



The 21th Budapest Nephrology School
August, 29, 2014

Online Haemodiafiltration

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Transplant**

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Effect of Membrane Permeability on Survival of Hemodialysis Patients

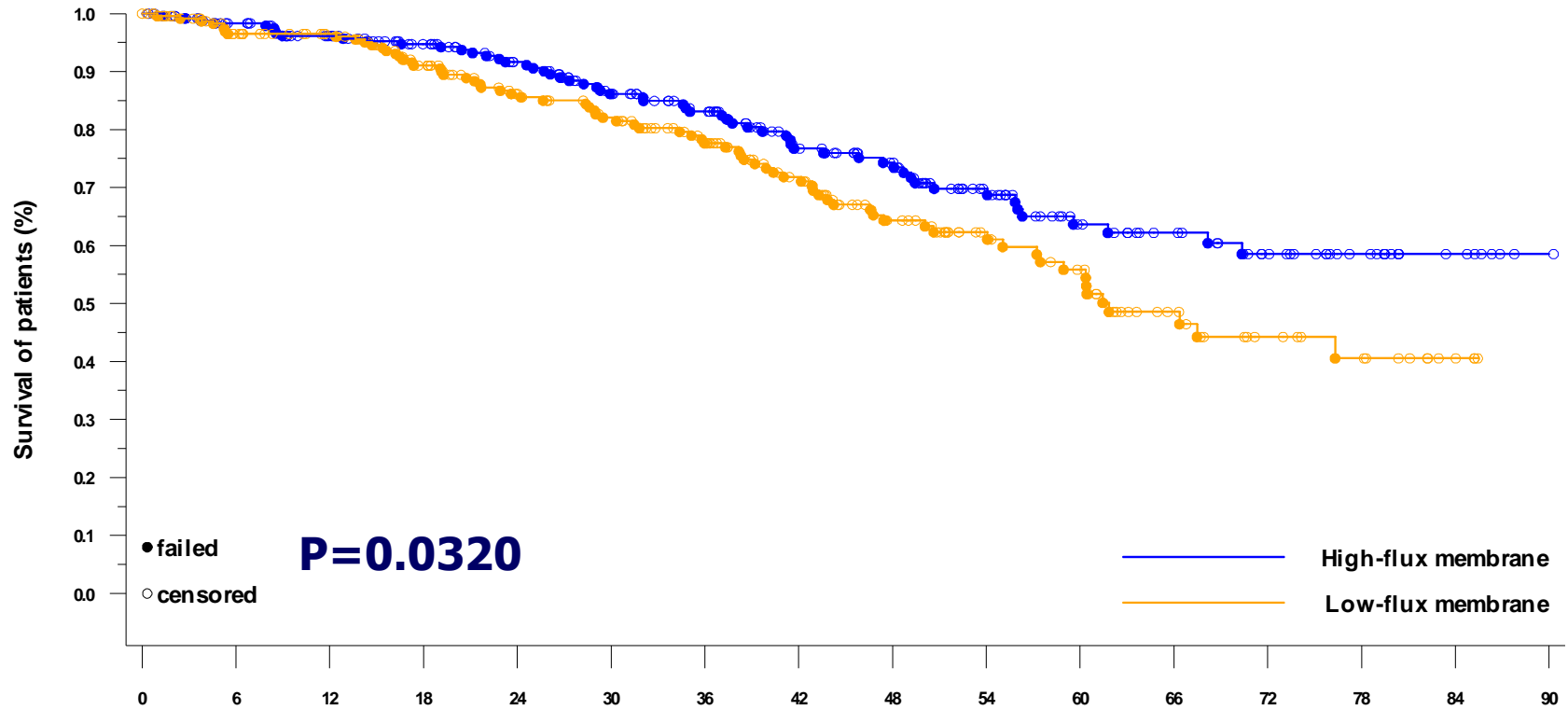
Francesco Locatelli,^{*} Alejandro Martin-Malo,[†] Thierry Hannedouche,[‡] Alfredo Loureiro,[§] Menelaos Papadimitriou,^{||} Volker Wizemann,[¶] Stefan H. Jacobson,^{**} Stanislaw Czekalski,^{††} Claudio Ronco,^{‡‡} and Raymond Vanholder,^{§§}
for the Membrane Permeability Outcome (MPO) Study Group

J Am Soc Nephrol 20: 645 – 654, 2009

MPO : Kaplan-Meier Survival Analysis

: Survival time - whole study time - Albumin ≤ 4
 - Kaplan-Meier analysis -
 Intention-to-treat, n=492

$\leq 4\text{g/dl Alb}$



P=0.0320

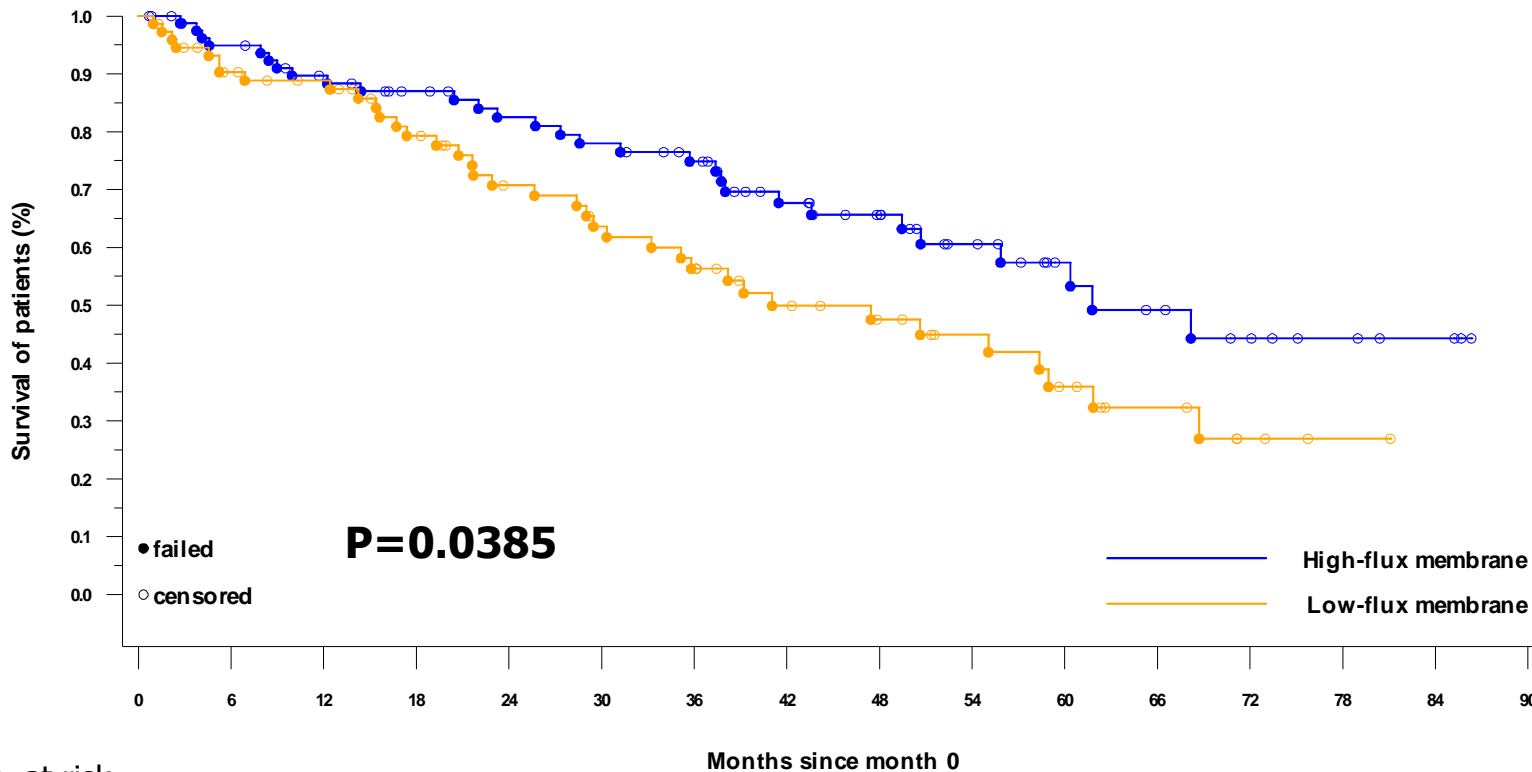
No. at risk

| | | | | | | | | |
|-----------|-----|-----|-----|-----|----|----|----|---|
| High-flux | 250 | 212 | 173 | 134 | 85 | 44 | 26 | 7 |
| Low-flux | 243 | 202 | 152 | 117 | 67 | 41 | 15 | 3 |

Months since month 0

MPO : Kaplan-Meier Survival Analysis Subgroup Analysis – Diabetics*

*Pts. with both serum albumin ≤ 4 and > 4 g/dl albumin



| | Months since month 0 | | | | | | | | | | | | | | |
|-------------|----------------------|----|----|----|----|----|----|----|----|----|----|----|----|----|----|
| No. at risk | 0 | 6 | 12 | 18 | 24 | 30 | 36 | 42 | 48 | 54 | 60 | 66 | 72 | 78 | 84 |
| High-flux | 83 | 67 | 55 | 46 | 27 | 14 | 7 | 3 | | | | | | | |
| Low-flux | 74 | 59 | 40 | 29 | 19 | 11 | 3 | 0 | | | | | | | |

High-flux or low-flux dialysis: a position statement following publication of the MPO study

- MPO study provides sufficient evidence **to upgrade the strength of guideline 2.1 to a level 1A (strong recommendation, based on high-quality evidence):** high-flux HD should be used to delay long-term complications of hemodialysis in the case of high-risk patients (comparable to the low-albumin group of the MPO study)
- Because the substantial reduction of an intermediate marker (beta2-microglobulin) in the high-flux group of the MPO study, **synthetic high-flux membranes should be recommended even in low-risk patients (level 2b: weak recommendation, low quality evidence)**

Quality of dialysis procedure

HDF



● Water quality and distribution system



● Dialysate

● Extracorporeal circuit



● Dialysis dose and frequency



● Membranes and convective treatments



● Online treatments

Observational studies on the effect of Haemofiltration and/or Haemodiafiltration on mortality risk

| | Design | Treatments (patients) | Sample size | Relative risk reduction | P value |
|------------------------------|-------------------------|--|--------------------|--|----------------|
| Locatelli et al. 1999 | Historical, prospective | HDF or Haemofiltration (188) HD (6,256) | 6,444 | 10% | NS |
| Canaud et al. 2006 | Historical, prospective | LF-HD (1,366) HF-HD (546) Low-efficiency HDF (156) High-efficiency HDF (97) | 2,165 | 35% (High-efficiency HDF vs LF-HD) | 0.01 |
| Panichi et al. 2008 | Prospective | Bicarbonate-HD* (424) HDF (204) On-line HDF (129) | 757 | 22% (HDF and On-line HDF vs Bicarbonate-HD) | 0.01 |

LF-HD: low-flux haemodialysis; HF-HD: high-flux haemodialysis; HDF: haemodiafiltration; * Including LF-HD (403 patients) and HF-HD (21 patients)

Randomised studies on the effect of Hemofiltration and/or Hemodiafiltration on mortality risk

| | Design | Treatments (patients) | Sample size | Relative risk reduction | P value |
|------------------------------|-------------------------|---|-------------|-------------------------|-------------|
| Locatelli et al. 1996 | Randomised, prospective | Cuprophane-HD (132) LF-HD (147) HF-HD (51) HDF (50) | 380 | | NS |
| Wizemann et al. 2000 | Randomised, prospective | HDF (23) LF-HD (21) | 44 | | NS |
| Santoro et al. 2008 | Randomised, prospective | On-line Hemofiltration (32) LF-HD (32) | 64 | 55% | 0.05 |
| Locatelli et al. 2010 | Randomised, prospective | LF-HD (70) On-line Hemofiltration (36) On-line HDF (40) | 146 | | NS |

LF-HD: low-flux hemodialysis; HF-HD: high-flux hemodialysis; HDF: hemodiafiltration

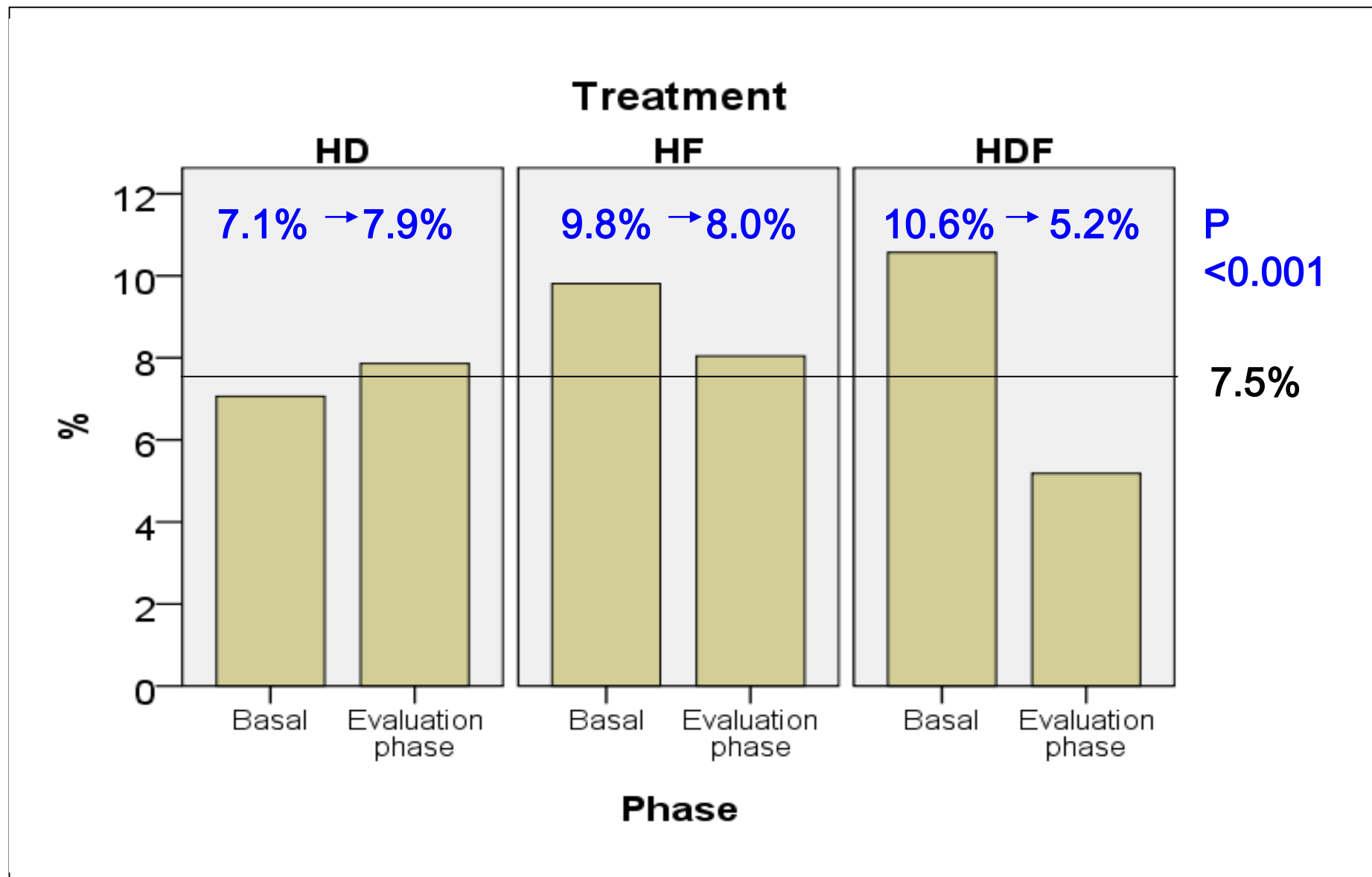
Convective Therapies: Outcomes

- **Intradialytic Cardiovascular Stability**
- **Beta2 microglobulin**
- **Phosphataemia**
- **Anaemia and ESA Dose**
- **Inflammation**
Mortality

Hemofiltration and Hemodiafiltration Reduce Intradialytic Hypotension in ESRD

Francesco Locatelli,^{*} Paolo Altieri,[†] Simeone Andrulli,^{*} Piergiorgio Bolasco,[‡] Giovanna Sau,[†] Luciano A. Pedrini,[§] Carlo Basile,^{||} Salvatore David,[¶] Mariano Feriani,^{**} Giovanni Montagna,^{††} Biagio Raffaele Di Iorio,^{‡‡} Bruno Memoli,^{§§} Raffaella Cravero,^{||||} Giovanni Battaglia,^{¶¶} and Carmine Zoccali^{***}

Sessions with intradialytic hypotension (%)



Tolerance of CKD patients receiving HDF and HF versus HD

F.Locatelli B. Canaud, *Nephrol Dial Transplant.* 2012 Aug;27(8):3043-8

| Author, Year | HDF vs Comp | Type of study | β 2-M | Survival | Tolerance |
|-------------------------|---------------------------------------|-------------------------------|-------------------|----------|-----------|
| Locatelli F et al, 1996 | LF-HD vs cuprophan-HD vs HF-HD vs HDF | RCT | ↓ (HF-HD and HDF) | = | = |
| Wizemann V et al, 2000 | HDF vs LFHD | RCT | ↓ | = | = |
| Bosch JP et al, 2006 | HDF vs LFHD vs HFHD | Historical prospective cohort | ? | ↑ 45% | ↑ |
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| Schiffl H et al, 2007 | HDF vs HFHD + UPD | RCT | ↓ | = | = |
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| Santoro A et al, 2008 | HF vs HFHD | RCT | ↓ | ↑ 18% | ↑ |
| Tiranathanagul K 2009 | HDF vs HFHD | Prospective controlled study | ↓ | = | ↑ |
| Vilar E et al, 2009 | HDF vs HFHD | Historical prospective cohort | ↓ | ↑ 34% | ↑ |
| Locatelli F et al, 2010 | HDF & HF vs LFHD | RCT | ↓ | = | ↑ ↑ |

Convective Therapies: Outcomes

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Long-term effects of high-efficiency on-line HDF on uraemic toxicity

Multicentre prospective randomized cross-over study

Laboratory values and dialysis adequacy parameters at the end of the 2 periods

| 6 months x 2 | LF-HD (n=62) | OI-HDF (n=62) | P-value |
|--------------------------|------------------|------------------|--------------------|
| eKt/V urea | 1.44±0.26 | 1.60±0.31 | < 0.0001 |
| Urea, basal, mg/dL | 143 ± 25 | 133 ± 23 | 0.004 |
| End session, mg/dL | 36 ± 12 | 29 ± 10 | <0.0001 |
| Beta2-m | 33.5±11.8 | 22.2±7.8 | < 0.0001 |
| tHcy, µmol/L | 18.7 ± 8.2 | 15.4 ± 5.0 | 0.003* |
| ADMA, µmol/L | 0.97 ± 0.40 | 0.84 ± 0.37 | 0.2 |
| P | 5.0±1.4 | 4.6±1.3 | 0.008 |
| iPTH | 228±177 | 203±154 | 0.03 |
| Triglycerides, mg/dL | 167 ± 87 | 148 ± 77 | 0.008* |
| Total cholesterol, mg/dL | 175 ± 45 | 176 ± 45 | 0.9 |
| Albumin | 4041±391 | 3919±393 | 0.004 |
| Albumin, g/dL | 4041 ± 391 | 3919 ± 393 | 0.004* |
| CRP | 6.65±6.07 | 5.49±5.46 | 0.03 |
| Potassium, mmol/L | 5.2 ± 0.6 | 5.2 ± 0.7 | 0.8 |
| Bicarbonate, mmol/L | 21.8 ± 2.1 | 21.7 ± 1.9 | 0.6 |

β2-M of CKD patients receiving HDF and HF versus HD

F.Locatelli B. Canaud, *Nephrol Dial Transplant.* 2012 Aug;27(8):3043-8

| Author, Year | HDF vs Comp | Type of study | β2-M | Survival | Tolerance |
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| Jirka et al, 2006 | HDF vs LFHD vs HFHD | Historical prospective cohort | ? | ↑ 36% | = |
| Schiffl H et al, 2007 | HDF vs HFHD + UPD | RCT | ↓ | = | = |
| Vinhas J et al, 2007 | HDF vs HFHD | Prospective controlled study | ? | ↑ 50% | ↑ |
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| Vilar E et al, 2009 | HDF vs HFHD | Historical prospective cohort | ↓ | ↑ 34% | ↑ |
| Locatelli F et al, 2010 | HDF & HF vs LFHD | RCT | ↓ | = | ↑ ↑ |

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Long-term effects of high-efficiency on-line HDF on uraemic toxicity

Multicentre prospective randomized cross-over study

Laboratory values and dialysis adequacy parameters at the end of the 2 periods

| | 6 months x 2 | LF-HD (n=62) | OI-HDF (n=62) | P-value |
|---|-------------------|------------------|------------------|--------------------|
| Relative urea index | eKt/V urea | 1.44±0.26 | 1.60±0.31 | < 0.0001 |
| Urea, mg/dL | | 36 ± 12 | 29 ± 10 | <0.0001 |
| End session, mg/dL | | 9.8 ± 2.2 | 9.1 ± 2.2 | <0.0001 |
| Creatinine, mg/dL | | 33.5±11.8 | 22.2±7.8 | < 0.0001 |
| Beta-2-microglobulin, mg/L | Beta2-m | 10.7 ± 0.2 | 10.4 ± 0.0 | 0.0001 |
| ADMA, µmol/L | | 0.97 ± 0.40 | 0.84 ± 0.37 | 0.2 |
| Calcium, mg/dL | | 9.6 ± 0.8 | 9.7 ± 0.7 | 0.3 |
| Phosphorus, mg/dL | P | 5.0±1.4 | 4.6±1.3 | 0.008 |
| Calcium-phosphorus product, mg ² /dL | | 47.0 ± 13.1 | 44.4 ± 13.0 | 0.001 |
| Intact parathyroid hormone-related protein, pg/mL | iPTH | 228±177 | 203±154 | 0.03 |
| Total cholesterol, mg/dL | | 175 ± 45 | 176 ± 45 | 0.9 |
| HDL, mg/dL | | 44.7 ± 12.4 | 49.2 ± 12.7 | <0.0001* |
| Albumin, g/L | Albumin | 4041±391 | 3919±393 | 0.004 |
| C-reactive protein, mg/L | | 6.65 ± 6.07 | 5.49 ± 5.46 | 0.02* |
| Serum ferritin, µg/L | CRP | 6.65±6.07 | 5.49±5.46 | 0.03 |
| Parathyroid hormone-related protein, pg/mL | | 0.2 ± 0.0 | 0.2 ± 0.1 | 0.8 |
| Bicarbonate, mmol/L | | 21.8 ± 2.1 | 21.7 ± 1.9 | 0.6 |

Long-term effects of high-efficiency on-line HDF on uraemic toxicity

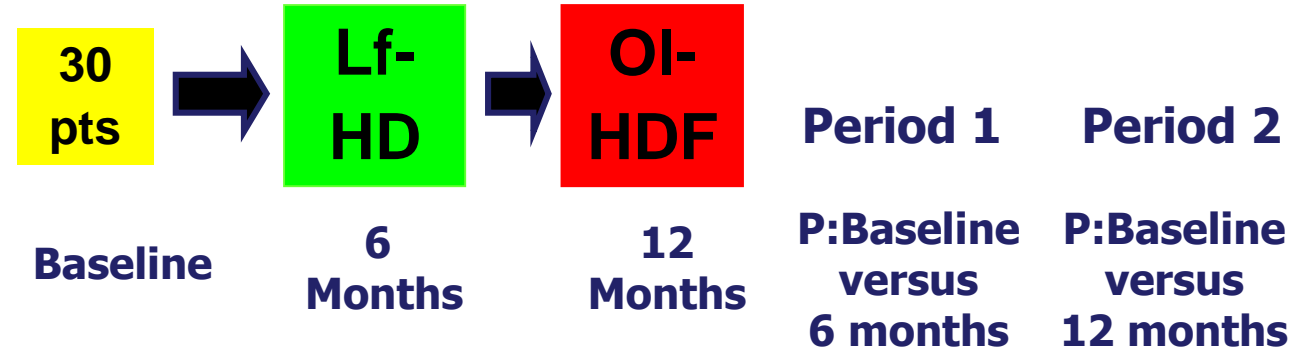
Multicentre prospective randomized cross-over study

Phosphate binders and 1-25 OH Vit D

| | Low Flux-HD | On line-HDF | P-value |
|-------------------------------------|------------------------------|------------------------------|-------------|
| Ca (acetate/carbonate), g/day | <i>n</i> = 35 2.54 ± 1.36 | <i>n</i> = 34 2.67 ± 1.45 | 0.6 |
| Al hydroxide, g/day | <i>n</i> = 16 2.98 ± 1.99 | <i>n</i> = 16 3.10 ± 1.97 | 0.9 |
| Sevelamer, mg/day | 5120±2001 | 3947±2016 | 0.04 |
| 1-25 OH cholecalciferol, µg/week | <i>n</i> = 38 2.25 ± 1.64 | <i>n</i> = 38 2.38 ± 1.83 | 0.8 |

Effect of post-dilutional on-line HDF on serum calcium, phosphate and PTH in uraemic patients

Prospective trial



Study group: $n=30$

| | | | | | |
|--|-----------|-----------|-----------|----|---------|
| Calcium (mg/dl) | 8.9 ± 0.8 | 9.1 ± 0.7 | 8.9 ± 0.6 | NS | NS |
| Serum phosphate (mg/dL) | 5.3 ± 0.7 | 5.1 ± 1.0 | 4.0 ± 0.7 | NS | <0.0001 |
| PTHint (ng/mL) | 319 ± 163 | 307 ± 167 | 194 ± 98 | NS | <0.0001 |
| Controls: $n=35$ (Lf-HD) | | | | | |
| Calcium (mg/dl) | 9.1 ± 0.6 | 9.2 ± 0.6 | 9.2 ± 0.5 | NS | NS |
| Serum phosphate (mg/dL) | 5.0 ± 0.5 | 5.1 ± 0.4 | 5.2 ± 0.5 | NS | NS |
| PTHint (ng/mL) | 276 ± 182 | 242 ± 149 | 294 ± 189 | NS | NS |

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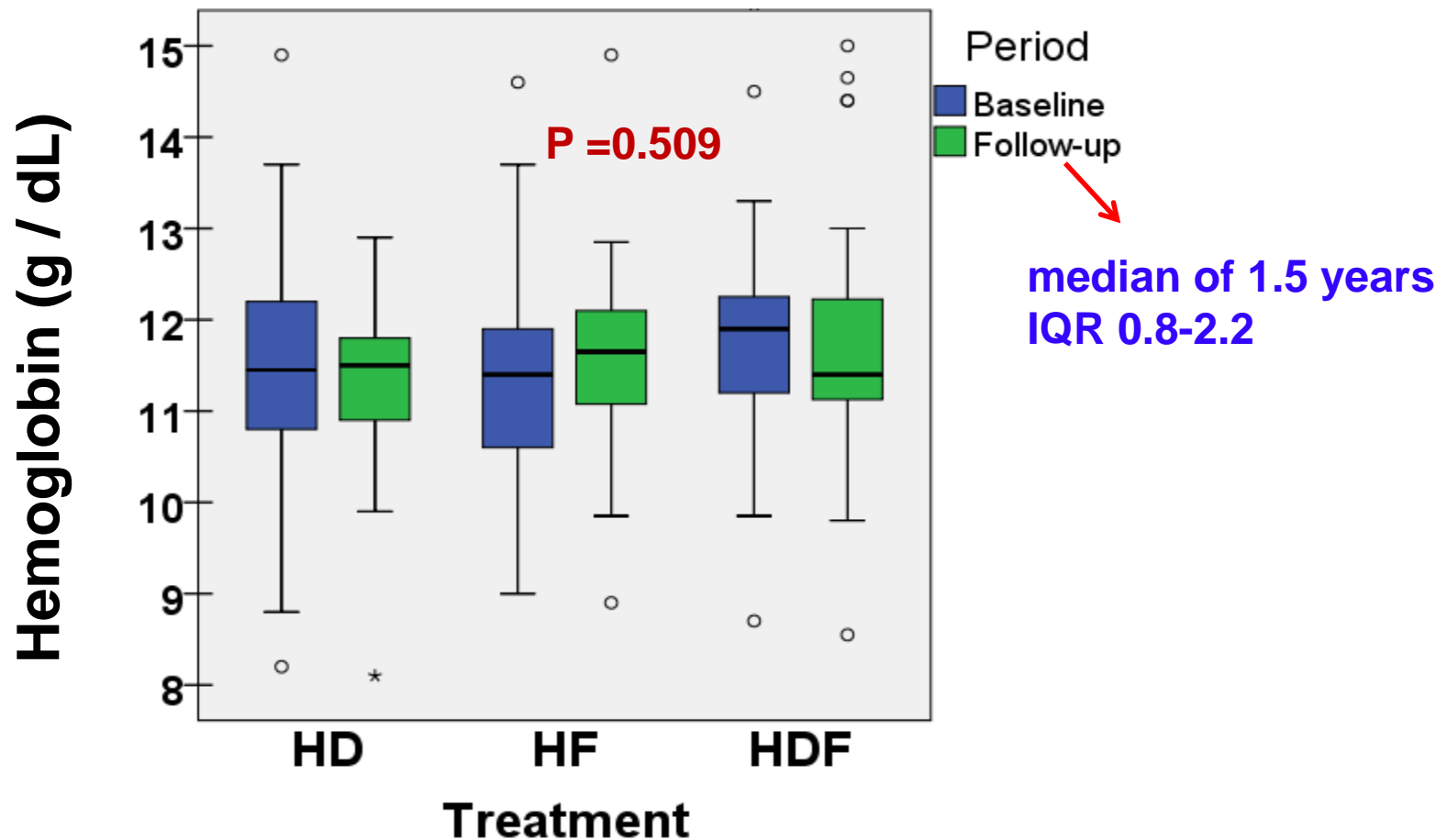
Randomised studies on the effect of Convective Treatments on Anaemia correction

| | Analysis | Treatments (patients) | Sample size | Haemoglobin Haematocrit | Epo dose |
|--------------------------------------|----------------------|---|-------------|----------------------------|----------|
| Locatelli et al. 1996 | Secondary | Cuprophane-HD (132) LF – Ps HD (147) HF – Ps HD (51) HDF Ps (50) | 380 | (HF-HD vs LF-HD) | NA |
| Locatelli et al. 2000 | Primary | HF-PMMA HD (42) Cellulose-HD (42) | 84 | = | = |
| Ward et al. 2000 | Primary | On-line HDF vs HF-HD | 44 | = | |
| Wizemann et al. 2000 | Primary | LF-HD (21) On-line HDF (23) | 44 | = | = |
| Ayli et al. 2004 | Primary | HF-HD vs LF-HD | 48 | | ↓ |
| Vaslaki et al. 2006 | Primary (cross-over) | On-line HDF vs HD | 70 | | ↓ |
| Locatelli et al. 2009 | Secondary | LF-HD (375) HF-HD (363) | 738 | = | = |
| Andrulli.. and Locatelli 2010 | Primary | HF-HD+ Vit. E coated membranes vs | 20 | = | = |
| | Secondary | HF-HD | | = | ↓ |

LF-HD: low-flux haemodialysis; HF-HD: high-flux haemodialysis; HDF: haemodiafiltration; NA: not available; Ps: Polysulphone; BK-F polymethylmetacrylate

Baseline and follow-up haemoglobin values in online HF and online HDF vs low-flux HD

A total of 146 patients were centrally randomized to HD (70 patients), HF (36 patients) or HDF (40 patients)



Convective Therapies: Outcomes

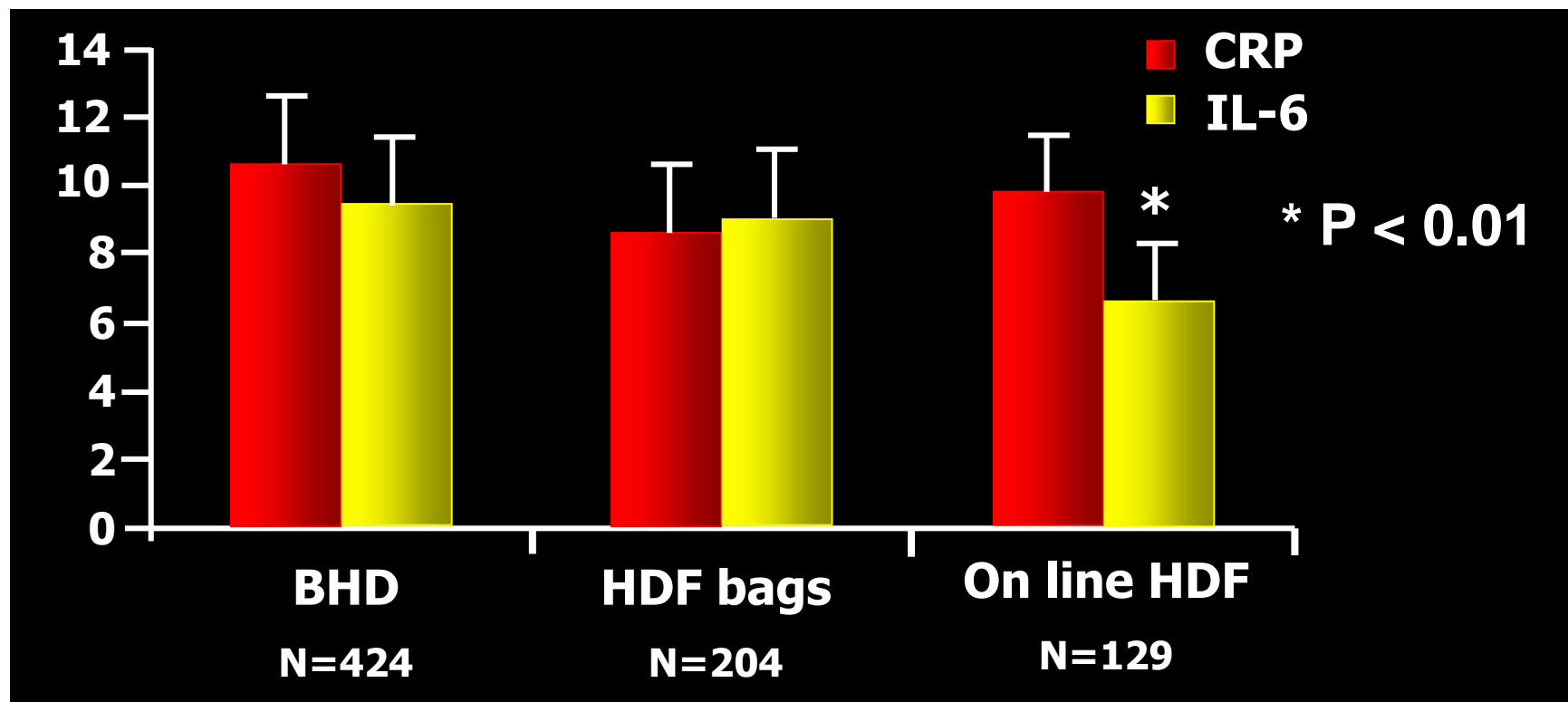
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Chronic inflammation and mortality in HD: effect of different renal replacement therapies.

Results from the RISCAVID study

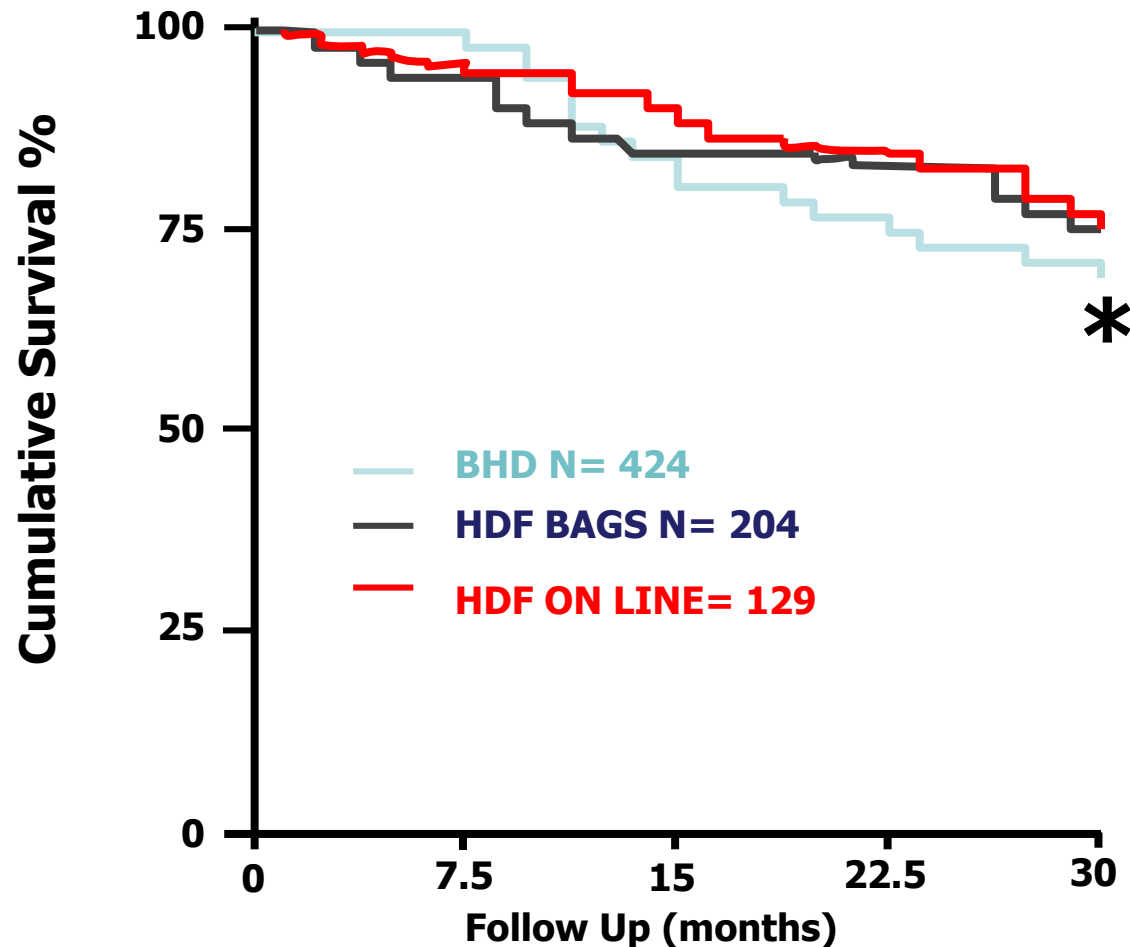
Prospective observational trial

Inflammatory markers and dialytic techniques



Chronic inflammation and mortality in HD: effect of different renal replacement therapies. Results from the RISCAVID study

Prospective observational trial

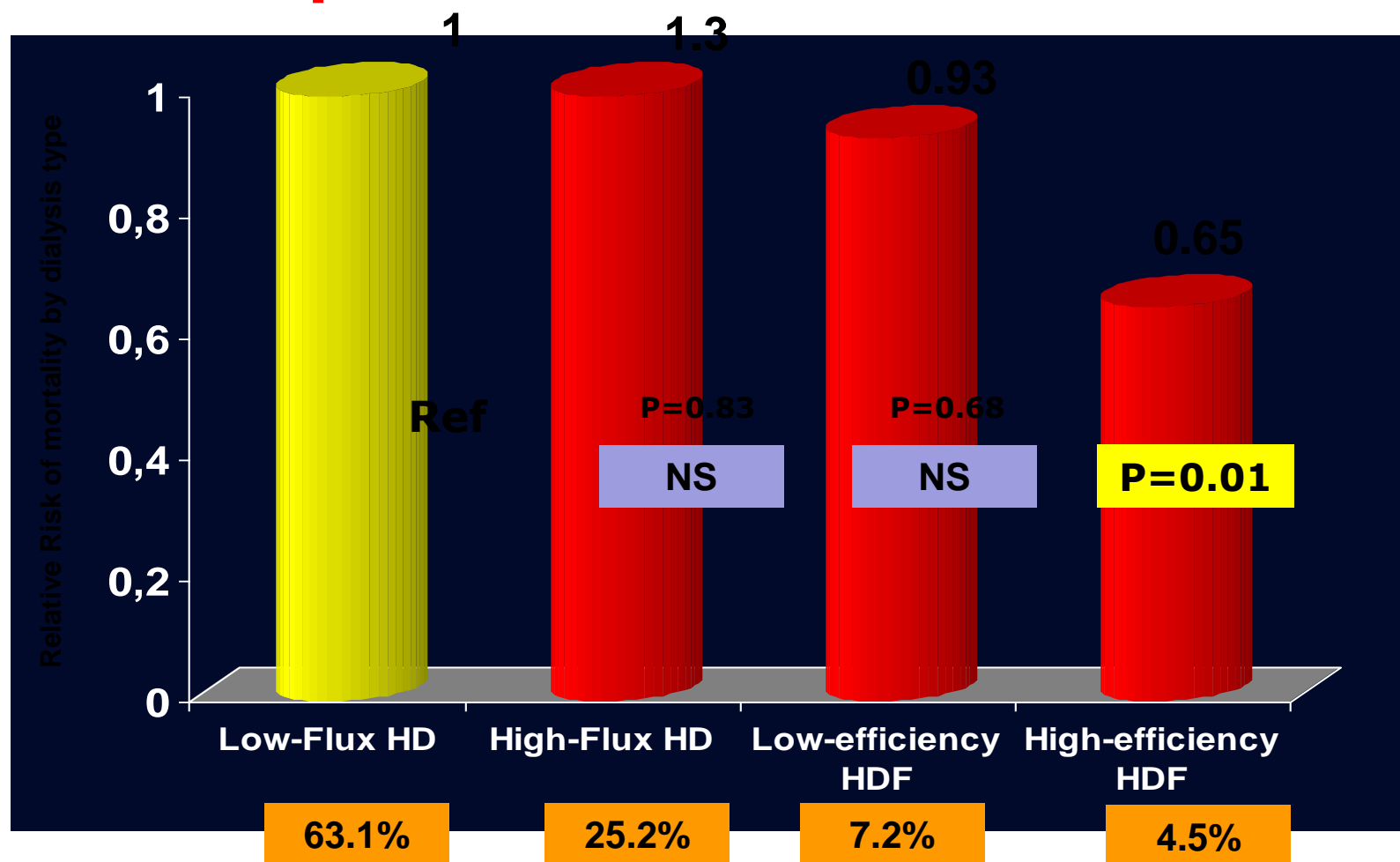


Convective Therapies: Outcomes

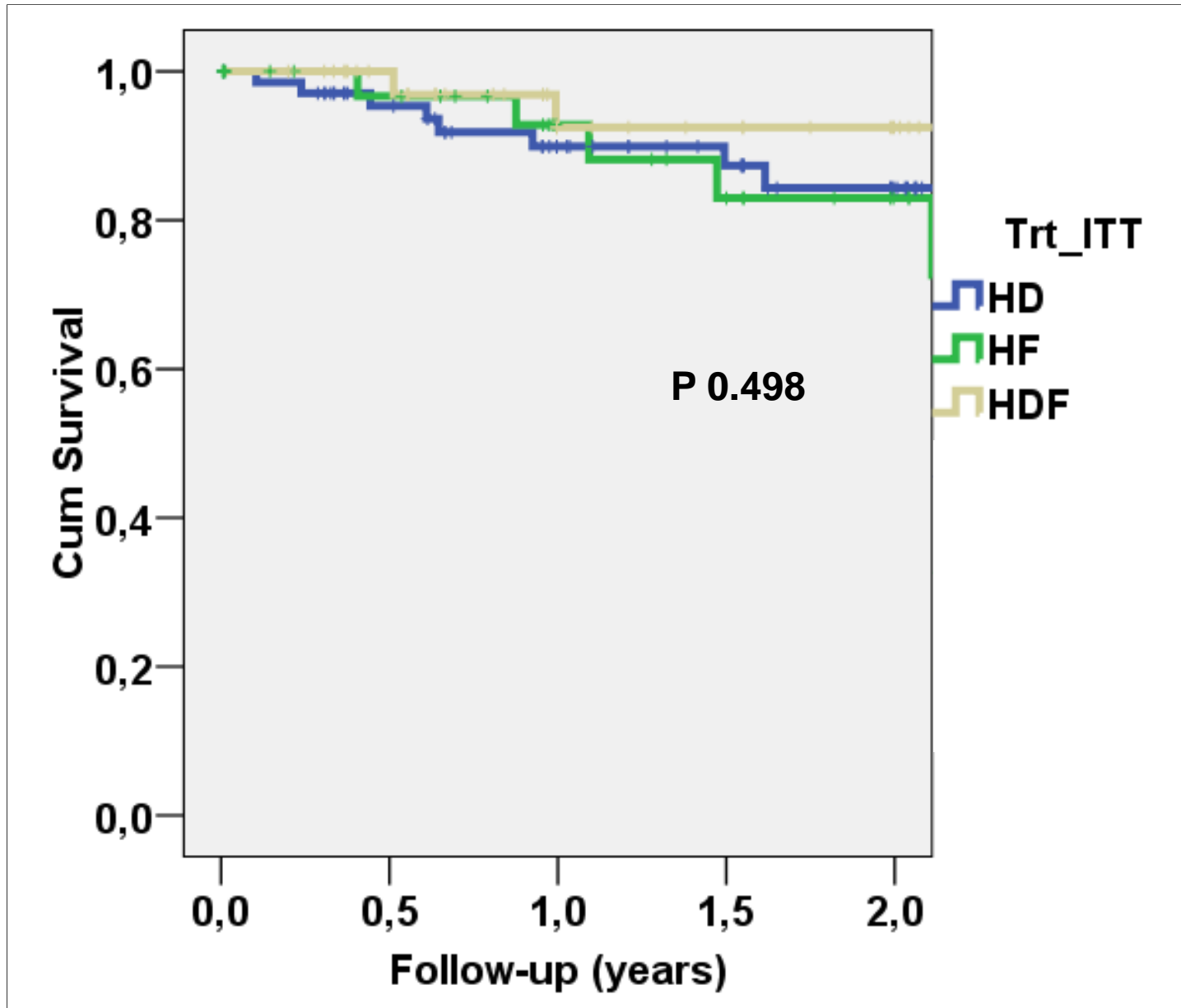
- Intradialytic Cardiovascular Stability
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 - Inflammation
- Mortality**

Mortality risk for patients receiving HDF versus HD

European results from the DOPPS



Patient survival



Survival of CKD patients receiving HDF and HF versus HD

Locatelli F. and Canaud B. Nephrol.Dial Transpl. 2012

| Author, Year | HDF vs Comp | Type of study | β 2-M | Survival | Tolerance |
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Outcomes of CKD patients receiving HDF versus HD

Locatelli F. and Canaud B. Nephrol.Dial Transpl. 2012

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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

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Is hemodiafiltration the future?

Barriers to its large use

Barriers to larger use of Hemodiafiltration

- Lack of convincing evidence of survival benefit
- Lack of convincing cost saving - varies from country to country
- Safety concerns using large volume of on-line prepared substitution fluid
- Regulatory issues regulation of on-line fluid preparation (cumbersome and costly)
- Inadequate vascular access for Q_b requirements
- Education and training
- Cost of OL-HDF machine

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;
enrollment closed
Dec 31, 2010;
Results by Dec ,
2014?

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

CLINICAL RESEARCH

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Hemofiltration and Hemodiafiltration Reduce Intradialytic Hypotension in ESRD

Francesco Locatelli,^{*} Paolo Altieri,[†] Simeone Andrulli,^{*} Piergiorgio Bolasco,[‡] Giovanna Sau,[†] Luciano A. Pedrini,[§] Carlo Basile,^{||} Salvatore David,[¶] Mariano Feriani,^{**} Giovanni Montagna,^{††} Biagio Raffaele Di Iorio,^{‡‡} Bruno Memoli,^{§§} Raffaella Cravero,^{||||} Giovanni Battaglia,^{¶¶} and Carmine Zoccali^{***}

J Am Soc Nephrol 2010 21:1798-807

Effect of Online Hemodiafiltration on All-Cause Mortality and Cardiovascular Outcomes

Muriel P.C. Grooteman,^{*†} Marinus A. van den Dorpel,[‡] Michiel L. Bots,[§] E. Lars Penne,^{*||} Neelke C. van der Weerd,^{*} Albert H.A. Mazairac,^{||} Claire H. den Hoedt,^{‡||} Ingeborg van der Tweel,[§] Renée Lévesque,[¶] Menso J. Nubé,^{*†} Piet M. ter Wee,^{*†} and Peter J. Blankestijn,^{||} for the CONTRAST Investigators

^{*}Department of Nephrology, VU University Medical Center, Amsterdam, The Netherlands; [†]Institute for Cardiovascular Research, VU Medical Center, Amsterdam, The Netherlands; [‡]Department of Internal Medicine, Maastrad Hospital, Rotterdam, The Netherlands; [§]Julius Center for Health Sciences and Primary Care, University Medical Center Utrecht, Utrecht, The Netherlands; ^{||}Department of Nephrology, University Medical Center Utrecht, Utrecht, The Netherlands; and [¶]Department of Nephrology, Centre Hospitalier de l'Université de Montréal, St. Luc Hospital, Montréal, Canada

CONTRAST

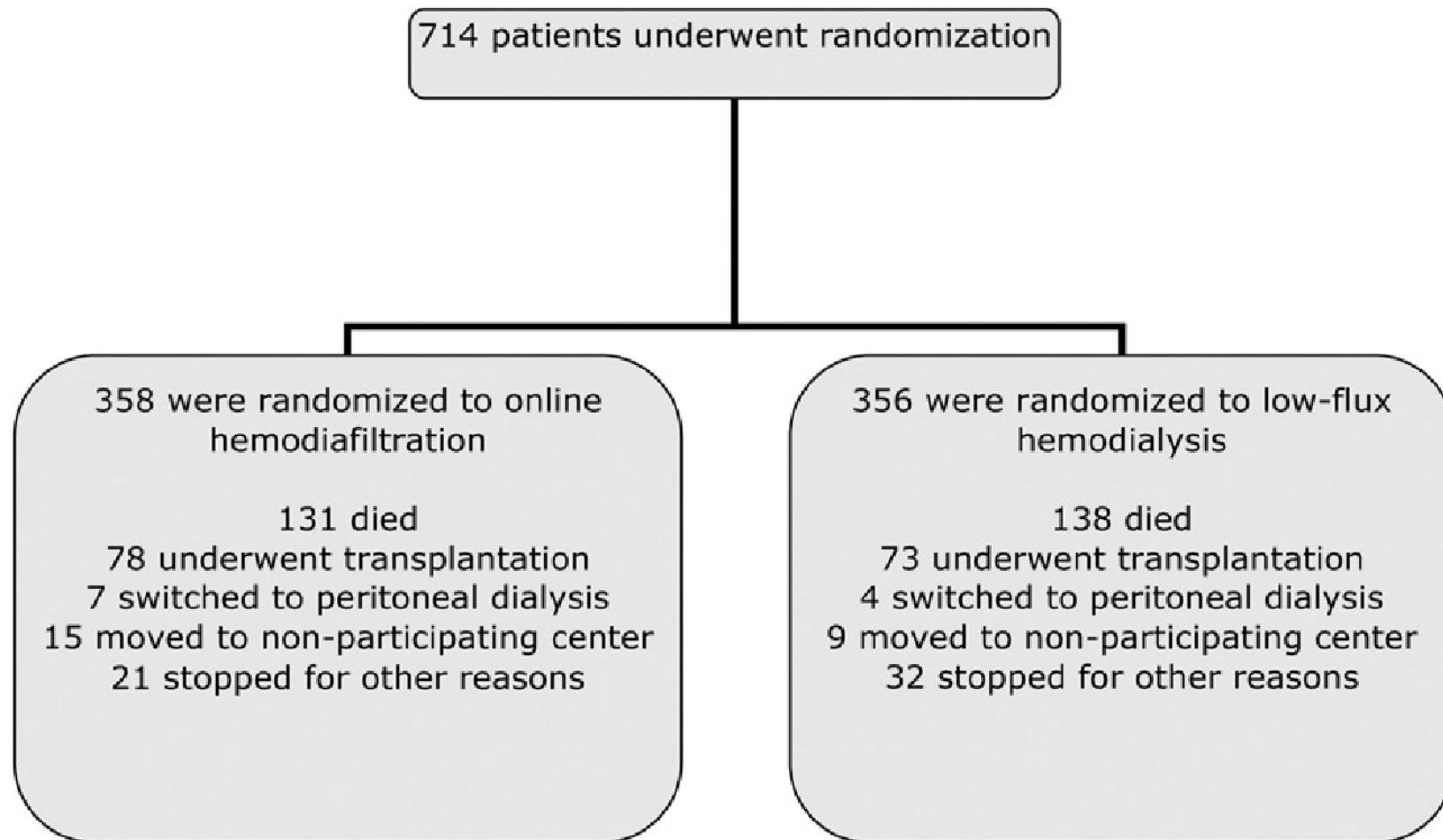


Figure 1. Enrollment, randomization, and follow-up of study participants. For mortality and cardiovascular events, all patients were followed until the end of the study.

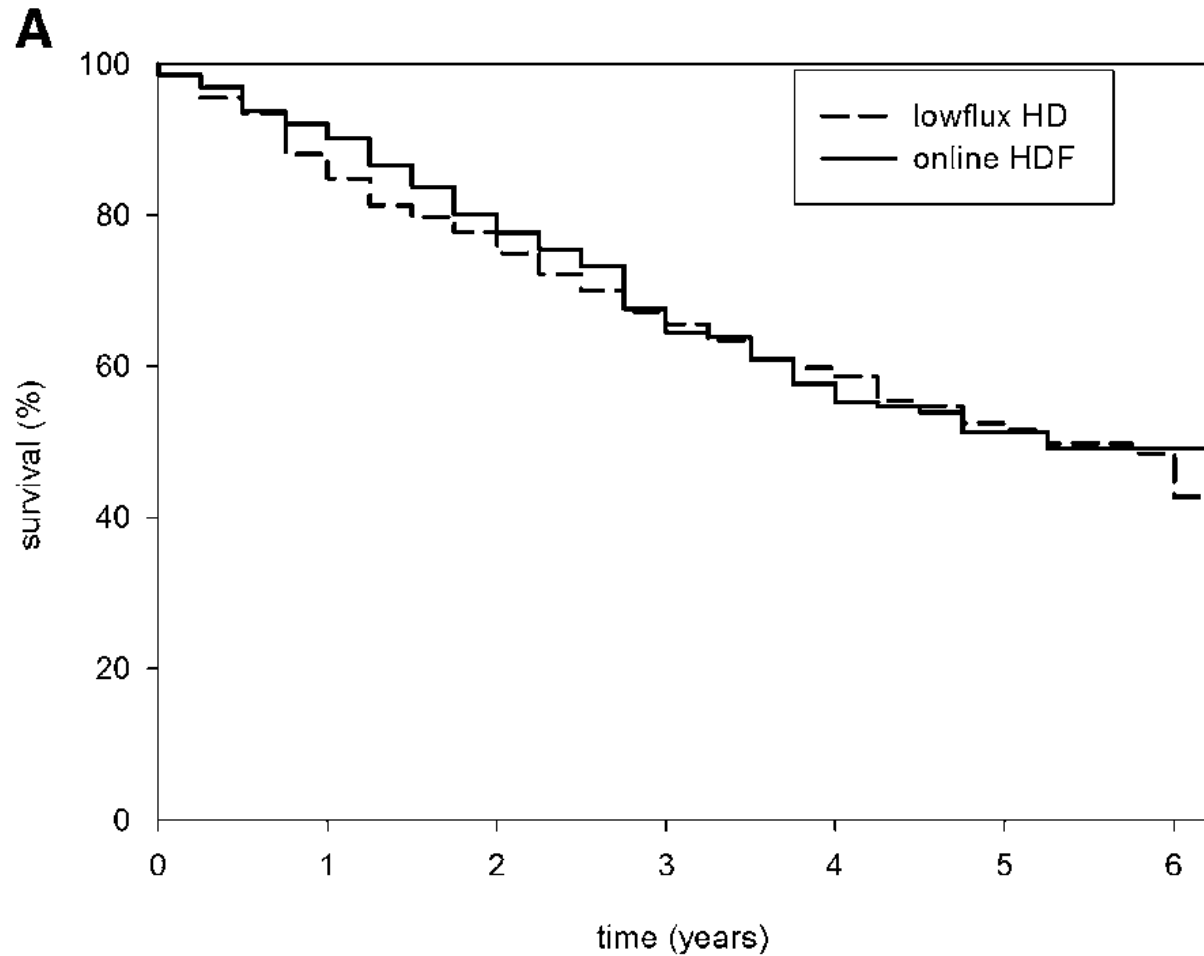
Primary outcome

| | Online Hemodiafiltration | | Low-Flux Hemodialysis | | HR (95% CI) ^a |
|--|---------------------------------|---------------------------|------------------------------|---------------------------|--------------------------|
| | Number of Events | Person-Years of Follow-Up | Number of Events | Person-Years of Follow-Up | |
| Primary out-come: all-cause mortality | 131 | 1085 | 138 | 1085 | 0.95 (0.75–1.20) |

^a Obtained through unadjusted Cox proportional hazards models

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



Patients at risk

| | | | | | | | | | | | | | |
|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|----|----|----|----|
| HD | 356 | 337 | 307 | 269 | 230 | 201 | 169 | 140 | 102 | 83 | 65 | 52 | 32 |
| HDF | 358 | 346 | 324 | 287 | 237 | 203 | 160 | 131 | 103 | 77 | 57 | 44 | 18 |

Risk of all-cause mortality by achieved convection volume

82 missing and 206 deaths instead of 269

| | HD | Online Hemodiafiltration Convection Volume Tertiles | | | <i>P</i> 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

<http://ndt.oxfordjournals.org/>

Nephrol Dial Transplant (2013) 28: 192–202

doi: 10.1093/ndt/gfs407

Advance Access publication 9 December 2012

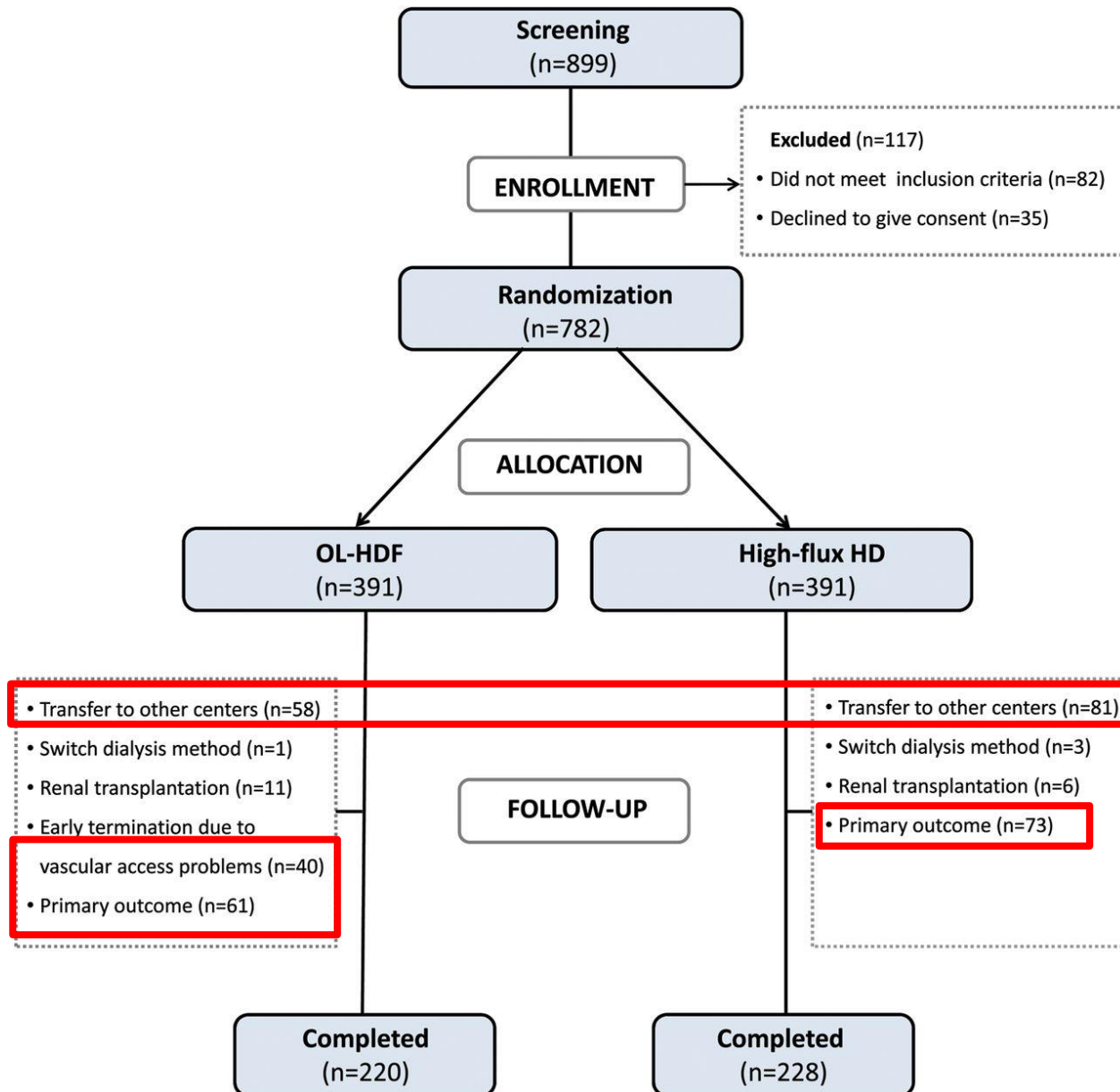
Mortality and cardiovascular events in online haemodiafiltration (OL-HDF) compared with high-flux dialysis: results from the Turkish OL-HDF Study

Ercan Ok¹, Gulay Asci¹, Huseyin Toz¹, Ebru Sevinc Ok¹, Fatih Kircelli¹, Mumtaz Yilmaz¹, Ender Hur¹, Meltem Sezis Demirci¹, Cenk Demirci¹, Soner Duman¹, Ali Basci¹, Siddig Momin Adam², Ismet Onder Isik², Murat Zengin², Gultekin Suleymanlar³, Mehmet Emin Yilmaz⁴ and Mehmet Ozkahya¹ and On behalf of the ‘Turkish Online Haemodiafiltration Study’

¹Division of Nephrology, Ege University School of Medicine, Izmir, Turkey, ²Fresenius Medical Care Dialysis Clinics, Turkey, ³Division of Nephrology, Akdeniz University School of Medicine, Antalya, Turkey and ⁴Division of Nephrology, Dicle University School of Medicine, Diyarbakir, Turkey

Correspondence and offprint requests to: Ercan Ok; E-mail: ercan.ok@ege.edu.tr

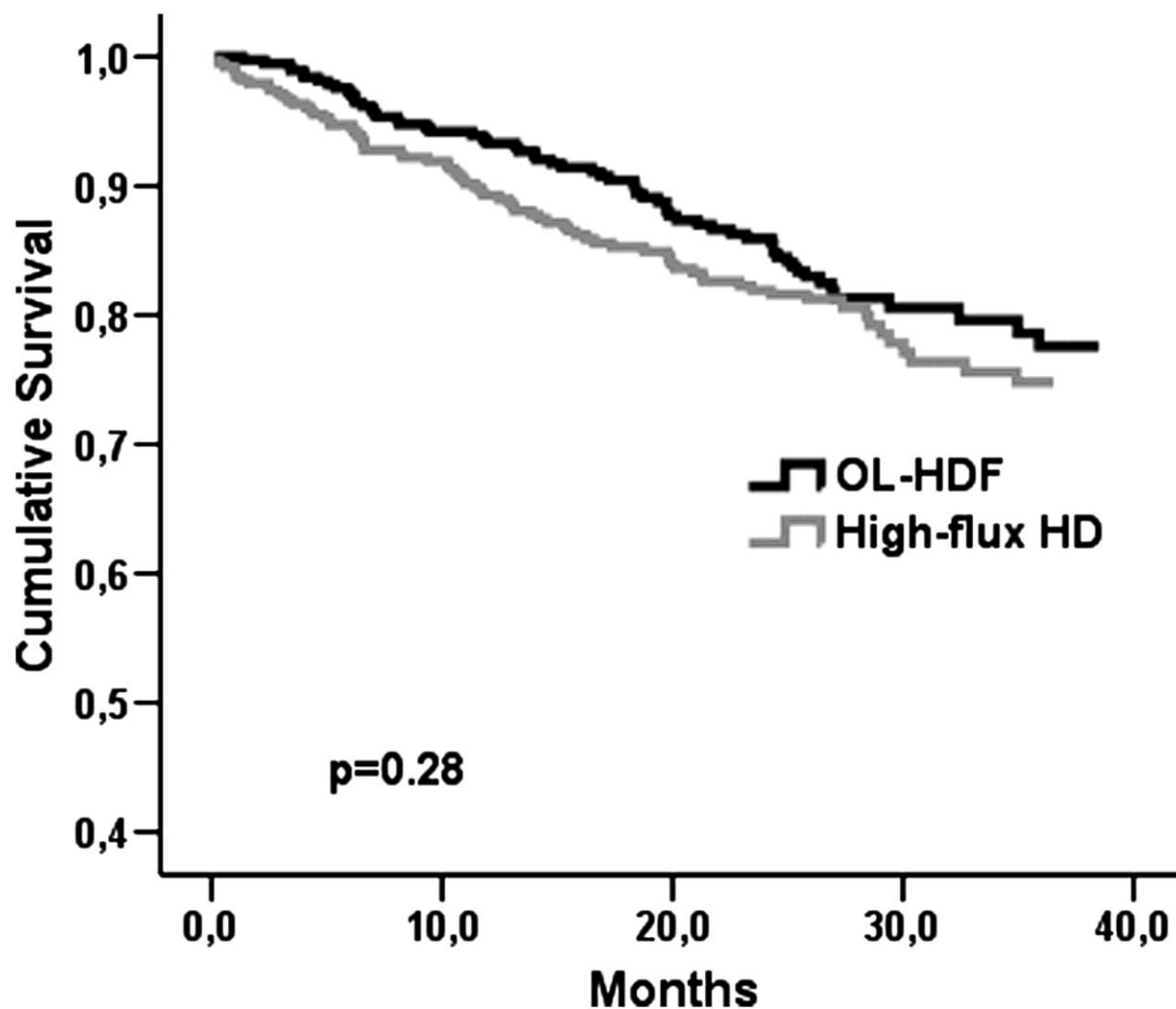
Flow chart of study participation.



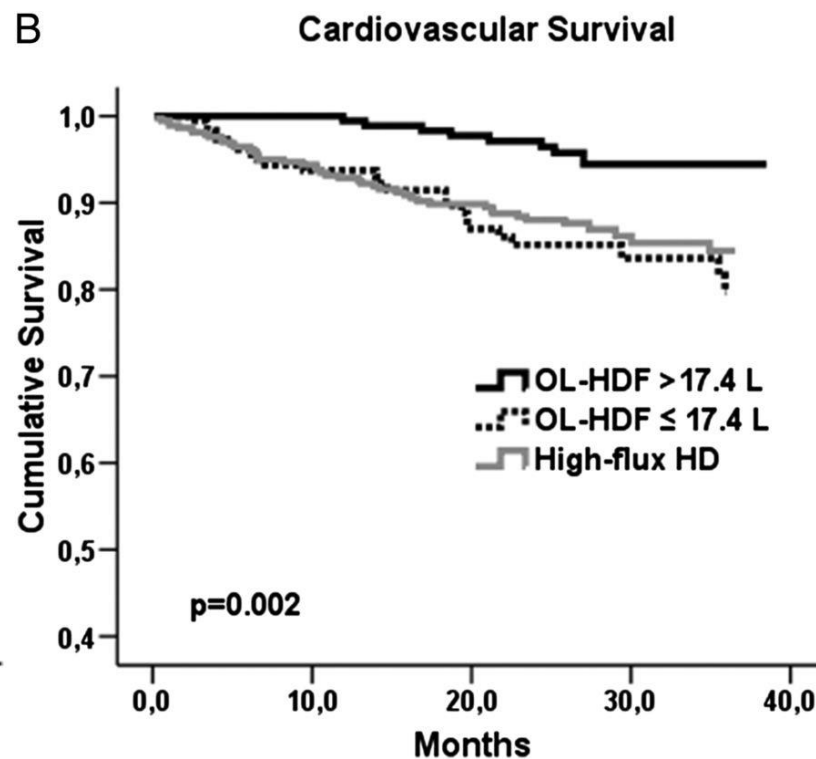
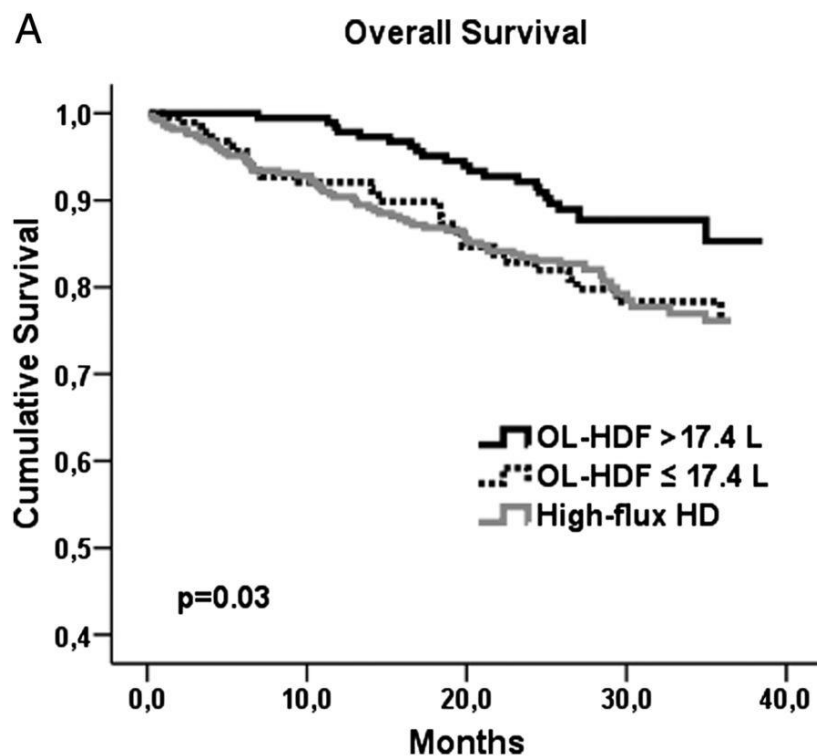
Mortality

| | All patients (<i>n</i> = 782) | OL-HDF (<i>n</i> = 391) | High-flux HD (<i>n</i> = 391) |
|--|-----------------------------------|-----------------------------|-----------------------------------|
| Overall mortality (<i>n</i> , %) | 117 (15.0) | 52 (13.3) | 65 (16.6) |
| Cardiovascular mortality (<i>n</i> , %) | 76 (9.7) | 32 (8.1) | 44 (11.2) |
| Noncardiovascular mortality (<i>n</i> , %) | 41 (5.2) | 20 (5.1) | 21 (5.3) |

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



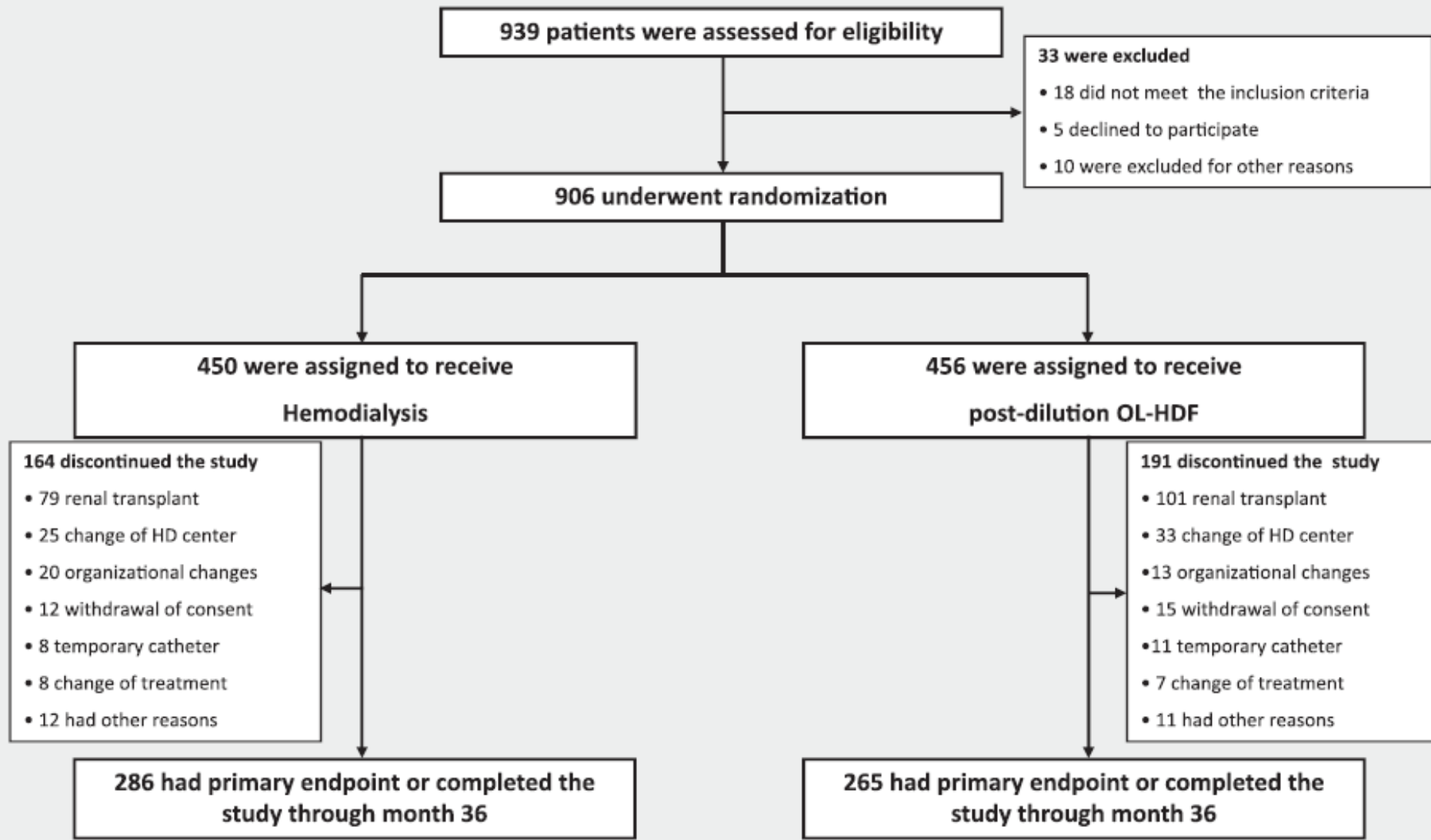
Overall (A) and cardiovascular survival (B) among the treatment groups



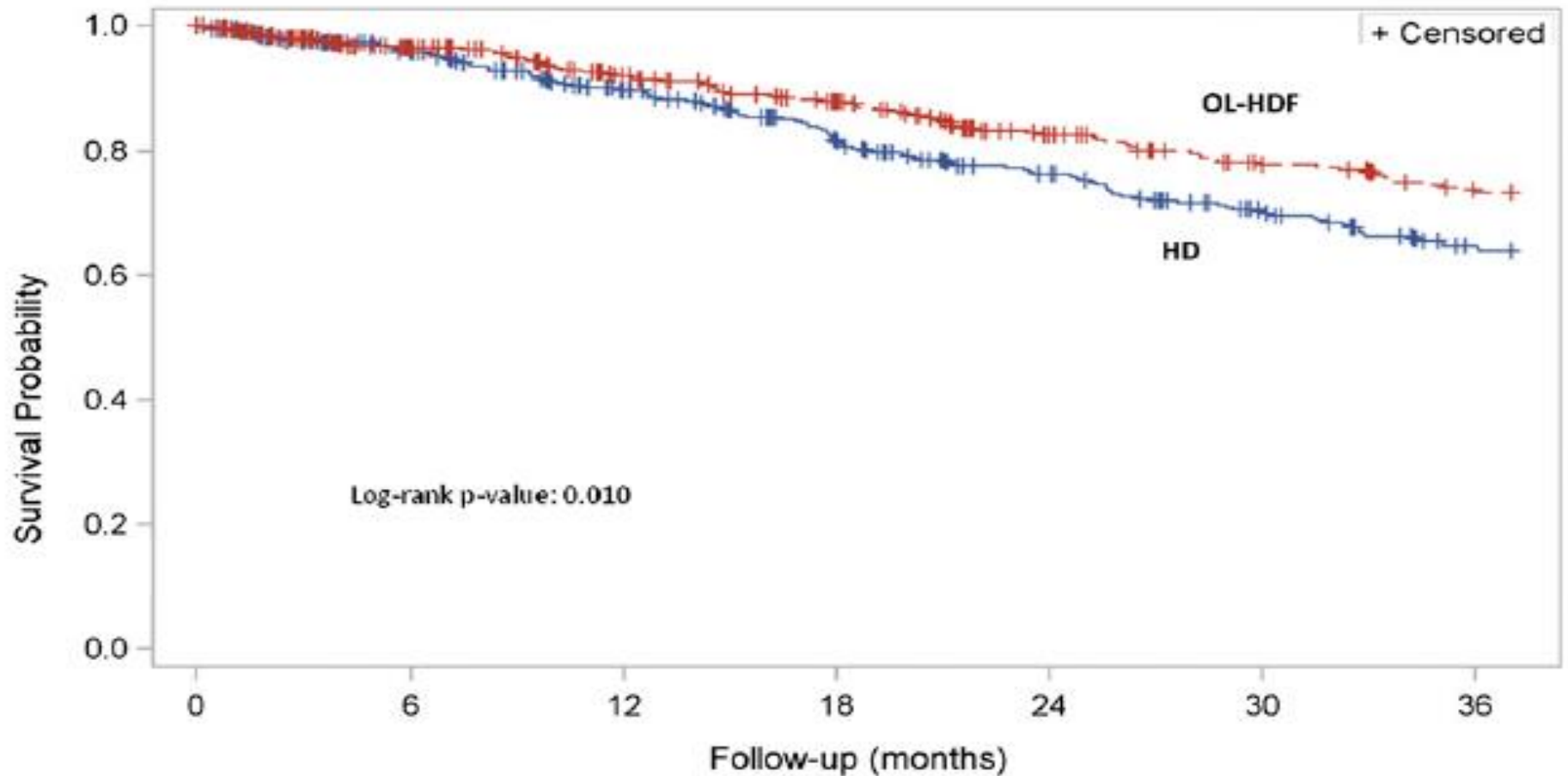
High-Efficiency Postdilution Online Hemodiafiltration Reduces All-Cause Mortality in Hemodialysis Patients

Francisco Maduell,^{*} Francesc Moreso,[†] Mercedes Pons,[‡] Rosa Ramos,[§] Josep Mora-Macià,^{||} Jordi Carreras,[¶] Jordi Soler,^{**} Ferran Torres,^{††‡‡} Josep M. Campistol,^{*} and Alberto Martinez-Castelao,^{§§} for the ESHOL Study Group

Study Populations

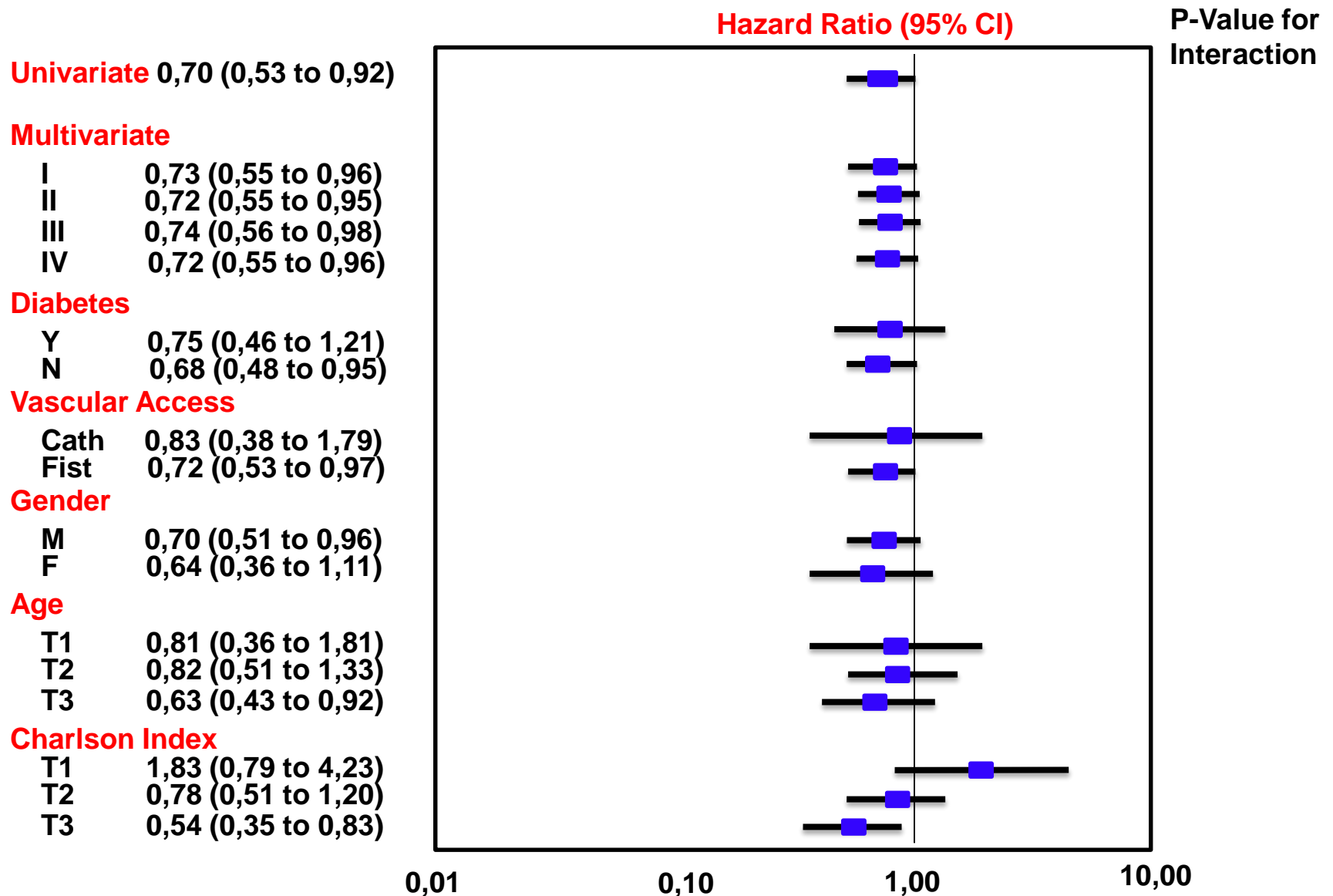


36 months survival in the intention to treat population ($p=0,001$ by the long rank test)



| | | | | | | | |
|--------|-----|-----|-----|-----|-----|-----|-----|
| HD | 450 | 388 | 327 | 275 | 235 | 196 | 165 |
| OL-HDF | 456 | 367 | 318 | 284 | 232 | 200 | 179 |

Analyses for the main outcome showing HRs (95% CIs) for the intervention based on relevant variable that were found to be independent predictors for all-cause mortality



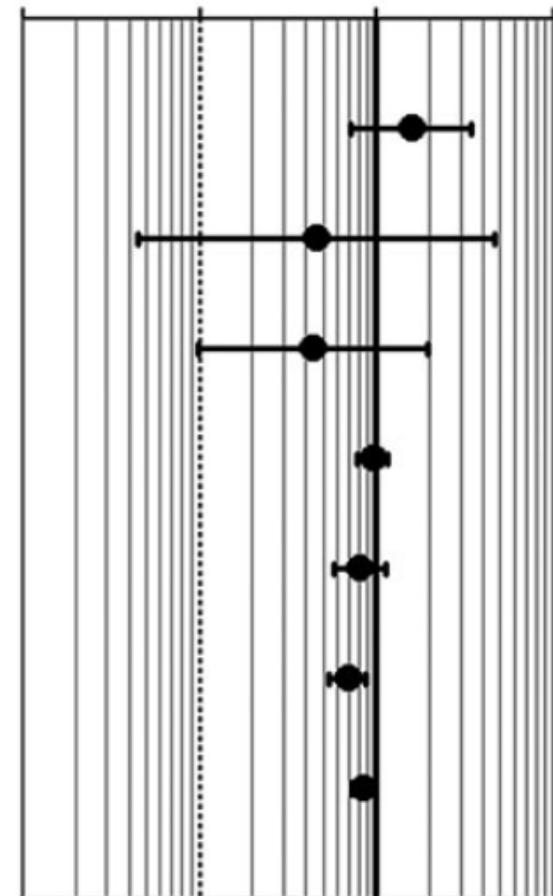
Clinical Evidence on Hemodiafiltration: A Systematic Review and a Meta-analysis

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 EUDIAL¹ – an official ERA-EDTA Working Group

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

| Studyname | 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 |

Relative Risk
 favours HDF 0.01 0.1 1 10 favours HD

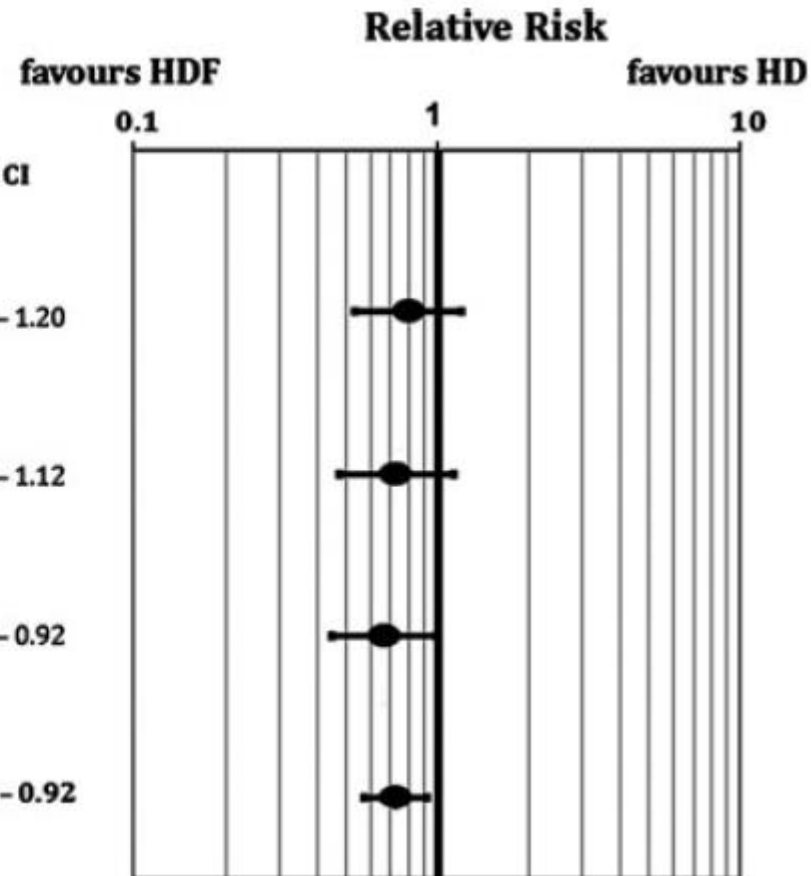


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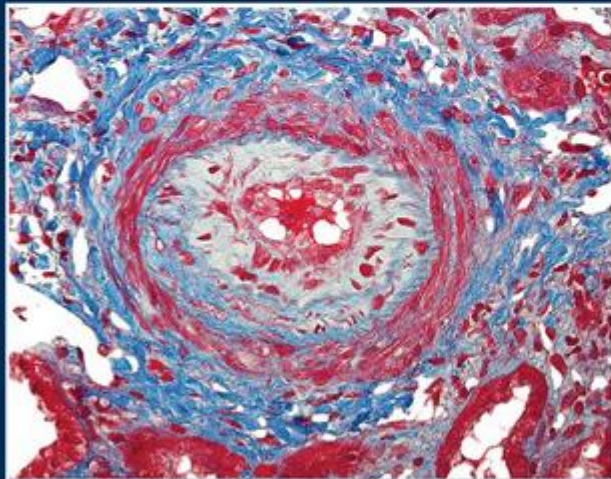
Meta-analysis of all RCTs comparing CARDIOVASCULAR MORTALITY in patients treated with HD or HDF

| 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 |



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Thrombotic Microangiopathy Following IV Abuse of the Opioid Agonist Oxycodone, p. 1022

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Therapies

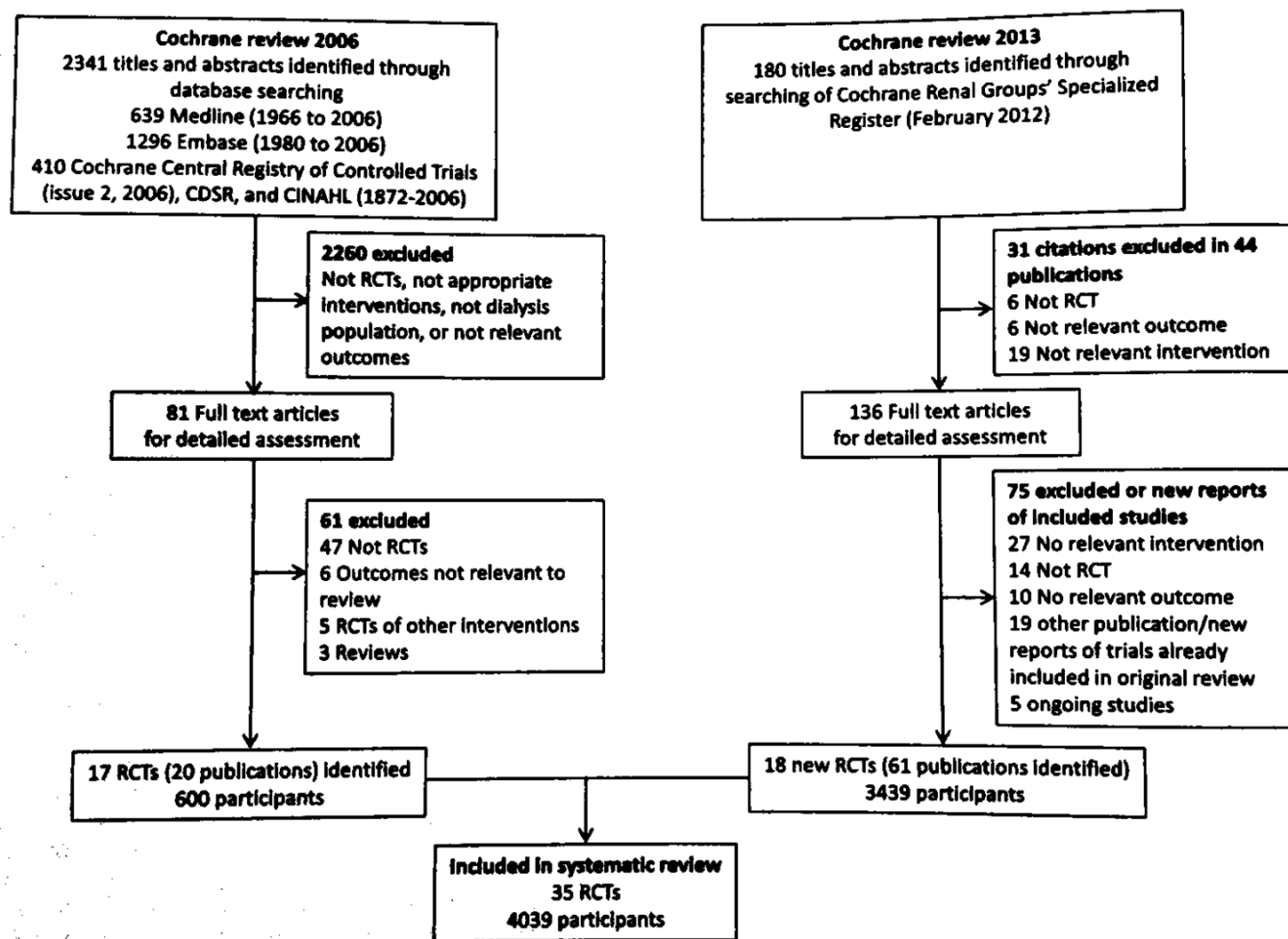
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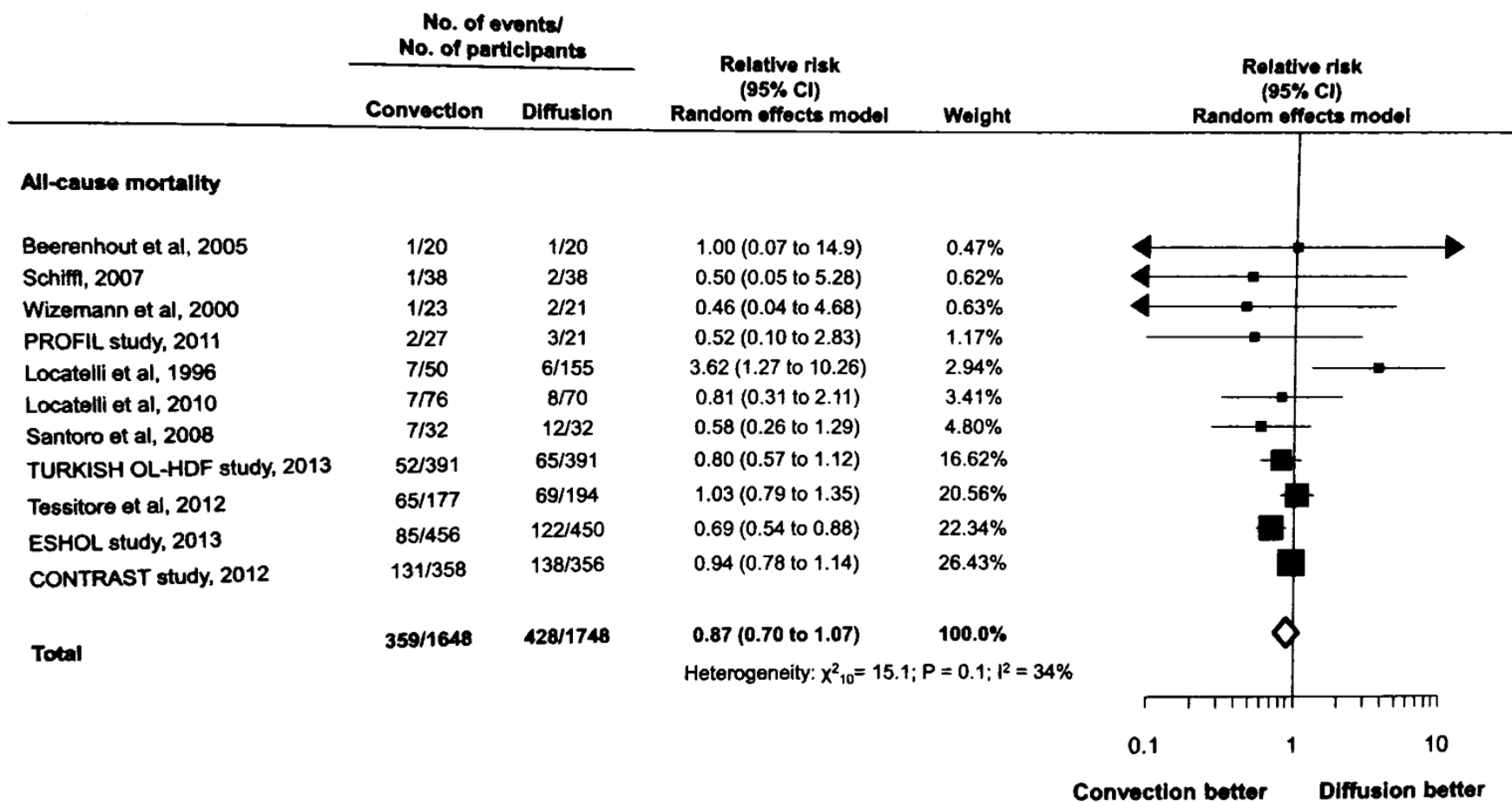
Convective Versus Diffusive Dialysis Therapies for Chronic Kidney Failure: An Updated Systematic Review of Randomized Controlled Trials

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}



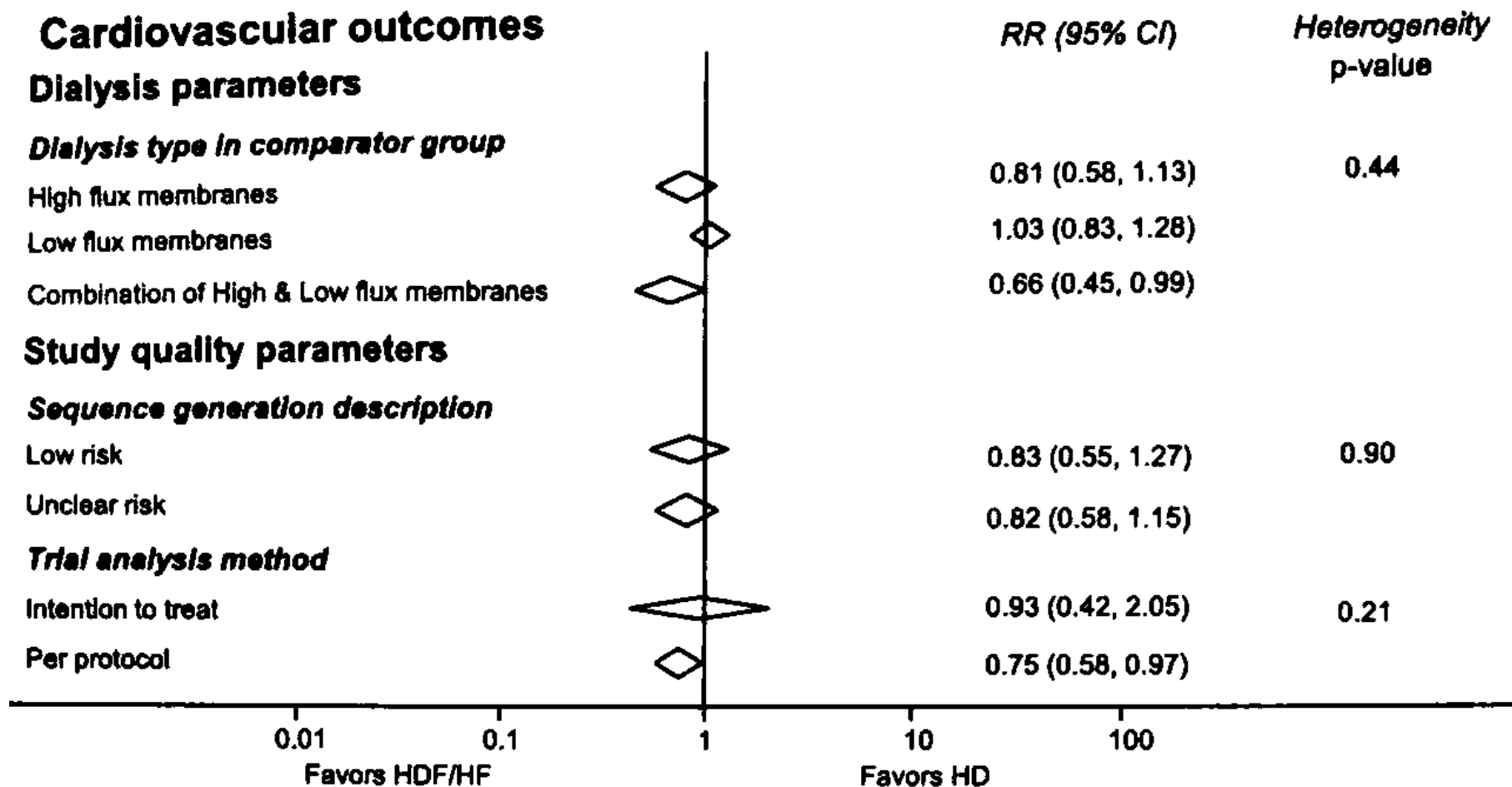
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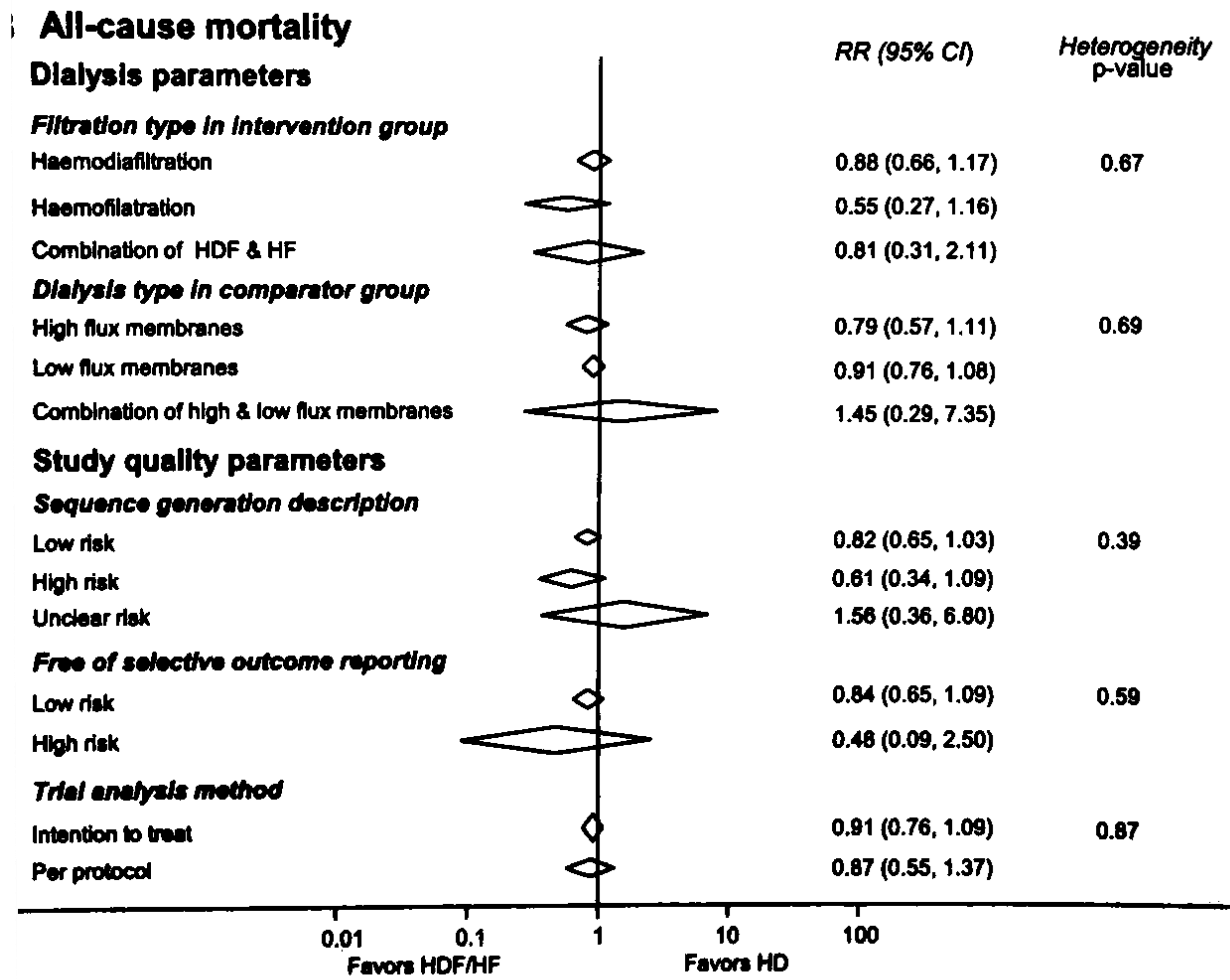
Effect of Hemodiafiltration or Hemofiltration Compared With Hemodialysis on Mortality and Cardiovascular Disease in Chronic Kidney Failure: A Systematic Review and Meta-analysis of Randomized Trials

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
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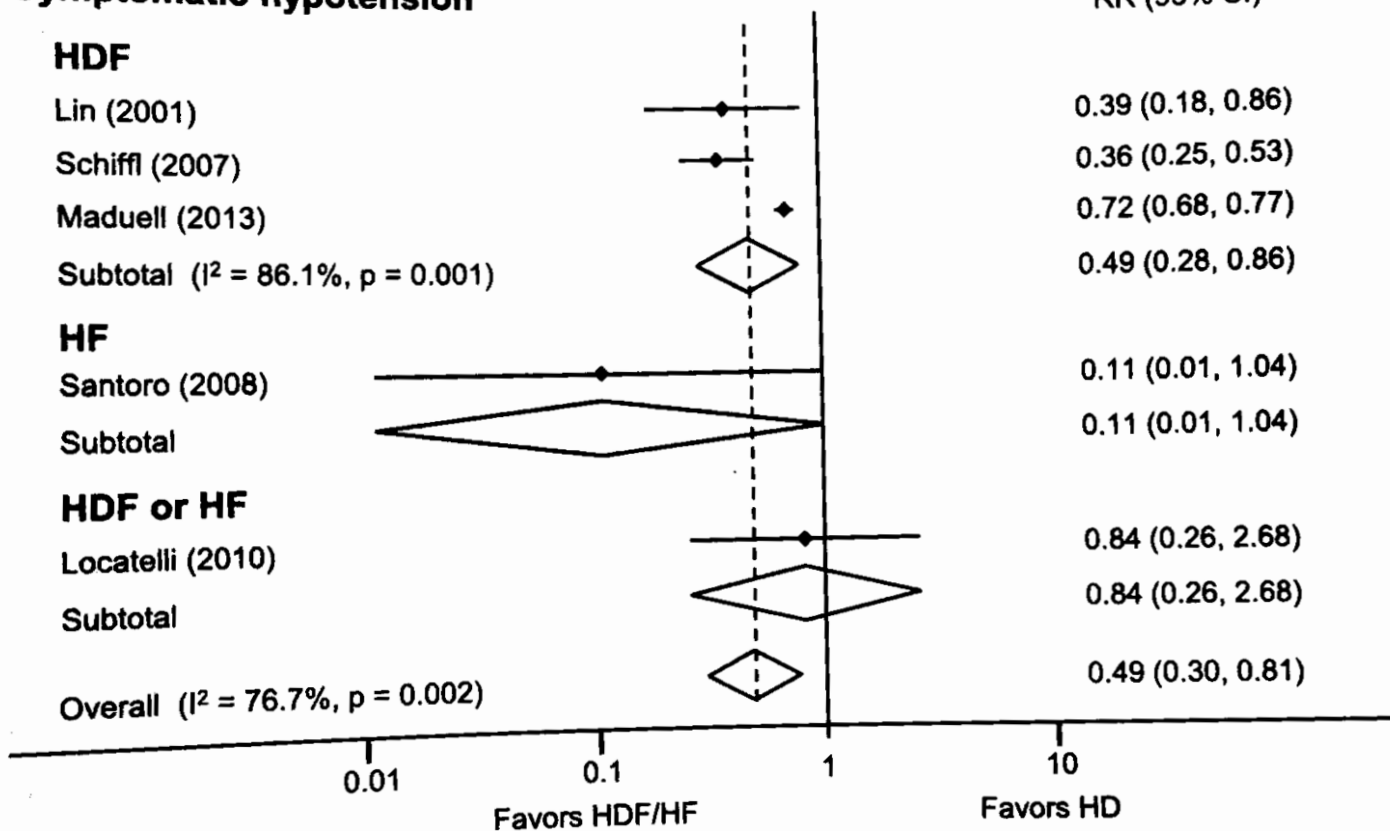
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Meg J. Jardine, MBBS, PhD, FRACP^{1,2}

Symptomatic hypotension



CONCLUSIONS

- Online Haemodiafiltration, is an established RRT modality in routine clinical practice for over two decades.
- Several clinical studies have reported upon the improved patient outcomes with Online Haemodiafiltration.
- Ever since the DOPPS data indicating that patient high-efficiency Online Haemodiafiltration improves outcomes, the focus has been on randomised controlled trials examining the impact of high convective volumes on patient survival.

CONCLUSIONS

- OL-HDF currently represents the most technically advanced dialysis treatment available.
- Widespread clinical experience with this RRT modality for ~ 3 decades has confirmed its safety and efficacy.
- Widespread implementation of this technique has been delayed pending conclusive evidence of its benefits from randomized studies.

The results of the ESHOL Study should be considered as an important step towards making OL-HDF a gold standard treatment for patients with CKD.

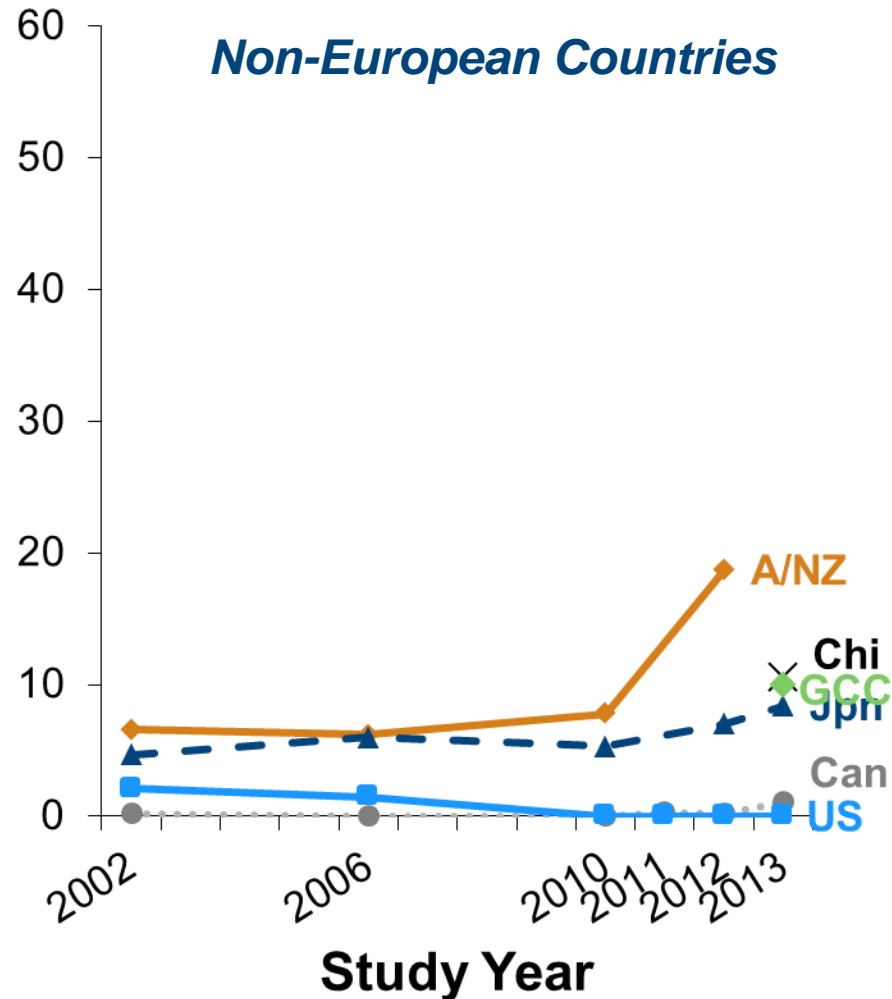
Locatelli, F. & Hörl, W. H. Nat. Rev. Nephrol. Advance online publication 16 April 2013

HDF Trends by Country

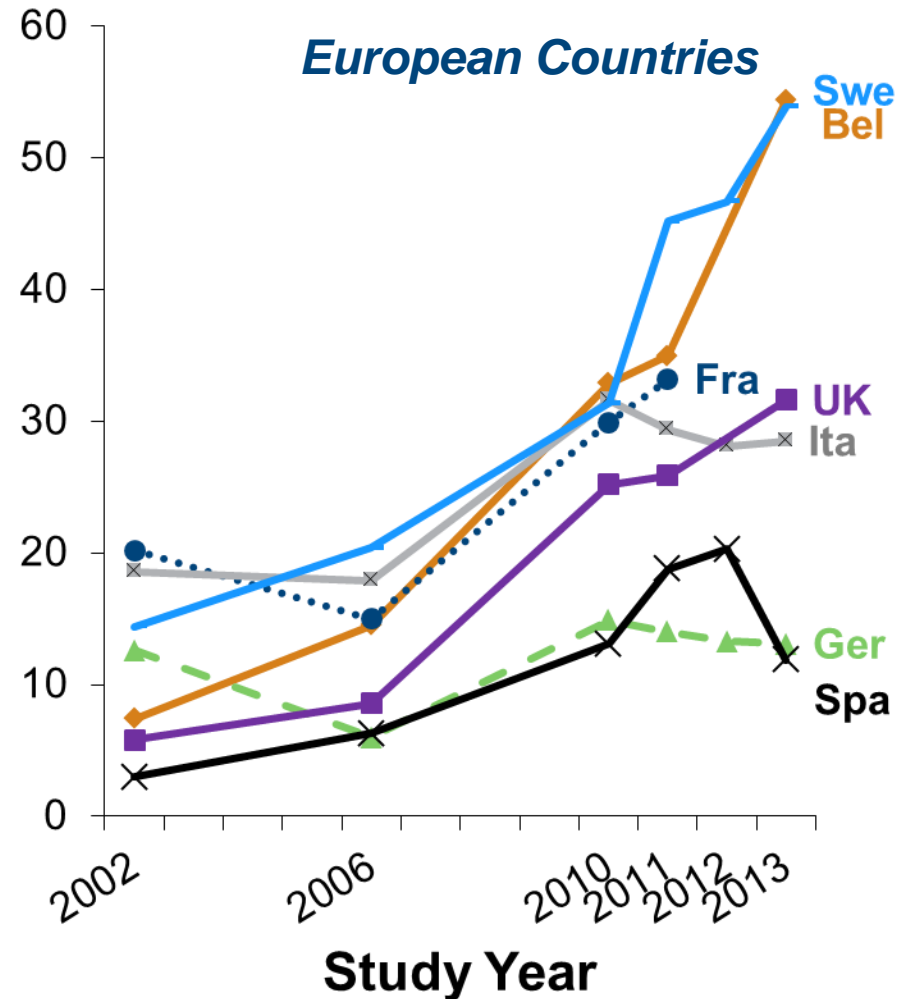
– DOPPS 2-5 (2002-2013) –

HDF (%)

Non-European Countries



European Countries





Frank Gotch

Blood Purif 2013;35:93-105

How Can We Improve the Solute and Fluid Transport Prescriptions in Hemodialysis to Improve Patient Outcomes?

there is no support for the recommendation of the routine use of hemodiafiltration

Francesco Pope



Nat Rev Nephrol 9:316-318, 2013

A step towards making online haemodiafiltration a gold standard

The results of the ESHOL study should be considered as an important step towards making OL-HDF a gold standard treatment for patients with chronic kidney disease.



Francesco Locatelli