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Reprocessing dialysers for multiple uses: recent analysis of death risks for patients

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Abstract

Background. Reprocessing dialysers is a common cost-saving practice in the USA. It began when patients were treated with bio-incompatible cellulosic membranes that were associated with medical complications, but has continued for economic reasons despite the current use of more biocompatible non-cellulosic membranes. A dialysis services and product provider using primarily its own non-cellulosic membranes recently embarked on a staged programme to stop reprocessing dialysers. Approximately a quarter of 71 000 patients had been switched from reuse to single use by July 1, 2001. The transition offered a unique opportunity to re-evaluate death risk associated with the reuse practice.

Methods. Patients were classified as reuse or single use as of July 1, 2001. Survival time measurements started on that date (Lag0) and at four 30 day intervals after it (Lag30, Lag60, Lag90 and Lag120). Thus, patients must have been treated in their reuse group after Lag0 for at least 30, 60, 90 or 120 days, respectively. Survival time was evaluated during 1 year following the lag date using the Cox method in unadjusted, case mix-adjusted and case mix plus other measure-adjusted models.

Results. All analyses suggested favourable survival advantage among patients treated with single use dialysers. The differences were statistically significant at all lag times in the unadjusted models but became significant only at later lag times in the case mix- and case mix plus other measure-adjusted models. For example, single use/reuse hazard ratios in the case mix-adjusted models at Lag0–Lag120 were 0.96 (NS), 0.96 (NS), 0.94 ($P=0.02$), 0.93 ($P=0.02$) and 0.92 ($P=0.01$), respectively.

Conclusions. A risk benefit appears associated with abandonment of the dialyser reuse practice, although the benefit may lag behind the change. In the USA, the relative risk burden associated with the reprocessing of dialysers may have changed over time with the evolution of clinical practice.

Keywords: haemodialysis; mortality

Introduction

The reprocessing of disposable dialysers was first proposed for economic reasons [1]. Early studies suggested that the reprocessing and reuse of dialysers manufactured using cellulosic membranes conferred medical benefits to patients, apparently rendering the membrane more biocompatible with blood [2]. In the USA, therefore, the clinical community adopted them as cost-saving measures in response to federal dialysis treatment price reductions. Only 19% of dialysis units reprocessed dialysers in 1980. The fraction increased to 61% by 1985 and increased further to 80% in 2000 [3].

Dialysers using synthetic membranes have largely replaced those using cellulosic membranes in recent years. More than 80% of dialysis units used cellulosic dialysers in 1990 while <25% used any dialysers with a synthetic membrane. Those statistics were reversed by 2000 such that <25% of facilities used any cellulosic dialysers while >80% used synthetic membrane dialysers [4]. The synthetic membranes are more biocompatible than their cellulosic predecessors so the reuse-associated medical benefit probably disappeared. The rationale for reusing synthetic membrane dialysers thus became purely financial.

During 2000, Fresenius Medical Care (North America) (FMCNA) embarked on a staged programme to discontinue the reprocessing of dialysers in its clinics. Reuse facilities were disassembled on dates selected by administrative staff for operational convenience, after which no patient in the unit was treated with a reprocessed dialyser. The evolution from universal reuse to single use provided a unique

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opportunity to evaluate possible changes of reuse-associated death risk in a population of patients after switching from treatment with reprocessed to single use dialysers. We therefore selected the sample of patients prevalent on July 1, 2001 to compare the annual death risk between patients using and not using reprocessed dialysers.

Methods

We adopted a null hypothesis of 'no difference' of survival between patients treated with single use and reused dialysers. The clinical consequences, if any, resulting from discontinuing reuse could be either adverse, due for example to repeatedly exposing blood to a new membrane surface as in the past, or beneficial, due for example to discontinued exposure of patients to some element of the reuse process. Any such consequence would probably lag behind the actual date of the change. Possible adverse consequences of discontinuing reuse may also lag behind the conversion date because increased exposure to trace industrial products or repeated inflammatory insults may be cumulative, requiring time to become clinically manifest. Similarly, any pathophysiology consequent to the reuse process may require time to repair after discontinuing the practice. We therefore adopted an analytical strategy evaluating patient survival in terms of minimum required lengths of time, lag periods, since reuse had been discontinued.

The initial sample included all patients treated in an FMCNA dialysis facility on July 1, 2001 for whom a dialyser make and model was available, and who were treated using a dialyser manufactured by the Dialysis Products Division of FMCNA. All dialysers manufactured by FMCNA use polysulfone membranes and are coded to distinguish dialysers for which reuse is permitted and possible, from models for which it is not.

Patients were assigned in a primary analysis cluster to the reuse group if they were treated using a reusable dialyser and to the single use group if they were treated with a single use dialyser. The cluster included three analysis sets depending on the level of statistical adjustment (unadjusted, case mix-adjusted and case mix plus other-adjusted). Each analysis set included five individual analyses. The first 1 year survival period started on July 1, 2001 (Lag0). One year analyses were also performed using the same sample, minus dying and censored patients, at four 30 day intervals after July 1 (Lag30, Lag60, Lag90 and Lag120). Thus, patients at each lag period must have been treated in their particular reuse group for at least 30, 60, 90 or 120 days, respectively, and survival times were determined for 1 year from those dates.

Survival curves were constructed using the Kaplan–Meier method, and possible significance between curves was evaluated at 6 months and 1 year using the log-rank test implemented by the SAS statistical system (SAS Institute, Carey, NC). The core analytical technique was survival time analysis using a proportional hazards model (Cox) to evaluate the single use/reuse death hazard ratio during 1 year, with censoring for traditional reasons such as transplantation, facility change, therapy change or loss to follow-up, and also if the dialyser reuse designation changed after the original reuse group assignment. Intention-to-treat analyses in which patients were not censored if the dialyser reuse designation changed were also performed. The proportional hazards assumption was evaluated for all analyses by including a time-dependent explanatory variable in the models. Proportionality was confirmed for all except the Lag30 models.

Three levels of statistical adjustment (i.e. the analysis sets) were used with the models: (i) unadjusted; (ii) case mix adjustment; and (iii) case mix plus other adjustment. The case mix adjustments included age, gender, race (black, white, other), diabetes (yes or no) and vintage (< 6 months, 6 months–1 year, 1–2 years and >2 years of dialysis prior to July 1, 2001); this set was considered the primary set for each cluster. The other adjustment measures included serum albumin concentration, alkaline phosphatase, bicarbonate, systolic blood pressure, body surface area, serum calcium, phosphorus, creatinine, ferritin, blood haemoglobin concentration, serum iron, the urea clearance × dialysis time product (Kt) and white blood cell count, all of which were significantly associated with death risk ($P < 0.01$). The average value for the 3 months before the analysis start date (July 1 plus the lag period) was used in these analyses. A single clinical laboratory (Spectra Clinical Laboratories, Rockleigh, NJ) performed all laboratory determinations. The urea reduction ratio (URR) and Kt were estimated by established techniques. The Daugirdas and the Daugirdas/Schneditz algebraic approximations were used, respectively, to estimate a single pool Kt indexed to a volume of urea distribution, spKt/V, and an equilibrated Kt/V, eKt/V.

We supplemented the primary cluster analyses by adjusting the single use/reuse hazard ratio for the year 2000 standardized mortality ratio (SMR) of the facilities in which patients were treated to evaluate whether facilities administratively selected for conversion to non-reuse may have systematically had lower mortality rates than others. Two separate analyses were performed. SMR was regarded as a continuous measure in the first. It was regarded as an ordinal measure in the second. Facilities were grouped as having an SMR above (high SMR), below (low SMR) or within (average SMR) the 80% confidence interval of ~1.0 given the facility size. The methods are described elsewhere [5].

Finally, a nominal date for discontinuing reuse operations was determinable for the majority but not all dialysis facilities (792 of 1078 facilities; 73.5%). We therefore evaluated an alternative analysis cluster using that nominal conversion date in addition to dialyser type (reuse or single use) when assigning patients to reuse or single use groups. We assumed that patients had been treated with dialysers that had not been reprocessed before the facility conversion date if a single use dialyser was used; we assumed the patient had been treated with a reprocessed dialyser if a reusable dialyser was used. All patients were deemed treated with dialysers that had not been reprocessed after the facility conversion date because reuse capability had been discontinued. Thus, all patients were assigned to the single use group if the facility nominal conversion date was before July 1, 2001. If the date was after July 1, patients treated with single use dialysers were assigned to the single use group while patients treated with reusable dialysers were assigned to the reuse group until the facility conversion date.

Results

Data and patient sample

Table 1 compares the distributions of selected measures among the reuse and single use patients on July 1, 2001 in the primary analysis cluster. Patients in the single use group tended to be slightly younger and were more likely to be male (and thus tended to be slightly larger and have higher creatinine concentration) than patients in the reuse group. The Kt was slightly higher but the URR, spKt/V and eKt/V were slightly lower in single use patients than in reuse patients. Albumin, haemoglobin and phosphorus were not different between the groups. Single use patients were slightly more likely to be diabetic.

Table 2 shows the patient counts at the start of each lag period and the reasons for patient attrition between periods. Between 1.9 and 2.6% of patients were lost each month due to traditional censoring reasons, 3.1–5.2% were lost because dialyser reuse status changed and 1.4–1.5% died. The proportion of reuse patients decreased from 74.5 to 71.5% during these 4 months.

Table 1. Sample attributes

Variable	Reuse ($n=52\,985$)		Single use ($n=18\,137$)		P
	Mean	SD	Mean	SD	
Age	61.0	15.1	59.7	15.4	<0.001
Gender (% male)	51.8		54.8		<0.001
Race (% white)	48.3		48.9		<0.001
Diabetes (% yes)	44.6		46.4		<0.001
Vintage (years)	3.4	3.6	3.4	3.8	NS
Albumin (g/dl)	3.8	0.4	3.8	0.4	NS
Creatinine (mg/dl)	9.0	3.2	9.3	3.3	<0.001
Haemoglobin (g/dl)	11.5	1.2	11.6	1.2	NS
Phosphorus (mg/dl)	6.0	1.6	6.0	1.6	NS
White blood cells ($10^3/\mu l$)	7.5	4.2	7.6	2.6	0.002
Systolic BP (mmHg)	150.9	19.9	150.6	20.1	0.084
Kt (l/Rx)	49.6	10.9	50.2	11.1	<0.001
URR (%)	70.2	6.9	69.8	7.1	<0.001
spKt/V	1.35	0.28	1.33	0.27	<0.001
eKt/V	1.15	0.23	1.14	0.23	<0.001
Body surface area (m^2)	1.82	0.25	1.85	0.27	<0.001

NS indicates $P>0.100$.

Primary analysis cluster

Figure 1 is a composite of four survival curves at Lag0, 30, 60 and 120 days. There was no significant difference between the curves at 6 months for Lag0 and Lag30; the difference was significant at 6 months for Lag60, Lag90 ($P=0.002$; not shown) and Lag120. The differences were significant at 1 year for all lag periods. Visual examination of the curves suggests that the reuse and single use curves tended to diverge late during the 1 year observation period when the lag period was short. They tended to diverge much earlier in the observation period when the lag period was longer.

Table 3 shows the results of the primary analysis cluster. While the unadjusted analyses all suggested a significant survival advantage for single use at each lag period, significance did not emerge for the case mix- or the case mix plus other-adjusted models until the lag period was $\geq$60 days. The case mix- and the case mix plus other-adjusted models suggested, respectively, a 7.6 and a 9.7% survival advantage associated with single use at Lag120. The intention-to-treat analyses implied similar survival patterns in all three sets. The hazard ratios at Lag0–Lag120 in the case mix-adjusted set, for example, were 0.950 (NS), 0.956 (NS), 0.931 ($P=0.009$), 0.921 ($P=0.003$) and 0.909 ($P<0.001$), respectively.

Differences by SMR

We adjusted the single use/reuse death hazard ratio for the SMR of the facility in which patients were treated. The mean SMRs among facilities reusing and not reusing dialysers were 1.02 and 0.96, respectively ($t=1.07$, NS). The single use/reuse hazard ratios were 0.948 ($P=0.049$), 0.953 ($P=0.091$), 0.921 ($P=0.005$), 0.910 ($P=0.002$) and 0.892 ($P<0.001$) at Lag0–Lag120

Table 2. Patient counts and (%) of patients at the start of each lag period

Lag time	Start	Censored[a]	Switched[b]	Died[c]	Carried[d]	% on reuse[e]
0	71 122 (100.0)	1870 (2.6)	3462 (4.9)	1004 (1.4)	64 786 (91.1)	74.5
30	64 786 (100.0)	1351 (2.1)	3350 (5.2)	915 (1.4)	59 170 (91.3)	74.1
60	59 170 (100.0)	1197 (2.0)	1842 (3.1)	817 (1.4)	55 314 (93.5)	73.0
90	55 314 (100.0)	1067 (1.9)	2429 (4.4)	815 (1.5)	51 003 (92.2)	72.4
120	51 003	NA	NA	NA	NA	71.5
All lags	71 122 (100.0)	5485 (7.7)	11 083 (15.6)	3551 (5.0)	51 003 (71.7)	NA

[a]Censored due for transplant, change of facility, change of therapy or loss to follow-up.
[b]Censored for switching reuse status.
[c]Died during lag period.
[d]Carried over to the next lag period.
[e]The percentage of patients reusing dialysers at the start of the lag period.
NA = not applicable.

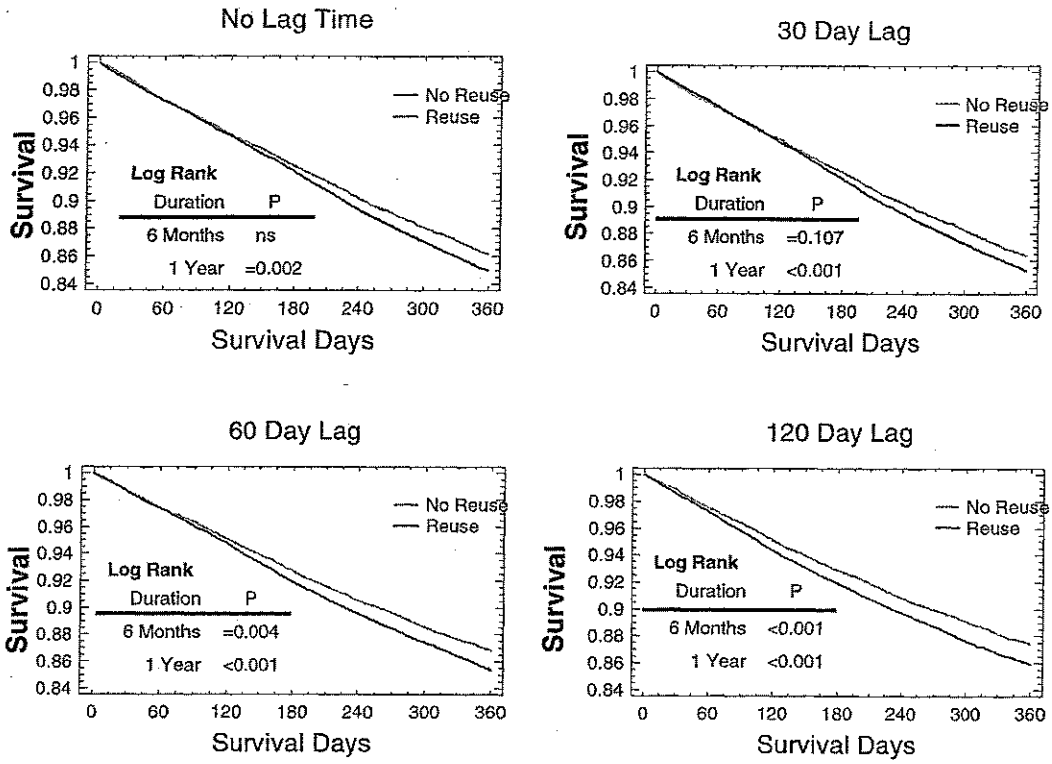

Fig. 1. Curves comparing the survival of patients treated with reusable and single use dialysers for at least the number of 'lag days' shown at the top of each panel. Log rank tests evaluating possible differences between the curves at 6 months and 1 year are shown. 'ns' indicates $P > 0.150$. The log rank statistics at Lag90 was significant at 6 months ($P = 0.002$) and at 1 year ($P < 0.001$).

Table 3. Cox regression analyses of survival comparing patients treated with reusable and single use dialysers

Model	χ^2	P[a]	Hazard ratio[b]	95% CI[c]	
				Lower	Upper
Lag = 0 days					
Unadjusted	9.4	0.002	0.922	0.876	0.971
Case mix	2.2	NS	0.961	0.911	1.031
Case mix + lab	2.5	NS	0.952	0.895	1.012
Lag = 30 days					
Unadjusted	7.8	0.005	0.927	0.878	0.977
Case mix	1.6	NS	0.964	0.913	1.019
Case mix + lab	2.9	0.089	0.946	0.888	1.008
Lag = 60 days					
Unadjusted	14.0	< 0.001	0.899	0.850	0.950
Case mix	4.8	0.029	0.938	0.886	0.993
Case mix + lab	6.5	0.011	0.918	0.859	0.980
Lag = 90 days					
Unadjusted	14.6	< 0.001	0.893	0.843	0.947
Case mix	5.4	0.021	0.932	0.878	0.989
Case mix + lab	8.2	0.004	0.904	0.844	0.989
Lag = 120 days					
Unadjusted	16.2	< 0.001	0.884	0.832	0.939
Case mix	6.2	0.012	0.924	0.868	0.983
Case mix + lab	7.8	0.005	0.903	0.840	0.970

[a]The associated probability of no association between reuse status and death hazard.
[b]The ratio of death hazard of single use patients to patients reusing dialysers.
[c]The upper and lower 95% CI enclose the 95% confidence interval of the hazard ratio.
NS indicates $P > 0.100$.

when SMR was regarded as a continuous measure. Similar ratios were 0.945 (NS), 0.968 (NS), 0.933 ($P = 0.019$), 0.919 ($P = 0.006$) and 0.898 ($P < 0.001$) when SMR was grouped by high, average or low SMR. Thus, the SMR-adjusted analyses suggested interpretations similar to those implied by Table 3.

Alternative analysis cluster: the nominal facility conversion date

Facilities were assigned a nominal date for discontinuing reuse that differed among facilities. Some patients may have been treated with single use dialysers before a facility's nominal conversion date. Few, if any, patients continued to be treated with reprocessed dialysers after the conversion date. However, some patients may have been treated with reusable dialysers that were not reprocessed after the conversion date to consume the inventory of reusable dialysers remaining at hand.

We evaluated the fractions of patients using reusable and single use dialysers before and after the nominal conversion date in each dialysis unit. A total of 8.3% of patients were treated with single use dialysers in the median facility 30 days before the conversion date; a similar statistic 30 days after the conversion date was 96.1% so that only 3.9% were treated with multiple use dialysers that were used only once. Thus, conversion to single use dialysers was rapid after the conversion date.

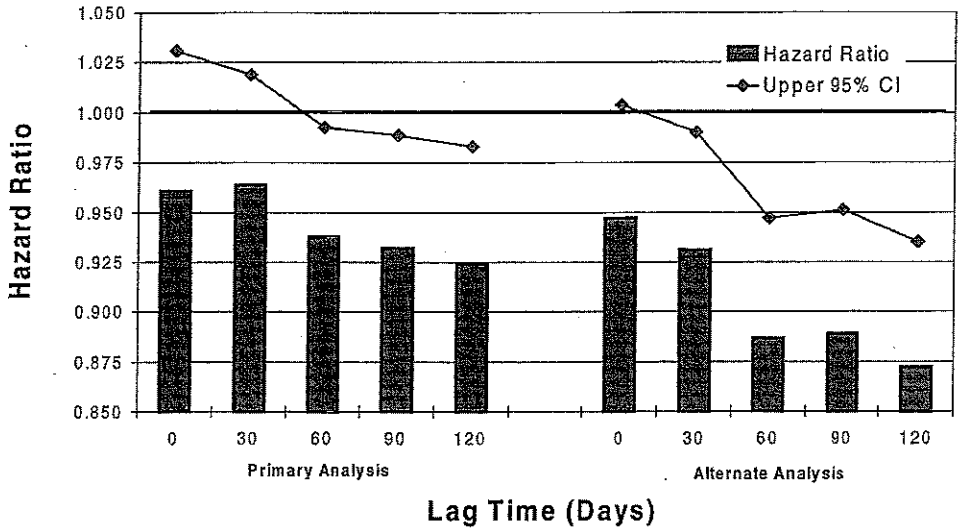

Fig. 2. The case mix analysis set from the primary analysis cluster is compared with a similar set from the second alternative analysis cluster. The single use/reuse hazard ratios and their upper 95% confidence intervals for each lag interval are shown. A horizontal, dark line is added at hazard = 1.000 to facilitate reading the chart.

Figure 2 compares the case mix-adjusted analysis set from the primary cluster with that from the alternative analysis cluster. Both analysis clusters imply decreasing (improving) single use/reuse hazard ratios over time and both imply a risk advantage for patients assigned to the single use group. The risk ratios were lower and the upper 95% confidence interval of the ratio fell below 1.000 earlier in the alternative cluster than in the primary cluster.

The unadjusted sets suggested a significant risk benefit associated with single use at all lag periods in both the primary and alternative clusters. The case mix plus other-adjusted sets in both the primary and alternative clusters were similar to the case mix-adjusted sets shown in Figure 2 except the hazard ratios tended to suggest a slightly greater risk benefit for single use at each lag period.

Supplementary information: prevalent reuse practices

Evaluation of the reuse practices among those 873 facilities (81%) for which data were available on July 1, 2001 indicated that the majority (75%) used formaldehyde disinfection with bleach cleaning and a single type of reuse machine. However, peracetic acid (19%), glutaraldehyde (1%), citric acid (1%) and heat-based (< 1%) disinfection were also used instead of formaldehyde (79%). While the majority of units using peracetic acid used no additional cleaning step, nearly one-third used bleach cleaning and an additional 6% used a water cleaning step. Most units using formaldehyde disinfection used a single machine to assist the process, but nearly 5% used another type. Units using peracetic acid-based disinfection used three different machine types. Thus, the combinations of disinfection (five disinfectants), cleaning methods (four methods) and assist machines (three machines) were sufficiently complex to preclude evaluating fully saturated statistical models. There were no statistically significant survival differences, however, among patients treated in facilities using formaldehyde *vs* peracetic acid disinfection or using bleach *vs* not using bleach as a cleaning step for any of the three statistical adjustments (the sets) used here. The median number of uses per dialyser and the maximum number of reuses among units practising reuse were 5.0 (interquartile range = 4.0–6.8) and 9.0 (7.0–12.5), respectively.

Discussion

Early research suggested that medical as well as financial benefits attended the reuse of dialysers. The white blood cell count fell sharply during the first few minutes of treatment with new dialysers manufactured with cellulosic membranes [6,7] and was substantially less when the dialyser was reprocessed [7]. Furthermore, a syndrome that included puritis, rash and asthma-like symptoms, called the 'first use syndrome', sometimes attended first use but not reprocessed dialysers. The white cell decrease observed with new cellulosic dialysers was much greater than seen with dialysers manufactured using new synthetic membranes [7]. Thus, the reprocessing of cellulosic dialysers appeared to enhance their biocompatibility.

Polysulfone is a synthetic membrane. Clinics affiliated with FMCNA embarked on a programme to discontinue reuse in 2000. Approximately 25% of patients had switched from reuse to single use by July 2001. These data suggest that a mortal risk benefit may attend a change to single use dialysers. The hazard associated with reuse was modest, ranging between 5 and 10%. However, it was consistent. All 55 single use/reuse hazard ratios were <1.0, suggesting a survival advantage for single use. The ratios became greater and more significant at and after Lag60 in the adjusted analyses.

Data from the late 1980s suggested possible risk associated with reuse using some disinfectants but not with others [8–10]. Later studies suggested that disinfectant-associated risk disappeared during the early 1990s [11]. The statistical adjustments made by those analyses differed among the studies [8–11] and were made across provider type, dialyser model and reprocessing disinfectant. Furthermore, both those attributes and the reuse process could contribute to, or be associated with, medical co-morbidity, for which the analyses were also adjusted. The statistical adjustments, therefore, could adjust for a pathology that was actually caused by the reuse practice. As such, the effect of multiple statistical adjustments to a target of interest, such as reuse-associated relative survival, may be difficult to evaluate. The analyses chosen here were more parsimonious, being restricted to one large provider network, one commonly used membrane type and one point in time among clinics evolving from reuse to single use practice, so that both procedures were being used in a large patient population. Finally, these analyses are patient specific because our proxies assigned reuse status based on information for each patient. Other similar efforts generally assigned a patient's reuse status using facility-based surveys indicating whether or not the unit practised reuse. As such, non-reusing patients might be misclassified as reuse patients.

We chose a model that did not distinguish between different types of reuse practice such as number of uses, the disinfectant chemical, supplementary cleaning procedures or what device was used to assist the reuse process. Available reuse guidelines [12,13] suggest that factors other than those are just as important to the reuse practice. We thus chose to classify patients into reuse and single use groups ignoring possible subclassifications.

The most common disinfectant used here was formaldehyde, whereas the most common used in the USA has a peracetic acid base [4]. Most early studies, however, suggested that the use of formaldehyde was associated with mortal risk comparable with single use [8–11] while peracetic acid was associated with greater risk [8–10].

Reprocessing dialysers is essentially limited remanufacturing that involves the cleaning and disinfection of a medical device. The practice is subject to few controls in the USA. Manufacturers could not follow such an uncontrolled practice for first use dialysers under current regulations in the USA (United States Code of Federal Regulations, Title 21, Parts 1, 26, 110, 211, 860, 876. April 1, 2003). The exposure of membranes to different disinfection chemicals and processes may alter those membranes in unpredictable ways [14]. Hence, the membrane used may not be functionally equivalent to the membrane purchased if it has been reprocessed. Simply said, dialysis facilities and regulatory agencies that oversee their operation in the USA do not require the levels of process control or quality surveillance that are required of manufacturers before a product is used to treat patients.

The reuse of dialysers is much less prevalent in Europe than in the USA [15–17]. A recent survey (Fresenius International, Internal Market Survey, 2004) suggests that reuse prevalence among patients in the 25 European Union countries is ~5% but that the statistic is heavily influenced by a single country (Poland; 85%). The practice is negligible (< 1%) in most EU (20 out of 25) countries and is legally proscribed in three (Portugal, Spain and France). Existing EU rules (Council of European Communities: Medical Device Directive 93/42/EEC—Annex 1, 13.6) require manufacturers to provide information about proper practice for reprocessing devices, including sterilization and preservation of functional integrity, if they are intended for reuse. The UK has implemented the requirement by formally assigning the legal responsibility for reuse of non-reusable devices to users, i.e. physicians, clinics and hospitals [Device Bulletin 2000(04), Medicines and Healthcare Products Regulatory Agency, Department of Health, UK]. The reuse prevalence in the UK, once nearly 25% [15] and more recently ~10% [15,17], now appears to be ~2% (Fresenius Market Survey).

Some speculate that apparent better survival among European than American dialysis patients may be due in part to differences of reuse exposure [18]. Those differences may also derive in part from demographic differences, prevalence of co-morbidities, differences in the use of vascular access and the delivered dose of dialysis [19], with special reference to the length of each treatment [18]. However, differences in the prevalence and nature of the reuse practice could also play a role [18,19]. It is clear, however, that medical, social, political and legal attitudes about reusing dialysers are very different in Europe from those in the USA whether or not retrospective epidemiological studies such as this and others [8–11] report mortality differences associated with the practice. Indeed, the differences in attitudes toward the practice are particularly noteworthy because clinicians and policy makers on both continents have access to much the same clinical literature.

These findings should be qualified by several considerations. First they, like all current studies of reuse practice, evolve from retrospective data and there was no attempt to randomize patients between reuse and single use groups. The attribute differences between groups that did exist, however, were small, and favourable risk associates were not confined to either group. Furthermore, statistical adjustment for a large number of measures did not extinguish the risk benefit associated with single use.

Secondly, individual patients were not coded as 'reuse' or 'single use' in our data. Thus, we used proxies for assigning patients to groups. Our initial choice was the dialyser type with which the patient was treated. Single use dialysers were probably never reprocessed. Multiple use dialysers were probably reused before the nominal facility conversion date but not reused after it. Indeed, this alternative proxy was associated with a more dramatic survival advantage than our primary

proxy and may reflect better accuracy in classifying patients by reuse practice.

Thirdly, reuse practice was not randomized within dialyser type. Differences in either the membrane or its transport capacity could account for part or all of the differences observed here even though all dialysers used a polysulfone membrane. Such an interpretation would require belief that there exist meaningful survival differences associated with dialyser models within each manufacturer. If so, there must also exist meaningful survival differences between the dialysers in common use sold by different manufacturers. There is little current evidence for such a belief particularly over a short observation period (1 year) or conversion horizon (a lag of 60 days). In any event, the dialysers associated with the risk benefit in this analysis are not reusable.

Further to this point, the proxies for 'small molecule' (urea) removal were similar between the groups; the measures indexed to body size (the URR, spKt/V and eKt/V) were if anything greater in the reuse group. We did not measure a proxy for the clearance of larger molecules. A recent trial, however, did not identify a meaningful survival difference between patients treated at higher or lower clearances [20].

Fourthly, it is possible that low mortality dialysis units were selected for early conversion to single use operation. Conversion date decisions were made by regional administrative staff and were not medical decisions. It is unlikely that administrators examined the mortality statistics of facilities when deciding the conversion schedule. Even so, adjustment for facility SMR did not extinguish the survival advantage associated with single use. Finally, if administrators had made their decisions based on criteria associated with facility mortality, the difference between reuse and single use would probably have been immediate rather than improving with time as it appears to have done here.

Fifthly, these studies were limited to one membrane type. We cannot say whether or not similar studies using different membranes might give different results, suggesting either more or less risk associated with their reuse. Furthermore, we cannot say that different remanufacturing methods that use different cleaning agents, disinfection methods and process strategies might be more or less safe than others, particularly as they are used with different membrane types. Data are available, however, suggesting that different reprocessing methods change different membranes in different ways [14].

While we cannot say with absolute certainty that the differences reported here were due solely to the reprocessing of dialysers, the preponderance of evidence suggests this to be the case. The materials from which dialysers are manufactured have changed over the years. It is reasonable to speculate that the balance of medical risk may have favoured the reprocessing of dialysers years ago when most artificial kidneys were manufactured using cellulosic membranes. Now that most dialysers are manufactured using more biocompatible membranes, the risk associated with reuse may have changed, causing a different balance. If so, the medical community and those who pay for dialysis services should consider the balance between the prices paid for treatment and the risk borne by patients when evaluating dialyser reuse practice in the USA. Such a reappraisal might suggest either that the reuse practice should be abandoned or that dialysis facilities, with or without the assistance of manufacturers, should be held to higher standards of process validation and control that are similar to those required for first use dialysers.

Conflict of interest statement. J.M.L. is an officer and a full-time employee of FMCNA. Z.L. and N.O. are full-time employees of FMCNA. E.G.L. is paid consultant to FMCNA and was president of its predecessor organization, National Medical Care, which developed and adopted reuse practices for its clinics. FMCNA manufactures and sells dialysers, and is a large provider of dialysis services.

References

1. Shaldon S, Rae AL, Rosen SM *et al.* Refrigerated femoral venous–venous haemodialysis with coil for rehabilitation of terminal uraemic patients. *Br Med J* 1963; 1: 1716–1717
2. Lowrie EG, Hakim RM. The effect on patient health of using reprocessed artificial kidneys. *Proc Dial Transplant Forum* 1980; 10: 86–91
3. Tolkars JI, Alter MJ, Arduino MJ. National surveillance of dialysis-associated diseases in the United States, 2000. *Semin Dial* 2002; 15: 162–171
4. US Renal Data System. Excerpt from the USRDS 2002 Annual Data Report (Chapter 11). *Am J Kidney Dis* 2003; 41: S177–S188
5. Lowrie EG, Teng M, Lacson E *et al.* Association between prevalent process measures and facility-specific mortality rates. *Kidney Int* 2001; 60: 1917–1929
6. Henderson LW, Miller ME, Hamilton RW, Norman ME. Hemodialysis leukopenia and polymorph random mobility—a possible correlation. *J Lab Clin Med* 1975; 85: 191–197
7. Hakim RM, Lowrie EG. Effect of dialyzer reuse on leukopenia, hypoxemia and total hemolytic complement system. *Trans Am Soc Artif Intern Organs* 1980; 26: 159–163
8. Held PJ, Wolfe RA, Gaylin DS *et al.* Analysis of the association of dialyzer reuse practice and patient outcomes. *Am J Kidney Dis* 1994; 23: 692–708
9. Feldman HI, Kinosian M, Bilker WB *et al.* Effect of dialyzer reuse on survival of patients treated with hemodialysis. *J Am Med Assoc* 1996; 276: 620–625
10. Feldman HI, Bilker WB, Hackett MH *et al.* Association of dialyzer reuse with hospitalization and survival rates among U.S. hemodialysis patients: do co morbidities matter? *J Clin Epdemiol* 1999; 52: 209–217
11. Collins AJ, Ma JZ, Constantini EG, Everson SE. Dialysis unit and patient characteristics associated with reuse practices and mortality: 1989–1993. *J Am Soc Nephrol* 1998; 9: 2153–2156
12. National Kidney Foundation report on dialyzer reuse. Task Force on reuse of dialyzers, Council on dialysis, National Kidney Foundation. *Am J Kidney Dis* 1997; 30: 859–871
13. American National Standard. *Reuse of Hemodialyzers.* Association for the Advancement of Medical Instruments, Arlington, VA; 1996: 805–820

14. Cheung AK, Agoda LY, Daugirdas JT *et al.* Effect of hemodialyzer reuse on clearances of urea and beta2-microglobulin. The Hemodialysis (HEMO) Study Group. *J Am Soc Nephrol* 1999; 10: 117–127
15. Valderrabano F, Berthoux FC, Jones EHP, Mehls O. Report on management of renal failure in Europe, XXV, 1994 End stage renal disease report. *Nephrol Dial Transplant* 1996; 11 [Suppl 1]: 2–21
16. Vinhas J, Pinto dos Santos J. Haemodialyzer reuse: facts and fiction. *Nephrol Dial Transplant* 2000; 15: 5–8
17. Brown C. Current opinion and controversies of dialyzer reuse. *Saudi J Kidney Dis Transplant* 2001; 12: 352–363
18. Shaldon S. Adequacy of long-term dialysis. *Curr Opin Nephrol Hypertens* 1992; 1: 197–202
19. Lameire N. Management of the hemodialysis patient: a European perspective. *Blood Purif* 2002; 20: 93–102
20. Eknoyan G, Beck GJ, Chueng AK *et al.* Effect of dialysis dose and membrane flux in maintenance hemodialysis. *N Engl J Med* 2002; 347: 2010–2019

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