Machine Learning Model Development and Validation for Early Detection of Stiff-Person Syndrome Using Administrative Claims Data

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Introduction

- Stiff-Person Syndrome is a rare neurologic disorder characterized by rigidity, spasms, and overlapping features with conditions such as multiple sclerosis, Parkinson's disease, and anxiety disorders. These similarities create diagnostic complexity, leading to frequent misdiagnosis and **delayed recognition**.
- Research applying machine learning to Stiff-Person Syndrome diagnosis has been minimal, with only **one** prior study testing a machine learning model on the data of **less than one hundred** patients. This study seeks to advance that work by developing and testing a new Transformer-based algorithm on large-scale claims data and identifying the key clinical factors that differentiate Stiff-Person Syndrome from related conditions.

Objectives

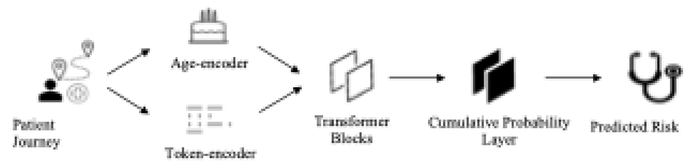
- Evaluate the performance of a Transformer-based machine learning model in identifying patients with Stiff-Person Syndrome using large-scale United States claims data.
- Identify key clinical features that differentiate Stiff-Person Syndrome from related neurologic and musculoskeletal disorders.
- Explore demographic characteristics and prescribing provider specialties associated with Stiff-Person Syndrome in real-world claims data.

Methods

- A retrospective study was conducted using the United States longitudinal administrative claims database, **Forian**, from 2017 to 2025. Two cohorts were created. The first included patients diagnosed with Stiff-Person Syndrome identified by ICD-10 code G25.82. The second was a comparator group of patients with conditions resembling Stiff-Person Syndrome, including Parkinson's disease and ankylosing spondylitis, while excluding any patients with an SPS diagnosis.
- To ensure data quality, patients were required to maintain continuous enrollment with claims activity every twelve months across consecutive two-year intervals and a minimum follow-up of two years. After applying these criteria, the final population included **2,933 patients** with Stiff-Person Syndrome and **108,708** with differential diagnoses.
- The **primary endpoint** was to evaluate the ability of a Transformer-based machine learning model to predict Stiff-Person Syndrome patients based on symptomology and time-based diagnostic events. Secondary objectives included identifying clinical features contributing to prediction, demographic characteristics, and provider specialties.

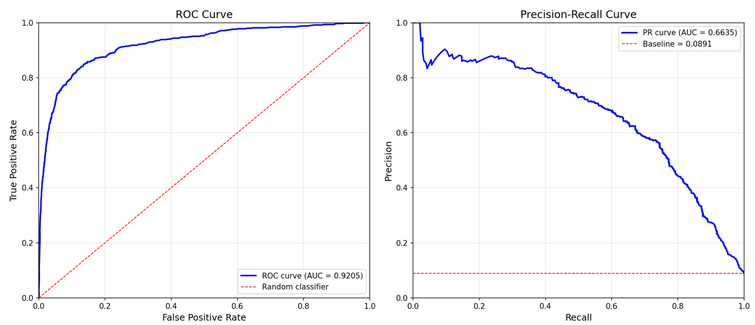
Methods (cont.)

- Model performance was assessed using the area under the receiver operating characteristic curve (AUROC) and the area under the precision–recall curve (AUPRC).
- Patient medical histories were represented as longitudinal sequences of diagnostic codes preceding the index date. These sequences trained the Transformer model to recognize temporal patterns and predict the likelihood of Stiff-Person Syndrome within a 60-month window. Model interpretability was achieved using integrated gradients to highlight clinical features relevant for earlier recognition.
- Model Architecture:



Results

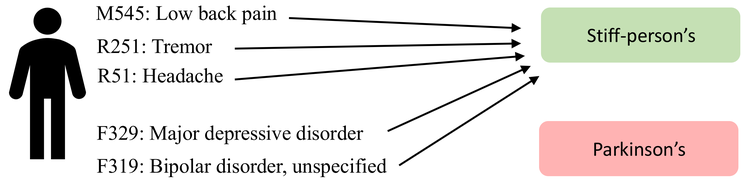
- The model achieved an **AUROC of 0.92** and an **AUPRC of 0.67** in highly imbalanced data, with positive samples accounting for **~ 9%**
- Performance remained stable even at lower prevalence thresholds, supporting robustness.



- AUPRC measures how well the model balances finding true cases (recall) while minimizing false positives (precision), which is especially important for rare diseases where the majority class can dominate traditional metrics. The high AUPRC demonstrates robust detection performance despite Stiff-Person Syndrome affecting only about nine percent of the cohort.

Results (cont.)

- Feature attribution analysis using integrated gradients identified musculoskeletal features such as muscle spasm and low back pain, psychiatric comorbidities such as bipolar disorder, and systemic comorbidities as key signals.



- Exploratory analyses showed that patients with Stiff-Person Syndrome had a lower mean age than comparators (58.7 vs. 71.8 years) and a more imbalanced male-to-female ratio (0.54 vs. 1.02). The top diagnosing specialties were neurology, internal medicine, and family medicine.

Conclusions/Implications

- This study demonstrates the potential of large-scale administrative claims data and machine learning for rare disease detection. The Transformer model achieved strong performance by industry standards and successfully identified both known and novel clinical features of Stiff-Person Syndrome. Early recognition of these symptom patterns could reduce the diagnostic delay faced by patients and reduce healthcare burden. The identification of neurology, internal medicine, and family medicine as key diagnosing specialties underscores the importance of collaboration between specialties and primary care to improve timely diagnosis and management of this rare neurologic condition.
- The study demonstrates an innovative**, scalable, and economically feasible** pathway for early diagnosis of Stiff-Person Syndrome by leveraging **easily accessible** claims data, offering a forward-looking framework that can be extended to **more rare diseases.**

Acknowledgments/Disclosure

- Special thanks to Ambit Inc. for providing free access to the Forian claims data used in this study.