16th ISFA 41st ISBP Joint World Congress San Diego, California, USA August 5-7, 2027

# Emerging Innovations in Dialysis Membrane Technology: Improving Outcomes in ESRD Care: A Look Beyond the Horizon in USA

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# Disclosure

Relevant Financial Relationships
Advisor: GSK, Nipro

Relevant Non-Financial Relationships
President, International Society for Apheresis
Secretary, International Society for Blood Purification
Former Board Member, American Society for Apheresis
Former Member, JCA Special Issue Committee

Slides
Some slides modified from collaborators in ISBP Hawaii 2025 (29 speakers)

Off Label Usage
Any will be identified clearly

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# Outline: Innovations in Extracorporeal Blood Purification

Compress one century into less than one hour

At the end of the session; delegates will have/be able to:

1. Give a brief History and Evolution of hemodialysis and Apheresis
2. Modern Extracorporeal blood purification circuits
3. Evolution of dialysis membranes and technology related to dialysis and data concerning survival: High-flux membranes, HDF
4. Proven innovations in Clinical Trials; Improved outcomes (mortality, convenience): What to use HDF vs HDx
5. ~~Innovations in the Horizon: Wearable & Portable Dialysis, Bio-Artificial Kidney~~
6. ~~AI & Machine Learning in Hemodialysis~~
7. ~~Remote Monitoring & Telehealth in Dialysis~~

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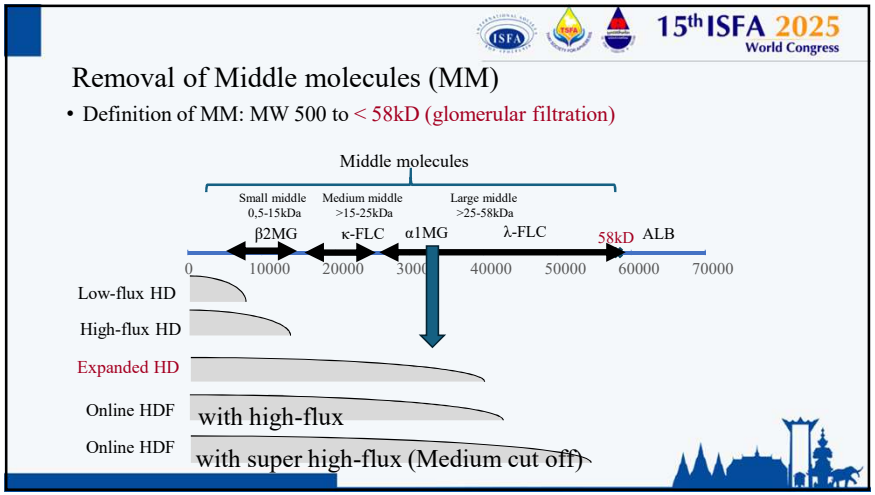
ISBP International Society of Blood Purification

## ISBP 2025 Kidney Health Congress

**Honolulu, Hawaii, August 20–22, 2025**

**Patient-centered perspectives: Mortality, Tolerability, quality of life, and innovation in expanded HD therapies**

29 Speakers from USA, Europe, Asia and Oceania
205 Delegates from all around the world.


## Classification of hemodialysis membranes

| Category | Ultrafiltration coefficient[1]* (mL/h/mmHg/m²) | β2-microglobulin | | Albumin | |
|---|---|---|---|---|---|
| | | Clearance[2]* (mL/min) | Sieving coefficient[1]* | Loss into dialysate[3]* (g) | Sieving coefficient[1]* |
| Low-flux | < 12 | < 10 | - | 0 | 0 |
| High-flux | 14~40 | 20~80 | < 0.7~0.8 | < 0.5 | < 0.01 |
| Medium cut-off | 40~60 | > 80 | 0.99 | 2~4 | < 0.01 |
| Protein-leaking | > 40 | > 80 | 0.9~1.0 | 2~6 | 0.01~0.03 |
| High cut-off | 40~60 | - | 1.0 | 9~23 | < 0.2 |

1*: In vitro
2*: For conventional hemodialysis with a blood flow rate of 300~400 mL/min. Includes contributions from diffusion, Convection, and adsorption.
3*: For 4 h of conventional hemodialysis.

Storr M, et al. Nephrol Dial Transplant 33 (Suppl 2) 2018

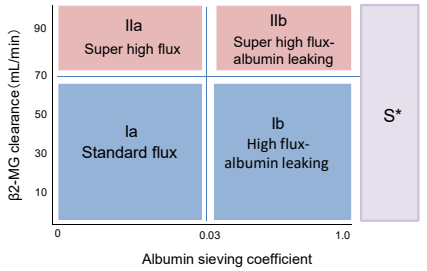


## Old and new classifications of dialyzers in Japan

Old classification

| Old Japanese classification | β2-MG clearance (mL/min) |
|---|---|
| I | < 10 |
| II | ≥ 10-30 |
| III | ≥ 30-50 |
| IV | ≥ 50-70 |
| V | ≥ 70 |

New classification 2023




∗ Definition of type S dialyzer: Excellent biocompatibility, ability to remove solutes by adsorption, anti-inflammatory and anti-oxidative properties. Currently, only PMMA dialyzers qualify.

JSDT 2017
Abe M, et al. Sci Rep. 2024

## USA Dialysis Overview

Dialysis Machines and Centers:
- Estimated market: $6.6 billion (2025)
- 7,556 dialysis centers nationwide

Dialysis Patient Distribution:
- Total patients: 516,837
- In-center hemodialysis: 433,396
- Home dialysis: 78,407
- Nursing facility: 5,034

Key Trends in Dialysis Care:
- Machines: 75,000–150,000 est
- Growth in home dialysis adoption
- Most use of high-flux membranes (NCDC and HEMO)
- Technological innovations in dialysis systems
- Focus on patient safety and biocompatibility



## Clinical Evidence for the use of high volume HDF and HDs

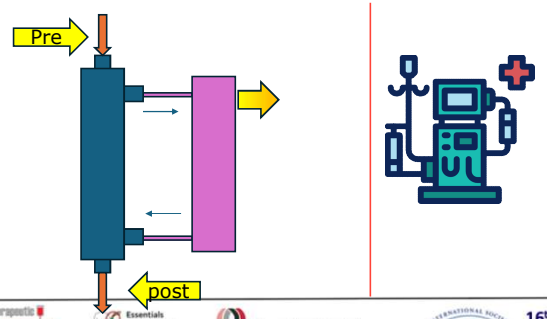
High Volume HDF vs HDs (Super high flux)



## High volume Hemodiafiltration (HDF)



## Basics






Required for this technique
- Dialysis machine
- Bloodline
- Endotoxin retention filters
- Water
- Acid & base

## The evidence efficacy of HDF

Therapeutic Apheresis Academy · Essentials and Advances in Apheresis Therapies · International Society of Blood Purification (ISBP) · ISFA · 16th ISFA 41st ISBP Joint World Congress San Diego, California, USA August 5-7, 2027



## HDF — The story of HDF

**ESHOL study**
906 dialysis patients (ES)

Study type: prospective, randomized, open-label
open-label clinical trial
Follow up: 3 years

- HD (n=450, HF 92%-LF 8%)
- Online-HDF(n=456) (≥18 L/session)

- Online-HDF reduction in all cause mortality
- Subgroup analysis
  - Online-HDF (≥23.1 L/Session) Risk reduction reduction in mortality (0.60- 23.1 L, 0.55-≥ 25.4 L, 0.55-≥ 25.4 L)
    - Related with Stroke and infection mortality infection mortality reduction
    - Reduction in all-cause hospitalizations in hospitalizations in HDF group

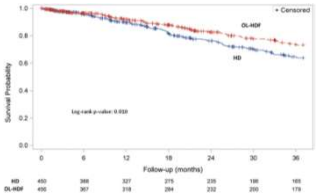



Table 4. Risk of all-cause mortality results by achieved convective volume, convective volume/BMI, and convective volume/BSA

| | Hemodialysis | OL-HDF | | | | |
|---|---|---|---|---|---|---|
| | | Tertile 1 | Tertile 2 | Tertile 3 | | |
| Convective volume (L/session) | | <23.1 | 23.1–25.4 | >25.4 | | |
| n (%) | 124 (26.4) | 33 (22.9) | 27 (18.2) | 25 (16.0) | 0.03 | 0.003 |
| HR (95% CI) | Ref. | 0.90 (0.61–1.31) | 0.60 (0.39–0.9) | 0.55 (0.34–0.84) | 0.01 | 0.001 |
| Convective volume/BMI (L/kg per m²) | | <0.9 | 0.9–1.1 | >1.1 | | |
| n (%) | 124 (26.4) | 25 (17.3) | 32 (21.9) | 26 (17.9) | 0.05 | 0.03 |
| HR (95% CI) | Ref. | 0.62 (0.4–0.94) | 0.74 (0.49–1.08) | 0.66 (0.42–0.99) | 0.04 | 0.02 |
| Convective volume/BSA (L/m²) | | <13.2 | 13.2–14.8 | >14.8 | | |
| n (%) | 124 (26.4) | 29 (20.0) | 29 (19.9) | 25 (17.2) | 0.06 | 0.01 |
| HR (95% CI) | Ref. | 0.73 (0.49–1.11) | 0.66 (0.43–0.98) | 0.62 (0.39–0.93) | 0.04 | 0.01 |

n (%) indicates the number of exits (% of exits from total of group participants). BMI, body mass index; BSA, body surface area.
[a]P value for the statistical significance test (Fisher's exact test; log-rank test).
[b]P value for the trend test (Cochran-Armitage trend test; log-rank test).

Ref: Maduell F *et al.* High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. J Am Soc Nephrol.2013



## HDF — The story of HDF

**Efficacy of High volume HDF therapy**

| | HD | Online HDF convection volume, delivered BSA-standardized in L/1.73 m² per treatment <19 | 19–23 | >23 |
|---|---|---|---|---|
| All-cause mortality | | | | |
| Crude | 1 | 0.91 (0.74–1.13) | 0.88 (0.72–1.09) | 0.73 (0.59–0.91) |
| Adjusted | 1 | 0.83 (0.66–1.03) | 0.93 (0.75–1.16) | 0.78 (0.62–0.98) |
| CVD mortality | | | | |
| Crude | 1 | 1.00 (0.71–1.40) | 0.71 (0.50–1.01) | 0.69 (0.48–0.98) |
| Adjusted | 1 | 0.92 (0.65–1.30) | 0.71 (0.49–1.03) | 0.69 (0.47–1.00) |
| Infections | | | | |
| Crude | 1 | 1.50 (0.93–2.41) | 0.96 (0.56–1.65) | 0.56 (0.30–1.08) |
| Adjusted | 1 | 1.50 (0.92–2.46) | 0.97 (0.54–1.74) | 0.62 (0.32–1.19) |
| Sudden death | | | | |
| Crude | 1 | 1.24 (0.80–1.91) | 0.91 (0.57–1.47) | 0.60 (0.35–1.03) |
| Adjusted | 1 | 1.09 (0.69–1.74) | 1.04 (0.63–1.70) | 0.69 (0.39–1.20) |

body surface area (BSA)

**Increasing of convection volume will decrease the risk of all-cause mortality**
**With comparison between HD vs HDF according to 4 big RCT study held in Europe**
**European mindset is "more convection for better mortality"**

Ref: Blankestijn PJ *et al.* Clinical evidence on haemodiafiltration. Nephrol Dial Transplant. 2018



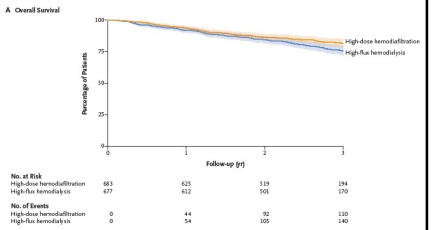
## HDF — The story of HDF

**CONVINCE study**
1360 dialysis patients

Study type: multinational, randomized, controlled
controlled trial
Follow up: >2 years to 3 years

- HD-HF (n=683)
- Online-HDF (n=677) (≥25.3 L/session)

- High volume HDF had a lower risk of death death
- Sub analysis :
  - Preexisting CVD: No difference
  - No preexisting CVD: mortality lower in online-lower in online-HDF
  - Preexisting Diabetes: No difference difference
  - No Preexisting diabetes: mortality lower in mortality lower in online-HDF




Ref: Blankestijn PJ *et al.* Effect of Hemodiafiltration or Hemodialysis on Mortality in Kidney Failure. N Engl J Med. 2023

# Expanded Hemodialysis by Super high flux

( HDs )



## Expanded Hemodialysis

HDs

### Key Concept

- Middle molecular weight molecule removal
- Low protein leakage



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## Expanded Hemodialysis

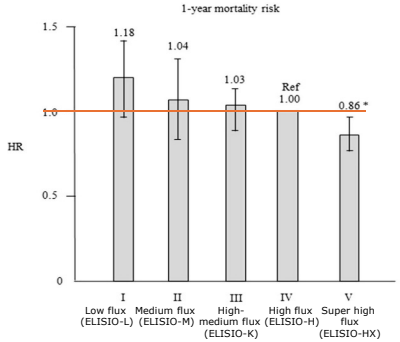
HDs

203 008 dialysis patients

Study type: Japanese Society for Dialysis Therapy Renal Data Registry (JRDR)
Follow up: 2 years

- Type I (n=2 087)
- Type II (n= 1 721)
- Type III (n= 8 349)
- Type IV (n= 165 082)
- Type V (n=25 769)

- Type V has a lower Hazard ration of all cause mortality

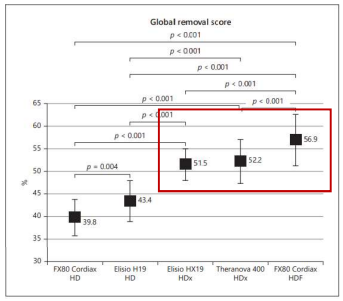



Ref: Abe M *et al.* High-Performance Membrane Dialyzers and Mortality in Hemodialysis Patients: A 2-Year Cohort Study from the Annual Survey of the Japanese Renal Data Registry. Am J Nephrol. 2017



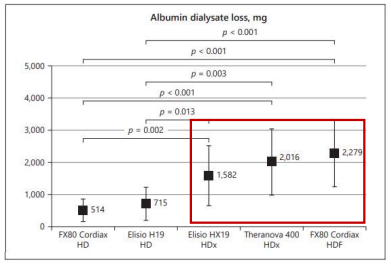
## Efficacy and Safety of the Medium Cut-Off Elisio HX Dialyzer

Francisco Maduell[a, b] José Jesús Broseta[a] Diana Rodríguez-Espinosa[a]
Jimena Del Risco-Zevallos[a] Miquel Gómez[a] Lida M. Rodas[a]
Marta Arias-Guillén[a] Manel Vera[a] Néstor Fontseré[a]
Maria del Carmen Salgado[c] Nayra Rico[c]




| | FX80 Cordiax HD | Elisio H19 HD | Elisio HX19 HDx | Theranova 400 HDx | FX80 Cordiax HDF |
|---|---|---|---|---|---|
| Urea (60 Da) (pI 7.4–8.5) | 81.3±5.2 | 82.7±5.5 | 83.4±5.7[a] | 81.7±6.7 | 82.2±6.8 |
| Creatinine (113 Da) (pI 11.19) | 74.4±5.7 | 75.4±5.5 | 75.7±6.5 | 75.0±6.3 | 75.5±6.5 |
| Phosphate (245 Da) (pI 4.7) | 58.6±11 | 56.2±13 | 58.1±11 | 60.5±10 | 58.6±12 |
| $\beta_2$-Microglobulin (11,818 Da) (pI 5.3–5.7) | 73.7±5.5 | 73.5±6.9 | 77.6±5.5[b,c] | 76.9±7.3 | 83.2±4.8[a] |
| Myoglobin (17,200 Da) (pI 6.8–7.4) | 36.8±9.6 | 50.5±7.6[b] | 66.1±7.1[a] | 67.6±7.3[a] | 74.0±6.6[a] |
| kFLC (22,500 Da) (pI 6.0–6.2) | 64.9±6.6 | 68.8±8.1 | 77.2±4.9[a] | 77.5±5.7[a] | 83.6±4.1[a] |
| Prolactin (23,000 Da) (pI 6.5) | 42.7±8.7 | 48.3±6.2[a] | 65.1±6.0[a] | 64.7±8.5[a] | 72.0±8.2[a] |
| $\alpha_1$-Microglobulin (33,000 Da) (pI 3.8–4.2) | 7.3±7.1 | 8.6±7.7 | 17.1±7.8[a] | 19.3±10.5[a] | 24.8±10.4[a] |
| $\alpha_1$-A. Glycoprotein (41,000 Da) (pI 2.8–3.8) | 6.8±6.9 | 7.7±5.9 | 8.4±5.8 | 11.3±7.4 | 14.6±10.6[a] |
| kFLC (45,000 Da) (pI 4.8–6.2) | 23.3±7.2 | 27.6±9.9 | 44.1±7.5[a] | 47.7±7.1[a] | 57.2±9.2[a] |
| Albumin BR-IN (MW 66,000 Da) (pI 4.7) | 9.8±5.6 | 10.7±5.5 | 8.6±5.0 | 8.1±6.1 | 9.8±6.2 |

MW, molecular weight; pI, isoelectric point. [a]$p < 0.05$ versus FX80-HD. [b]$p < 0.001$ versus FX80-HD. [c]$p < 0.01$ versus Elisio-HD. [d]$p < 0.001$ versus FX80-HD, Elisio-HD, Elisio-HDx, and Theranova-HDx. [e]$p < 0.001$ versus FX80-HD and Elisio-HD. [f]$p < 0.05$ versus FX80-HD and Elisio-HD. [g]$p < 0.01$ versus FX80-HD and Elisio-HD. [h]$p < 0.05$ versus FX80-HD, Elisio-HD, and Elisio-HDx.



## Expanded Hemodialysis

**CARTOON study**
80 dialysis patients

Study type: multicenter, prospective, open-label, open-label, randomized trial
Follow up: 1 years

- Online-HDF (n=37) (≥19.5 L/session)
- HDx-HF (n=43)

- None inferiority in all cause mortality and mortality and cardiovascular mortality mortality

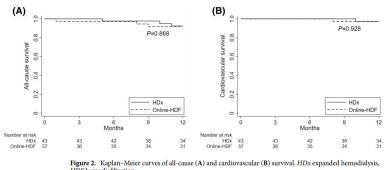



Figure 2. Kaplan–Meier curves of all-cause (A) and cardiovascular (B) survival. *HDx* expanded hemodialysis, *HDF* hemodiafiltration.

Ref: Lee Y *et al.* Cardiovascular Risk Comparison between Expanded Hemodialysis Using Theranova and Online Hemodiafiltration (CARTOON): A Multicenter Randomized Controlled Trial.Sci Rep. 2021



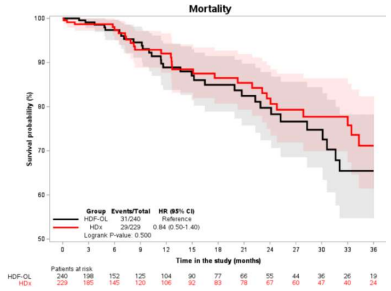
## Expanded Hemodialysis

**MOTheR study**
xxx dialysis patients- preliminary 469

Study type: multicenter, open-label, prospective, prospective, randomized study
Follow up: 2 years

- Online-HDF (n=x pre n=240) (≥23 L/session) L/session)
- HDx (n=xx pre n= 229)

- **Preliminary 469:** HDx is not inferior to OL-HDF in reducing the all-cause mortality outcome outcome




Ref: de Sequera P *et al.* Trial design of the MOTheR HDx study: a multicenter, open-label, prospective, randomized study to explore the morbidity and mortality in patients dialyzed with the Theranova HDx in comparison with online hemodiafiltration Clin Kidney J. 2023



## HDF vs. HDs

### Technical synopsis

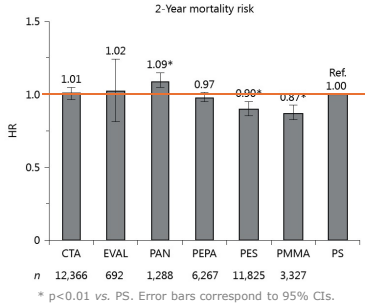
| Technical requirements | High volume HDF | Patient | High volume HDF |
|---|---|---|---|
| | Dialysis machine | | Good vascular access |
| | Bloodline | | Stable patients |
| | More steps to set it up | | Hemodynamically stable (>20 L/session) |
| | Endotoxin retention filters | | Without coagulation issues |
| | Pure Water – **high** volume | | Without preexisting CVD |
| | Acid & base- high volume | | |
| | Trained nursing staff | | |
| Technical requirements | HDx | Patient | HDx |
| | Pure Water –**low** volume | | All HD patients |
| | Dialyzer- super high flux | | |
| | Rest is standard for HD | | |



| | HDF | Cost Savings | | HDs |
|---|---|---|---|---|
| | | HDF | HDs | |
| Dialysis machine | Specialized machine | | ✓ | Any machine |
| RO – water quality & volume | High volume | | ✓ | Same as current |
| Bloodlines | Dedicated bloodlines | | ✓ | Same as current |
| Substitution line | Required | | ✓ | Not needed |
| Special procedure/difficulty & training | Clinicians & physician training required | | ✓ | No change to current practice |
| Treatment preparation & clinical workflow | More time & steps required | | ✓ | No change to current practice |
| Facility space | More space required | | ✓ | No change |
| Patient qualification | Limited patient population | | ✓ | Any patients |
| Treatment reimbursement | HDF reimbursement needed | | ✓ | Special reimbursement? (to cover higher dialyzer cost) |

## PES membranes

**ELISIO-PES membrane**




* p<0.01 *vs.* PS. Error bars correspond to 95% CIs.

- Hazard Ratios were significantly lower in PES *versus* PS

Ref: Abe M *et al.* High-Performance Membrane Dialyzers and Mortality in Hemodialysis Patients: A 2-Year Cohort Study from the Annual Survey of the Japanese Renal Data Registry. Am J Nephrol. 2017

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## Prediction in US Dialysis Environment

Conclusion moving towards HDs can achieve similar treatment outcome with HDF treatment; HDs will become standard

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## ELISIO-HX is

**"Super high flux" and "PES membrane material"**

**"The world's "only dialyzer "with both**

*Live longer,*
*Live better,*

## Summary

What type of dialysis membrane should be used?

1. Old classifications of dialyzers and mortality in patients on hemodialysis
   - ✓ Compared with low-flux and high-flux dialyzers, super high-flux dialyzers (Type IV and V) might be beneficial for patients on hemodialysis
   - ✓ Although type IV and V dialyzers are classified as super high-flux membrane dialyzers, our findings indicate superiority of the type V dialyzer
2. New classifications of dialyzers and mortality in patients on hemodialysis
   - ✓ Compared with standard flux (Type Ia) dialyzers, super high-flux (Type IIa and IIb ) and Type S dialyzers might be beneficial for patients on hemodialysis
3. Difference between MCO and super high flux membrane
   - ✓ HD with Theranova 500® has proven to be very similar in efficacy to OL-HDF, although with a significantly higher albumin loss.
   - ✓ HD with Elisio 21HX™ resulted in less albumin loss than with Theranova 500®.





## Outline

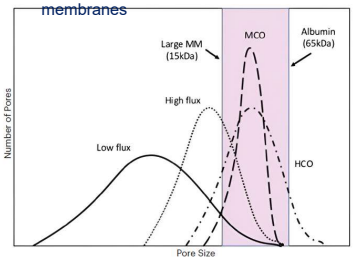
What type of dialysis membrane should be used?

1. Old classification of dialyzers and mortality in patients on hemodialysis
2. New classification of dialyzers and mortality in patients on hemodialysis
3. Difference between medium cut-off and super high-flux membrane



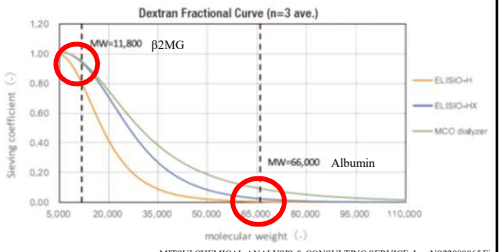
## Difference between MCO and super high flux membrane

Pore size distribution in dialysis membranes




Wolley M, et al. Clin J Am Soc Nephrol. 2018

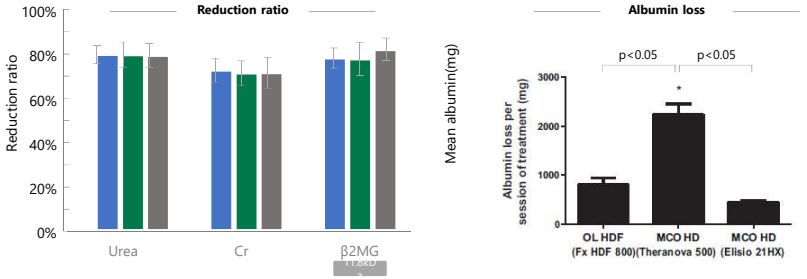
Sharp cut-off technology




MITSUI CHEMICAL ANALYSIS & CONSULTING SERVICE, Inc: NS22080065 Fig

## OL-HDF with FxCordiax HDF 800™, Theranova 500® and Eli 21HX™ dialyzer

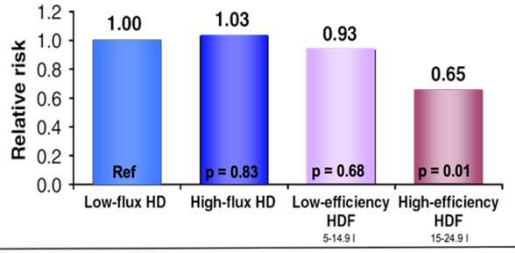
ELISIO HX HD VS Theranova HD VS FX Cordiax HDF




Martinez-Miguel P, et al.

## Mortality risk for patients receiving high efficiency HDF *vs*. HD is reduced

European Results from DOPPS




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

*Kidney Int 2006; 69:2087-2093*



## Randomized clinical trials in Europe evaluating HDF vs HD

JASN 2012

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

NDT 2013

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

JASN 2013

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

Kidney Int 2017

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

## Methods

**1 Primary outcome**

- Death from any cause

**2 Secondary outcomes**

- Cause-specific mortality
- Composite fatal & nonfatal CV events
- Kidney Tx
- Any cause/infection-related recurrent hospitalizations

- Hospitalization reasons → recorded during trial period
- Wide variety of frequent adverse events in trial population → reporting restricted to only serious events
- Findings regarding PROs & cost-effectiveness not reported in this publication

*CV (Cardiovascular) events include death from: CV causes, nonfatal myocardial infarction, nonfatal stroke, therapeutic coronary procedure (coronary-artery bypass graft, percutaneous transluminal coronary angioplasty, or stenting), therapeutic carotid procedure (endarterectomy or stenting), and vascular intervention (revascularization, percutaneous transluminal angioplasty, or stenting), or peripheral limb amputation.*

# Routine Use of HDF in 2025

**1. Europe: Spain**: highest adoption online HDF (~50%). **France, Italy, Germany, Netherlands and Belgium**: Significant use.

**2. Asia: Japan**: Increasing adoption, conventional HD remains dominant. **South Korea**: Growing interest. **China**: Some centers are integrating HDF, but HD remains the primary modality.

**3. Middle East; Turkey**: High adoption rates. **Saudi Arabia & UAE**: Expanding use

**4. Australia & New Zealand**

- HDF is available but not as widely adopted as in Europe. Some centers are using it selectively for specific patient selectively for specific patient populations.

**5. North America (U.S. & Canada)**

- HDF is not yet widely used in the U.S. due to regulatory and reimbursement challenges, though interest is challenges, though interest is growing.
- Canada has some centers offering HDF, but it is not routine practice.



## MoTheR HDx Trial
## Morbimortality in Patients Dialyzed With the Theranova HDx

- Multicenter, Open-label, Prospective, Randomized Study of MCO vs. HDF
  - Adult ESKD ICHD patients
  - Intervention: HDx with Theranova MCO dialyzer
  - 700 patients in Spain for up to 36-month duration
  - In process
- Combined Outcome
  - All cause mortality
  - Stroke (ischemic or hemorrhagic)
  - Acute coronary syndrome (angina and myocardial infarction)
  - Peripheral arterial disease (amputation or revascularization)
  - Ischemic colitis (mesenteric thrombosis)
- Preliminary Result
  - HDx with Theranova dialyzer non-inferior to HDF

• Ortiz Patricia De Sequera, et al. , #3472 Preliminary data from mother hdx study: a multicentre open-label rct study to explore the morbimortality with the theranova hdx vs ol-hdf, *NDT*Volume 38, Issue Supplement_1, May 2023, gfad063.3472,

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