e.g. when we assess acute kidney injury (AKI) in a cohort of patients before and after elective surgery or procedure. The concept still holds when serum creatinine is measured at any previous time point (optimally by the same assay), assuming that the condition of the patient was stable at the time of sampling and has not substantially changed until the period of interest. However, quite often a patient may present to medical attention without any prior measurement of serum creatinine. In such a case, we must decide whether to use some other value to approximate the baseline (such as creatinine on admission, creatinine on discharge or a nadir creatinine), or to make the best possible estimate based on statistical inferences from the characteristics of the population from which the patient comes. We agree with Pickering and Endre [1], who suggest determining the baseline creatinine by a reproducible process of thoughtful assessment and selection of the most appropriate value from available creatinines, and we agree a prior measurement will almost always be superior to any estimated value. However, we believe that the specific approach to deriving a baseline creatinine should also depend on the specific use of RIFLE criteria. When AKI is an endpoint for a clinical trial or for a biomarker validation study, it is quite reasonable to adjudicate cases on the basis of all the available data (e.g. values and patterns of serum creatinine over time). In an individual case, the most reasonable estimate of baseline creatinine could well be a convalescent value obtained after discharge. However, when AKI is being used as an enrolment criterion or is being diagnosed for clinical management, we do not have the luxury of waiting for multiple creatinines. In such circumstances, it will be necessary to make the best estimate given what data are available. We should bear in mind that as much as 30% of the variability of serum creatinine can be explained from demographic and anthropometric variables [2] (such as age, gender, race, weight and height), so, in fact, our estimate will be better if we use them. The most common formula [i.e. back-calculating with modification of diet in renal disease (MDRD)] ascribes the same glomerular filtration rate to all patients irrespective of age, gender and race, and while it is clear that this approach cannot be ‘quite right’, no substitute has been yet shown to perform significantly better. The adjudicated hierarchical approach suggested by Pickering and Endre corresponds to the rational clinical reasoning, obviates the need for inter-laboratory calibration efforts (it would mostly compare sequential creatinine values measured in one lab) and its bias may be more easily predicted and analysed. However, it is probably best suited for clinical trials, where AKI can be adjudicated after the fact. We recommend that all studies using RIFLE/AKI criteria should report how baseline creatinine was ascertained. Furthermore, clinicians and researchers alike should recognize that estimating baseline creatinine using the MDRD equation is prone to considerable bias particularly for RIFLE-Risk [3] and to gauge their clinical and scientific decision making accordingly.

Conflict of interest statement. None declared.

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Advance Access publication 17 March 2011

Phosphate binders in a European haemodialysis population

Sir,

We have read with great interest the article authored by Floege et al. [1]. They have reported the result of a study conducted by the Analysing Data, Recognising Excellence and Optimising Outcomes (ARO) investigators on a randomly selected population of 7970 patients from 11 countries who underwent haemodialysis (HD) treatment between January 2005 and December 2006 at a European Fresenius Medical Care dialysis facility. The main finding was a U-shaped pattern of the adjusted relative risk of mortality that was obtained as a result of both baseline and time-dependent analyses of serum intact parathyroid hormone and phosphate levels. A phosphate level of >1.78 mmol/L or <1.13 mmol/L was associated with a significant increase in the relative risk of death. These results reinforce most observational studies reported previously [2,3]. Surprisingly, they also reported the absence of phosphate binder (PB) medication in >50% of cases (baseline analysis), which resulted in a mean serum phosphate level of 1.5 ± 0.4 mmol/L. This is in contrast to the data reported by the dialysis outcomes and practice pattern study wherein 90.2% HD patients were under PB medication [2]. The observation of Floege et al. is in agreement with our results with the Tassin population that was under a long dialysis schedule (3 × 5 to 3 × 8 h weekly) and a large protein intake (1.23 ± 0.3 g/kg/J), achieving a mean serum phosphate level of 1.4 ± 0.4 mmol/L with only 50% of the patients taking PB [4]. However, Floege et al. reported no data on the dialysis schedule and dietary phosphate intake that can help explain
these unexpected results. We are also questioning about differences in the PB medication among the 11 participating countries.

After investigating the reasons for the very low numbers of PB prescription, we strongly suggest a separate analysis of the patients on the basis of the PB medications and the serum phosphate level to understand the association of these parameters with the outcomes. Apart from some particular dialysis schedule including long and/or daily strategies, phosphataemia remains an important marker of nutrition in cases of conventional HD. The use of PBs could be associated with a better outcome when associated with a higher protein intake, but this remains a speculation.

We encourage the ARO investigators to provide more observational data from European countries to improve our understanding of the association between mineral metabolism disorders, their treatments and outcomes.

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In our population, we observed a significant interaction between phosphate level, phosphate binder use and mortality (P = 0.02). As can be seen in Table 1, this interaction is being driven by the lack of an association between low phosphate levels and mortality in those treated with a phosphate binder compared to those untreated.

In principle, this observation is consistent with the data of Isakova et al. [1], who noted a reduced mortality in haemodialysis patients treated with a phosphate binder. However, in that study, most of the benefit was observed in patients with high phosphate levels, whereas in our study patients treated to low phosphate levels appeared to benefit most from a phosphate binder.

**Conflict of interest statement.** None declared.

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**Is there a link between thrombotic thrombocytopenic purpura and anti-glomerular basement membrane disease?**

Sir,
We read with interest the article by Torok et al. [1]. They reported a 43-year-old Caucasian male who had developed thrombotic thrombocytopenic purpura (TTP) followed by anti-glomerular basement membrane (anti-GBM) disease.

Table 1. Association between phosphate levels and mortality in the ARO population according to whether or not a participant is taking a phosphate binder at baseline

<table>
<thead>
<tr>
<th>Phosphate (mmol/L)</th>
<th>Not taking phosphate binders</th>
<th>Taking phosphate binders</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1.13</td>
<td>1.29 (1.08–1.55)</td>
<td>1.00 (0.75–1.34)</td>
</tr>
<tr>
<td>1.13–1.78</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>&gt;1.78</td>
<td>1.32 (1.07–1.64)</td>
<td>1.33 (1.04–1.71)</td>
</tr>
</tbody>
</table>

*Adjusted for demographics (age, gender, country, body mass indexBMI, smoking status), medical history (chronic kidney disease aetiology, history of diabetes, history of cardiovascular disease (CVD), history of Cancer), dialysis parameters (vintage, vascular access type, Kt/V, blood flow), markers of inflammation (serum albumin, C-reactive protein), CVD medications (anti-hypertensive drugs, ACE inhibitors, oral anticoagulants, anti-aggregants), vitamin D use and other lab parameters (PTH, calcium, haemoglobinHb, ferritin, cholesterol, blood leucocytes) and miscellaneous (hospitalization, change in vascular access type).

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**Reply**

Jean and Vanel raise some interesting questions about the management of dialysis patients in Europe and the association between phosphorous and mortality, especially when considering the use of phosphate binders. In the ARO population, the majority of patients (>80% in all countries) have three dialysis sessions per week, with the median duration of each session being 4 h. Unfortunately, ARO does not contain data allowing us to estimate dietary phosphate intake. We cannot fully exclude underreporting of phosphate binder use in some countries. Moreover, dosing equivalence between different phosphate binders used in this cohort, which is really difficult to establish, prevented us from looking at a dose-dependent effect. However, we found no relationship between the prevalence of phosphate binder use and phosphate levels at baseline.