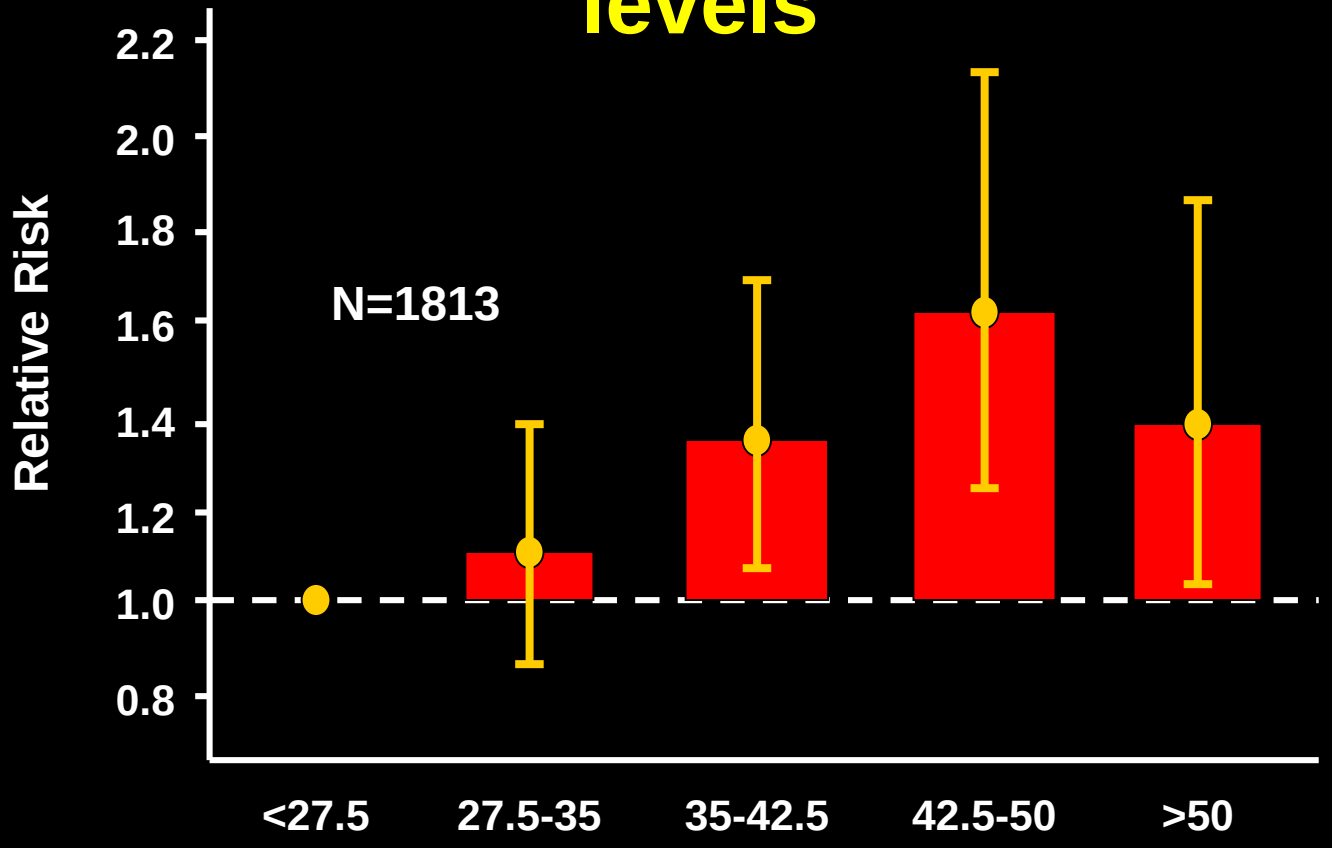
Pages 546-555

Serum β-2 Microglobulin Levels Predict Mortality in Dialysis Patients: Results of the HEMO Study

Alfred K. Cheung,* Michael V. Rocco,† Guofen Yan,‡ John K. Leypoldt,* Nathan W. Levin,§ Tom Greene,‡ Lawrence Agodoa,‖ James Bailey,¶ Gerald J. Beck,‡ William Clark,# Andrew S. Levey,** Daniel B. Ornt,†† Gerald Schulman,‡‡ Steven Schwab,§§ Brendan Teehan,‖‖ and Garabed Eknoyan;¶¶ for HEMO Study Group

**VA Salt Lake City Healthcare System and Department of Medicine, University of Utah, Salt Lake City, Utah; †Department of Medicine, Wake Forest University, Winston-Salem, North Carolina; ‡Department of Biostatistics & Epidemiology, Cleveland Clinic Foundation, Cleveland, Ohio; §Renal Research Institute, New York, New York; ‖National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland; ¶Department of Medicine, Emory University, Atlanta, Georgia; #Baxter Corporation, McGaw Park, Illinois; **Department of Medicine, Tufts-New England Medical Center and Tufts University, Boston, Massachusetts; ††Department of Medicine, University of Rochester, Rochester, New York; ‡‡Department of Medicine, Vanderbilt University, Nashville, Tennessee; §§Department of Medicine, Duke University, Durham, North Carolina; ‖‖Department of Medicine, Lankenau Hospital, Philadelphia, Pennsylvania; and ¶¶Department of Medicine, Baylor College of Medicine, Houston, Texas*

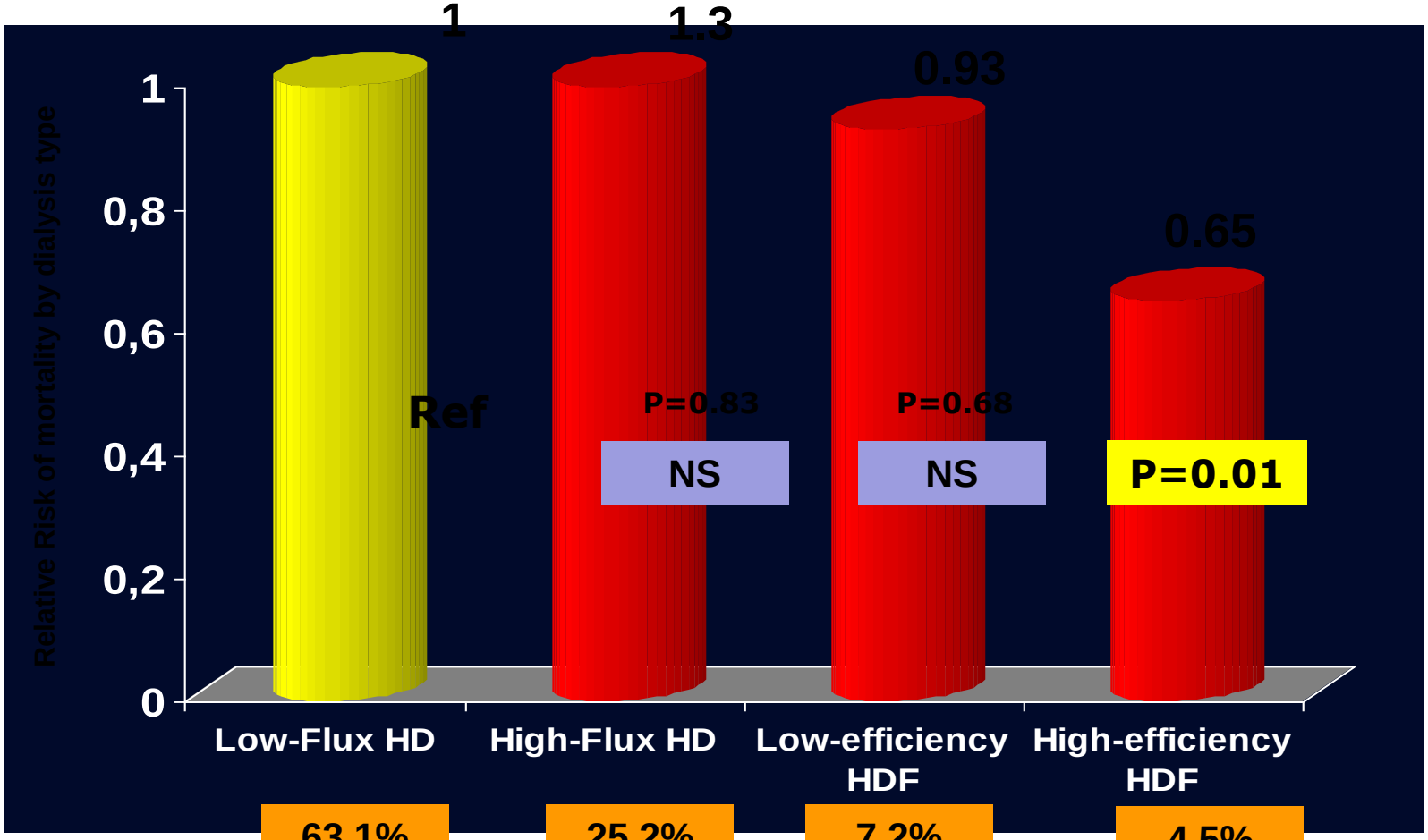
Association of all-cause mortality with cumulative mean pre-dialysis serum β2M levels



Time-dependent Cox regression analysis: RR 1.11 (1.05-1.19) per 10 mg/L increase

Cheung AK et al. J Am Soc Nephrol 2006; 17: 546-555

Mortality risk for patients receiving HDF versus HD
European results from the DOPPS



Canaud B et al. Kidney Int 2006; 69: 2087-2093

KDIGO Controversies Conference

Novel techniques and innovation in blood purification:
How can we improve clinical outcomes in hemodialysis?

14-15 October, 2011
Paris, France

CONFERENCE LEADERS

Christopher T Chan, MD – Conf. Co-Chair
University of Toronto
Toronto, CANADA
Christopher.Chan@uhn.on.ca

Bertram Kasiske, KDIGO Co-Chair
Hennepin County Medical Center
Minneapolis, MN, UNITED STATES
kasis001@umn.edu

Nathan Levin, MD – Conf. Co-Chair
Renal Research Institute
New York, NY, UNITED STATES
nlevin@rriny.com

Kai-Uwe Eckardt, MD – KDIGO Co-Chair
University Hospital Erlangen
Erlangen, GERMANY
Kai-Uwe.Eckardt@uk-erlangen.de

Francesco Locatelli, MD – Conf Co-Chair
Alessandro Manzoni Hospital
Lecco, ITALY
f.locatelli@ospedale.lecco.it

Is Hemodiafiltration the future?

CHAN CT… LOCATELLI F. ET AL KIDNEY INT. 2013 JAN 16

Do we have randomized control trials comparing HDF and HD?

Randomized clinical trials in Europe evaluating HDF vs HD

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

715 enrolled
JASN 2012

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

70 HD; 40 HDF
& 36 HF patients
JASN 2010

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

410 patients
Kidney Int. 2017

Catalonian Trial
ESHOL
HFHD vs HDF
300/300
CV events
Mortality
24 months

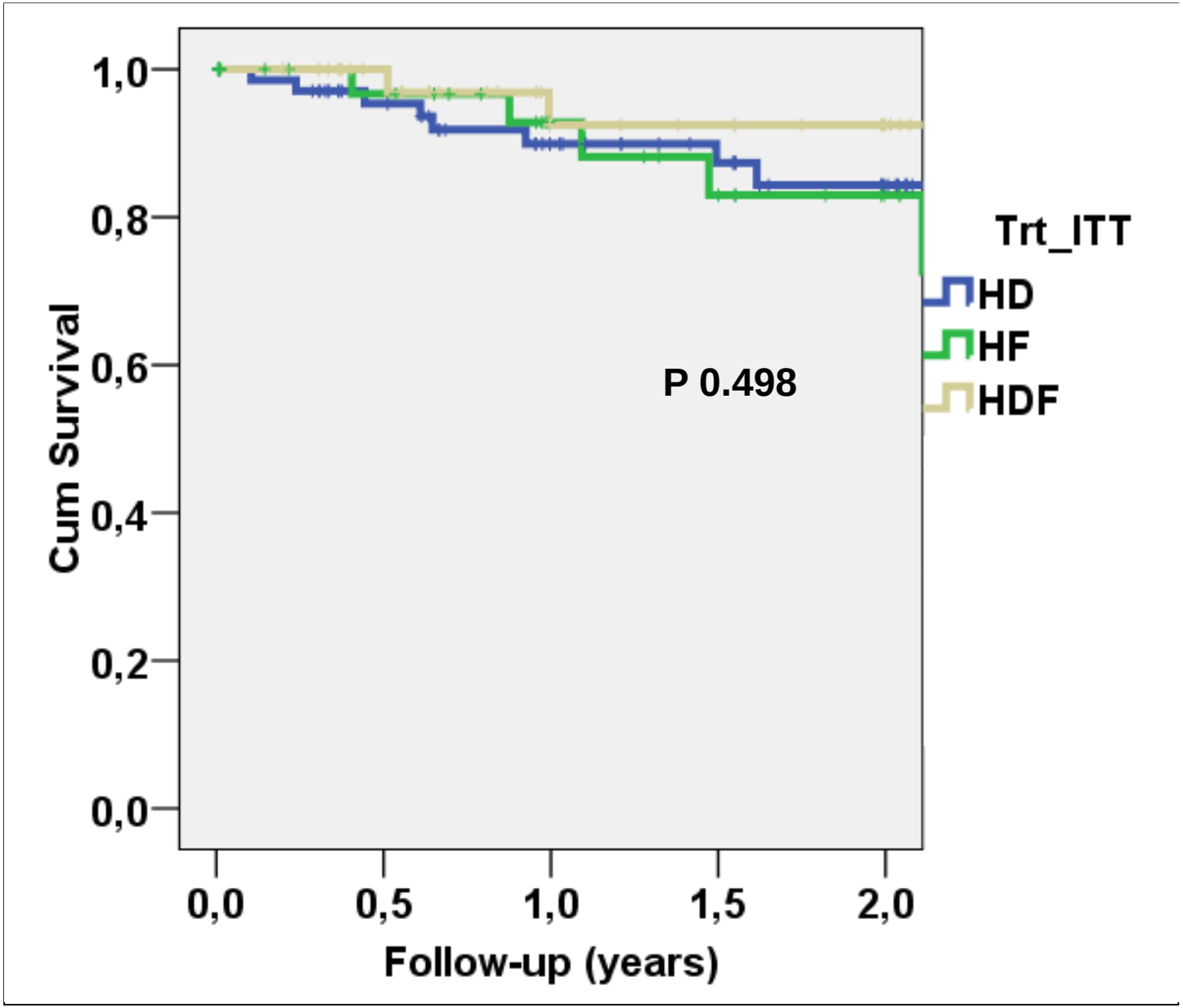
~900 patients;
JASN 2013

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

~ 800 patients
NDT 2012

Is HDF able to improve Survival?

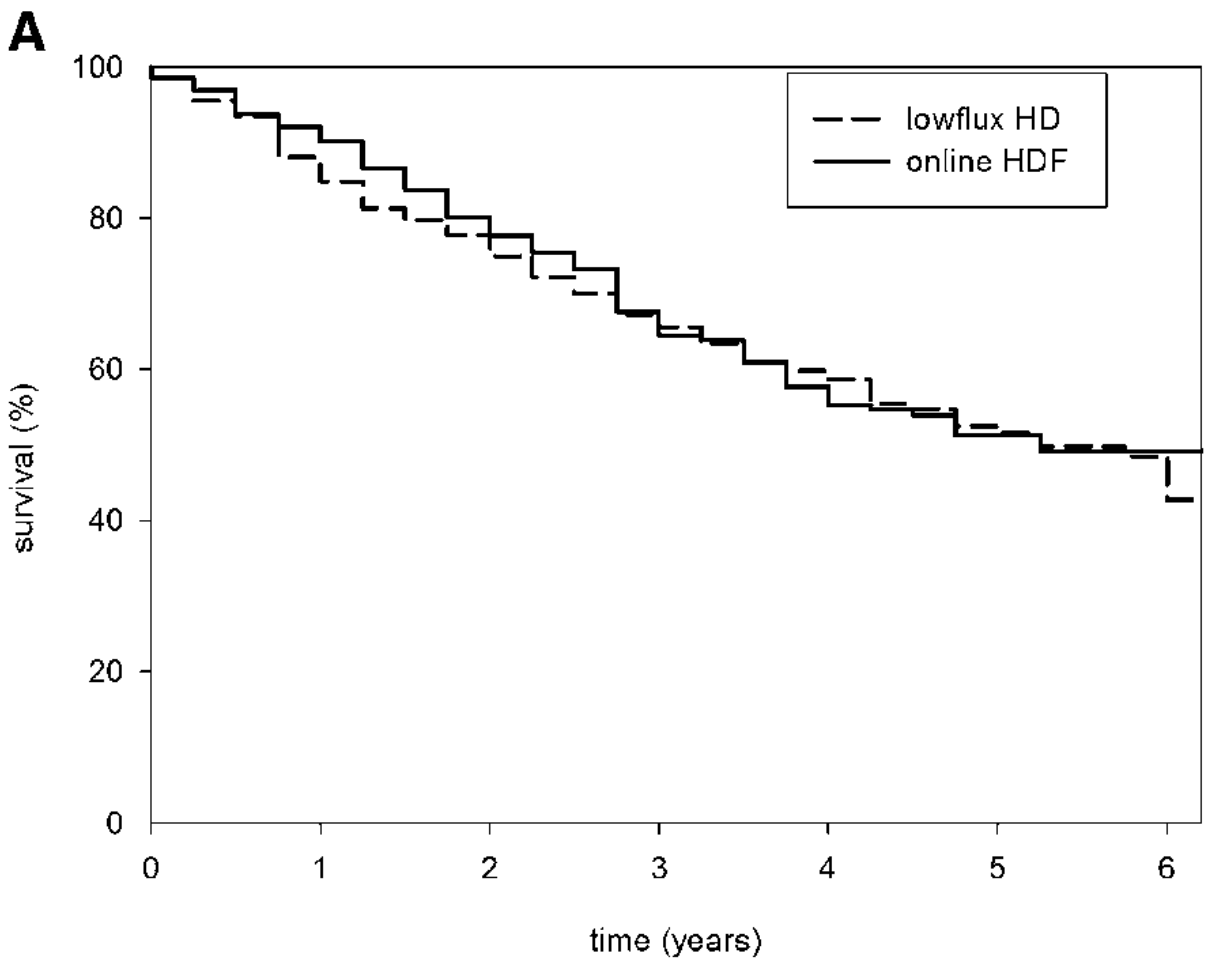
Patient survival



Locatelli et al. J Am Soc Nephrol. 2010; 21(10):1798-807

All-cause mortality was not affected by treatment

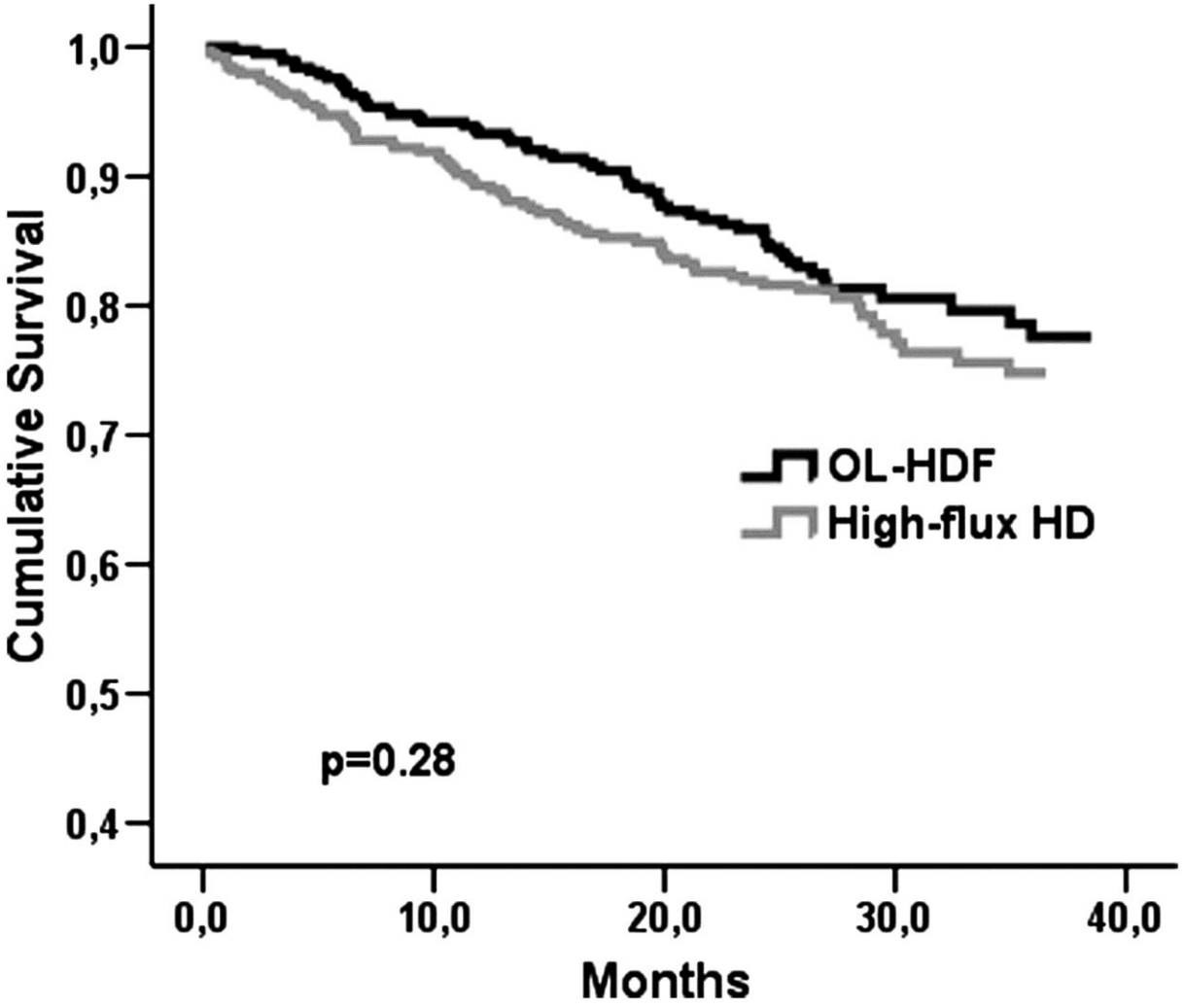
Survival curves for time to death from any cause based on life table analyses using 3-month time periods



Grooteman M P et al. JASN 2012;23:1087-1096

JASN

Composite event-free survival in patients treated with OL-HDF and high-flux HD

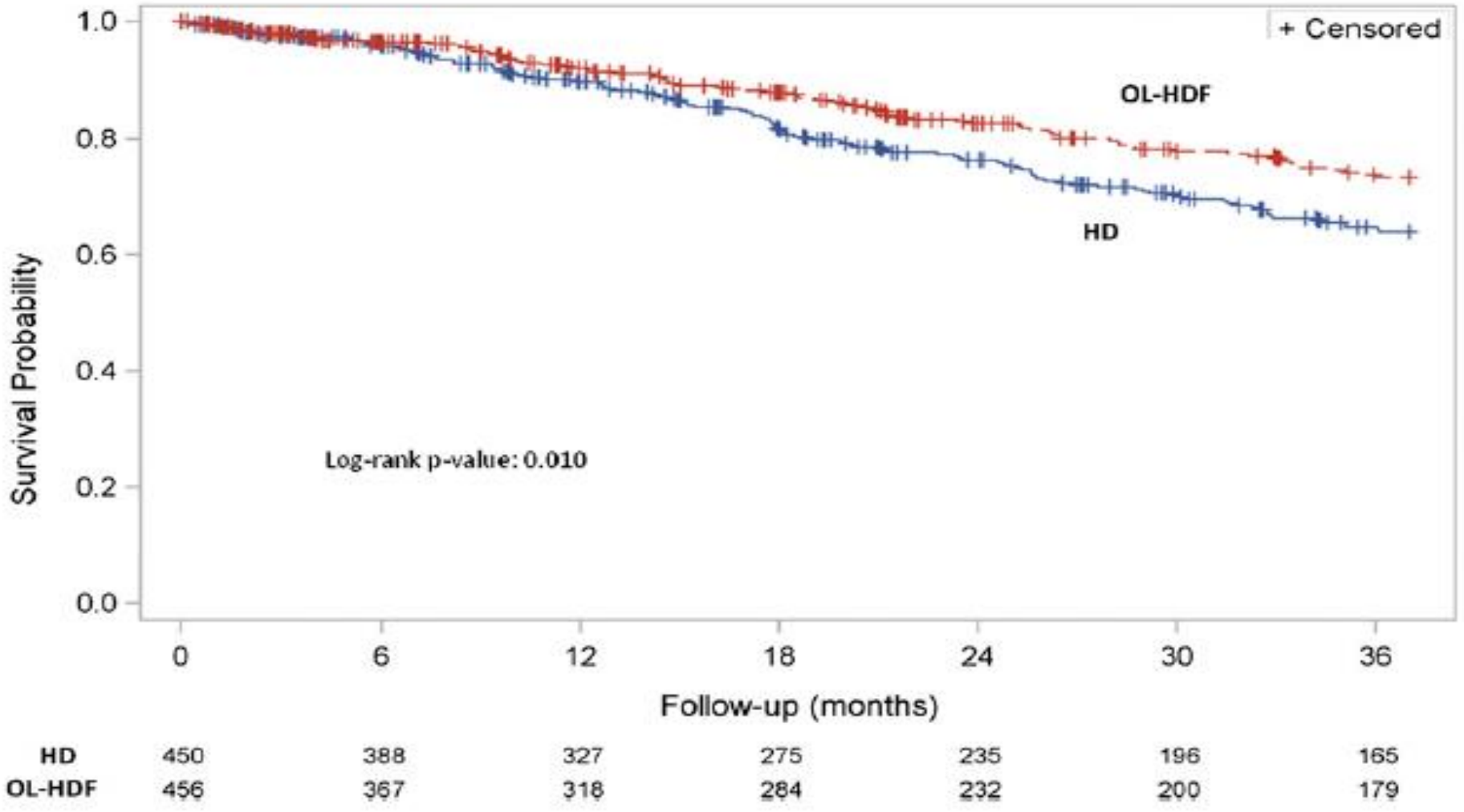


Ok E et al. Nephrol. Dial. Transplant. 2013;28:192-202

NDT Nephrology Dialysis Transplantation

36 months survival in the intention to treat population

(p=0,001 by the long rank test)



F. Maduell et al. J Am Soc Nephrol 24: 2013

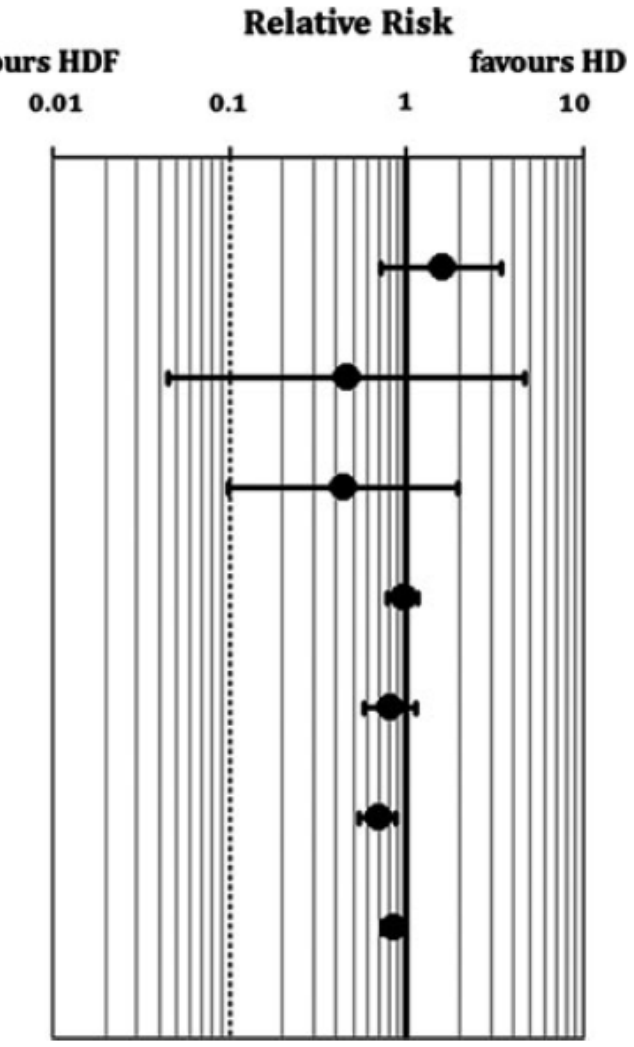
Seminars in Dialysis

Clinical Evidence on Hemodiafiltration: A Systematic Review and a Meta-analysis

Ira M. Mostovaya,* Peter J. Blankestijn,* Michiel L. Bots,† Adrian Covic,‡ Andrew Davenport,§ Muriel P.C. Grooteman,¶** Jörgen Hegbrant,†† Francesco Locatelli,‡‡ Raymond Vanholder,§§ Menso J. Nubé,¶** and on behalf of the EUDIAL[1] – an official ERA-EDTA Working Group

Meta-analysis of all RCTs comparing *MORTALITY* in patients treated with HD or HDF

Study name	Weight	HDF (Events/Pat)	HD (Events/Pat)	RR	95% CI
Locatelli 1996 et al. (9)	0.03	7/50	26/279	1.56	0.72 – 3.42
Wizemann et al. (11)	0.01	1/23	2/21	0.46	0.045 – 4.68
Locatelli 2010 et al. (10)	0.01	2/40	8/70	0.44	0.10 – 1.96
Grooteman et al. (12)	0.48	131/358	138/356	0.94	0.78 – 1.15
Ok et al. (13)	0.16	52/391	65/391	0.80	0.57. – 1.12
Maduell et al. (14)	0.31	85/456	122/450	0.69	0.54 – 0.88
Pooled	**1.00**	**278/1318**	**361/1567**	**0.84**	**0.73 – 0.96**



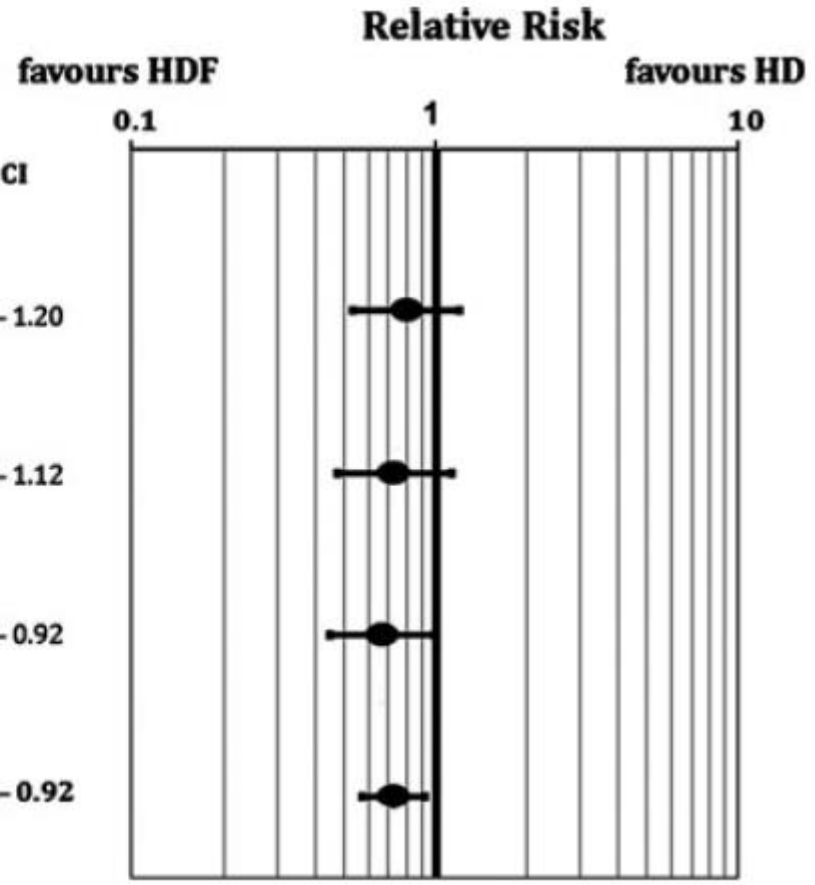
Seminars in Dialysis

Clinical Evidence on Hemodiafiltration: A Systematic Review and a Meta-analysis

Ira M. Mostovaya,* Peter J. Blankestijn,* Michiel L. Bots,† Adrian Covic,‡ Andrew Davenport,§ Muriel P.C. Grooteman,¶** Jörgen Hegbrant,†† Francesco Locatelli,‡‡ Raymond Vanholder,§§ Menso J. Nubé,¶** and on behalf of the EUDIAL[1] – an official ERA-EDTA Working Group

Meta-analysis of all RCTs comparing *CARDIOVASCULAR MORTALITY* in patients treated with HD or HDF

Study name	Weight	HDF (Events/Pat)	HD (Events/Pat)	RR	95% CI
Grooteman et al. (12)	0.30	37/358	46/356	0.80	0.53 – 1.20
Ok et al. (13)	0.26	32/391	44/391	0.73	0.47 – 1.12
Maduell et al. (14)	0.44	37/456	55/450	0.66	0.57 – 0.92
Pooled	1.00	106/1205	145/1197	0.73	0.57 – 0.92



Convective Versus Diffusive Dialysis Therapies for Chronic Kidney Failure: An Updated Systematic Review of Randomized Controlled Trials

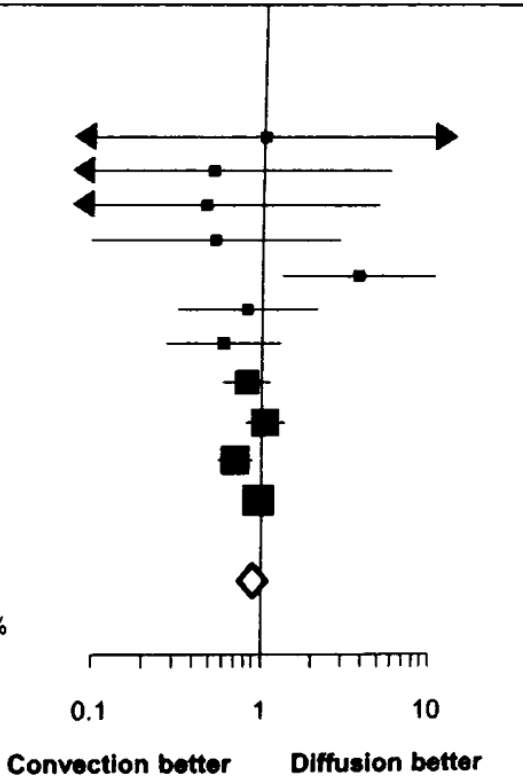
Ionut Nistor, MD,[1,2,] Suetonia C. Palmer, MBChB, PhD,[3,*] Jonathan C. Craig, MBChB, DCH, MM, PhD,[4] Valeria Saglimbene, MSc,[5] Mariacristina Vecchio, MSc,[6] Adrian Covic, MD, PhD,[1] and Giovanni F.M. Strippoli, MD, PhD, MM, MPH[4,5,6]*

AJKD AMERICAN JOURNAL OF KIDNEY DISEASES

VOL 63, NO 6
JUNE 2014

	No. of events/ No. of participants		Relative risk (95% CI) Random effects model	Weight
	Convection	Diffusion		
All-cause mortality				
Beerenhout et al, 2005	1/20	1/20	1.00 (0.07 to 14.9)	0.47%
Schiffl, 2007	1/38	2/38	0.50 (0.05 to 5.28)	0.62%
Wizemann et al, 2000	1/23	2/21	0.46 (0.04 to 4.68)	0.63%
PROFIL study, 2011	2/27	3/21	0.52 (0.10 to 2.83)	1.17%
Locatelli et al, 1996	7/50	6/155	3.62 (1.27 to 10.26)	2.94%
Locatelli et al, 2010	7/76	8/70	0.81 (0.31 to 2.11)	3.41%
Santoro et al, 2008	7/32	12/32	0.58 (0.26 to 1.29)	4.80%
TURKISH OL-HDF study, 2013	52/391	65/391	0.80 (0.57 to 1.12)	16.62%
Tessitore et al, 2012	65/177	69/194	1.03 (0.79 to 1.35)	20.56%
ESHOL study, 2013	85/456	122/450	0.69 (0.54 to 0.88)	22.34%
CONTRAST study, 2012	131/358	138/356	0.94 (0.78 to 1.14)	26.43%
Total	**359/1648**	**428/1748**	**0.87 (0.70 to 1.07)**	**100.0%**

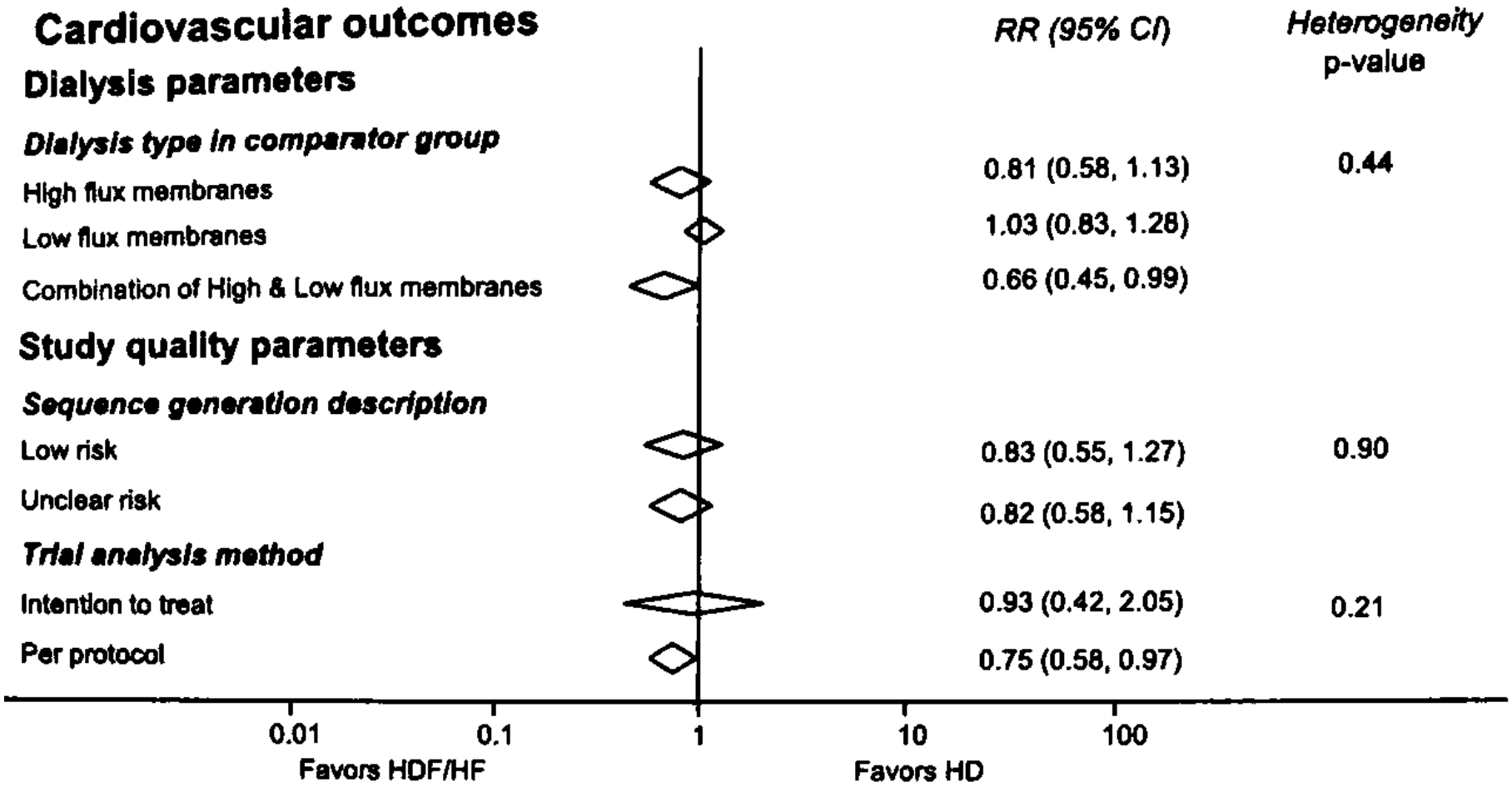
Heterogeneity: $\chi^2_{10} = 15.1$; $P = 0.1$; $I^2 = 34\%$



Effect of Hemodiafiltration or Hemofiltration Compared With Hemodialysis on Mortality and Cardiovascular Disease in Chronic Kidney Failure: A Systematic Review and Meta-analysis of Randomized Trials

Amanda Y. Wang, MBBS, FRACP,[1] Toshiharu Ninomiya, MD, PhD,[1]
Anas Al-Kahwa, BSc(Med),[1,2] Vlado Perkovic, MBBS, PhD, FRACP,[1]
Martin P. Gallagher, MBBS, PhD, FRACP,[1,2]
Carmel Hawley, MBBS (Hons), M Med Sci, FRACP,[3] and
Meg J. Jardine, MBBS, PhD, FRACP[1,2]

AJKD
AMERICAN JOURNAL OF KIDNEY DISEASES
VOL 63, NO 6
JUNE 2014



Nephrol Dial Transplant (2014) 0: 1–8
doi: 10.1093/ndt/gfu347

ndt
Nephrology Dialysis Transplantation

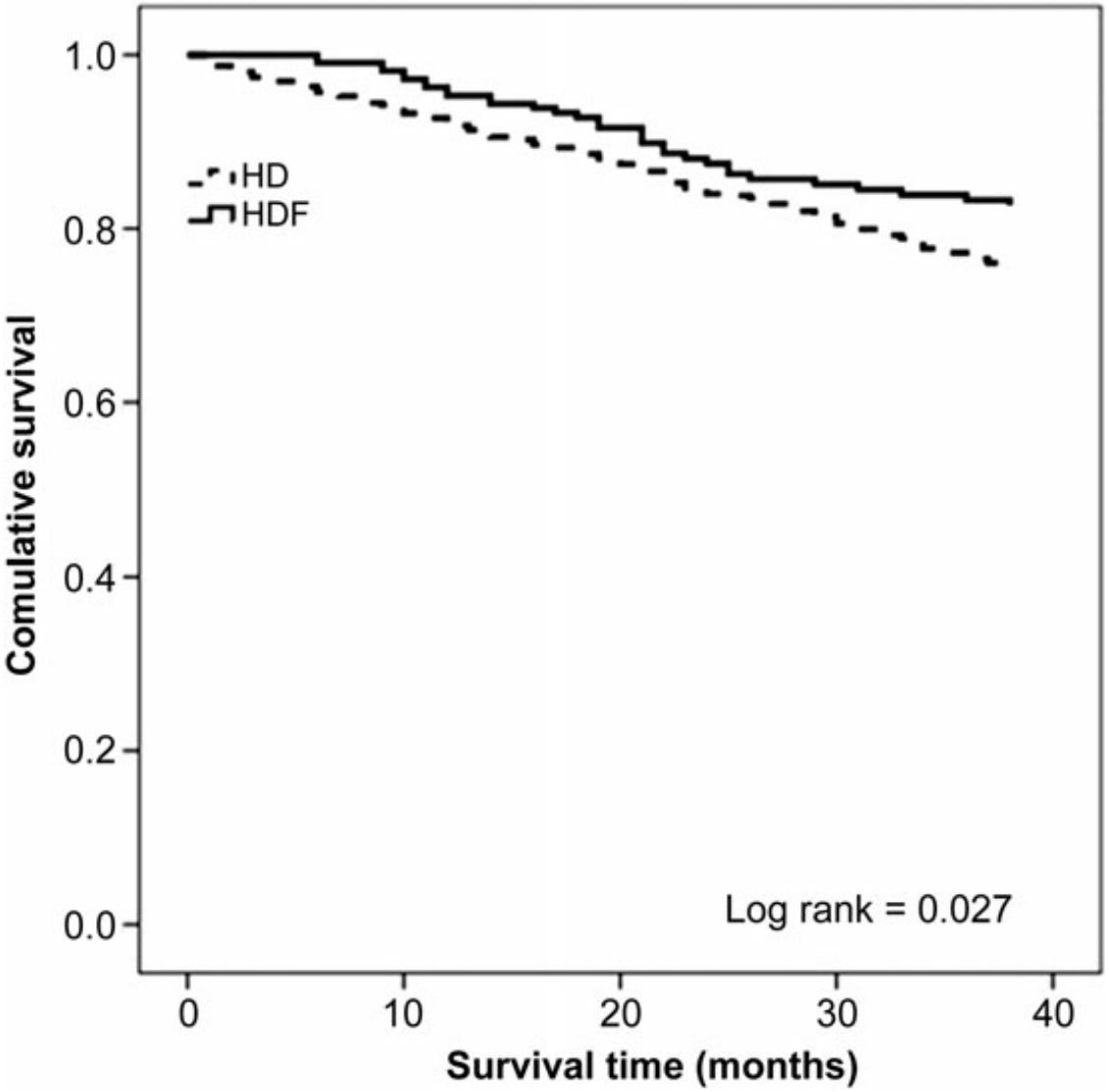
Original Article

New insights into the effect of haemodiafiltration on mortality: the Romanian experience

Dimitrie Siriopol[1], Bernard Canaud[2], Stefano Stuard[2], Gabriel Mircescu[3], Ionut Nistor[1] and Adrian Covic[1]

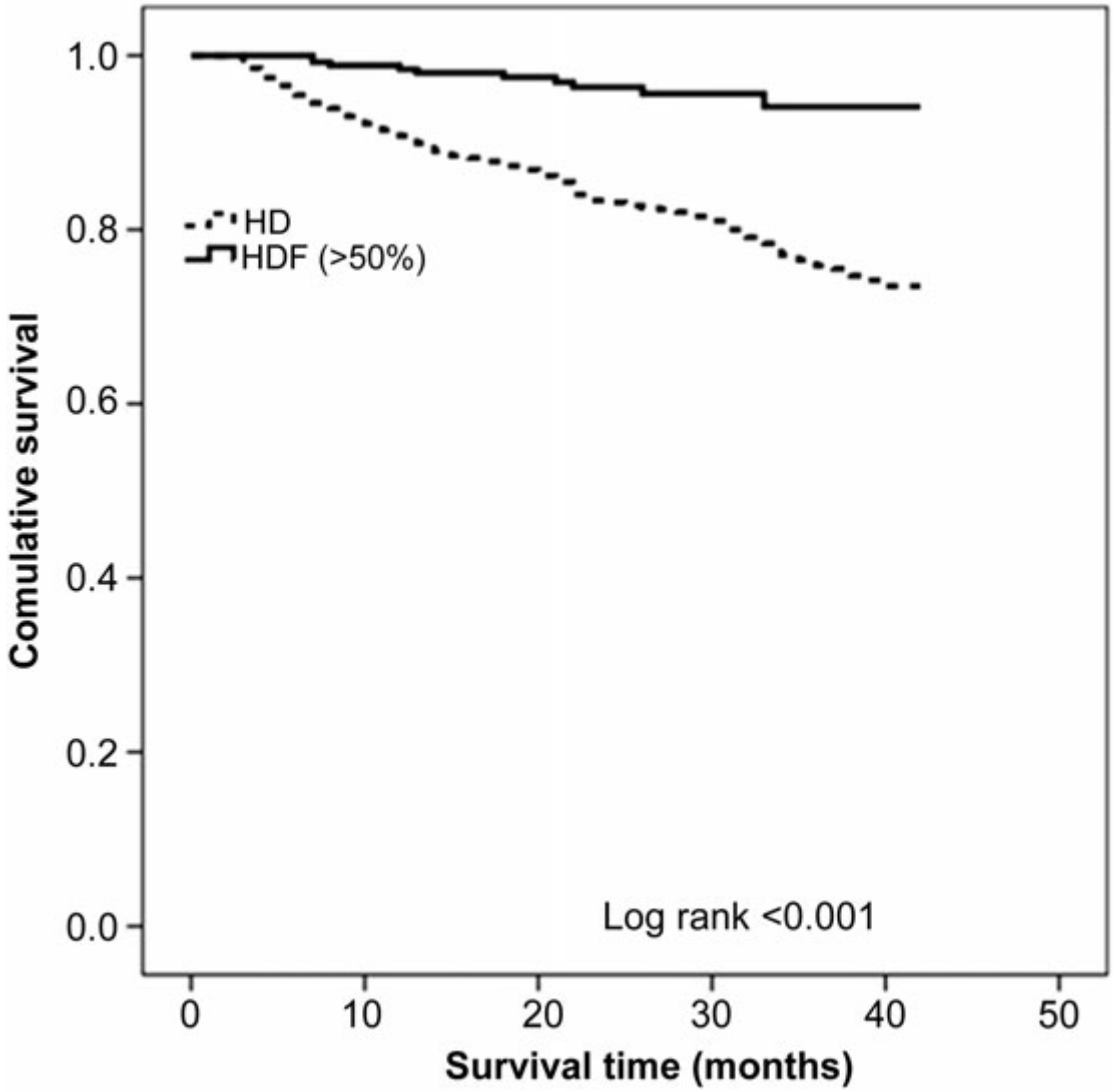
[1]Nephrology Department, Gr. T. Popa University of Medicine and Pharmacy, Iasi, Romania, [2]Fresenius Medical Care, Bad Homburg, Germany and [3]Nephrology Department, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

The effect of haemodiafiltration *on mortality*: the Romanian experience*: prevalent patients*



Siriopol et al Nephrol Dial Transpl 2015; 30: 294-301

The effect of haemodiafiltration on *mortality:* the Romanian experience: *incidence patients*



Siriopol et al Nephrol Dial Transpl 2015; 30: 294-301

The effect of haemodiafiltration *on mortality*: the Romanian experience: *prevalent patients*

Table 4. Univariate and multivariate Cox survival analysis for the prevalent patients

	HR[a]	95% CI	P
Unadjusted	0.67	0.46–0.96	0.03
Adjusted			
Model 1	0.64	0.44–0.92	0.02
Model 2	0.62	0.39–0.98	0.04
Model 3	0.58	0.36–0.93	0.02

Model 1: age, gender, Charlson index score, dialysis vintage; Model 2: CRP, albumin, systolic blood pressure; Model 3: variables in model 1 + variables in model 2.
[a]Hazard ratio for HDF group versus HD group.

Siriopol et al Nephrol Dial Transpl 2015; 30: 294-301

The effect of haemodiafiltration *on mortality*
The Romanian experience: *incidence patients*

- ***2447 patients started dialysis (2181 HD and 266 HDF) during the observation period.***

- ***Patients in the HDF group maintained a reduced risk for all-cause mortality (HR = 0.20, 95% CI 0.11–0.38 for the univariate and HR = 0.24, 95% CI 0.13–0.46 for the fully adjusted model).***

Siriopol et al Nephrol Dial Transpl 2015; 30: 294-301

Hemodiafiltration (5,526 pts) Versus Hemodialysis and Survival in Patients With ESRD: The REIN Registry

HR for

All-cause mortality	**HR : 0.84 (0.77-0.91)**
Cardiovascular mortality	**HR : 0.73 (0.61-0.88)**

In patients treated exclusively with HDF (2,254)

All-cause mortality	**HR : 0.77 (0.67-0.87)**
Cardiovascular mortality	**HR : 0.66 (0.50-0.86)**

Mercadal et al.AJKD 68, 2, 247–255

Hemodiafiltration Versus Hemodialysis and Survival in Patients With ESRD
The REIN Registry

At the facility level, increasing the percentage of patients using HDF from 0% to 100% was associated with

HRs for

All-cause mortality	**0.87 (0.77-0.99)**
Cardiovascular mortality	**0.72 (0.54-0.96)**

Mercadal et al.AJKD 68, 2, 247–255

Nephrol Dial Transplant (2017) 1–7
doi: 10.1093/ndt/gfx277

ndt
Nephrology Dialysis Transplantation

ORIGINAL ARTICLE

Mortality risk in patients on hemodiafiltration versus hemodialysis: a 'real-world' comparison from the DOPPS

Francesco Locatelli[1], Angelo Karaboyas[2], Ronald L. Pisoni[2], Bruce M. Robinson[2,3], Joan Fort[4], Raymond Vanholder[5], Hugh C. Rayner[6], Werner Kleophas[7,8], Stefan H. Jacobson[9], Christian Combe[10], Friedrich K. Port[2] and Francesca Tentori[2,11]

[1]Department of Nephrology and Dialysis, Alessandro Manzoni Hospital, ASST Lecco, Lecco, Italy, [2]Arbor Research Collaborative for Health, Ann Arbor, MI, USA, [3]Department of Internal Medicine, University of Michigan, Ann Arbor, MI, USA, [4]Nephrology Department, University Hospital Vall d'Hebron, Barcelona, Spain, [5]Department of Nephrology, University Hospital, Ghent, Belgium, [6]Heart of England NHS Foundation Trust, Birmingham, UK, [7]MVZ DaVita Rhein-Ruhr, Dusseldorf, Germany, [8]Department of Nephrology, Heinrich-Heine-University, Dusseldorf, Germany, [9]Division of Nephrology, Karolinska Institute, Danderyd Hospital, Stockholm, Sweden, [10]Centre Hospitalier Universitaire de Bordeaux, Bordeaux, France and [11]Vanderbilt University, Nashville, TN, USA

Correspondence and offprint requests to: Francesco Locatelli; E-mail: f.locatelli@asst-lecco.it

Background

- ***Online HDF is one of the most efficient dialysis techniques, though evidence supporting a positive impact of HDF on clinical outcomes is inconclusive***
- ***1 of 3 trials showed a survival benefit for HDF vs. HD***
  - ***Subgroup analyses showed patients randomized to HDF who received the highest convection volumes had lower risk of adverse events***
- ***Use of high-volume HDF subsequently increased in many European countries, while online production of replacement fluid is not available in North America.***
  - ***We studied the association of HDF with mortality in the 'real-world' clinical setting, studying a contemporary DOPPS cohort in countries where HDF is available***

F. Locatelli et al.,Nephrol. Dial. Transplant. 2017

DOPPS

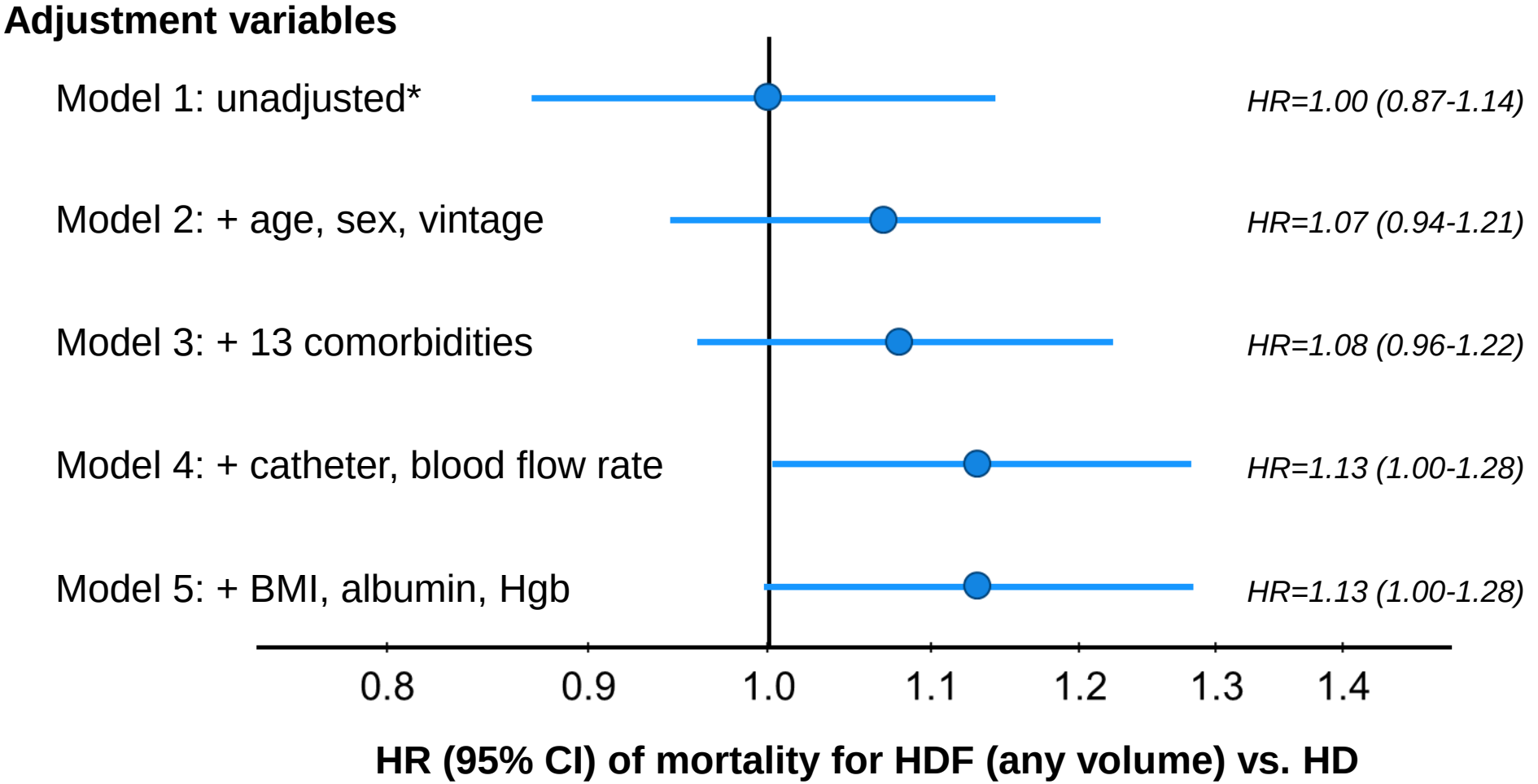
Methods

- ***N=8567 patients from 7 European countries in DOPPS phases 4-5 (2009-2015) with vintage >90 days***
  - ***N=2012 (23%) patients were on HDF, about half had replacement fluid volume >20L***
- ***Adjusted Cox regression was used to estimate the association between HDF (both overall and high-volume) and mortality (vs. HD)***
  - ***All-cause, CV, and infection-related mortality***
  - ***Also examined whether facility practice of treating more patients with HDF was associated with survival***

DOPPS

F. Locatelli et al., Nephrol. Dial. Transplant. 2017

Association between HDF (vs. HD) and all-cause mortality, by level of adjustment



*Unadjusted Cox model stratified by DOPPS phase and country and accounted for facility clustering

F. Locatelli et al.,Nephrol. Dial. Transplant. 2017

DOPPS

Treatment tolerance and patient-reported outcomes favor online hemodiafiltration compared to high-flux hemodialysis in the elderly

Marion Morena[1,2,3], Audrey Jaussent[4], Lotfi Chalabi[5], Hélène Leray-Moragues[6], Leila Chenine[6], Alain Debure[7], Damien Thibaudin[8], Lynda Azzouz[9], Laure Patrier[10], Francois Maurice[11], Philippe Nicoud[12], Claude Durand[13], Bruno Seigneuric[14], Anne-Marie Dupuy[1], Marie-Christine Picot[4], Jean-Paul Cristol[1,2,3] and Bernard Canaud[2,15]; for the FRENCHIE Study Investigators[16]

[1]Laboratoire de Biochimie, CHU de Montpellier, Montpellier, France; [2]Institut de Recherche et de Formation en Dialyse, Montpellier, France; [3]PhyMedExp, INSERM U1046, CNRS UMR9214, Université de Montpellier, Montpellier, France; [4]Département de l'Information Médicale, CHU de Montpellier, Montpellier, France; [5]Association pour l'Installation à Domicile des Epurations Rénales (AIDER), Montpellier, France; [6]Service de Néphrologie, CHU de Montpellier, Montpellier, France; [7]ATS, Saint-Denis, France; [8]Service de Néphrologie, CHU de Saint Etienne, Saint-Etienne, France; [9]Association Régionale pour le Traitement de l'Insuffisance Rénale Chronique, Saint-Priest-en-Jarez, France; [10]AIDER, Nîmes, France; [11]Centre Hémodialyse du Lez, Castelnau le Lez, France; [12]Centre de Néphrologie du Mont Blanc, Sallanches, France; [13]Polyclinique Saint Martin, Pessac, France; [14]Service de Néphrologie, CHU de Toulouse, Toulouse, France; and [15]Université de Montpellier, Néphrologie, Montpellier, France

Morena M et al KI 91-6 1495-1509, 2017

Kaplan-Meier Curve for 24-months Survival
Intention to Treat

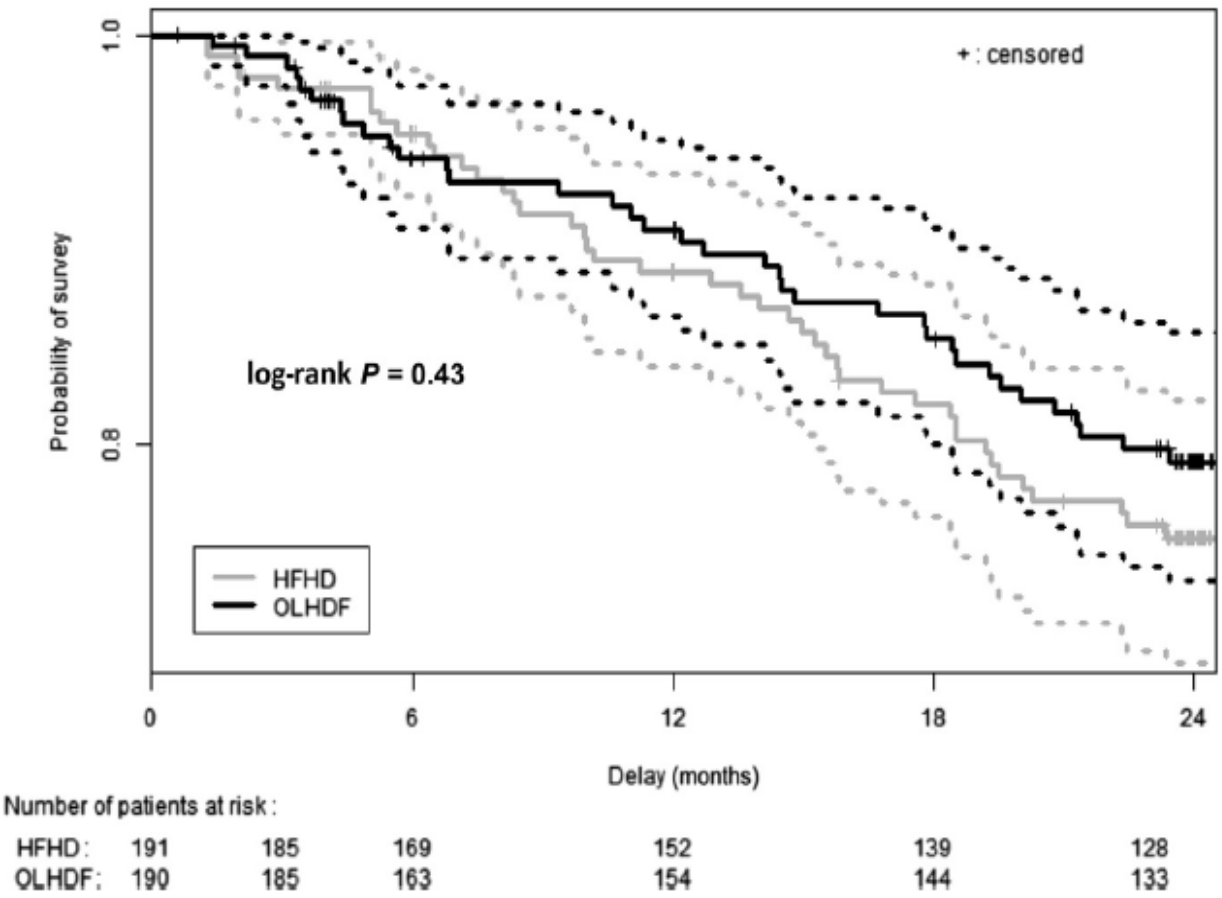


Figure 4| Kaplan-Meier curve for 24-month survival in the intention-to-treat population. HFHD, high-flux hemodialysis; OLHDF, online hemodiafiltration.

Morena M et al KI 91-6 1495-1509, 2017

Are the highest convection volumes in HDF mandatory for improving patient survival?

Risk of all-cause mortality by achieved convection volume

82 missing and 206 deaths instead of 269

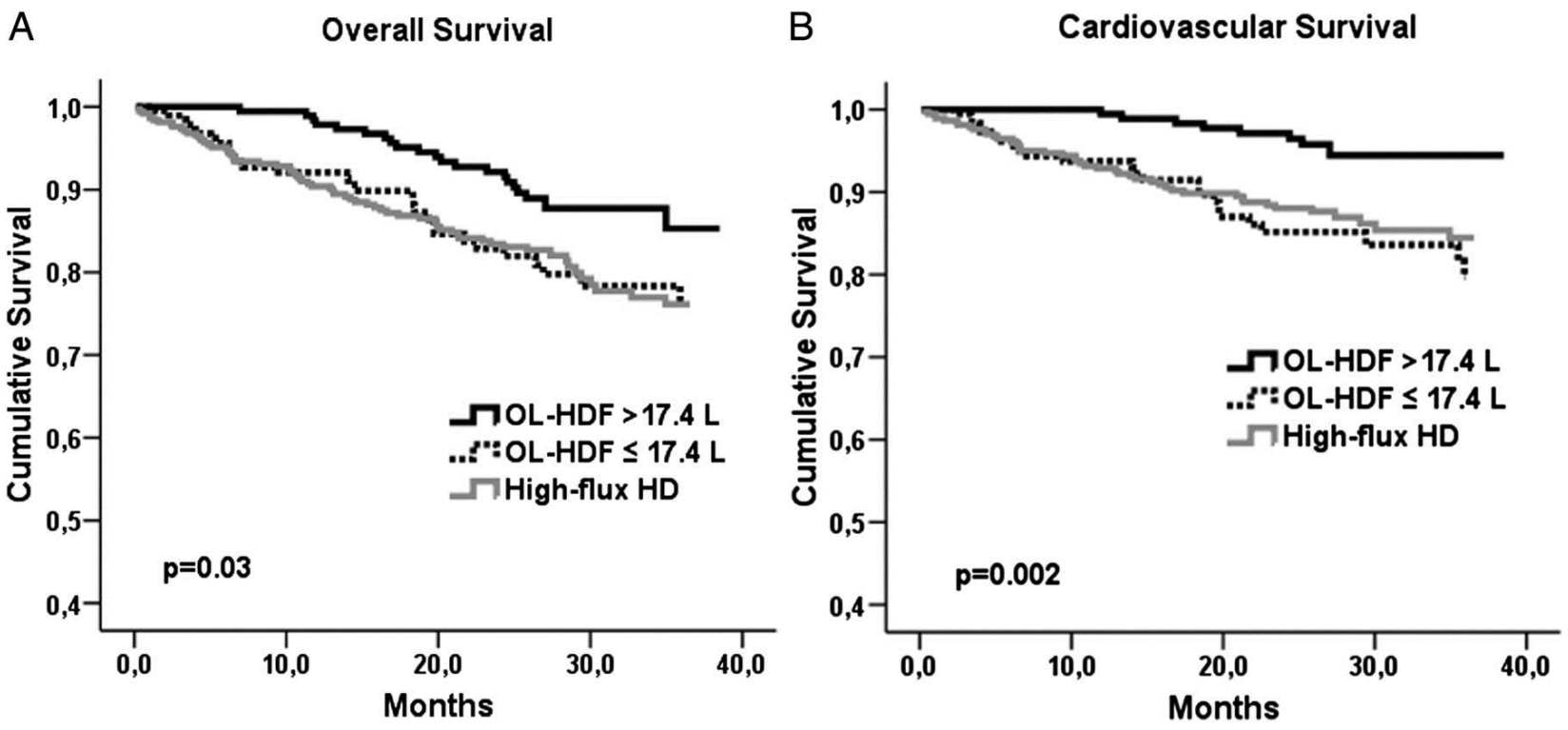
	HD	Online Hemodiafiltration Convection Volume Tertiles			*P* for Trend
		<18.17 L	18.18–21.95 L	>21.95 L	
Total mortality					
crude	1.0	0.95 (0.66–1.38)	0.83 (0.57–1.22)	0.62 (0.41–0.93)	0.010
adjusted [a]	1.0	0.79 (0.53–1.14)	0.77 (0.51–1.14)	0.65 (0.42–0.99)	0.012
adjusted [b]	1.0	0.80 (0.52–1.24)	0.84 (0.54–1.29)	0.61 (0.38–0.98)	0.015

[a] Adjusted for age, sex, previous vascular disease, diabetes, previous transplantation, spKt/V, baseline eGFR, baseline albumin, baseline creatinine, baseline hematocrit, and use of α- and β-blockers, calcium antagonists, and angiotensin converting inhibitors at baseline

[b] Adjusted for the above-mentioned determinates as well as for center differences

Grooteman MPC et al J Am Soc Nephrol 23: 1087–1096, 2012

Overall (A) and cardiovascular survival (B) among the treatment groups



Ok E et al. Nephrol. Dial. Transplant. 2013;28:192-202

NDT Nephrology Dialysis Transplantation

ndt
Nephrology Dialysis Transplantation

Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials

Sanne A.E. Peters[1,2], Michiel L. Bots[2], Bernard Canaud[3,4], Andrew Davenport[5], Muriel P.C. Grooteman[6], Fatih Kircelli[7], Francesco Locatelli[8], Francisco Maduell[9], Marion Morena[4,10,11], Menso J. Nubé[6], Ercan Ok[7], Ferran Torres[12,13], Mark Woodward[1,14,15] and Peter J. Blankestijn[16] on behalf of the HDF Pooling Project Investigators

Peters S.A.E…..Locatelli F. et al. Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials. Nephrol Dial Transplant (2015) 0: 1–7

HR and 95% CIs for *all-cause mortality and cause-specific mortality* by delivered BSA-standardized convection volume in litres per 1.73 m2 per treatment with standard HD as a reference

Table 3. HR and 95% CIs for all-cause mortality and cause-specific mortality by delivered BSA-standardized convection volume in litres per 1.73 m^2 per treatment with standard HD as a reference

Cause	Online HDF: BSA-adjusted convection volume (L/session)		
	<19	19–23	>23
All-causes			
Unadjusted	0.91 (0.74; 1.13)	0.88 (0.72; 1.09)	0.73 (0.59; 0.91)
Adjusted	0.83 (0.66; 1.03)	0.93 (0.75; 1.16)	0.78 (0.62; 0.98)
Cardiovascular			
Unadjusted	1.00 (0.71; 1.40)	0.71 (0.50; 1.01)	0.69 (0.48; 0.98)
Adjusted	0.92 (0.65; 1.30)	0.71 (0.49; 1.03)	0.69 (0.47; 1.00)
Infections			
Unadjusted	1.50 (0.93; 2.41)	0.96 (0.56; 1.65)	0.56 (0.30; 1.08)
Adjusted	1.50 (0.92; 2.46)	0.97 (0.54; 1.74)	0.62 (0.32; 1.19)
Sudden death			
Unadjusted	1.24 (0.80; 1.91)	0.91 (0.57; 1.47)	0.60 (0.35; 1.03)
Adjusted	1.09 (0.69; 1.74)	1.04 (0.63; 1.70)	0.69 (0.39; 1.20)

Values are HRs and 95% CI.
Adjusted for age, sex, albumin, creatinine, history of cardiovascular diseases and history of diabetes.

Peters SAE…Locatelli F. et al. Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials. Nephrol Dial Transplant (2015) 0: 1–7

New insights into the effect of haemodiafiltration *on mortality*: the Romanian experience

- ***The baseline median convective volume was 22.2L/session,higher than that achieved in the CONTRAST Study, but lower than that from the ESHOL Study, and in our analysis it was not associated with mortality risk.***
- ***This is in contrast with the findings from the three RCT, where in all post hoc analyses an association between higher convection volumes and better survival***

Siriopol et al Nephrol Dial Transpl 2015; 30: 294-301

Risk of all-Cause Mortality in HDF by achieved Convection Volume

***A recent meta-analysis* using uni-variate meta-regression analysis *found no effect of achieved convection volume on all-cause mortality* .**

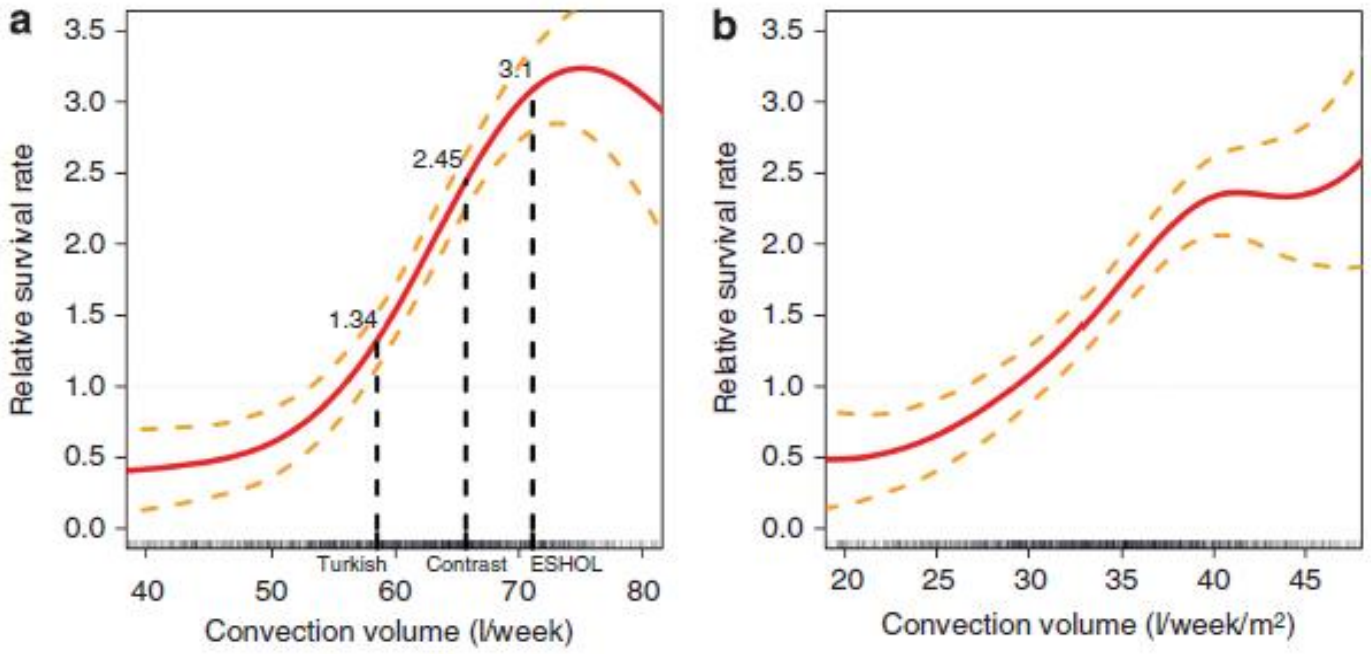
Nistor et al: Am J Kidney Dis 2014; 63: 654–667.

Risk of all-Cause Mortality in HDF by achieved Convection Volume

- ***Although this dose–effect relation is promising, it should be interpreted with caution, as these post hoc analyses must be viewed as cohort analyses***
- ***adequate multivariable adjustments should be made to reduce potential confounding.***

Siriopol et al Nephrol Dial Transpl 2015; 30: 294-301

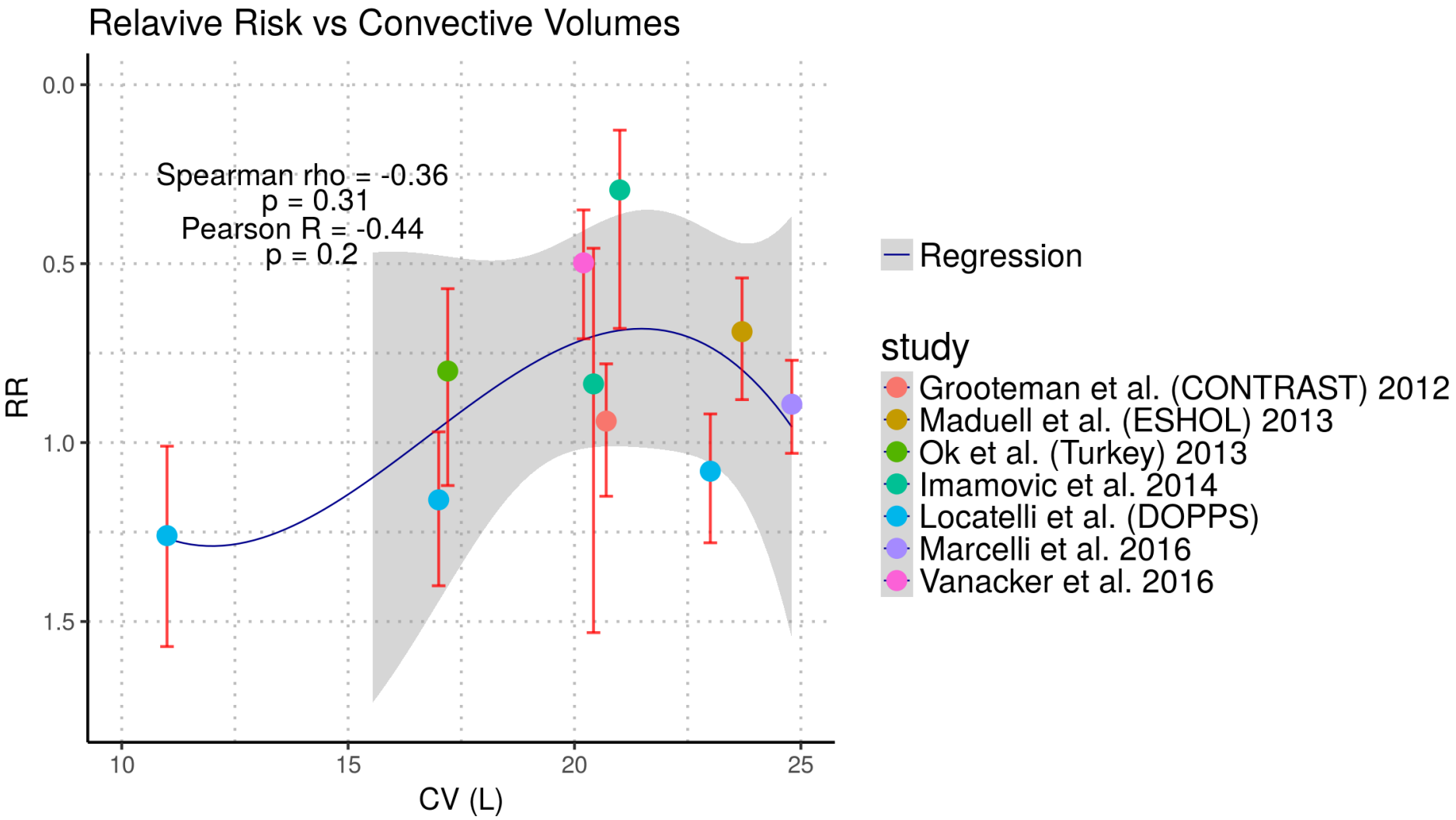
Optimal convection volume for improving patient outcomes in an international incident dialysis cohort treated with online hemodiafiltration



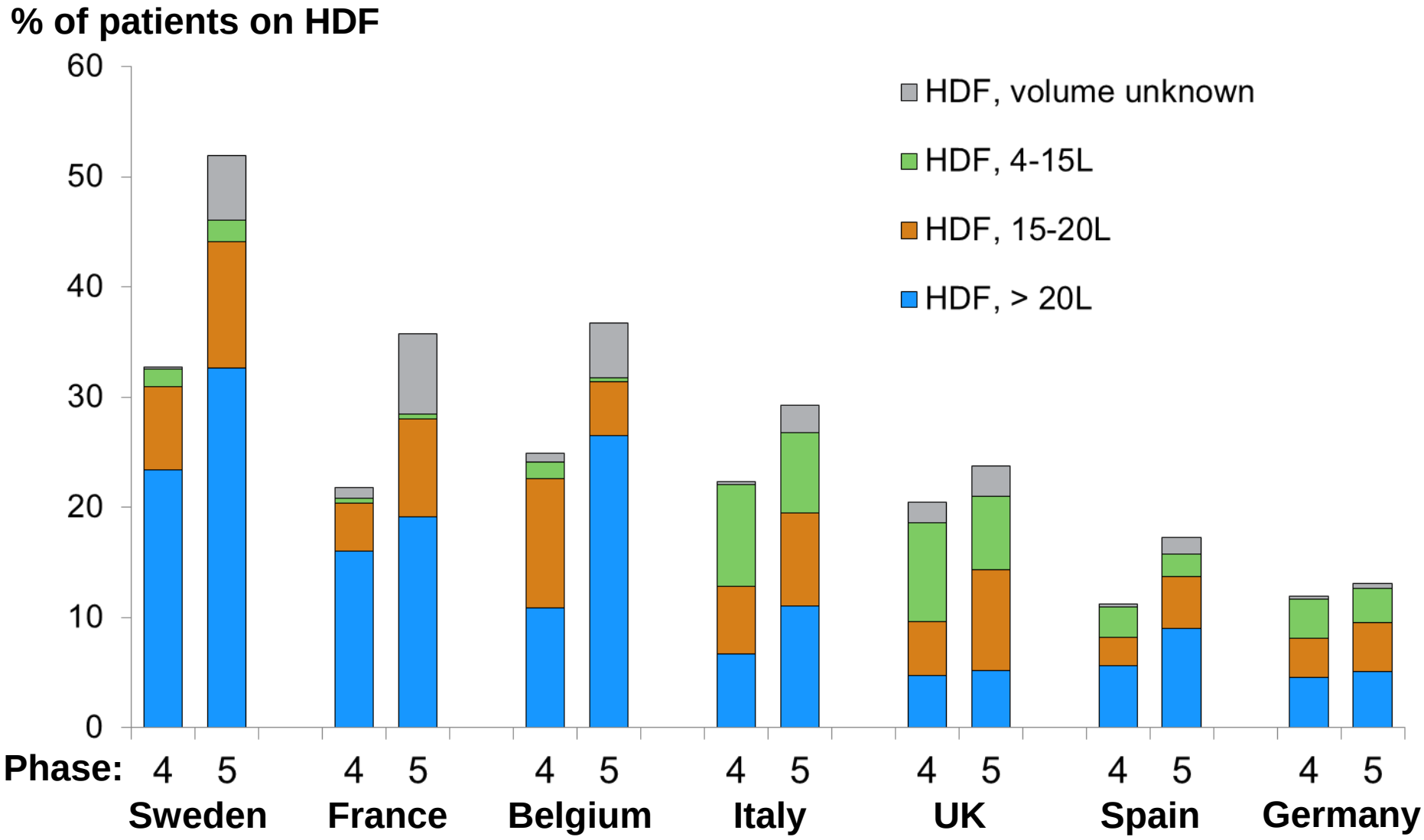
Canaud B.et al. Kidney International (2015) 88, 1108–1116; doi:10.1038/ki.2015.139

Does the survival advantage for haemodiafiltration depend upon the delivered convective volume?

F. Carfagna and F. locatelli ; submitted 2018



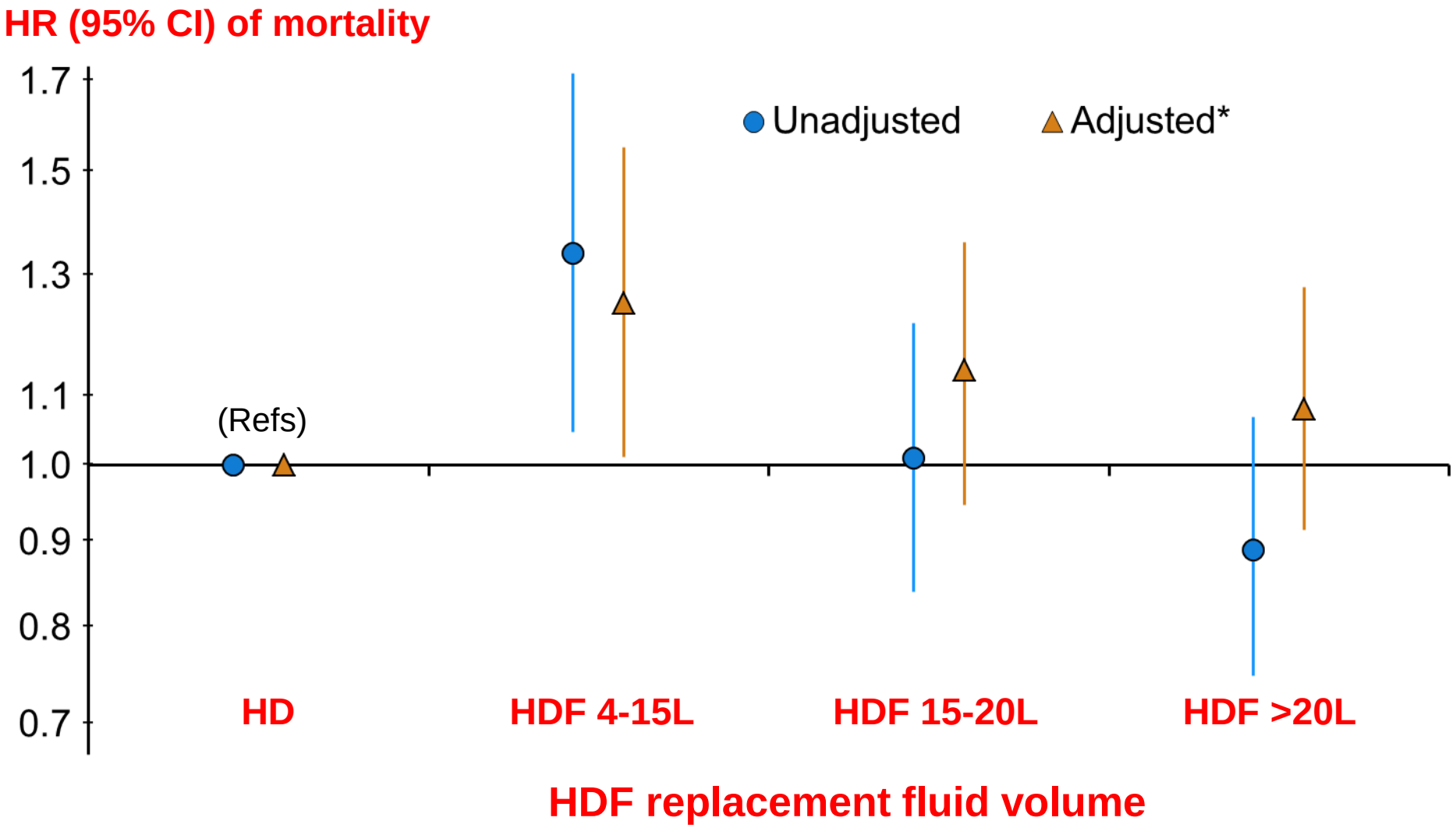
HDF use, by Replacement Fluid Volume



DOPPS phase 4: 2009-2011, DOPPS phase 5: 2012-2015

F. Locatelli et al., Nephrol. Dial. Transplant. 2017

HDF Replacement Fluid Volume and Mortality



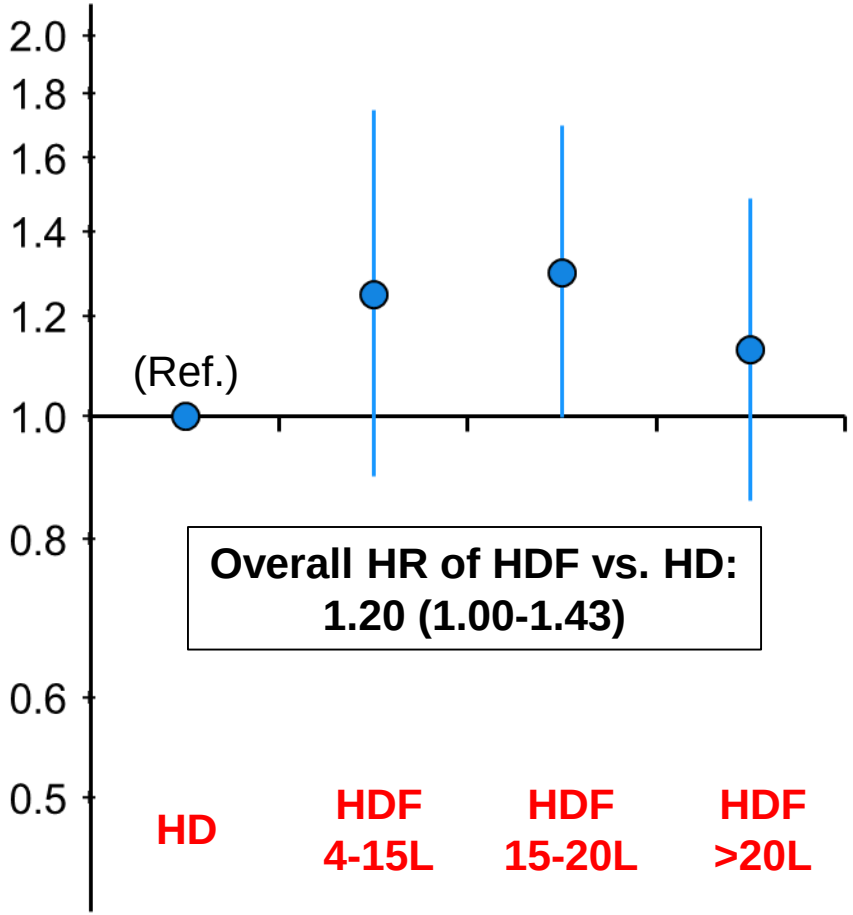
Both Cox models stratified by DOPPS phase and country and accounted for facility clustering
*Adjusted for age, sex, vintage, 13 comorbidities, vascular access, blood flow rate, BMI, albumin, hemoglobin

DOPPS

F. Locatelli et al.,Nephrol. Dial. Transplant. 2017

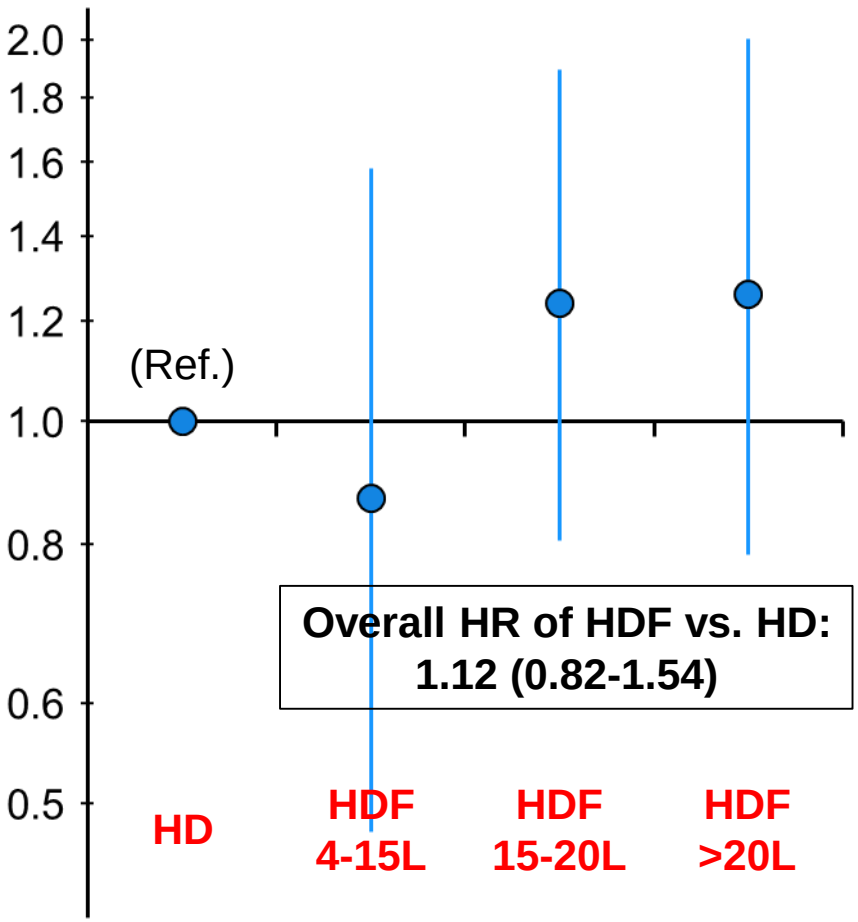
HDF and cause-specific mortality

HR (95% CI) of CV mortality



HDF replacement fluid volume

HR (95% CI) of Infection mortality



HDF replacement fluid volume

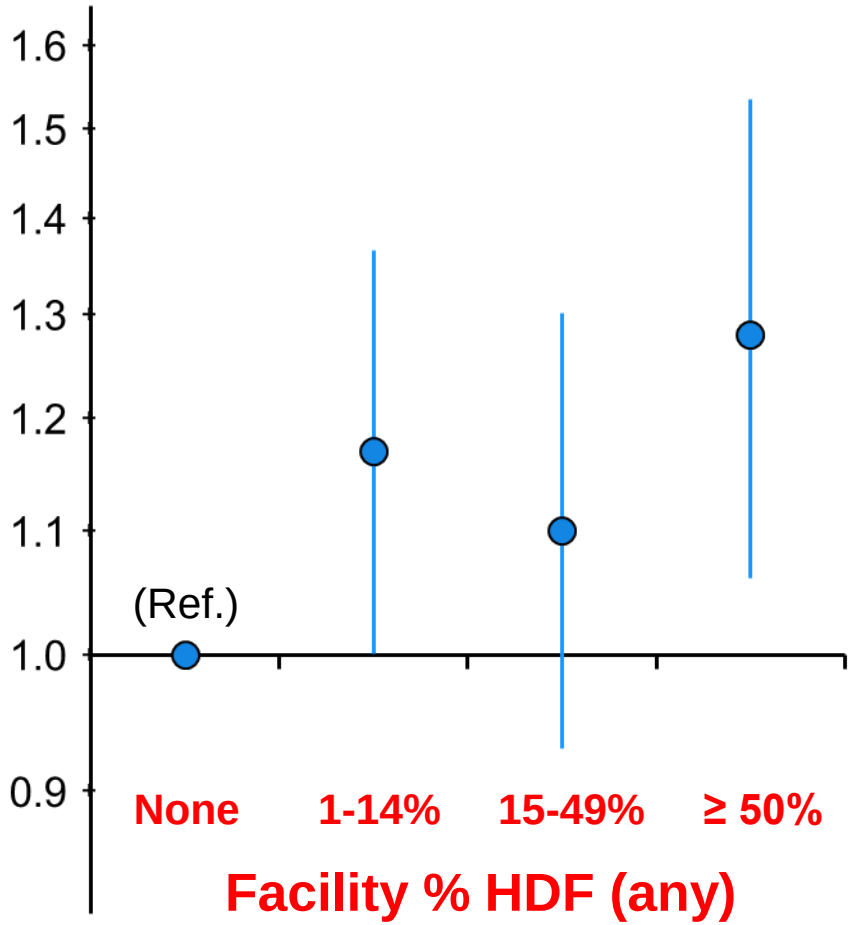
Cox models stratified by DOPPS phase and country, accounted for facility clustering, and adjusted for age, sex, vintage, 13 comorbidities, vascular access, blood flow rate, BMI, albumin, hemoglobin

DOPPS

F. Locatelli et al.,Nephrol. Dial. Transplant. 2017

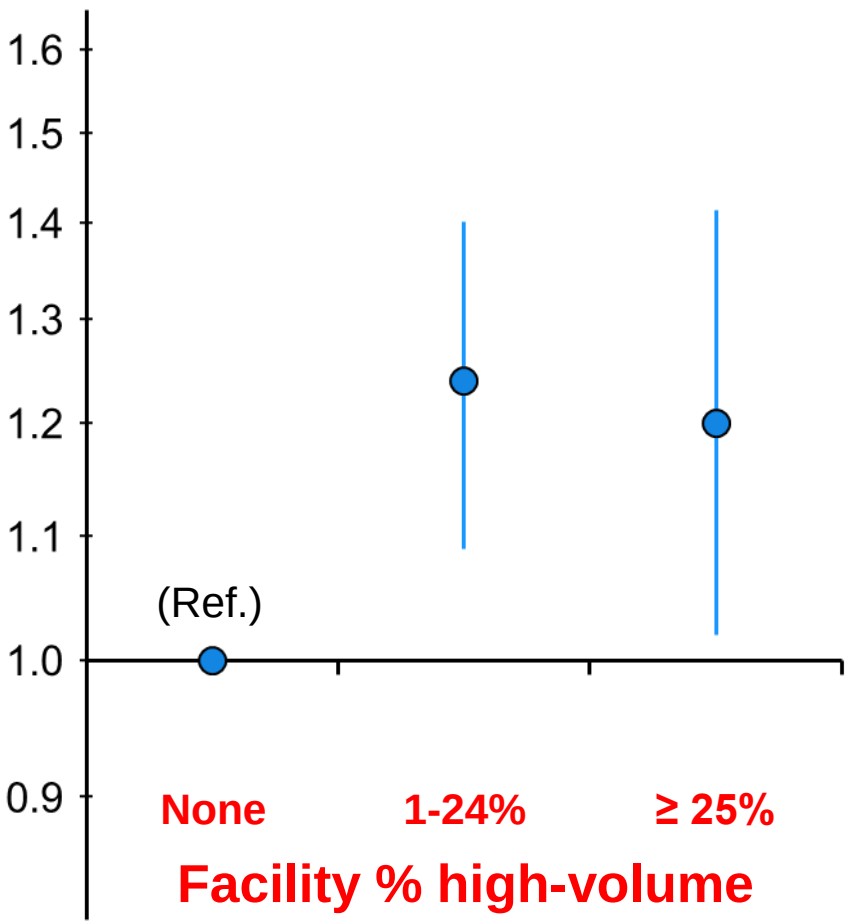
Facility % HDF and mortality

HR (95% CI) of mortality



Facility % HDF (any)

HR (95% CI) of mortality



Facility % high-volume HDF (>20 L)

Cox models stratified by DOPPS phase and country, accounted for facility clustering, and adjusted for age, sex, vintage, 13 comorbidities, vascular access, blood flow rate, BMI, albumin, hemoglobin, and 5 facility-level covariates: % catheter use, % Kt/V < 1.2, % albumin < 3.5 g/dL, % phosphorus > 5.5 mg/dL, mean hemoglobin

DOPPS

F. Locatelli et al.,Nephrol. Dial. Transplant. 2017

Conclusions

- ***This analysis of current HDF practices does not support the notion that HDF is a superior treatment in comparison to HD, even focusing on HDF with the highest convection volumes***

- ***Further trials specifically designed for testing the effect of different convection volumes of HDF vs. HD on clinical outcomes are necessary***

DOPPS

F. Locatelli et al., Nephrol. Dial. Transplant. 2017

Original Report: Patient-Oriented, Translational Research

American Journal of Nephrology

Am J Nephrol 2017;46:288–297
DOI: 10.1159/000481669

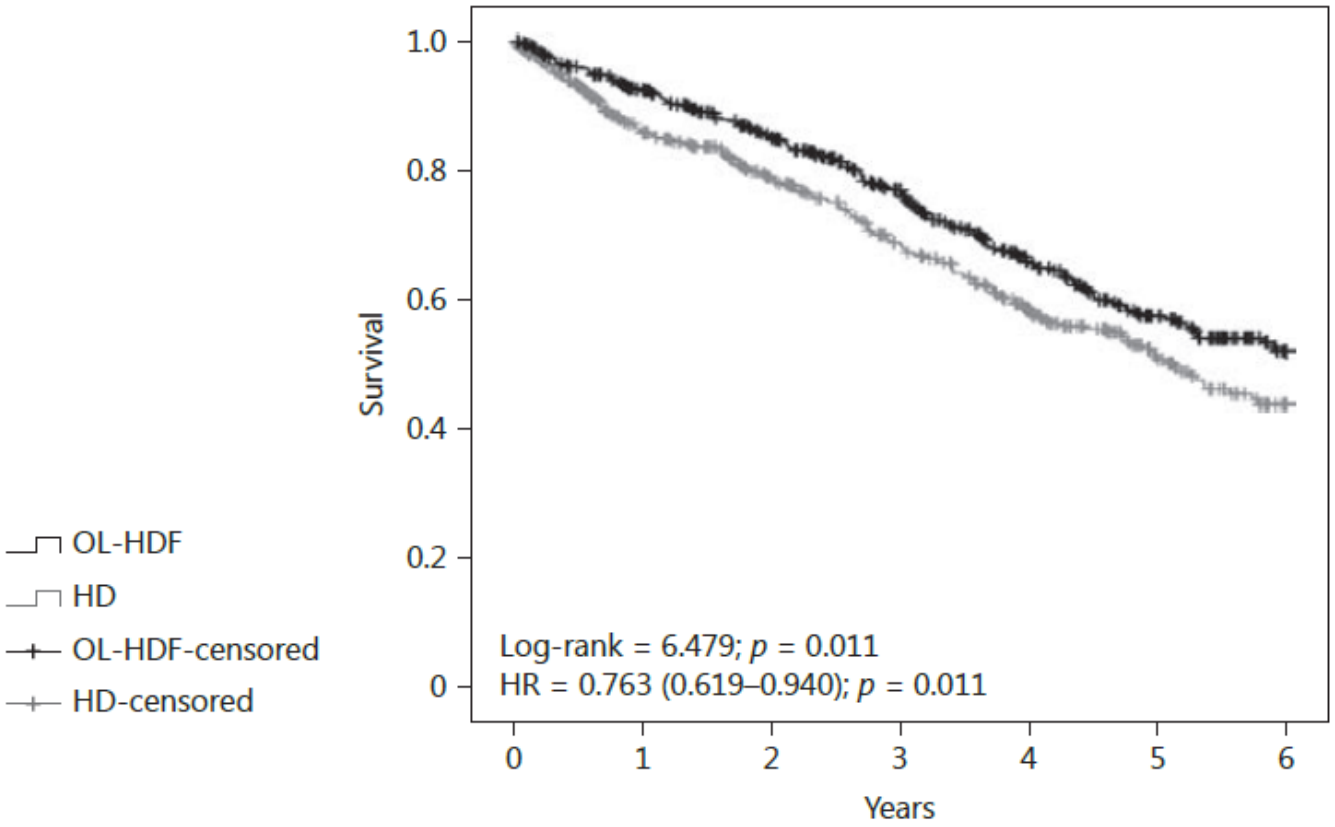
Received: August 1, 2017
Accepted: September 18, 2017
Published online: October 17, 2017

Hemodiafiltration Reduces All-Cause and Cardiovascular Mortality in Incident Hemodialysis Patients: A Propensity-Matched Cohort Study

Francisco Maduell[a] Javier Varas[b] Rosa Ramos[b] Alejandro Martin-Malo[c]
Rafael Pérez-Garcia[d] Isabel Berdud[b] Francesc Moreso[b] Bernard Canaud[e]
Stefano Stuard[e] Adelheid Gauly[e] Pedro Aljama[c] Jose Ignacio Merello[b]

[a]Department of Nephrology, Hospital Clínic, Barcelona, Spain; [b]Dirección Médica, Fresenius Medical Care, Madrid, Spain; [c]Department of Nephrology, Hospital Universitario Reina Sofía, Córdoba, Spain; [d]Servicio de Nefrología, Hospital Universitario Infanta Leonor, Madrid, Spain; [e]Fresenius Medical Care, Bad Homburg, Germany

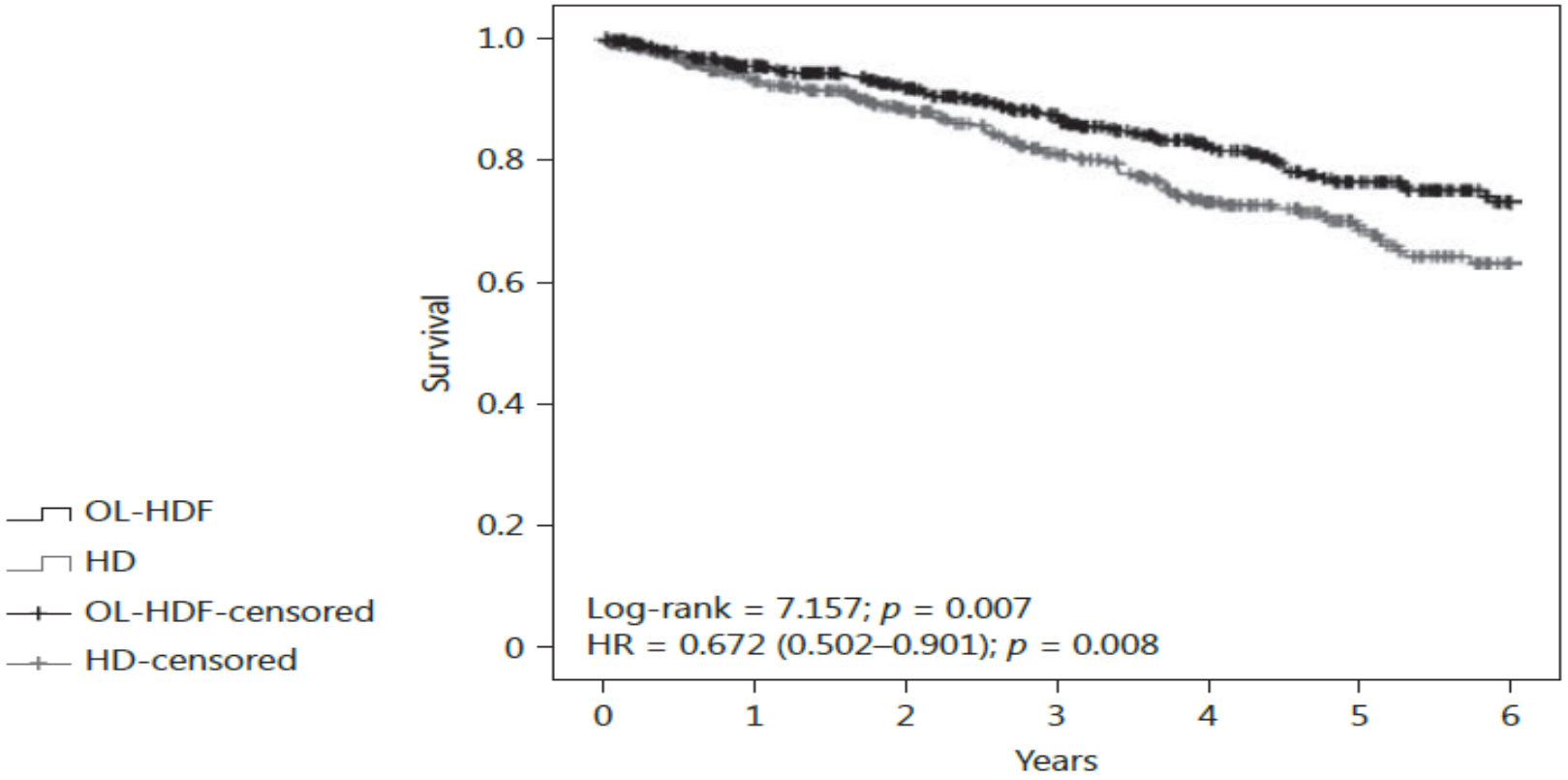
Kaplan-Meier analyses comparing all-cause mortality between HDF and high-flux HD,PSM cohort



		0.0	1.0	2.0	3.0	4.0	5.0	6.0
HD	Event	506	65	94	129	159	175	185
	At risk		362	288	221	154	86	45
OL-HDF	Event	506	37	70	102	137	158	168
	At risk		428	355	267	184	125	68

Maduell F. et al. Am J Nephrol 2017;46:288–297

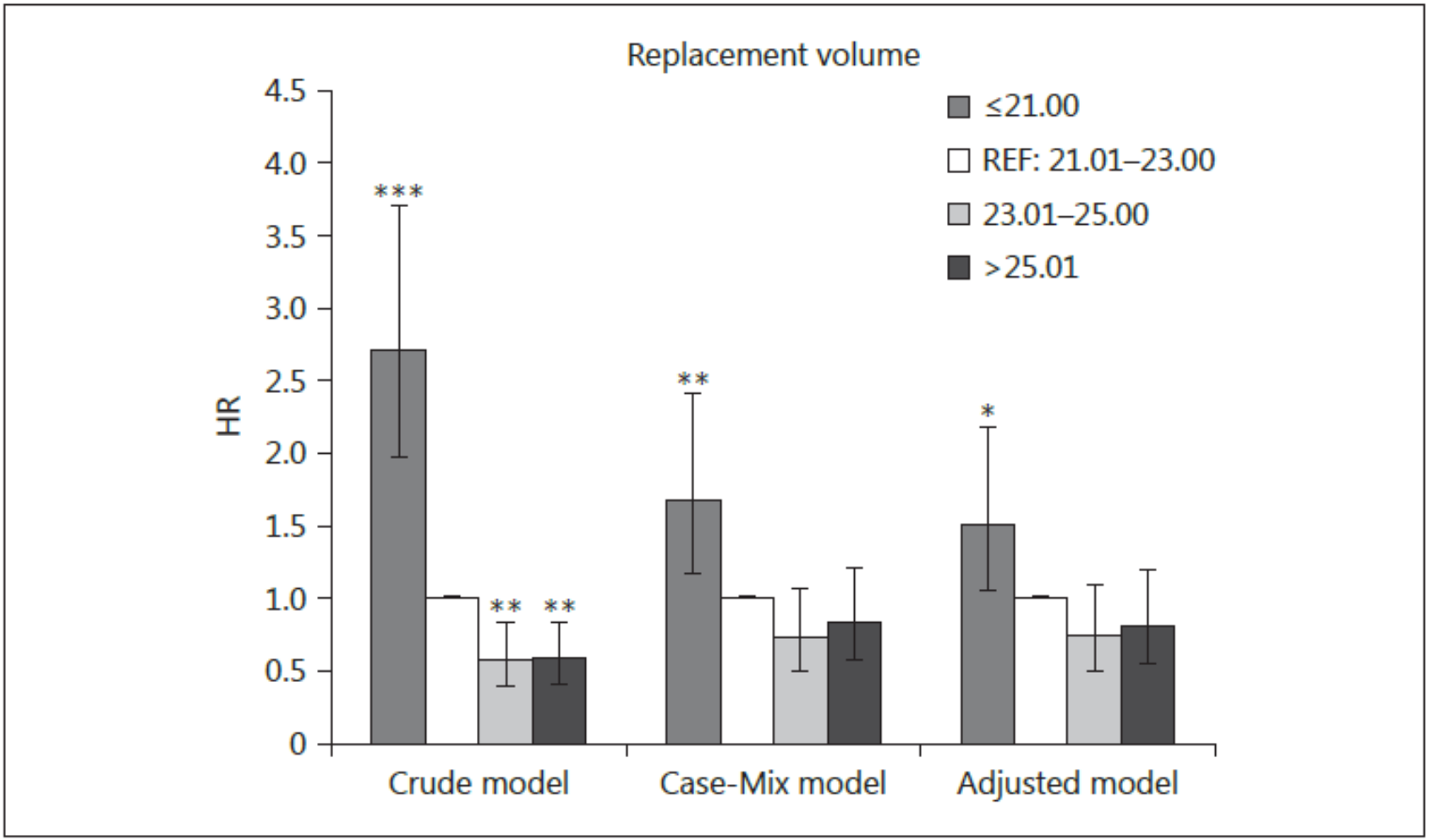
Kaplan-Meier analyses comparing CV mortality between HDF and high-flux HD PSM cohort



		0.0	1.0	2.0	3.0	4.0	5.0	6.0
HD	Event	506	30	47	69	88	95	101
	At risk		362	288	221	154	86	45
OL-HDF	Event	506	21	36	52	66	77	81
	At risk		428	355	268	184	125	68

Maduell F. et al. Am J Nephrol 2017;46:288–297

Association between all Cause Mortality and Convective Volumes



Maduell F. et al. Am J Nephrol 2017;46:288–297

Nephrol Dial Transplant (2018) 1–9
doi: 10.1093/ndt/gfy035

ndt
Nephrology Dialysis Transplantation

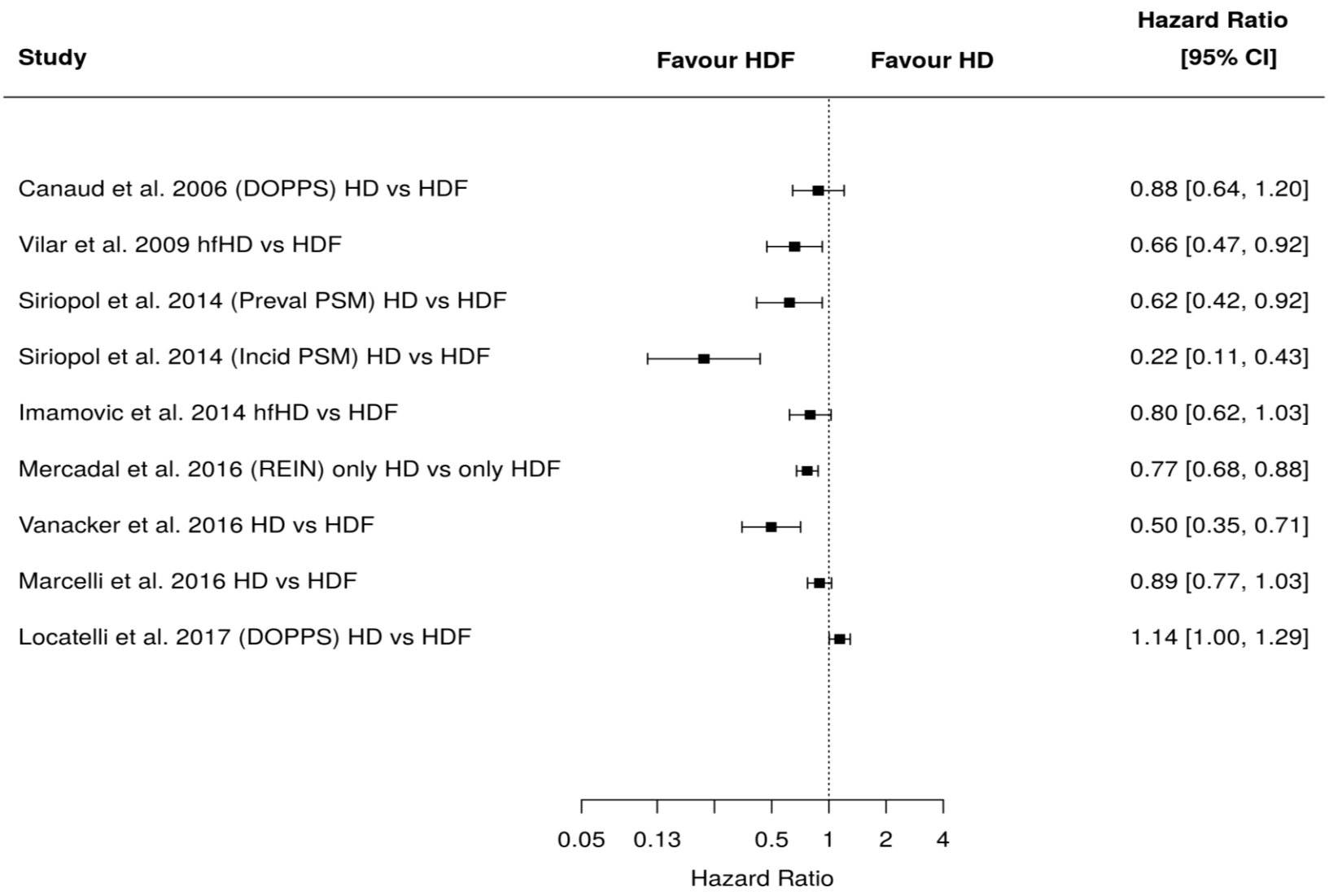
Haemodialysis or haemodiafiltration: that is the question

Francesco Locatelli, Fabio Carfagna, Lucia Del Vecchio and Vincenzo La Milia

Department of Nephrology and Dialysis, Alessandro Manzoni Hospital ASST Lecco, Lecco, Italy

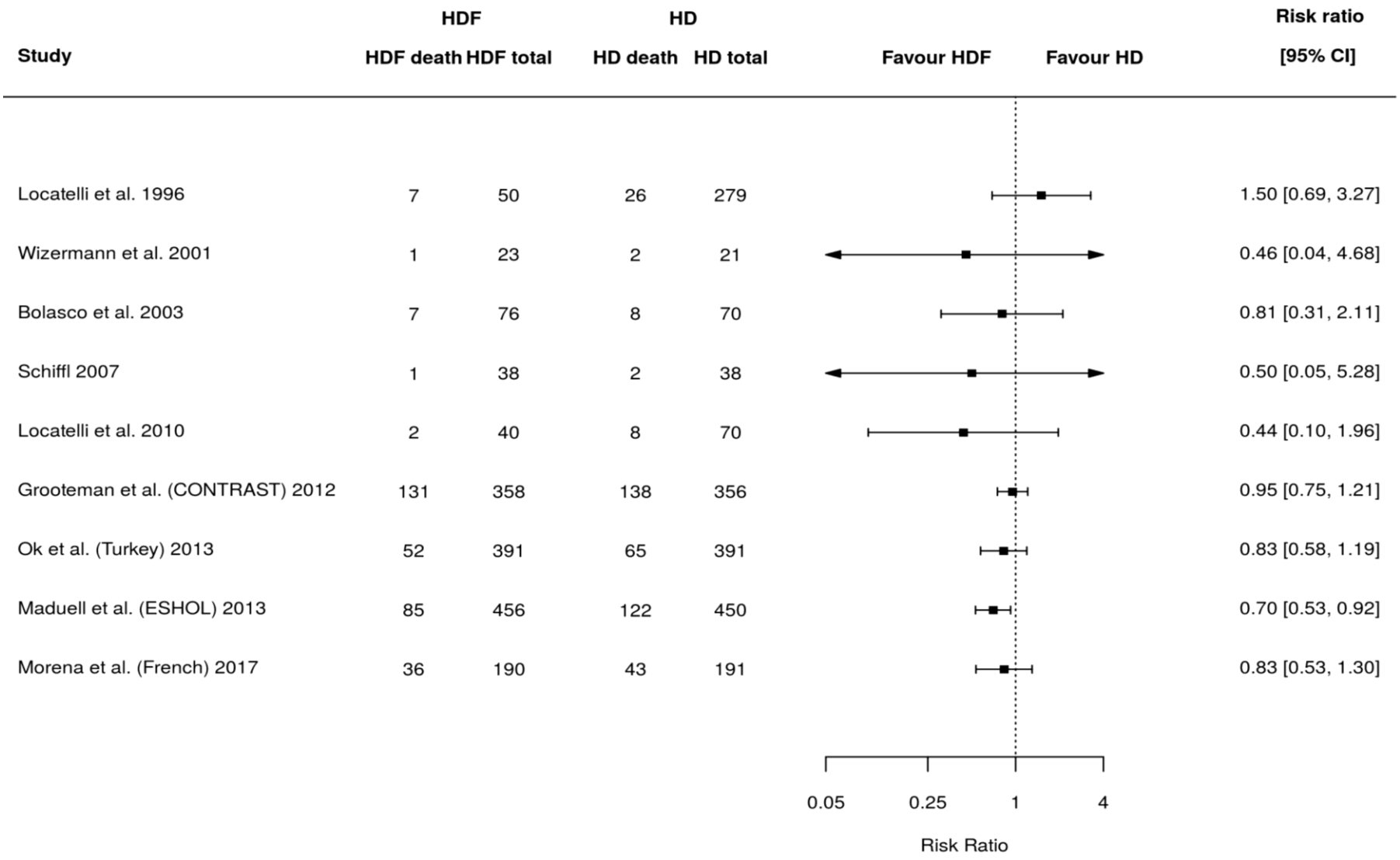
Correspondence and offprint requests to: Francesco Locatelli; E-mail: f.locatelli@asst-lecco.it

Observationals Study on HDF



F. Locatelli ,F. Carfagna,L. Del Vecchio, V. La Milia: Nephrol. Dial. Transplant. 2018

Randomised Studies on HDF



F. Locatelli ,F. Carfagna, L.Del Vecchio, V. La Milia Nephrol. Dial. Transplant. 2018

HDF vs HD: all Cause and cardiovascular mortality in metanalysis

Study	Cardiovascular mortality	All-cause mortality
Susantitaphong *et al.* [38]	Reduced in HDF	No difference
Wang *et al.* [36]	No difference	No difference
Mostovaya *et al.* [39]	Reduced in HDF	Reduced in HDF
Nistor *et al.* [37]	Reduced in HDF	No difference
Peters *et al.* [76]	Reduced in HDF	Reduced in HDF

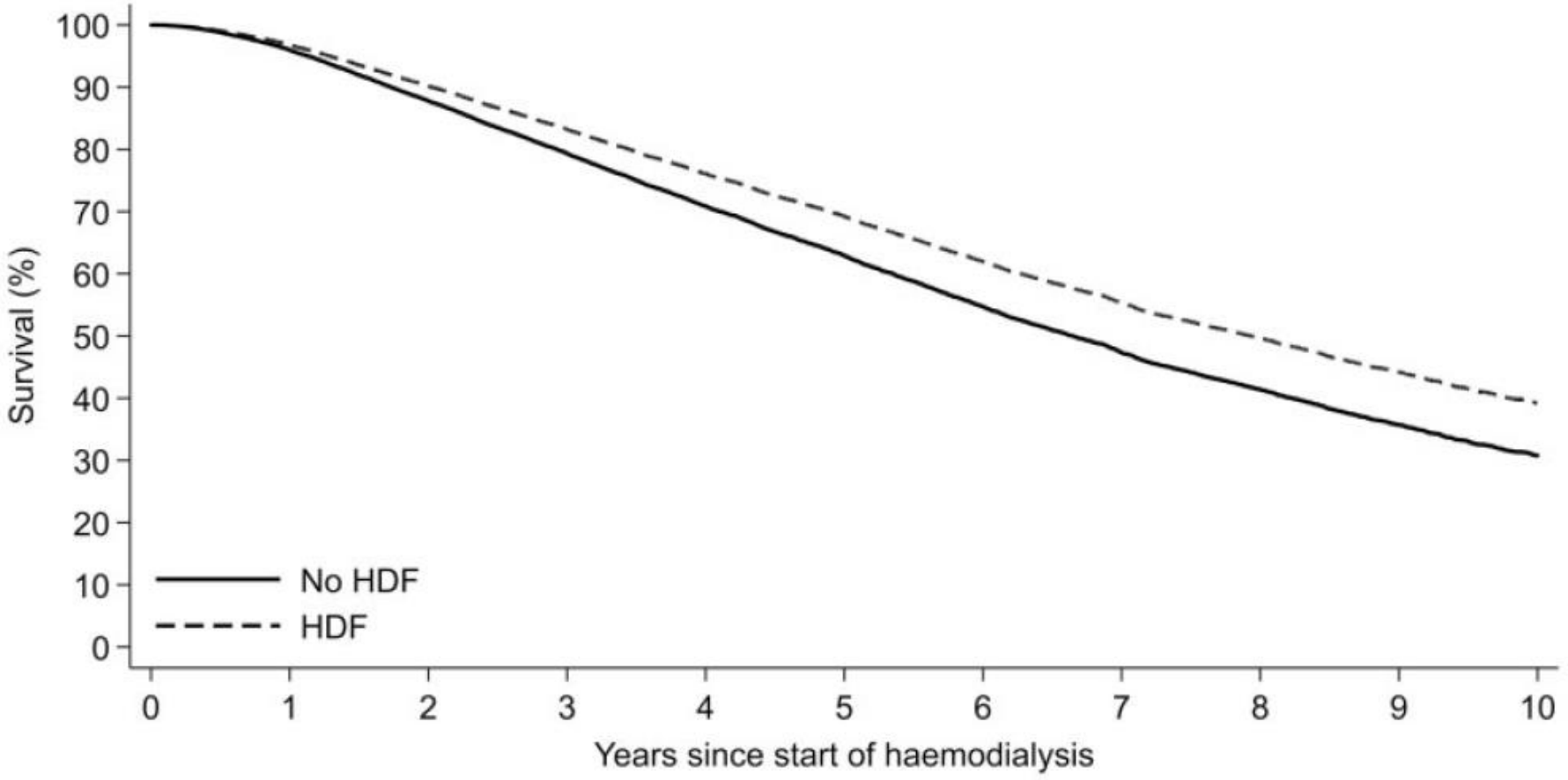
F. Locatelli ,F. Carfagna, L. Del Vecchio, V. La Milia Nephrol. Dial. Transplant. 2018

HDF vs HD: Main Clinical Parameters in Randomized Trials

Study	Groups	Phosphate	Anaemia	Cardiovascular mortality	All-cause mortality
Locatelli *et al.* [20]	HD versus HDF	–	–	–	No difference
Wizemann *et al.* [65]	HD versus HDF	No difference	No difference	–	No difference
Bolasco *et al.* [66]	HD versus HDF/HF	–	–	–	No difference
Schiffl [67]	hf-HD versus HDF	Decreased pre-treatment levels in HDF	No difference	–	No difference
Locatelli *et al.* [34]	HD versus HDF	–	No difference	–	No difference
Grooteman *et al.* (CONTRAST) [59]	HD versus HDF	Decreased pre-treatment levels in HDF	Increased Hb in HDF	No difference	No difference
Ok *et al.* (Turkey) [60]	HD versus HDF	No difference	Decreased ESA dose in HDF	No difference	No difference
Maduell *et al.* (ESHOL) [35]	HD versus HDF	No difference	No difference	No difference	Decreased in HDF
Panichi *et al.* [61]	lf-HD versus hv-HDF	–	Decreased ERI in HDF	–	–
Morena *et al.* (French) [40]	hf-HD versus HDF	Decreased pre-treatment levels in HDF	No difference	No difference	No difference

F. Locatelli ,F. Carfagna, L. Del Vecchio, V. La Milia Nephrol. Dial. Transplant. 2018

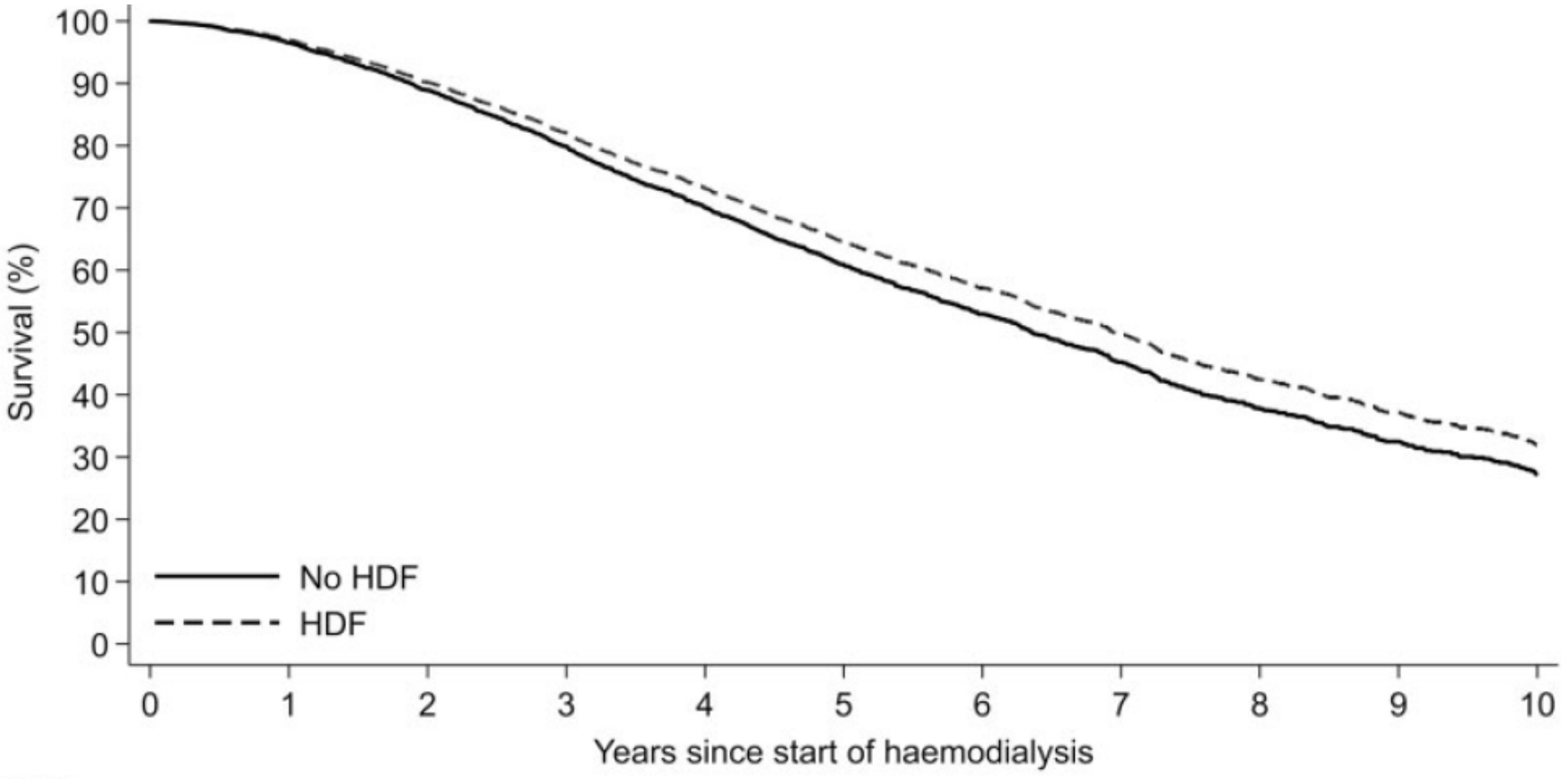
Modeled survival curves comparing patient survival between 4110 patients managed with haemodiafiltration (HDF) and 22 851 patients managed with haemodialysis by country. The difference between the groups was statistically significant for Australia (P<0.001)



Patients											
No HDF	20,418	16,984	13,105	10,069	7,566	5,690	4,088	2,957	2,058	1,429	976
HDF	730	680	757	714	640	536	420	279	235	172	115

See E.J.et al.Nephol.Dial.and Transplant 2018

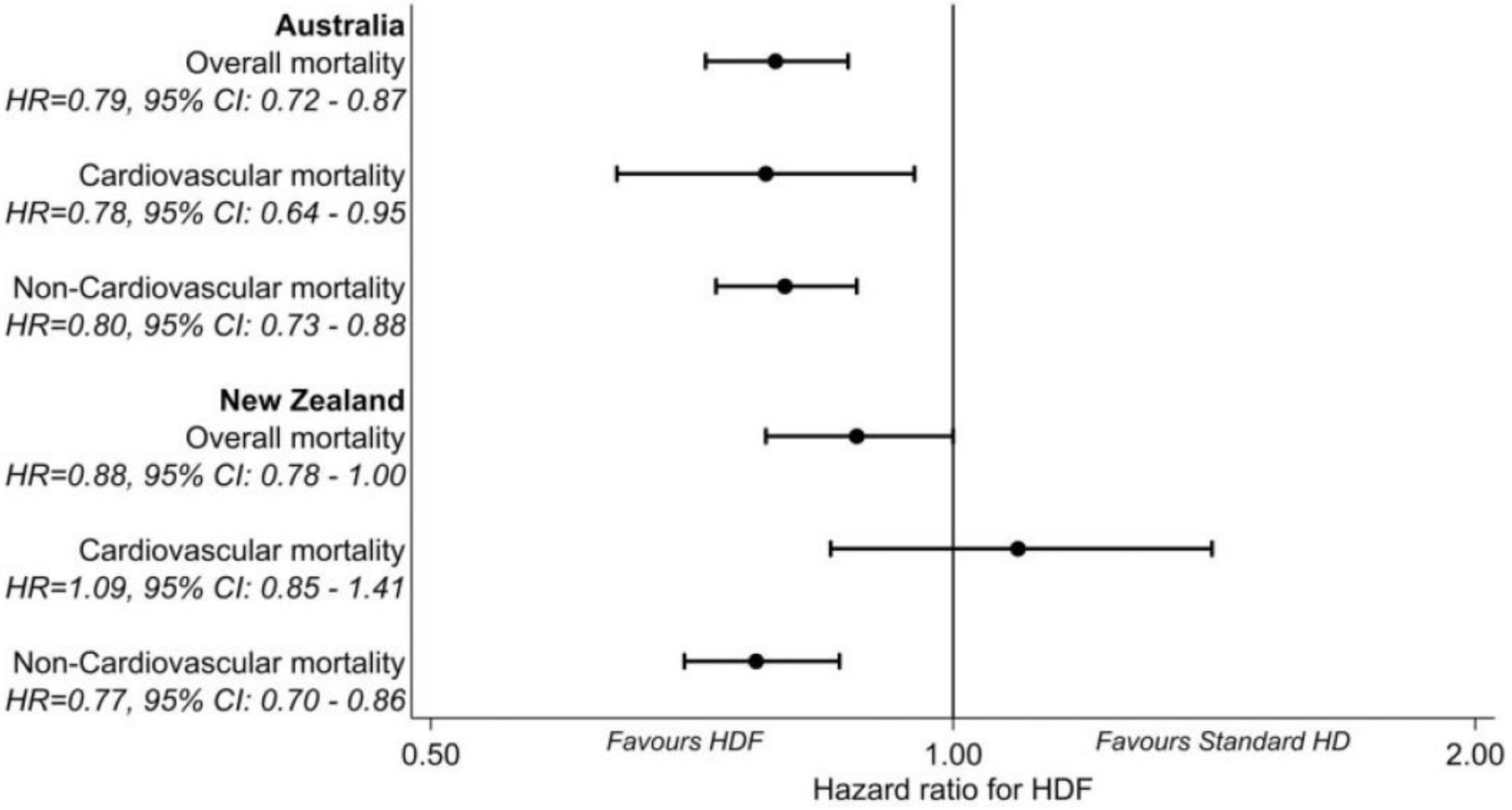
Modeled survival curves comparing patient survival between 4110 patients managed with haemodiafiltration (HDF) and 22 851 patients managed with haemodialysis by country. The difference between the groups was statistically significant for New Zealand (P<0.001)



Patients											
No HDF	3,350	2,697	2,163	1,701	1,278	954	686	491	355	233	156
HDF	399	288	231	188	150	133	101	83	53	44	29

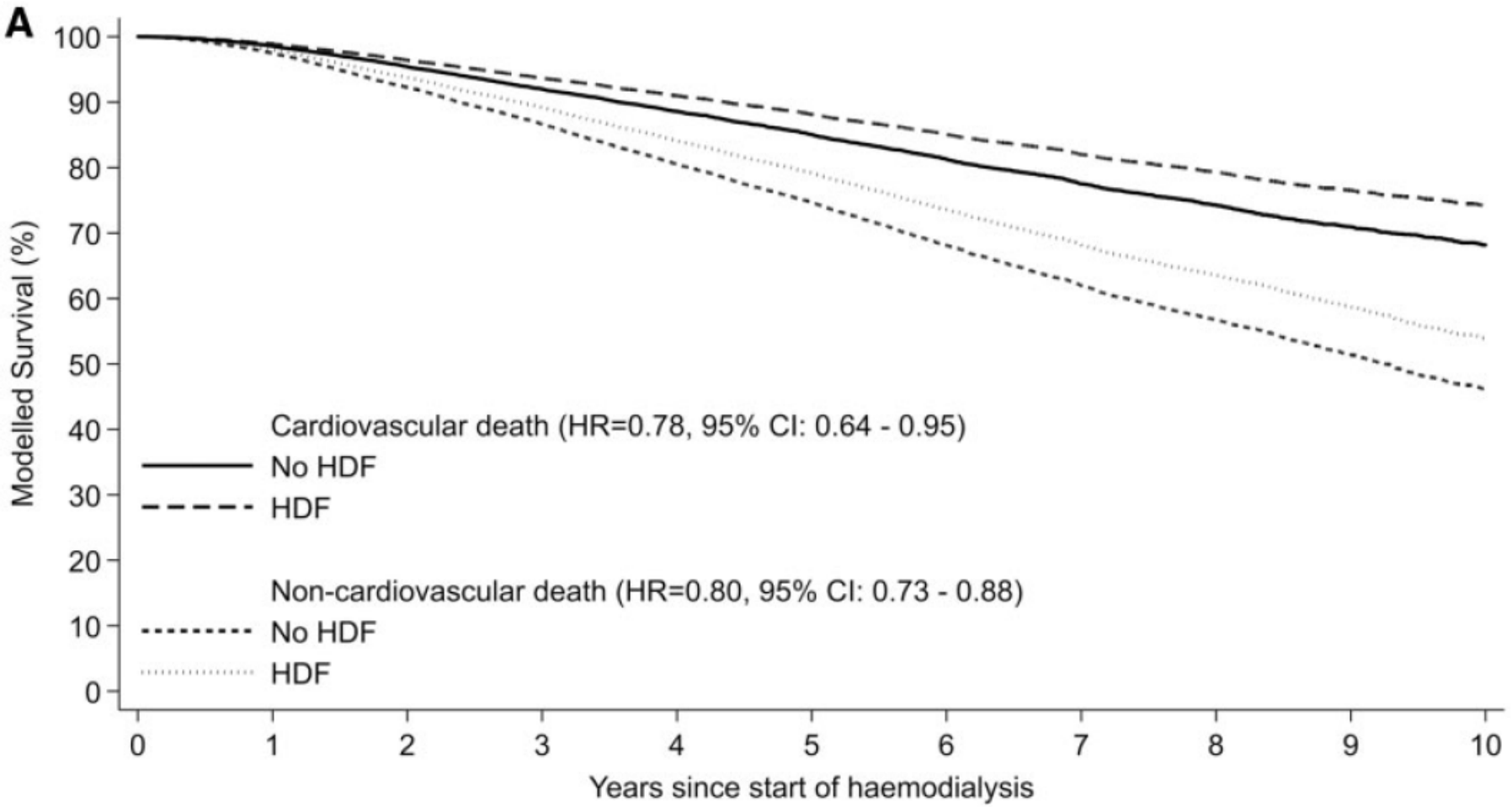
See E.J.et al.Nephol.Dial.and Transplant 2018

Multivariable Cox regression model comparing all - cause mortality and multivariable cause – specific regression models comparing cardiovascular and non – cardiovascular mortality between 4110 patients managed with Haemodiafiltration and 22851 patients with standard haemodialysis by country



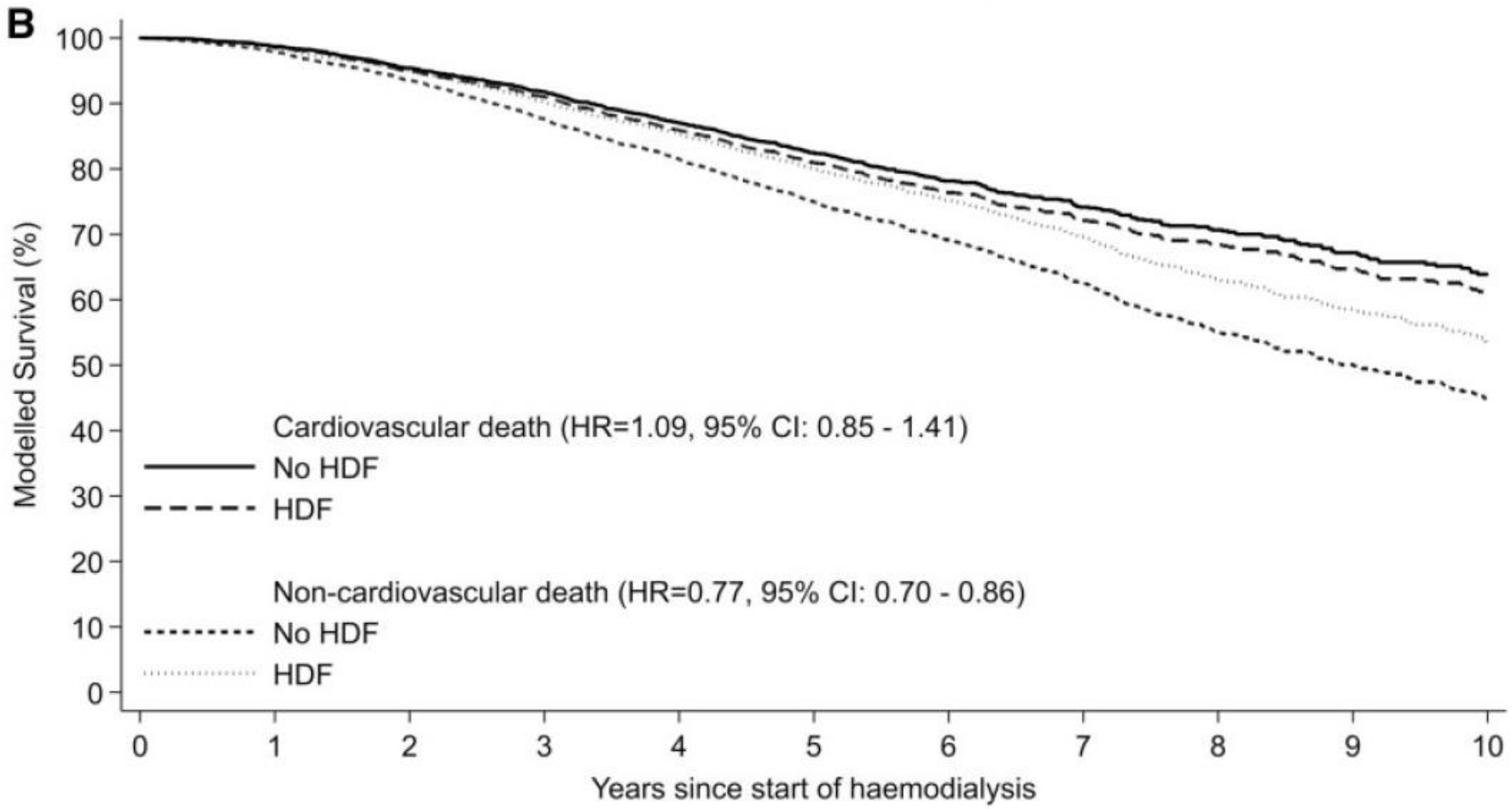
See E.J.et al.Nephol.Dial.and Transplant 2018

Multivariate cause-specific regression models comparing cardiovascular and non-cardiovascular mortality between patients managed with HDF and HD in Australia



See E.J.et al.Nephol.Dial.and Transplant 2018

Multivariate cause-specific regression models comparing cardiovascular and non-cardiovascular mortality between patients managed with HDF and HD in New Zealand



See E.J.et al.Nephol.Dial.and Transplant 2018

Conclusions

- ***The analyses of current HDF practices do not support the notion that HDF is a superior treatment in comparison to HD, even focusing on HDF with the highest convection volumes***

- ***Further trials specifically designed for testing the effect of different convection volumes of HDF vs. HD on clinical outcomes are necessary***