



# Incidence and Management of Clozapine-Induced Myocarditis in a Large Tertiary Hospital



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## Background

- Clozapine is an effective antipsychotic agent that is reserved for the management of treatment-resistant schizophrenia
- Clozapine is associated with severe adverse events, including myocarditis
- Mechanism is postulated to be an Type I hypersensitivity (up to 66% present with eosinophilia)
- The reported incidence ranges from 0.06% to 3.88%
- The purpose of this study is to evaluate the incidence and management of clozapine-induced myocarditis at St Paul's Hospital (SPH)

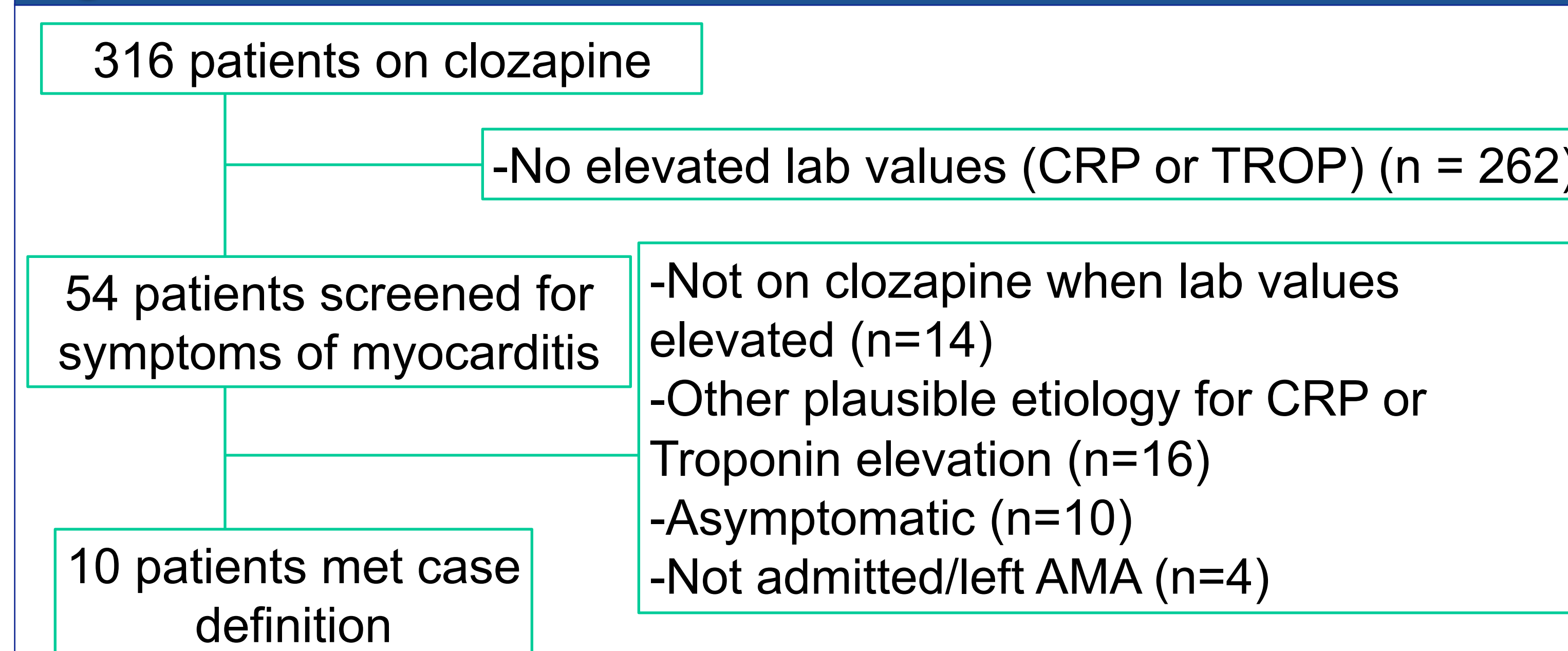
## Objectives

- **Primary:**
- To determine the incidence of clozapine-induced myocarditis at SPH and compare that to what is described in the literature
- To describe patient outcomes after clozapine-induced myocarditis
- **Secondary:**
- To determine potential risk factors for clozapine-induced myocarditis
- To determine common management approaches for clozapine-induced myocarditis

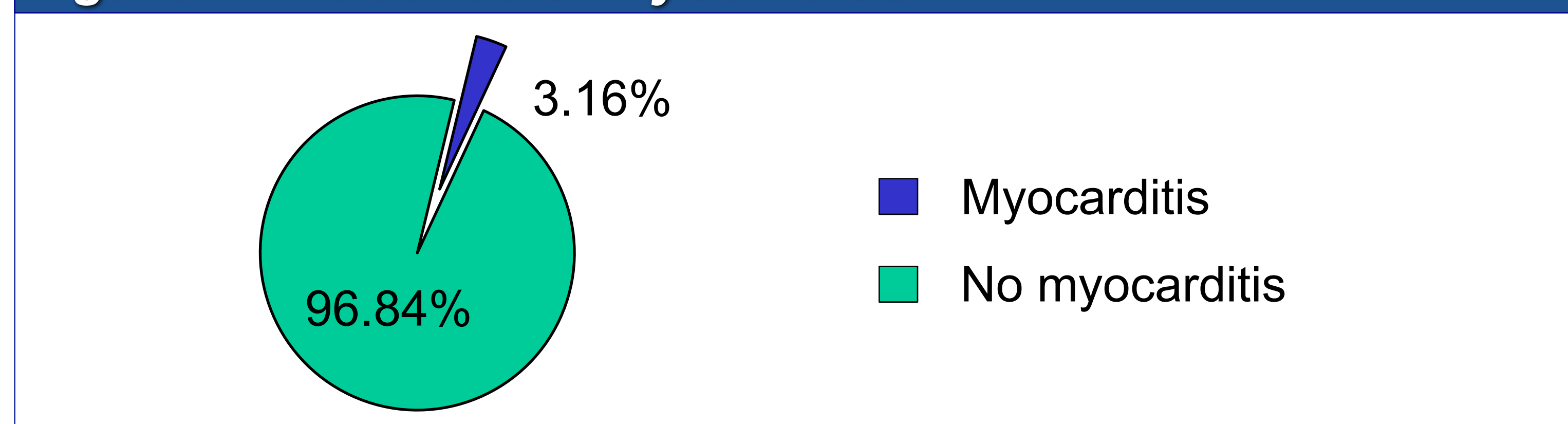
## Methods

- **Design:** Retrospective review
- **Population:** Adult patients on psychiatric units on clozapine at SPH between January 1, 2010 and July 31, 2016
- **Analysis:** Descriptive statistics
- **Case definition of clozapine-induced myocarditis:** At least 1 of the following signs or symptoms:
  - Lightheadedness with postural BP change or resting SBP < 100mmHg
  - Fatigue with ↓ exercise tolerance
  - Chest pain/discomfort/pressure
  - Palpitations with HR > 100 bpm or > 30 bpm above baseline
  - SOB
  - Peripheral edema
  - Fever
- **AND** Elevation in high sensitivity trop T (>14ng/L) OR trop I (>0.05mcg/L) OR CRP >50mg/L, in the absence of alternative plausible etiologies

### Figure 1: Patient Flow Chart



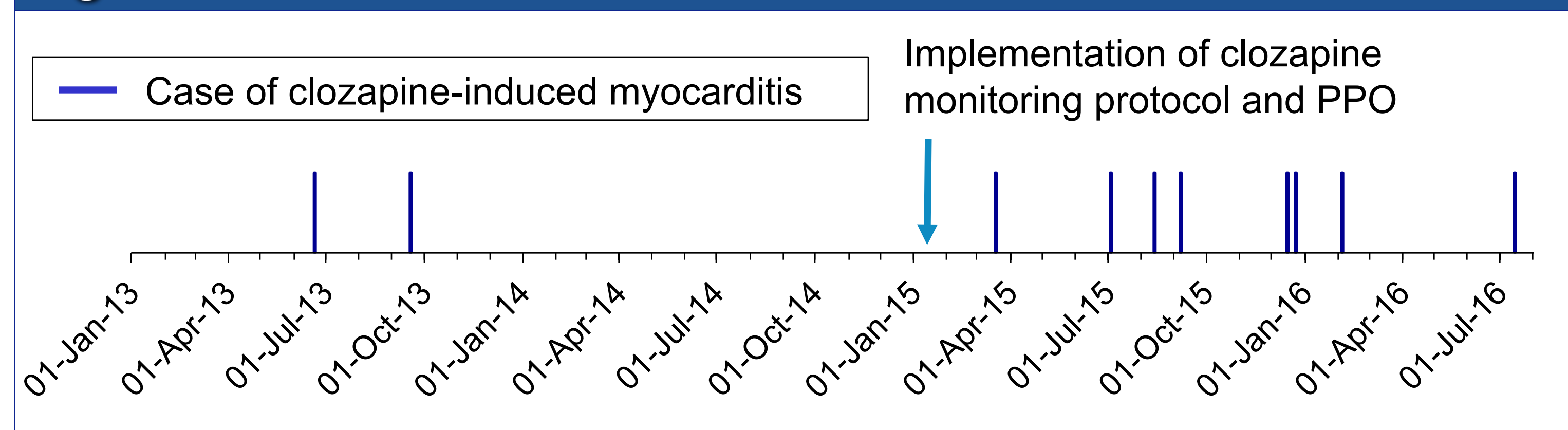
### Figure 2: Incidence of Myocarditis



### Table 1: Demographic Characteristics of Cases (N = 10)

Median age [y, (range)]	48.5 (26-57)		
Male Sex (%)	70		
Median BMI [BMI (range)]	28.5 (19.8-35.7)		
Ethnicity	60% Caucasian		
History of illicit drug use:	7 (70%)		
<b>Concomitant Meds</b>		<b>Comorbidities</b>	
Other antipsychotic	80%	Dyslipidemia	50%
Divalproex	50%	HCV	30%
Benzodiazepine	20%	HTN	20%
Lithium	10%	T2DM	10%
Gabapentin	10%	History of ACS	10%
		HIV	10%

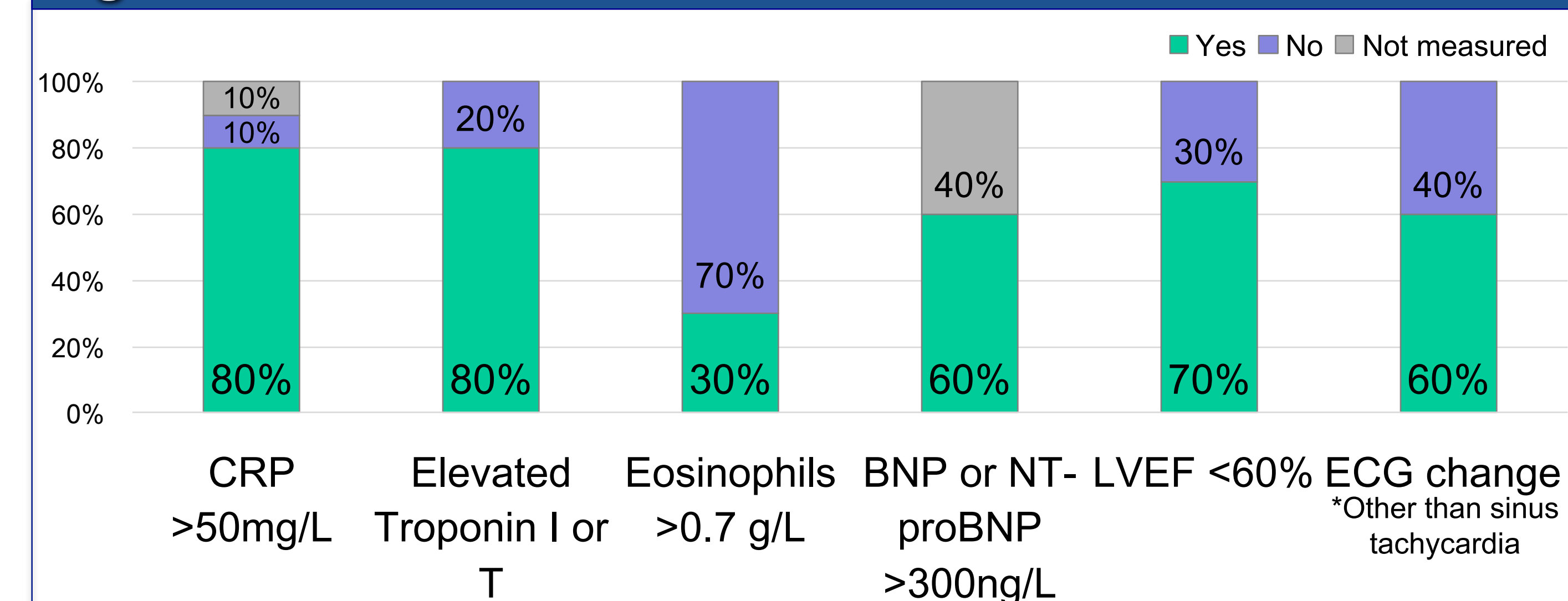
### Figure 3: Timeline of Events



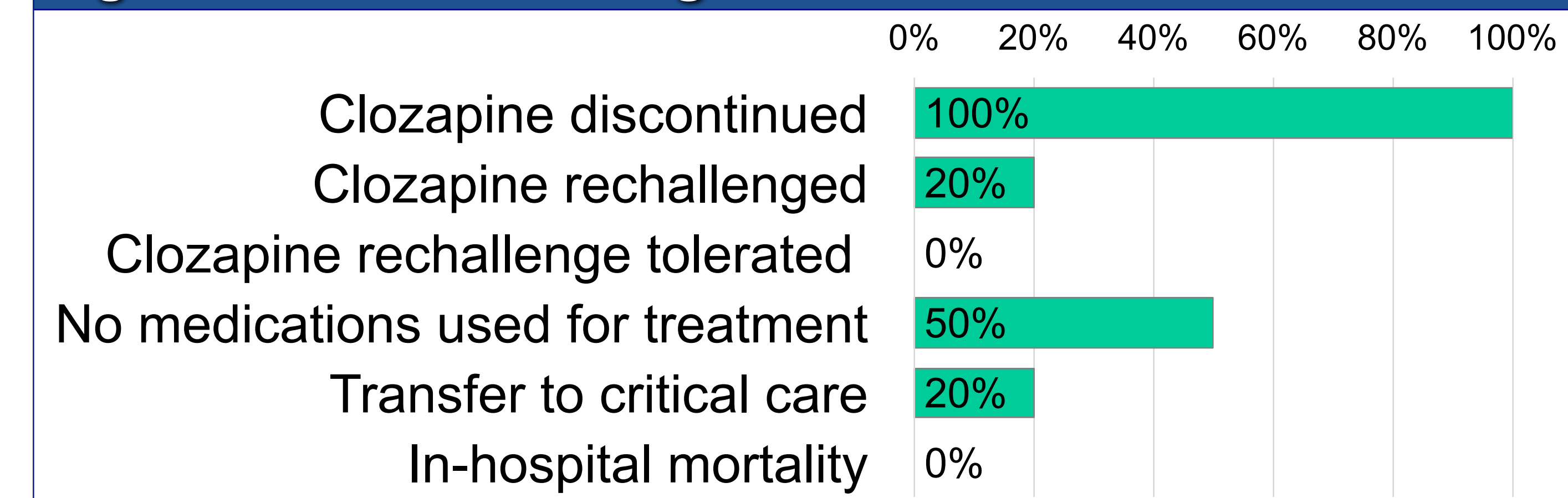
### Table 2: Characterization of Clozapine Use

Clozapine dose at onset of suspected myocarditis [mg, (range)]	200mg (100mg-550mg)
New clozapine starts: n = 9 <sup>^</sup>	
Initial dose (mg)*	12.5 (12.5-25)
Dose titration (mg/d)*	11.31 (5.9-25)
Time to onset of suspected myocarditis (days)*	16 (10-22)
*Data presented in median (range)	
<sup>^</sup> 1 patient was on clozapine prior to admission, at 450mg/d, which was increased to 550mg/d before onset of signs and symptoms of myocarditis	

### Figure 4: Lab Values and Cardiac Tests



### Figure 5: Patient Management and Outcomes



## Limitations

- Retrospective study; post discharge data not available
- Lack of generally accepted diagnostic criteria
- Logistic regression not completed due to small number of cases

## Conclusions

- The incidence of clozapine-induced myocarditis at SPH was 3.16%, within range of what has been reported in the literature
- Most cases occurred after implementation of a clozapine monitoring protocol and pre-printed order
- The mortality rate was 0% and symptoms were managed without medications in 50% of patients
- Additional research is necessary to further elucidate potential risk factors for this adverse event