Introduction:
A major clinical goal in peritoneal dialysis (PD) is delaying technique failure, which occurs when patients require permanent transfer to hemodialysis.

Studies have reported a lower risk of technique failure in centers treating more PD patients, leading to recommendations for minimum patient volumes.

However, these studies have not explored robustness to residual confounding or the impact of interventions to increase patient exposure to high-volume centres, making policy prescriptions premature.

We explored the robustness to residual confounding and estimated plausible effects of policies to change centre volumes using data from a French PD registry.

Methods:
Data source:
- Registre de Dialyse Péritonéale de Langue Française (80% coverage).

Population analyzed:
- Adult patients initiating PD between 1/1/2000 and 31/12/2009, followed-up until 1/1/2010 in metropolitan France (public and association centres only).

Variables:
- Centre volume as median number of patients on PD per day over the 12 months prior to initiating PD.
- Outcomes of time to death, technique failure, renal transplantation.
- Potential confounders of age, sex, Charlson comorbidity index (minus age score), diabetes, previous haemodialysis or transplantation, type of assistance, and type of centre.

Statistical analysis:
- Multiple imputation by chained equations of missing variables.
- Calculation of adjusted cause-specific hazard ratios (cs-HRs) and sub-distribution hazard ratios (sd-HRs) with robust-variance Cox and Fine & Gray regression models, respectively.
- Probabilistic analysis of sensitivity to residual confounding by:
  - extracting centre random effect from mixed-effects Cox model;
  - imputing confounder by \( \hat{Y} = \exp(\beta X^T + \beta X_T) \) with \( \hat{V}_{w,c} \) and \( \hat{R}_{w,c} \) as volume and random effect after normalization and standardization;
  - re-estimating the adjusted Cox regression model including \( B \); and
  - calculating cs-HR and 95%CI from the median regression coefficient and median standard deviation over 1,000 runs under scenarios of low \((R_1-R_0<0.5)\), mid \((R_1-R_0=1.0)\), and high \((R_1-R_0>2.0)\) confounding.
- Estimation of impact of intervention to change centre volumes by:
  - postulating probability distributions for changes in patients’ exposure to centre volume for different interventions (table 1);
  - predicting outcome cumulative incidences at 5 years after PD initiation from the Fine & Gray models (pre-intervention);
  - drawing a new volume from the distributions and predicting cumulative incidences using this new value (post-intervention); and
  - calculating the difference in pre- and post-intervention cumulative incidences over 1,000 simulation runs and reporting the median difference with 95% central prediction intervals.

Conclusion:
Patients initiating PD in high-volume centres had a reduced risk (cs-HR) and cumulative incidence (sd-HR) of technique failure. This reduced risk (cs-HR) was robust to scenarios of residual strong confounding, suggesting that it may be a causal effect.

Patients in high-volume centres had no change in risk (cs-HR) for transplantation and death but had an increased cumulative incidence (sd-HR) of these outcomes in higher-volume centres. This was simply the result of the longer time spent on PD in these centres, where the risk (cs-HR) of technique failure was lower.

Hypothetically intervening to shift patients to high-volume centres only modestly reduced the cumulative incidence of technique failure. The largest benefit was from intervention 1, which induced a large change in volume exposures and so would probably be unrealistic in a real-world setting.

These findings raise questions about the relevance of the highly protective cs-HRs found in this and previous studies for health-services policy. It may be more fruitful to pursue other interventions to reduce technique failure.

Table 1 Hypothetical interventions to change patients’ exposure to centre volume

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Description</th>
<th>Change in cumulative incidence</th>
<th>Difference</th>
<th>95% central interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intervention #1</td>
<td>Close centres and divert patients to existing centres</td>
<td>-0.002</td>
<td>-0.006 to 0.002</td>
<td></td>
</tr>
<tr>
<td>Intervention #2</td>
<td>Close centres and divert patients to existing centres</td>
<td>-0.001</td>
<td>-0.007 to 0.005</td>
<td></td>
</tr>
<tr>
<td>Intervention #3</td>
<td>Close centres and divert patients to new larger centres</td>
<td>-0.002</td>
<td>-0.009 to 0.005</td>
<td></td>
</tr>
<tr>
<td>Intervention #4</td>
<td>Increase patients initiating PD in smaller centres without closing centres</td>
<td>-0.009</td>
<td>-0.010 to 0.009</td>
<td></td>
</tr>
</tbody>
</table>

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