Exploring Schizophrenia Treatment Pattern Based on Treatment Sequences Analysis through Temporal Clustering Method in a Japan Retrospective Claims Database

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BACKGROUND

Schizophrenia is affecting 0.56% of the Japanese population. The estimated annual burden exceeds 3.5 million yen per patient (approximately US$30,000).
Prescribing patterns are complex and characterized by treatment switching, discontinuation, relapse and poor adherence to antipsychotic medication.

OBJECTIVE

This study aims to improve the knowledge of schizophrenia treatment patterns in the real world, based on Japan's retrospective claims (JMDC) through a visual representation of Patients Treatment Sequences.

METHODS

12,000 patients taking at least one antipsychotic drug between 2009 and 2013 were selected from JMDC claims, an employment-based administrative database containing the medical and pharmacy claims from ten different payers.
The aim of this method is to perform a clustering of patients' profiles.

A temporal clustering method consists in three main steps:

- Treatment Sequences Alignment
- Hierarchical Agglomerative Clustering
- Graphical representation & Image Smoothing

RESULTS

Of the 23 treatments most frequently used, sulpiride was the most frequent first line treatment (Fig 5).

Patients taking sulpiride (first line) showed low persistence with a mean and median time to discontinuation of approximately 6 and 3 months, respectively. In subsequent lines, sulpiride was prescribed in combination with olanzapine.

Risperidone was the second most frequent first line treatment. Patients initiating risperidone presented a mean and median time to discontinuation of 7 and 3 months respectively.

STEP 1 TREATMENT SEQUENCES ALIGNMENT

Patients' treatment sequences present two dimensions: **temporal dimension and treatment information**. Thus, a pairwise match needs to be found between patients which includes the treatment information along with the temporal component. In this order, the data needs to be transformed using the Temporal Needleman Wunsch (TNW) algorithm.

- TNW was run with temporal treatment sequences as inputs (as shown in Fig 1)
- A Pairwise temporal sequence alignment performed to obtain the **similarity matrix.**
- The Similarity matrix was converted to a **distance matrix** representing pair distances of the treatment sequences.

Fig1: Treatment sequence temporal representation

Patient_ID	Treatment, duration (months)
Patient_1	T1,10.D,4.T2,12.T3,5

T1 : Treatment 1 **10** : 10 months D : Discontinuation

STEP 2 HIERARCHICAL AGGLOMERATIVE CLUSTERING (HAC)

- Clustering on the previous distance matrix using HAC with Euclidean Distance and Ward's Linkage Criterion.
- Automatic bootstrapping-based validation technique to select the best number of patients' profiles (clusters) based on several clustering indices like the Rand index, Jaccard index, Fowlkes & Mallows index and the Silhouette Coefficient.
- Identification of the best number of clusters: the best average score across all the clustering indices.

STEP 3 IMAGE PROCESSING ON THE CLUSTERED DATA

- Transformation of the data from table to image (Fig 2)
- Results classified by cluster index (Fig 3).
- Each cluster represents a patient profile (Fig 3).
- Image Smoothing to improve visibility (Fig 4).

Fig 2: Representation of treatment lines

Patient_ID	Treatment, duration (months)
Patient_1	T1,10.D,4.T2,12.T3,5
Patient_2	T1,5.T2,4.T4,16.D,6
Patient_3	T5,10.T6,21
Patient_4	T2,2.D,2.T2,2.T4,6.T7,19

Legend
T1 : Treatment 1
T2 : Treatment 2
.
.
.
T7 : Treatment 7
D : Discontinuation

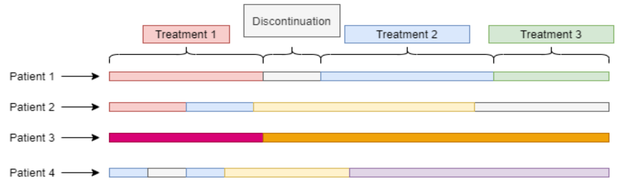


Fig 3: Clustered index

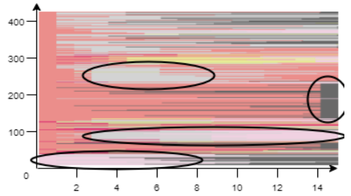


Fig 4: Image processing

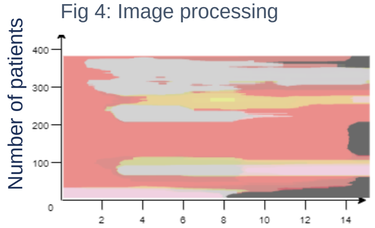
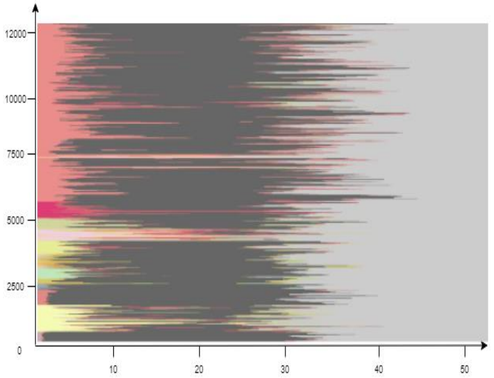
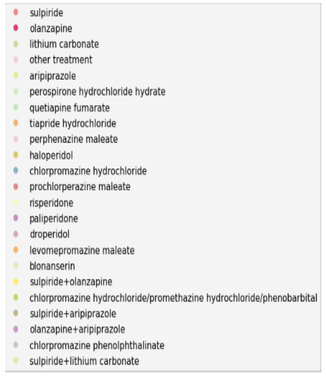


Fig 5: Image processing





CONCLUSION

Overall, patients with schizophrenia present high discontinuation and low persistence which can explain poor psychiatric response along with worsening symptoms in most of real-world cases.
Artificial Intelligence methods can provide a better RWE understanding of antipsychotic treatment sequences for these patients. This applied study demonstrates the good performance of combining Machine Learning & Image Processing techniques to reveal hidden patterns in real world tabular data, while presenting temporal correlations in an interpretable graphical format.