Clinical trial feasibility

• Clinical trials are expensive, time consuming and can result in cancelled trials and can have costly amendments.
• Using a data-driven approach for feasibility allows for an overall understanding of the population of interest and characteristics of the population by examining inclusion/exclusion criteria for the population of interest.
• By enabling the CDM, and OHDSI tools we are able to mimic protocol populations using observational data to better understand how inclusion/exclusion criteria affect the population in a timely, concise and reproducible manner.
Using OHDSI tools to conduct clinical trial feasibility

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ABSTRACT

Background: Observational data has been used in support of various epidemiological studies including safety assessments, characterization and outcomes research. A novel use of observational data that is enabled through the use of OHDSI tools in assessing clinical trial feasibility.

Methods: Using the tools from the OHDSI network we are able to apply standard methods to effectively assess inclusion criteria for a potential clinical trial population. A case study example has been executed to illustrate feasibility.

Results: The result of using observational data has provided efficiencies in protocol design, the ability to address operational questions, and potentially avoid protocol amendments. The case study demonstrates the ability to adequately generate useful information for relevant inclusion criteria.

Conclusions: Insights gained by protocol simulation can be adapted to enhance how clinical trials are designed and conducted. By using the common data model, standard vocabularies and OHDSI tools we are able to deliver results in a standard, concise, timely and reproducible manner.

BACKGROUND

- The use of observational data in retrospective analyses has been thoroughly explored and studied. Applying this data in the use of clinical trial feasibility has been a new application of the data.
- By utilizing the OMOP common data model (OMOP CDM) and the current OHDSI tools, the ability to utilize the data in clinical trial feasibility is possible and can address operational questions, provide insight in overall population eligibility, impact protocol design, and possibly avoid protocol amendments for a clinical trial.

METHODS

- Typical clinical trial feasibility lifecycle (Figure 1.): 3. Each criteria of interest is applied to the index population (or inclusion criteria) in ATLAS.

RESULTS

- In less than 9 months, the team has used ATLAS to answer over 20+ protocol-related questions using various criteria including assessing the impact of individual protocol criteria, operational questions to determine cohort selection and patient characteristics prior to drafting protocols.
- The types of insights gained by various protocols are: insights of inclusion criteria, assessing impact of changing thresholds for inclusion criteria, and checking for adequate match rates amongst the population found in the retrospective observational data cohort.
- Of the 4 inclusion criteria in the case study, 2 can be adequately be addressed in the tools. Of the 5 exclusion criteria, 3 can be simulated in observational data.
- The overall match rate for this population is 56.60% based on the criteria entered (Table 1) and individual match criteria are displayed in Table 2 for the Truven CCAF database (a large US commercialized claims database).
- The criteria that have lower than a 90% match rate were: bipolar disorder in all time prior, no more than 3 previous antidepressants in all time prior.

Table 1. Summary of index population and match percentage

<table>
<thead>
<tr>
<th>Match Rate</th>
<th>56.60%</th>
</tr>
</thead>
</table>

Table 2. Inclusion criteria from MDD protocol simulation

<table>
<thead>
<tr>
<th>Inclusion Criteria</th>
<th>N</th>
<th>% Satisfied</th>
<th>% To Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>No current MDD with psychosis</td>
<td>388,798</td>
<td>98.06%</td>
<td>1.94%</td>
</tr>
<tr>
<td>No bipolar disorder in all time prior</td>
<td>359,603</td>
<td>92.59%</td>
<td>7.41%</td>
</tr>
<tr>
<td>No current obsessive-compulsive disorder</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
<tr>
<td>No current borderline personality disorder</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
<tr>
<td>No current eating disorder</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
<tr>
<td>No current schizophrenia in all time prior</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
<tr>
<td>No substance abuse diagnosis the prior 12 months</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
<tr>
<td>No diagnosis of suicidal ideation in the prior 183 days</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
<tr>
<td>No more than 3 previous antidepressants in all time prior</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
<tr>
<td>No antidepressant use greater than 183 days (6 months)</td>
<td>11,010</td>
<td>96.37%</td>
<td>3.63%</td>
</tr>
</tbody>
</table>

CONCLUSIONS

- The ability to analyze clinical trial feasibility thorough observational data may provide substantial insights in avoiding amendments, recruitment challenges and protocol design.
- By utilizing the common data model across various databases, the analysis to be simulated in different populations and geographies which can be representational of recruitment regions.
- The OHDSI tools can facilitate many assumptions in a protocol for clinical trial feasibility prior to which is a valuable proposition. The tools provide a strong framework to conduct the analysis in a standardized and reproducible manner.

REFERENCES


CONFLICT OF INTEREST STATEMENT

Rupa Makadia, Jamie Forlenza, Frank DeFalco, Chris Knoll, and Patrick Ryan are full time employees of Janssen Research & Development, a unit of Johnson & Johnson. The work on this study was part of their employment. They also hold pension rights from the company and own stock and stock options.
Background

- Clinical trial feasibility analyses address operational questions, provide insight in overall population eligibility, impact protocol design, and can potentially avoid protocol amendments for a clinical trial. At Janssen this utility is provided to clinical teams by identifying appropriate protocols and pre-protocol documents that may be studied using observational data (mainly claims databases).

- To date we have conducted more than 70 analyses within a time span of two and a half years. This analysis is limited to 30 programs/protocols that are posted on clinicaltrials.gov across five therapeutic areas.

- This study provides an understanding how of observational data can inform clinical trial design using the OHDSI framework and tools.
Methods

• The results of each of the analyses are summarized into a dataset which includes therapeutic area, key analysis questions, the number of criteria evaluated by domain (administrative, condition, drug, measurement, observation, and procedure), age distribution, individual results, match rates (the proportion of persons to match all criteria in the index cohort), data sources, and cohort size were recorded.

• Statistics were calculated by therapeutic area for various metrics, specifically: match rate, data domains of criteria, percentage of criteria evaluated/not evaluated which reflect the degree to which the criteria from the CT could be implemented in the observational data.
Results

• In total, 17% represent protocols recruiting from pediatric populations, while 7% were mixed adult and child and 76% adult.

• Table 1 gives the overall statistics of criteria by type and percent evaluated. Overall each protocol has on average 33.1 criteria with 55.59% of criteria that can evaluated through available observational data.

Table 1. Overall statistics of evaluated programs using the clinical trial feasibility framework

<table>
<thead>
<tr>
<th>Therapeutic Area ‡</th>
<th>N</th>
<th>Average number protocol criteria</th>
<th>Average number inclusion criteria</th>
<th>Average number exclusion criteria</th>
<th>Percent protocol criteria implemented</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNS</td>
<td>9</td>
<td>34.5</td>
<td>11.1</td>
<td>23.4</td>
<td>48.18%</td>
</tr>
<tr>
<td>CVM</td>
<td>4</td>
<td>29.0</td>
<td>9.0</td>
<td>20.0</td>
<td>59.89%</td>
</tr>
<tr>
<td>IDV</td>
<td>4</td>
<td>28.3</td>
<td>11.5</td>
<td>16.8</td>
<td>53.21%</td>
</tr>
<tr>
<td>IMM</td>
<td>7</td>
<td>51.0</td>
<td>16.8</td>
<td>34.1</td>
<td>57.23%</td>
</tr>
<tr>
<td>ONC</td>
<td>6</td>
<td>22.6</td>
<td>8.7</td>
<td>14.0</td>
<td>59.44%</td>
</tr>
<tr>
<td>Overall</td>
<td>30</td>
<td>33.1</td>
<td>11.4</td>
<td>21.7</td>
<td>55.59%</td>
</tr>
</tbody>
</table>

‡ Therapeutic area: (CNS=Central Nervous System, CVM=Cardiovascular & Metabolism, IDV=Infectious disease & Vaccines, IMM=Immunology, ONC=Oncology)
Results

• The proportion of criteria in a protocol vary by domain with conditions making up over 30% of the protocol criteria across domains followed by drugs, procedures, observations, measurements and administrative criteria.

• In all TA’s conditions make up the majority of criteria that is evaluated with at least 27% of condition criteria evaluated.

• Administrative data is not evaluated in any TA due to the lack of this data type, examples include: consent to participate or adherence to protocol guidelines. Measurement data which is mainly laboratory data is evaluated for less than 1% of criteria due to lack of completeness of data for all persons in the disease cohorts.

• The differences in the amount of criteria by domain represent comorbidities that are relevant to individual TA’s, for example immunology and oncology have a larger proportion of drug criteria compared to cardiovascular protocols.
Results

- The match rates vary among the TA’s and by protocol. The matching population can vary from ~3% to 70% depending on the index population and disease area.
Conclusions

• Our study demonstrates the value of using the OHDSI tools to support generating real-world evidence that can meaningfully inform clinical trial design. The observed diversity in match rates and impact of criteria demonstrate the need for feasibility to gain additional insights.

• Clinical trial inclusion criteria can often, but not always, be evaluated in observational data. When these criteria can be evaluated, they are most often based on prior conditions and medication history of the patient.

• The impact of inclusion criteria on the proportion of patients from a target population that satisfy all criteria can be evaluated using OHDSI tools, and the substantial variability shown in this study demonstrates that different types of insights can be obtained in different circumstances.

• While the use of observational data should be tailored to the particular clinical problem and the needs of the decision-making stakeholders, we believe a consistent process for applying standardized analytics can be applied to trial feasibility to meaningfully inform clinical development.

• Future research would be to evaluate the results from published trials against our implementation to determine the generalizability using observational data.
Thank You

Janssen Research & Development