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The mortality and hospitalization rates associated with the long interdialytic gap in thrice-weekly hemodialysis patients

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Excess mortality and hospitalization have been identified after the 2-day gap in thrice-weekly hemodialysis patients compared with 1-day intervals, although findings vary internationally. Here we aimed to identify factors associated with mortality and hospitalization events in England using an incident cohort of 5864 hemodialysis patients from years 2002 to 2006 inclusive in the UK Renal Registry linked to hospitalization data. Higher admission rates were seen after the 2-day gap irrespective of whether thrice-weekly dialysis sequence commenced on a Monday or Tuesday (2.4 per year after the 2-day gap vs. 1.4 for the rest of the week, rate ratio 1.7). The greatest differences in admission rates were seen in patients admitted with fluid overload or with conditions associated with a high risk of fluid overload. Increased mortality following the 2-day gap was similarly independent of session pattern (20.5 vs. 16.7 per 100 patient years, rate ratio 1.22), with these increases being driven by out-of-hospital death (rate ratio 1.59 vs. 1.06 for in-hospital death). Non-white patients had an overall survival advantage, with the increased mortality after the 2-day gap being found only in whites. Thus, fluid overload may increase the risk of hospital admission after the 2-day gap and that the increased out-of-hospital mortality may relate to a higher incidence of sudden death. Future work should focus on exploring interventions in these subgroups.

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KEYWORDS: hemodialysis; interdialytic events; mortality; out-of-hospital death

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Excess admissions and deaths have been identified after the 2-day break (long interdialytic gap) in three times a week hemodialysis (HD).[1–4] Increases in mortality of between 20 and 40% compared with the rest of the week have been described, although the findings vary from country to country. For instance in the Dialysis Outcomes and Practice Patterns (DOPPS) analysis,[2] the greatest increases in mortality in European patients dialyzing Tuesday/Thursday/Saturday (Tue/Thu/Sat) were on Saturdays, whereas Japanese patients dialyzing Monday/Wednesday/Friday (Mon/Wed/Fri) had highest mortality on Fridays. Possible explanations for the weakening of the association outside of the USA may relate to the longer dialysis treatment times routinely employed in these countries compared with the USA during the respective study periods.[5] Fluid retention and hyperkalemia are associated with a higher incidence of cardiac death in HD patients,[6,7] and increased interdialytic intervals would be likely to enhance this risk.

Increased hospitalization rates(~60 to 90%) after the long gap are best described in US cohorts with greater increases noted for cardiovascular admissions.[1] However, given the variations identified in mortality patterns internationally, it may not be safe to assume that this problem also exists in other health-care systems. Patients with other chronic conditions are more likely to be hospitalized after the weekend, making it important to distinguish between this phenomenon and any variations driven by dialysis session patterns.[8–10] The simultaneous increase in hospitalization and mortality after the 2-day gap may be a manifestation of the heightened workload on admitting hospitals and their staff.[11]

If current dialysis sessional patterns are genuinely associated with increased risks of hospitalization and death then there is a need to find solutions. We aimed to clarify, in a large incident cohort of patients from a single country, whether dialysis pattern (Mon/Wed/Fri or Tue/Thu/Sat) is associated with an increase in admissions and deaths after the long break. We also aimed to understand the factors associated with hospitalization and death in these circumstances and the demographic and clinical characteristics of affected patients.

RESULTS

Following the exclusion of patients receiving HD in centers that did not employ hospital episode statistics (HES) to code dialysis attendance (68%) and extended periods of time admitted while coded as being on the HD modality (8%), 5864 incident HD patients from 36 centers accounting for 10,878 patient years were available for analysis. Median time available for analysis per patient was 1.3 years. HD patterns were broken down as follows: Mon/Wed/Fri—6816 treatment years (50.2%), Tue/Thu/Sat—6274 treatment years (47.3%), and Tuesday/Thursday/Sunday (Tue/Thu/Sun)—322 treatment years (2.5%). Overall, 13.5% of patients moved from one dialysis pattern to another for >5% of their treatment time. The demography of the patients when first observed is detailed in Table 1. The lower mortality rate in most deprived was attenuated by direct standardization with age (rate per 100 patient years, most to least deprived: 16.9, 17.0, and 17.7) and has been fully reversed following comprehensive adjustment in previous analyses.[12]

Admissions after the long break

The mean emergency admission rate was 1.54 admissions per patient year, and this was highest after commencement of regular HD as renal replacement therapy (RRT; 2.52 annualized admissions for the first 3 months, 1.69 for the subsequent 9 months, $P<0.001$). For those who died, admissions increased exponentially toward death. There was an increase in admissions after the long break (2.38 per year for the first HD session of the week, HD1 vs. 1.40 per patient year for the rest of the week; ratio of admission rates (RR) 1.69, 95% confidence interval (CI) 1.63-1.76: $P<0.001$), which was observed for both Mon/Wed/Fri, Tue/Thu/Sat, and Tue/Thu/Sun patients (Figure 1). Admission rates for HD3 for Mon/Wed/Fri (Friday) and Tue/Thu/Sat (Sat) patients were similar (1.67 and 1.71 admissions per year, $P=0.4995$).

These increased admission rates are shown according to the reason for admission in Table 2, with the greatest increases being seen for admissions associated with fluid overload. The relationship between admission rates and patient demography is presented in Supplementary Table S2 online.

Table 1 | Demography of patients when first entering the observation period, with emergency admission rate and mortality rate per 100 patient years while observed, stratified by the demographic group

Demography at entry into study	Proportion of cohort	Emergency admission rate (per year; 95% CI)	Crude mortality rate (per 100 patient years)
Age<40 years[a]	11.9%	1.51 (1.44–1.59)	5.53 (4.23–7.00)
Age 40–65 years	37.9%	1.52 (1.48–1.55)	11.98 (10.96–13.07)
Age>65 years	50.2%	1.57 (1.54–1.61)	23.85 (22.57–25.18)
Male	62.3%	1.52 (1.49–1.55)	18.02 (17.01–19.05)
Female	37.7%	1.58 (1.54–1.62)	16.03 (14.83–17.30)
White	83.0%	1.54 (1.52–1.57)	18.82 (17.92–19.74)
Non-white	17.0%	1.62 (1.58–1.66)	9.84 (8.50–11.33)
Least deprived tertile	32.2%	1.62 (1.58–1.66)	19.02 (17.56–20.56)
Intermediate deprivation	32.4%	1.56 (1.51–1.60)	17.39 (16.02–18.80)
Most deprived tertile	34.7%	1.62 (1.58–1.66)	15.66 (14.43–16.94)
Dialysis ⩽1 year[b]	82.2%	1.91 (1.85–1.96)	17.67 (16.19–19.21)
Dialysis >1 year	17.8%	1.41 (1.38–1.43)	17.11 (16.20–18.04)
Arrhythmia	4.7%	2.00 (1.90–2.10)	18.02 (17.01–19.05)
Congestive cardiac failure	19.1%	2.19 (2.13–2.26)	26.15 (22.63–29.91)
Chronic obstructive pulmonary disease	6.7%	2.33 (2.22–2.43)	33.49 (31.09–35.98)
Acute myocardial infarction	14.9%	2.12 (2.06–2.19)	35.78 (31.98–39.90)
Valvular heart disease	5.5%	2.02 (1.92–2.12)	30.69 (28.30–33.18)
Lymphoma/myeloma	4.1%	2.29 (2.12–2.47)	31.11 (27.47–35.09)
Connective tissue disease	3.6%	1.82 (1.68–1.96)	49.61 (42.07–57.75)
Peptic ulcer disease	5.4%	2.13 (2.02–2.24)	23.07 (18.62–28.26)
Neurological disease	4.9%	2.41 (2.29–2.53)	25.55 (21.99–29.52)
Cancer (previous or active)	8.5%	1.82 (1.74–1.90)	30.37 (26.49–34.66)
Vascular intervention/stent	4.6%	2.00 (1.90–2.10)	32.28 (28.93–35.92)
Cerebrovascular accident	9.7%	2.25 (2.17–2.33)	27.27 (23.74–31.18)
Depression	3.0%	2.62 (2.46–2.79)	34.52 (31.53–37.65)
Diabetes	34.1%	1.90 (1.86–1.95)	24.32 (19.61–29.53)
Coronary artery bypass graft	5.8%	1.93 (1.84–2.03)	20.65 (19.23–22.16)
Claudication	8.1%	2.39 (2.30–2.48)	20.68 (17.77–23.93)
Comorbid score 0[c]	33.4%	1.38 (1.33–1.42)	5.17 (4.41–6.02)
Comorbid score 1	28.6%	1.68 (1.62–1.74)	12.75 (11.47–14.09)
Comorbid score 2	17.1%	2.12 (2.04–2.20)	19.39 (17.52–21.41)
Comorbid score 3 or more	20.1%	2.42 (2.36–2.48)	36.37 (34.06–38.75)

Abbreviation: CI, confidence interval.
[a]Mean age 62.7 years (s.d. 15.8 years).
[b]Mean dialysis vintage 6.5 months (s.d. 13.8 months).
[c]Mean comorbid score 1.35 (s.d. 1.39).[12]

Significantly higher admission rates after the long break were seen in patients with the comorbid conditions of the following: congestive cardiac failure (3.61 on HD1 vs. 1.97 admissions/year for the rest of the week, RR 1.83 vs. 1.64 for those without the condition, *P*-value for difference in rate ratio 0.015); chronic obstructive pulmonary disease (4.04 on HD1 vs. 2.05 admissions/year for the rest of the week, RR 1.97 vs. 1.66 for those without, *P*-value for difference in RR 0.002); and pre-dialysis systolic blood pressure in excess of 150 mm Hg (2.40 on HD1 vs. 1.34 for the rest of the week, RR 1.79 vs. 1.62 for those without, *P*-value for difference in RR 0.04).

The relative increase in admissions after the long break remained constant throughout the first 2 years of treatment (RR 1.71 for first 3 months vs. 1.66 for subsequent 21 months, *P*-value for difference in RRs = 0.67). Similarly, the relative increase in admissions after the long break was not significantly higher approaching death (RR 1.79 for last 3 months of life vs. 1.66 for the preceding 9 months, *P*-value for difference in RRs = 0.178). Admission rates and relative increases according to time are plotted in Figure 2.

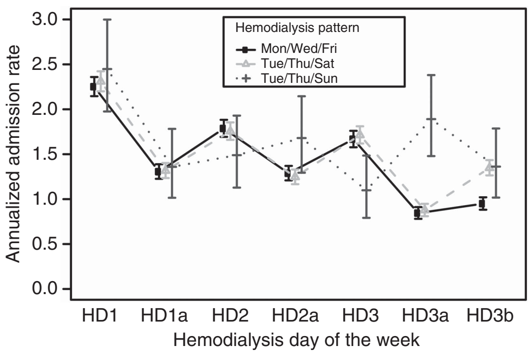

Figure 1 | Admission rates stratified by dialysis pattern. Hemodialysis (HD1) represents Monday in a patient dialyzing on a Monday/Wednesday/Friday (Mon/Wed/Fri) regime, Tuesday in a patient who dialyzes on a Tuesday/Thursday/Saturday (Tue/Thu/Sat) regime, and Sunday in patients who dialyzed on a Tuesday/Thursday/Sunday (Tue/Thu/Sun) regime. The day after the first HD session was assigned HD1a, HD2 for the second HD session etc. Irrespective of dialysis pattern, HD1 was always the day after the long gap.

Deaths after the long break

Overall mortality rate on HD therapy was 17.3 per 100 patient years. The mortality rate after the long break was 20.5 per 100 patient years (95% CI 18.3–22.8) compared with 16.7 (95% CI 15.9–17.6) for the rest of the week (RR 1.22, 95% CI 1.08–1.38, $P<0.001$). This increase was identical for patients dialyzing Mon/Wed/Fri and Tue/Thu/Sat. This increase in deaths was only observed with out-of-hospital deaths, which had a much larger increase in deaths after the long break (8.2 vs. 5.2 per 100 patient days, RR 1.59, $P<0.001$). Of the 32.4% of deaths occurring out-of-hospital (606 of 1873), 79% of those occurred on dialysis days (HD1, HD2, and HD3) were reported without a corresponding HD session being coded, suggesting that the majority of deaths occurred before HD was due (5.3 vs. 1.4 deaths per 100 patient years, $P<0.001$). The in-hospital mortality rate remained constant across the week at 11.7 per 100 patient days (RR of HD1 to the rest of the week 1.06, $P=0.47$). These data are shown in Figure 3. Again these findings were observed for both Mon/Wed/Fri and Tue/Thu/Sat patients (out-of-hospital mortality RR 1.70 and 1.50, $P<0.001$ and 0.008, respectively).

The overall mortality rate limited the majority of subgroup analyses. Reviewing mortality rates according to day of the week according to ethnicity, lower mortality rates were observed in non-white patients (9.8 per 100 patient years) compared with white patients (18.8 per 100 patient years, RR 0.52, 95% CI 0.47–0.63, $P<0.001$). In addition to this survival advantage, unlike whites, non-white patients did not appear to have an increase in mortality after the long break (9.0 per 100 patient years on HD1 vs. 10.0 for the rest of the week, RR 0.90, $P=0.617$, compared with 22.8 on HD1 vs. 18.1 for the rest of the week in white patients, RR = 1.26, $P=<0.001$). These differences persisted following age and comorbidity standardization and are shown in Figure 4.

The increased admission rate approaching death was greater in those dying in-hospital compared with patients dying out-of-hospital; however, the association with the long gap was weaker. A greater increase in admissions after the long gap prior to death was seen in those who subsequently died out-of-hospital (Supplementary Figure S1 online).

Table 2 | Admission rates after the 2-day break, the rest of the week, and the associated rate ratio for seven specific reasons for admission

Reason for admission	HD1 admission rate per year	Rest of the week admission rate per year	Ratio for HD1 to rest of the week
Chest pain	0.19 (0.17–0.21)	0.11 (0.1–0.12)	1.74 (1.52–1.99)
Overload	0.17 (0.15–0.19)	0.08 (0.07–0.08)	2.12 (1.83–2.45)
Falls/fracture/trauma	0.49 (0.45–0.53)	0.26 (0.25–0.27)	1.86 (1.71–2.02)
Sepsis	0.49 (0.46–0.53)	0.30 (0.29–0.31)	1.65 (1.52–1.79)
Vascular access	0.08 (0.06–0.09)	0.06 (0.06–0.07)	1.16 (0.95–1.42)
Vascular event	0.16 (0.14–0.18)	0.11 (0.1–0.11)	1.44 (1.25–1.67)
Other	0.72 (0.68–0.76)	0.44 (0.42–0.45)	1.64 (1.53–1.75)

Abbreviation: HD, hemodialysis.
Numbers in brackets represent 95% confidence limits. Grouping of reasons for admission available in Supplementary Materials online.

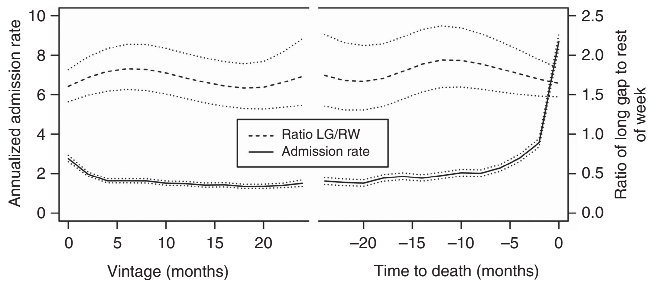

Figure 2 | Admission rates according to time on dialysis/approaching death. Ratio long gap (LG)/rest of the week (RW): the ratio of admissions after the LG compared with the RW. Dotted lines adjacent to ratio and admission rate lines are the 95% confidence intervals for the ratio and rates, respectively.

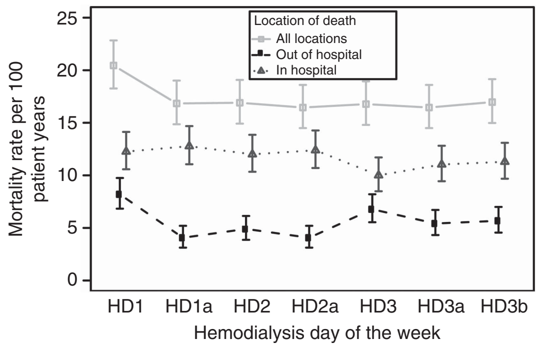

Figure 3 | Mortality per 100 patient years according to day of the week, stratified by location of death. HD, hemodialysis.

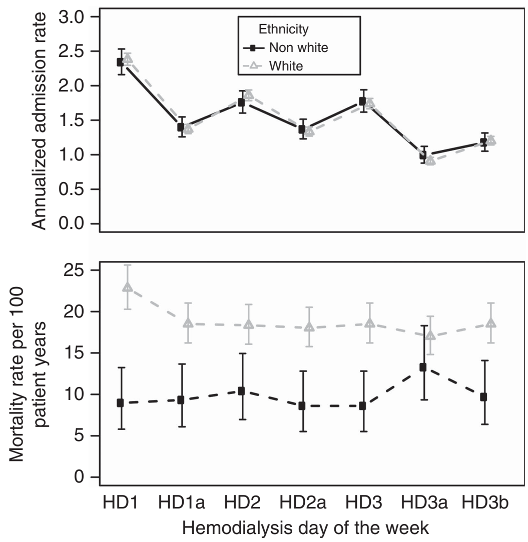

Figure 4 | Comparable admission rates but lower mortality rates with no increase after the long gap in non-white hemodialysis (HD) patients compared with white hemodialysis patients.

The patterns of both admission rates and mortality were similar in summer (April to September) and winter (October to March). Admission rates were identical in these periods, whereas mortality was higher in winter (19.2 vs. 15.3 per 100 patient years, RR 1.26, $P<0.001$).

Sensitivity analysis

Patients excluded from the analysis (see methods) showed similar admission rates and a similar pattern of admission rate by day of the week to included patients, although it was not possible to map these to dialysis session pattern (Supplementary Figure S2 online). Mortality in these excluded patients was greater at 19.3 per 100 patient years ($P<0.001$), largely owing to the deaths associated with greater time in-hospital (18.6 days per year compared with 12.8 days per year, $P<0.001$; Supplementary Figure S3 online).

The increase in mortality on HD3a observed in non-white patients was driven by both Mon/Wed/Fri and Tue/Thu/Sat patients, despite a larger proportion of non-white patients receiving Tue/Thu/Sat regimes. Adherence with attendance at dialysis sessions, estimated using mean HD sessions per week in included patient treatment time, was identical (2.78, $P=0.74$).

DISCUSSION

This study has identified an excess of admissions and deaths over the long gap in three times a week HD, irrespective of dialysis session pattern. Admissions for fluid overload and falls were notably higher after the long gap. Greatest increases in admissions were observed in patients with conditions such as congestive cardiac failure, hypertension, and pulmonary disease, comorbidities which may be more susceptible to the increases in volume over the long gap. Despite this hypothesis, there was no increase in admissions over the long gap with increasing time on dialysis, a surrogate for residual urine volume. Excess mortality was limited to patients dying out-of-hospital and patients of white ethnicity.

This study adds to previous national and international analyses detailing events over the long interdialytic interval. Whereas previous analyses by DOPPS identified variations in the mortality pattern when compared with dialysis schedule,[2] this study has demonstrated strong associations with both Mon/Wed/Fri and Tue/Thu/Sat patients. Despite concerns of a ‘Monday morning’ admission phenomenon seen with patients with coronary artery disease, chronic obstructive pulmonary disease, and congestive cardiac failure,[8–10] admissions in patients dialyzing on Tue/Thu/Sat regimes had the highest admission rate on a Tuesday. We explicitly quote similar admission rates on the third HD session in both groups to illustrate no drop in admissions because the HD session occurs at a weekend in Tue/Thu/Sat, making a weekend lag effect in admissions an unlikely explanation for these observations. The association was also found in the small proportion of patients dialyzing Tue/Thu/Sun. This national investigation shows identical trends irrespective of dialysis pattern.

Beyond the perhaps unsurprising increase in fluid overload after the long gap, the increased incidence of falls- and

trauma-related admissions warrants thought. Previous studies have shown increased fall risk in patients with greater comorbidity and lower pre-dialysis blood pressure, potentially increasing the patient's susceptibility to intradialytic hypotension owing to the greater ultrafiltration requirements following the long gap.[13]

Notably, the annualized all-cause mortality rate over the dialysis week is similar to that presented by Foley *et al.*[1] for patients dialyzing between 2005 and 2008. This US cohort reports on patients starting during an earlier era, but this finding mirrors those of recent DOPPS reports of comparable HD mortality rates in North America and Europe.[14] Analytical methods differ between these studies due to how time admitted to hospital contributes to the analysis. Given data showing dialysis treatment length in the UK has generally exceeded that in North America,[5] one might have expected that the increased solute clearance and ultrafiltration this extended time might offer would modulate the above increases in event rates. Session length was incompletely reported to the UKRR and may be confounded by patients with a propensity to present with fluid overload preferentially receiving augmented treatment regimes.

The increase in out-of-hospital mortality is thought provoking. First, despite a 69% increase in admissions after the long break, and the increase in workload associated with this, there is no increase in-hospital mortality. One might assume that deaths over the weekend at home might be uncovered on a Monday; however, the out-of-hospital mortality rate in Tue/Thu/Sat patients was still greatest on a Tuesday. That 79% of out-of-hospital deaths on dialysis days occurred before hemodialysis had taken place might suggest that excessive fluid removal necessitated by the 2-day break is unlikely to be a major factor accounting for the observed excess mortality.

Because of the established lower mortality rate in non-white patients and their prevalence in UK dialysis programs (17% in this cohort), analysis of ethnicity was limited to white and non-white. The lower mortality rate across the dialysis week despite identical admission rate profiles suggests that hospital-associated mortality for non-white patients is also lower than white patients throughout the week. The lack of an increase in the mortality after the long gap does not explain the previously described survival advantage of non-whites[15,16] but may contribute to it. Questions may be raised as to why white patients tolerate the long interdialytic interval worse than non-white patients. If hyperkalemia is the explanation for the increased out-of-hospital mortality rate then dietary potassium intake, body composition, and total clearance—residual kidney function plus delivered dialysis dose—may differ between these ethnic groups.[15,17,18] It has been previously shown that overall comorbid burden does not differ significantly between these groups.[12] The nonsignificant increase in mortality after the third HD session in non-whites (Figure 4) is unexplained and may relate to adherence issues toward the end of the dialysis week in this group.[19] We were unable to identify any issues with non-adherence in this patient group but recognize that our analysis technique may be insensitive to this. Additional limitations to this observational study include our inability to evaluate the impact of directly measured residual kidney function (although we found no association with dialysis vintage—Figure 2), dialysis session length, shortened sessions because of compliance issues, or sessional potassium levels on interdialytic events. The anonymized nature of the data set prevented us from performing a HES validation exercise with manual case note review. We have insufficient cohort size to explore Tue/Thu/Sun patients to reliably exclude a lag in the identification of patients dying at the weekend who are discovered at the beginning of the week or other mortality associations. Data processing and preparation of our manuscript were greatly simplified by focusing on conventional (thrice-weekly) HD, and as a result we are unable to comment on any survival advantage or disadvantage associated with twice-weekly HD.[20]

Planning an intervention to reduce mortality over the long break should clearly be focused on re-evaluating the standard dialysis pattern. More recent lessons from the Frequent Dialysis Network have shown that longer session length may not be the solution, with deleterious effects on residual renal function and increased mortality at 3 years seen in nocturnal dialysis patients when compared with standard three times a week regimes.[21,22] More encouraging is the survival advantage seen in patients randomized to shorter more frequent in-center sessions.[23] Furthermore, we should ensure that three sessions a week are delivered reliably by exploring adherence to dialysis schedules and the temporary introduction of longer gaps due to transitions between hemodialysis patterns and seasonal holiday dialysis rescheduling.

We need to understand the underlying mechanisms for these issues in relation to the long gap, such as fluid overload and electrolyte disturbance. We need also to be able to identify whether there are particular patient phenotypes conferring increased risk. This knowledge would allow us to be better able to target interventions such as minimizing interdialytic intervals or deploying other measures to limit fluid and biochemical accumulation. This study does offer insight into which patient groups might be best targeted for greatest improvements in survival, hospitalization, and potentially reduced health-care costs or greatest quality-adjusted life year gains.

MATERIALS AND METHODS

Patients and data

Information on incident patients starting RRT in England between 1 January 2002 and 31 December 2006 was collected by the UK Renal Registry (UKRR), a disease registry collecting modality, laboratory and the outcome data from electronic downloads from clinical computer systems within renal centers. Patient follow-up data were available to the end of 2009. These data were then linked to hospital admission data in the form of HES data set by a third party, the Research Capability Programme. All secondary-care activity irrespective of payer is collected via HES, which records diagnosis, procedure, location, and mortality information for each hospitalization in England. As HES only covers England, patients

and centers residing outside England were excluded. As these data sets contain similar demographical information, their combination reduced missing data on ethnicity and comorbidity to ~1%.

Demographic information was updated on a weekly basis, with comorbidity informed from ICD10 diagnosis codes extracted from admissions prior to the week in question using commonly applied comorbid diagnosis code groupings.[24] The presence of individual comorbid conditions was determined, and an overall comorbid score derived from the survival of incident patients on RRT in England.[12] Agreement for comorbidity supplied through UKRR and that derived from HES immediately prior to starting RRT was 93%; however, because of anonymization verification of admission-specific data was not possible. Blood pressure values were taken from the most recent downloaded quarterly bloods collected in the 6 months prior to the week in question. Non-white was defined as patients coded as Black, South Asian, or other from either data set.

Dialysis pattern

HD treatment pattern was determined in centers that routinely used HES to record outpatient HD treatment attendance. As recording HD attendance was not mandatory at this time, steps were taken to ensure that the appropriate frequency of outpatient HD sessions was being recorded by renal centers contributing data to the analysis. Periods of time when the modality recorded via UKRR was coded as HD was compared with HES-recorded outpatient HD attendance for individual HD units within renal centers, with HD units contributing appropriate HD attendance counts being retained. For each HD treatment week attendances for outpatient HD were compared with established three times a week HD patterns. The first recognized three times a week pattern was carried forward until significant deviation and/or the establishment of a new HD pattern for 4 consecutive weeks. Incident RRT patients could be included in the analysis if they started RRT on a different modality between 2002 and 2006 and then transferred to HD at a later date.

Admissions and deaths

Emergency admissions (defined by HES coding of admission method) and deaths identified through HES and UKRR. Data during these weeks were then compared with the assigned dialysis pattern for that week. Entire weeks where a patient was admitted to hospital were excluded. For mortality analyses, the week after the admission week was also included in order to obtain a robust in-hospital and out-of-hospital mortality rate. A death out-of-hospital was defined as a recorded death via the UKRR without a corresponding HES-recorded death during an admission. Reasons for admission were derived from the Healthcare Cost and Utilization Project mapping of ICD10 diagnosis codes to reason for admission groups.[25] The ICD10 codes employed in the reported groups are available in Supplementary Table S1 online.

Statistical methods

In this analysis, HD1 represents Monday in a patient dialyzing on a Mon/Wed/Fri regime and Tuesday in a patient who dialyzes on a Tue/Thu/Sat regime. Patients who dialysed on at Tue/Thu/Sun regime were assigned Sunday as their HD1. The day after the first HD session was assigned HD1a, HD2 for the second HD session, HD2a for the day after the second session, HD3 for the third HD session, with HD3a and HD3b for the 2 days after this final HD session. Irrespective of dialysis pattern, HD1 was always the day after the long gap.

The rates of admissions or deaths are reported in admissions per patient year and deaths per 100 patient years, respectively, using individual dialysis days or breaks as discrete patient time intervals where appropriate. The primary end point was the relative increase in the event rate on HD1 compared with the rest of the week. Confidence intervals around individual HD day event rates and the RR of HD1 to the rest of the week were determined using the Poisson distribution. Days admitted to hospital were subtracted from days at risk for admission; however, a patient was classed as at risk of death for all the time they received HD. Differences in the increase in events after the long gap compared with the rest of the week (RR) between groups were tested for using the rate interaction test. Sensitivity analyses were performed comparing admissions and deaths in the included and excluded patient treatment time (dialysis weeks) to ensure dialysis pattern assignment and exclusion techniques detailed above did not bias analyses.

DISCLOSURE

All the authors declared no competing interests.

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SUPPLEMENTARY MATERIAL

Table S1. ICD10 codes for reasons for admission mapped to the nine reasons for admission groups reported.
Table S2. Demographic variables and their influence on admission rates over the dialysis week.
Figure S1. Overall admission rate and increases in admission after the two day gap approaching death stratified by location of death.
Figure S2. Similar admission rates and trend over the week in patients and treatment time included and excluded in the analysis.
Figure S3. Lower mortality rates seen in the selected patients and treatment time compared to unselected.
Supplementary material is linked to the online version of the paper at http://www.nature.com/ki

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