Identifying the treatment gap of undiagnosed tardive dyskinesia: an analysis of unstructured electronic health record data

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BACKGROUND

- **Tardive dyskinesia (TD)** is a severe and involuntary movement disorder, which is commonly associated with prolonged antipsychotic treatment.
- TD is likely underreported and misdiagnosed in real-world clinical practice.[1,2]
- Understanding the proportion of patients who may experience TD but receive no formal diagnosis could support the characterisation of patient populations that may benefit from novel therapeutic interventions, such as vesicular monoamine transporter type 2 (VMAT2) inhibitors.

- **Electronic health records (EHRs)** can be used to assemble large, naturalistic cohorts of patients who are representative of those receiving routine mental healthcare. EHRs typically include structured data on demographics, diagnoses and prescribed medication but most of the clinical information is stored in unstructured data fields that comprise documentation of clinical assessments and treatment.

STUDY AIMS

- Identify the number and proportion of patients with a history of antipsychotic treatment who
  - Have a recorded ICD diagnosis of TD in structured EHR data
  - Have no recorded ICD diagnosis of TD in structured EHR data, but evidence of clinical features of TD documented in unstructured EHR data

METHOD

Data source and cohort assembly

- A retrospective study using NeuroBlu database version 21R1.[3]
- The database contains de-identified EHR data recorded between 1999 and 2021 across 25 US mental healthcare sites.
- A cohort of patients treated with antipsychotic medication was assembled.

Identifying diagnosed tardive dyskinesia

- SQL was used to identify patients with ICD-codes mapped to TD (ICD-9 333.85, ICD-10 G24.01).

Identifying evidence of clinical features of tardive dyskinesia

- Clinical features of tardive dyskinesia documented within unstructured EHR data were extracted through manual review.
- A total of 25,376 unique text-strings which described psychomotor function as part of the mental state examination were reviewed.
- Text-strings which contained relevant key words were categorised as indicating a possible diagnosis of tardive dyskinesia.
- Here, features of tardive dyskinesia were defined using key words manually derived from the Abnormal Involuntary Movement Scale[4] and independently validated by a trained psychiatrist.

RESULTS

Overall cohort: patients treated with antipsychotics
N = 363,043

Patients with evidence of clinical features of TD documented in unstructured EHR fields
N = 4,243
mean [SD] age = 39.1 years [14.9], 41% male

Patients with an ICD diagnosis of TD in structured EHR fields
N = 116

Patients with evidence of clinical features of TD documented in unstructured EHR fields AND an ICD diagnosis of TD in structured EHR fields
N = 54

Of the 4,243 patients with evidence of clinical features of TD documented in unstructured EHR fields, < 1% also had an ICD diagnosis of TD recorded in structured EHR fields

The most frequently clinician-recorded features of TD were extremity movements and unspecified symptoms (Table 1, Figure 1).

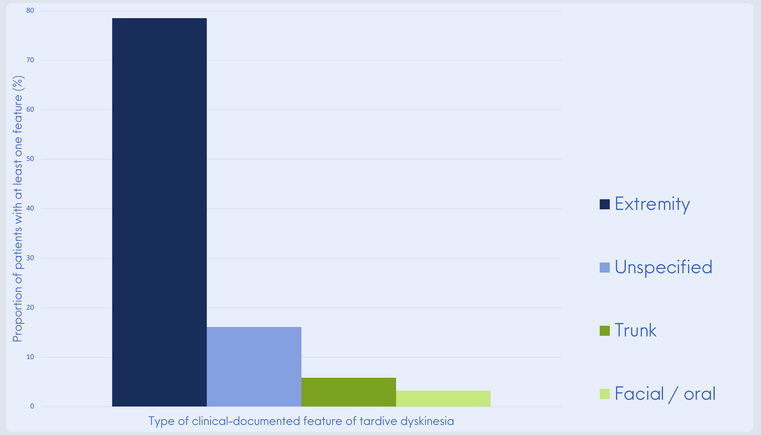

Figure 1. Proportion of patients with clinical features of tardive dyskinesia recorded in unstructured portions of the EHR. Each clinical feature was mapped to one of four categories of the AIMS scale.

Table 1. Number and proportion o patients with at least one clinical feature of tardive dyskinesia recorded in unstructured portions of electronic health records, grouped by type of feature.

Type of TD feature documented	Number of patients identified, n (%)	Example text-string documented in unstructured EHR
Extremity movements	3,329 (78.5)	"wringing of hands"
Unspecified movements	685 (16.1)	"tardive dyskinesia present"
Trunk movements	247 (5.8)	"hip gyrations", "rocking back and forth"
Facial / oral movements	135 (3.2)	"oral buccal smacking/puckering/chewing"

DISCUSSION

- Findings demonstrate that clinical features of TD may be frequently recorded by clinicians in unstructured EHR data but not be formally recorded as a diagnosis in structured fields.
- The lack of recording of a structured TD diagnosis in over 99% of patients with evidence of TD recorded in unstructured fields could represent a substantial missed opportunity for treatment.
- While involuntary facial and oral movements have been estimated to account for up to 60-80% of TD cases, our data suggest that broader features of a "tardive dyskinesia syndrome" may be frequently documented during clinical assessment.
- Alternatively, other motor symptoms, such as akathisia, Parkinsonian symptoms or tremor, could have been misattributed.
- The present study highlights a pressing need for clinicians to better recognise and diagnose TD to close the treatment gap and increase access to treatments for affected patients.

References

1. Brown P, Funk SC. Tardive dyskinesia: Barriers to the professional recognition of an iatrogenic disease. Journal of Health and Social Behavior. 1986 Jun 1:116-32.
2. Weiden PJ, Mann JJ, Haas G, Mattson M, Frances A. Clinical nonrecognition of neuroleptic-induced movement disorders: a cautionary study. Am J Psychiatry. 1987 Sep 1;144(9):1148-53.
3. Patel R, Wee SN, Ramaswamy R, Thadani S, Tandi J, Garg R, Calvanese N, Valko M, Rush AJ, Rentería ME, Sarkar J. NeuroBlu, an electronic health record (EHR) trusted research environment (TRE) to support mental healthcare analytics with real-world data. BMJ open. 2022 Apr 1;12(4):e057227.
4. Lane, R. D., Glazer, W. M., Hansen, T. E., Berman, W. H., & Kramer, S. I. (1985). Assessment of tardive dyskinesia using the Abnormal Involuntary Movement Scale. *Journal of Nervous and Mental Disease.*

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