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Original Article

The short- and long-term impact of multi-disciplinary clinics in addition to standard nephrology care on patient outcomes

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Abstract

Background. This two country case control study of incident dialysis patients evaluates the outcomes of patients exposed to formalized multi-disciplinary clinic (MDC) programmes *vs* standard nephrologist care.

Methods. Patients commencing dialysis in two centres (Vancouver, Canada and Cremona, Italy) were evaluated at and after dialysis start, as a function of MDC exposure *vs* nephrologist care alone. Only chronic kidney disease patients, with longer than 3 months of exposure to nephrology care, who had not previously received kidney replacement therapy were included. Study outcomes included laboratory parameters and survival. The MDC was similar in both countries and average exposure was 6–8 h per patient-year, as compared to 2–4 h for standard care. All patients had equal access to resources prior to dialysis and with respect to dialysis start, as all had been referred to the same local nephrology practices.

Results. During the evaluation period 288 patients commenced dialysis after receiving more than 3 months nephrology care prior to dialysis. There were no major demographic differences between the cohorts. Mean duration of nephrology care prior to dialysis was 42 months, and dialysis was initiated at similar low glomerular filtration rate (GFR), though statistically significantly different (7.0 and 8.4 ml/min/m^2, $P = 0.001$). The MDC patients had higher haemoglobin (102 *vs* 90 g/l, $P < 0.0001$), albumin (37.0 *vs* 34.8 g/l, $P = 0.002$) and calcium levels (2.29 *vs* 2.16 mmol/l, $P < 0.0001$) at dialysis start. Survival was significantly better in the MDC group demonstrated by Kaplan–Meier analysis ($P = 0.01$). Cox proportional hazards analysis demonstrated standard nephrology clinic *vs* MDC attendance was a statistically significant independent predictor of death (hazards ratio = 2.17, 95% confidence interval 1.11–4.28) after adjusting for other variables known to impact outcomes.

Conclusions. This analysis of outcomes in two different countries suggests that despite equal and long exposure to nephrology care prior to dialysis, there appears to be an association of survival advantage for those patients exposed to formalized clinic care in addition to standard nephrologist follow-up. While other known predictors of survival such as adequacy of dialysis and severity of illness measures were not included in the model, those parameters require time on dialysis to be accumulated. Thus, the data do suggest that knowledge of patient status at the time of dialysis start is important. Further research is needed to determine which specific components of care both prior to dialysis and after its commencement are most important with respect to outcomes.

Keywords: chronic disease management; chronic kidney disease; multi-disciplinary clinic; nephrology; outcomes; survival

Introduction

Mortality and morbidity of kidney failure patients remains high despite the many advances in dialysis treatment [1–4]. Indeed, kidney failure is a culmination of a complex set of processes with widespread pathophysiological consequences. It is well recognized that much of the disease burden is well established prior to the initiation of dialysis therapy [5,6]. Opportunity thus exists for proactive intervention to modify disease progression and risk factors associated with poor outcomes.

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Although it is believed that a nephrology team is important in the management of patients with kidney disease [3,7–10], there is no uniform definition of such a team, nor a description of implementation practices. Given that multi-disciplinary teams impact on health care resources, it is imperative to evaluate their effectiveness in comparison to current clinical practice. The impact of a multi-disciplinary team clinic has been studied in other disciplines such as diabetology [11,12], cardiology [13–15], rheumatology [16,17] and oncology [18] and shown to benefit patient care and outcomes.

There is substantial evidence that late referral leads to poor outcomes for patients with kidney disease and that early referral is of benefit [19–22]. The unique purpose of this study was to examine patient outcomes as a function of two different clinical care model exposures, both over a prolonged period of pre-dialysis time: that is, we sought to examine the question of the effect of different care when late referral is not an issue. We compare two cohorts of patients who commenced dialysis in two countries. All patients had been exposed to conventional nephrologist care or nephrologists and multi-disciplinary team care for an extended period of time. We evaluated the impact of care prior to dialysis on survival and other objective parameters shown to influence long-term outcomes [23,24]. This study extends previous observations [8] into the current era, and internationally, in order to improve the generalizability of the findings.

Patients and methods

This study of incident dialysis patients examines those patients initiating dialysis in two tertiary care institutions: St Paul's Hospital (SPH), University of British Columbia, Vancouver, Canada and Istituti Ospitalieri di Cremona, Italy. In the Canadian cohort, patients commencing chronic dialysis at SPH during calendar years 1997 and 1998 were considered for inclusion. In the Italian cohort, all patients commencing dialysis in Cremona from 1 January 1999 until 30 June 2002 were considered. The total cohort of dialysis patients during the time periods was 352, but only adult patients (over the age of 18 years) and those followed by nephrologists for more than 3 months were eligible for inclusion for this analysis, given the specific questions being addressed. The 3 month convention attempts to remove patients with 'late referral' based on duration of time needed for education, modality selection and access creation in non-urgent manner. All patients gave informed consent and local ethics boards of each respective institution approved the study.

Patients were categorized according to prior exposure to a multi-disciplinary clinic-based education and follow-up programme and compared with a concurrent cohort who received standard nephrologist care in the same centres. Details of the MDC are described below. Patients were excluded if they had a failed kidney transplant or had been on dialysis previously for any reason.

In both countries, the dialysis centres are accessed by patients who are from the same referral group practice and referral base of nephrologists. All nephrologists in each centre had the same opportunity to access facilities and personnel of the multi-disciplinary clinic for their patients. The reasons for non-referral or non-attendance at the clinic were not obtained. Care after dialysis initiation was standardized and managed according to unit practices, and standardized.

Details of the multi-disciplinary clinic have been described in more detail elsewhere [8]. Briefly, the formal programmes in both Canada and Italy have a standardized philosophy including educational programmes as well as regular, protocolized clinic and laboratory follow-up of patients with chronic kidney disease. The frequency of both visits and laboratory tests is predetermined based on the level of kidney function with reminder systems to facilitate follow-up. Regularly scheduled bloodwork and clinical examinations and prespecified educational topics are reviewed with each patient.

In the Canadian centre, the complete formalized multi-disciplinary clinic team consists of a nurse educator, physician, social worker, nutritionist, and pharmacist, though exposure to each individual is varied depending on level of glomerular filtration rate (GFR). In the Italian centre the team consists of programme-dedicated nephrologists and multi-disciplinary nurses responsible for implementation of recommended diagnostic and intervention strategies, information, education and support. The formal team accesses the nutritionist, psychologist, and social worker when necessary.

In both countries the average duration of exposure of the patient to the team is approximately 1.5 h per visit (range 1–2.5 h). The average number of visits per patient-year depends on the protocol, determined by level kidney function. For the purposes of this analysis, it is estimated at five visits per year (including a specialized education visit for treatment modality selection at 2 h), thus total exposure to the clinic team is approximately 8 h ($4 \times 1.5 + 2$ h) per patient-year. The average duration of visits to the nephrology office is estimated to be 0.5 h based on office booking schedules. For the purposes of comparison, the number of visits to nephrologist offices is estimated to be the same number: 5 ($4 \times 0.5 +$ the same 2 h specialized education session). Thus, patients attending nephrology offices had 'exposure' for ~4 h per patient-year. Note that the timing of the 2 h educational session was left to the discretion of the nephrologist for the standard nephrology care patients; however, the same staff from the multi-disciplinary clinic performed it. Thus all patients were exposed to the identical information session.

In Italy, patients in the formal programme participate in three 2 h educational dialysis orientation meetings over 3 months, culminating in additional 6 h of education exposure. Those patients who do not attend the programme receive orientation to dialysis by the physician in charge and the programme team; the timing of this is again at the discretion of the

nephrologist, and occurs closer to dialysis start than those attending the formal programme.

Data collection and measurements

Data were collected on all patients at the time of dialysis initiation, by research assistants. Baseline data included demographics, diabetic status, aetiology of kidney failure, date of first nephrology referral and dialysis modality. Serial laboratory data were collected on all patients at the time of dialysis initiation and at follow-up intervals of 6 and 12 months. Patient status (on dialysis, deceased, transplanted, discontinued treatment, or moved) was also obtained at the end of the study period for each cohort.

Statistical analysis

Descriptive analyses are presented as mean ± standard deviation. Continuous variables were compared using the Student's *t*-test or Wilcoxon rank-sum test depending on distribution. Categorical variables were compared using the chi-squared test. Multiple linear regression was used to investigate independent predictors of short-term outcomes (differences in laboratory data at dialysis initiation) adjusting for age, sex, race, diabetes, aetiology of kidney failure, estimated kidney function at dialysis initiation, country and attendance of multi-disciplinary clinic (MDC). Survival on dialysis was examined using the Kaplan–Meier method and survival by clinic attendance was compared using the log-rank test. Patients were censored at transplant, moving away, and end of study period. Cox proportional hazards modelling was used to examine hazard ratios for death as outcome. Multivariate modelling explored the impact of MDC on survival adjusting for variables found previously to impact on survival: age, gender, race, diabetes, duration of follow-up prior to dialysis and country. A *P*-value of <0.05 for two-sided tests was considered significant.

Results

The total eligible cohort of 288 patients consisted of 152 patients in the Canadian cohort and 136 patients in the Italian cohort. During the time period of interest, 352 people started dialysis, of which 64 (18%) were referred to nephrologists <3 months prior to dialysis start. These study cohort populations are similar in demographics to those described in national registries from both Canada and Italy [1,25,26]. The only cohort difference between the two countries was racial distribution. All data were thus combined with country and race factored into analyses.

Table 1 demonstrates the demographic and initial laboratory data at dialysis initiation for the 288 eligible patients: note that all patients had an average of 42 months of nephrology care prior to dialysis. Comparisons between those patients seen in the MDC ($n=132$) *vs* standard nephrology care ($n=156$) are presented. Age and race are statistically significantly different between the two groups, with those exposed to the MDC being younger (64 *vs* 60 years) and of different racial composition (more East Indian and less Asians). Analysis of the age distributions confirms similar ranges in both groups.

Patients in both groups commenced dialysis at mean levels of kidney function that were low (below 9 ml/min/1.73 m^2). The estimated GFR using the 'four variable' (abbreviated) Modification of Diet in Renal Disease (MDRD) study equation [27], was statistically significantly different between the two groups: those attending the MDC started dialysis with mean GFR values of 8.4 ml/min/1.73 m^2, *vs* those receiving standard nephrology care alone, who had a mean GFR of 7.0 ml/min/1.73 m^2 (a mean difference between the groups of 1.4, 95% CI: 0.6–2.2, ml/min/1.73 m^2). In both cohorts, ~60% commenced haemodialysis, and 40% commenced peritoneal dialysis therapy. Home-based haemodialysis therapy was not an option at the time of study.

Short-term outcomes: differences in laboratory outcomes at dialysis initiation

Table 2 describes the laboratory data at dialysis initiation as a function of MDC exposure or standard nephrologist care. There were significant differences

Table 1. Summary demographics at dialysis initiation

	Entire cohort	Standard nephrologist office care	Nephrologist and multi-disciplinary clinic	*P*[a]
N (%)	288	156	132	
Clinic duration (months)	41 ± 34	43 ± 34	40 ± 33	0.4
Age (years)	62 ± 16	64 ± 16	60 ± 17	0.02
Female (%)	39.9	43.6	35.6	0.2
Diabetes (%)	33.7	33.3	34.1	0.9
Race (%)				0.001
Caucasian	72.1	66.4	78.9	
Asian	17.1	25.0	7.8	
East Indian	6.4	3.3	10.2	
Other	2.5	2.6	2.3	
Aetiology of kidney failure (%)				0.5
Diabetes	22.3	20.5	24.4	
Hypertension	20.2	21.2	19.1	
GN[b]/Autoimmune	24.7	23.1	26.7	
Cystic disease	7.3	5.8	9.2	
Chronic kidney disease[c]	13.6	16.0	10.7	
Other	11.8	13.5	9.9	
Dialysis Modality[d] (% HD)	60.4	61.5	59.1	0.7

[a] *P*-value denotes comparison between those patients seen in the nephrologist and multi-disciplinary clinic *vs* standard nephrologist office care.
[b] GN, glomerulonephritis.
[c] Not otherwise specified.
[d] Percentage of those starting dialysis, HD, haemodialysis (*vs* peritoneal dialysis).

with respect to haemoglobin (102 *vs* 90 g/l, $P < 0.0001$), albumin (37.0 *vs* 34.8 g/l, $P = 0.002$) and calcium (2.29 *vs* 2.16 mmol/l, $P < 0.0001$) levels in those patients followed in the multi-disciplinary clinic *vs* those followed by nephrologist alone. The difference in haemoglobin levels persists during the first year, while the values for calcium and albumin become similar over the course of dialysis. Note that phosphate levels were not different.

In a multivariate model, MDC was independently associated with higher haemoglobin ($\beta = 12.5 \pm 1.9$, $P < 0.001$), calcium ($\beta = 0.14 \pm 0.03$, $P < 0.001$) and albumin ($\beta = 2.2 \pm 0.7$, $P = 0.002$) at dialysis initiation after adjusting for age, sex, calculated GFR at dialysis start, race, diabetes, aetiology of kidney failure, and country of treatment.

Table 2. Laboratory data (mean ± standard deviation) at dialysis start, 6 and 12 months post-dialysis

	Standard nephrologist office care	Nephrologist and multi-disciplinary clinic	*P*
Kidney function at dialysis start			
Creatinine (μmol/l)	707 ± 188	650 ± 225	0.03
GFR[a] (ml/min/m^2)	7.0 ± 2.6	8.4 ± 3.8	0.001
Haemoglobin (g/l)			
Dialysis start	90 ± 14	102 ± 18	<0.0001
6 months	108 ± 15	116 ± 16	<0.0001
12 months	110 ± 17	120 ± 16	<0.0001
Albumin (g/l)			
Dialysis start	34.8 ± 5.3	37.0 ± 5.4	0.002
6 months	36.5 ± 4.5	37.0 ± 4.7	0.4
12 months	36.9 ± 4.6	37.0 ± 4.2	0.9
Calcium (mmol/l)			
Dialysis start	2.16 ± 0.27	2.29 ± 0.21	<0.0001
6 months	2.33 ± 0.24	2.32 ± 0.22	0.9
12 months	2.28 ± 0.21	2.29 ± 0.17	0.6
Phosphate (mmol/l)			
Dialysis start	1.73 ± 0.55	1.73 ± 0.54	0.9
6 months	1.56 ± 0.51	1.61 ± 0.43	0.4
12 months	1.61 ± 0.47	1.59 ± 0.44	0.8

[a]GFR estimated by abbreviated MDRD formula.

Long term outcomes: survival analysis

Patients were followed for a median of 14 months after dialysis start. There were differences in important clinical outcomes after dialysis initiation. In the standard nephrology group 12 patients had been transplanted, one had transferred and 46 had died; in those followed by the MDC, seven had been transplanted, two had transferred, and 13 had died. Figure 1 demonstrates the difference in survival after dialysis initiation, between patients who attended the MDC *vs* those who received standard care, using Kaplan–Meier analysis. Note the statistically significant survival advantage of those attending the MDC over those patients in the standard nephrology cohort ($P = 0.01$).

Multivariate modelling revealed only age and MDC to be significant predictors of survival (Figure 2). Age per 5 years (hazards ratio = 1.36, 95% confidence interval 1.21–1.54) and standard nephrology clinic *vs* MDC attendance (hazards ratio = 2.17, 95% confidence interval 1.11–4.28) were statistically significant independent predictors of death.

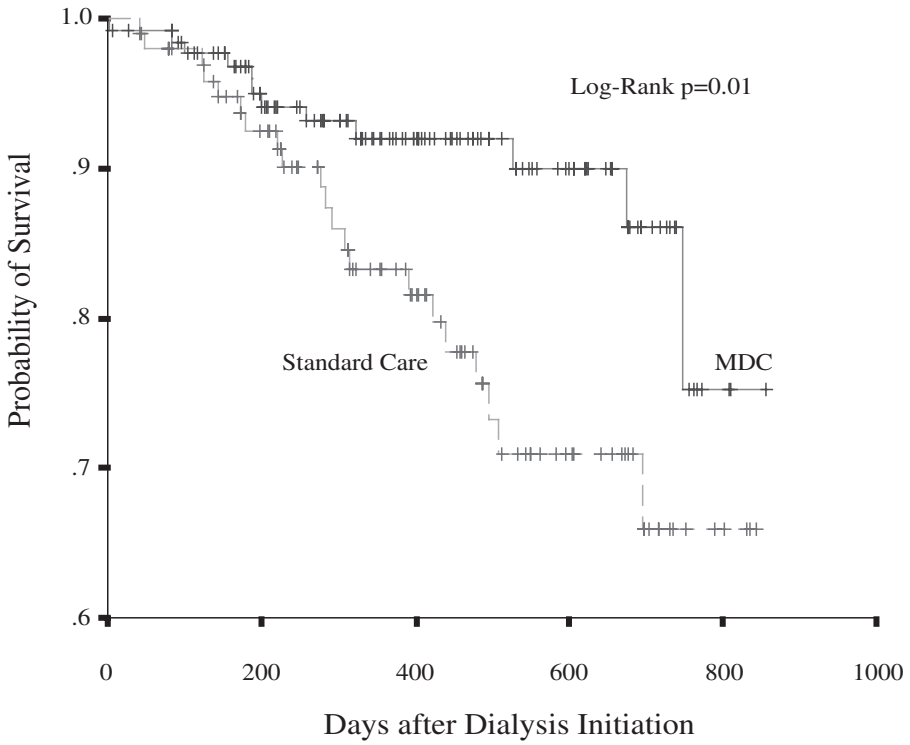

Fig. 1. Kaplan–Meier survival after starting chronic dialysis therapy. Comparison is made between patients seen prior to dialysis initiation in the multi-disciplinary clinic (MDC) *vs* standard nephrology care.

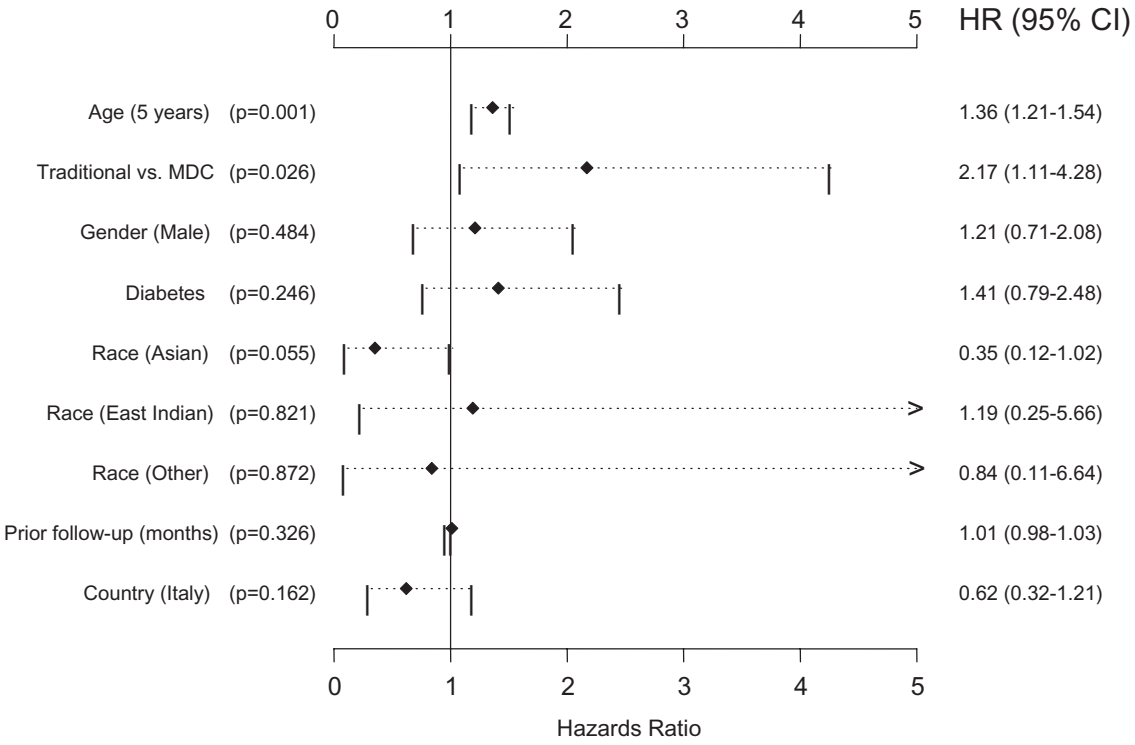

Fig. 2. Risk of death according to multivariate Cox proportional hazards modelling. Comparitor for race is Caucasion.

Discussion

This two country observational study is the first to demonstrate an association between an exposure to formal MDC-based care and survival benefit of patients starting dialysis. Despite similar long exposure times to expert care, those patients exposed to the formalized clinic had higher levels of serum haemoglobin, albumin, and calcium at dialysis start than those followed by standard nephrology care. These measures may be viewed as markers of exposure to care (e.g. nutrition counselling) and have been shown in numerous publications to be associated with a decrease in morbidity and mortality [23,24]. In fact this analysis demonstrates that MDC care impacts on these parameters independent of GFR: that is, the findings of better laboratory parameters are not explained by higher GFR in that cohort receiving MDC care.

The survival advantage of the multi-disciplinary clinic cohort persists despite adjusting in the Cox proportional hazards model for baseline variables known to impact survival: e.g. age, gender, race and diabetes. There were two major differences in the demographics of the cohorts: age and race. The statistically significant 4 year difference in age is of questionable clinical importance. Racial differences are less easy to interpret and may represent patient preference for care patterns, cultural attitudes or a combination of both. As this study seeks to describe the outcomes of exposure to a specific treatment, this finding does not change the conclusions, but does raise further questions for exploration. Of note Asian/Oriental race is usually associated with better outcomes and East Indian and Caucasian with worse outcomes. Thus, the racial distribution differences would serve to bias the analysis against the formalized clinic cohort. While there was a statistical difference between the two groups with respect to GFR at dialysis start, the clinical importance of $1.4\,ml/min/1.73\,m^2$ at levels below $9\,ml/min/1.73\,m^2$ is not clear, but unlikely to account for all the findings. Importantly, we did not adjust for haemoglobin and albumin in the survival analysis, as these variables were themselves impacted directly by our treatment of interest: MDC exposure. Therefore, statistically we could not adjust for a phenomenon that occurred as a consequence of the treatment of interest, at a time point after the exposure. Thus, while it is well known that lower values of haemoglobin and albumin at dialysis start impact on long-term outcomes, our analysis demonstrates one mechanism by which these values may be modifiable in a cohort known to nephrologists for a prolonged period of time. Furthermore, we did not adjust for factors which would have been evidence after dialysis start (such as adequacy of dialysis, severity of illness measures) as our analysis was confined to those factors which would exist prior to dialysis intiation. While it is clear that survival is impacted by adequancy of dialysis and other factors, these factors would not be known to clinicians at the time of initiation, and thus would not be available to inform clinicans as to prognosis: this analysis

clearly describes the importance of status at dialysis initiation.

The data from the two countries are not concurrent; this is due to the late implementation of the formal programme in Italy, which was modelled after the Vancouver programme. Nontheless, the similarlity of the programmes, as one was based on the other, despite the different time periods, allows us to combine the data. Importantly, the results demonstrate that even in a more current era, with increasing awareness of the importance of care prior to dialysis, differences in outcomes are maintained.

This study is not a randomized control trial (RCT), thus the nature of the cohort design does not allow us to rule out a referral or case mix bias affecting our results. However, it is important to stress that all patients had equal opportunities to be referred to the clinic, given that the group of university affiliated physicians belonged to the same practice group in the same geographical area, and used the same hospital and educational resources. While attitudinal differences between physicians may exist, the knowledge of the importance of haemoglobin, albumin and other parameters is probably identical. The analysis confirms similar time of follow-up, and similar patient cohorts, apart from age and ethnicity. We are unable to know with certainty if there are other unmeasured variables impacting on these results such as blood pressure control or aspects of patients' attitudes. The possibility of selection bias of course remains a weakness of this study, and for this reason we advocate the need for a RCT in order to definitively answer the questions posed herein.

There has been only one RCT in patients with kidney disease, published by Harris *et al*. [28], which did not demonstrate a benefit to case management in chronic kidney disease. The intervention in that study was very different to our study as it was limited to written suggestions made to primary care physicians and the assigned clinic patients did not receive any specific treatment or preparation for kidney replacement therapy. This is in contrast to our study in which treatments were implemented directly by clinical staff. Thus, failure to show a benefit in the Harris study may well have been due to the failure of individual primary care physicians to implement the recommendations from the clinic. There are numerous examples of benefit of the MDC in chronic illnesses, which do demonstrate benefit in patient outcomes [11–18]. The current analysis specifically compares sophisticated clinic programs, which include protocolized objectives of care, specific treatment regimens and education to solitary nephrology care. Given the difficulties in conducting randomized control trials of care delivery systems, this study is of value. Indeed, a recent review by Powe [29] describes the need for carefully conducted studies such as this where exposure time, methods and outcomes are carefully tracked, as an alternative to the RCT. We believe the current analysis demonstrates the value of this approach, but does not obviate the need for randomized control trials, as mentioned above.

The reasons for improved laboratory and clinical outcomes despite similar length of time exposed to nephrology expertise are not clear but are probably multi-factorial as the finding argues for the potential added value of a team managing the complex set of factors within individual patients with chronic kidney disease (CKD). We are not able to determine which individual aspects of the programmes are responsible for the findings. It is likely that variables or combinations of variables, such as attitudes and compliance that are difficult to measure may contribute. As we do not have reliable data regarding initial GFR at time of initial referral in all patients, it is possible that slower progression of those exposed to MDC care may account for the findings. This would require additional confirmation with extended studies. Certainly the duration of individual patient exposure per interaction of at least 2 times longer (8 *vs* 4 h), despite similar total patient exposure in months, could be important. We hypothesize that a number of qualitative, not just quantitative, differences in exposure contributed to the outcomes. Importantly, the actual time spent with the patients may overtly reinforce the importance of the condition to the patients, thereby influencing patient compliance and thus outcomes.

We chose to focus on only those persons who had been exposed to nephrologists for >3 months prior to dialysis start. This 3 month cut-off is a construct derived from the literature; importantly for this analysis, it serves to eliminate those patients truly referred late. Current guidelines suggest that up to 6 months in advance of dialysis initiation may be needed for adequate vascular access maturation and optimization of care [30,31]. Nonetheless, even using this 3 month cut-off, the exposure to nephrologists in both groups of interest (formal clinic and nephrology alone) still averaged 42 months: well over 3 years of clinical care. This study then describes the outcomes of patients followed for substantial periods of time. The finding that patients chose haemodialysis 60% of the time irrespective of care model is interesting. It is noted that 60% is well below the national average in both countries (Canada 72%, Italy 89%; and in both regions ~70%) thus indicating the higher propensity for these patients to choose home-based peritoneal dialsysis as their treatment of choice. This corroborates other studies of early *vs* late referral which demonstrate that those referred early are more likely to choose independent-based care than those who are referred later [22].

There is increasing recognition of the importance of CKD [32,33] and a growing number of CKD patients. It is imperative to develop evidence-based strategies that maximize outcomes. The importance of early referral to nephrologists is not disputed and has been well described by many authors to date [19–22]. Early referral is essential to identify the myriad of abnormalities, and plans for their treatment

is best achieved in consultation with specialist care. However, it may be that the ability of individual nephrologists to attend to the multiple and complex aspects of care in this patient group, in the absence of formal clinic teams, is limited. Publications using United States [24,34] and Canadian data [35] demonstrate that even the care of patients with CKD who are known to nephrologists continues to be suboptimal. Our study corroborates these findings.

In summary, this study suggests that even after appropriate and timely referral to a nephrologist, there is additional value of a multi-disciplinary team in optimizing both short, and long-term patient outcomes [33,36]. Uniquely, we extend observations of previous studies and demonstrate a potential survival advantage of formal MDCs. The value of each of the components of the clinic programme (i.e. personnel, protocol driven laboratory/visit schedule and treatment plans) is not known. Research needs to be undertaken to prospectively follow patients from entry into the nephrology/MDC care to confirm these findings and determine whether other objectives of the clinic, such as delaying progression, are met.

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Conflict of interest statement. The authors do not declare any conflicts of interest that may impact the validity or credibility of the findings or statements. The preparation of this study and the manuscript were independently conceived and not funded by any outside sources.

[See related article by Mendelssohn (this issue pp. 10–12)]

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