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Switching from high-flux dialysis to hemodiafiltration: Cost-consequences for patients, providers, and payers

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Abstract

Hemodiafiltration (HDF) achieves a more efficient reduction of the uremic toxic load compared to standard high-flux hemodialysis (HF-HD) by virtue of the combined diffusive and convective clearances of a broad spectrum of uremic retention solutes. Clinical trials and registry data suggest that HDF improves patient outcomes. Despite the acknowledged need to improve survival rates of dialysis patients and the survival benefit HDF offers, there is little to no utilization in some countries (such as the US) in prescribing HDF to their patients. In this analysis, we present the healthcare value-based case for HDF (relative to HF-HD) from the patient, provider, and payor perspectives. The improved survival and reduced morbidity observed in studies conducted outside the US, as well as the reduced hospitalization, are attractive for each stakeholder. We also consider the potential barriers to greater utilization of HDF therapies, including unfounded concerns regarding additional costs of HDF, e.g., for the preparation and microbial testing of quality of substitution fluids. Ultrapure fluids are easily attainable and prepared from dialysis fluids using established "online" (OL) technologies. OL-HDF has matured to a level whereby little additional effort is required to safely implement it as all modern machine systems are today equipped with the OL-HDF functionality. Countries already convinced of the advantages of HF-HD are thus well positioned to make the transition to OL-HDF to achieve further clinical and associated economic benefits. Healthcare systems struggling to cope with the increasing demand for HD therapies would therefore, like patients, be beneficiaries in the long term with increased usage of OL-HDF for end stage kidney disease patients.

1 | INTRODUCTION

By 2040, chronic kidney disease (CKD) is estimated to become the fifth leading cause of death globally.[1,2] As the burden of CKD escalates and current costs being unsustainable, dialysis care providers and payors need not only to be prepared for future demand in kidney replacement therapy (KRT) but to improve patient outcomes while reducing costs.[3] Among populations with access to dialysis, mortality remains high and outcomes suboptimal.[4] Although survival rates of patients on dialysis have improved globally over the years, they are still considered unsatisfactory even in high-income populations.[3,5] Unadjusted 5-year survival of end-stage kidney disease (ESKD) patients on kidney replacement therapy (KRT) was 41% in the USA, 48% in Europe, and 60% in Japan.[3] Hemodialysis (HD) is the predominant KRT modality in these regions. Because providers in most countries outside of the US are rewarded based upon patient health outcomes, the gap in survival between the US, Europe and Japan requires reassessment of KRT management strategies to ensure better delivery of HD therapies with reduced procedure-related effects that impact patient wellbeing as well as costs.[6,7]

1.1 | Why high-flux dialysis is still a sub-optimal modality

According to DOPPS (Dialysis Outcomes and Practice Patterns Study), MONDO and United States Renal Data System (USRDS), differences in patient populations and variations in dialysis practice patterns may account for some of the aforementioned differences in survival outcomes.[3,5,8,9] Modifiable dialysis practices including HD treatment modality, duration, frequency and location of treatment, vascular access, medication, water quality, and patient compliance which all impact dialysis adequacy and survival rates.[10] The choice of treatment modalities for HD includes low-flux HD (LF-HD), high-flux HD (HF-HD), and hemodiafiltration (HDF), of which there are several variants, the main two being online HDF (OL-HDF) and online high-volume HDF (HV-HDF; i.e., substitution volumes >21 L per session, post-dilution mode).[11–13] The switch from LF-HD to HF-HD, backed by secondary analyses of the US HEMO and the European MPO trials that showed a survival advantage in certain patient groups, convinced nephrologists of the benefits of increased dose of dialysis as well as of more intensive removal of a broad spectrum of uremic toxins.[12–14] It also fuelled the belief that patient outcomes could be improved further with modalities that are even more efficient in terms of their detoxification capabilities.[15]

2 | STRIVING FOR "MORE INTENSIVE" DIALYSIS: HEMODIAFILTRATION

Hemodiafiltration (HDF), as the designation indicates, is modality that combines the principles of hemodialysis (HD) and hemofiltration (HF) that was pioneered in the US in the 1970s to target removal of larger uremic retention solutes involved in uremia.[16–18]

The original HDF procedures were cumbersome as fluid removed by ultrafiltration (other than that removed to compensate for interdialytic fluid gain) had to be substituted with an equivalent volume of highly pure substitution fluid using several bottles or bags.[16] The advent of "online" (OL) preparation of substitution fluid—from the existing dialysis fluids—resolved the dilemma and established the platform for OL-HDF and its different variants in use today.[19] Achievement of maximal ultrafiltration rates (relative to the blood flow rates) according to the individual needs of patients is the key to maximizing convective clearances with HDF.[20] A body of clinical evidence indicates that HDF, particularly at high substitution volumes (> 21 L per treatment) provides survival benefits for patients; this has given rise to the concept of *convective dose* which considers the total ultrafiltration volume (volume due to substitution and weight loss.[21–25] To our knowledge to date, no studies have shown any inferiority or detrimental effects attributed to OL-HDF.[26] Further, previous studies that were unable to demonstrate any superiority of OL-HDF (over HF-HD) probably applied substitution volumes below 21 L per treatment, as the convective dose concept only became evident subsequently after the initial set of clinical studies on OL-HDF.[26]

3 | HEMODIAFILTRATION: THE VALUE BASED HEALTH CARE PERSPECTIVE

Concerns regarding the future global sustainability of dialysis have increased in recent years. In a recent review Himmelfarb et al.,[4] as current *costs* are not sustainable (even for high-income countries), there is urgent need to develop new approaches and dialysis modalities that reduce costs, improve patient outcomes, and increase accessibility. This statement, from leading opinion leaders in nephrology addressing the current and future landscape of dialysis, essentially embodies the core tenet of value-based healthcare (VBHC) of achieving the *best* (*clinical*) *outcomes* at adequate *costs*.[27,28] The benefits of a VBHC system extend to *patients*, *providers*, *payers*, suppliers, and society as a whole.[29]

Provision of dialysis is one of the most cost-intensive medical interventions whereby lifelong KRT—sometimes up to three decades or beyond—is delivered.[30,31] It represents a disproportionately high financial burden to healthcare systems and society at large, and the need for KRT is projected to increase more steeply.[32,33] Recognizing the need for action, many initiatives have applied the VBHC framework to CKD and dialysis care.[34] The analyses of Busink et al.[35] reveals that translation of VBHC into value-based renal care (VBRC) is possible and even desirable if an optimal treatment pathway for CKD patients is to be achieved. Such a transition requires an organizational change in health system setup and should include a strategy focusing on full care responsibility: the patient outcome perspective and economic analysis need to be the center of attention while also considering societal and environmental aspects. A further example of VBHC endeavors that evaluate cost implications of KRT, the National Institute for Health and Care Excellence[36] England conducted a systematic review and applied economic models to compare HDF with Hf-HD.[36]

3.1 | The patient: HDF improves survival rates as well general well-being

While patients value longevity, the overarching desire of patients is reducing symptom burden and achieving maximal functional and social rehabilitation.[4,38] Three major European RCTs have investigated survival and morbidity rates of HDF compared to HD.[37,39,40] The Pooling Data Study compiled the data from the three RCTs and additional data from the FRENCHIE study, all report survival benefits for patients treated with HV-HDF.[23,41–43] After pooling all data, the reported numbers needed to treat (NNTs) were 32 (all-cause mortality) and 75 (CVD-mortality) for high volume HDF treatments per year, meaning that 32/75 patients need to be treated with high volume HDF to prevent one death per year related to all-cause/CVD mortality respectively.[42] Similarly, by taking the mortality rates from the ESHOL Study (that compared HF-HD and HV-HDF) and calculating the projected survival difference between the two groups of 100 HF-HD and 100 HDF patients, after 6 years, 12 patients more would have survived in the HDF group than in the HD group (Figure 1).[37]

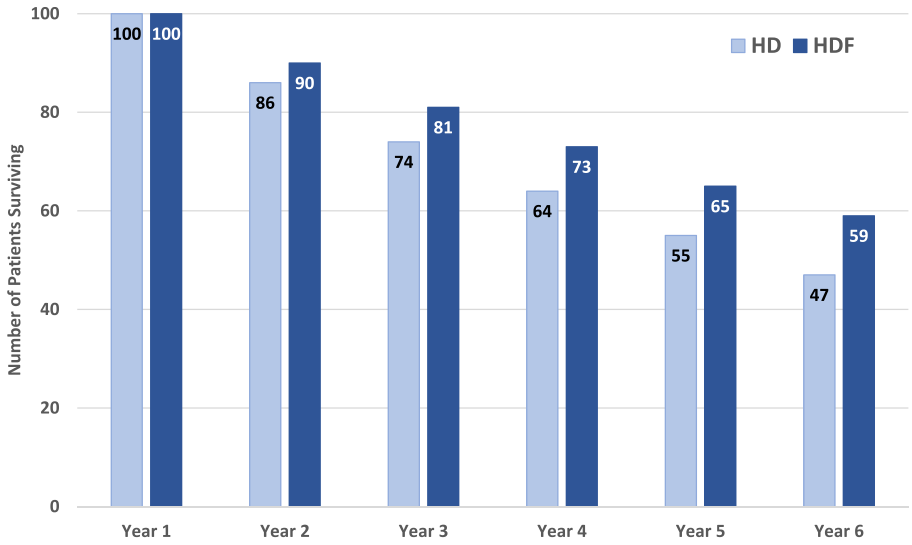

FIGURE 1 The number of surviving HD and HV-HDF patients over a period of 6 years according to the mortality rates reported in the ESHOL study.[37] Survival calculations are based on these mortality rates and NNT (numbers needed treat, measure used in communicating the effectiveness of a health-care intervention), starting with 100 patients in both groups

3.2 | The provider: HDF enables cost-saving

Ethical considerations aside, if patients live longer, providers of KRT would profit from being able to treat each patient for extended periods. This longevity incentive compels providers of dialysis therapies to develop or implement treatment strategies for which there is evidence of improved survival rates.[44] Recently, data from a large provider of HD services showed a reduction of mortality when key indicators of HD performance are systematically implemented in combination with HDF.[45]

Because of the very nature of current delivery of HD—intermittent, regular, and long-term—clinical outcomes are intricately linked to costs and profitability.[46,47] Intermittent dialysis results in severe systemic stress inducing both acute (during HD session) as well as chronic (interdialytic period) *hemodynamic stress*, both of which result respectively in hypotensive and hypertensive episodes.[48–50] Subsequent correctional interventions to deal with adverse events have considerable cost repercussions for providers of HD therapies.[51] HDF, particularly at higher convective volumes, could provide beneficial effects towards reducing such adverse reactions observed in HD patients.[25,52]

The principal *cost-incurring components* involved in the care of all HD patients are infrastructure (care unit setting and physician/nurse fees), HD treatment (disposables, machines, and solutions), medications (heparin, erythropoietin, iron, or for comorbid conditions), transportation (in some countries), diagnostics/lab testing (regular session-related blood or fluid monitoring), and waste disposal (packaging and biowaste).[53] In a budget constrained environment, it is apparent that each of these components could contribute to cost savings by improving efficiencies or reducing waste.[54,55] However, cost optimization processes, if conducted injudiciously without due consideration to the physiological and medical consequences, are often to the detriment of the patient who then receives suboptimal therapy leading to poor outcomes. Most additional costs incurred attributed directly to the HD treatment session or its consequences (short- or long-term) are costs related to hospitalization to address or correct adverse events.

3.3 | How HDF enables cost savings through reduced hospitalization

Hospitalization is an important cost factor for providers who are not reimbursed for the sessions missed.[56–60] A recent analysis estimated the potential cost-savings associated with reducing hospital admissions associated with online HV-HDF relative to HF-HD.[61] As economic models built upon payment systems and structures outside of the US may be difficult to apply to US, the analysis estimated the potential cost-savings associated with reducing hospital admissions with online HV-HDF (vs. HF-HD) based on published studies and average cost of hospitalization derived from USRDS cost data. The overall rate ratio of all-cause hospital admissions was 0.78 (with 95% CI of 0.67–0.90 in patients on HV-HDF vs. HF-HD); this translates into significant cost savings due to hospitalization with HV-HDF observed for averted hospitalization and missed in-center treatment sessions as shown in Figure 2.

3.4 | The payer: HDF curtails overall costs for long-term sustainability

Longevity means increased burden of care, but this could partially be compensated by incentivizing general well-being (reduced morbidity) so that a patient is able to lead as normal a life as possible and contribute to society.[62] However, every hospitalization means significant extra costs for the payer (healthcare system), depending on the severity of the incidence and duration of stay, planned or unplanned. During the hospitalization period, HD therapy must nevertheless be continued at the prescribed intervals and even may be more if the patient's volume status is impacted and/or if they are more catabolic. Although costs for HD treatments conducted in hospital are covered by specific reimbursement schemes, hospitals may need to charge higher amounts as the therapy is not usually conducted in the same streamlined way as in specialist dialysis facilities.[63]

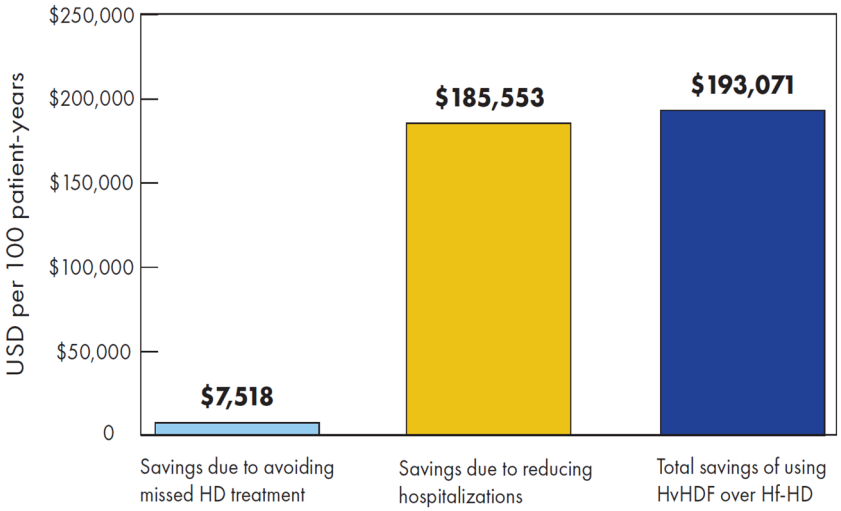

FIGURE 2 Potential cost-savings associated with avoiding missed in-center HD treatments and reducing hospitalizations for healthcare providers. The parameters used for the calculations: (A) average cost of hospitalization was derived from USRDS and adjusted to 2021 ($17,181); (B) average hospital stay of 6.42 days; (C) assuming thrice weekly HD would result in 2.75 missed HD treatments/hospitalization; (D) similar reimbursement rate ($253.13/treatment for in-center Hf-HD and Hv-HDF); similar treatment costs for both

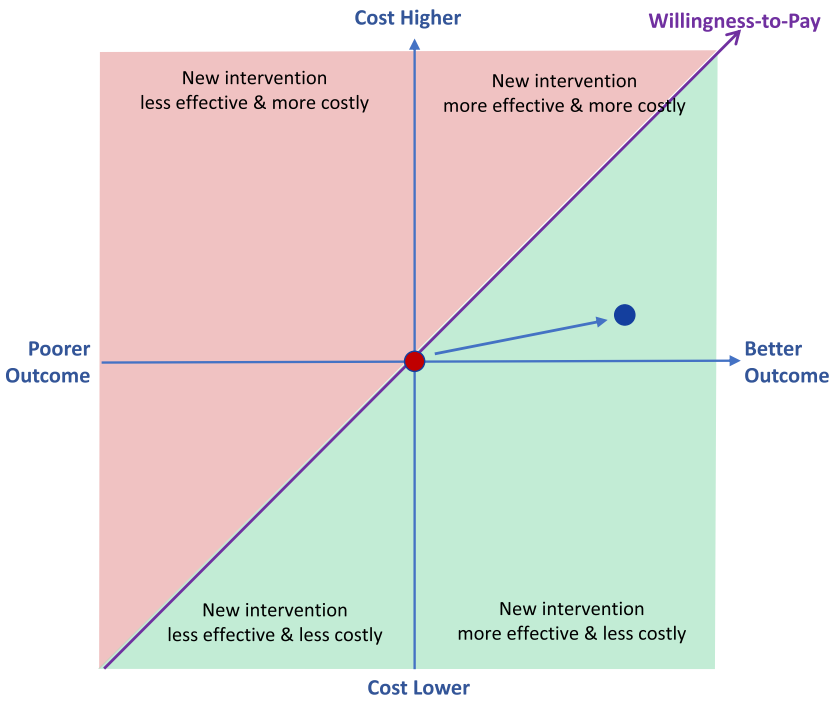

FIGURE 3 Graph illustrating how payers (health care systems) evaluate additional value of HDF (blue spot) relative to HF-HD (current standard of care, or comparator; in the middle, red spot). The value of a new intervention is examined by plotting costs (*y* axis) against clinical effectiveness or outcomes (*x* axis). The willingness to pay of a health system for additional value a new intervention is delivering runs diagonally across the four quadrants; if the intervention is above the line (red region), it is deemed as being unfavorable

The NICE initiative from England conducted a systematic review and applied economic models to compare HDF with HF-HD.[36] NICE recommends that in-center HDF should be considered rather than in-center HD in hospital or satellite dialysis units. This evidence-based recommendation aims at reducing variation in the availability and quality of NHS treatments and care, as well as promoting individualized and integrated care in England. In their assessment, NICE considered HDF be cost-effective: It improves survival of HD patients (incident and prevalent) and leads to less dialysis-related amyloidosis.[64,65] Concurrently, according to European studies, non-direct dialysis procedure-related categories, such as medication, are positively impacted, for example, reducing requirements for erythropoiesis stimulating agents by 9%.[37,39] Thus, HDF achieves a better outcome over cost ratio than HD, which is at the center aspect of the provision of VBHC. It should be noted that NICE did not consider hospitalization for the cost-effectiveness analysis as the evidence was judged to be inconclusive when assessing the literature, because insufficient substitution volumes (<21 L) were used in two of the four studies.

A *cost-effectiveness* (*CE*) *analysis* like the one conducted by NICE for HDF evaluates the effectiveness of two or more treatments relative to their cost. It is the most commonly applied health economic evaluation and is typically carried out by *health technology assessment* (*HTA*) agencies based on published evidence (i.e., *evidence-based medicine*).[36,66,67] The CE plane is used to illustrate the results of a CE analysis, by plotting the costs (*y* axis) against health outcomes (*x* axis) of a new intervention: usually compared to the "current standard of care" which is plotted at the origin (Figure 3). Technologies falling on or below this threshold are judged to be cost-effective. Whether a

technology is cost-effective in a case where outcomes are improved but costs are higher, it depends on the stakeholders' willingness to pay (WTP).

4 | IMPLEMENTATION OF HDF

The transition from Hf-HD to HDF has gained pace in recent years as there is a conviction of its clinical and economic advantages as well as it being safe and as simple a modality to implement as regular HD.[26]

4.1 | Current worldwide uptake of HDF

OL-HDF is an established treatment option used routinely for thousands of patients in Europe and Asia Pacific (AP). Globally in 2018, about 10% of patients were on HDF, 26% of these being in Europe, and 11% in AP.[68] The HDF patient average growth rate of 12% to 24% is far above the total patient HD growth rate of 6.6%. In 2016, an estimated 80,000 European patients with ESKD and 160,000 worldwide were being treated by OL-HDF. Of the 2.82 million patients on HD, 286,000 patients were on HDF (representing a 18% compound annual growth rate since 2009) with 278,000 (97% of

TABLE 1 Perceived barriers to a greater utilization in clinical practice of OL-HDF

	Perceived barrier to prescription of OL-HDF treatment modality[a]	Comments
1.	HDF is a more costly therapy than Hf-HD	NICE analysis and US Study show HDF to be more cost-effective.
2.	The evidence level for HDF is not sufficient to indicate its superiority over Hf-HD	Sufficient evidence from large RCTs, and real-world evidence (clinical experiences; > 10% of HD population globally treated with OL-HDF.
3.	HDF procedure technically more complex, requires more nursing care time/session. Staff need to undergo extensive training programs.	After initial training, it is as simple to perform as standard HD with technology advancements: nurse–patient ratio maintained.
4.	HDF requires additional microbiological testing for water, dialysis, or substitution fluids quality	Ensuring high water and dialysis fluid quality is mandatory for all forms of HD therapies.
5.	Infusion of large volumes of fluid is not safe for patient	Millions of treatments are performed annually: no reported adverse events linked specifically to fluid quality issues.
6	Fluid infusion is laborious (lack of awareness of 'online' substitution fluid production from normal dialysis fluid)	A misconception: probably from treatment of acute kidney failure in ICU where HDF is performed with sterile bag solutions.
7.	Requires additional expenditure/new machines	When old machines are replaced, all newer versions today have the OL-HDF functionality
8.	Machine disinfection regimes are more time-consuming	Machine disinfection regimes do not change with application of OL-HDF.
9.	Requires special (more costly) dialyzers	The same (high-flux) dialyzers used for Hf-HD are also applicable for OL-HDF
10.	To be fully effective, HDF requires very high blood flows	Similar high blood flows that are advantageous for Hf-HD also
11.	There are special requirements for vascular access	Fistula first
12.	Lack of nephrologists championing HDF in US/belief HDF is for acute kidney failure only (see point 6 above).	No FDA approval (510 k clearance) of online production of substitution fluid - a hindrance for nephrologists aware of clinical benefits of HDF.
13.	Additional reimbursement (e.g., US) may be required.	Saline savings via online priming and additional functions (e.g., Autoflow, Ecoflow) enable adjustment of fluid usage according to needs in each session.

[a]In no order of importance.

HDF patients) utilizing the OL-HDF modality. Germany, France, Italy, Russian Federation, Great Britain, Spain, and Portugal are the countries with the largest HDF patient populations. In the AP region, Japan and China are the most prominent countries in terms of HDF share, accounting for 82,600 and 47,420 patients, respectively, with a share of 26 and 10%.

4.2 | Perceived barriers/impediments for the greater uptake of HDF

Despite the rapid rise in the application of HDF worldwide (particularly but not exclusively in most high-income countries), the reasons that prevent an even greater application of HDF need to be examined. Table 1 lists some of the perceived barriers that hinder a more widespread usage of OL-HDF to treat KRT patients. While the individual perceptions and reservations of nephrologists in assessing the published data may prevent them from offering HDF to their patients, overall country-specific policy, mostly related to cost, regulatory and/or reimbursement issues are the greater deterrence, even when physicians are convinced of its clinical value. The case is different for the US, where HDF is absent because regulatory approval of the therapy in the US is pending and no HDF machines are available. Whereas outside the US HDF is regarded as a standard of care, in the US, it is an unknown therapy and not included in the nephrology training curriculum. Consequently, there are questions raised as to what extent non-US clinical trial data can be extrapolated to the US. Once the therapy is available, data from US-based trials would help evaluate the incremental benefit of HDF in the US.

5 | CONCLUSIONS

All KRT therapies aim not just to sustain, but to prolong patient lives with an acceptable quality of life. The obligation to produce benefit for individual patients is a duty of physicians and healthcare systems alike.[69] By advocating the case of the clinical and cost-effectiveness of OL-HDF in this publication, we prompt the question how the renal care community can give even more patients access to this treatment modality.[70]

Today, scientific or clinical considerations alone do not determine the mode of dialysis delivered to patients. Provision of HD is intricately linked to cost-containment; a conflict of interest arises between bedside care providers (doctors and nurses) and dialysis center management teams involved in administrative and procurement operations. However, by achieving better patient outcomes at the same or lower costs, OL-HDF meets the core prerequisites of patients, providers, and payers alike. There are certainly areas requiring further refinement through the acquisition of more evidence, but the current data and clinical experience with HDF are sufficiently strong to suggest its superiority over conventional HD (including high-flux HD) based upon clinical endpoints derived from RCTs and real-world evidence.[26] Several millions of OL-HDF treatment sessions are carried out safely annually without increased procedure-specific incidences. Globally, even though the US has not yet had the opportunity to offer this modality option to its ESKD population, HDF represents a new paradigm shift in KRT with potentially promising results, particularly when OL-HDF is delivered with high substitution volumes (>21 L).[26,43,71,72]

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REFERENCES

1. Kalantar-Zadeh K, Jafar TH, Nitsch D, Neuen BL, Perkovic V. Chronic kidney disease. *Lancet*. 2021;398(10302):786-802.
2. Foreman KJ, Marquez N, Dolgert A, et al. Forecasting life expectancy, years of life lost, and all-cause and cause-specific mortality for 250 causes of death: reference and alternative scenarios for 2016-40 for 195 countries and territories. *Lancet*. 2018;392(10159):2052-2090.
3. Thurlow JS, Joshi M, Yan G, et al. Global epidemiology of end-stage kidney disease and disparities in kidney replacement therapy. *Am J Nephrol*. 2021;52(2):98-107.
4. Himmelfarb J, Vanholder R, Mehrotra R, Tonelli M. The current and future landscape of dialysis. *Nat Rev Nephrol*. 2020;16(10):573-585.
5. United States Renal Data S. USRDS 2018 annual data report: Atlas of end-stage renal disease in the United States, Chapter 5: Mortality. *Am J Kidney Dis*. 2019;2:411-426.
6. Vanholder R, Davenport A, Hannedouche T, Kooman J, Kribben A, Lameire N, Lonnemann G, Magner P, Mendelssohn D, Saggi SJ, Shaffer RN, Moe SM, van Biesen W, van der Sande F, Mehrotra R and Dialysis Advisory Group of American Society of N. Reimbursement of dialysis: a comparison of seven countries. *J am Soc Nephrol* 2012;23(8):1291-1298.
7. Saunders MR, Lee H, Chin MH. Early winners and losers in dialysis center pay-for-performance. *BMC Health Serv Res*. 2017;17(1):816-824.
8. Saran R, Bragg-Gresham JL, Levin NW, et al. Longer treatment time and slower ultrafiltration in hemodialysis: associations with reduced mortality in the DOPPS. *Kidney Int*. 2006;69(7):1222-1228.
9. Usvyat LA, Haviv YS, Etter M, et al. The MONitoring Dialysis Outcomes (MONDO) initiative. *Blood Purif*. 2013;35(1–3):37-48.
10. Ashby D, Borman N, Burton J, et al. Renal association clinical practice guideline on haemodialysis. *BMC Nephrol*. 2019;20(1):379-414.
11. Susantitaphong P, Siribamrungwong M, Jaber BL. Convective therapies versus low-flux hemodialysis for chronic kidney failure: a meta-analysis of randomized controlled trials. *Nephrol Dial Transplant*. 2013;28(11):2859-2874.
12. Eknoyan G, Beck GJ, Cheung AK, et al. Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Engl J Med*. 2002;347(25):2010-2019.
13. Tattersall J, Canaud B, Heimburger O, et al. High-flux or low-flux dialysis: a position statement following publication of the Membrane Permeability Outcome study. *Nephrol Dial Transplant*. 2010;25(4):1230-1232.
14. Locatelli F, Gauly A, Czekalski S, et al. The MPO study: just a European HEMO Study or something very different? *Blood Purif*. 2008;26(1):100-104.
15. Thomas G, Jaber BL. Convective therapies for removal of middle molecular weight uremic toxins in end-stage renal disease: a review of the evidence. *Semin Dial*. 2009;22(6):610-614.
16. Henderson LW. The beginning of clinical hemofiltration: a personal account. *ASAIO j*. 2003;49(5):513-517.

17. Ronco C, Cruz D. Hemodiafiltration history, technology, and clinical results. *Adv Chronic Kidney Dis*. 2007;14(3):231-243.
18. Tattersall J, Martin-Malo A, Pedrini L, et al. EBPG guideline on dialysis strategies. *Nephrol Dial Transplant*. 2007;22(Suppl 2):ii5-ii21.
19. Canaud B. The early years of on-line HDF: how did it all start? How did we get here? *Contrib Nephrol*. 2011;175:93-109.
20. Canaud B, Bowry SK. Emerging clinical evidence on online hemodiafiltration: does volume of ultrafiltration matter? *Blood Purif*. 2013;35(1–3):55-62.
21. Bowry SK, Canaud B. Achieving high convective volumes in on-line hemodiafiltration. *Blood Purif*. 2013;35(Suppl 1):23-28.
22. Canaud B, Koehler K, Bowry S, Stuard S. What is the optimal target convective volume in on-line hemodiafiltration therapy? *Contrib Nephrol*. 2017;189:9-16.
23. Davenport A, Peters SA, Bots ML, et al. Higher convection volume exchange with online hemodiafiltration is associated with survival advantage for dialysis patients: the effect of adjustment for body size. *Kidney Int*. 2016;89(1):193-199.
24. Marcelli D, Kopperschmidt P, Bayh I, et al. Modifiable factors associated with achievement of high-volume post-dilution hemodiafiltration: results from an international study. *Int J Artif Organs*. 2015;38(5):244-250.
25. Blankestijn PJ, Fischer KI, Barth C, et al. Benefits and harms of high-dose haemodiafiltration versus high-flux haemodialysis: the comparison of high-dose haemodiafiltration with high-flux haemodialysis (CONVINCE) trial protocol. *BMJ Open*. 2020;10(2):e033228.
26. Canaud B, Blankestijn PJ, Grooteman MPC, Davenport A. Why and how high volume hemodiafiltration may reduce cardiovascular mortality in stage 5 chronic kidney disease dialysis patients? A comprehensive literature review on mechanisms involved. *Semin Dial*. 2021;35(2):117-128.
27. Porter ME. Value-based health care delivery. *Ann Surg*. 2008;248(4):503-509.
28. Porter ME. A strategy for health care reform—toward a value-based system. *N Engl J Med*. 2009;361(2):109-112.
29. NEJM Catalyst. What Is Value-Based Healthcare?. 2017. Accessed January 20, 2022. 10.1056/CAT.17.0558
30. Vanholder R, Lameire N, Annemans L, Van Biesen W. Cost of renal replacement: how to help as many as possible while keeping expenses reasonable? *Nephrol Dial Transplant*. 2016;31(8):1251-1261.
31. Vanholder R, Annemans L, Brown E, et al. Reducing the costs of chronic kidney disease while delivering quality health care: a call to action. *Nat Rev Nephrol*. 2017;13(7):393-409.
32. Braun L, Sood V, Hogue S, Lieberman B, Copley-Merriman C. High burden and unmet patient needs in chronic kidney disease. *Int J Nephrol Renovasc Dis*. 2012;5:151-163.
33. Mushi L, Marschall P, Flessa S. The cost of dialysis in low and middle-income countries: a systematic review. *BMC Health Serv Res*. 2015;15:506-515.
34. Verberne WR, Das-Gupta Z, Allegretti AS, et al. Development of an international standard set of value-based outcome measures for patients with chronic kidney disease: a report of the International Consortium for Health Outcomes Measurement (ICHOM) CKD Working Group. *Am J Kidney Dis*. 2019;73(3):372-384.
35. Busink E, Canaud B, Schroder-Back P, et al. Chronic kidney disease: exploring value-based healthcare as a potential viable solution. *Blood Purif*. 2019;47(1–3):156-165.
36. NICE National Institute for Health and Care Excellence. RRT and conservative management - Cost-effectiveness analysis: HDF versus high flux HD. NICE guideline [NG107]; 2018.
37. Maduell F, Moreso F, Pons M, et al. High-efficiency postdilution online hemodiafiltration reduces all-cause mortality in hemodialysis patients. *J am Soc Nephrol*. 2013;24(3):487-497.
38. Jawed A, Moe SM, Moorthi RN, Torke AM, Eadon MT. Increasing nephrologist awareness of symptom burden in older hospitalized end-stage renal disease patients. *Am J Nephrol*. 2020;51(1):11-16.
39. Ok E, Asci G, Toz H, et al. Mortality and cardiovascular events in online haemodiafiltration (OL-HDF) compared with high-flux dialysis: results from the Turkish OL-HDF Study. *Nephrol Dial Transplant*. 2013;28(1):192-202.
40. Canaud B, Morena M, Leray-Moragues H, Chalabi L, Cristol JP. Overview of clinical studies in hemodiafiltration: what do we need now? *Hemodial Int*. 2006;10(Suppl 1):S5-S12.
41. Peters SA, Bots ML, Canaud B, et al. Blankestijn PJ and HDFPPI. Haemodiafiltration and mortality in end-stage kidney disease patients: a pooled individual participant data analysis from four randomized controlled trials. *Nephrol Dial Transplant*. 2016;31(6):978-984.
42. Nube MJ, Peters SAE, Blankestijn PJ, et al. Mortality reduction by post-dilution online-haemodiafiltration: a cause-specific analysis. *Nephrol Dial Transplant*. 2017;32(3):548-555.
43. Morena M, Jaussent A, Chalabi L, et al. Treatment tolerance and patient-reported outcomes favor online hemodiafiltration compared to high-flux hemodialysis in the elderly. *Kidney Int*. 2017;91(6):1495-1509.
44. Roundtable on Population Health Improvement, Board on Population Health and Public Health Practice and Institute of Medicine. *Financing Population Health Improvement: Workshop Summary*. Washington (DC): National Academies Press (US); 2015.
45. Garbelli M, Ion Titapiccolo J, Bellocchio F, Stuard S, Brancaccio D, Neri L. Leveraging digital transformation to empower clinical governance: enhancement in intermediate clinical endpoints and patients' survival after implementation of a continuous quality improvement program in a large dialysis network. *Nephrol Dial Transplant*. 2021;37(3):469-476.
46. Just PM, de Charro FT, Tschosik EA, Noe LL, Bhattacharyya SK, Riella MC. Reimbursement and economic factors influencing dialysis modality choice around the world. *Nephrol Dial Transplant*. 2008;23(7):2365-2373.
47. van der Tol A, Lameire N, Morton RL, van Biesen W, Vanholder R. An international analysis of dialysis services reimbursement. *Clin J am Soc Nephrol*. 2019;14(1):84-93.
48. McIntyre CW. Recurrent circulatory stress: the dark side of dialysis. *Semin Dial*. 2010;23(5):449-451.
49. Canaud B, Kooman JP, Selby NM, et al. Dialysis-induced cardiovascular and multiorgan morbidity. *Kidney Int Rep*. 2020;5(11):1856-1869.
50. Canaud B, Chazot C, Koomans J, Collins A. Fluid and hemodynamic management in hemodialysis patients: challenges and opportunities. *J Bras Nefrol*. 2019;41(4):550-559.
51. European Renal Association European Dialysis and Transplant Association. *ERA-EDTA Registry: ERA-EDTA Registry Annual Report 2014*. Amsterdam (NL): Academic Medical Center; 2016.
52. Ethier I, Nevis I, Suri RS. Quality of life and hemodynamic effects of switching from hemodialysis to hemodiafiltration: a Canadian controlled cohort study. *Can J Kidney Health Dis*. 2021;8:20543581211057717.
53. Kaur G, Prinja S, Ramachandran R, Malhotra P, Gupta KL, Jha V. Cost of hemodialysis in a public sector tertiary hospital of India. *Clin Kidney J*. 2018;11(5):726-733.
54. Piccoli GB, Nazha M, Ferraresi M, Vigotti FN, Pereno A, Barbero S. Eco-dialysis: the financial and ecological costs of dialysis waste products: is a 'cradle-to-cradle' model feasible for planet-friendly haemodialysis waste management? *Nephrol Dial Transplant*. 2015;30(6):1018-1027.
55. Ferraresi M, Nazha M, Vigotti FN, et al. Ecodialysis: first strategies to limit damages and reduce costs. *G Ital Nefrol*. 2014;31(5):1-6.

56. Flythe JE, Kimmel SE, Brunelli SM. Rapid fluid removal during dialysis is associated with cardiovascular morbidity and mortality. *Kidney Int*. 2011;79(2):250-257.
57. Mitema D, Jaar BG. How can we improve the quality of life of dialysis patients? *Semin Dial*. 2016;29(2):93-102.
58. Henderson LW. Dialysis in the 21st century. *Am J Kidney Dis*. 1996; 28(6):951-957.
59. Rhee CM, Chou JA, Kalantar-Zadeh K. Dialysis prescription and sudden death. *Semin Nephrol*. 2018;38(6):570-581.
60. Rabindranath KS, Strippoli GF, Roderick P, Wallace SA, MacLeod AM, Daly C. Comparison of hemodialysis, hemofiltration, and acetate-free biofiltration for ESRD: systematic review. *Am J Kidney Dis*. 2005; 45(3):437-447.
61. Ficociello L, Farahati F, Mullon C and Anger MS. Potential cost savings associated with the reduction of hospital admissions by using online high-volume hemodiafiltration (Hv-HDF) vs. high-flux hemodialysis (Hf-HD) (Abstract). 2021. Accessed January 20, 2022. https://www.asn-online.org/education/kidneyweek/2021/program-abstract.aspx?controlId=3611227
62. Drummond M, Federici C, Busink E, Apel C, Kendzia D, Brouwer W. Performance-based risk-sharing agreements in renal care: current experience and future prospects. *Expert Rev Pharmacoecon Outcomes Res*. 2021;21(2):197-209.
63. CostHelper, Inc. Dialysis cost—how much does dialysis cost? 2021. Accessed January 20, 2022. https://health.costhelper.com/dialysis.html
64. Ramponi F, Ronco C, Mason G, et al. Cost-effectiveness analysis of online hemodiafiltration versus high-flux hemodialysis. *Clinicoecon Outcomes Res*. 2016;8:531-540.
65. AlSaran K, Mirza K. Cost-effectiveness of online hemodiafiltration. In: Karkar AS, ed. *Advances in hemodiafiltration*. Rijeka (Croatia): IntechOpen; 2016.
66. Sendi PP, Briggs AH. Affordability and cost-effectiveness: decision-making on the cost-effectiveness plane. *Health Econ*. 2001;10(7): 675-680.
67. Black WC. The CE plane: a graphic representation of cost-effectiveness. *Med Decis Making*. 1990;10(3):212-214.
68. Canaud B, Kohler K, Sichart JM, Moller S. Global prevalent use, trends and practices in haemodiafiltration. *Nephrol Dial Transplant*. 2020; 35(3):398-407.
69. Schröder-Bäck P, Duncan P, Sherlaw W, Brall C, Czabanowska K. Teaching seven principles for public health ethics: towards a curriculum for a short course on ethics in public health programmes. *BMC Med Ethics*. 2014;15:73-82.
70. Alquist M, Bosch JP, Barth C, et al. Knowing what we do and doing what we should: quality assurance in hemodialysis. *Nephron Clin Pract*. 2014;126(3):135-143.
71. Locatelli F, Karaboyas A, Pisoni RL, et al. Mortality risk in patients on hemodiafiltration versus hemodialysis: a 'real-world' comparison from the DOPPS. *Nephrol Dial Transplant*. 2018;33(4):683-689.
72. Marcelli D, Scholz C, Ponce P, et al. High-volume postdilution hemodiafiltration is a feasible option in routine clinical practice. *Artif Organs*. 2015;39(2):142-149.

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