Evaluating Patient Count Vs Hospitalization Risk for Common Clinical Trial Eligibility Criteria: A Case Study for Relapsed/Refractory Lymphoma/Leukemia

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Background
- Clinical trials remain essential for generating medical evidence.
  - Within the same disease domain, common eligibility criteria (CEC) patterns can be observed as many of the same criteria might be applied for safety reasons and/or reducing study population heterogeneity, but at the expense of reducing available patients who might benefit from participation.
  - Objective: To assess the tradeoff in patient count vs hospitalization risk when using different CEC sets, by using adult relapsed/refractory (r/r) lymphoma/leukemia trials as a case study.

Methods
General Procedure

- Data Sources
  - Trial Enrollment Data
  - ClinicalTrials.gov
  - EHR

- 23 trials available for r/r lymphoma/leukemia
- Provides candidate eligibility criteria
- Provides patient data (from a large academic medical center) for cohort construction

CEC Identification

- Select concepts appearing in at least 25% of all trials
- Remove concepts if too vague or not reasonably captured in EHR
- Manually cross-check concepts to original ClinicalTrials.gov source text

Cohort Construction

- Rx = portion of relevant chemotherapy or corticosteroid
- Dx = lymphoma or leukemia diagnosis
- Outcome = hospitalization (length of stay >1 day)

Analysis

- Perform power calculations to identify powered CEC sets
- Create scatterplot between CEC patient count and hospitalization risk for each powered CEC set
- Apply k-means clustering to identify CEC patterns

Results

- There were 9 CEC found, with no prior malignancy found to be the most restrictive

<table>
<thead>
<tr>
<th>CEC Label</th>
<th>CEC Description</th>
<th>Number of Trials (N)</th>
<th>Patient Count (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Start</td>
<td>NA</td>
<td>23 (100)</td>
<td>663 (100)</td>
</tr>
<tr>
<td>No HIV</td>
<td>No HIV within the past 365 days</td>
<td>20 (86.96)</td>
<td>614 (98.56)</td>
</tr>
<tr>
<td>No HIV/HCV</td>
<td>No HIV/HCV within the past 365 days</td>
<td>19 (82.61)</td>
<td>613 (98.39)</td>
</tr>
<tr>
<td>Not pregnant</td>
<td>No evidence of current pregnancy within the past 60 days</td>
<td>19 (82.62)</td>
<td>612 (98.94)</td>
</tr>
<tr>
<td>No prior chemotherapy or radiotherapy within the past 14 days (excludes index)</td>
<td>16 (78.26)</td>
<td>590 (94.70)</td>
<td></td>
</tr>
<tr>
<td>No prior malignancy (beside lymphoma, leukemia, non-melanoma skin cancer, melanoma in situ, carcinoma in situ of the cervix, benign tumor, or lipomatous tumor) within the past 1095 days</td>
<td>17 (73.91)</td>
<td>313 (50.24)</td>
<td></td>
</tr>
<tr>
<td>Adequate eGFR</td>
<td>Most recent eGFR measure within the past 180 days &gt;30 mL/min/1.73 m²&lt;sup&gt;2&lt;/sup&gt; (per MDRD equation)</td>
<td>11 (47.83)</td>
<td>525 (84.27)</td>
</tr>
<tr>
<td>No infection</td>
<td>No active infection within the past 30 days</td>
<td>10 (43.48)</td>
<td>604 (96.65)</td>
</tr>
<tr>
<td>Adequate ANC</td>
<td>Most recent ANC measure within the past 180 days &gt;1000/mm³</td>
<td>9 (39.13)</td>
<td>587 (94.22)</td>
</tr>
<tr>
<td>No corticosteroid</td>
<td>No prior corticosteroid use within the past 7 days (excludes index)</td>
<td>9 (39.13)</td>
<td>612 (98.23)</td>
</tr>
</tbody>
</table>

- Of 511 possible CEC sets, only 256 (50%) were powered; all included the CEC of no prior malignancy
- Combining no infection and no prior chemotherapy suggests the lowest hospitalization risk, but at the expense of the smallest available number of patients to recruit (i.e., Cluster 5)

Conclusions

- This procedure demonstrates a possible approach for better estimating and addressing the effect of eligibility criteria on patient counts and safety risk
- Trial sample and EHR data can greatly impact results, so CEC found to have muted effects from this analysis might not necessarily hold in other environments or different data sources

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