



Pioneering Patient Safety: Leveraging AI to Predict Adverse Drug Outcomes

Capstone Showcase

August 18, 2023

Oscar Courbit & Hermine Tranié

Takeda team: Saurabh Awasthi, Dona M. Ely, Maria Camila Marengo

Faculty Advisor: Alexandre Jacquillat

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

Costly clinical trials

Multimodal data

Complex drug patient interactions

Large-scale data

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

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

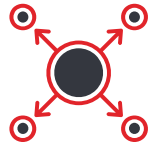
Deployment: Web App

The screenshot shows a web application interface with a sidebar on the left containing navigation links: About, Causal Inference, Predictive Modeling, The Creators, Oscar Courbit, Hermine Tranie, Acknowledgments, Mentors, and Computer Science Student & Web App. The main content area features the Takeda, MIT Management Sloan School, and Operations Research Center logos. Below the logos is a welcome message and a 'Project Description' section. The project description states the goal is to provide a decision support tool for pharmacovigilance teams to understand causal relationships between concomitant drugs and adverse events, and to predict adverse events based on multiple factors like demographics, concomitant drugs, dosage, and past adverse drug reactions. It also mentions the goal is to help Takeda better understand adverse events and improve drug safety. A 'Pages' section lists 'Causal Inference' and 'Predictive Modeling' with brief descriptions of their functions.

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?

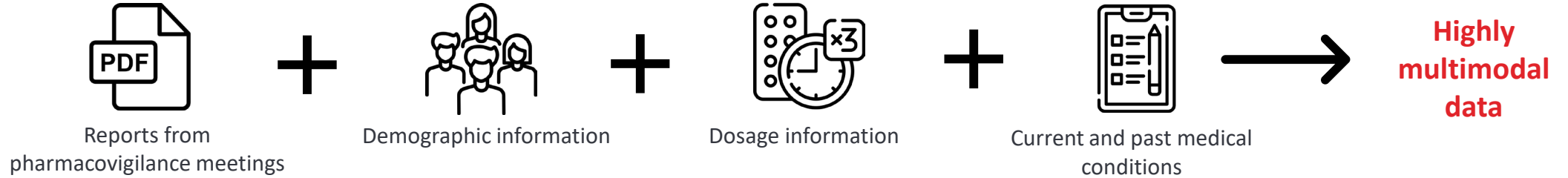


What are the **key population subgroups** that are at **higher risk of developing a given adverse event?**



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:



Drug 1

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

Drug 2

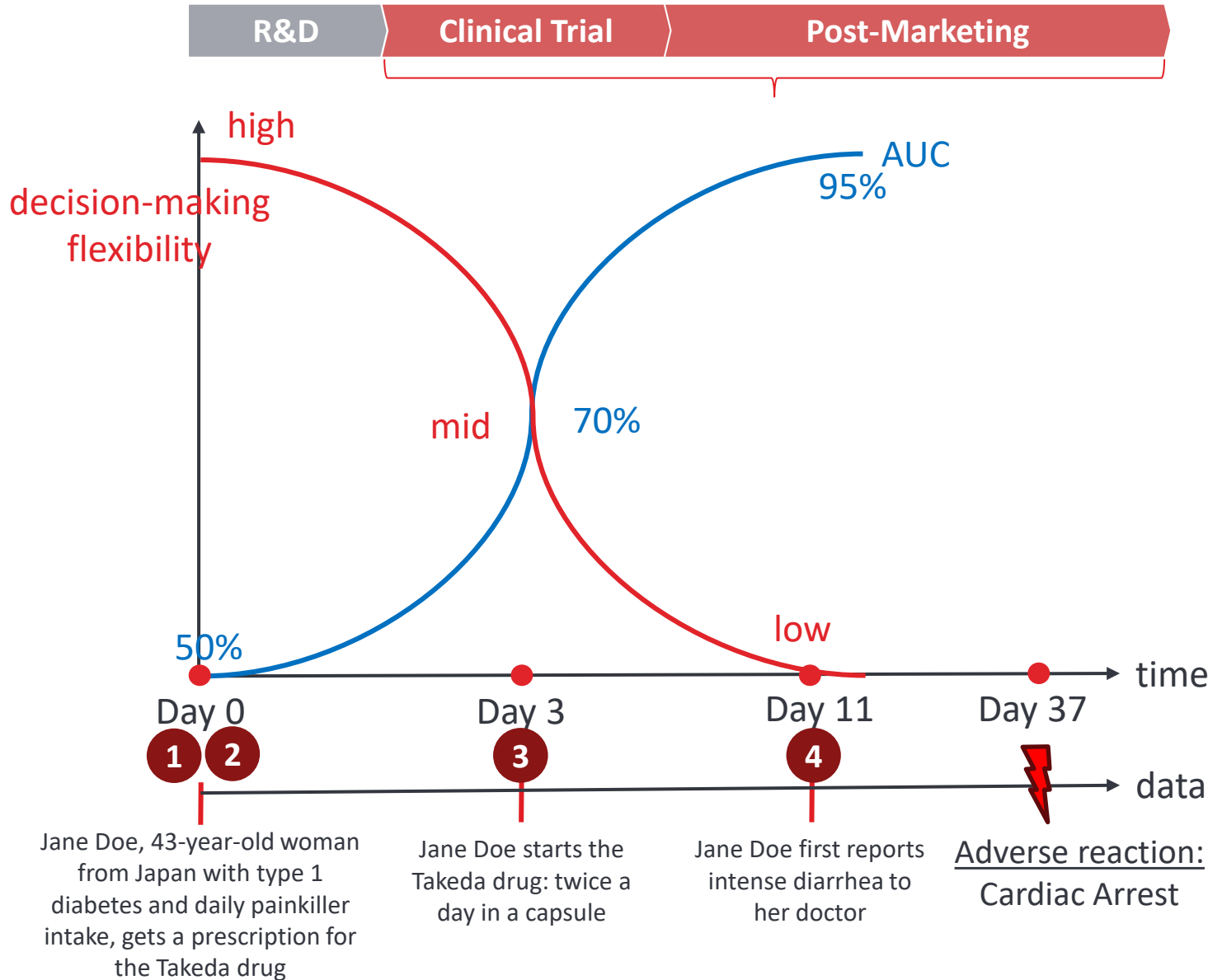
- Uric acid in the blood
- Adverse event: Steven Johnson Syndrome, Toxic Epidermal Necrolysis
- 56 out of 16393 patients faced this issue

Drug 3

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

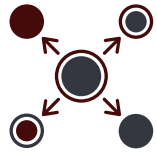
→ Very varied cases, drugs and patients

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

For any problem there is always a solution...



CHALLENGE



SOLUTION

"fancy" models used



IMPACT

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

PRE-PROCESSING

CAUSAL INFERENCE

PREDICTIVE MODELING

POST-PROCESSING

Product Demo – Predictive Modeling



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

- **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.

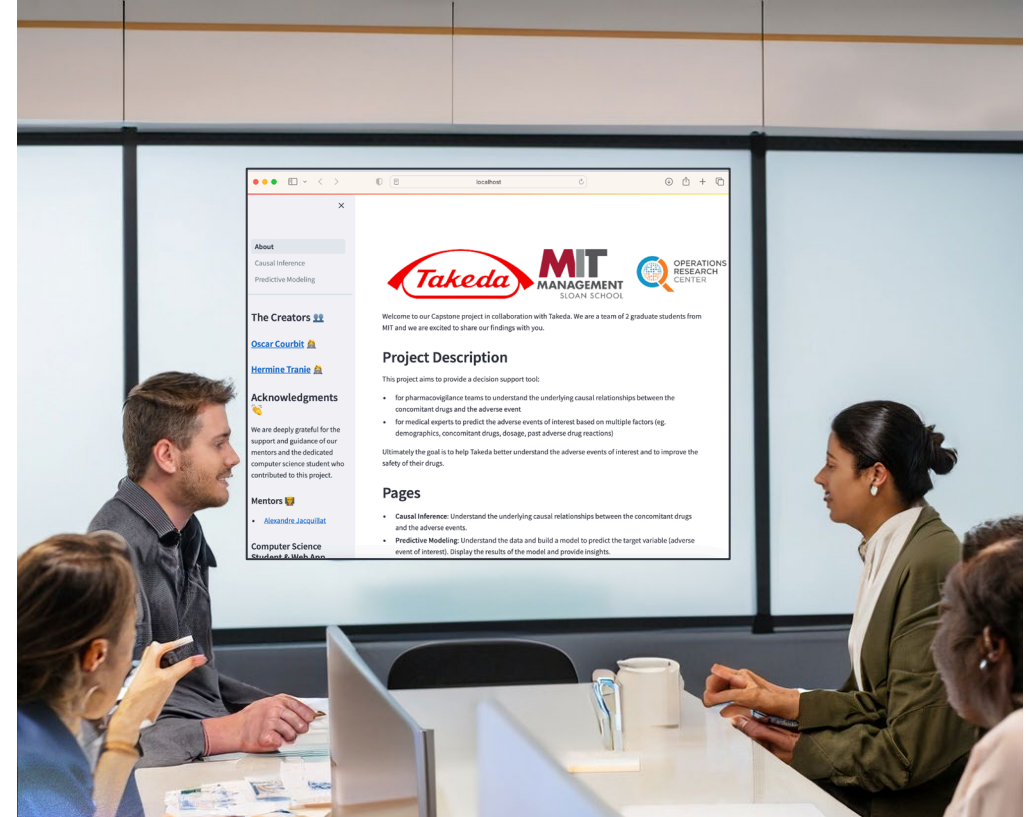
Transforming Pharmacovigilance: Bolstering Patient Safety and Paving the Way for Efficient, Data-Driven Decisions



BEFORE



AFTER



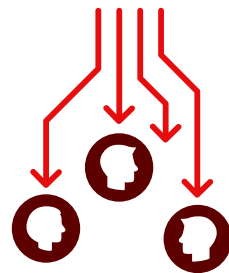


Next Steps and Future Work



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.

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



Better Health, Brighter Future