

Natural language processing assisted chart review of patients with suspected or diagnosed clozapine induced myocarditis (CIM)

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Background

Clozapine-induced myocarditis (CIM) is a potentially fatal adverse drug reaction. It has an underestimated prevalence due to heterogeneous clinical presentations, and the underutilization of gold standard diagnostic interventions (Cardiac MRI)¹. Clinical investigations performed are heterogeneous, though electrocardiograms (ECGs), C-reactive protein (inflammatory marker) and troponin tests (cardiac damage marker), are commonly used and recommended for CIM monitoring. As there are no specific international classification of diseases (ICD) codes for CIM, definitive case identification for research purposes relies on clinical review of patient records. Natural language processing (NLP) can increase the efficiency of electronic chart reviews by identifying relevant notes containing information about clozapine side effects.

Study Objectives

1. To identify cohorts of patients with suspected and definitively diagnosed CIM
2. To characterize the demographic, diagnostic, and treatment-related characteristics of these patients
3. To quantify discrepancies between documented clinical suspicion/diagnosis of CIM and the presence of ICD diagnosis codes

Methods

- **Data Source:** Neuroblu (25r2) – a longitudinal de-identified EHR database for US psychiatric patients was used for the analysis.
- **Inclusion Criteria:** availability of clinical notes containing evidence of clozapine exposure and a clinical concern for CIM. No diagnostic restrictions were imposed.
- **Notes identification:** Unstructured notes were screened using keyword searching then processed by a transformer model (GLiNER-BERT). This model was fine-tuned for side effect recognition based on a training dataset of 11,408 annotated sentences from clinical notes. A team of psychiatrists annotated these notes. The model had an F1 score of 0.84 for the classification of drug side-effects.
- **Notes review:** Identified notes were manually reviewed by a psychiatrist to identify notes where the documenting clinician had documented either a suspicion for CIM or a confirmed diagnosis.
- **Additional extracted variables:** age, sex, race, psychiatric comorbidities, CIM diagnosis status, clozapine treatment decisions, indicators of CIM suspicion, investigations performed, evidence of valproate exposure.
- **Analysis method:** Descriptive statistics comparing diagnosed vs suspected CIM according to extracted variables.

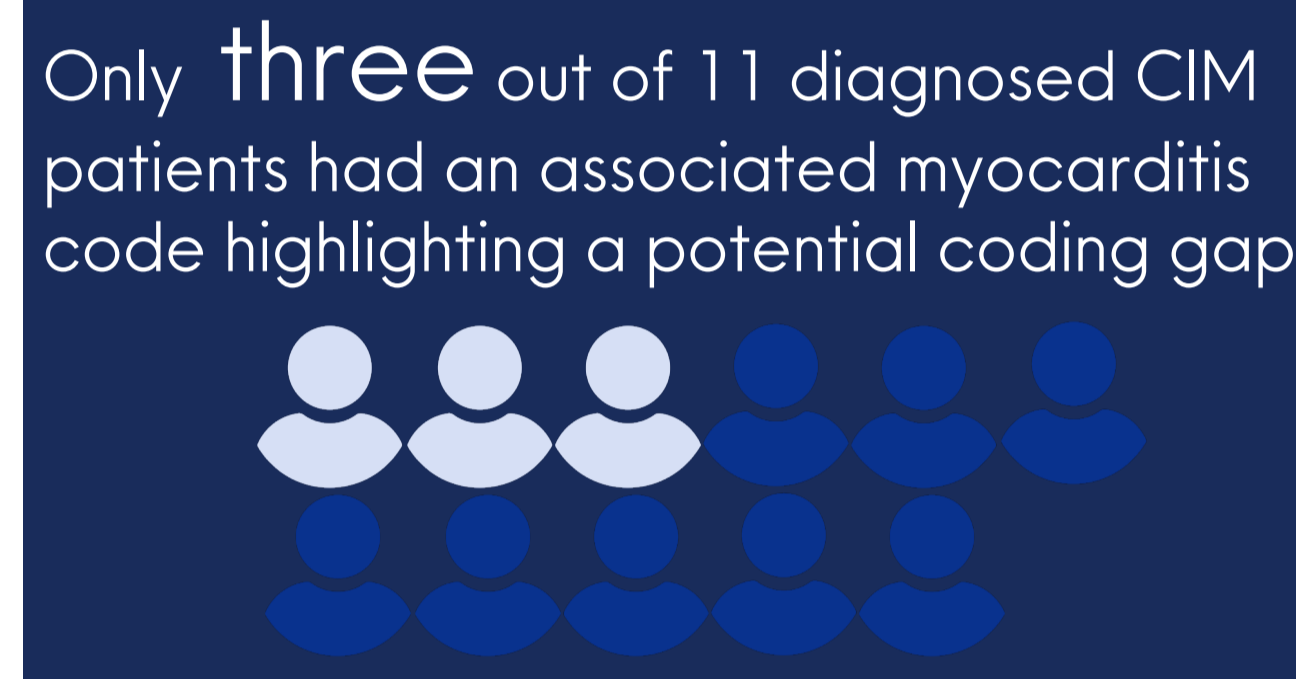
Results

48 patients were included in the final study cohort. 11 had a documented CIM diagnosis and 37 had suspected CIM.

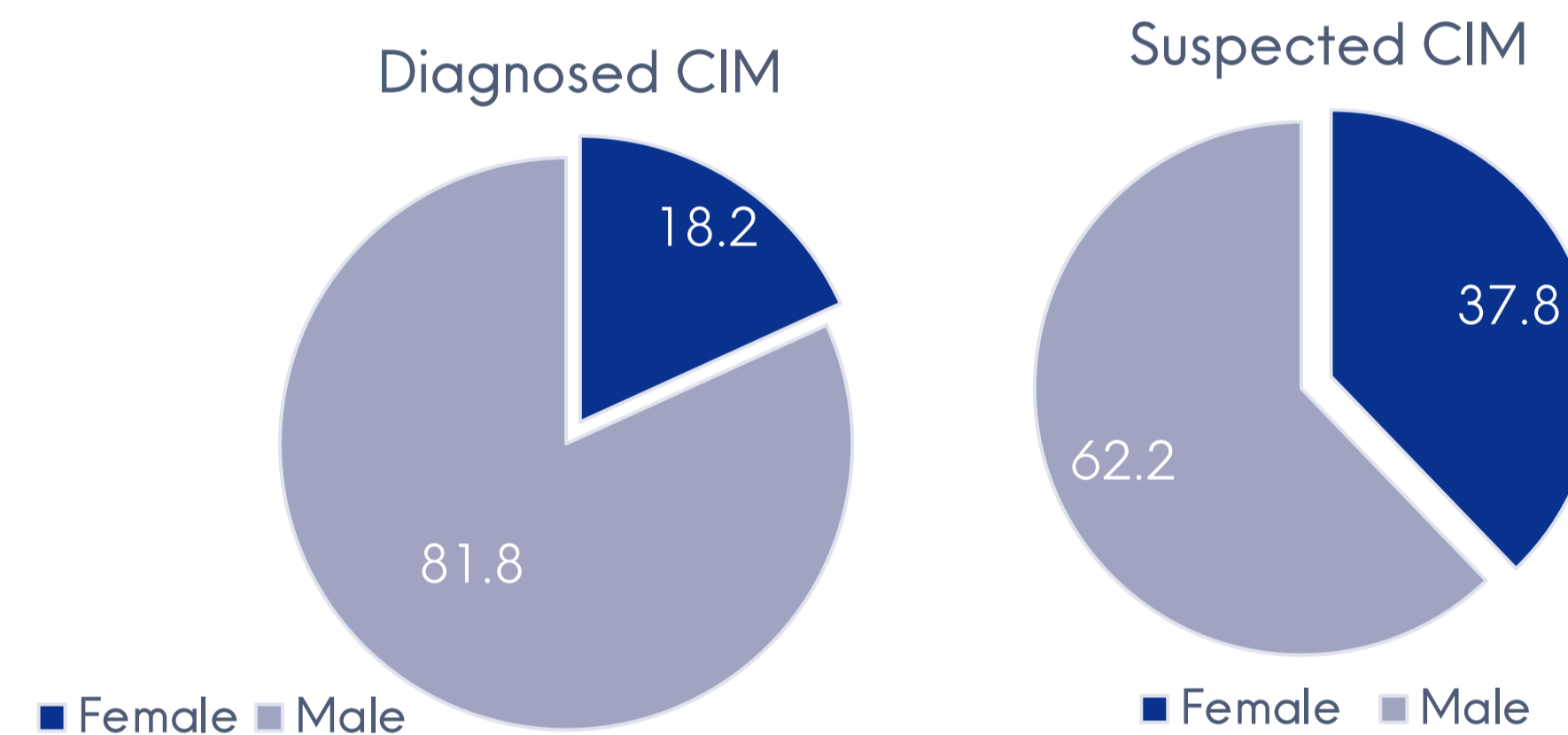
3/11 (27.3%) diagnosed CIM patients had an associated myocarditis code, while 5/37 (13.5%) suspected patients did.

All patients in the cohort had schizophrenia. The commonest comorbidities were mood disorders (67%), substance use disorders (56%), and anxiety disorders (44%).

Table 1 provides demographics for the total cohort and for diagnosed and suspected CIM patients.



The male:female ratio for CIM cases was 4.5:1



Diagnosed patients tended to be older, male, and African American.

Table 1: Cohort Demographics

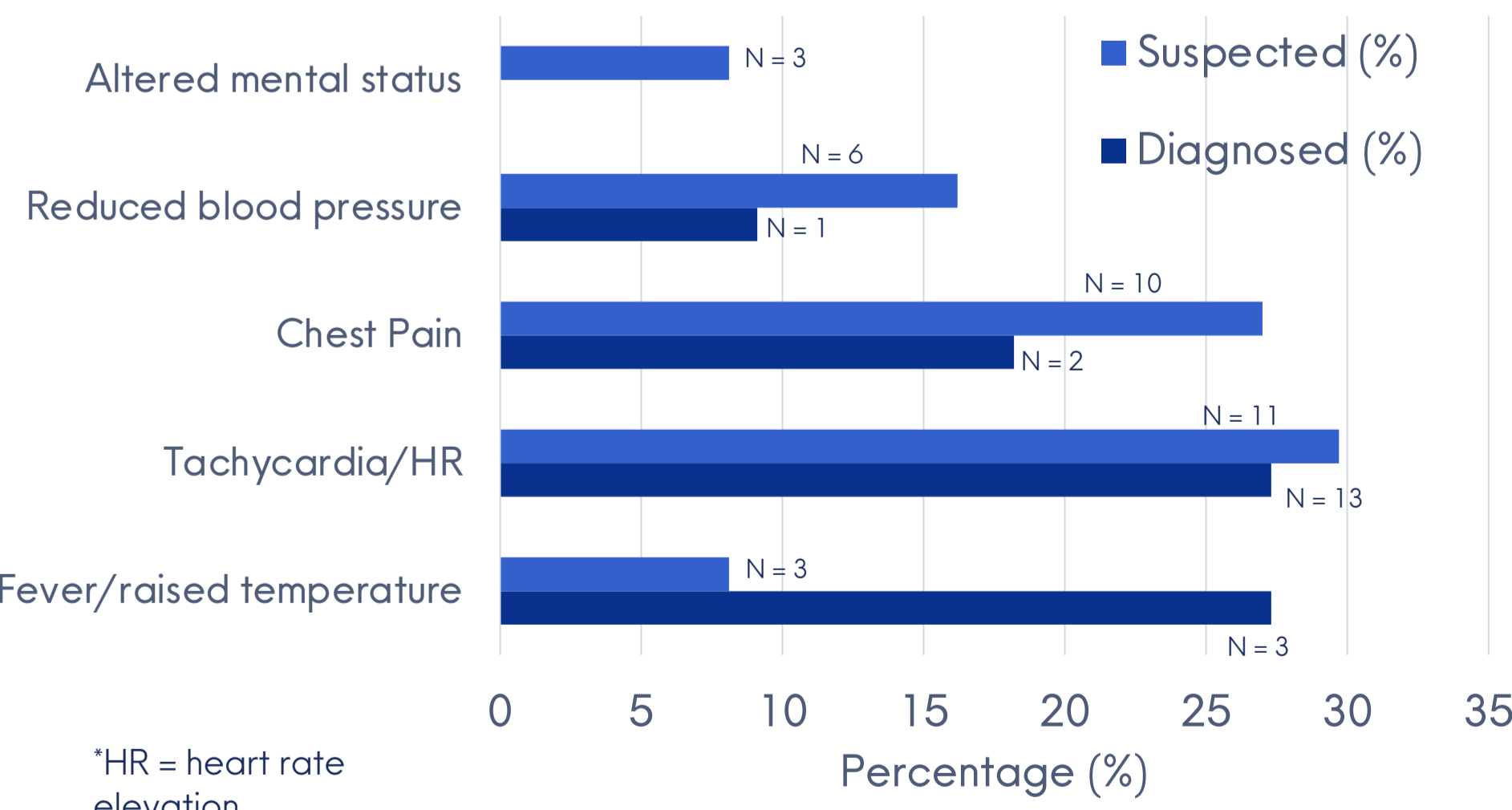
	Diagnosed (n=11)	Suspected (n=37)	Total (N=48)
Mean age (SD)	43.9 (13.0)	38.4 (13.2)	39.6 (13.2)
Sex			
Female	2 (18.2%)	14 (37.8%)	16 (33.3%)
Male	9 (81.8%)	23 (62.2%)	32 (66.7%)
Race			
Black or African American	7 (63.6%)	21 (56.8%)	28 (58.3%)
White	2 (18.2%)	4 (10.8%)	6 (12.5%)
Asian	0 (0.0%)	6 (16.2%)	6 (12.5%)
Other Race	2 (18.2%)	3 (8.1%)	5 (10.4%)
Unknown	0 (0.0%)	3 (8.1%)	3 (6.25%)

Chest pain and raised heart rate were the primary signs/symptoms that drove concern for CIM in suspected and diagnosed patients.

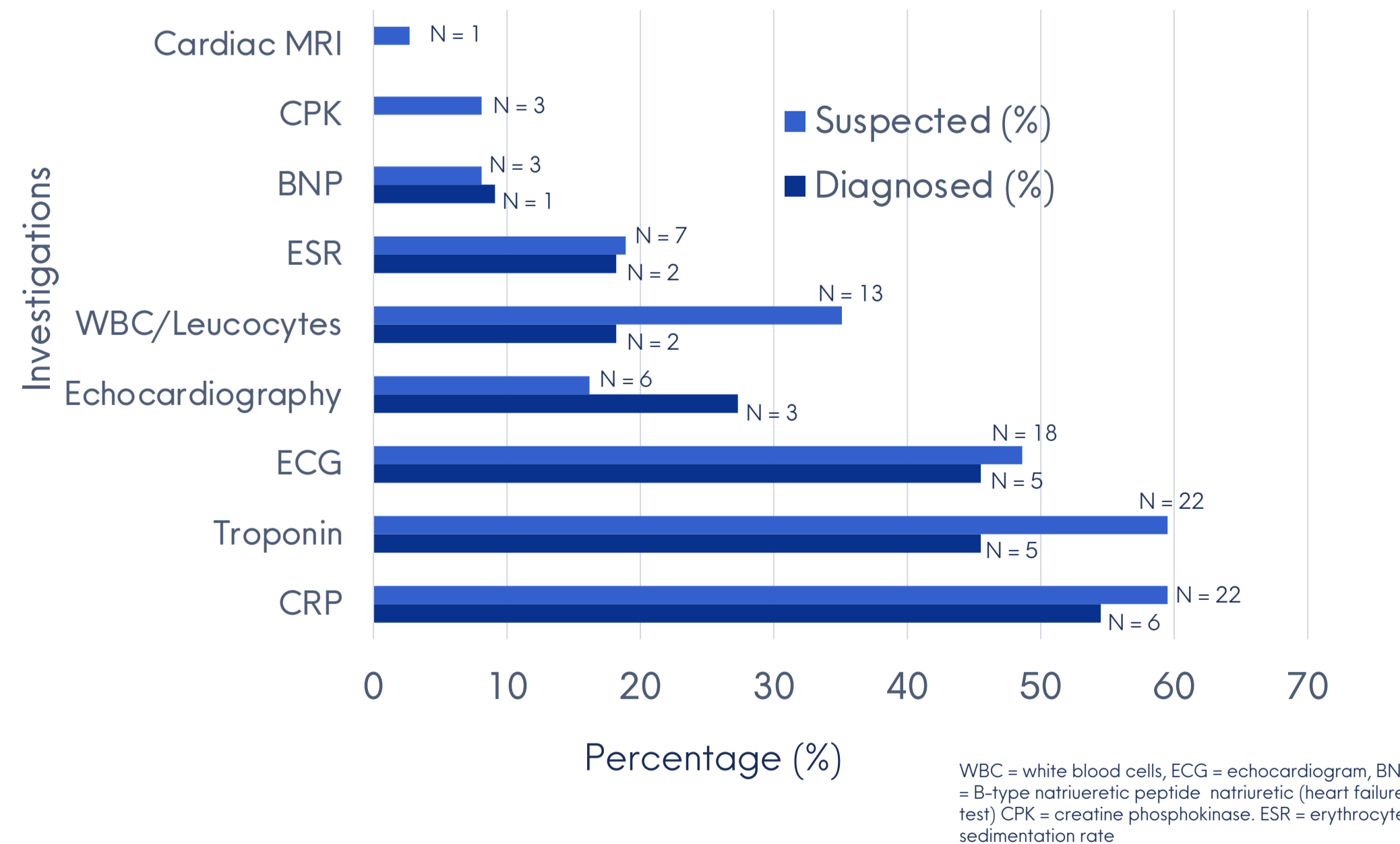
No diagnosed CIM cases had documented cardiac MRI use. CRP and troponin remained the primary investigations in both groups

Clozapine is stopped at higher rates in diagnosed CIM. Recent or concurrent sodium valproate exposure occurred at higher rates in diagnosed patients, and it is a known risk factor for CIM²

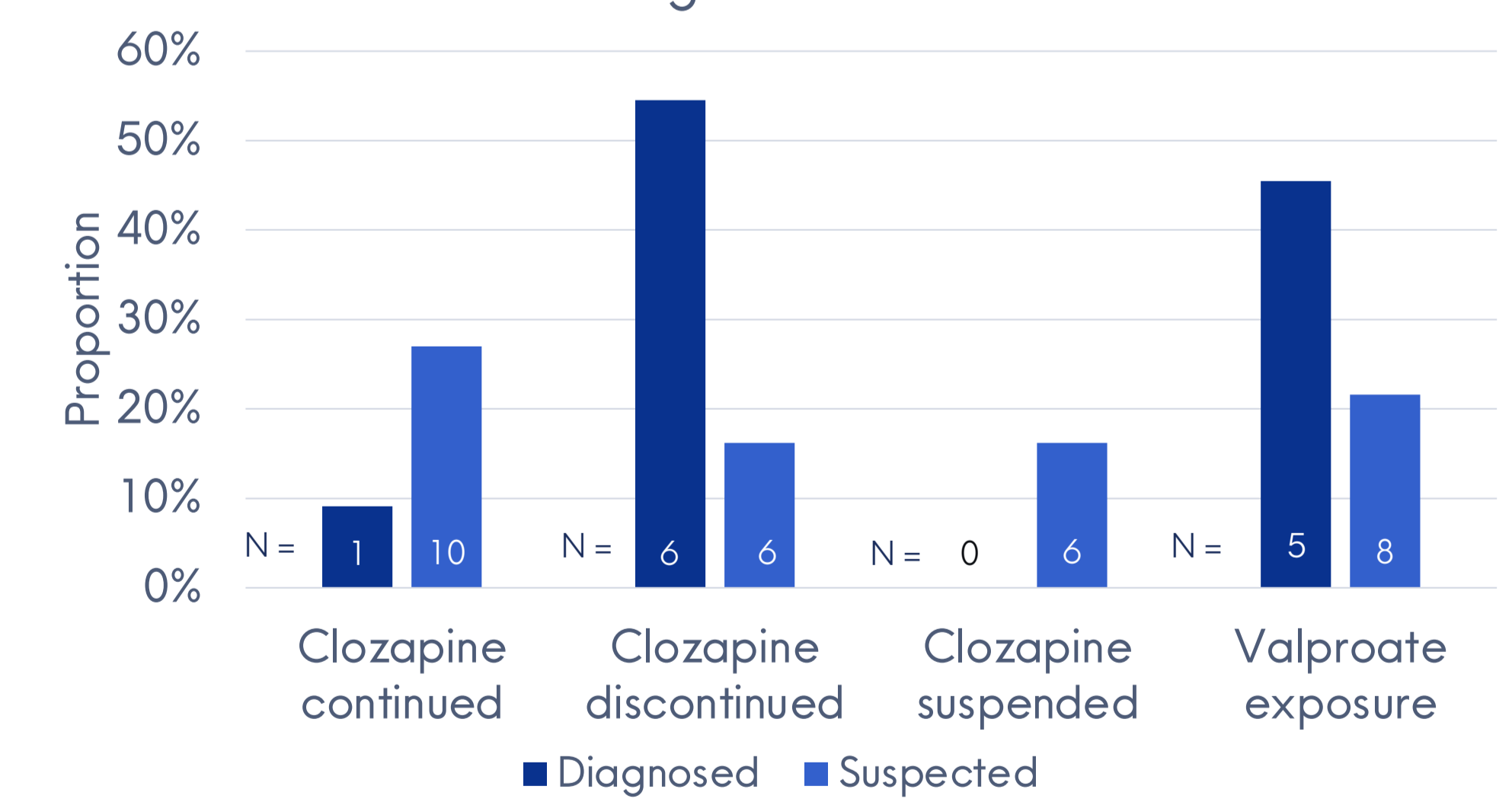
The five commonest signs and symptoms that caused concern for CIM



Investigations performed in suspected versus diagnosed CIM patients



Treatment correlates of suspected vs diagnosed CIM



Limitations

1. This study is limited by a small sample size and a purely descriptive analysis, which prevents firm conclusions from being made about the relationship between study variables
2. This study only used specialist psychiatric EHR data so it likely underestimates the presence of CIM diagnoses, ICD codes, and advanced investigations (such as cardiac MRIs), which may have occurred in different healthcare settings.
3. As the analysis focuses on clinical documentation, observed signs and symptoms associated with CIM may not represent the full spectrum of symptomatology
4. Finally, because some suspected CIM patients may still be undergoing cardiac investigation, definitive CIM diagnoses might only be captured in future records that are currently unavailable for analysis.

Conclusions

1. There is preliminary evidence for a diagnostic coding gap for confirmed CIM cases

2. NLP methods are useful for identifying rare and poorly coded disorders

3. Gold standard investigations for CIM are possibly underused which may lead to misdiagnosis and premature treatment cessation

References

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2. Vickers M, Ramani V, Malacova E, Eriksson L, McMahon K, Moudgil V, et al. Risk factors for clozapine-induced myocarditis and cardiomyopathy: a systematic review and meta-analysis. *Acta Psychiatrica Scandinavica*. 2022;145(5):442-55.

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