

Renal Care in the USA Set for Change in 2026 and Beyond *Customised care options expand on results from pivotal trial and FDA clearance*

Two significant events in the first half of this year have informed new debate around how the standard of care for hemodialysis patients in North America should develop:

- Results from a pivotal, long-term clinical trial (MOTheR)[1] that directly compared Hemodiafiltration (HDF) and expanded hemodialysis in more than 500 patients have been presented at the European Renal Association (ERA) Congress.[2]
- The U.S. Food and Drug Administration (FDA) has published 510(k) clearance for a new dialyser that will enable an 'Expanded Hemodialysis with super high-flux membrane,'[3] (HDs) approach to be introduced to the North American market, bringing the States in line with other, already established, markets around the world.

In this article we look at the science behind the two treatment modalities, compare the growing body of clinical evidence for each and contrast the practical implications for adoption in the North American healthcare system.

Elevating Patient Care

Around the world, individual physicians and healthcare providers strive to bring the highest standard of affordable care to their patient populations. In the context of renal disease in North America, this translates currently into the Centre for Disease Control and Prevention (CDC) estimating that, in 2026, 14% of U.S. adults, or around 37 million people, will have chronic kidney disease.[4] With the USRDS (United States Renal Data System) annual report 2025 noting almost 500,000 Americans receiving dialysis,[5] there is a large opportunity to make a meaningful impact on the lives of patients through middle molecule focused therapies that are built around individual patient needs.

The care patients receive will likely change over time, as new developments come to the fore and new therapies or treatment modalities emerge. Focusing on hemodialysis, for example, initial research in the 1970s[6] introduced HDF as a treatment modality that could not only remove the toxins from the blood that 'standard,' hemodialysis achieved, but also eliminate some important so-called 'middle molecules,' that are associated with increased inflammation, cardiovascular events, reduced quality of life and increased mortality.

Since then, the HDF modality has been refined and further developed to the point where it has gained some traction around the world. Interestingly, PubMed returns 4,810 all-time hits for Hemodiafiltration, with annual publication numbers still growing.

Many of these publications have proposed the idea that each new development in HDF should/would mean it becomes the standard for advanced renal care. However, a systematic review[7] of the available evidence in 2005 concluded: 'It is not possible on the basis of effectiveness to prefer one extracorporeal renal replacement therapy modality to the other for end-stage kidney disease because significant differences in clinically important outcomes have not been shown by available published RCTs.'

In addition, it is important to note that even in the areas of the world where HDF has seen the most adoption (namely Europe and Japan), a variety of challenges mean it is only able to be used for a portion of the total patient population.[8]

More recently, an alternative approach to middle molecule removal that is based on newly designed dialyser membrane technology has been commercialised. Known as 'Expanded Hemodialysis,' (expanded HD) the first approved products for clinical use were introduced in Japan in 2008 and now, with the recent FDA 510k authorisation of ELISIO-HX, super high-flux dialyser for expanded solute removal (HDs), physicians have an additional treatment pathway for their patients within the United States.

The new expanded HD treatment modality maintains the principle of a single stage process and is therefore compatible with most existing dialysis equipment. It allows improved dialysis performance without the need to adapt day-to-day procedures.

As with HDF, markets outside North America have embraced the clinical evidence that supports the roll-out of expanded HD but, until the recent FDA approval of ELISIO-HX and the integration of expanded HD into their programme of dialysis care by one of the largest U.S. dialysis providers (DaVita Inc.),[9] adoption of Expanded HD in the North American healthcare system has been limited, leaving patients behind.

Science Compared

Although conceived decades apart, HDF and expanded HD were both developed to allow nephrologists to more closely mimic the clearance achieved by a healthy kidney. As clinical knowledge grew, a consensus was quickly reached that the removal of 'middle molecules' – specifically those in the 12–60 KDa range – was a key factor in improving mortality and quality of life for patients.[10,11,12]

Hemodiafiltration (HDF) is an advanced form of dialysis in which a patient's blood passes through a highly permeable dialyser, removing waste products and excess fluid by diffusion and convection, while sterile replacement fluid is infused into the blood – typically before or after the filter – to maintain volume as larger amounts of plasma water are filtered. In practice, this combination approach is performed in a specifically designed HDF system.

In contrast, expanded HD relies on a re-engineering of the core dialysis membrane to extend the performance envelope of a standard dialysis set-up (Figure 2). With expanded HD, there is no additional infrastructure, specialised equipment, or changes to treatment

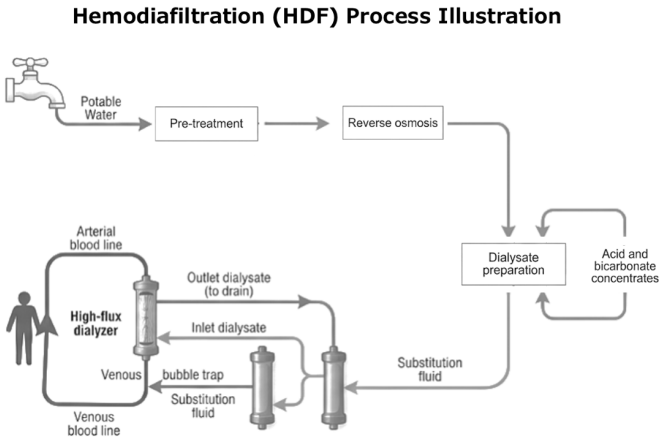


Figure 1. Diagram shows a typical flow for an HDF set-up and an example system

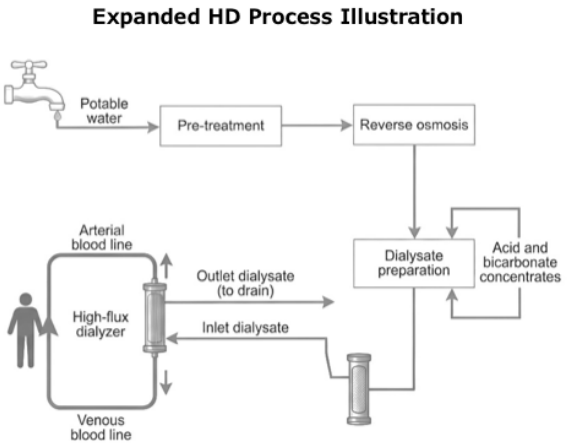


Figure 2. Diagram showing the expanded HD process, from water treatment and dialysate preparation to blood filtration and dialysate disposal.

procedures required as the engine for improvement sits within the technology of the dialyser itself.

A key consideration when designing a medium cut-off dialyser is to assess and choose the core membrane material and structure: the newly FDA approved dialyser (ELISIO-HX) is made from polyethersulfone (PES) and features a super high-flux class membrane, that is precisely engineered with sharp-cut off technology. Research has shown (see Table 1) that this membrane material has improved safety and efficacy profile compared to other materials. In addition, this dialyser's membrane is not made using Bisphenol A and features a newly designed hollow fibre structure, bigger pore size and a specific geometry allowing higher performance compared to standard high flux membranes.

A contemporaneous review of the development of this new class of membranes, published in 2017[13] concluded: *'We believe that the best application is the new therapy called 'expanded hemodialysis…' This new therapy is likely to modify the outcome of end-stage kidney disease patients, thanks to the enhanced removal of molecules traditionally retained by current dialysis techniques.'*

Global Lessons

A significant body of clinical evidence has been built up that defines and proves the performance of HDF and expanded HD and makes relevant comparisons of the two modalities. Studies in the mid-2010s focused on the performance of new polymers and their influence on overall mortality risk before, researchers in the early 2020s published studies that compared expanded HD with conventional HD and with HDF.

No.	Category	Year	Name	Author	Reference	Takeaway
1	Super High-flux	2021	High-performance dialyzers and mortality in maintenance hemodialysis patients	Abe M. et al.	DOI: 10. 1038/ s41598-021-91751-w	Type V dialyzers (containing HDs membrane) were associated with significantly lower I-year au-cause mortality versus
2	PES membrane	2017	High-Performance Membrane Dialyzers and Mortality in Hemodialysis Patients: A 2-Year Cohort Study from the Annual Survey of the Japanese Renal Data Registry	Abe M. et al.	DOI: 10.1159/ 000478032	Type IV dialyzers. Fully adjusted analysis: HR 0.878, corresponding to a 12.2% lower mortality risk vs Type lV. Propensity score-matched analysis: HR 0.862, corresponding to a 13.8% lower mortality risk vs Type 'V.
3	PES membrane	2016	The Choice of Hemodialysis Membrane Affects Bisphenol A Levels in Blood	Bosch-Panadero E. et al.	DOI:10.1681/ ASN.201SO 30312	Nationwide cohort study in Japan HD patients, 2-year follow-up)-Mortality rates may differ depending on dialyzer membrane type. PES membranes showed 10% lower mortality risk compared with PS.
4	ELISIO-HX (HDs membrane)	2022	Clinical performance comparison of two medium cut-off dialyzers	Krieter D.H. et aL	DOI: 10.1111/ 1744-9987.18919	Shows broad middle molecule removal (up to —45 kDa, e.g., AFLC) Comparable overall removal performance to Theranova (MCO reference) Significantly lower albumin loss: HDs membrane: 0.77±0.25 g/session Theranova: 2.14±0.45 g/session (—3x higher)
5	ELISIO-HX (HDs membrane)	2022	Comparison ot2 medium cutoff dialyzers versus on-line hemodiafiltration regarding depurative ability and albumin loss	Martinez-Miguel P. et al.	DOI: 10.1111/ a01.14466	Similar removal performance ot HX to HOF with 21.1 ± 3.9 L/ session Comparable etticacyvs MCO competitor (Theranova) Significantly lower albumin loss across all comparators: HDs membrane: —0.44 g/session HOF: -0.82 g Theranova: —2.25 g/session
6	ELISIO-HX (HDs membrane)	2022	Efficacy and Safety of the Medium Cut-Ott Elisio HX Dialyzer	Maduell F. etal.	DOI: 10.1159/ 000524644	Expanded HD clearly superior to conventional HD Expanded HD comparable efficacy to MCO dialyzers (Theranova) Expanded HD slightly below high-volume HDF (–31 L), but close in performance Albumin loss: HDs dialyzer: – 1.6 g/session Theranova (HDx): – 2.0 g/session HDF (post-dilution, —31 L): – 2.3 g/session

Table 1: Selected publications illustrating key milestones in HD development.

Fast forward to earlier in 2026, when results from the largest long-term clinical trial (MOTheR) directly compared Hemodiafiltration (HDF) and expanded hemodialysis (expanded HD) were presented at the European Renal Association (ERA) Congress.[14] MOTheR is a multi-centre, open label, prospective, 1:1 randomised, parallel group trial that recruited 552 incident haemodialysis patients (270 HDx, 282 OL HDF).

The researchers sought to determine whether expanded HD is non-inferior to OL-HDF at reducing a composite outcome of all-cause mortality, stroke, acute coronary syndrome, peripheral artery disease and ischemic colitis. Secondary endpoints of safety, mortality and quality of life measures were also set.

Follow-up was 23.6 months in the expanded HD group and 19.9 months in the OL-HDF group. During follow-up, the two groups had similar mortality rates (20.2% [n=53/262] vs 21.4% [n=58/271], respectively). The two groups were also similar in incidence rates of the composite end point (expanded HD, 14.6 events per 100 person-years and OL-HDF, 16.9 events per 100 person-years [incidence rate ratio, 0.87]).

The non-inferiority test was statistically significant (P=0.011), confirming the non-inferiority of expanded HD to OL-HDF and indicating that the safety profiles with respect to mortality and major cardiovascular events were similar between the two groups.

The authors concluded: 'The results of the MOTheR study demonstrate that expanded HD is non-inferior to OL-HDF for the prespecified composite endpoint.'

Removing the Barriers to Adoption

The introduction of any new technology or patient pathway always takes time but as noted throughout this article, based on the clinical evidence that reports significant improvements in removing the middle molecules responsible for sub-optimal outcomes and quality of life impacts compared to standard HD, the adoption of HDF and expanded HD has progressed in several markets around the world, notably Asia and Europe.

Clearly, both give physicians options for raising the bar for dialysis patients, however there are patient eligibility requirements, along with regulatory challenges and significant infrastructure and equipment limitations, for example, for HDF. These issues make HDF a suitable treatment option for a portion of the patient population, while expanded HD – performed on standard dialysis equipment – offers an easily scalable opportunity to raise the bar for a broad portion of the hemodialysis population.

Against this background, and to add further US market-specific data and experience, a series of trials and studies using the new HDs dialyser are planned to start now that F.D.A. 510(k) clearance has been obtained. The upcoming studies will measure a variety of data points including mortality, hospitalisation, removal performance, albumin retention, medication reduction and overall quality of life metrics.

Conclusion

Researchers and clinicians seem aligned on the opinion that the new treatment modalities now available mark a significant shift in the quality of care they can provide for their dialysis patients. Both HDF and expanded HD have met the mark in terms of safety and efficacy and are now growing in adoption outside of the U.S. where they are becoming common options for improving care. The recent commitment from major US providers to scale up expanded HD is underpinned by the new clinical evidence from the most recent European clinical trial showing that expanded HD is non-inferior to HDF and the availability of the new HDs dialyser. The simplicity and practical advantages of expanded HD finally look set to drive the adoption of the therapy in North America, transforming US dialysis outcomes.

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