Pioneering Patient Safety: Leveraging AI to Predict Adverse Drug Outcomes

Capstone Showcase
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Better Health, Brighter Future
Executive Summary

We turned an exploratory project on how to use AI to guide pharmacovigilance into an operational, interactive app that detects adverse events during clinical trials and post-marketing.

Qualitative and Quantitative Insights

- **Quantitative:** good classification metric, statistically significant treatment effect
- **Qualitative:** systematically and rapidly detect an adverse event

We can **accurately identify 100% of our adverse event of interest** while reducing the population to watch by ~85% for one of the drugs.

Business Value

- **Robustness:** earlier detection
- **Safety:** mitigated risks
- **Efficiency:** significant cost savings opportunities

**Deployment: Web App**

Welcome to our Capstone project in collaboration with Takeda. We are a team of 2 graduate students from MIT and we are excited to share our findings with you.

**Project Description**

- For pharmaceutical firms to understand the underlying causal relationships between the concomitant drug and the adverse event
- For medical experts to predict the precise event of interest (e.g., multiple factors like demographics, concomitant drugs, dosage, post-adverse drug reaction)

Ultimately, the goal is to help Takeda better understand the adverse event of interest and to improve the safety of new drugs.

**Costs:**

- $77-$138 Billion annual cost of Adverse Drug Reactions in the US

**Business Value Deployment:** Web App

- **Costly clinical trials**
- **Multimodal data**
- **Complex drug patient interactions**
- **Large-scale data**
Using data analytics and AI to support Takeda’s mission: patient safety

How can we **assess our drug’s actual impact** compared to other drugs that a patient is taking?

What are the **key population subgroups** that are at higher risk of developing a given adverse event?

How can we predict **whether a patient is going to develop this adverse event**?
To analyze patient risk, we are focusing on 3 Drug Event Combinations that were pulled from the patient database:

Reports from pharmacovigilance meetings + Demographic information + Dosage information + Current and past medical conditions → Highly multimodal data

**Drug 1**
- Lung cancer
- Adverse event: Cardiotoxicity
- 52 out of 1147 patients

**Drug 2**
- Uric acid in the blood
- Adverse event: Steven Johnson Syndrome, Toxic Epidermal Necrolysis
- 56 out of 16393 patients faced this issue

**Drug 3**
- Hypertension and heart failure
- Adverse event: Rhabdomyolysis
- 62 out of 19647 patients faced this issue

→ Very varied cases, drugs and patients
The 4 analytics models built will allow Takeda to act at three different stages of the patient-drug interaction process.

1. Do we continue developing this drug?
   Predict adverse event based on demographics data

2. Is there a causal relationship between the initiation of the Takeda product and the adverse event?
   Analyze influence from other drugs

3. Do we market this drug?
   Add dosage information to prediction

4. What do we add to the label?
   Add initial light reaction

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Jane Doe, 43-year-old woman from Japan with type 1 diabetes and daily painkiller intake, gets a prescription for the Takeda drug.

- Day 0: Jane Doe starts the Takeda drug: twice a day in a capsule.
- Day 3: Jane Doe reports intense diarrhea to her doctor.
- Day 11: Adverse reaction: Cardiac Arrest.
- Day 37: AUC 95% decision-making flexibility.
For any problem there is always a solution...

<table>
<thead>
<tr>
<th>CHALLENGE</th>
<th>SOLUTION</th>
<th>IMPACT</th>
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| 1) Multimodal & Unstructured Data | • Natural Language Processing  
• Graph Concomitant Product Analysis | ➢ Extracted 5000+ Drugs  
➢ Selected Representative Drugs |
| 2) Many Concomitant Factors | • Regress and Compare for Causal Effect of Drugs | ➢ Identified 45+ Causal Drugs |
| 3) High Class Imbalance | • Ensemble Learning and Undersampling | ➢ Increased AUC from 0.50 to 0.95 |
| 4) Need for Interpretability | • Interpretable Trees  
• Robustness of Feature Significance | ➢ Found 5 Highly Significant Features  
➢ At No Cost on Performance |
# Empowering Lives: Redefining Patient-Centric Impact

## Precision Empowerment

1) **Empowering Patient Confidence**
   - Refined *drug labels* empower patients

2) **Vigilance in Vulnerability**
   - Swift identification of susceptible patient subgroups

## Unveiling Potential Dangers

3) **Informed Risk Reduction**
   - Expert insight into dangerous drug combinations (*risky concomitants*)

4) **Hidden Beneath the Surface**
   - Unveiling and preventing potential adverse events

## Bridging Boundaries

5) **Revolutionizing Generalizations**
   - Bridging clinical trials to real-world patient benefit

6) **Empowerment Through Adaptation**
   - Dynamic research redirection for ongoing patient safety

## Tailored Care

7) **Preserving Patient Well-being**
   - *Thousands of patients spared* from adverse reactions

8) **Global Influence, Individual Lives**
   - Impact on millions through Takeda’s reach

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**Massive Patient Reach**: Every year, **31 million patients** in more than **100 countries** rely on Drug 2 for their well-being. Our efforts directly influence their safety and quality of life. If our project was expanded to all other Takeda Drugs, number of patients impacted could be so much more!

**Unveiling Hidden Dangers**: The tip of the iceberg is the ~**30,000 serious adverse reactions** reported to Takeda. Beneath the surface, countless more adverse events may be prevented through our vigilant approach, ensuring patients remain shielded from harm.
Transforming Pharmacovigilance: Bolstering Patient Safety and Paving the Way for Efficient, Data-Driven Decisions
Future work

• **Expand training**: Train our models on the 51 other drugs that Takeda manufactures in the US and their most serious adverse reactions.

• **Safety improvement**: Track decisions made together with our solution to measure its impact.

Implementation

• **Validated results with product teams**.

• Our project was pre-selected by the HEVER* group in an **international effort** to bring AI to the pharmaceutical industry. If selected the project will be granted millions of dollars.

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* HEVER group: Gatherings of heads of R&D from big pharmaceutical companies
Thank you!

“A collaboration of multiple perspectives joining together to lead patient safety into the future!”
Head of Global Patient Safety Signal Management and Innovation, Takeda

“This work is a brilliant demonstration of the interest of AI in pharmacovigilance. It shows clearly the huge contribution of such approach in decision-making.”
President, Council for International Organizations of Medical Sciences

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