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 surveillance, characterisation 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 possibly avoid protocol amendments. The case study illustrates the ability to adequately simulate 7 out of 9 criteria and provide insights around selected criteria.

Conclusion: 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 have 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.)
  1.) Eligible protocols are identified in therapeutic areas that are of interest to the organization throughout the clinical trial lifecycle from trial design through active trials facing recruitment challenges. Additionally, review of inclusion/exclusion criteria that can be addressed through the data elements available in the CDM data.
  2.) Creation of concept sets and/or utilization of concept sets from standard vocabularies in ATLAS to describe the criteria set.
  3.) Each criteria of interest is applied to the index population (or inclusion criteria) in ATLAS.
  4.) The individual match percentages for each criteria and overall match criteria are evaluated for each protocol.
  5.) Results are shared with clinical team.
- A case study for a major depressive disorder (MDD) protocol has been entered through the process and results generated and evaluated; Inclusion and exclusion criteria are shown in Figure 2 from clinicaltrials.gov.
- The index population was defined as people having a condition occurrence of a primary condition of MDD in the 2014 calendar year between the ages of 21 and 64 and with at least 180 days prior. All people matching those criteria must also have antidepressant use greater than 1825 days (60 months) all time prior, no diagnosis of suicidal ideation in past 365 days, no substance abuse diagnosis 6 months prior to index, no current obsessive compulsive disorder, no current bipolar disorder in all time prior, no more than 3 previous antidepressants in all time prior, no diagnosis of suicidal ideation in past 365 days, no more than 3 previous antidepressants in all time prior, no antidepressant use greater than 1825 days (60 months) all time prior.

RESULTS
- In less than 9 months, the team has used ATLAS to answer over 20 protocol questions with regard to various criteria including assessing the impact of individual protocol criteria, operational questions pertaining to cohort selection and population characteristics prior to drafting protocols.
- The types of insights gained by various protocols are: insights of inclusion criteria, assessing impact of changing 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 addressed in the tools. Of the 5 exclusion criteria, 5 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 CCAE database (a large US commercially insured claims database).
- The criteria that have lower than a 90% match rate were: no 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 N</th>
<th>Index population</th>
</tr>
</thead>
<tbody>
<tr>
<td>56.60%</td>
<td>318,950</td>
</tr>
</tbody>
</table>

Table 2. Inclusion criteria from MDD protocol simulation

<table>
<thead>
<tr>
<th>Inclusion Rule</th>
<th>N</th>
<th>% Satisfied</th>
<th>% To-Gain</th>
</tr>
</thead>
<tbody>
<tr>
<td>No current MDD with psychosis</td>
<td>309,510</td>
<td>97.04%</td>
<td>1.31%</td>
</tr>
<tr>
<td>No bipolar disorder in time prior</td>
<td>282,586</td>
<td>95.38%</td>
<td>4.62%</td>
</tr>
<tr>
<td>No current obsessive compulsive disorder</td>
<td>318,520</td>
<td>99.87%</td>
<td>0.13%</td>
</tr>
<tr>
<td>No current borderline personality disorder</td>
<td>316,888</td>
<td>99.35%</td>
<td>0.65%</td>
</tr>
<tr>
<td>No current eating disorder</td>
<td>314,022</td>
<td>98.45%</td>
<td>1.55%</td>
</tr>
<tr>
<td>No schizophrenia in all time prior</td>
<td>315,981</td>
<td>99.07%</td>
<td>0.93%</td>
</tr>
<tr>
<td>No substance abuse diagnosis 6 months prior to index</td>
<td>302,983</td>
<td>94.99%</td>
<td>5.01%</td>
</tr>
<tr>
<td>No diagnosis of suicidal ideation in past 365 days</td>
<td>318,342</td>
<td>99.81%</td>
<td>0.19%</td>
</tr>
<tr>
<td>No more than 3 previous antidepressants in all time prior</td>
<td>227,125</td>
<td>71.27%</td>
<td>28.73%</td>
</tr>
<tr>
<td>No antidepressant use greater than 1825 days (60 months) all time prior</td>
<td>310,340</td>
<td>97.30%</td>
<td>2.70%</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 representative of recruitment regions.
- The OHDSI tools can facilitate many assumptions in a protocol for clinical trial feasibility a priori 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 and Development, a unit of Johnson and 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.