While it is not possible to conclude from this report that the incidence of FSGS in the Scottish population is not increasing as this is not a longitudinal study, it does support the finding that FSGS is not the commonest cause of nephrotic syndrome in northern European populations, and that membranous nephropathy remains the dominant histological finding.

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Quantifying the discontinuity of haemodialysis dose with time-averaged concentration (TAC) and time-averaged deviation (TAD)

It is with great interest that we have read the analysis of Daugirdas et al. on the effects of spacing of discontinuous haemodialysis on weekly dose of dialysis [1]. The authors showed that (contrary to other measures) the change in maximum concentration (‘peak’) associated with intermittent dialysis and attained at the end of the long dialysis interval best captured the increase in the weekly dose, especially when changing from ill- to well-spaced treatments.

Long before the introduction of equivalent renal clearance [2] and so-called standard Kt/V [3], Lopot et al. compared different modes of dialysis by computing the time-averaged deviation (TAD) and plotted this measure against the time-averaged concentration (TAC) of urea [4,5]. For $c(t)$, representing the time-dependent urea nitrogen concentration (in millimole per litre), and $T$, representing the duration of 1 week (10 080 min), TAC and TAD are given as

$$TAC = \frac{1}{T} \int_0^T c(t) \, dt,$$

and

$$TAD = \frac{1}{T} \int_0^T |c(t)−TAC| \, dt,$$

respectively.

Both $TAC$ and $TAD$ are obtained in units of concentration (millimole per litre).

We would like to show that such an analysis is useful to present results reported in [1].

Repeating the model calculations for the treatment modes (A, B, C and D) described in [1], we computed TAC and TAD (Table 1), and plotted TAD against TAC (Figure 1). In this representation, the standard mode A characterized by three well-spaced treatments per week is located in the range covered by the rectangle indicating normal haemodialysis, as specified in [5]. A change in duration, frequency, or spacing of treatments represents a new state and the transition to a new location in the TAC/TAD plot. For example, doubling the frequency (mode C) reduces both TAC as well as TAD and causes a diagonal transition from A to C. The gain in weekly clearance computed from $G/peak$, where $G$ is the urea generation rate, is +18% (Table 2). The ill-spaced schedule causes an increase in both TAC and TAD (mode B), and most importantly, a loss in weekly clearance by −27%

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**Table 1.** Weekly Kt/V computed from different reference concentrations (TAC, meanpre, peak, TAC + TAD) for treatment modes (A to D) normalized for $G$, $T$ and $T$, as described in [1]

<table>
<thead>
<tr>
<th>Transition</th>
<th>TAC</th>
<th>Meanpre</th>
<th>Peak</th>
<th>TAC + TAD</th>
</tr>
</thead>
<tbody>
<tr>
<td>A→B</td>
<td>16.9%</td>
<td>31.1%</td>
<td>−27.1%</td>
<td>−25.9%</td>
</tr>
<tr>
<td>A→C</td>
<td>9.1%</td>
<td>28.8%</td>
<td>18.0%</td>
<td>18.2%</td>
</tr>
<tr>
<td>A→D</td>
<td>93.4%</td>
<td>98.9%</td>
<td>55.4%</td>
<td>88.4%</td>
</tr>
<tr>
<td>C→D</td>
<td>77.2%</td>
<td>54.5%</td>
<td>31.7%</td>
<td>59.4%</td>
</tr>
</tbody>
</table>

*Transition described in [1].

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**Table 2.** Percentage of gain or loss in weekly Kt/V (Table 1) computed from different reference concentrations (TAC, meanpre, peak and TAC + TAD) for transitions between different treatment modes (A to D)

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**Fig. 1.** Location of treatment modes (A to D) varying by duration, frequency and spacing of treatments in the ‘Lopot-plot’ (the rectangle represents the range of standard haemodialysis prescription, and the arrows and numbers represent the transitions and the gain (and loss) in weekly Kt/V as derived from $G/peak$).
(Table 2). Interestingly, the transition from a well- to an ill-spaced treatment mode also follows the diagonal in the TAD/TAC plot. The effects of spacing and frequency appear to be related. Mode D may be reached from A by doubling the treatment frequency, or from C by doubling the treatment time.

TAD is a measure of treatment discontinuity, decreasing with increased treatment frequency and improved spacing of treatments. Such information could be useful to correct for effects observed with intermittent treatment modes. The weekly Kt/V computed from the sum of TAC and TAD, as G/(TAC + TAD), was smaller than that calculated from TAC alone (because TAD was always larger than zero) but larger than that calculated from ‘meanpre’ (G/meanpre) as suggested by Gotch [3], with the important exception of the ill-spaced treatment mode B (Table 1). When investigating the gains or losses for transitions between modes, the new reference concentration G/(TAC + TAD) performed well compared to that proposed in [1] as it captured the reduction in dose anticipated for ill-spaced treatment modes (A→B, Table 2). It also exhibited increased sensitivity for transitions A→D and C→D.

In summary, treatment modes, including those examined in [1], appear to be well characterized by their location in the ‘Lopot-plot’, with characteristic effects on TAD which therefore could be used to compute an improved weekly Kt/V.

Conflict of interest statement. None declared.

1. Daugirdas JT Tattersall J. Effect of treatment spacing and frequency on three measures of equivalent clearance, including standard Kt/V. Nephrol Dial Transplant 2009; doi: 10.1093/ndt/gfp446

doi: 10.1093/ndt/gfp656

To the editors,

Korohoda et al describe the effects of haemodialysis spacing and frequency on an equivalent clearance defined as G/(TAC + TAD) • 10 080/V [1]. This is based on the time-averaged deviation concept of Lopot et al [2] and incorporates both the time-averaged concentration of urea during the week as well as its deviation from the average value. Korohoda et al conclude that, in terms of ‘gain’ with optimal treatment spacing, the G/(TAC + TAD) equivalent clearance performs better than stdKt/V in that it does penalize for poorly spaced treatments, while stdKt/V does not. In this respect, Lopot's G/(TAC+TAD) clearance provides similar results to G/peak as described in our paper [3]. The G/(TAC+TAD) clearance shows a gain similar to that with stdKt/V on moving from 3 to 6 treatments per week. The gain was somewhat greater than with G/peak.

We believe this is an important contribution and it shows that we may not yet know which is the best equivalent urea clearance to use (though these analyses suggest that perhaps we should consider using G/(TAC+TAD) or G/peak rather than stdKt/V). Further work that might be useful would be a comparison of how these candidate equivalent urea clearances differentially track removal of other important uraemic toxins such as phosphate when using various dialysis schedules and treatment spacings. Not including Lopot's time-averaged deviation concept in the original analysis [3] was an oversight on our part. Korohoda et al now have corrected this important omission.

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3. Daugirdas JT, Tattersall J. Effect of treatment spacing and frequency on three measures of equivalent clearance, including standard Kt/V. Nephrol Dial Transplant 2009; doi: 10.1093/ndt/gfp676

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