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# Outcomes on home haemodialysis: registry challenges

Mark S. MacGregor

John Stevenson Lynch Renal Unit, NHS Ayrshire & Arran, Crosshouse Hospital, Kilmarnock, Scotland

*Correspondence and offprint requests to*: Mark S. MacGregor; E-mail: Mark.MacGregor@aaaht.scot.nhs.uk

**Abstract**
Health care policy is encouraging expansion of home haemodialysis, aiming to improve patient outcomes and reduce cost. However, most patient outcome data derive from retrospective observational studies, with all their inherent weaknesses. Conventional thrice weekly home haemodialysis delivers a 22–51% reduction in mortality, but why should that be? Frequent and/or nocturnal haemodialysis reduces mortality by 36–66%, with comparable outcomes to deceased donor kidney transplantation. Approaches which might improve the quality of future observational studies are discussed. Patient-relevant outcomes other than mortality are also discussed.

**Keywords:** home haemodialysis; frequent dialysis; nocturnal dialysis; lean management; patient registries

Currently, there is a desire to expand home haemodialysis [1], driven by studies demonstrating lower costs than in-centre haemodialysis [2] and by evidence of better patient outcomes. Prevalence rates vary dramatically between and within countries from 0 to 58 per million population [3], suggesting considerable opportunity to increase utilization. So how strong is the evidence for improved outcomes and what further studies are required?

## Conventional haemodialysis

Several early studies demonstrated improved survival for patients treated with thrice weekly haemodialysis at home [4, 5]. This review is limited to more recent studies (Table 1), after home haemodialysis prevalence had started to decline in most countries.

In a single-centre US study, patients survived longer on home than hospital haemodialysis or peritoneal dialysis [6–8], but were younger, had fewer co-morbidities and were less likely to have higher risk renal diseases. The survival advantage persisted after multivariate adjustment using a Cox regression. In a retrospective study from two centres in the west of Scotland [9], home haemodialysis patients were compared to age- and sex-matched peritoneal dialysis patients, with diabetics excluded. Survival was excellent in both groups, but superior in the home haemodialysis patients. Co-morbidity analysis was limited, but there were fewer smokers and fewer electrocardiograph abnormalities in the home haemodialysis patients. A single-centre Swiss study compared home to in-centre haemodialysis [10]. Controls were matched for age, sex, primary renal disease and dialysis vintage. Despite the low proportion of patients treated with home haemodialysis, controls could not be found for 44%. Even after matching, home haemodialysis patients still had fewer co-morbidities (not statistically significant). Kaplan–Meier analysis showed a substantial survival advantage for home patients and significantly fewer hospital admissions. Covariates were assessed in a Cox model (age, gender, renal disease co-morbidity, smoking status, marital status and year of starting dialysis) and the survival advantage persisted. Both groups of patients were only dialysed 2.3–2.5 times per week for 9.4–9.5 h per week, limiting generalizability in the modern era.

Using the Case Mix Severity study (a nearly random sample of US dialysis patients), home haemodialysis patients were compared to in-centre patients using Cox regression [11]. There were difficulties defining whether patients were on home haemodialysis, because of patients receiving assisted home haemodialysis, and self-care haemodialysis patients in-centre, but a stringent definition was used, which required patients to be receiving home haemodialysis training on Day 30 after starting dialysis. Home haemodialysis patients were younger and less likely to have diabetic nephropathy, congestive heart failure, myocardial infarctions, strokes or obesity. After multivariate analysis (including age, gender, race, diabetic nephropathy and co-morbidity), a substantial survival advantage persisted for home haemodialysis. A confirmatory analysis using all patients in the United States Renal Data System (USRDS) database also showed a survival advantage, though less impressive, and not adjusted for co-morbidity. It should be noted that hospital haemodialysis in the USA had generally poor outcomes at this time making it difficult to interpret these results. In a recent registry analysis from England and Wales [12], home haemodialysis patients were compared to age- and sex-matched controls treated with hospital haemodialysis, satellite haemodialysis or peritoneal dialysis. Home haemodialysis patients were more likely to be white, less likely to be socially deprived and had lower risk renal diseases. They were also more likely

**Table 1.** Home haemodialysis survival studies

| Author | Setting | Incident years | Home HD group | Comparator group | Mortality |
|---|---|---|---|---|---|
| Conventional haemodialysis | | | | | |
| Grant (1992) | West of Scotland | 1982–1988 | 139 | 139 PD | 3 years: 93.8 versus 86.2% |
| Mailloux (1996) | USA | 1970–1993 | 74 | 687 Hospital HD | RR 0.49 |
| Woods (1996) | National sample, USA | 1986–1987 | 70 | 3102 Hospital HD | RR 0.58 (95% CI 0.35–0.95) |
| | National population, USA | | 418 | 43 122 Hospital HD | RR 0.78 (95% CI 0.67–0.90) |
| Saner (2005) | Berne, Switzerland | 1970–1995 | 58 | 58 Hospital HD | 5 years: 93 versus 64%<br>10 years: 72 versus 48% |
| Nitsch (2010) | England and Wales | 1997–2005 | 225 | 900 Hospital HD | RR 0.68 (95% CI 0.44–1.03) |
| | | | | 450 Satellite HD | RR 1.06 (95% CI 0.55-2.04) |
| | | | | 900 PD | RR 0.61 (95% CI 0.40–0.93) |
| Frequent haemodialysis | | | | | |
| Blagg (2006) | US SDHD | 2003–2004 | 117 | USRDS HD | SMR 0.39 (95% CI 0.19–0.51) |
| Kjellstrand (2008) | US/European SDHD | 1982–2005 | 415 | USRDS HD and transplant | SMR 0.34 (95% CI 0.20-0.54) |
| Pauly (2009) | Toronto NHD | 1994–2006 | 177 | 531 USRDS DD transplant | RR 1.15 (95% CI 0.66–2.00) |
| | | | | 531 USRDS LD transplant | RR 1.96 (95% CI 1.10–3.57) |
| Johanssen (2009) | US NHD | 1997–2006 | 94 | 940 Hospital HD | RR 0.36 (95% CI 0.22–0.61) |
| | US SDHD | | 43 | 430 Hospital HD | RR 0.64 (95% CI 0.31–1.31) |

HD, haemodialysis; PD, peritoneal dialysis; DD, deceased donor; LD, live donor; RR, risk ratio.

to be wait-listed for kidney transplantation. This study did not assess co-morbidity other than renal disease, but used wait-listing for transplantation as a surrogate marker of global health status. Cox models (incorporating age, gender, renal disease, ethnicity, social deprivation, wait-listing for transplant and time-dependent variables for home haemodialysis and transplantation) showed a significant survival advantage of home haemodialysis compared to peritoneal dialysis. An advantage of similar magnitude was seen compared to hospital haemodialysis but did not achieve significance. There was no difference compared to satellite haemodialysis, but that analysis was limited by lack of power. Interestingly, patients did not start home dialysis for a median of 12 months after starting renal replacement therapy, so none of these patients would have been included in the US study. Patients were maintained on home haemodialysis for a median of only 18 months. Cost-effectiveness might be improved by reducing the time to start home haemodialysis.

It is clear from these studies that the survival benefit of home haemodialysis is explained at least partly by patient selection; but despite varied statistical approaches, all show residual unexplained survival advantage after adjustment. While this could be due to confounding by unmeasured factors, are there other possibilities? Anecdotally, patients dialysing at home sometimes perform additional sessions. While not equivalent to frequent haemodialysis, these sessions may be performed at crucial times such as when fluid overloaded or after a potassium-rich meal. Psychosocial factors offer other intriguing possibilities. Patients who are more engaged with their own care may improve disease control [13]. Mechanisms are uncertain, but improved adherence may contribute. Secondly, patients whose psychological preference is to control their environment may have reduced stress and better outcomes when the treatment approach is congruent with their psychological preferences [14, 15]. Conversely, patients who prefer to give others control might not benefit from home haemodialysis.

## Frequent haemodialysis

More recently, studies have examined patient outcomes on short-daily haemodialysis (SDHD) and nocturnal haemodialysis (NHD), mostly performed at home. In a small US study, mortality of 117 patients on SDHD (16% in-centre) followed for up to 2 years was substantially lower when compared to the USRDS population using the standardized mortality ratio (SMR), adjusting for age, sex, race and renal disease [16]. In a combined US/European population of 415 SDHD patients (36% in-centre), survival was substantially better than the USRDS population, again using the SMR approach [17]. Perhaps more impressively, the home SDHD patients had equivalent survival to deceased donor kidney transplant recipients. The Toronto group compared survival of 177 NHD patients to 531 deceased donor and 531 live donor kidney transplant recipients from the USRDS, matched for race, diabetes and prior treatment duration with conventional haemodialysis [18]. NHD patients had significantly more vascular disease and cancer. Cox regression showed no difference in survival between NHD and deceased donor transplant patients, although live donor transplants had superior survival. A recent five-centre US study compared outcomes in 94 NHD and 43 SDHD home patients to the USRDS population using propensity score matching [19]. Survival was significantly better after Cox regression for NHD but was not significant for SDHD. Disappointingly, hospitalization was not improved for either group. The conventional haemodialysis control group were somewhat unusual in that they dialysed for only 3 h per session (compared to 2.9 h for SDHD), but for 3.5 times per week, and this may have confounded the results, particularly for the SDHD group.

In these studies, mortality improvement is impressive, with a 36–66% reduction compared to a 22–51% improvement with conventional home haemodialysis. But these studies suffer from the same limitations of any retrospective observational data. Two studies have in part addressed

the issue of patient selection by showing comparable survival to deceased donor kidney transplant recipients, a group which should be at least as selected. It remains unclear how much of the improved survival in these studies is due to frequent dialysis and how much to dialysis at home. The Frequent Dialysis Network trials should cast some light on this issue [20] by comparing SDHD to conventional haemodialysis in-centre and NHD to conventional haemodialysis at home; but these studies are only powered to compare composite end points incorporating mortality, left ventricular mass and quality of life. The SDHD study showed significant improvement in both composites with hazard ratios of 0.61 and 0.70 respectively [21]. Mortality at one year was 4% in the SDHD arm ($n = 125$) and 7.5% in the control arm ($n = 120$).

## Research challenges

If one accepts that a randomized trial of home haemodialysis with power to assess mortality is unlikely to be performed, then what can further observational research add? A large, multinational retrospective observational study of outcomes may still be of value as numbers remain relatively small in the studies above. Nevertheless, despite multivariate analysis a retrospective study will always be severely limited by unmeasured confounders. The FREEDOM study is a prospective observational study of SDHD using the NxStage® machine [22] and has started to report benefits including reduced depression, improved sleep quality and reduced recovery time after dialysis. Establishing a similar, detailed, large prospective observational study of the various types of home haemodialysis may address some of the problems of confounding (e.g. co-morbidity) more convincingly.

**Table 2.** Comparison of impact of different haemodialysis modalities, using a lean approach of value to patient

| | CHD | CHHD | SDHD | NHD |
|---|---|---|---|---|
| Transport to dialysis (min/week)[a] | 90 | 0 | 0 | 0 |
| Waiting to start dialysis (min/week)[a] | 75 | 0 | 0 | 0 |
| Machine set-up (min/week) | 0 | 90 | 180 | 180 |
| Dialysis (min/week) | 810 | 810 | 810 | 0[b] |
| Machine tear-down (min/week) | 0 | 90 | 180 | 180 |
| Waiting for transport (min/week)[a] | 45 | 0 | 0 | 0 |
| Transport home (min/week)[a] | 90 | 0 | 0 | 0 |
| Recovery from dialysis (min/week)[c] | 1140 | 1275 | 210 | 60 |
| Total treatment time (min/week) | 2250 | 2265 | 1380 | 420 |
| Remaining waking time (min/week)[d] | 4470 | 4455 | 5340 | 6300 |
| Value-added time | 67% | 66% | 79% | 94% |
| Non-value-added time | 33% | 34% | 21% | 6% |

Value-added time is the remaining waking time, and non-value added time is the total treatment time, both expressed as a percentage of total waking hours. CHD, conventional haemodialysis (thrice weekly for 4.5 h per session); CHHD, conventional home haemodialysis; SDHD at home (six times weekly for 2.25 h per session); NHD (six times weekly for 6 h per session).

[a]Data from MacGregor and Allan [28].

[b]Dialysis takes place during sleep.

[c]Data from Lindsay *et al.* [26].

[d]Assumes average of 8 h sleep per night.

Which outcomes should we be studying? Mortality is attractive as a definitive binary outcome, but other outcomes are also important to patients' lives. End points such as blood pressure, left ventricular mass [20, 23] or serum phosphate [24] can be used but are in essence surrogates for mortality. The early literature addressed impact on quality of life and psychosocial functioning but to a limited extent, and there is scope for more detailed research [25]. Lindsay [26] published a seminal study asking patients the simple question, 'How long does it take you to recover from a dialysis session?' and demonstrated dramatic differences between conventional haemodialysis (7 h 5 min), SDHD (34 min) and NHD (9 min). One could combine such data with the lean management approach [27] of defining activity as value-added or non-value-added from the patient's perspective (Table 2). This could lead to innovative end points, which may capture the impact of dialysis on patients' lives in a more rounded fashion. At the very least, we should be debating the issue of trial end points with our patients.

## Conclusion

Observational data have consistently shown improved mortality with home haemodialysis, and frequent dialysis seems to add an even greater benefit approaching that of deceased donor kidney transplantation. However, these retrospective observational studies are likely to overestimate benefit. As randomized trials seem unlikely, prospective observational studies offer the most promise to deliver more reliable evidence. Consideration should also be given to assessing a range of end points in addition to mortality, with a particular focus on those that represent the overall impact of dialysis on patients' lives.

*Conflict of interest statement.* None declared.

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