PLANNING AND CONDUCTING CLAIMS DATA ANALYSES: THE EXAMPLE OF GERMAN CLAIMS DATA STUDIES

Finding the unexplored value of your product.

Ingress White Paper No. 2
by Thomas Wilke

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1 BACKGROUND

The value proposition of a pharmaceutical product is generally based on its efficacy/safety profile as shown in clinical studies. Also, both market approval and reimbursement decisions are based on clinical evidence. However, health authorities as well as prescribers/insurers are increasingly aware of the fact that the real-world-effectiveness/safety profile of a treatment may differ from its efficacy/safety profile as shown in clinical studies. So, real-world evidence (RWE) data are getting more important for reimbursement discussions with health authorities for the following reasons:

- Products may have benefits/disadvantages that cannot be shown in clinical studies (e.g., adherence/persistence benefits).
- Patients in real life may differ from patients included in clinical studies.
- There may also be patient subgroups that benefit more/benefit less from the new treatment, which have not been addressed in clinical trials.
- Physicians’ behavior in real life may differ from that in clinical studies.
- RWE data may be the basis for pay for performance contracts between pharmaceutical companies and health insurers and/or health authorities. Here, health authorities may use provisional reimbursement systems, which require additional real-life data to be collected and evaluated after a pre-defined period of time.
- Also, health insurers are increasingly interested in the real-life resource use/costs associated with treatments. Given tight financial constraints these institutions are facing, they are willing to pay only higher “real-world prices” for new treatments if these are associated with a higher “real-world benefit”.

The main purpose of RWE studies is to collect data about the real-world treatment of patients and the real-world effectiveness/safety profile of specific treatments. Claims data studies are an important RWE study option.
2 CLAIMS DATA ANALYSES – STUDY TYPES AND ADVANTAGES/DISADVANTAGES: THE EXAMPLE OF GERMAN CLAIMS DATA

A particular feature of claims data sets is that they cover all treatment areas (inpatient treatment, outpatient treatment, outpatient prescriptions, days absent from work, other claims, such as rehabilitation clinic stays or medicinal prescriptions). Please note that prescription data are available in the database in a very detailed manner: product number ("Pharmazentralnummer") describing drug and package size, prescription date, date of submission to pharmacy, type of prescribing physician, defined daily dosage for specific product, list price of drug. However, please also note that inpatient medication treatment is regularly not available in a claims dataset. Sickness funds do not reimburse inpatient medication treatment costs separately, but reimburse on a Diagnosis Related Groups (DRG) basis (DRG then includes medication costs).

Table 1: Main data in the German claims-based data set

<table>
<thead>
<tr>
<th>Socio-demographic characteristics</th>
<th>Inpatient care</th>
<th>Outpatient care</th>
<th>Outpatient medication (prescriptions only)</th>
<th>Other data</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age</strong></td>
<td>Data about initial diagnoses including day of admission</td>
<td>All physicians’ visits including type of physician (esp. GPs and specialists in different specialist groups)</td>
<td>Type of medication (medication number – in Germany: PZN), ATC code, number of packs, dates of prescription and of dispensing pharmacy</td>
<td>Costs for outpatient devices/other supportive measures</td>
</tr>
<tr>
<td><strong>Gender</strong></td>
<td>All documented diagnoses/procedures (also: cardiovascular/diabetes-related outcomes including date of clinical event)</td>
<td>Documentati of diagnoses/measures (EBM, GONr, OPS)</td>
<td>Prescribing physician</td>
<td>Outpatient surgeries</td>
</tr>
</tbody>
</table>
In Germany, most patients (about 90%) are insured by a public sickness fund. Willingness of these sickness funds to provide claims data for scientific analysis depends on several factors:

- Research objectives and scientific quality of study protocol;
- Legal framework; the German “Sozialgesetzbuch” (SGB) requires every sickness fund to do a detailed evaluation of every proposed analysis before delivering data to a research institute.
- Statement of data protection institutions; IPAM/Ingress are, based on prior experience, prepared to meet every requirement in this respect.

In the last five years, IPAM, as exclusive network partner of Ingress health, did > 20 different claims data analyses based on German health fund data. The main advantages of claims data analyses can be summarized as follows:

- Access to high patient numbers/long observational periods
- Bias resulting from study site/patient selection is minimal
- Bias resulting from study itself (because physicians/patients know that they are part of the study) is non-existent.
The main disadvantages are that claims data analyses can mostly be done only in a retrospective way and that certain outcomes of interest are not available in claims databases. Based on claims data available in Germany, the following outcomes could be analyzed:

- **Excellent**
  - Direct medical costs
  - Death
  - Major clinical outcomes which are associated with inpatient/outpatient diagnoses such as stroke, amputation etc.
  - Incidence/prevalence of diseases in a health care fund population
  - Treatment patterns (outpatient/inpatient treatment and medication treatment)
  - Treatment switches or time to next line of treatment

- **Good**
  - Treatment-adherence/persistence, based on claims filed for prescriptions
  - Drug/other treatment overuse/underuse if compared to evidence-based guidelines
  - Analysis of factors associated with certain outcomes

- **Poor**
  - Clinical surrogate outcomes like disease progression (if not associated with specific diagnoses/specific drug treatment), lung function, viral load or other laboratory values etc.
  - Patient-reported outcomes like pain, HrQoL, preferences etc.

The most applied claims study types are the following:

- **Epidemiological study** exploring incidence/prevalence of a disease/disease stage and assessing risk factors for incidence/prevalence
- **Explorative claims data analysis**, analyzing treatment of patients and corresponding treatment outcomes; in some cases, this is compared to evidence-based guidelines
- **Explorative, multivariate analysis** assessing factors associated with certain disease stages/outcomes or treatment patterns
- **Cost-of-treatment studies**
- **Comparative studies** comparing effectiveness/safety/costs associated with alternative treatments
  - Propensity score matching-based comparisons
  - Multivariable statistical analyses such as logistic regression, Cox survival models or GLM/gamma regression analyses.
3 SUMMARY AND CHECKLIST

Claims data analyses are a very important and attractive option, if a company is generally interested in real-world data. Ingress health, based on a year-long experience of claims data studies and based on general access to these data (dependent on final approval by health funds) in many major European countries, can support you in planning/conducting your claims data analysis. The following checklist helps you in planning a claims data analysis; if all questions can be answered positively, your claims data analysis is a well-planned scientific study.

Checklist: Planning of a claims-based data study

<table>
<thead>
<tr>
<th>Checklist point</th>
<th>General study planning</th>
<th>Shows high scientific quality – high probability that results can be published in a peer-reviewed journal</th>
</tr>
</thead>
</table>
| 1. Based on the value proposition/target product profile of your product, and a possible general need for epidemiological data, did you define the outcomes/endpoints you are interested in? Are these outcomes/endpoints well acknowledged in the scientific community and do they matter for patients? | No – please revise your outcome/endpoint planning.  
Yes – continue with planning process. |                                                                                           |
| 2. Did you do a thorough/systematic literature review regarding your area of interest? | Yes                                                                                           |                                                                                           |
| 3. Did you develop an a priori study protocol which has been discussed in a peer-review by internal/external experts?  
Did you make sure that the definition of outcomes (which may consist of a combination of diagnoses and prescriptions) is in line with scientific/clinical practice? | Yes                                                                                           |                                                                                           |
| 4. Will the results (irrespective of their “direction”) be published?            | Yes                                                                                           |                                                                                           |

1 Based on Ingress-Health experience and www-strobe-statement.org.
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<th>Question</th>
<th>Answer</th>
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<tr>
<td>5. Did you choose the best-possible study design to derive outcome data in the most representative way possible?</td>
<td>Yes</td>
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<tr>
<td>6. Will the study sample be representative?</td>
<td>Yes</td>
</tr>
<tr>
<td>7. Did you define inclusion/exclusion criteria for study centers/patients? Did you do a realistic sample size planning?</td>
<td>Yes</td>
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<tr>
<td>8. Did you describe all descriptive/endpoint variables in the study protocol? Are the descriptive variables sufficient for a detailed sociodemographic/clinical characterization of the study patients?</td>
<td>Yes</td>
</tr>
<tr>
<td>9. Did you describe the planned statistical analyses in the study protocol? Are these analyses sufficient/scientifically accepted?</td>
<td>Yes</td>
</tr>
<tr>
<td>10. Did you describe the different forms of bias in your study protocol? Did you plan for specific measures to account for that, for example scenario analyses?</td>
<td>Yes</td>
</tr>
<tr>
<td>11. Will the study be steered by a scientific steering board, which may consist of members of the company, the institution conducting the study, the health fund providing the data and independent experts?</td>
<td>Yes</td>
</tr>
<tr>
<td>12. Did you implement the necessary data protection measures? Normally, a data protection concept is needed.</td>
<td>Yes</td>
</tr>
<tr>
<td>13. Will the study be conducted by an institution which has experience/a track-record in claims data analyses?</td>
<td>Yes</td>
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</tbody>
</table>
Thomas has 14 years of experience in leading/conducting German/international real-world evidence studies. He published several papers about the topic of treatment-adherence and persistence. He has a wealth of experience with respect to the German market, chart reviews, prospective studies and patient reported outcomes. Thomas has an above-average access to German claims data and has a well-known reputation for conducting claims data analyses in Germany.

Thomas holds a PhD degree in Economics from the University of Duisburg, Germany, and a Diploma degree in Economics from the University of Duisburg. From 2001–2004 Thomas worked for the Boston Consulting Group. Since 2004, he has worked as a professor at the University of Applied Sciences Wismar. Furthermore, he is the head of an institute in health economics and has published in many international journals.
5 INGRESS HEALTH WHITE PAPERS

- No.1: Thomas Wilke (2016): RWE study planning: a systematic approach
- No. 2: Thomas Wilke (2016): Planning and conducting of claims data analyses: the example of German claims data studies
- No. 3: Thomas Wilke (2016): Planning and conducting pragmatic trials
- No. 4: Sabrina Mueller/Thomas Wilke (2016): Treatment adherence/persistence studies: measurement of adherence/persistence
- No. 5: Sabrina Mueller/Thomas Wilke (2016): Treatment adherence/persistence studies: measurement of causes of non-adherence
- No. 7: Bart Heeg and Maarten Postma (2016): Real world effectiveness, cost-effectiveness and reimbursement
We strongly believe that the future of health technology reimbursement in the EU will be based on provisional reimbursement, corresponding outcomes based managed entry schemes and health economic evaluations. This belief is based on trends in digitalization of patient outcomes in clinical practice, the increasing number of drugs approved with conditional market authorization by EMA and an increase in outcomes based managed entry schemes in the EU.

This shift from reimbursement to conditional reimbursement requires a change of mind-set in industry as in the past when developing RWE studies manufacturers often did not (need to) consider the health economic perspective. We also strongly believe that a lot of products are underutilized because clinical trials did not show their value in terms of, e.g., reduced side effects, improved quality of life and/or compliance.

Therefore, Ingress health, with its combined and integrated health economic and real-world evidence expertise and passion for the field, will be successful in optimizing your products’ pre- and post-marketing value proposition.

For more information, please visit www.ingress-health.com