

*Original Article*

## **Haemodialysis prescription, adherence and nutritional indicators in five European countries: results from the Dialysis Outcomes and Practice Patterns Study (DOPPS)**

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### **Abstract**

**Background.** The Dialysis Outcomes and Practice Patterns Study (DOPPS) is a prospective, observational study designed to evaluate practice patterns in random samples of haemodialysis facilities and patients across three continents. Participating countries include France, Germany, Italy, Spain and the UK (Euro-DOPPS), Japan and the USA. DOPPS data collection has used the same questionnaires and protocols across all participating countries to assess components of dialysis therapy and outcomes. This study focuses on dialysis prescription, adherence and nutrition among the Euro-DOPPS countries.

**Methods.** In each Euro-DOPPS country, patients were selected randomly from 20–21 representative facilities. Simple means and frequencies were calculated to compare relevant data elements to gain insights into differences in therapeutic aspects among nationally representative patients. Participants entering the study within 90 days of beginning dialysis therapy were excluded from these analyses.

**Results.** Among the five countries, mean delivered dose as measured by normalized urea clearance (Kt/V) varied from 1.28 to 1.50 and was accompanied by differences in dialysis prescription components, including blood flow rates, treatment times, and dialyser membrane and flux characteristics. By country, a

nearly 2-fold difference was observed in indicators of patient adherence and management (skipping and shortening dialysis, hyperkalaemia, hyperphosphataemia and high interdialytic weight gain). Indicators of malnutrition varied substantially.

**Conclusions.** This study demonstrates differences in the management of haemodialysis patients across Euro-DOPPS and offers opportunities for improving dialysis dose, adherence and nutrition. Correlation of differences in practice patterns at the dialysis unit level with patient outcomes will offer new insights into improving dialysis therapy.

**Keywords:** adherence; dialysis dose; Europe; haemodialysis; nutritional parameters; outcomes

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### **Introduction**

A study of survival rates among haemodialysis patients in Europe, Japan and the USA in the 1980s showed large differences among these regions [1]. This study, however, was based on registry data, which had not been collected in a standardized way across countries and did not allow for comparisons in relation to variations in dialysis prescription and patient adherence.

The Dialysis Outcomes and Practice Patterns Study (DOPPS) evaluates several components of facility practice and patient outcomes using nationally representative samples of haemodialysis patients from seven countries (France, Germany, Italy, Japan, Spain,

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the UK and the USA). Identical questionnaires and protocols have been used to evaluate patient characteristics, a variety of practice patterns and patient outcomes [2,3]. Previous studies have shown that the relative risk of mortality is lower with three treatment characteristics: higher dialysis dose [4–6], improved patient adherence to therapy [7] and better nutritional status indicators [8]. These studies set the stage for the DOPPS and its primary aim of identifying cross-national differences in dialysis practice patterns and correlating these differences to variations in patient outcomes. The present study describes and evaluates the differences among the five European DOPPS countries (Euro-DOPPS) in three domains: (i) haemodialysis prescription; (ii) patient adherence; and (iii) nutritional indicators.

## Subjects and methods

### *Data source*

At study start, the DOPPS protocol was tested in a random sample of US patients and facilities, and study materials for Euro-DOPPS countries were professionally translated. In each Euro-DOPPS country, 20 haemodialysis facilities were selected randomly for study participation; the need for a replacement unit brought Germany's total to 21. Facilities were stratified by geographic region and facility type [France stratified by general, private, university and association facilities; Germany by clinics (medical centres), non-profit freestanding and private practice units; Italy by public and private units; Spain by academic and non-academic units; and the UK by centre and satellite units]. For efficiency, dialysis units with <25 patients were excluded, a decision that ruled out fewer than 5% of haemodialysis patients in the Euro-DOPPS countries.

Within each facility, 20–40 patients were selected randomly from a census of prevalent patients for detailed longitudinal follow-up, depending on the total number of patients in each unit. Patients who departed (due to transplantation, transferring to another unit or death) were replaced with randomly selected patients entering the dialysis facility during that interval. Euro-DOPPS data collection occurred between June 1998 and November 2000, with follow-up data collected every 4 months. The study was approved by appropriate review boards in each country. Appropriate patient consent was obtained at all study sites; units and patients remained anonymous to the investigators. A more detailed explanation of the study design and analytical methods for DOPPS have been published elsewhere [2].

### *Sample used for analysis*

There were 11 422 total patients in the 101 randomly selected units that participated in Euro-DOPPS. Information was collected on age, race, gender, whether diabetes was the primary cause of end-stage renal disease (ESRD), date of death, date and reason for patient entry and departure from the facility. Detailed patient information was collected from a random sample of 4591 patients from the 11 422 patients treated in the facilities during the study. Detailed data

contained information on topics such as co-morbidities, laboratory values, quality of life variables, medications, hospitalization history and vascular access history.

Out of the 4591 sample patients, 3039 patients who were enrolled in the study at least 90 days after their first-ever dialysis treatment were used in this analysis; 1552 patients who did not meet this criterion were excluded. Patients entering the study within 90 days of their first-ever dialysis treatment were removed because such patients are known to differ from patients in a steady state of haemodialysis treatment. In the dialysis dose/prescription analyses, only patients who had been on dialysis > 1 year and received three times weekly dialysis were used in order to minimize the effect of residual renal function on these statistics ( $n = 2498$ ).

### *Statistical analysis and formulae*

Simple means were calculated by country for the characteristics of interest. Also, an overall unweighted mean was calculated for each measurement. Statistical comparisons were made between individual countries and the overall Euro-DOPPS mean using linear regressions for continuous responses and logistic regressions for dichotomous responses. Linear regression was used to examine the trends in Kt/V over time. Each patient's first dose measurement (after being on dialysis at least 1 year) was modelled against the calendar year in which that measurement occurred. Differences in trends between countries were examined using interaction terms within this model.

The effects of facility clustering on standard error estimates were addressed in these analyses using the generalized estimating equation procedure specifying facility-level clustering and an exchangeable correlation matrix [9]. This method of analysis takes into account the fact that patients from the same facility may be more similar to each other than they are to patients from another facility. All analyses were performed using SAS version 8.2 (SAS Institute, Cary, NC).

'Prescribed' dialysis dose was calculated from patient volume, dialyser characteristics, prescribed blood flow rate and treatment time. 'Delivered' dialysis dose was measured using the single- and double-pool methods for calculating Kt/V [10]. Pre- and post-dialysis blood urea or urea nitrogen (BUN) measurements were used for Kt/V calculations, and the post-dialytic BUN or urea was standardized according to the facility's reported timing of post-dialysis blood sampling. Patients in facilities that drew blood immediately at the end of a dialysis session received the full Daugirdas adjustment for double-pool dose. Patients in facilities that waited 30 min received no adjustment for double-pool dose, as the rebound was presumed to have occurred within 30 min. Patients in facilities that waited between 0 and 30 min received a fraction of the Daugirdas adjustment for double-pool dose depending on facility-reported blood draw times and assuming that the rebound effect was fastest immediately at the end of dialysis and tapered off at 30 min afterward.

The patient measures of non-adherence used in this study were skipping of more than one dialysis session in 1 month, shortening a dialysis session by > 10 min in 1 month, serum potassium concentration of > 6.0 mEq/l, phosphate level of > 7.5 mg/dl or interdialytic weight gain (IDWG) > 5.7% of body weight (the last cut-off was based on a > 4 kg IDWG in a 70 kg patient). These definitions are identical to those used in a prior publication from a US Renal Data System

(USRDS) special study [7]. A session missed because of hospitalization was not considered non-adherence. IDWG was defined by the amount of weight removed during a haemodialysis session and is presented as the percentage of body weight removed. The prevalence of each adherence measure was calculated for the initial round of patients at time of entry into the study. Skipping and shortening status were evaluated for the 30 days prior to enrolment into the DOPPS. IDWG was calculated from the most recent haemodialysis treatment before enrolment, and potassium and phosphorus measurements were those obtained on or before the enrolment date. The non-adherence measures of IDWG, potassium and phosphate were adjusted for day of the week of the blood draw. All patients were adjusted to a Wednesday blood draw value to ensure comparability.

To assess nutritional status, a number of laboratory indicators were investigated, including pre-dialysis BUN, serum albumin, serum creatinine, serum potassium, serum phosphorus, weight, IDWG, body mass index (BMI), modified subjective global assessment (mSGA) and normalized protein catabolic rate (nPCR or nitrogen appearance rate). Serum albumin was adjusted for the method of measurement (bromo-cresol green, bromo-cresol purple or other method). The mSGA [11] was used to gather subjective and objective aspects of patient medical history and physical examination. Data captured included weight loss and physical appearance, appetite, nausea, energy level and disease burden. The nPCR was determined using the two-point model of urea kinetics published by Depner and Daugirdas [12]:  $nPCR_{(g/kg/day)} = C_0 / (a + bKt/V + c/[Kt/V]) + 0.0168$ , where  $C_0$  is the pre-dialysis BUN in mg/dl and  $Kt/V$  is the single-pool estimate of dialysis dose. For patients who received dialysis three times weekly, appropriate coefficients (a, b, c) were used, depending on whether laboratory measurements were obtained at the beginning, middle or end of the week.

## Results

Table 1 shows demographic factors and patient modalities by country for haemodialysis patients who had been on dialysis >90 days upon entering the DOPPS. The overall average age was 59.5 years, with Italy displaying the highest mean age (61.3 years) and

the UK the lowest average age (56.6 years). In the UK, 62% of patients were male compared with 57% in each of the four other Euro-DOPPS countries. The size of facilities, as defined by the mean number of treated haemodialysis patients, was similar across countries, with the median size varying from 50 patients/facility in Spain to 59 patients/facility in France. The difference between the country mean and median indicates the presence of a skewed distribution, with some very large dialysis units in each country, particularly in Italy, where this difference was the greatest (Table 1).

Table 2 displays patient-level characteristics of dialysis dose. The delivered dialysis dose, assessed by single-pool  $Kt/V$  and double-pool  $eKt/V$  from measurements of pre- and post-dialysis BUN concentrations, averaged 1.37 and 1.24, respectively, in Euro-DOPPS overall. However, there was considerable country variation, with single-pool  $Kt/V$  ranging from 1.28 in Germany to 1.50 in France. Mean double-pool delivered dose was 6–19% lower than the prescribed dialysis dose in the five countries. Considerable country variation was observed in the components of prescribed dialysis dose. For example, mean haemodialysis treatment time varied from 217 min in Spain to 249 min in France and Germany; the mean blood flow rate ranged from 248 ml/min in Germany to 320 ml/min in Spain; and mean patient volume varied from 36.8 to 40.9 l across the five Euro-DOPPS countries.

Dialysers with the largest surface area and highest efficiency, according to the reported overall mass transfer coefficient ( $K_oA$ ), were used in Spain (Table 2). Synthetic membranes accounted for 41–74% of dialysers by country. High-flux dialysers were used predominantly in France (62%); these dialysers were used least frequently in the UK (20%). These findings indicate substantial variations by country regarding different components of the prescribed dose. Even larger variation in components of prescribed dose was seen when comparing across all facilities in Euro-DOPPS.

A time-trend analysis of changes in delivered dialysis dose in Euro-DOPPS during the data collection time interval from 1998 to 2000 indicated a small, but statistically significant, decline in delivered dialysis

**Table 1.** Demographics, modalities of care and facility size

Facility characteristics	Country					All Euro-DOPPS
	France	Germany	Italy	Spain	UK	
Sample size						
Facilities ( <i>n</i> )	20	21	20	20	20	101
Patients ( <i>n</i> )	672	571	600	576	620	3039
Age (years)	59.3	60.5	61.3	61.0	56.6 <sup>†</sup>	59.5
Male (%)	57	57	57	57	62	58
Facility size						
Mean no. of HD patients	62	61	65	53	61	61
Median no. of HD patients	59	56	54	50	58	55

Patients entering the study within 90 days of their first dialysis treatment were excluded from this analysis. Dialysis units with fewer than 25 patients were excluded.

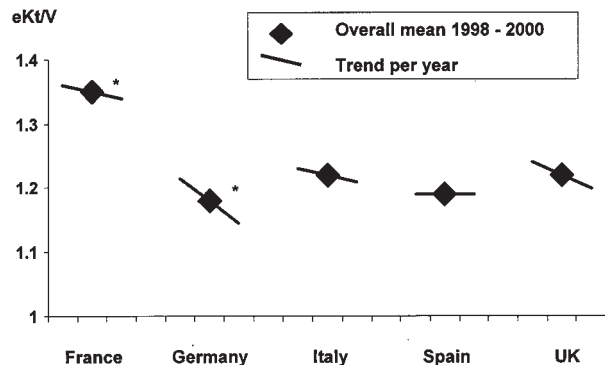
<sup>†</sup> $P < 0.01$  vs All Euro-DOPPS, accounting for facility clustering.

**Table 2.** Delivered dialysis dose and dialysis prescription

Measure	Country					All Euro-DOPPS
	France	Germany	Italy	Spain	UK	
Delivered dose (SP Kt/V)	1.51 <sup>‡</sup>	1.30*	1.32	1.32	1.38	1.38
% < 1.2 (SP Kt/V)	16 <sup>‡</sup>	40*	34	35	28	30
Delivered dose (DP eKt/V)	1.36 <sup>‡</sup>	1.19 <sup>†</sup>	1.22	1.20 <sup>†</sup>	1.23	1.25
% patients with either prescribed dose or components of dose measured	96*	91	87	96 <sup>†</sup>	90	92
Prescribed dose	1.68*	1.31*	1.46	1.46	1.23*	1.38
Duration of HD treatment (min)	249 <sup>†</sup>	251 <sup>†</sup>	221 <sup>†</sup>	216 <sup>‡</sup>	230	234
Blood flow rate (ml/min)	292	251 <sup>‡</sup>	307	322 <sup>‡</sup>	311	296
Patient volume (l)	37.8	40.7 <sup>‡</sup>	37.0 <sup>†</sup>	36.4 <sup>‡</sup>	39.4 <sup>†</sup>	38.2
Dialyser KoA (ml/min)	734	748	715*	861 <sup>†</sup>	744	760
Dialyser surface area (m <sup>2</sup> )	1.45 <sup>†</sup>	1.54	1.50	1.72 <sup>†</sup>	1.62	1.56
Synthetic membrane (%)	64	69	42 <sup>†</sup>	53	71	59
High-flux membrane (%)	60 <sup>†</sup>	54*	28*	49	19 <sup>‡</sup>	43

Patient dialysis dose was taken from the first haemodialysis treatment measured in the DOPPS after the first year on dialysis. Patients not on a thrice-weekly haemodialysis schedule were excluded from this analysis. SP, single pool; DP, double pool; HD, haemodialysis.

\* $P < 0.05$ ;  $^†P < 0.01$ ;  $^‡P < 0.0001$  vs All Euro-DOPPS, accounting for facility clustering.



**Fig. 1.** Mean eKt/V (double-pool) in Euro-DOPPS countries and trend per year. \*Indicates that the country mean was significantly different from overall average eKt/V. Trends were statistically significantly different ( $P < 0.05$ ) between: Germany and France, Germany and Spain, and Spain and the UK. Overall average slope was significantly negative ( $P < 0.001$ ).

dose (Figure 1). In Euro-DOPPS, the overall trend in single-pool Kt/V was a 0.03 decline per year. The decreasing trend in Kt/V was seen in each country except Spain. Various dialysis-related factors were evaluated to understand the reason for this declining trend in delivered dose in Euro-DOPPS, including changes in total body water, post-dialysis weight and blood flow rates, and trends in percentage of patients who skipped or shortened a haemodialysis session per month. The results indicated that the decrease in dose (ranging from 0 eKt/V per year in Spain to  $-0.07$  eKt/V per year in Germany) was primarily because of an increase in average patient weight and a decrease in blood flow rate during the 2 years of the study. The average patient weight increased by 1.8 kg/year in Euro-DOPPS (range of increase: 0.86 kg/year in Italy to 2.79 kg/year in the UK). The average blood flow rate decreased by 4.4 ml/min/year in Euro-DOPPS (range of average decrease:  $-1.7$  ml/min/year in Italy to  $-7.4$  ml/min/year in Germany).

When patients skip dialysis sessions, monthly delivered dialysis dose is lower than the prescribed dose. In European dialysis centres, however, this occurred very rarely ( $< 1\%$  per month, Table 3) compared with reports for the USA [7]. Shortening of sessions by 10 min or more at least once within a 30-day period occurred more frequently than sessions being skipped. The Euro-DOPPS average for shortened sessions was 9%, ranging from 12.6% in the UK to  $\sim 7\%$  in Spain and France (Table 3). Several other parameters may suggest problems with adherence and/or treatment issues. Overall, almost 20% of patients had hyperkalaemia of  $\geq 6.0$  mmol/l. This percentage varied from 10% in the UK to almost 30% in Italy. The pattern for hyperphosphataemia by country was different, with an average of 11.7% of patients having levels  $> 7.5$  mg/dl (2.42 mmol/l). This condition was most frequent in Germany (22%) and least frequent in Italy (4%). More detailed data by country are shown in Table 3. Intradialytic weight loss of  $> 5.7\%$  of dry weight is equivalent to an IDWG of  $> 4$  kg for a 70 kg patient. Relatively high IDWG values were observed in Italy and France, with the lowest IDWG values in the UK and Germany.

Analyses of mSGA data showed that 3.8% of patients were assessed with a cachectic or severely malnourished score, ranging from 2.3% in Italy to 6.5% in the UK (Table 4). Moderate or severe mSGA scores were indicated in 15% of patients, being slightly lower in Spain (11.2%) and somewhat higher in France (18%). Data on mean BMI showed only small variation and did not appear to correspond to the mSGA.

The average pre-dialysis serum albumin, a nutritional indicator and inflammatory marker, ranged from 3.73 g/dl in the UK to 4.14 g/dl in Germany (Table 4). The relatively high average albumin level in Germany may have resulted, in part, from Germany's practice of measuring serum albumin with a laboratory

**Table 3.** Adherence and treatment measures

Measure	Country					All Euro-DOPPS
	France	Germany	Italy	Spain	UK	
% Patients shortened session by $\geq 10$ min in past month	7.3	9.5	8.8	6.6	12.6	9.0
% Patients skipped $\geq 1$ session/month	0.3	0.9	0.5	0.5	0.8	0.6
Serum potassium $> 6.0$ mEq/l (%)	10.9 <sup>†</sup>	15.4	28.0 <sup>‡</sup>	27.3 <sup>‡</sup>	9.8 <sup>‡</sup>	18.0
Serum phosphorus $> 2.42$ mmol/l (or $> 7.5$ mg/dl) (%)	9.4	22.4 <sup>‡</sup>	3.8 <sup>‡</sup>	12.2	11.6	11.7
Serum phosphorus $> 2.10$ mmol/l (or $> 6.5$ mg/dl) (%)	21.3	38.5 <sup>‡</sup>	15.5 <sup>‡</sup>	22.6	21.9	23.8
IDWG $> 5.7\%$ body weight (%)	14.3 <sup>†</sup>	5.6	17.7 <sup>‡</sup>	7.5	3.4 <sup>†</sup>	9.8

Patients entering the study within 90 days of their first dialysis treatment were excluded from this analysis. IDWG, interdialytic weight gain <sup>†</sup> $P < 0.01$ ; <sup>‡</sup> $P < 0.0001$  vs All Euro-DOPPS, accounting for facility clustering.

**Table 4.** Nutritional Indicators

Measure	Country					All Euro-DOPPS
	France	Germany	Italy	Spain	UK	
Pre-BUN (mg/dl)	73.1*	66.6 <sup>†</sup>	75.7 <sup>†</sup>	72.1	64.8 <sup>†</sup>	70.8
Pre-dialysis albumin (g/dl)	3.87	4.17 <sup>†</sup>	3.98	3.98	3.72 <sup>‡</sup>	3.92
Pre-dialysis serum creatinine (mg/dl)	9.5	8.7*	9.8 <sup>†</sup>	9.1	9.2	9.3
Pre-dialysis serum potassium (mEq/l)	5.0 <sup>‡</sup>	5.3	5.5 <sup>‡</sup>	5.5 <sup>†</sup>	5.0 <sup>‡</sup>	5.3
Pre-dialysis serum phosphorus (mg/dl)	5.3*	6.5 <sup>‡</sup>	5.0 <sup>‡</sup>	5.4	5.6	5.5
nPCR (g/kg/day)	1.12*	0.97*	1.14 <sup>†</sup>	1.09	1.03 <sup>†</sup>	1.09
Weight (kg)	63.6 <sup>†</sup>	69.7 <sup>‡</sup>	63.9 <sup>†</sup>	63.5 <sup>‡</sup>	68.1 <sup>†</sup>	65.6
IDWG (%)	3.9*	3.0 <sup>†</sup>	4.2 <sup>‡</sup>	3.2	2.8 <sup>‡</sup>	3.5
BMI (kg/m <sup>2</sup> )	23.2 <sup>†</sup>	24.5 <sup>†</sup>	23.5	23.9	24.2	23.8
mSGA score (%)						
Moderately malnourished	18.0	14.1	16.1	11.2*	15.4	15.1
Severely malnourished	4.5	2.6	2.3	3.2	6.5 <sup>†</sup>	3.8

Patients entering the study within 90 days of their first dialysis treatment were excluded from this analysis. In Germany, albumin commonly is measured using total protein and serum protein electrophoresis, which may overestimate albumin compared with the direct method. BUN, blood urea nitrogen; nPCR, normalized protein catabolic rate; IDWG, interdialytic weight gain; BMI, body mass index; mSGA, subjective global assessment, modified to adapt to available DOPPS data.

\* $P < 0.05$ ; <sup>†</sup> $P < 0.01$ ; <sup>‡</sup> $P < 0.0001$  vs All Euro-DOPPS, accounting for facility clustering.

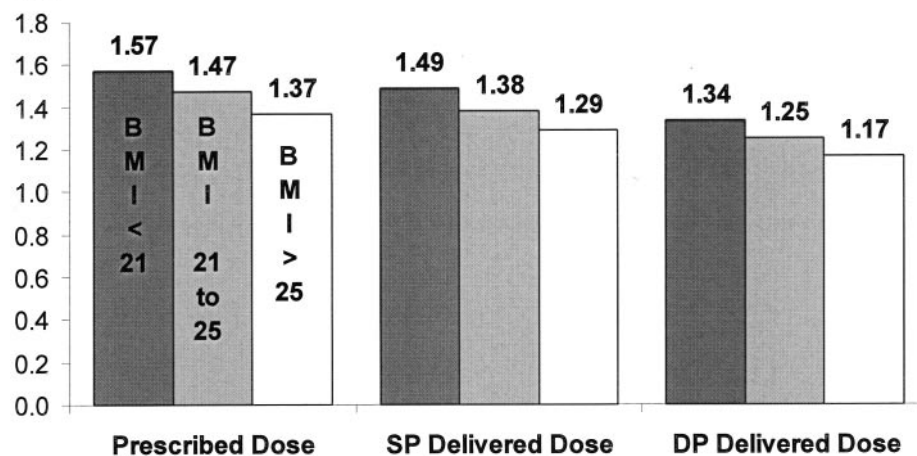
method relying on serum protein electrophoresis. Serum creatinine serves as a marker of muscle mass and dialysis dose, and its mean value ranged from 8.7 mg/dl (0.77 mmol/l) in Germany to 9.8 mg/dl (0.87 mmol/l) in Italy. The average BUN varied by country from 64.8 mg/dl to 75.7 mg/dl and showed little correlation to serum creatinine. Although BUN and creatinine both are dependent on dialysis dose, creatinine is probably a stronger indicator of muscle mass than of dialysis dose. The average nPCR was 1.09 g/kg, with lower values in Germany and the UK (0.97 and 1.03 g/kg, respectively) and relatively higher values in Italy and France (1.14 and 1.12 g/kg, respectively).

The average dialysis dose by BMI categories is presented in Figure 2. The relationships between BMI and prescribed Kt/V, single-pool Kt/V and double-pool Kt/V were similar, each showing that patients with the highest BMI received the lowest dialysis dose. The correlation between BMI and double-pool

Kt/V was modest, but statistically significant (generalized  $r = 0.3$ ,  $P = 0.0003$  after accounting for facility clustering) [13].

Considerable variation in monitoring nutrition was apparent across countries. Overall, 62% of Euro-DOPPS units did not measure nPCR, ranging from 20% of units in Spain to 90% in Germany (Table 5). Study coordinators also reported highly variable use of dietitians, ranging from 20% in Spain to 85% in the UK. These data were compared with reports from the patient questionnaire in which patients were asked if they had been counselled by a dietitian in the 6 months prior to study enrolment. Here again, wide variation was observed, spanning from 7% in Italy to 75% in the UK.

Finally, caloric oral supplements were prescribed for between 1 and 14% of patients, with the lowest percentages for Spanish and German patients (1 and 2%, respectively) and highest percentages for patients in the UK (14%).

**KtV\***

**Fig. 2.** Three measures of dialysis dose by patient body mass index. Patients entering the study within 90 days of their first dialysis treatment were excluded. BMI, body mass index. \*Adjusted for the time of the blood draw for post-dialysis BUN.

**Table 5.** Nutrition practices

Facility nutrition practices	Country					All Euro-DOPPS
	France	Germany	Italy	Spain	UK	
Sample size ( <i>n</i> , facilities)	20	21	20	20	20	101
Renal dietitian available (%)	50	29	25	20*	85 <sup>†</sup>	43
Patients reported having seen dietitian in past 6 months (%)	33	19 <sup>‡</sup>	7 <sup>‡</sup>	15 <sup>‡</sup>	75 <sup>‡</sup>	29
nPCR not measured (%)	80	90 <sup>†</sup>	60	20 <sup>‡</sup>	60	62
Oral supplements (%)	8	3*	8	6	19 <sup>‡</sup>	10

Practices are as reported by the study coordinators in the dialysis units. nPCR, normalized protein catabolic rate.

\* $P < 0.05$ ; <sup>†</sup> $P < 0.01$ ; <sup>‡</sup> $P < 0.0001$  vs All Euro-DOPPS.

## Discussion

### *Dialysis units in the Euro-DOPPS countries*

The haemodialysis units participating in Euro-DOPPS were randomly selected to be representative of the different types of haemodialysis units and geographic regions within each country, with the caveat that small units treating <25 chronic haemodialysis patients were excluded. The average facility size was nearly the same in all countries, after excluding centres with <25 prevalent patients. Since the random selection of facilities had been stratified by type of dialysis unit in order to be representative of all facilities in each country, the observed patterns of types of facilities reflect the distribution in each country.

### *Age*

Observed differences in the mean age of the prevalent sample suggest that several things may be occurring: variation in the selection of patients accepted for haemodialysis therapy, differential loss to transplantation and possibly differential mortality by age group. In the UK, the mean patient age was lower (57 years)

and the proportion of males higher (62%, Table 1). Efforts are still needed to distinguish to what extent the finding of a younger mean age in the UK may, in part, be a reflection of limited acceptance rates for the oldest patients, higher levels of peritoneal dialysis and a relatively high dialysis mortality rate (18.0% in 1999 as reported by the UK Renal Registry) [14]. Despite trends toward accepting older patients in the UK, the effects of prior preferential acceptance of younger patients persist in the age distributions of a current prevalent sample. An age increase of 4.2 years would be expected to be associated with a 10–20% higher mortality risk [15]. The age differences across the Euro-DOPPS countries are sufficiently large to account for substantial differences in mortality.

### *Dialysis prescription*

The dialysis dose, measured from pre- and post-dialysis urea or BUN or calculated according to Kt/V or eKt/V, showed variation by country. Since delivered dose was not measured in approximately one-quarter of German patients, 'prescribed' Kt/V was also used for comparisons across all five countries. Ranking of dose by country was similar for both

delivered and prescribed Kt/V. It is of interest, however, that dose was achieved by different means, including choice of dialyser (surface area, type of membrane and flux) and blood flow. Recent studies have demonstrated that use of high-flux synthetic membranes is associated with lower mortality risk at the same Kt/V [16]. Similarly, delivering the same dialysis dose by higher blood flow rates was associated with lower mortality [17]. This correlation has been observed consistently in Euro-DOPPS, as well as in US-DOPPS and Japan-DOPPS. Thus, a higher dose may be delivered through higher blood flow rates at no apparent disadvantage in terms of patient survival.

Mean treatment times varied across the Euro-DOPPS countries by 32 min, from 249 min per session in France to 217 min in Spain (Table 2). Previous studies show contradictory results for treatment time and mortality risk at the same Kt/V [18,19].

The HEMO study did not show a reduction in mortality risk with high dialysis doses or high flux in a randomized design [20]. The confidence intervals of these negative findings agree with the null hypothesis of no effect and also agree with the prior findings of some benefit with higher dose and high flux. The HEMO study did not evaluate low dose ( $< \text{Kt/V } 1.2$ ). Therefore, the findings that 30% of Euro-DOPPS patients receive doses of  $< 1.2 \text{ Kt/V}$  appear of serious concern, as they are likely to be associated with increased risk of mortality.

The finding of a lower dialysis dose for patients with higher BMI confirms similar results from the USA [5,21]. It indicates that dialysis dose is prescribed with only partial consideration of patient size. This finding suggests that prescription by time is more common than by a target Kt/V. Since studies have clearly shown lower mortality risk with larger BMI and higher dialysis dose [5,22,23], greater consideration of body size for dialysis prescription and greater focus on improved nutrition appear advisable. Previous DOPPS findings have shown that during the same study period, body weights increased while average blood flow rates decreased, suggesting that patient nutritional status is improving with time but is not accompanied by a corresponding increase in the dialysis prescription [24].

#### *Measures of adherence and nutritional status*

Measures of adherence with the dialysis schedule show that shortening dialysis treatment occurred among 9% of patients (Table 3). Skipping dialysis sessions was very rare, and both types of poor adherence were recorded less frequently in Euro-DOPPS than in the USA [7]. Adherence to dietary restrictions was only indirectly measured by the incidence of high levels of potassium, phosphorus and fluid intake, as these are also modified by adjustments to aspects of dialysis treatment such as treatment time, dialysis membrane and dialysate composition. Furthermore, the potassium content of the normal diet in each country will also influence the value of hyperkalaemia as a measure of

dietary adherence. As factors such as hyperkalaemia, large IDWG and hyperphosphataemia ( $> 6.5 \text{ mg/dl}$ ,  $2.1 \text{ mmol/l}$ ) are associated with mortality risk [7,25], further analysis by country, facility, regional diet and practice pattern are needed to identify ways to reduce the frequency of these problems. Furthermore, although a large IDWG is associated with higher mortality risk, the possibility still requiring further investigation is to examine for certain haemodialysis patients whether a moderate IDWG serves as a positive marker of nutritional intake rather than lack of adherence. For example, is a diet that maintains a good nutritional status associated with higher intake of liquids and, consequently, moderate IDWG?

Nutritional management appears to vary substantially among the Euro-DOPPS countries, when looking by country at such elements as the mSGA, nPCR, BMI and input from a dietitian. The DOPPS has already evaluated in detail the association between a low BMI and increased mortality risk in haemodialysis patients [8,11]. Since nutritional status is quite strongly associated with mortality risk [8,11], further study is needed to evaluate best practices, including the role of advice from dietitians and the use of dietary supplementation, which are shown to vary widely [26]. The reported association of dialysis dose with dietary protein intake [27] and patient albumin levels [28] also deserves further study.

Possible limitations of this study include noise due to use of different laboratories and potential misclassification or underascertainment of co-morbid conditions. Non-significant findings may suffer from noise and possible misclassification. However, significant findings might be more striking if there was less noise or less misclassification.

This study and two companion papers reviewing mortality and anaemia in the Euro-DOPPS countries [29,30] seek to present a comprehensive overview of the haemodialysis and anaemia practices and outcomes for the European study population. In the present study, the DOPPS provides international comparisons of haemodialysis therapy, adherence and nutrition among five large European countries with new descriptive information on differences in patient management. These data also indicate opportunities for improvements in patient care, through avoidance of low prescribed dialysis dose, counselling for better adherence and effective dietary instruction. Since dialysis dose, adherence and nutritional status have been associated with mortality, these DOPPS results provide an important base of information for promoting changes in haemodialysis practices that will probably lead to improvements in patient outcomes.

*Acknowledgements.* The Phase I Euro-DOPPS country investigators were: Bernard Canaud, MD and Christian Combe, MD (France); Jürgen Bommer, MD and Erwin Hecking, MD (Germany); Vittorio Andreucci, MD and Francesco Locatelli, MD (Italy); Luis Piera, MD and Fernando Valderrábano, MD (Spain); Roger Greenwood, MSc, MD and Hugh C. Rayner, MD

(UK). The work of the staff members at the 101 Euro-DOPPS units is gratefully acknowledged. DOPPS investigators from the USA include: Philip J. Held, PhD, Friedrich K. Port, MD, MS, Eric W. Young, MD, MS, Robert A. Wolfe, PhD, Donna L. Mapes, DNSc, Marcia L. Keen, PhD, David A. Goodkin, MD, Kenneth Chen, MD, and Bradley J. Maroni, MD. The DOPPS is supported by an unrestricted grant from Kirin-Amgen, Inc.

*Conflict of interest statement.* None declared.

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*Received for publication: 31.12.02*

*Accepted in revised form: 26.6.03*