Home Hemodialysis: Do We Need More Randomized Controlled Data?  
By John W. M. Agar  
When snake oil salesmen peddled their cure-alls, an undefended populace fell prey to the “best story,” the “best sell,” and the “most persuasive line.” Then, as remedy upon remedy failed to prove effective, to be safe, or to give value for money, greater scientific rigor was demanded of medical intervention. With statistical methods improving in parallel, “proof by clinical trial” emerged.

Trials of a single intervention—an active drug against a placebo, two active drugs head to head—are relatively simple to design and blind, the latter preferably applying to both investigators and subjects. If well designed and conducted, these trials commonly yield a useful and reliable answer.

Conversely, when multiple conflicting, competing, and differing factors exist in both trial arms—especially if these have an impact beyond the subject alone and affect the behavioral patterns, finances, and lifestyle of an entire family unit and their friends—the complexity and outcome interpretation becomes impossible. This has been a core “insurmountable” for the recent attempts to conduct randomized control trials (RCTs) of home versus conventional hemodialysis.

Although the RCT is commonly regarded as the gold standard trial method—and so it is for assessing single or even multiple but controllable interventions—RCT design, subject selection, and trial conduct are crucial. An RCT that poses the wrong question, recruits insufficient subjects, lacks adequate statistical power, selects the wrong end points, or inappropriately selects surrogate outcomes may grievously mislead or misdirect. Many believe that the two “landmark” RCTs in hemodialysis, the National Cooperative Dialysis Study (NCDS) (1) and the HEMO study (2), both inadvertently led to misinterpretations that fundamentally changed the course of dialysis by seriously impeding the very thing an RCT is supposed to ensure: improvement in outcomes. This has been most evident in the United States, where for 2 or 3 decades the blight of Kt/V urea, and gross inadequacies in dialysis duration that flowed from these RCTs, have directly diminished both patient and HDH have been unsuccessful, or if these modalities are not suitable for the patient. As stated before, PD is an excellent first dialysis modality for patients with ESRD. Transition from PD to HHD takes advantage of the significant patient benefits that accrue from both dialysis modalities and potentially avoids the appreciable lifestyle upheaval and deterioration in functional status that not infrequently accompanies the transfer to CHD. Moreover, the ability of PD patients to understand dialysis principles and to manage their own treatments puts them one step ahead for a successful HHD training experience. Given that only a small number of patients will quit PD because of failure to cope with home-based self-care treatments, we propose that a substantial proportion of patients in whom PD is unsuccessful could be transferred to HHD programs. To date, small studies have evaluated the feasibility and outcome of such a transition. However, even in centers with a specific interest in home-based dialysis, only a small proportion of patients completing PD therapy transferred directly to HHD. Although the more complicated HHD training can also limit the transition from PD to HHD, we believe that further evaluation and promotion of the integrated home dialysis model can significantly increase the overall capture for home dialysis modalities and improve patients’ care, quality of life, and outcomes. It is time to rethink our dialysis model to implement a home-first vision.

An Integrated Peritoneal Dialysis/Home Hemodialysis “Home-First” Vision: A Call to Action for an Integrated Home Dialysis—First System  
By Annie-Claire Nadeau-Fredette and David W. Johnson  
Dialysis leads to massive changes in an individual’s lifestyle. This is especially true for in-center conventional hemodialysis (CHD), which necessitates that patients constantly travel back and forth to their dialysis facility at least three times a week.

Home dialysis, which includes peritoneal dialysis (PD) and home hemodialysis (HHD), is an attractive alternative to CHD, allowing dialysis treatment in the patient’s own environment. Home dialysis also helps to preserve quality of life and gives patients a sense of empowerment. Patients who undergo dialysis at home generally have superior survival and quality of life compared with those who use a dialysis facility. From a socioeconomic perspective, home dialysis substantially reduces dialysis-related costs. It especially decreases the staff requirements at dialysis facilities and limits technique-related expenses, particularly for PD. These patient-centered and economic advantages have led to the promotion of home dialysis in many regions.

Traditionally, PD has been the most common form of home dialysis, accounting for 11 percent of the world’s total dialysis population and ranging between 2 percent and 74 percent of dialysis patients in different countries. PD offers several significant advantages compared with hemodialysis, including possibly enhanced survival in the first few years, better preservation of residual kidney function, greater suitability to incremental (progressive) dialysis, delayed need for fistula surgery, reduced erythropoietin requirements, reduced blood transfusion requirements, decreased risk of blood-borne infections, and higher levels of patient satisfaction with treatment. PD also delivers a more continuous form of dialysis and, by its home modality nature, helps to better maintain patient autonomy. Balanced against these advantages, a main limitation of PD is that many patients are unable to continue with the treatment after 2 or 3 years, often because of cause of infection (peritonitis), catheter-related problems, or inadequate removal of wastes or fluid. Given that PD is an excellent first dialysis modality because of its benefits and possibly early survival advantage, the classic integrated dialysis model (also known as the PD-first model) was proposed some years ago. According to this model, to achieve the best possible outcomes, patients would start dialysis with PD and then transfer to CHD when PD was no longer possible or no longer the best option for the patient. For example, a new dialysis patient would stay with PD for a few years and then switch to CHD when clearance or infection became an issue. Although interesting, this classic integrated dialysis model completely overlooked the important option of HHD.

Home HD can be performed according to a variety of regimens, including short daily (2.5 to 3 hours, five or more times per week), long (more than 5.5 hours, three to four times per week or long frequent [more than 5.5 hours, five or more times per week]), and interdialytic intervals of the chosen regimen. HHD provides high-quality dialysis and is more cost-effective than CHD. On top of the general advantages of home dialysis, such as independence and better quality and length of life, HHD has been shown to be associated with improved heart structure and function, blood pressure, and blood chemistry (including phosphate control). However, despite these clear advantages of HHD, the prevalent belief among kidney specialists that HHD is superior to CHD, and the growing interest in HHD over the past decade, the global uptake of HHD is very low (less than 5 to 10 percent) except in a few countries (such as Australia, New Zealand, and Uruguay).

Therefore, we propose a new integrated home dialysis model that should be the new paradigm of home-based dialysis. In this home-first model, a patient would begin dialysis with PD and then be referred to HHD once PD is no longer suitable. Hence, CHD would be considered only as a last resort, once both PD and HHD have been unsuccessful, or if these modalities are not suitable for the patient. As stated before, PD is an excellent first dialysis modality for patients with ESRD. Transition from PD to HHD takes advantage of the significant patient benefits that accrue from both dialysis modalities and potentially avoids the appreciable lifestyle upheaval and deterioration in functional status that not infrequently accompanies the transfer to CHD. Moreover, the ability of PD patients to understand dialysis principles and to manage their own treatments puts them one step ahead for a successful HHD training experience. Given that only a small number of patients will quit PD because of failure to cope with home-based self-care treatments, we propose that a substantial proportion of patients in whom PD is unsuccessful could be transferred to HHD programs. To date, small studies have evaluated the feasibility and outcome of such a transition. However, even in centers with a specific interest in home-based dialysis, only a small proportion of patients completing PD therapy transferred directly to HHD. Although the more complicated HHD training can also limit the transition from PD to HHD, we believe that further evaluation and promotion of the integrated home dialysis model can significantly increase the overall capture for home dialysis modalities and improve patients’ care, quality of life, and outcomes. It is time to rethink our dialysis model to implement a home-first vision.
Clinical Advantages of Home Hemodialysis

By Christopher T. Chan

Home hemodialysis (HHD) has emerged as an important alternative treatment option for patients with end stage renal disease. The renaissance of HHD is based in part on several established and potential clinical benefits. In addition, HHD also acts as a conduit for intensive hemodialysis, which is otherwise not feasible outside the United States, with the past 15 years focusing on the two more recent iterations of home hemodialysis treatment—extended-hour and high-frequency (usually nocturnal) home hemodialysis, and short daily home hemodialysis. Carl Kjellstrand, a greatly respected savant of hemodialysis, compiled a lexicon of home hemodialysis publications appearing before 2000. This list, even then, exceeded 600 articles and abstracts; since then it has more than doubled. Although all these were observational and cohort studies, they were nonetheless studies by reputable experts in this field. Not one recorded a lesser outcome for home care. Nor have any since. Yet, given that these were criticized for selection bias and a range of other “shortcomings,” an RCT was demanded to settle the disquiet that these articles supporting home hemodialysis were somehow selling a lie. Although I commend the authors of FHN(2) for their effort, a horrendous task gamely and honestly attempted, their fatally flawed study has seemingly swept aside this accumulated knowledge with one hopelessly underrecruited and underpowered RCT; FHN(2) suffered from all the recruitment biases it sought to exclude. Fewer than 55 percent of the subject numbers required by predefined statistical power were recruited, and the trial design proved resistant to randomization to center-based conventional care that the rules were altered in midtrial to permit the conventional arm to receive dialysis at home, where survival is twice that of in-center care (5). Even then, only 73 percent of those randomized to the home nocturnal arm performed their dialysis treatments as required by the trial design. Despite all this, the conclusion reported that extended-hour, high-frequency nocturnal home dialysis was no better than standard conventional hemodialysis. A fairer conclusion might have been that despite a clear trend to near-significance in favor of home-extended hour and high-frequency dialysis from only a third of the predicted number of study participants, the trial was a design, recruitment, and statistical failure. A more honest conclusion should have ‘fessed up to this. An excellent critique puts this brave, but failed, RCT into its proper perspective (6).

Do we need another RCT to resolve the issue? I contend, no. Ask yourself this question: has there ever been an RCT between transplantation and dialysis? No. If not, why not? It is simply because we know we can never fairly randomly assign patients to transplantation versus dialysis, any more than we can fairly randomize to one type of dialysis versus another. Yet, we universally acknowledge that “transplantation is the best therapy” and that “transplantation survival is better.” Will yet another RCT of dialysis modality add anything further? No, it will not. John W. M. Agar, MBBS, is affiliated with the Department of Renal Medicine at the Geelong Hospital in Victoria, Australia.

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well-being and survival. I dare suggest that the recent Frequent Hemodialysis Network 2nd arm trial—the FHN(2) trial (3)—of extended-hour home hemodialysis versus conventional hemodialysis is in the same category and risks leaving a similar misinterpretation. Yet, all three are RCT analyses…so, they must be right, eh? Such is the aura of the epithet “RCT” that any conclusion drawn by an RCT becomes “lone” in the blink of an eye. Like apologies that follow media errors, printed much later, recorded in small print, appearing on page 47 near the customary section, the error for which it “apologizes” long ingrates, dissenting opinions of RCT results either are dismissed or appear too late to alter the RCT “message.” This effect is amplified if the RCT in question has been long awaited and widely anticipated (advertised) to provide the “authoritative answer”—as was the case with the FHN trials. But although FHN(2) purported to yield an answer, it did not. Even more concerning, now that RCTs have garnered such a bulletproof aura that legislators and funding agencies now structure practice regulations and funding models based on their outcomes, an incorrect conclusion from FHN(2) risks enshrining a further grave dialysis misstep.

Towardowski and Misra (4) nicely summarized the complexity—no, the impossibility—of achieving fair trials and conduct and believable outcomes in an area as fraught as modality choice, wherein multiple competing comorbidities, socioeconomic circumstances, and expectations affect every dialysis patient differently. To be honest, dialysis patients are just not a homogenous group, and homogeneity of comparable groups is part and parcel of RCT selection and study.

There are now 60 or more years of worldwide accumulated experience in home hemodialysis, most of it outside the United States, with the past 15 years focusing on the extent of myocardial stunning.

The clinical benefits of HHD will be discussed and summarized in this overview article. In the past decade, there has been a substantial increase in both observational and randomized controlled data in the domain of HHD. Of note, survival advantage has been documented in cohorts of short daily hemodialysis and nocturnal hemodialysis. Overall, the survival rates of daily hemodialysis patients are in the range of 90 percent, 70 percent, and 50 percent at 1, 3, and 5 years, respectively. Similarly, the 1, 3, and 5-year survival rates for nocturnal hemodialysis are in the range of 95 percent, 90 percent, and 85 percent, respectively. Given that there is a specific selection bias in patients conducting intensive hemodialysis, investigators have also used kidney transplant recipients as a potential control group. Recently, Canadian nocturnal home hemodialysis patients were compared with a Canadian kidney transplant cohort (1). The kidney transplant patients had a 55 percent to 61 percent (depending on organ donor type) reduced risk of treatment failure or death during the study compared with patients using long and frequent HHD. The risk of being admitted to the hospital and spending a longer time in the hospital was higher for some kidney transplant patients for as long as a year after transplantation, but it was lower in the long term compared with dialysis patients.

HHD has also been documented to have improve ments in blood pressure regulation, preservation of left ventricular hypertrophy, restoration of left ventricular ejection fraction, normalization of phosphate control, and certain aspects of quality of life related to kidney disease. Other measurements of dialysis intrusiveness, such as recovery time from dialysis treatments, clearly favor HHD over in-center thrice-weekly hemodialysis. Moreover, quality of sleep and sleep apnea have also been improved, especially in the case of nocturnal home hemodialysis. Finally, as an attempt to restore the “unnaturalness” of dialysis, HHD has been shown to improve endothelial progenitor cells and diminish the extent of myocardial stunning.

End stage renal disease has traditionally been associated with a low conception rate and poor pregnancy outcomes. Longer weekly dialysis times and lower urea levels through pregnancy have been suggested to be protective. In a comparative analysis, conception rate, gestational age, and proportion of live birth were significantly higher in a cohort of nocturnal HHD patients than in a contemporary North American control group.

HHD has several important clinical advantages. It is, however, important to acknowledge that potential risks exist with any form of renal replacement therapy. In the case of HHD, further work is required to minimize potential adverse events (for example, vascular access infection or malfunction) and to improve patient-, facility-, and physician-level barriers. There is a growing appreciation for intensive HHD as an accepted first-line renal replacement therapy. Our community should be charged with enthusiasm to engage with all stakeholders to focus on optimizing the delivery of HHD.

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