Addressing treatment implementation bias in the construction of high dimensional propensity score

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### Background
- Formally, covariate for propensity score (PS) construction are assessed before treatment onset.
- However differences occurring in patient journeys after the decision to treat and before the treatment onset may bias the score (e.g. pre-chemotherapy assessment)

### Objectives
To address treatment implementation bias induced by differential patient journeys between the decision to treat and the treatment initiation.

### Methods
- **Study design**
  - Comparative effectiveness study to compare 1st-line advanced cancer treatments
  - **Intravenous agent**
  - **Oral treatment**
- **Data source**
  - Extraction from the French nationwide healthcare database (SNDS)
  - From 01/01/2009 to 12/31/2016
- **Study population**
  - 1,213 patients initiating an **intravenous** agent,
  - 2,442 patients initiating an **oral** agent.
- **Construction of the high dimensional Propensity Scores (hdPS)**
  - Different **hdPS models** to estimate the probability for a patient to be treated by an intravenous versus oral agent
    - 100 variables empirically selected from 5 dimensions
      - Long term disease registration
      - Hospital discharge diagnoses
      - Dispensed drugs
      - Performed laboratory tests
      - Performed medical procedures
    - Extra forced variables judged clinically pertinent by experts
    - Different covariates assessment period length
    - 1:1 matching on hdPS, and potentially other forced variables
- **hdPS performance assessment**
  - hdPS distributions
  - C-statistics value (the closer to 0.5 the better)
  - Number of matched-patient pairs
  - Number of variables with a standardized difference (SD) > 10% between the comparator groups
  - Number of variables associated with the outcome with SD>10%

### Results

#### Table 1. Comparison of successive hdPS models

<table>
<thead>
<tr>
<th></th>
<th>Model 1</th>
<th>Model 1.1</th>
<th>Model 2</th>
<th>Model 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Forced variables</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at initiation treatment</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Disease stage before index date</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Charlson comorbidity index</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Total healthcare costs</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Treatment of bone metastases</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Cancer specific procedure 1</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Dispensing of antineoplastic agents</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
<tr>
<td>Covariate assessment period length</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
<td>✔</td>
</tr>
</tbody>
</table>

#### hdPS distribution

- **Intravenous**
- **Oral**

Before matching

After trimming and matching 1:1

Not applicable

### Number of potential matched-patients pairs

<table>
<thead>
<tr>
<th>Matching strategy</th>
<th>hdPS (± 0.01)</th>
<th>hdPS (± 0.01)</th>
<th>hdPS (± 0.01)</th>
<th>hdPS (± 0.01)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of potential matched-patients pairs</td>
<td>273</td>
<td>765</td>
<td>830</td>
<td>716</td>
</tr>
<tr>
<td>Matching strategy</td>
<td>hdPS (± 0.01)</td>
<td>hdPS (± 0.01)</td>
<td>hdPS (± 0.01)</td>
<td>hdPS (± 0.01)</td>
</tr>
<tr>
<td>C-statistic value</td>
<td>0.713</td>
<td>0.614</td>
<td>0.586</td>
<td>0.603</td>
</tr>
<tr>
<td>Number of variables with SD &gt;10% and statistically associated with the outcome</td>
<td>Not applicable</td>
<td>52</td>
<td>48</td>
<td>17</td>
</tr>
</tbody>
</table>

### Conclusion
- Pre-exposure window should be routinely assessed and potentially excluded when constructing propensity score, especially when patients have followed distinct care pathways.
- Ideally, covariate assessment period should stop at the time treatments are decided upon and not yet started.

The Authors declare that there is no conflict of interest.

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