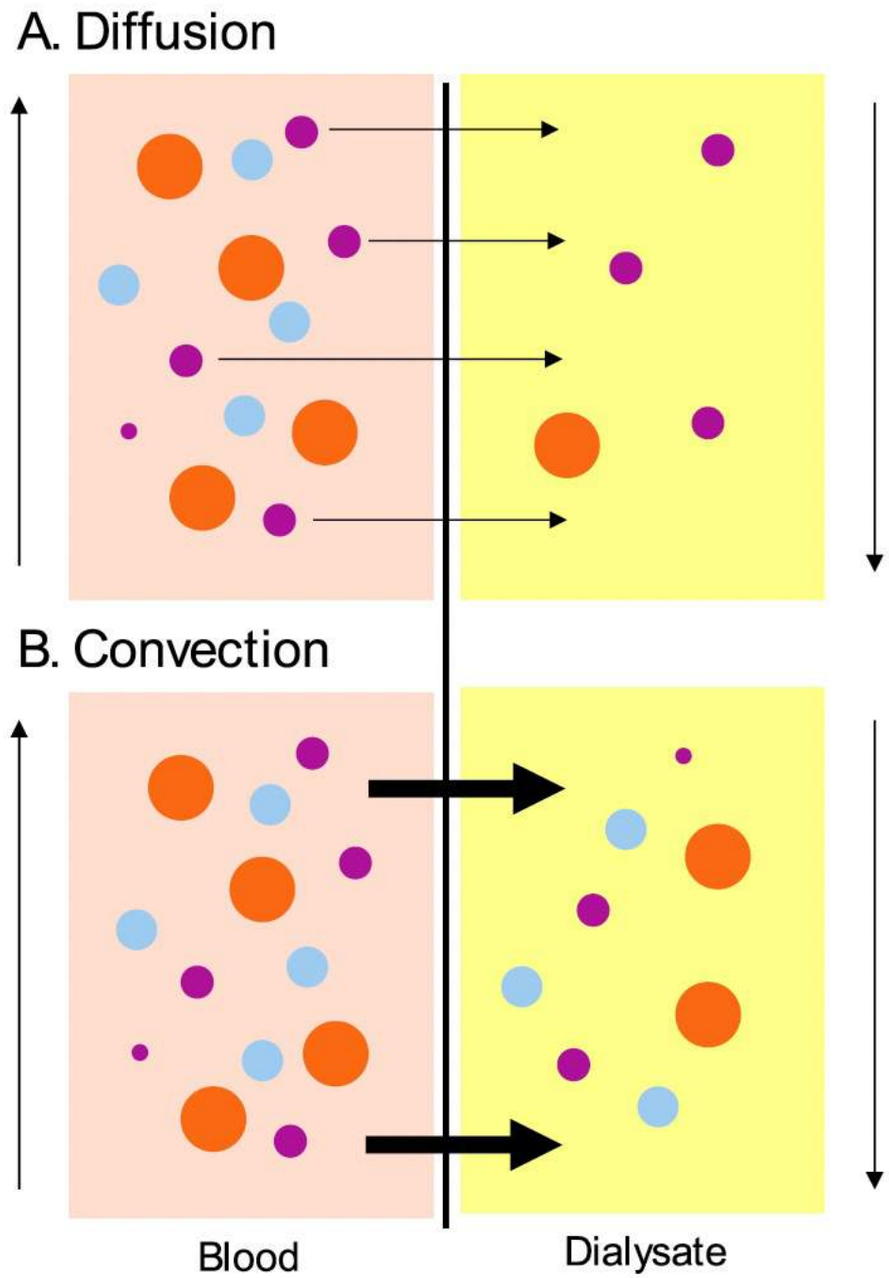
Hämodiafiltration versus Hämodialyse

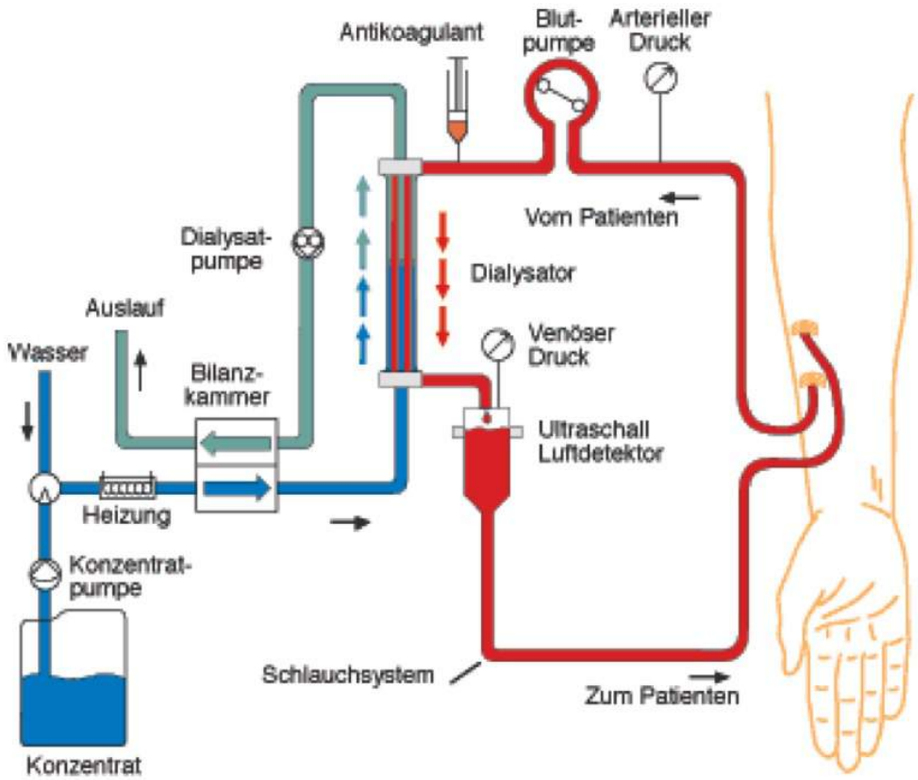
Helmut Reichel
Villingen-Schwenningen

Hemodiafiltration



Strippoli GFM, Green SC . *Clin Kidney J* 2024;https:/doi.org/10.1093/ckj/sfae035

Hemodiafiltration



Postulated advantages

- Enhanced clearance of middle molecules, larger molecules and protein-bound uremic toxins
- Better hemodynamic stability
- Reduced risk of cardiovascular complications
- Better phosphorus removal
- Reduction of oxdative stress and inflammatory reactions
- Amelioration of anemia
- Reduced risk of infections
- Improvement of neurological symptoms
- Improved clinical outcomes

Pedreros-Rosales C, et al. *Toxins* 2023; 15, 531. https://doi.org/10.3390/toxins15090531

Outcomes HDF vs HD (Cochrane-Review 2015)

Patient or population: men and women with end-stage kidney disease

Intervention: convective dialysis

Comparison: diffusive dialysis

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	No of partici-pants (studies)	Quality of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	Diffusion	Convection				
All-cause mortality	200 per 1000	Not significant	RR 0.87 (0.72 to 1.05)	11 (3396)	⊕⊕⊖⊖ **low**	Convective therapy has little or no effect on all-cause mortality
Cardiovascular mortality	100 per 1000	75 per 1000	RR 0.75 (0.81 to 0.92)	6 (2889)	⊕⊕⊖⊖ **low**	Convective therapy may reduce cardiovascular mortality
Nonfatal cardio-vascular events	130 per 1000	Not significant	RR 1.23 (0.93-1.63)	2 (1688)	⊕⊖⊖⊖ **very low**	Convective therapy has uncertain effects on non-fatal cardiovascular events
Health-related quality of life	Not estimable	Not estimable	Not estimable	8 (988)	⊕⊕⊖⊖ **very low**	Convective therapy has uncertain effects on health-related quality of life

*The **assumed risk** (e.g. the median control group risk across studies) is derived from data within dialysis registries for all-cause mortality and cardiovascular mortality and the reported event rate in the available study for nonfatal cardiovascular events (CONTRAST (Dutch) Study 2005). The **corresponding risk** (and its 95% confidence interval) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI). **CI:** Confidence interval; **RR:** Risk Ratio

GRADE (Grading of Recommendations Assessment, Development, and Evaluation) Working Group grades of evidence (Guyatt 2011).
Low quality: Indicates that our confidence in the effect estimate is limited: The true effect may be substantially difference from the estimated effect.
Very low quality: Indicated that we have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimated effect.

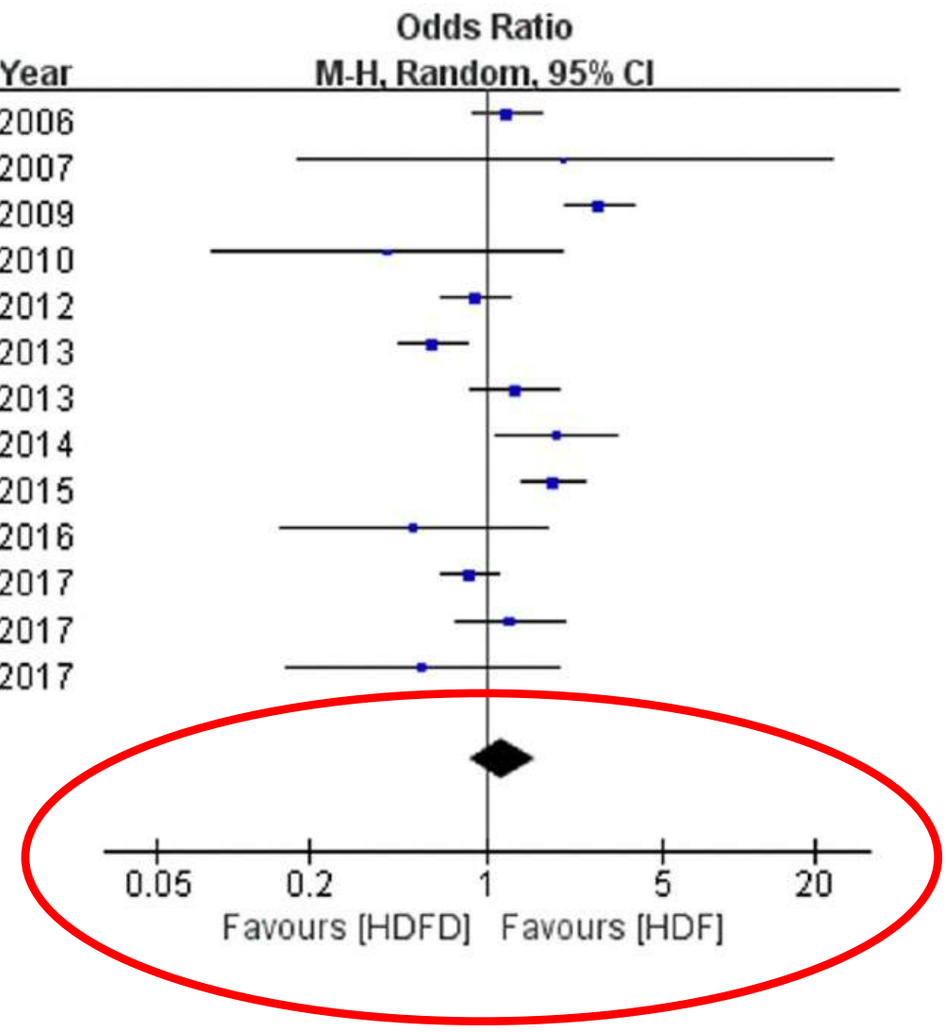
Nistor I, et al., *Cochrane Database Syst Rev* 2015; 5 :CD006258. https: //doi.org/10.1002/14651858

Mortality Outcomes HDF vs HD (Review 2023)

Study or Subgroup	HFHD Events	HFHD Total	HDF Events	HDF Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Canaud,2006	208	546	85	253	10.2%	1.22 [0.89, 1.66]	2006
Schiffl,2007	2	38	1	38	1.3%	2.06 [0.18, 23.68]	2007
Vilar,2009	369	626	79	232	10.1%	2.78 [2.03, 3.81]	2009
Locatelli F,2010	2	40	8	70	2.7%	0.41 [0.08, 2.02]	2010
Grooteman MP,2012	131	358	138	356	10.2%	0.91 [0.67, 1.23]	2012
Maduell F,2013	85	456	122	450	10.1%	0.62 [0.45, 0.84]	2013
Ok E,2013	65	391	52	391	9.5%	1.30 [0.88, 1.93]	2013
Imamović,2014	28	151	31	291	8.2%	1.91 [1.10, 3.32]	2014
Canaud,2015	149	795	88	795	10.4%	1.85 [1.39, 2.46]	2015
Djuric,2016	6	32	8	26	4.0%	0.52 [0.15, 1.75]	2016
Maduell F,2017	168	506	185	506	10.5%	0.86 [0.67, 1.12]	2017
Morena,2017	43	191	36	190	8.7%	1.24 [0.76, 2.04]	2017
Lei Lei,2017	5	34	8	34	3.9%	0.56 [0.16, 1.93]	2017
Total (95% CI)		**4164**		**3632**	**100.0%**	**1.16 [0.86, 1.57]**	
Total events	1261		841				

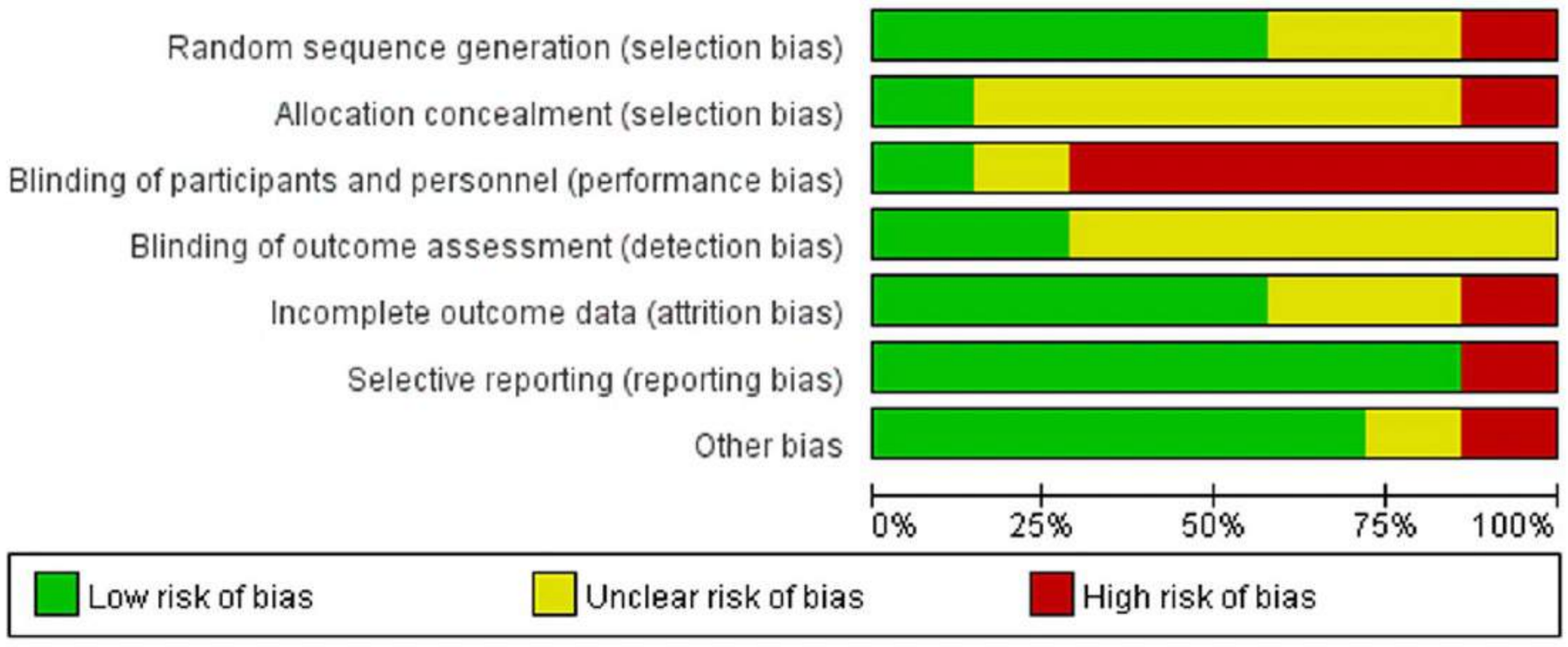
Heterogeneity: Tau² = 0.21; Chi² = 71.17, df = 12 (P < 0.00001); I² = 83%

Test for overall effect: Z = 0.95 (P = 0.34)



Ma S, et al. *Ren Fail* 2023, Vol. 45, No. 1, 2147436https://doi.org/10.1080/0886022X.2022.2147436

Bias risk diagram HDF vs HD studies (review 2023)



Ma S, et al. *Ren Fail* 2023, Vol. 45, No. 1, 2147436https://doi.org/10.1080/0886022X.2022.2147436

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

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ABSTRACT

In patients with ESRD, the effects of online hemodiafiltration on all-cause mortality and cardiovascular events are unclear. In this prospective study, we randomly assigned 714 chronic hemodialysis patients to online postdilution hemodiafiltration (n=358) or to continue low-flux hemodialysis (n=356). The primary outcome measure was all-cause mortality. The main secondary endpoint was a composite of major cardiovascular events, including death from cardiovascular causes, nonfatal myocardial infarction, nonfatal stroke, therapeutic coronary intervention, therapeutic carotid intervention, vascular intervention, or amputation. After a mean 3.0 years of follow-up (range, 0.4–6.6 years), we did not detect a significant difference between treatment groups with regard to all-cause mortality (121 versus 127 deaths per 1000 person-years in the online hemodiafiltration and low-flux hemodialysis groups, respectively; hazard ratio, 0.95; 95% confidence interval, 0.75–1.20). The incidences of cardiovascular events were 127 and 116 per 1000 person-years, respectively (hazard ratio, 1.07; 95% confidence interval, 0.83–1.39). Receiving high-volume hemodiafiltration during the trial associated with lower all-cause mortality, a finding that persisted after adjusting for potential confounders and dialysis facility. In conclusion, this trial did not detect a beneficial effect of hemodiafiltration on all-cause mortality and cardiovascular events compared with low-flux hemodialysis. On-treatment analysis suggests the possibility of a survival benefit among patients who receive high-volume hemodiafiltration, although this subgroup finding requires confirmation.

J Am Soc Nephrol 23: 1087–1096, 2012. doi: 10.1681/ASN.2011121140

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

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

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ABSTRACT

Retrospective studies suggest that online hemodiafiltration (OL-HDF) may reduce the risk of mortality compared with standard hemodialysis in patients with ESRD. We conducted a multicenter, open-label, randomized controlled trial in which we assigned 906 chronic hemodialysis patients either to continue hemodialysis (n=450) or to switch to high-efficiency postdilution OL-HDF (n=456). The primary outcome was all-cause mortality, and secondary outcomes included cardiovascular mortality, all-cause hospitalization, treatment tolerability, and laboratory data. Compared with patients who continued on hemodialysis, those assigned to OL-HDF had a 30% lower risk of all-cause mortality (hazard ratio [HR], 0.70; 95% confidence interval [95% CI], 0.53–0.92; P=0.01), a 33% lower risk of cardiovascular mortality (HR, 0.67; 95% CI, 0.44–1.02; P=0.06), and a 55% lower risk of infection-related mortality (HR, 0.45; 95% CI, 0.21–0.96; P=0.03). The estimated number needed to treat suggested that switching eight patients from hemodialysis to OL-HDF may prevent one annual death. The incidence rates of dialysis sessions complicated by hypotension and of all-cause hospitalization were lower in patients assigned to OL-HDF. In conclusion, high-efficiency postdilution OL-HDF reduces all-cause mortality compared with conventional hemodialysis.

J Am Soc Nephrol 24: 487–497, 2013. doi: 10.1681/ASN.2012080875

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

see commentary on page 1279

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]

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Large cohort studies suggest that high convective volumes associated with online hemodiafiltration may reduce the risk of mortality/morbidity compared to optimal high-flux hemodialysis. By contrast, intradialytic tolerance is not well studied. The aim of the FRENCHIE (French Convective versus Hemodialysis in Elderly) study was to compare high-flux hemodialysis and online hemodiafiltration in terms of intradialytic tolerance. In this prospective, open-label different in both groups. An improvement in the control of metabolic bone disease biomarkers and β2-microglobulin level without change in serum albumin concentration was observed with online hemodiafiltration. Thus, overall outcomes favor online hemodiafiltration over high-flux hemodialysis in the elderly.

Kidney International (2017) **91,** 1495–1509; http://dx.doi.org/10.1016/j.kint.2017.01.013

CONTRAST RCT: Postdilution HDF vs low flux HD: Beta-2-microglobulin removal

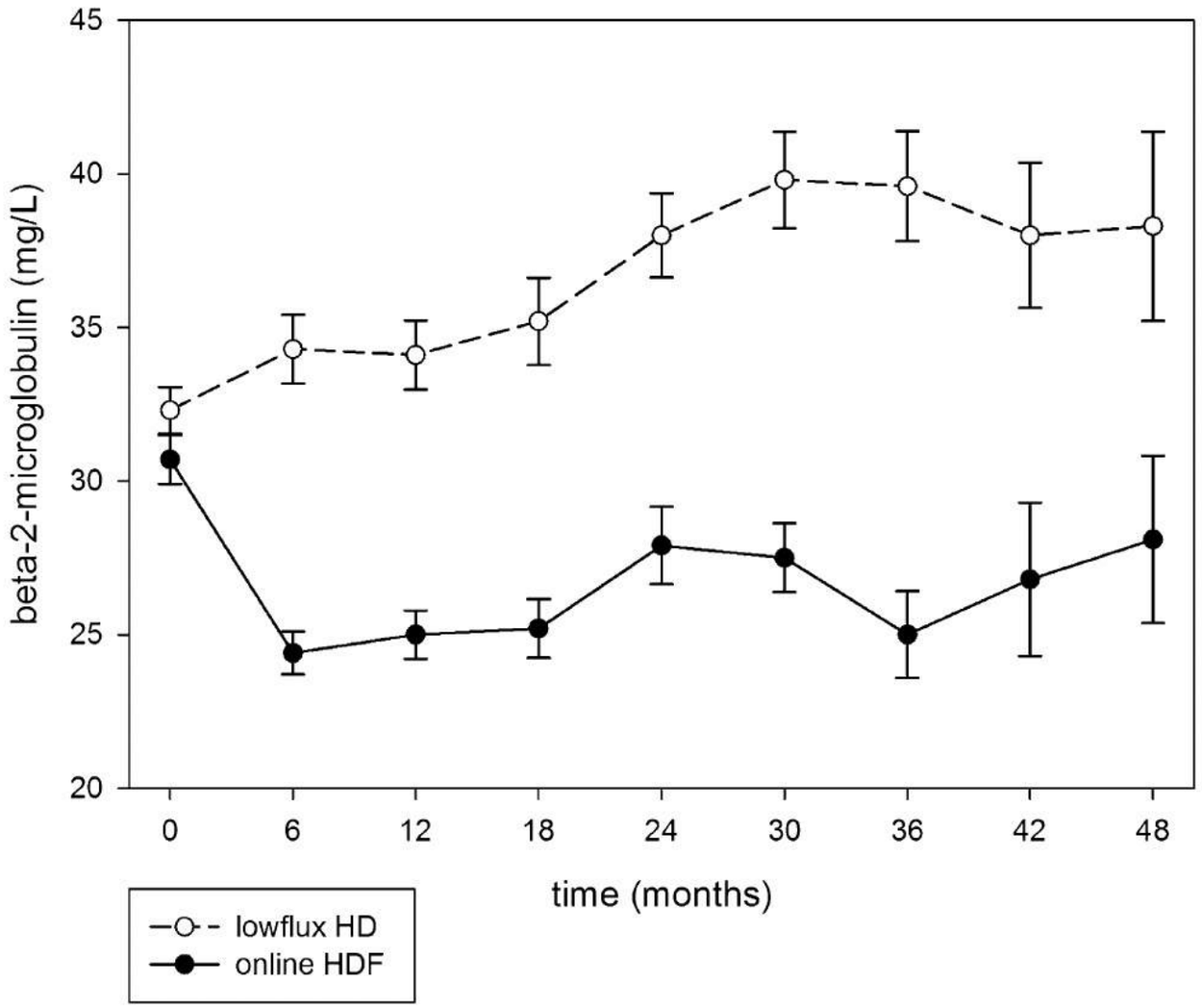
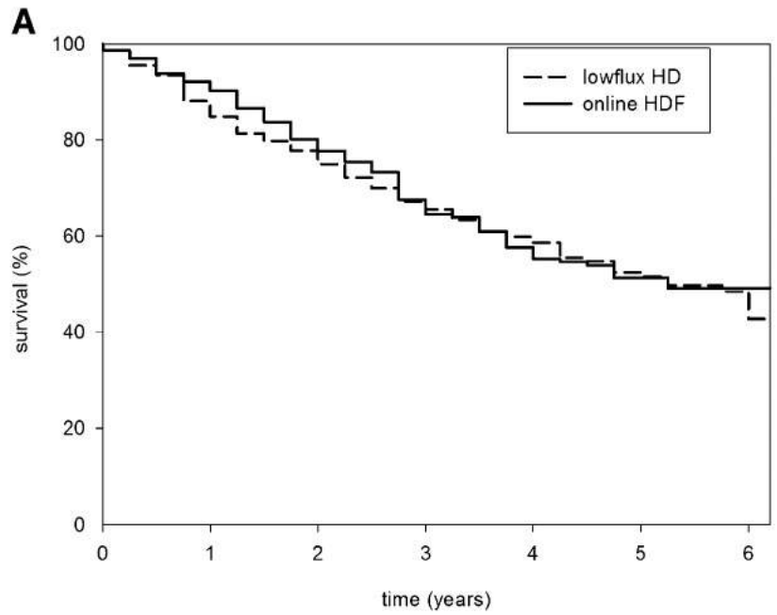


Figure 2. Predialysis β-2-microglobulin levels in patients treated with online hemodiafiltration and low-flux hemodialysis (mean ± SEM) using measurements of individuals at those time points. The difference between β-2-microglobulin levels for both treatments was significant ($P<0.001$).

n=714; mean follow-up 3.0 yrs

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

CONTRAST RCT: Postdilution HDF vs low-flux HD: Overall mortality (A) and cardiovascular mortality (B)



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

CONTRAST posthoc analysis: Outcomes according to convection volumes

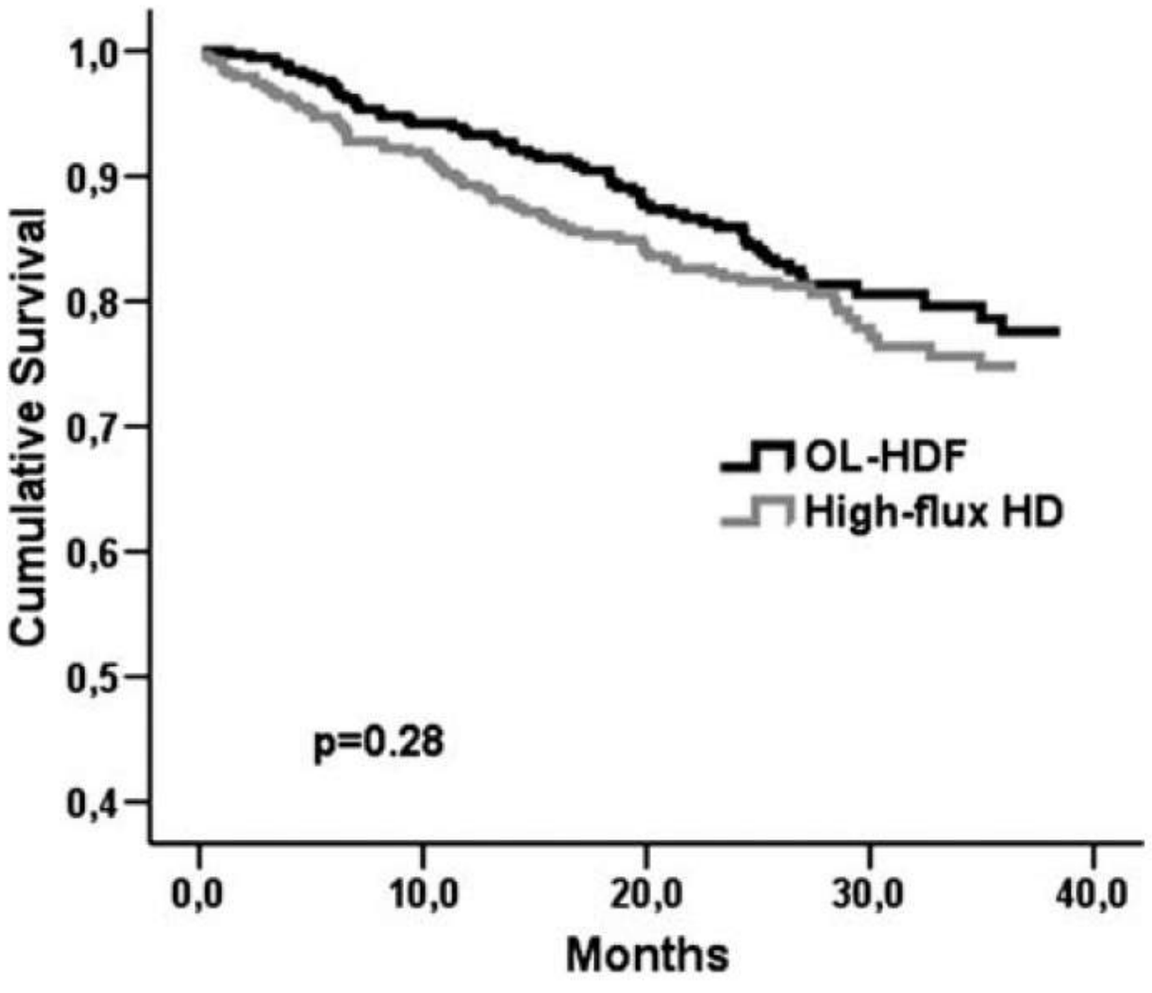
	Hemodialysis	Online Hemodiafiltration Convection Volume Tertiles			*P* for Trend
		<18.17 L	18.18–21.95 L	>21.95 L	
Total mortality					
crude	1.0	0.95 (0.66–1.38)	0.83 (0.57–1.22)	0.62 (0.41–0.93)	0.010
adjusted[a]	1.0	0.79 (0.53–1.14)	0.77 (0.51–1.14)	0.65 (0.42–0.99)	0.012
adjusted[b]	1.0	0.80 (0.52–1.24)	0.84 (0.54–1.29)	0.61 (0.38–0.98)	0.015
Fatal and nonfatal cardiovascular events					
crude	1.0	1.37 (0.94–1.98)	1.06 (0.72–1.56)	0.76 (0.50–1.16)	0.473
adjusted[a]	1.0	1.41 (0.92–2.11)	0.93 (0.62–1.40)	0.77 (0.48–1.21)	0.369
adjusted[b]	1.0	1.35 (0.86–2.11)	1.04 (0.66–1.62)	0.72 (0.44–1.19)	0.475

Results reported as HR and 95% confidence interval, from Cox proportional hazards models. Reference is treatment with low-flux hemodialysis.
[a]Adjusted for determinants of mortality, *i.e.*, 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 (82 missing, 206 deaths, 182 cardiovascular events).
[b]Adjusted for the above-mentioned determinates as well as for center differences (82 missing, 206 deaths, 182 cardiovascular events).

Overall: Relative mortality risk = 0.95 for hemodiafiltration versus HD (90% CI 0.75–1.20)

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

Turkish Online HDF Study: Postdilution HDF vs high-flux HD
Outcome: Overall mortality



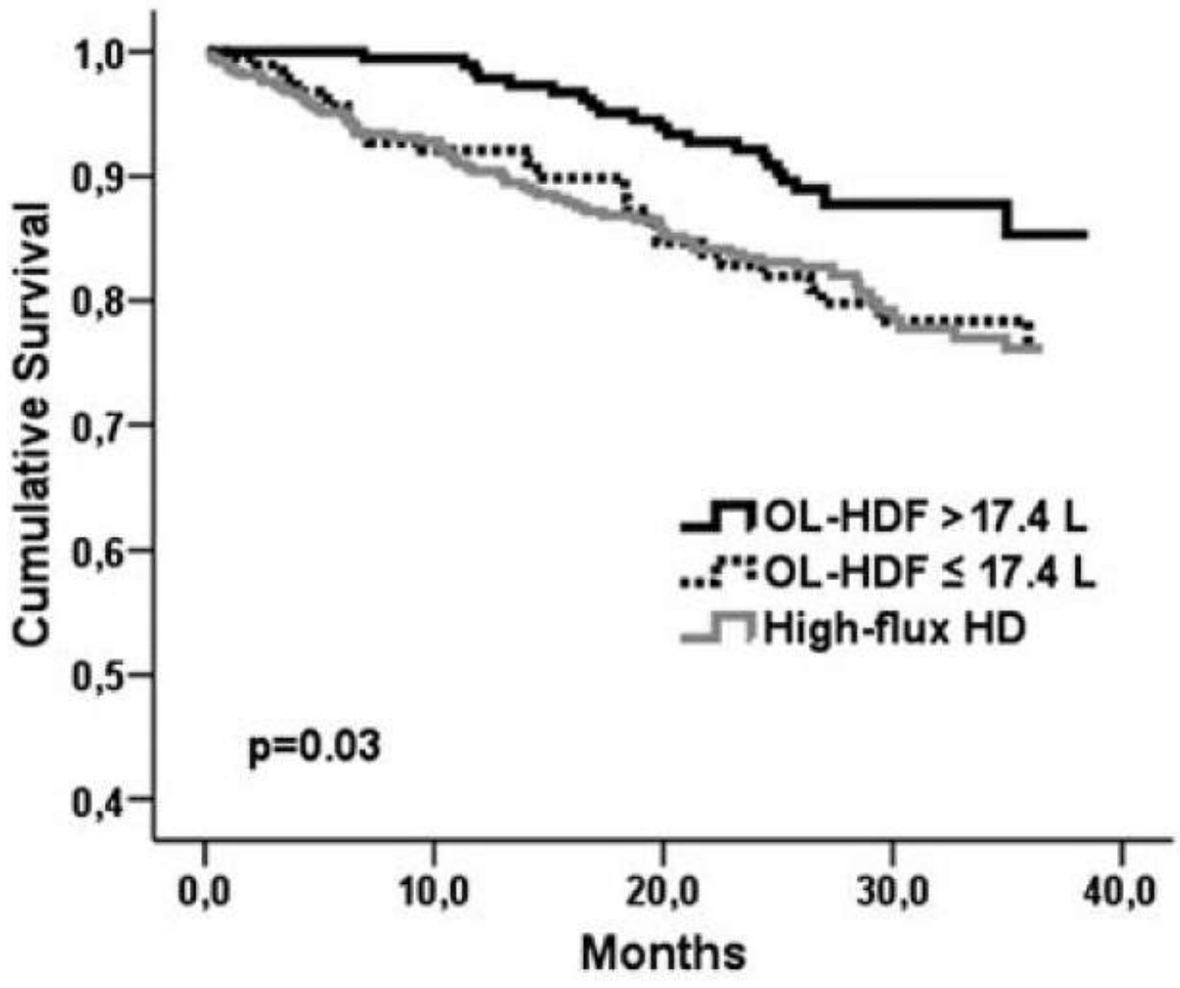
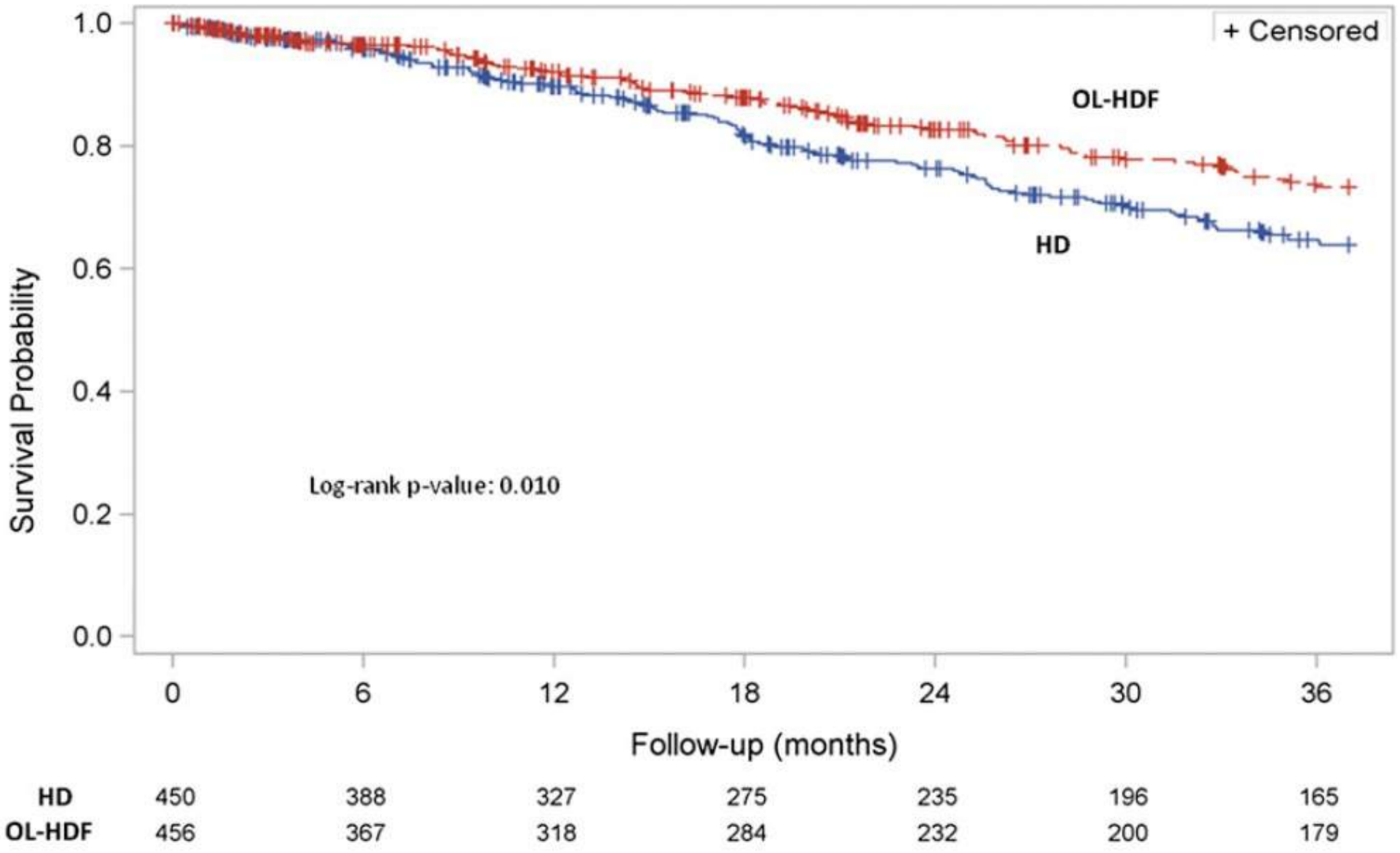


Fig. 2. Composite event-free survival in patients treated with OL-HDF and high-flux HD.

n=782, mean follow-up 22.8 months, median substitution volume 17.4 l

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

ESHOL RCT: Postdilution HDF vs high-flux HD
Outcome on overall mortality



n=906; mean follow-up 1,91 yrs; median quarterly convective volume 20.8-21.8 l/session

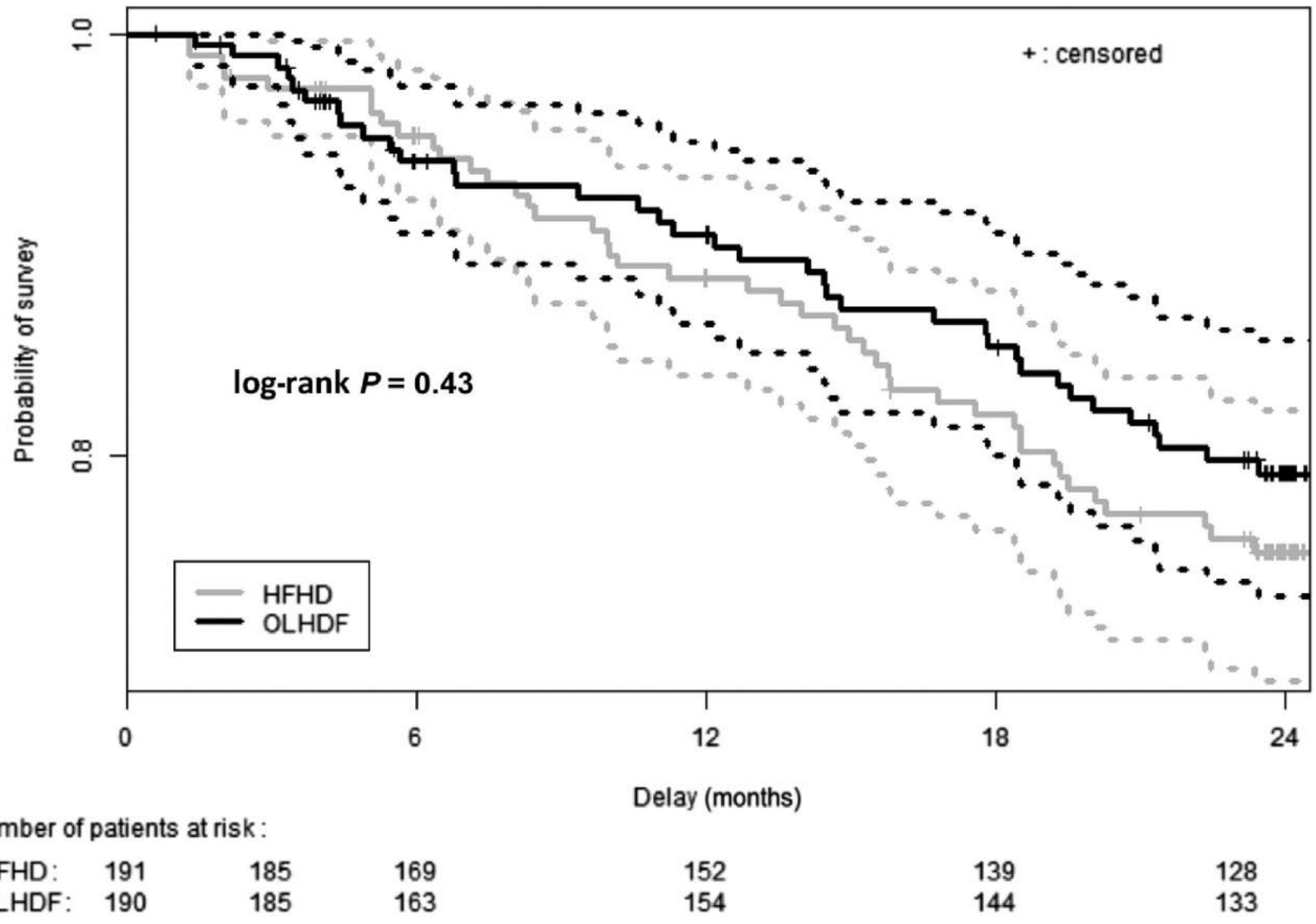
Maduell F, et al. *J Am Soc Nephrol* 2013;24:487-497

ESHOL RCT: Postdilution HDF vs high-flux HD
Mortality outcomes in subgroups

	Hemodialysis Group (*n*=450) (867.3 patient-years at risk)		OL-HDF Group (*n*=456) (863.1 patient-years at risk)		HR (95% CI)	*P*[a]
	Events	Events/100 Patient-Years	Events	Events/100 Patient-Years		
Death from any cause	122	14.1	85	9.8	0.70 (0.53–0.92)	0.01
Cardiovascular cause	55	6.3	37	4.3	0.67 (0.44–1.02)	0.06
Heart failure	10	1.2	7	0.8	0.69 (0.26–1.82)	0.46
Ischemic heart disease	15	1.7	14	1.6	0.93 (0.45–1.94)	0.86
Mesenteric thrombosis	6	0.7	5	0.6	0.84 (0.26–2.77)	0.78
Stroke	18	2.1	7	0.8	0.39 (0.16–0.93)	0.03
Dysrhythmia	5	0.6	3	0.3	0.59 (0.14–2.47)	0.46
Peripheral arteriopathy	1	0.0	1	0.0	0.97 (0.06–15.48)	0.98
Infection	22	2.5	10	1.2	0.45 (0.21–0.96)	0.03
Tumor	6	0.7	10	1.2	1.67 (0.61–4.59)	0.32
Sudden death	14	1.6	14	1.6	0.99 (0.47–2.08)	0.98
Cachexia	8	0.9	4	0.5	0.51 (0.15–1.70)	0.27
Death from other causes	17	2.0	10	1.2	0.59 (0.27–1.28)	0.18

Maduell F, et al. *J Am Soc Nephrol* 2013;24:487-497

FRENCH HDF study: Postdilution HDF vs high flux HD
Secondary outcome: overall mortality



n=381; age > 65 yrs, primary outcomes were intradialytic tolerance: positive effect of HDF and HRQoL: no effect of HDF; no effect of HDF on hospitalization

Morena M, et al. *Kidney Int* 2017;91:1495-1509

Indeterminate outcome of HDF RCTs

- Variations in study design
- Characteristics of patient study population
- Selection of control groups
- Possible selection bias
- Confounding factors (i.e. HD filter, targeted convection volume)

European HDF pooling project: Overall mortality and cause-specific mortality

Table 2. Risk ratio and HR and 95% CI of all-cause mortality and cause-specific mortality

Cause	HD			HDF			HR (95% CI) for HDF versus HD
	n	Events	Events/100 PY	*n*	Events	Events/100 PY	
All-causes	1369	410	12.10	1367	359	10.45	0.86 (0.75; 0.99)
Cardiovascular disease	1302	164	4.84	1289	128	3.73	0.77 (0.61; 0.97)
Infections	1302	77	2.27	1289	73	2.13	0.94 (0.68; 1.30)
Sudden death	1302	56	1.65	1289	56	1.63	0.99 (0.68; 1.43)

PY, person years.

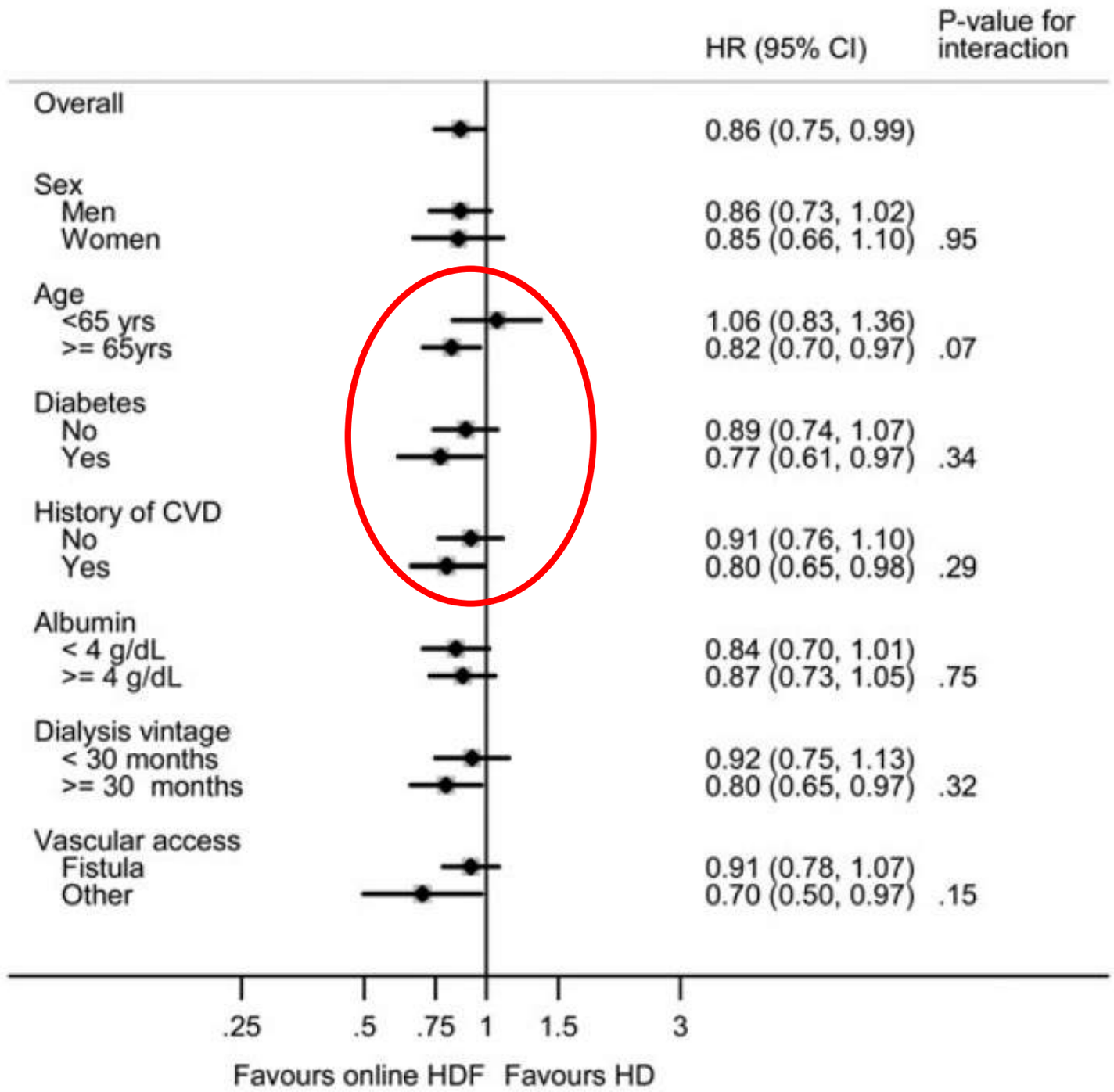
Completion of missing mortality follow-up data

- ESHOL 39% (352/355)
- French HDF study 11% (41/43)
- Turkish HDF study 25% (148/195)

n=2.793; median follow-up 2.5 yrs; mortality n=769; event rate/100 pts/yr 11.0

Peters SAE, et al. *Nephrol Dial Transplant* 2016;31:979-984

European HDF pooling project: Mortality in subgroups



Peters SAE, et al. *Nephrol Dial Transplant* 2016;31:979-984

European HDF pooling project: Effect of convection volume on outcomes

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, et al. *Nephrol Dial Transplant* 2016;31:978-984

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Hemodiafiltration or Hemodialysis on Mortality in Kidney Failure

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ABSTRACT

Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

CONVINCE: Methods

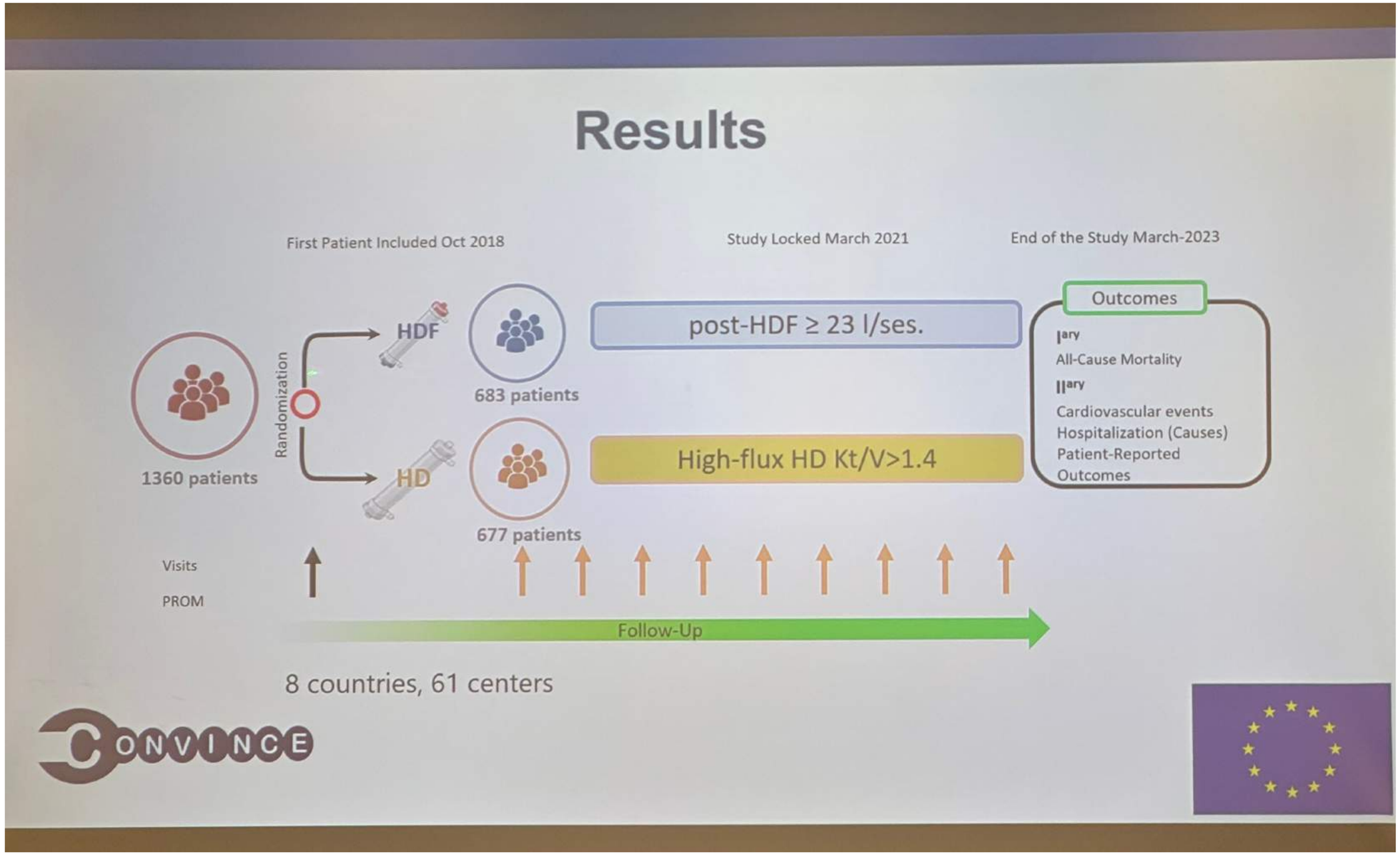
Prospective Randomized international multicenter clinical trial

Objectives	Description
Primary objective	To compare HDF when delivered consistently in high-dose, with high-flux HD-treatment in terms of all-cause mortality
Secondary objectives	1. Compare treatments in terms of cause-specific morbidity and mortality 2. Assess PROs to capture patient perspectives and compare between treatments 3. Assess cost-effectiveness of high-dose HDF

Supported by European Commission Research & Innovation Horizon 2020 program

Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

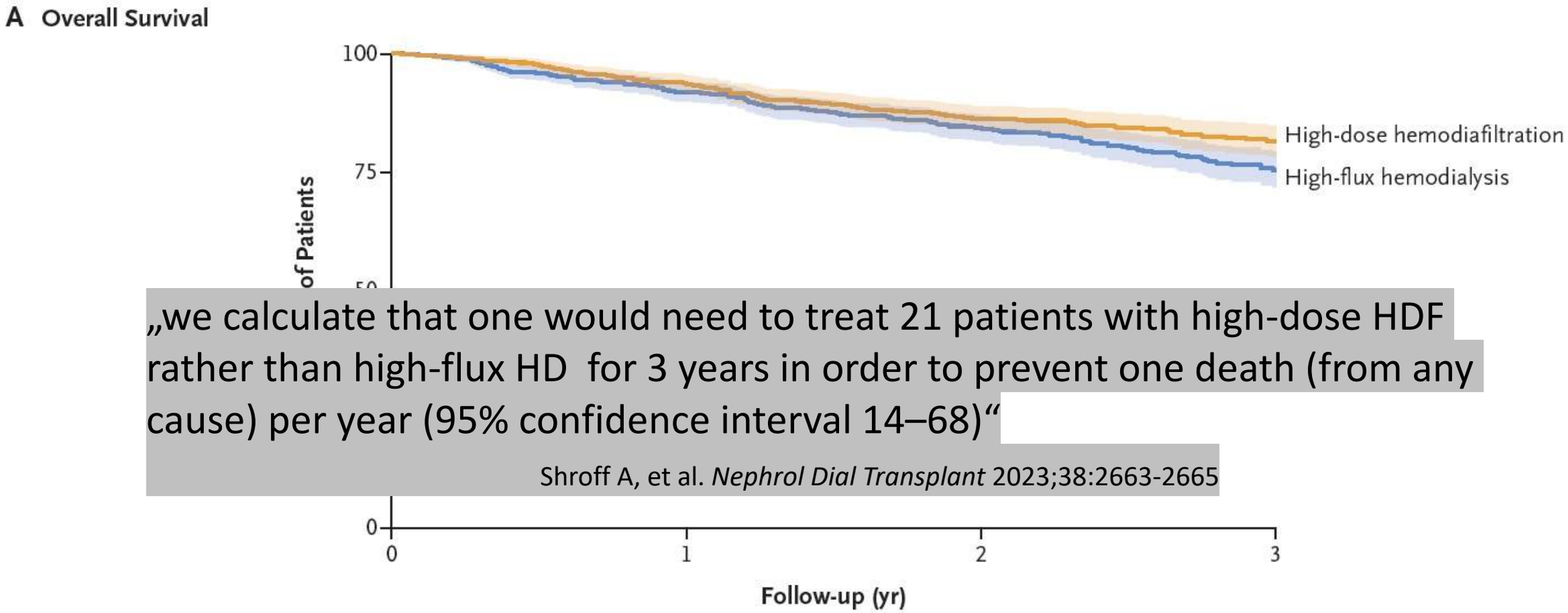
CONVINCE: Methods



61 clinics in 8 countries, 7 academic centers, 54 centers from dialysis providers; randomisation from: 11/2018-04/2021

Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

CONVINCE: Primary outcome overall survival



„we calculate that one would need to treat 21 patients with high-dose HDF rather than high-flux HD for 3 years in order to prevent one death (from any cause) per year (95% confidence interval 14–68)“

Shroff A, et al. *Nephrol Dial Transplant* 2023;38:2663-2665

HR 0.77 (0.65-0.93), p=0.005; 7.13 vs 9.19 events per 100 patient years, median follow-up 30 months

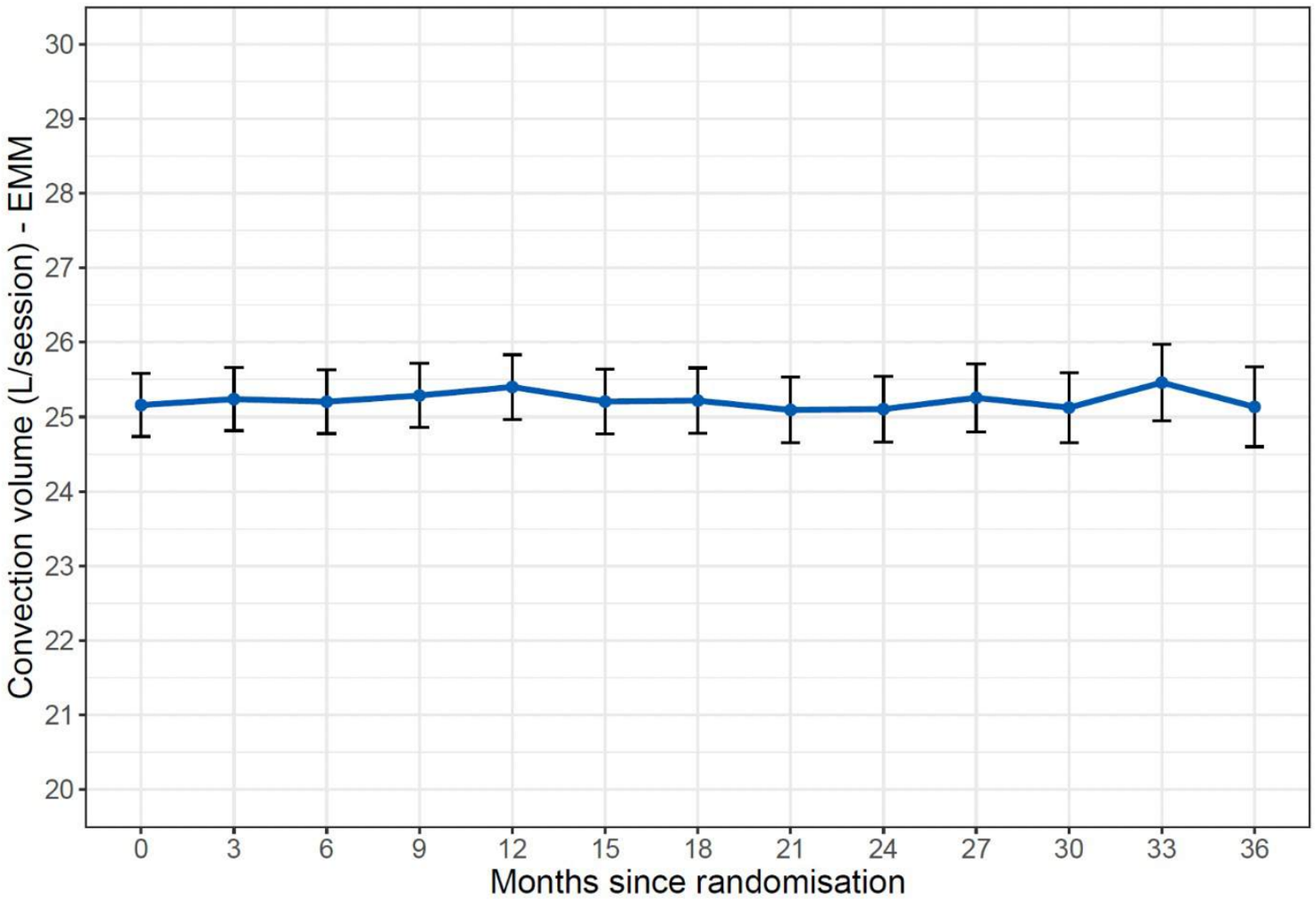
Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

CONVINCE: Patient characteristics and treatment modalities

Baseline data		
	HDF	High-flux HD
Age (yrs)	62.5 ± 13.5	62.3 ± 13.5
Blood flow (ml/min)	369 ± 54	367 ± 56
Median vintage (IQR) (months)	35 (16-78)	30 (14-67)
Median duration of session (IQR) (min)	240 (240-248)	240 (240-245)
Median single pool Kt/V (IQR)	1.61 (1.45-1.83)	1.61 (1.42-1.80)
Diabetes mellitus (%)	33.7	37.1
Any cardiovascular disease (%)	43.3	46.7

Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

Convection volume across visits for HDF group



Average levels during the trial and mean difference over time between treatment arms obtained through linear mixed models using the on trial measurements with adjustments for baseline measurements and trial site included as random effect. Values are means (95% CI). NA, not applicable.

Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

CONVINCE: Causes of death

Table 2. Primary and Secondary Outcomes.*

Variable	High-Dose Hemodiafiltration (N=683)		High-Flux Hemodialysis (N=677)		Hazard Ratio (95% CI)†
	no. (%)	*no. of events/ 100 patient-yr (95% CI)*	*no. (%)*	*no. of events/ 100 patient-yr (95% CI)*	
Primary outcome					
Death from any cause	118 (17.3)	7.13 (5.90–8.54)	148 (21.9)	9.19 (7.77–10.79)	0.77 (0.65–0.93)
Secondary outcomes					
Death					
Cardiovascular	31 (4.5)	1.87 (1.27–2.66)	37 (5.5)	2.30 (1.62–3.17)	0.81 (0.49–1.33)
Noncardiovascular	87 (12.7)	5.26 (4.21–6.48)	111 (16.4)	6.89 (5.67–8.30)	0.76 (0.59–0.98)
Infection-related					
Including Covid-19	38 (5.6)	2.30 (1.62–3.15)	54 (8.0)	3.35 (2.52–4.37)	0.69 (0.49–0.96)
Excluding Covid-19	23 (3.4)	1.39 (0.88–2.09)	33 (4.9)	2.05 (1.41–2.88)	0.68 (0.42–1.10)
Fatal or nonfatal cardiovascular outcome‡	136 (19.9)	9.05 (7.60–10.71)	126 (18.6)	8.48 (7.07–10.10)	1.07 (0.86–1.33)
Kidney transplantation	75 (11.0)	4.80 (3.77–6.01)	71 (10.5)	4.72 (3.69–5.96)	1.01 (0.71–1.44)
Recurrent hospitalization — no.§					
For any nonfatal cause	998	61.34 (57.59–65.27)	895	56.36 (52.73–60.18)	1.11 (0.98–1.25)
Infection-related					
Including Covid-19	234	14.32 (12.54–16.28)	219	13.92 (12.14–15.88)	1.06 (0.86–1.30)
Excluding Covid-19	152	9.34 (7.92–10.95)	156	9.82 (8.34–11.49)	0.97 (0.74–1.26)

7.13 vs 9.19 Events per 100 patient years, p=0.005

Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

CONVINCE: Causes of death

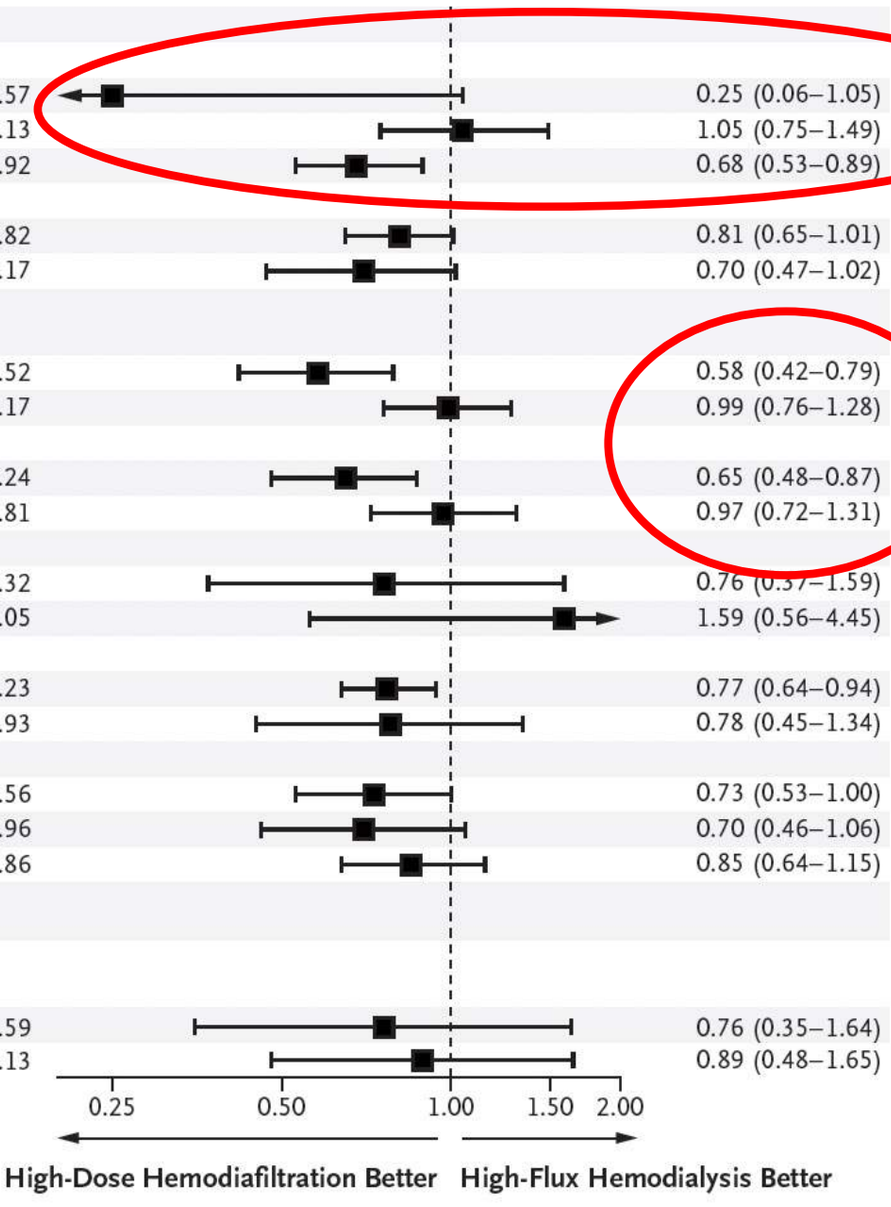
	HDF		High-flux HD		Hazard ratio
	no.	Events/100 pt yrs	no.	Events/100 pt yrs	
Overall	118	7.13	148	9.19	0.77 (0.65-0.93)
Cardiovascular	31	1.87	37	2.30	0.81 (0.49-1.33)
Non-cardiovascular	87	5.26	111	6.89	0.76 (0.59-0.98)
Infection-related	38	2.30	54	3.35	0.69 (0.49-0.96)
Infection-related (exluding COVID19)	23	1.39	33	2.05	0.68 (0.42-1.10)
No effect on hospitalization					

Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

CONVINCE: Overall survival in subgroups

B Risk of Death

Subgroup	High-Dose Hemodia-filtration	High-flux Hemodialysis	High-Dose Hemodia-filtration	High-flux Hemodialysis	Hazard Ratio (95% CI)
	no. of events/no. of patients		*rate/100 person-yr*		
Death from any cause					
Age					
<50 yr	2/121	8/119	0.64	2.57	0.25 (0.06–1.05)
50 to 65 yr	49/264	43/250	7.61	7.13	1.05 (0.75–1.49)
>65 yr	67/298	97/308	9.59	13.92	0.68 (0.53–0.89)
Sex					
Male	83/436	97/420	7.94	9.82	0.81 (0.65–1.01)
Female	35/247	51/257	5.74	8.17	0.70 (0.47–1.02)
Preexisting cardiovascular disease					
No	43/387	66/361	4.40	7.52	0.58 (0.42–0.79)
Yes	75/296	82/316	11.06	11.17	0.99 (0.76–1.28)
Preexisting diabetes					
No	54/453	76/426	4.72	7.24	0.65 (0.48–0.87)
Yes	64/230	72/251	12.50	12.81	0.97 (0.72–1.31)
Residual urinary output					
<1000 ml/24 hr	12/52	17/52	9.23	12.32	0.76 (0.37–1.59)
≥1000 ml/24 hr	6/30	3/26	6.67	4.05	1.59 (0.56–4.45)
Vascular access					
Fistula	97/558	123/557	7.16	9.23	0.77 (0.64–0.94)
Graft or catheter	21/125	25/120	6.98	8.93	0.78 (0.45–1.34)
Dialysis vintage					
<2 yr	37/267	51/281	5.59	7.56	0.73 (0.53–1.00)
2 to 5 yr	34/207	49/207	6.94	9.96	0.70 (0.46–1.06)
>5 yr	46/207	48/188	9.18	10.86	0.85 (0.64–1.15)
Death from cardiovascular causes					
Preexisting cardiovascular disease					
No	12/387	14/361	1.23	1.59	0.76 (0.35–1.64)
Yes	19/296	23/316	2.80	3.13	0.89 (0.48–1.65)



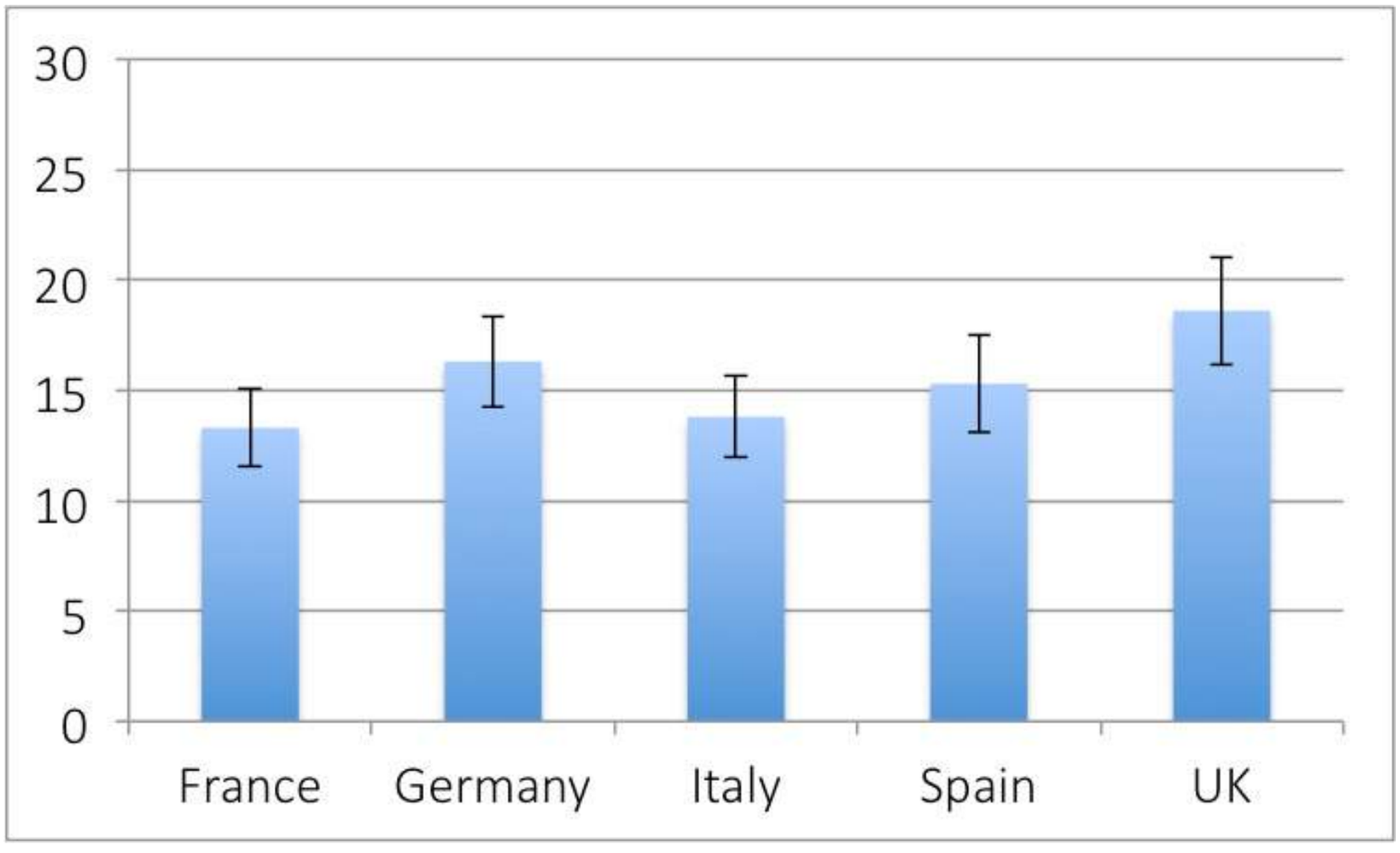
Blankestijn P, et al. *N Engl J Med* 2023;389:700-709

CONVINCE: Overall survival in subgroups

In der HDF Gruppe geringere Mortalität bei

- Älteren Patienten (> 65 Jahre); sehr niedrige event rate bei Patienten < 50 Jahre
- Patienten ohne Diabetes mellitus
- Patienten ohne kardiovaskuläre Erkrankung
- Patienten mit Eigengefäß-Shunt
- Patienten mit dialysis vintage < 2 years

Einjahres-Mortalitätsrate 1999-2000
(Dialysis Outcomes Practice Pattern Study)



Rayner FC, et al. *Nephrol Dial Transplant* 2004;19:108-120

Medianes Überleben älterer Hämodialysepatienten (Deutschland 2007-2013)

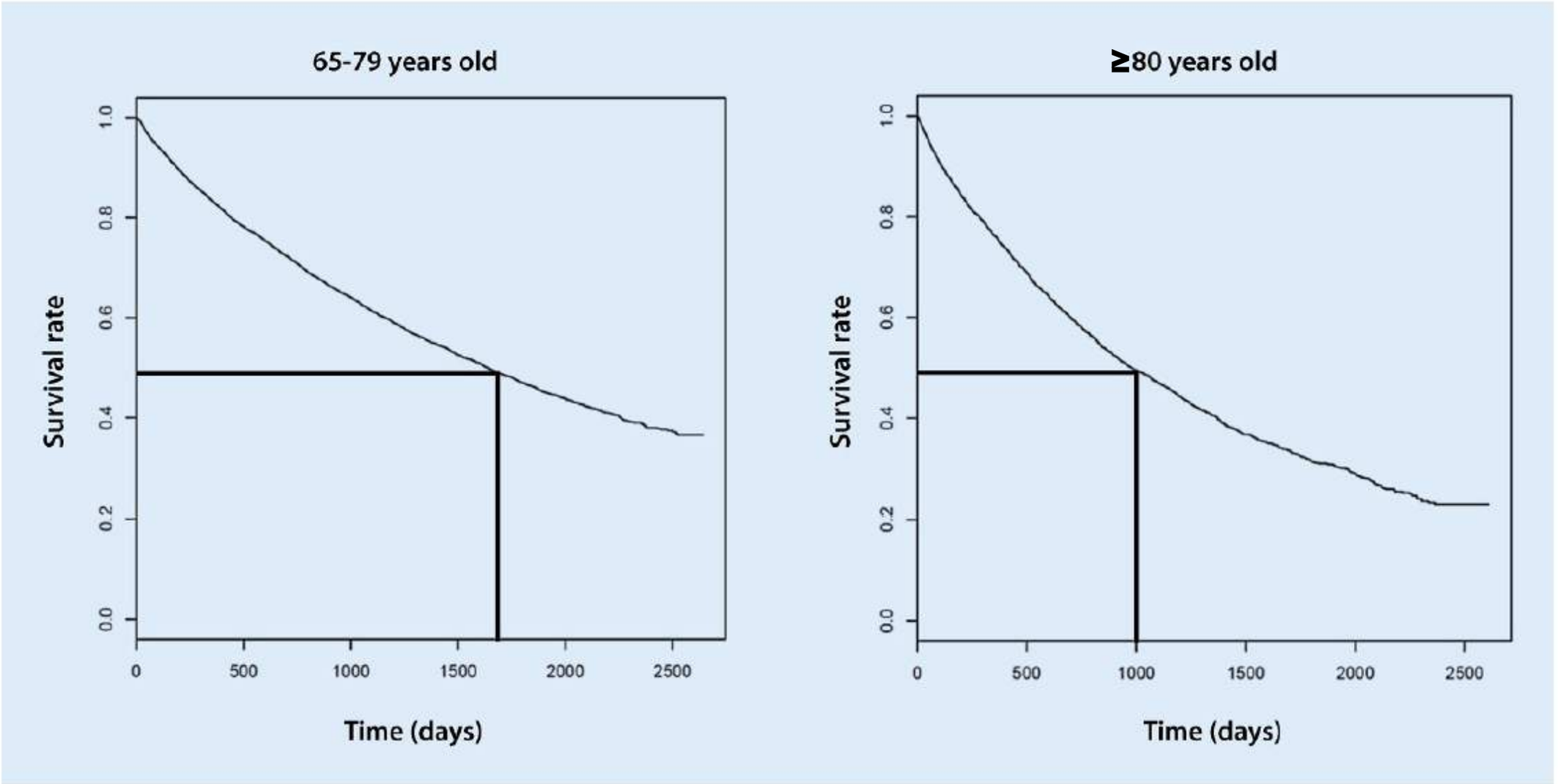


Fig. 2 ▲ Kaplan-Meyer analysis of mortality in elderly dialysis patients. Median survival time was 1638 days (4.5 years) in patients 65–79 years old and 978 days (2.68 years) in the oldest old (≥80 years at dialysis initiation)

Röhrig G, et al. *Z Gerontol Geriat* 2018;51:60–66

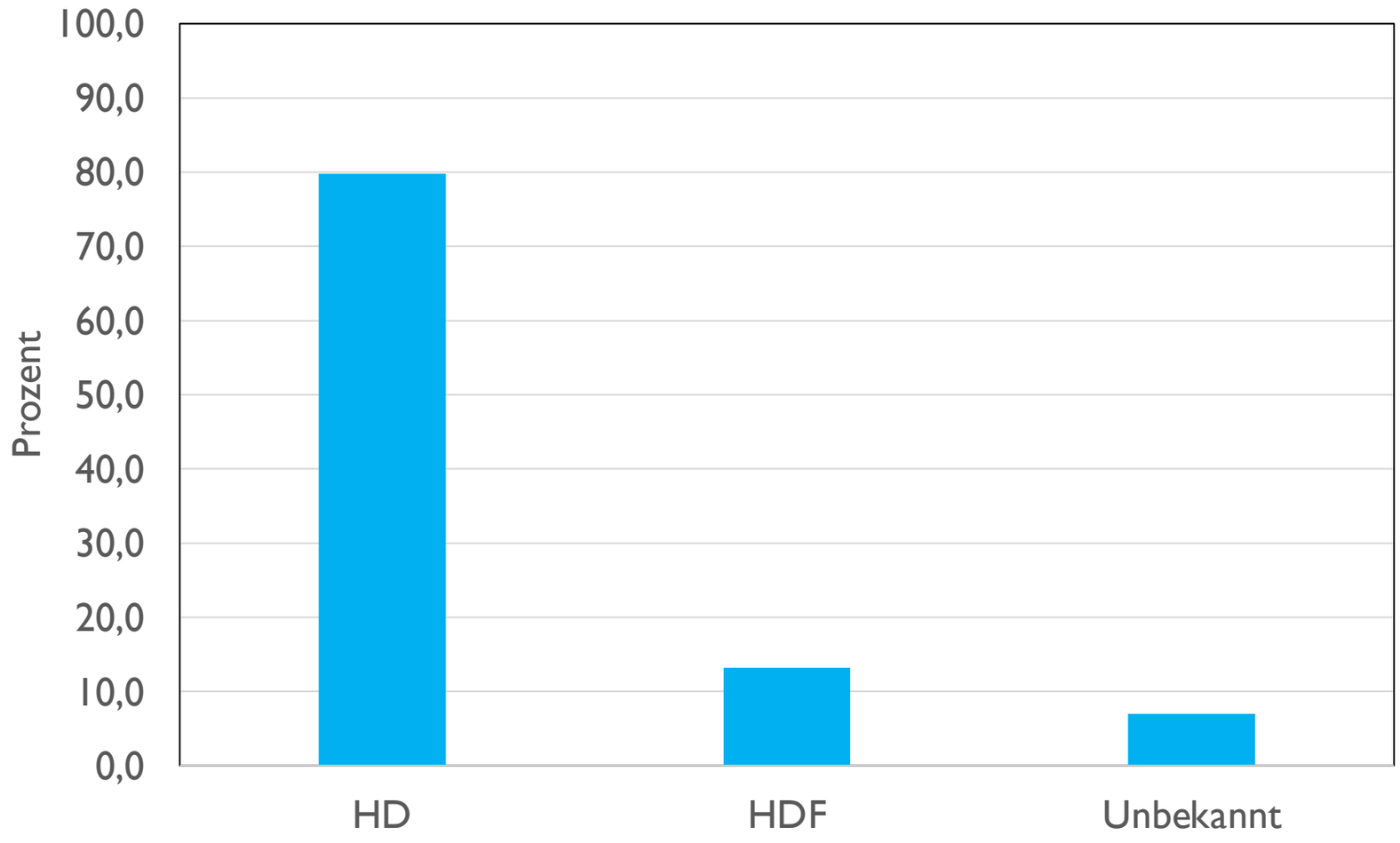
2012 ERA-EDTA Registry Annual Report: Mortality in dialysis patients

Table 7. One, two and five-year patient and graft survival probabilities (95% Confidence interval), for all patients and for patients above 65 years of age, adjusted for age, gender and primary diagnosis

	2006–10 cohort		2003–07 cohort		
	1 year	2 year	1 year	2 year	5 year
Incident RRT patients					
All patients	89.7 (89.5–89.8)	82.2 (82.0–82.5)	88.7 (88.5–88.9)	80.6 (80.3–80.9)	59.7 (59.3–60.0)
65–74	82.3 (81.8–82.8)	70.5 (70.0–71.1)	80.3 (79.8–80.7)	67.6 (67.1–68.2)	39.3 (38.7–39.9)
75+	72.6 (72.1–73.2)	56.7 (56.1–57.3)	70.4 (69.8–70.9)	53.2 (52.6–53.8)	21.3 (20.8–21.9)
Patient survival on dialysis					
All patients	88.3 (88.1–88.5)	79.7 (79.4–80.0)	86.9 (86.7–87.1)	77.5 (77.2–77.8)	52.5 (52.0–52.9)
65–74	81.9 (81.5–82.4)	69.7 (69.1–70.2)	79.9 (79.4–80.4)	66.9 (66.3–67.4)	36.7 (36.1–37.3)
75+	72.4 (71.9–73.0)	56.4 (55.8–57.0)	70.1 (69.5–70.7)	52.9 (52.2–53.5)	20.9 (20.4–21.5)

Pippias M, et al. *Clin Kidney J* 2015;8:248-261

Verteilung HD/HDF (Q3/2023)
Benchmarkingprogramm DN e.V.



n=7.903

Duttlinger J, Reichel H, unpublished

HD vs HDF (Q3/2023)
Benchmarkingprogramm DN e.V.

	HD	HDF
Age (yrs)	69.5 ± 14.5	66.4 ± 14.8
Dialysis vintage (yrs)	6.01	7.51
BC-Shunt (%)	68.1	71.2
Treatment time/session (min)	258	264
spKt/V	1.51 ± 0.44	1.57 ± 0.42
Diabetes (%)	42.8	34.3
Composite cardio-vascular disease (%)	67.2	55.3
Coronary heart disease (%)	35.6	30.3

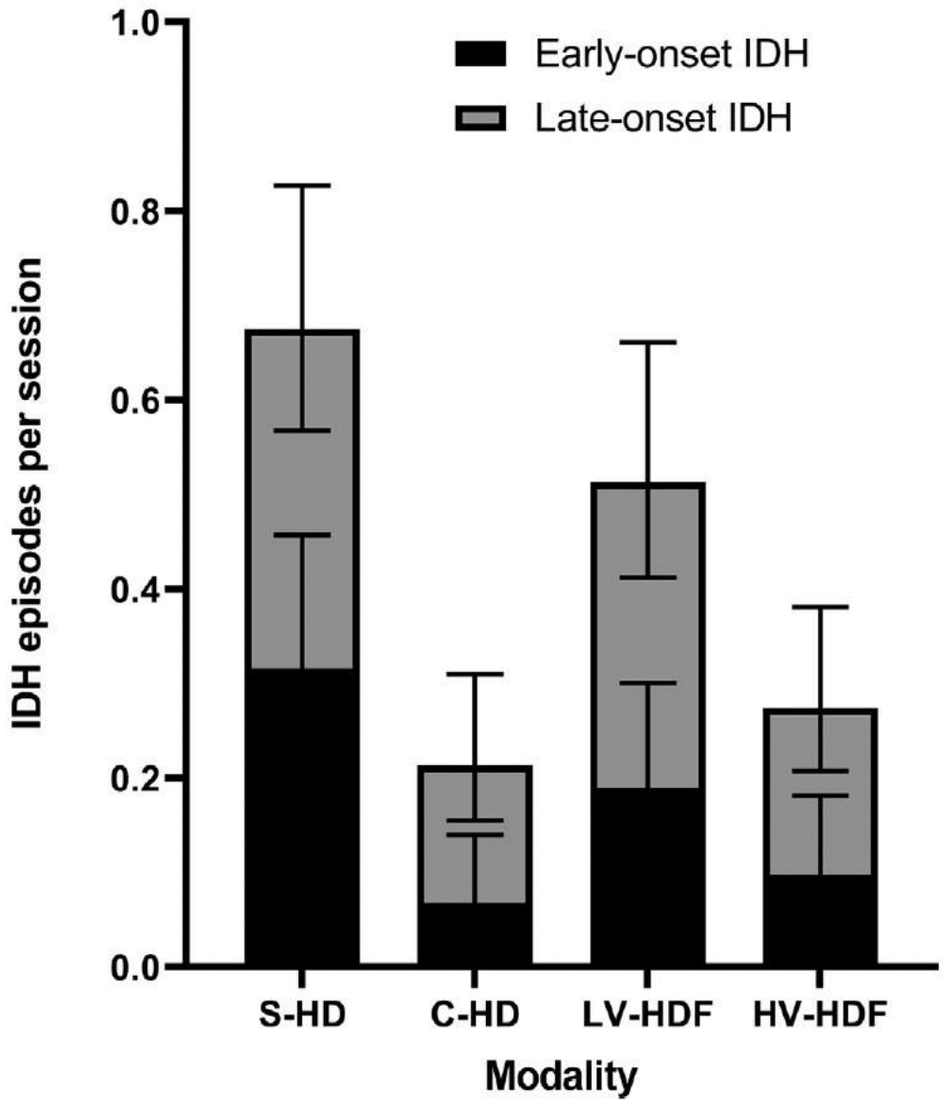
Duttlinger J, Reichel H, unpublished

Possible mechanisms for improved HDF outcomes

- Increased removal of uremic toxins
- Less endothelial dysfunction
- Reduction of inflammatory and oxidative stress
- Decreased exposure to circulating cardiovascular uremic toxins
- Improvement in hemodynamic stability

Canaud B, et al. *Semin Dial* 2022;35:117-128

HDF vs cool HD – effect on intradialytic hemodynamics



Crossover-RCT, n=40, 4 x 2 weeks

Rootjes PA, et al. *Kidney Int Rep* 2022;7:1980-1990

Zusammenfassung CONVINCE

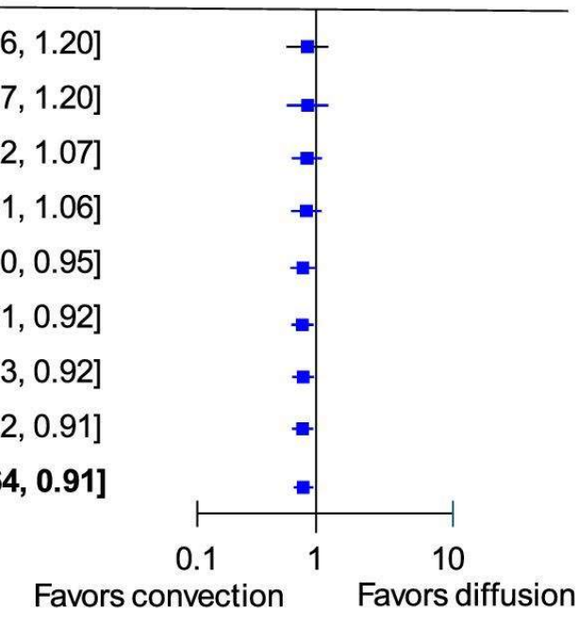
- High-volume HDF im Vergleich zu high-flux HD reduzierte das Mortalitätsrisiko in CONVINCE um 23% (hazard ratio [HR] 0.77)
- Größter positiver Effekt bei Patienten > 65 Jahre ohne kardiovaskuläre Erkrankung und Diabetes mellitus, Dialysetherapie < 2 Jahre und arteriovenösem Shunt
- Kein Effekt bei Patienten mit vorbestehender kardiovaskulärer Erkrankung und mit vorbestehendem Diabetes mellitus und kein Unterschied bei kardiovaskulärem Mortalitätsrisiko

Zusammenfassung CONVINCE

- Anteil von Infektionen an Todesursachen höher als Anteil kardiovaskulärer Erkrankungen; unklarer Effekt von COVID19?
- Mortalitätsrisiko durch Infektionen in CONVINCE durch high-volume HDF reduziert
- Studien-Effekte getriggert durch Reduktion non-cardiovascular and infection-related deaths
- Insgesamt niedrige event rate (Mortalität) und geringe Komorbiditäten (im Vergleich zu einer gesamten Dialysepopulation)
- *European HDF pooling project:* Kein signifikanter Effekt von high-volume HDF auf Mortalität durch Infektionen, Reduktion kardiovaskulärer Todesursachen
  (Peters SAE, et al. *Nephrol Dial Transplant* 2016;31:978-984)

Cumulative meta-analysis of convective therapy on risks of cardiovascular mortality

Study	Cumulative participants		Cumulative risk ratio 95% confidence interval	
	Convection	Diffusion		
Santoro 1999	177	194	0.82	[0.56, 1.20]
+ Beerenhout 2005	197	214	0.83	[0.57, 1.20]
+ CONTRAST (Dutch) Study 2005	555	570	0.81	[0.62, 1.07]
+ Schiffl 2007	593	608	0.80	[0.61, 1.06]
+ ESHOL Study 2011	1049	1058	0.76	[0.60, 0.95]
+ TURKISH HDF 2013	1440	1449	0.75	[0.61, 0.92]
+ Morena 2017	1634	1643	0.76	[0.63, 0.92]
+ FINESSE 2019	1697	1704	0.75	[0.62, 0.91]
+ CONVINCE 2023	**2380**	**2381**	**0.76**	**[0.64, 0.91]**



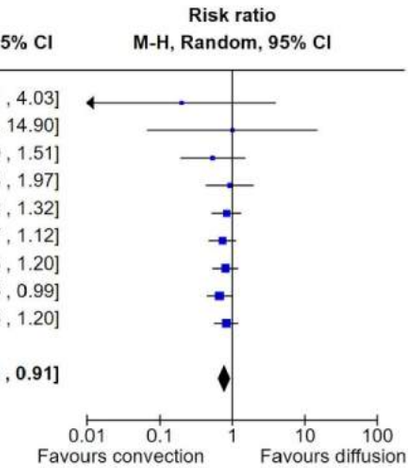
Strippoli GFM, Green SC . *Clin Kidney J* 2024;https:/doi.org/10.1093/ckj/sfae035

Risks of death due to cardiovascular cause and all causes with convective therapy versus diffusive therapy

A. Cardiovascular death

Study	Convection Events	Convection Total	Diffusion Events	Diffusion Total	Weight	Risk ratio M-H, Random, 95% CI
Schiffl 2007	0	38	2	38	0.3%	0.20 [0.01 , 4.03]
Beerenhout 2005	1	20	1	20	0.4%	1.00 [0.07 , 14.90]
FINESSE 2019	5	63	9	61	2.9%	0.54 [0.19 , 1.51]
Morena 2017	12	194	13	194	5.4%	0.92 [0.43 , 1.97]
CONVINCE 2020	31	683	37	677	14.4%	0.83 [0.52 , 1.32]
TURKISH HDF 2013	32	391	44	391	16.6%	0.73 [0.47 , 1.12]
CONTRAST (Dutch) Study 2005	37	358	46	356	18.8%	0.80 [0.53 , 1.20]
ESHOL Study 2011	37	456	55	450	19.8%	0.66 [0.45 , 0.99]
Santoro 1999	36	177	48	194	21.4%	0.82 [0.56 , 1.20]
Total (95% CI)		**2380**		**2381**	**100.0%**	**0.76 [0.64 , 0.91]**
Total events:	191		255			

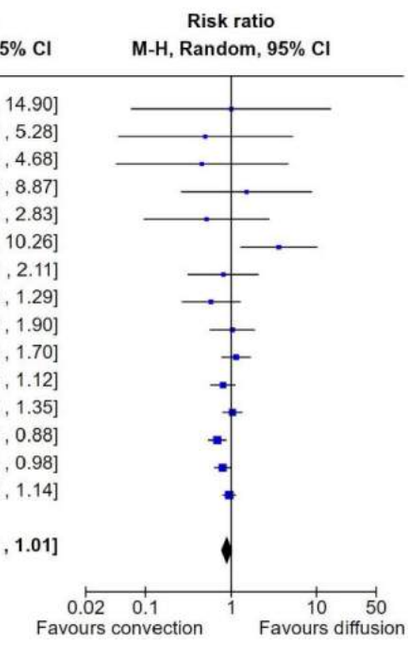
Heterogeneity: Tau² = 0.00; Chi² = 2.33, df = 8 (P = 0.97); I² = 0%
Test for overall effect: Z = 3.03 (P = 0.002)



B. Death from all causes

Study	Convection Events	Convection Total	Diffusion Events	Diffusion Total	Weight	Risk ratio M-H, Random, 95% CI
Beerenhout 2005	1	20	1	20	0.2%	1.00 [0.07 , 14.90]
Schiffl 2007	1	38	2	38	0.3%	0.50 [0.05 , 5.28]
Wizemann 2000	1	23	2	21	0.3%	0.46 [0.04 , 4.68]
HDFIT 2019	3	97	2	98	0.6%	1.52 [0.26 , 8.87]
PROFIL Study 2011	2	27	3	21	0.6%	0.52 [0.10 , 2.83]
Locatelli 1994	7	50	6	155	1.6%	3.62 [1.27 , 10.26]
Bolasco 2003	7	76	8	70	1.8%	0.81 [0.31 , 2.11]
Santoro 2005a	7	32	12	32	2.6%	0.58 [0.26 , 1.29]
FINESSE 2019	16	63	15	61	4.2%	1.03 [0.56 , 1.90]
Morena 2017	41	194	36	194	8.4%	1.14 [0.76 , 1.70]
TURKISH HDF 2013	52	391	65	391	10.8%	0.80 [0.57 , 1.12]
Santoro 1999	65	177	69	194	14.2%	1.03 [0.79 , 1.35]
ESHOL Study 2011	85	456	122	450	16.0%	0.69 [0.54 , 0.88]
CONVINCE 2020	118	683	148	677	18.0%	0.79 [0.64 , 0.98]
CONTRAST (Dutch) Study 2005	131	358	138	356	20.4%	0.94 [0.78 , 1.14]
Total (95% CI)		**2685**		**2778**	**100.0%**	**0.88 [0.77 , 1.01]**
Total events:	537		629			

Heterogeneity: Tau² = 0.01; Chi² = 18.30, df = 14 (P = 0.19); I² = 24%
Test for overall effect: Z = 1.85 (P = 0.06)



Strippoli GFM, Green SC . *Clin Kidney J* 2024;https:/doi.org/10.1093/ckj/sfae035

Abschließende Punkte

- Konzeptionell verbessert HDF durch zusätzliche Konvektion die Dialyse-Qualität
- Generalisierbarkeit der CONVINCE- und HDF-Studien-Ergebnisse?
- Mechanismen?
- Lebensqualität (HRQoL)
- Cost-effectiveness/sustainability
- Daten vom *High-volume haemodiafiltration vs high-flux haemodialysis Registry Trial (H4RT)* werden Ende 2025 erwartet