ONLINE SUPPLEMENTARY MATERIAL

STEPS IN THE INTERVENTIONS SIMULATIONS

The figure below summarizes the steps in the simulations used to calculate the intervention effects. The steps were run 1,000 times for each intervention.

Randomly choose one imputed dataset

"Pre-intervention"

- Draw non-parametric bootstrap sample

Run adjusted Fine & Gray model for outcomes

"Post-intervention"

- Simulate intervention effects as in Table 1

Predict cumulative incidence of each outcome at 5 years after PD initiation for each patient using pre-intervention variable values

Calculate median cumulative incidence over all patients (CPPreAll)

Predict cumulative incidence of each outcome at 5 years after PD initiation for each patient using post-intervention variable values

Calculate median cumulative incidence over all patients (CPPostAll)

Calculate "average treatment effect" of the intervention (ATE = CP(PostAll) - CP(PreAll))

Calculate 95% central prediction interval as 1st and 3rd quartiles of ATE
FRAMEWORK FOR INTERVENTIONS SIMULATIONS

In this section, we present the assumptions about variable relationships we made in developing the model for volume-outcome associations in peritoneal dialysis. We assume readers are familiar with directed acyclic graphs (DAGs). Excellent introductions to DAGS in epidemiology can be found elsewhere.\(^1\)–\(^3\)

Effect of the volume exposure variable

Like others, we assumed that volume does not directly change patient outcomes itself but that its effects are, rather, mediated by factors such as team experience and financial resources available for peritoneal dialysis in a centre.\(^4\)–\(^7\) This is shown in the DAG in Figure 1, where volume in one time period changes experience and resources in the next time period (black arrows). In volume-outcome research in other areas, experience and resources in one time period may also change volume in the next time period (grey arrows in Figure 1). This would occur if a centre with better performing teams and better financing for peritoneal dialysis attracted new patients in greater numbers.\(^8\) We assumed that this is not an important factor in the French health system.

A patient starting peritoneal dialysis in a centre in a given time period is therefore exposed to experience and resource levels which are jointly determined by the volume, experience, and resources in the preceding period. As centre volumes were fairly constant over time in our dataset, we worked on the basis that centres with the same volume had the same experience and resource levels in any given time period, conditional on other potentially relevant covariables (e.g. type of centre) which are not shown in Figures 1 and 2 for simplicity. We therefore handled volume as a time-invariant variable in the analysis.\(^1\)

\(^1\) We note, however, that our measure of centre volume is relevant even if volume were a time-varying variable in our dataset. It is a useful decision tool for patients choosing a centre at the moment of peritoneal dialysis initiation under a
**Interaction between volume, resources, and experience**

We considered an underlying causal mechanism involving an interaction between volume, resources, and experience to be likely. In this, we assumed that:

- any beneficial effect of high volumes would only be realized in the presence of sufficient experience and resources;
- high volumes with low experience and resources would likely have a negative impact on patient outcomes; and
- the effect of low volumes with high experience and/or resources was unclear.

Under this approach, volume, experience, and resources can be thought of as components in the sufficient-component-cause framework standard in epidemiology\(^9\) and so presented in a sufficient-component-cause DAG as proposed by Vanderweele and Robins\(^10\) (Figure 2). The +, −, and ± signs show an anticipated direction of effect which is positive, negative, and uncertain respectively. Note that we only show the DAG for the outcome of transfer to haemodialysis.

We estimated the volume-outcome effects using observational data in a system which we assume to be stable, as explained above. This meant that the level of experience was at the expected level for each centre’s volume, i.e. only the VE path in Figure 2 was represented in the data. Similarly, we assumed that funding was mostly adequate for each centre’s volume (which seemed reasonable in the French system), i.e. only the VR path in Figure 2 was represented in the data. We therefore considered that the only paths estimable from our system where centre volumes after initiation follow the same pattern as those in the dataset analyzed. Further, it is a relevant measure for predicting the effects of interventions to change centre volumes providing that the same condition applies (i.e. the centre volumes after the intervention time follow the same pattern as those of the corresponding volume centre in the dataset).
dataset were those shown in Figure 3. Of course, an intervention to change centre volume without changing experience and resources would activate the other paths but we do not consider it possible to estimate these paths from this (and perhaps most) observational dataset.

**A priori confounders of the volume-outcome effect**

The DAG in Figure 4 shows the relationships between variables which we considered likely *a priori* and the DAG in Figure 5 the unblocked paths after adjustment on the confounders based on Figure 4. We note that, based on these assumed relationships, additionally adjusting on nephropathy may have improved the adjustment for the unmeasured variable *major concurrent illnesses*; however, as we were concerned about sparse cells in the regression model, we did not do include nephropathy as a covariable. Figure 5 also shows the open confounding path through unmeasured variables, the importance of which we explored in the sensitivity analysis.

**Interventions to change centre volume**

Figures 6 and 7 are a graphical representation of the assumptions underlying the four interventions explored in the article. For clarity, we have removed most of the covariables shown in the previous DAG.

Figure 6 represents the patient-diversion interventions #1, #2, and #3 in the main article which would close small centres and divert patients to larger centres. For all three interventions, the figure shows the core assumption that the intervention changes the distribution of centre volume (as defined in Table 1 in the main article). We assume that resources provided to the centres are adequate for their post-intervention volumes. Figure 6 also shows that these patient-diversion interventions may have the additional effects of changing the type of centre
in which patients initiated peritoneal dialysis, as explored in intervention #3, as well as changing patients’ travel time to the centres which may affect outcomes (discussed in the main article and below).

Figure 7 represents intervention #4 in which a larger proportion of patients initiate peritoneal dialysis in existing centres. As patients would stay in their existing centres, arrows indicating a change in type of centre and a change in travel time have been removed. We still assume that centres will receive adequate resources for their post-intervention patient volumes.

**The possibility of estimating the impact of travel time**

A potentially important pathway in interventions 1, 2, and 3 is the impact of travel time on technique failure. We argue that this path would plausibly have a negative impact on technique failure. It may be possible to estimate an association between travel time and technique failure in datasets where patients’ addresses and their treating centres are geocoded in a geographic information system (GIS). However, we are not convinced that this effect can be reliably estimated from observational data produced from a relatively stable system in which patients have the possibility of being treated near their homes, as in France. Under such a system, those patients travelling further for peritoneal dialysis probably choose to do so and therefore plausibly differ from those who seek care locally, with little reason to expect the impact of travel time on technique failure to be the same for these different patient groups. We note that this is a different situation from countries, such as Australia and Canada, where some patients live far from the nearest dialysis service. This may allow a better estimation of any distance-outcome association, but these cases pose well-known, additional challenges such as confounding by socioeconomic and cultural factors.
**Meaning of the above assumptions for interpreting the intervention results**

The above considerations imply that the simulation results apply to health systems in which i. centre volumes stabilize after the initial change induced by the intervention, ii. sufficient time passes to allow centres to acquire appropriate experience, and iii. appropriate resources are provided to centres.


Figure 1: Directed acyclic graph showing assumed relationships between centre volume, resources, and experience.
Figure 2: Sufficient-causation directed acyclic graph showing assumed relationship between centre volume, resources, and experience with transfer to haemodialysis.
Figure 3: Sufficient-causation directed acyclic graph showing the paths estimable from the observational dataset used in the article.
Figure 4: Directed acyclic graph showing assumed relationships between centre volume, transfer to haemodialysis, and other variables.
Figure 5: Directed ayclic graph after conditioning on variables

- Centre volume
- U: unmeasured variables
- Type of peritoneal dialysis
- Transfer to HD
- Peritoneal dialysis vs. haemodialysis
- Diabetes
- U: Major concurrent illnesses
- U: Frailty
- Comorbidity index
- Centre type
- Sex
- Type of assistance
- Nephropathy
- Previous treatment
Figure 6: Sufficient-causation directed acyclic graph for the patient-diversion interventions

**Intervention:**
Close small centres

- Volume at PD initiation
- U: Resources for PD

- Transfer to haemodialysis

- Centre type
- VR
- VnotR

U: Change in travel time
Figure 7: Sufficient-causation directed acyclic graph for the prioritise-peritoneal-dialysis intervention

**Intervention:**
Increase patients starting PD in centres

- Volume at PD initiation
- U: Resources for PD

Centre type

- Transfer to haemodialysis

U: Change in travel time
UNADJUSTED AND ADJUSTED CAUSE-SPECIFIC HAZARD RATIOS AT 30 DAYS, ONE YEAR, AND FIVE YEARS OF FOLLOW UP

As noted in the main text, we estimated the cs-HRs of each centre-volume group for each outcome at 30 days and one year of follow up in addition to 5 years of follow up after initiation of peritoneal dialysis. This aimed to examine the association of “early” technique failure and to explore any effect from depletion of susceptibles. The results are in the figure below. Note that the model for transplantation did not converge at 30 days’ follow up owing to very few events at this time.
UNADJUSTED AND ADJUSTED SUBDISTRIBUTION HAZARD RATIOS AT FIVE YEARS OF FOLLOW UP

Unadjusted estimates

Adjusted estimates

Transfer to haemodialysis

Death

Hazard ratio

Centre volume (median patients per day)
Transplantation

Hazard ratio

Centre volume (median patients per day)

Transplantation

Hazard ratio

Centre volume (median patients per day)
# Adjusted Hazard Ratios at Five Years of Follow Up in Complete-Case and Imputed-Dataset Analyses

<table>
<thead>
<tr>
<th>Centre volume</th>
<th>0 to 10</th>
<th>11 to 20</th>
<th>21 to 30</th>
<th>31 to 40</th>
<th>41 to 50</th>
<th>51 to 60</th>
<th>&gt;60</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Complete case</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Technique failure</strong></td>
<td>cs-HR (95%CI)</td>
<td>ref.</td>
<td>0.82 (0.69 to 0.99)</td>
<td>0.78 (0.63 to 0.97)</td>
<td>0.58 (0.45 to 0.75)</td>
<td>0.57 (0.41 to 0.79)</td>
<td>0.40 (0.26 to 0.64)</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>cs-HR (95%CI)</td>
<td>ref.</td>
<td>0.96 (0.80 to 1.16)</td>
<td>1.05 (0.87 to 1.27)</td>
<td>1.05 (0.85 to 1.30)</td>
<td>1.06 (0.84 to 1.34)</td>
<td>0.96 (0.73 to 1.27)</td>
</tr>
<tr>
<td><strong>Transplantation</strong></td>
<td>cs-HR (95%CI)</td>
<td>ref.</td>
<td>0.92 (0.71 to 1.20)</td>
<td>0.77 (0.59 to 1.00)</td>
<td>0.79 (0.61 to 1.02)</td>
<td>0.91 (0.61 to 1.35)</td>
<td>1.00 (0.69 to 1.44)</td>
</tr>
<tr>
<td><strong>Imputed datasets</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Technique failure</strong></td>
<td>cs-HR (95%CI)</td>
<td>ref.</td>
<td>0.77 (0.65 to 0.90)</td>
<td>0.70 (0.57 to 0.87)</td>
<td>0.55 (0.43 to 0.69)</td>
<td>0.54 (0.40 to 0.73)</td>
<td>0.37 (0.26 to 0.53)</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>cs-HR (95%CI)</td>
<td>ref.</td>
<td>1.00 (0.87 to 1.14)</td>
<td>1.06 (0.91 to 1.24)</td>
<td>1.05 (0.88 to 1.25)</td>
<td>0.99 (0.80 to 1.23)</td>
<td>0.98 (0.80 to 1.19)</td>
</tr>
<tr>
<td><strong>Transplantation</strong></td>
<td>cs-HR (95%CI)</td>
<td>ref.</td>
<td>1.00 (0.80 to 1.27)</td>
<td>0.80 (0.63 to 1.01)</td>
<td>0.80 (0.62 to 1.02)</td>
<td>0.92 (0.63 to 1.34)</td>
<td>0.99 (0.71 to 1.40)</td>
</tr>
<tr>
<td><strong>Complete case</strong></td>
<td>sd-HR (95%CI)</td>
<td>ref.</td>
<td>0.75 (0.63 to 0.90)</td>
<td>0.72 (0.58 to 0.91)</td>
<td>0.56 (0.45 to 0.71)</td>
<td>0.55 (0.41 to 0.75)</td>
<td>0.39 (0.28 to 0.53)</td>
</tr>
<tr>
<td><strong>Technique failure</strong></td>
<td>sd-HR (95%CI)</td>
<td>ref.</td>
<td>1.07 (0.92 to 1.25)</td>
<td>1.17 (0.99 to 1.39)</td>
<td>1.14 (0.94 to 1.38)</td>
<td>1.17 (0.95 to 1.44)</td>
<td>1.16 (0.95 to 1.41)</td>
</tr>
<tr>
<td><strong>Death</strong></td>
<td>sd-HR (95%CI)</td>
<td>ref.</td>
<td>1.18 (0.89 to 1.57)</td>
<td>1.00 (0.75 to 1.33)</td>
<td>1.05 (0.77 to 1.42)</td>
<td>1.14 (0.76 to 1.70)</td>
<td>1.30 (0.89 to 1.91)</td>
</tr>
<tr>
<td><strong>Transplantation</strong></td>
<td>sd-HR (95%CI)</td>
<td>ref.</td>
<td>1.24 (0.95 to 1.62)</td>
<td>1.10 (0.84 to 1.43)</td>
<td>1.21 (0.90 to 1.62)</td>
<td>1.26 (0.87 to 1.82)</td>
<td>1.44 (1.04 to 2.00)</td>
</tr>
</tbody>
</table>

*cs-HR, cause-specific hazard ratio; 95%CI, 95% confidence interval*