

# Intensified home hemodialysis: clinical benefits, risks and target populations

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## ABSTRACT

Intensive home hemodialysis (IHHD) has emerged as an alternate treatment option for patients with end-stage renal disease and has several established and potential clinical benefits. These clinical advantages need to be tempered against a growing appreciation of the risks of IHHD, including a potentially higher rate of vascular access interventions. Identifying who might be an eligible and optimal candidate for IHHD is paramount to its expansion as an important form of renal replacement therapy. In the following review, we will provide a working definition of IHHD, discuss its major clinical benefits/risks and identify potential target populations to whom this therapy can be provided.

**Keywords:** intensive hemodialysis, populations, target

## INTRODUCTION: WHAT IS INTENSIFIED DIALYSIS?

An increasing number of patients are being considered for home hemodialysis. One of the major advantages of dialyzing at home is its flexibility. In addition, provision of dialysis in the home environment allows exposure to different treatment regimens. Simply, intensive home hemodialysis (IHHD) refers to home hemodialysis with an increase in dialysis frequency (days/week) or session length above a standard conventional hemodialysis (CHD) schedule. However, it is important to recognize that CHD schedules are not standardized. Traditionally, CHD has been defined as 4 h/session and 3 sessions/week, but there is a wide variation in the session length when examining data from international registries and cohorts. In a registry study of Australian and New Zealand hemodialysis patients, 38 and 73% of facility and home CHD patients received >4.5 h per session, respectively [1]. In contrast, the dialysis outcomes and practice patterns

study 4 study identified that the session length is typically <240 min in North America and most European countries (although shorter frequent dialysis is also included) [2]. Acknowledging that there are differences in CHD session length, there are three predominant IHHD regimens that are commonly identified. Short-daily hemodialysis (SDHD) is characterized by an increase in dialysis frequency (5 or more sessions per week) and decrease in session length (2.5–3 h). Long hemodialysis consists of 3–4 weekly sessions of >5.5 h. Long-frequent hemodialysis involves an increase in both frequency (5 or more weekly sessions) and session length (>5.5 h). Both long and long-frequent IHHD can be provided overnight while a patient sleeps [nocturnal hemodialysis (NHD)]. Because of the increase in dialysis time for long and long-frequent hemodialysis, there are some special considerations that need to be made; provided patients are not hypercalcemic, dialysis bath calcium concentration should be maintained at 1.5 mmol/L to avoid a negative total body calcium balance [3]. Patients receiving longer treatment schedules may also require phosphate additives due to the tendency toward hypophosphatemia due to improved phosphate clearance [4]. A summary of typical dialysis frequencies, session lengths and dialyzate/blood flows for CHD and IHHD are noted in Table 1 [5].

## CLINICAL BENEFITS

### Survival

Several studies have evaluated survival in SDHD and NHD. However, no well-powered randomized controlled trial (RCT) has been performed, and most data are extracted from observational studies. Overall, survival rates were reported in an SDHD cohort of 262 patients with 1-, 3- and 8-year patient survival of  $92 \pm 2$ ,  $73 \pm 4$  and  $54 \pm 7\%$ , respectively [7]. Similarly, 1-, 3- and 5-year survival was 98, 92 and 83%, respectively, in

**Table 1. Intensive home hemodialysis regimens**

	Dialysis regimen				
	CHD	NxStage	Short daily hemodialysis	Long hemodialysis <sup>a</sup>	Long frequent <sup>a</sup>
Frequency (sessions/week)	3	5+	5+	3–4	5+
Duration (hours/session)	4	2.5–3.5	2.5–3	>5.5	>5.5
Dialyzate flow (mL/min)	500–800	100–200	500–800	300–500	300–500
Blood flow (mL/min)	200–400	400	400	200–400	200–300
std $K_t/V_{urea}^b$	2.50 (12 h/week)	–	3.75 (13.5 h/week)	3.75 (26.8 h/week)	5.82 (40.2 h/week)

<sup>a</sup>Can be performed as NHD.

<sup>b</sup>Adapted from the Frequent Hemodialysis Network analysis of solute clearance [6]. Clearances reflect median weekly values, and are model-based calculations for provided weekly treatment times. std  $K_t/V_{urea}$  denotes standardized  $K_t/V_{urea}$ .

an Australian cohort of 286 extended-hours hemodialysis patients (mostly home nocturnal) [8]. Finally, the overall survival (including patient and technique survival) has been assessed in a cohort of 247 NHD Canadian patients with a 1- and 5-year survival of 95.2 and 80.1%, respectively [9].

Additionally, improved survival compared with matched cohorts of CHD or the standardized mortality ratio for CHD patients is described for SDHD [10, 11] and NHD [12–14]. A large study including all patients starting renal replacement therapy between 1996 and 2007 in Australia and New Zealand showed a reduction in the adjusted mortality for patients with frequent/extended home hemodialysis [hazard ratio (HR) 0.53, 95% confidence interval (CI) (0.41–0.68)] compared with in-center CHD. Patients on conventional home hemodialysis had a similar decrease in mortality risk, however, among them, 61% had a dialysis session length of >5 h [1].

### Blood pressure

Blood pressure reduction has been one of the most consistent benefits of IHHD in randomized and non-randomized studies [15–21]. The Frequent Hemodialysis Network (FHN) trial showed a significant reduction in systolic blood pressure among the NHD cohort after 12 months of follow-up [–9.7 (–16.9, –2.5) mm Hg] with a significant decrease in the number of antihypertensive agents. No difference was seen in the CHD control group, although a large proportion was receiving their treatment at home. This emphasizes the effect of intensive hemodialysis on blood pressure and not only home treatment *per se* [18]. Ambulatory 24 h blood pressure decreased in a small randomized crossover trial after 8 weeks of NHD compared with the previous CHD phase despite the absence of significant decrease in patients' post-dialysis weight [20]. The mechanism of blood pressure reduction in NHD is speculated to be related to reductions in total peripheral resistance and plasma norepinephrine over and above changes in volume status [20, 21].

In SDHD, improvement of blood pressure was retrospectively described among 32 US patients after conversion from CHD to SDHD [19]. The London Daily/Nocturnal Study also showed a decreased blood pressure in the SDHD group with a parallel reduction in their extra-cellular fluid volume [17]. Similar results with a reduction in blood pressure and extra-cellular fluid content were found in a randomized crossover study with 12 patients receiving SDHD in Italy [22]. Unlike

NHD, a reduction in fluid overload seems to be the main mechanism for blood pressure reduction in SDHD [17].

### Left ventricular geometry

Improvement in left ventricular mass index as measured by 2D echography has been reported in observational studies of SDHD [17, 22] and NHD [15, 17] cohorts. A meta-analysis including frequent and extended hemodialysis performed at home and in-center reported a favorable reduction in left ventricular mass index in both groups [23]. Two RCTs have evaluated cardiac geometry in home NHD cohorts. A reduction in the left ventricular mass was demonstrated in a Canadian RCT with 52 prevalent dialysis patients. The 26 patients randomized to NHD had significant improvements in the left ventricular mass compared with the CHD group with a difference of 15.3 g [(1.0–29.6 g),  $P = 0.04$ ] between the two groups after 6 months [24]. In contrary, the FHN trial did not find a statistically significant effect of NHD on left ventricular hypertrophy (LVH) compared with CHD. However, a large proportion of the 92 patients had no LVH at the time of their enrollment in the study and the trial also enrolled a smaller number of patients than expected [18].

### Phosphate control and mineral metabolism

Phosphate control improvement is described with SDHD and to a higher degree with NHD. The FREEDOM trial showed a modest reduction in phosphate after the 12-month SHDH period ( $5.5 \pm 1.3$  to  $5.2 \pm 1.6$  mg/dL,  $P = 0.01$ ) [25]. Two RCTs evaluated phosphate control with NHD. The FHN Nocturnal trial demonstrated a reduction of 1.24 mg/dL (95% CI 0.68–1.79) in the mean phosphate compared with the CHD group. By the end of the study period, 73% of NHD patients did not need phosphate binders compared with 8% in the CHD group [18]. Similar findings were described in the RCT from two Canadian centers with a significant reduction in phosphate (0.49 mmol/L, 95% CI 0.24–0.74) for the NHD group compared with the CHD group after 6 months. The decline in intact parathyroid hormone (PTH) was also more frequent for NHD patients compared with CHD (60 versus 20%,  $P = 0.003$ ); however, no significant changes in the median PTH level were found [24, 26].

### Quality of life

The influence of IHHD on quality of life (QOL) has been evaluated in multiple studies with most of them showing an improvement in kidney-specific domains [18, 24, 27–29]. No change in global QOL as assessed by EuroQol 5-D was demonstrated in the Alberta Kidney Disease Network RCT for the NHD group compared with the control CHD group after the 6-month follow-up. However, significant improvements in kidney-specific domains QOL and burden of kidney disease were reported among NHD patients [24]. The FHN trial, did not find a significant difference between the conventional and NHD groups. Nonetheless, both groups improved their QOL during follow-up and, as mentioned above, a large proportion of the CHD patients received their dialysis treatments at home [18]. The London Daily/Nocturnal Hemodialysis Study (which included 11 SDHD patients, 12 NHD patients and 22 CHD patients serving as controls) also demonstrated improvements in kidney-specific QOL [29]. In addition to QOL, mood improvement can be seen with IHHD. Depression symptoms were specifically assessed in the FREEDOM study. The Beck Depression Inventory (BDI) score was significantly improved after 12 months of SDHD compared with baseline, both in the per-protocol and intention-to-treat analysis ( $P < 0.001$ ) [25]. The nocturnal FHN also showed a greater improvement in the BDI score for the NHD group compared with CHD; however, it did not reach significance [18].

### Quality of sleep

Restless legs syndrome (RLS) is a major issue for many patients on dialysis. The FREEDOM study evaluated changes in RLS prevalence and severity in a prospective cohort of 235 patients treated with SDHD. At baseline, 40% of patients suffered from RLS. Among them, the adjusted mean International Restless Leg Score decreased from baseline (18) to 4 months (13) and 12 months (11) in the per-protocol analysis, ( $P = 0.001$ ). Among the 127 patients that completed the 12-month RLS survey, the prevalence of RLS decreased from 35 to 26% after 12 months of SDHD ( $P = 0.05$ ) [30].

NHD has been associated with a reduction in the frequency of sleep apnea episodes. In a cohort study, 14 patients underwent a polysomnography during CHD therapy and 6–15 months after conversion to NHD. The frequency of apnea and hypopnea episodes decreased from  $25 \pm 25$  to  $8 \pm 8$  episodes per hour of sleep for a night on NHD ( $P = 0.03$ ). The effect was more pronounced among the seven patients with severe sleep apnea syndrome with a reduction from  $46 \pm 19$  to  $9 \pm 9$  per hour ( $P = 0.006$ ) [31].

### Fertility

Dialysis has been associated with a low conception rate and poor pregnancy outcomes, including spontaneous abortion, premature delivery and low gestational weight. For instance, a pregnancy rate of 3.3 per 1000 patient-years was reported between 1996 and 2008 in the Australian and New Zealand dialysis population with a live birth rate of 1.84 per 1000 patient-years during the same period [32]. Endocrine abnormalities leading to a reduction in the fertility rate include dysregulation of

the pituitary–hypothalamic axis, higher but constant levels of luteinizing hormone, lower levels of estrogen and progesterone and finally, decreased prolactin clearance resulting in hyperprolactinemia [33]. Longer weekly dialysis time [34] and lower urea level [35] throughout pregnancy have been related to better outcomes including increased gestational age and birth weight. Although published data are still scarce, intensive dialysis appears to improve outcomes of pregnant woman with end-stage renal disease. In a report of intensive NHD patients, conception rate increased to 16% after conversion from CHD to NHD. Among the seven pregnancies that occurred, one resulted in an elective abortion, while all the other women delivered living infants at a mean gestational age of  $36.2 \pm 3$  weeks and birth weight of  $2417.5 \pm 657$  g. Maternal complications were also fewer. Dialysis time among this cohort of women was higher than any other pregnancy reports with a weekly dialysis time increased from  $36 \pm 10$  h before the pregnancy to  $48 \pm 5$  h during the pregnancy [36]. It is postulated that intensive dialysis could partially restore the pituitary–hypothalamic axis by increasing toxin clearance. Furthermore, a better control of fluid status and blood pressure could also favorably influence pregnancy outcomes. Intensive dialysis could also improve fertility in men by increasing testosterone level and decreasing hyperprolactinemia [37].

### RISKS

Intensive hemodialysis performed in a home setting has been associated with several clinical benefits, which need to be balanced with emerging adverse signals. A Cochrane systematic review is presently underway to evaluate the benefits and harms of HHD in comparison with CHD [38]. Of note, we will focus on vascular access events, buttonhole infections and loss of residual kidney function.

#### Access-related events

Concerns of an increased rate of vascular access interventions and adverse events were raised with the FHN trial. Patients receiving (in-center) SDHD had a significantly shorter time to first vascular event (repair, loss or access-related hospitalization) compared with the CHD group (HR 1.76; 95% CI 1.11–2.79;  $P = 0.017$ ). Most of these events were vascular access repairs or losses and a higher risk was observed for patients dialyzing with an arteriovenous fistula (HR 1.90; 95% CI 1.11–3.25;  $P = 0.02$ ). Most of the risk was driven by vascular access repair as opposed to access loss [39, 40]. A similar trend was observed in the nocturnal cohort, although the time to first access-related event did not reach statistical significance (HR 1.81; 95% CI 0.94–3.48;  $P = 0.076$ ). Similar to the daily trial, the highest risk was observed among patients with arteriovenous access (HR 3.23; 95% CI 1.07–10.35;  $P = 0.038$ ) [18, 40]. An association between dialysis frequency and vascular access-related events (infections and interventions) was also reported in an observational Australian study. Among 286 patients receiving extended-hours hemodialysis, those with  $>3.5$  sessions per week had a lower cumulative vascular access survival compared with patients with 3.5 sessions or less ( $P < 0.001$ ). A continuous increase in the number of sessions per week was also associated with higher vascular access events in

a multivariable analysis (HR 1.56 per session, 95% CI 1.03–2.36). Most of these events were infections (60%) and access-related events were predictors of mortality in a multivariable analysis (HR 2.85, 95% CI 1.14–7.15) [8] (Table 2).

### Buttonhole infections

Buttonhole cannulation (BH) technique is widely used in IHHD. It is perceived as an easier self-cannulation technique for patients and has been associated with decreased pain, faster cannulation and lower risk of hematoma [27, 41, 42]. Within the last several years, concerns have been raised about an increased risk of infection for IHHD patients using the BH cannulation technique. In an observational Australian cohort study including 63 NHD patients and 172 CHD patients, BH cannulation was used in 94% of NHD patients and 10% of CHD patients. In a multivariable analysis, those who were using BH technique with NHD had an increased risk of septic dialysis-related events compared with the CHD group [incidence rate ratio 3.0 (95% CI 1.04–8.66),  $P = 0.04$ ]. The authors did not comment on topical antibiotic use among patients with BHs [27]. Although not performed in a home dialysis population, an RCT evaluating BH versus rope ladder cannulation in 140 patients on CHD also found a higher rate of *Staphylococcus aureus* bacteremia and fistula abscesses requiring intravenous antibiotics in the group using the BH technique ( $P = 0.003$ ) [43]. A systematic review recently performed by Mustafa *et al.* for the Canadian Society of Nephrology (CSN) described a bacteria rate of 0.15–0.60 events per 1000 patient-days with BH cannulation. These rates were withdrawn from four reports among IHHD cohorts and led the authors to highlight the potential risk associated with BH cannulation [44]. Furthermore, another retrospective Canadian study evaluated rates of *S. aureus* bacteremia in 56 NHD patients using the BH technique, before and after the establishment of prophylaxis topical mupirocin. The infection rate [events/1000 arteriovenous (AVF)-days] decreased from 0.23 to 0.03 with the topical antibiotic in the ‘intention-to-treat’ analysis [OR 6.4; 95% CI (1.3–32.3);  $P = 0.02$ ]. Although there was a significant reduction in the infection rate with topical mupirocin, it was still higher compared with CHD patients with a native AVF during the same period (0.005/1000 AVF-days) [45]. As a result, the Canadian Society of Nephrology recommends mupirocin antibacterial cream when BH cannulation is used in patients undergoing NHD [46].

### Residual kidney function

Residual kidney function has been associated with clinical benefits in dialysis patients [47]. Nonetheless, a significant decline in residual kidney function is appreciated during the first year of dialysis, especially in patients undergoing hemodialysis [48]. This reduction in residual kidney function might be even more pronounced among IHHD patients. In the FHN trial, patients undergoing NHD experienced a more rapid decline in residual kidney function compared with the CHD group. At 4 and 12 months, 52 and 67% of NHD patients with initial residual kidney function became anuric compared with 18 and 36% in the CHD group, respectively ( $P = 0.015$  for 4 months,  $P = 0.06$  for 12 months) [18, 49]. Reasons behind

this earlier drop in residual kidney function with NHD include changes in blood pressure and extracellular fluid volume, reduction in osmotic load and possible increased inflammatory response and platelet activation [50] with more intensive hemodialysis. We acknowledge that residual kidney function (calculated using 24-h urine output) may have been underestimated in the IHHD group because of differences in the timing of collections. It is unclear whether this effect would have been observed if residual kidney function was measured by other means [51].

## WHO IS ELIGIBLE FOR IHHD?

### Contraindications

When a motivated patient wishes to undergo IHHD, there are few absolute contraindications to treatment. Lack of suitable vascular access, uncontrolled psychosis (a situation in which a patient may be harmful to themselves) and lack of a caregiver (if patients are dependent) are important contraindications to any home hemodialysis modality, including IHHD [52]. Difficulty with anticoagulating the dialysis circuit (due to bleeding risk) has historically been considered a contraindication to long and long-frequent IHHD [52]. However, the use of large volume continuous saline infusion (Bioflow®) or regional anticoagulation with citrate [53] also permits anticoagulation-free long and long-frequent IHHD. Finally, an emerging observation for patients being considered for IHHD is the possibility of increased vascular access interventions due to more frequent schedules. Provided there is no major indication for frequent hemodialysis, CHD patients who have a high baseline rate of vascular access interventions may be better suited for long hemodialysis (three times/week) or an alternative home modality such as peritoneal dialysis (PD).

### Surmountable patient barriers to adoption of IHHD

Lack of motivation/interest, unwillingness to change, fear of isolation, perceived burden on caregivers and fear of cannulation are commonly cited barriers to home hemodialysis including IHHD [54–56]. In addition, when a caregiver is not available, physical limitations (such as reduced vision, limited manual dexterity or poor strength) may interfere with patients’ ability to cannulate, set up the machine and provide treatment. Fear of cannulation may be especially relevant in short daily and long frequent IHHD regimens for which cannulation attempts are more frequent. While many of these factors are important barriers to IHHD, they can be overcome. Nurse-assisted cannulation practice protocols have been used with some success to alleviate patients’ fear of cannulation [57]. While patients sense a high burden on their caregivers, the perspective of caregivers is that burden is minimal [58]. Nevertheless, provision of respite care may alleviate some of the burden on care providers [59]. Finally, fear of isolation can be addressed by provision of respite care, ongoing nurse-led home visits and a well-defined nursing/technical support system for patients [60].

**Table 2. Adverse events associated with intensive hemodialysis**

Author (year)	Country	Study design	Population	Specific variable of interest	Risk for intensive group
<b>Vascular access events</b>					
FHN trial group (2010, 2013)	North America (USA, Canada)	RCT, 245 patients	Intensive: in-center SDHD, 6 × 1.5–2.75 h Standard: in-center, CHD, 3 × 2.5–4 h	First vascular event (repair, loss or access-related hospitalization)	HR 1.90 (1.11–3.25), P = 0.017
FHN trial group (2011, 2013)	North America (USA, Canada)	RCT, 87 patients	Intensive: NHD patients, ≥6 h per treatment, std $K_t/V \geq 4.0$ Standard: CHD patients, 3 × ≥2.5 h, $eK_t/V > 1.1$ , std $K_t/V > 2.0$	First vascular event (repair, loss or access-related hospitalization)	HR 1.81 (0.94–3.48), P = 0.076
Jun <i>et al.</i> (2013) [8]	Australia	Retrospective observational study, 286 patients	(1) More intensive: >3.5 sessions per week Less intensive: ≤3.5 sessions per week (2) Continuous increase in the number of sessions	(1) Survival free of vascular access-related events (infections and interventions) (2) Vascular access-related events	(1) Unadjusted KM curve: shorter survival for intensive group, P < 0.001 (2) HR 2.85 per dialysis session (1.14–7.15), P = 0.04
<b>BH infections</b>					
Van Eps <i>et al.</i> (2010) [21]	Australia	Retrospective observational study, 235 patients	Intensive: NHD (94% with BH) Standard: CHD (10% with BH)	Septic dialysis-related events <sup>a</sup> : BH in NHD compared with CHD	IRR 3.0 (1.04–8.66), P = 0.04
Nesrallah <i>et al.</i> (2010) [45]	Canada	Retrospective observational pre–post study	(1) Intensive: NHD, 56 patients with BH, pre–post-mupirocin (2) Intensive versus 298 CHD patients with AVF	Rates of <i>S. aureus</i> bacteremia: (1) Pre/post topical mupirocin (2) Post-mupirocin compared with CHD patients	(1) OR 6.4 (1.3–32.3) P = 0.02 2–0.03/1000 AVF-days versus 0.005/1000 AVF-days
<b>Residual kidney function</b>					
FHN trial group (2011, 2013)	North America (USA, Canada)	RCT, 87 patients	Intensive: NHD patients, ≥6 h per treatment, std $K_t/V \geq 4.0$ Standard: CHD patients, 3 × ≥2.5 h, $eK_t/V > 1.1$ , std $K_t/V > 2.0$	Proportion of patients with initial residual kidney function who became anuric (NHD versus CHD)	4 months: 52 versus 18%, P = 0.015 12 months: 67 versus 36%, P = 0.06

$eK_t/V$ , equilibrated  $K_t/V$ .

<sup>a</sup>Septic dialysis-related events defined by: admission to hospital with suspicious of dialysis access infection or fever/rigor requiring antibiotic coverage or clinical suspicion of access infection.

### Facility and physician-level barriers

While the majority of this review is focused on patients, there are barriers to adoption of IHHD at the level of physicians and facilities. In a survey of Australian nephrologists, 16 and 38% cited a lack of nephrologist expertise and physical infrastructure as barriers to home hemodialysis [61]. The former may be addressed by increasing exposure to home hemodialysis in nephrology fellowship programs; a survey of trainees revealed that only 16% felt well-trained in home hemodialysis [62]. In addition to infrastructure, the cost of IHHD may be perceived as a barrier to uptake. Multiple cost comparisons have been performed, and on balance, IHHD appears to provide benefit at reduced or equivalent cost compared with CHD [63, 64]. Furthermore, higher electricity and water costs for IHHD patients (which is also a perceived barrier [61]) may be offset by an increased opportunity for employment (see target populations, below).

### Caregiver-dependent patients

Cohort studies have identified that IHHD patients tend to be younger and relatively healthier compared with those receiving CHD [25, 65]. Compared with CHD, it has been shown that patients and caregivers generally prefer a home-based dialysis therapy (which would include IHHD) [66]. Furthermore, in a cohort study, caregiver dependency for IHHD administration (primarily in the form of NHD) was not associated with a difference in time to first hospitalization, death or technique failure after adjustments for baseline comorbidity, age, gender, access, race and pre-IHHD dialysis vintage time [67]. While these results are promising, it is anticipated that additional supports for elderly, frail and dependent patients who are interested in IHHD will be needed. Nonetheless, expansion of IHHD to include dependent patients is an achievable goal.

### Crash starts

While it is optimal to provide patients with adequate pre-dialysis modality education, a large number of patients initiate dialysis late for unavoidable reasons [68]. These patients may not have enough information to make an informed modality decision. However, even ‘crash starts’ can be successfully instituted on IHHD after appropriate in-hospital education [69].

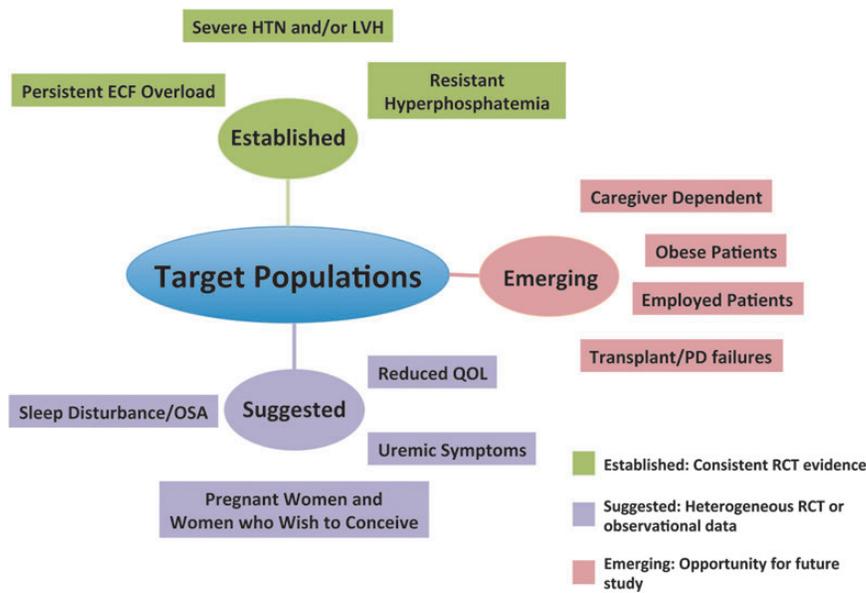
### Employed patients

IHHD may be a preferred choice for working patients. It has been shown that patients receiving home dialysis (both peritoneal dialysis and home hemodialysis) have higher rates of employment compared with those receiving CHD, even after adjustment for case-mix differences, demographics and end-stage renal disease duration [70]. IHHD in the form of nocturnal home hemodialysis has the potential for even higher rates of employment compared with conventional home hemodialysis; one can surmise that overnight dialysis allows patients more freedom during daytime working hours.

## TARGET POPULATIONS

Patients with severe obstructive sleep apnea, resistant hyperphosphatemia, persistent uremic symptoms, difficult to control hypertension and refractory extracellular fluid overload are candidates for IHHD (Figure 1). As suggested by the current body of literature, women on dialysis who wish to conceive and women who have conceived on CHD/PD can be successfully transitioned to an intensified hemodialysis regimen, which in turn, is associated with potential improvement(s) in fertility and fetal outcomes. While these considerations are persuasive, IHHD should not be restricted to patients with only the complications listed above.

In addition to those potential target populations, there are emerging patient groups to whom IHHD may also be considered (Figure 1).



**FIGURE 1:** Established, suggested and emerging patient groups to whom IHHD may be considered. ECF, extracellular fluid volume; HTN, hypertension; LVH, left ventricular hypertrophy; OSA, obstructive sleep apnea; QOL, quality of life.

### Transplant failures and PD failures

Transition from kidney failure to dialysis is associated with a higher risk of mortality and reduced quality of life (measured by the physical health composite), compared with transplant naïve patients. Thus far, there is little evidence to guide us on the relative potential benefit of IHHD versus CHD after graft loss. One can speculate that utilization of a home dialysis modality in this patient population may reduce the loss of independence, time and freedom that is associated with transitioning to in-center dialysis after graft loss. Similarly, patients who experience technique failure while on PD (i.e. due to loss of membrane function, severe peritonitis necessitating catheter removal or mechanical complications) may be optimal patients to transition to IHHD, as they can maintain on dialysis without being uprooted from their home. In addition, the more gentle hemodynamic fluctuations associated with IHHD most approximates volume changes in peritoneal dialysis. Whether transitioning patients with a failed renal transplant or after PD failure impacts outcomes remains to be seen in future studies.

### Morbid obesity

Amongst younger dialysis patients, morbid obesity has been shown to be a risk factor for mortality [71]. Is IHHD a feasible treatment option for patients who are obese? In a small descriptive study, IHHD was successfully performed in patients with a BMI of  $\geq 30$  kg/m<sup>2</sup>, with good clinical outcomes. Consideration for preferential transitioning of obese patients to IHHD over other dialysis modalities is also a subject for future studies.

### CONCLUSION

Intensive home hemodialysis has a number of important clinical advantages. While there are risks, they also present an opportunity for ongoing quality improvement initiatives to further optimize delivery of IHHD. There is a growing appreciation that the paradigm of candidacy for IHHD is changing. As the worldwide burden of kidney disease continues to increase, research should focus on optimizing the delivery of IHHD.

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### CONFLICT OF INTEREST STATEMENT

None declared.

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