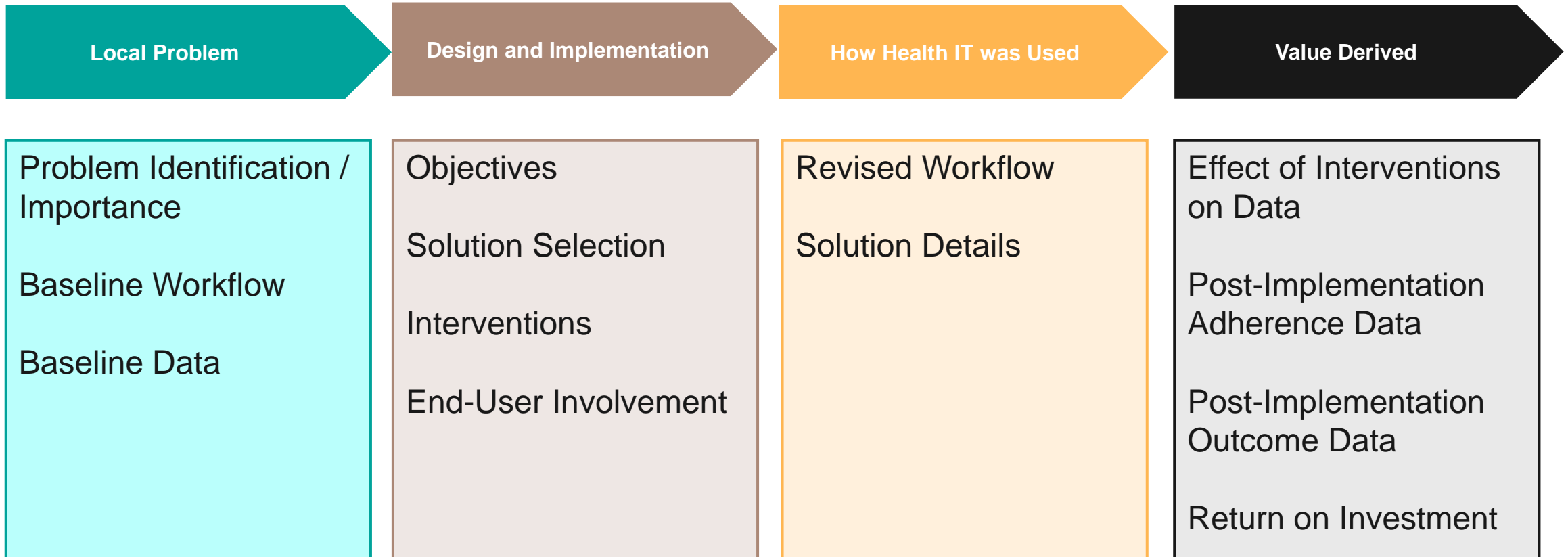


# 1

## Monitoring Protocol for Clozapine-induced Myocarditis

# Agenda



## Overview of Clozapine



- 25-30% of all individuals with schizophrenia meet criteria for treatment resistance (Remington 2010)
- Clozapine is the only antipsychotic with proven efficacy (Remington, Addington et al. 2017)
- Substantial side-effects

Side Effect	Prevalence
Agranulocytosis	Rare (<1%)
Constipation	60%
Myocarditis	<5%

- CAMH houses the largest clozapine clinic in North America (~750 patients)
- Goal to double volume over a 5-year period

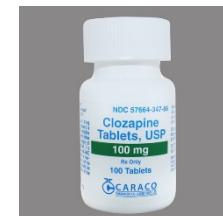
## Problem Identification

### Problem Identification

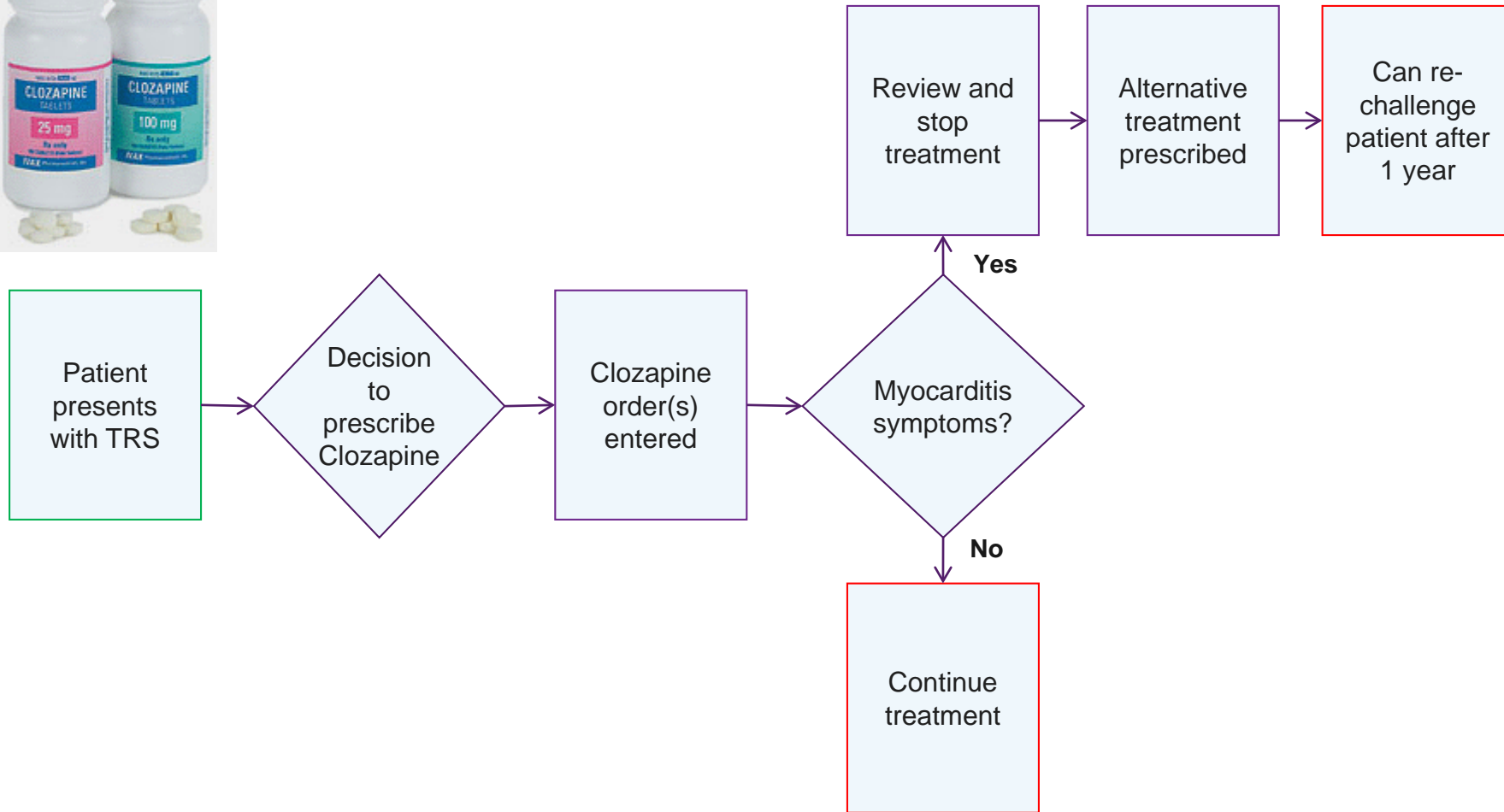
- Clinical symptoms of myocarditis noted in patients treated with clozapine
- An expert was consulted who determined that the cause was myocarditis
- Agranulocytosis is the only standard monitoring for clozapine treatment

### Why is this Important?

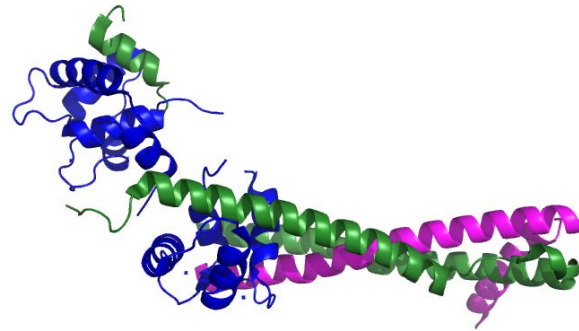
- Clozapine-induced Myocarditis is a **potentially fatal yet likely under diagnosed complication of Clozapine therapy**
  - Incidence estimated ~ 3%
  - Develops within the first 4 weeks of Clozapine initiation and titration
  - Hypersensitivity reaction with a fatality rate of **10%**



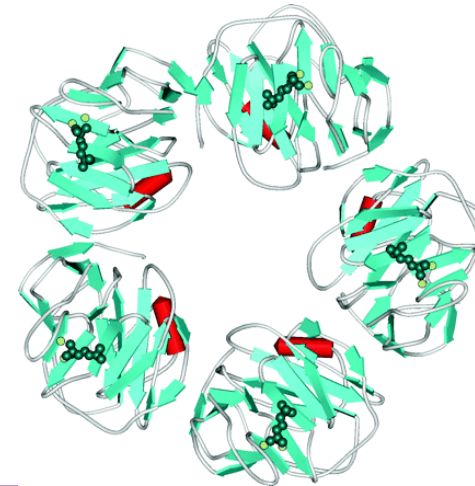
# Baseline Workflow



# Myocarditis Monitoring



Cardiac Troponin Positive



C-Reactive Protein > 50

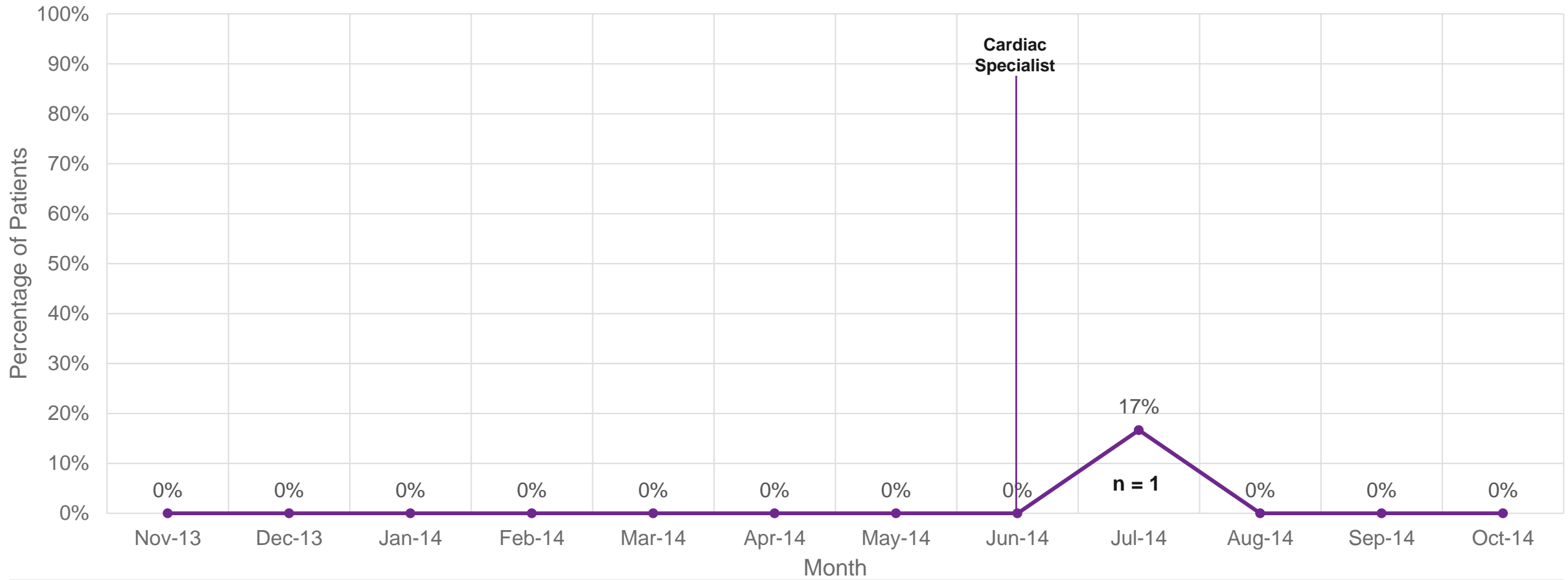


Suspected myocarditis

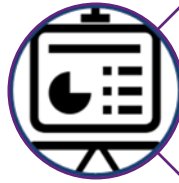
# Baseline Data

	<b>Nov 2013 – Oct 2014</b>
Myocarditis Monitoring Protocol	4.2%

## Clozapine-naïve Patients with Myocarditis Monitoring Protocol



## Objectives



Standardize myocarditis monitoring protocol for Clozapine-naïve patients



Increase compliance to myocarditis monitoring protocol



Discontinue Clozapine for patients showing warning signs of myocarditis



Streamline ordering process to save clinician time and prevent errors



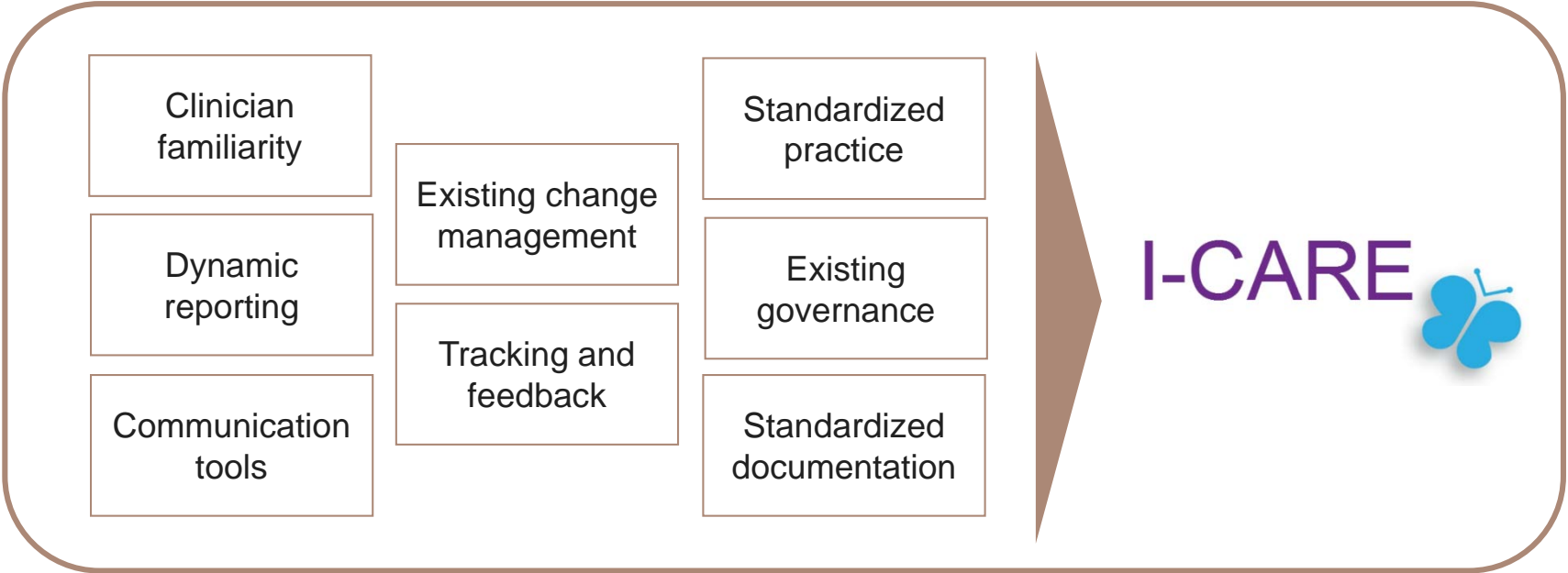
# Solution Selection

CAMH identified a method to increase myocarditis monitoring for Clozapine patients.

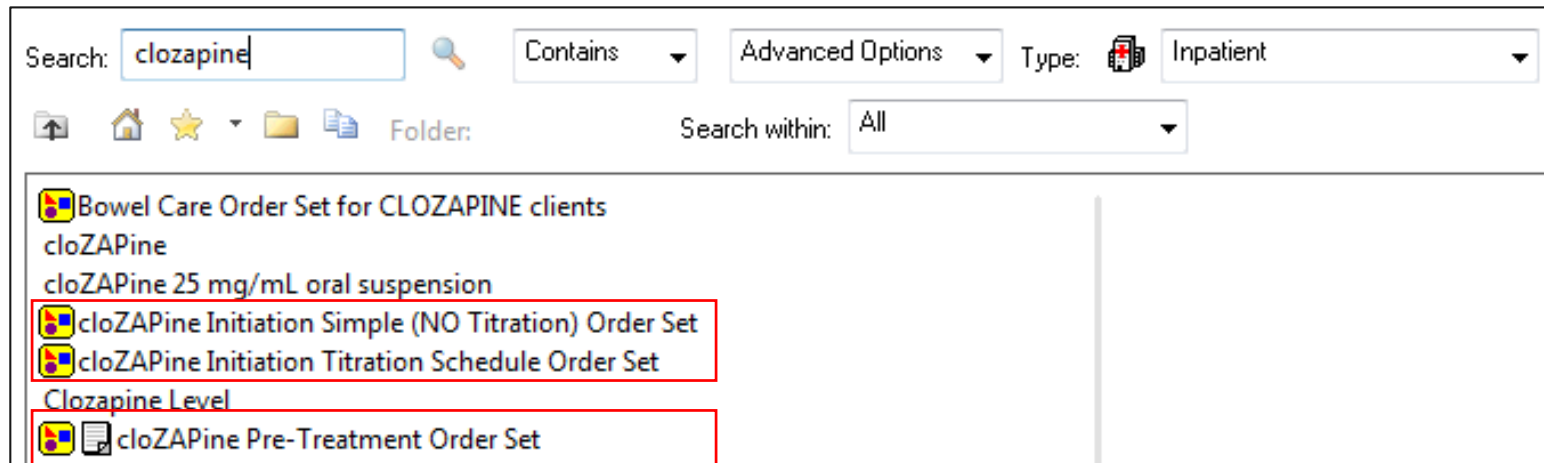
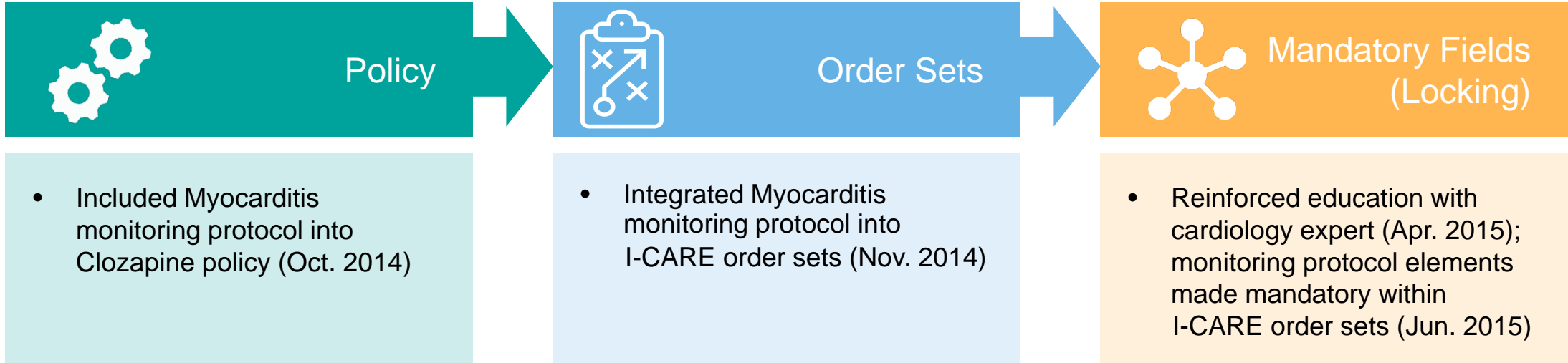


The implementation of I-CARE provided an opportunity to standardize care through order sets.

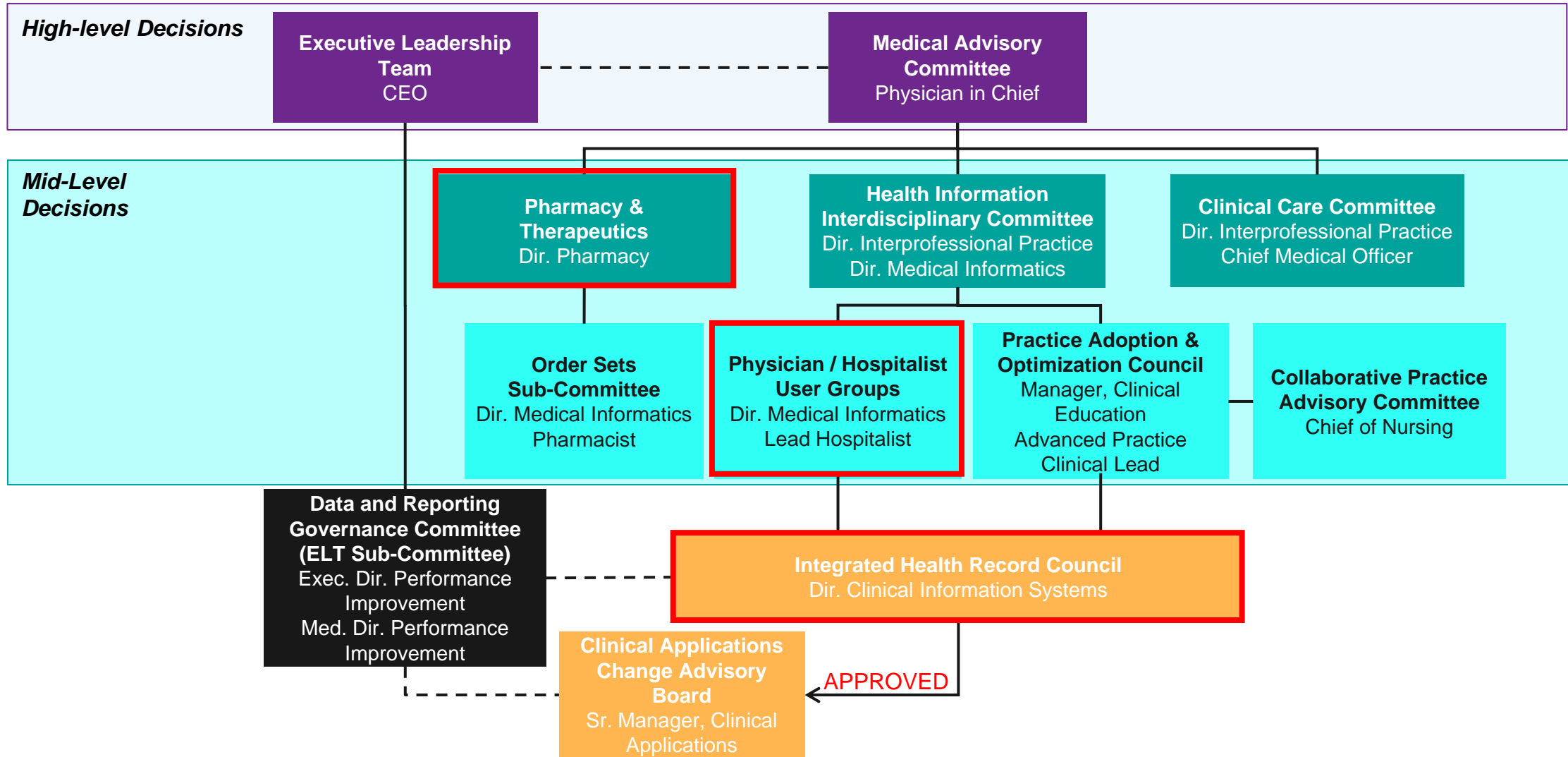
-Decision to standardize practice through order sets was made through the Hospitalist User Group and the Pharmacy and Therapeutics Committee



# Interventions



# Strategic Governance



## End-User Involvement

### Integrated Health Record Committee

- Chairs: Dir. Interprofessional Practice, Dir. Medical Informatics
- Includes clinicians and other stakeholders
- Initial approval of need

### Hospitalist User Group

- Chair: Medical Head, Hospitalist Services
- Developers and subject matter experts for Clozapine Order Sets
- Representation from physicians, nurses, Pharmacy, Professional practice, and Health Records

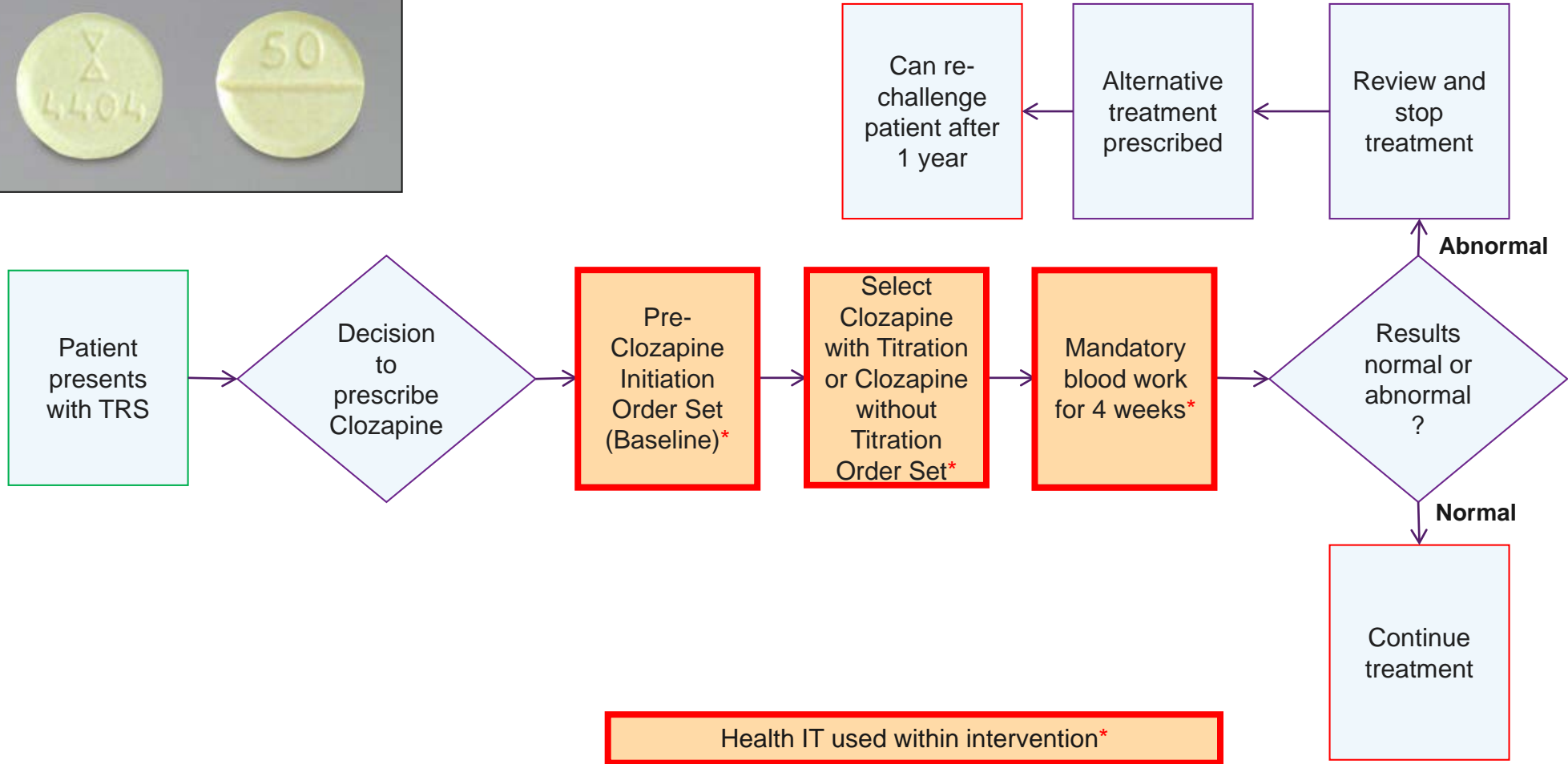
### Physician User Group

- Chair: Chief Medical Information Officer
- Representation of front-line physicians
- Contains 15 physicians from throughout CAMH

### Pharmacy & Therapeutics

- Co-chairs: Appointed Physician and Dir. Pharmacy
- Owners and approvers of Order Set
- Includes a minimum of 6 physicians, 4 pharmacists

# Revised Workflow



# Mandatory Monitoring Protocol

### Pre-initiation

- Baseline ECG, CRP, and Troponin
- Identification of pre-existing cardiac disease

cloZAPine Pre-Treatment Order Set (Initiated Pending)			
Assessment & Monitoring			
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Height	T;N, Routine, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Weight	T;N, Routine, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Circumference- Waist (Waist Circumference)	T;N, Routine, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Blood Pressure	T;N, Routine, Daily
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Heart Rate (Pulse)	T;N, Routine, Daily, Brachial
Laboratory Services			
To enter lab orders for Diabetic client/patients, please select the Metabolic Monitoring Order Set from the Assessment & Monitoring category.			
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	CBC	T;N, Whole Blood, Stat Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Glucose Fasting	T;N, Plasma, Stat Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	AST	T;N, Serum, Stat Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	ALT	T;N, Serum, Stat Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Lipid Panel	T;N, Serum, Stat Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Alkaline Phosphatase (ALP)	T;N, Serum, Stat Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Hemoglobin A1c (HbA1C)	T;N, Whole Blood, Routine Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	C-Reactive Protein (CRP)	T;N, Serum, Routine Collect, Once
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Troponin I (High Sensitivity)	T;N, Serum, RT Collect, Once
Diagnostic Services			
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Electrocardiogram (QS) (ECG (QS))	T;N, Routine, Reason for ECG: Pre Clozapine
<input checked="" type="checkbox"/>	<input checked="" type="checkbox"/>	Electrocardiogram (CS) (ECG (CS))	T;N, Routine, Reason for ECG: Pre Clozapine
<input type="checkbox"/>	<input type="checkbox"/>	Electroencephalogram- Standard (QS) (EEG Standard (...))	T;N, Routine
<input type="checkbox"/>	<input type="checkbox"/>	Electroencephalogram- Standard (CS) (EEG Standard (...))	T;N, Routine

Troponin lab test

CRP lab test

# Mandatory Monitoring Protocol

## Post-initiation

- Weekly clinical assessments
- CRP and Troponin monitoring x 4 weeks
- Regular Agranulocytosis monitoring

Component	Status	Dose ...	Details	Order Com...
<b>cloZAPine Initiation Simple (NO Titration) Order Set (Initiated Pending)</b>				
<b>Assessment &amp; Monitoring</b> Before prescribing, the MD must receive confirmation from CSAN that the client/patient has been approved to receive cloZAPine. The client/patient must have an active CSAN number before the first prescription is entered. Contact the cloZAPine Program Site Coordinator or phone CSAN at 1-800-267-2726. See cloZAPine policy section 6.2.				
<input type="checkbox"/>			Vital Signs Order Set	
<input type="checkbox"/>			Metabolic Monitoring Order Set	
<input checked="" type="checkbox"/>			Bowel Care Order Set for CLOZAPINE clients	Initiated Pen...
<input checked="" type="checkbox"/>			Bowel Monitoring	T;N, Routine, qAM and qHS Alert MD/N...
<b>Medications</b>				
Treatment: initial dose of Clozapine only:				
<input checked="" type="checkbox"/>			cloZAPine	12.5 mg, Oral, Form: Tab, qHS, First Dose: T;2100
<b>Laboratory Services</b>				
Reassess client/patient after 6 months.				
<input checked="" type="checkbox"/>			CBC	T+7;N, Whole Blood, Routine Collect, q1wk
<input checked="" type="checkbox"/>			C-Reactive Protein (CRP)	T+7;N, Serum, Routine Collect, q1wk for 4 week(s)
<input checked="" type="checkbox"/>			Troponin I (High Sensitivity)	T;N, Serum, RT Collect, q1wk for 4 week(s)
Order a cloZAPine Level (plasma concentration) AT LEAST 5 days after reaching doses (when maintaining at) 300 mg, 400 mg and 500 mg, and AT LEAST 5 days after every dose increase past 500 mg.				
<input type="checkbox"/>			Clozapine Level	T;N, Plasma, Routine Collect, Once
<b>Consults/Referrals</b>				
<input checked="" type="checkbox"/>			Request to Dietitian	T;N, Routine, Reason: Constipation prevention/management
<input checked="" type="checkbox"/>			Request to Pharmacist	T;N, Routine, Reason: Constipation prevention/management

Troponin lab test

CRP lab test

4 week duration

# Effect of Interventions on Data



Intervention

- Included Myocarditis monitoring protocol into Clozapine policy (Oct. 2014)

- Integrated Myocarditis monitoring protocol into I-CARE order sets (Nov. 2014)

- Reinforced education with cardiology expert (Apr. 2015); monitoring protocol elements made mandatory within I-CARE order sets (Jun. 2015)

Effect

- Increased clinical awareness and regulations to educate staff about clozapine-induced myocarditis and the effective monitoring protocol

- Integration of monitoring protocol increased speed of ordering and provided a visual reminder about the monitoring protocol for clinicians

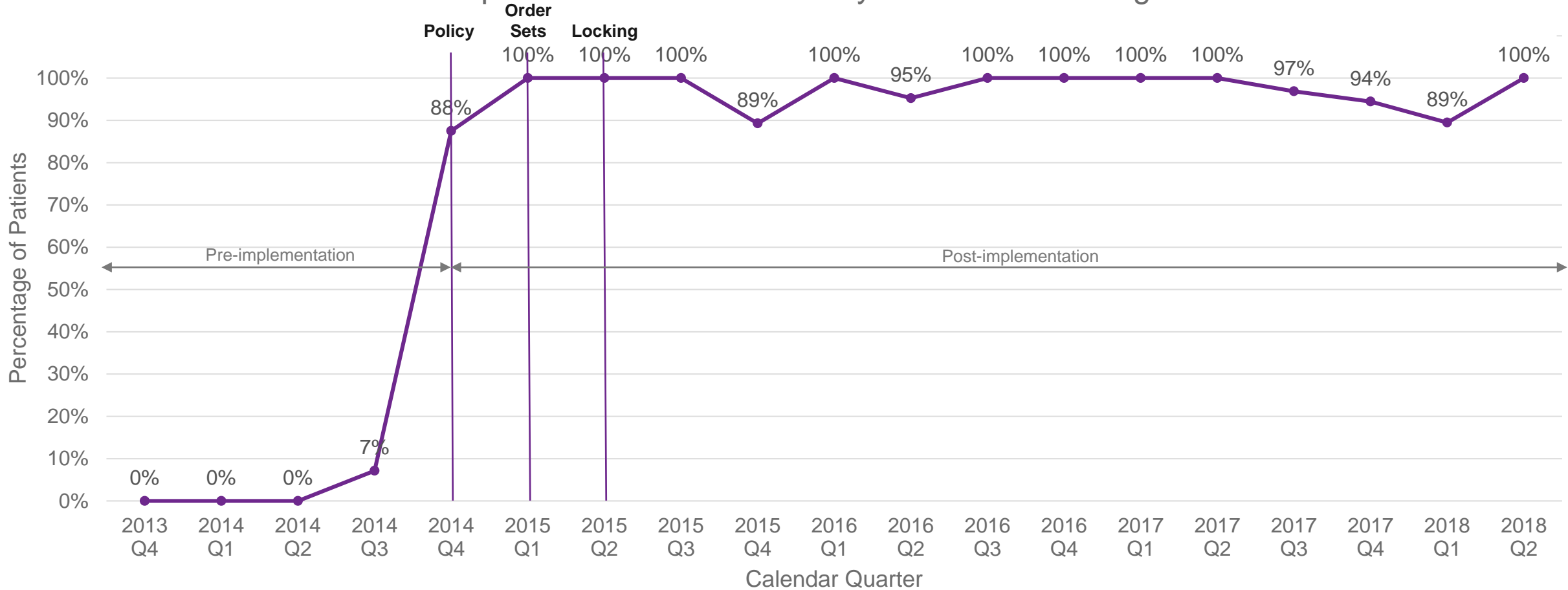
- Increased clinical awareness and enforced regulations to standardize practice for Clozapine-naïve patients



# Post-Implementation Adherence Data

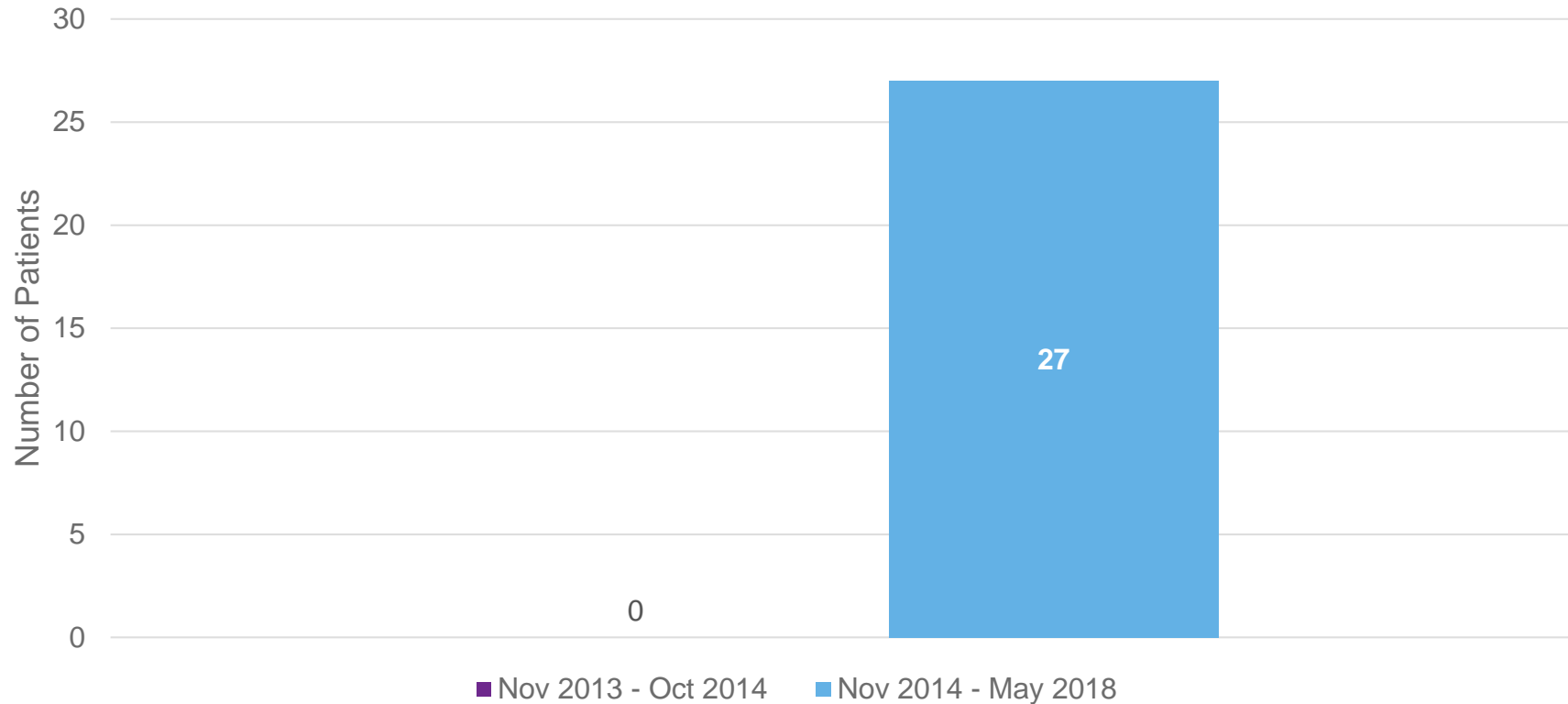
	<b>Nov 2013 – Oct 2014</b>	<b>Nov 2014 – May 2018</b>
<b>Myocarditis Monitoring Protocol</b>	4.2%	97.0%

## Clozapine-naive Patients with Myocarditis Monitoring Protocol



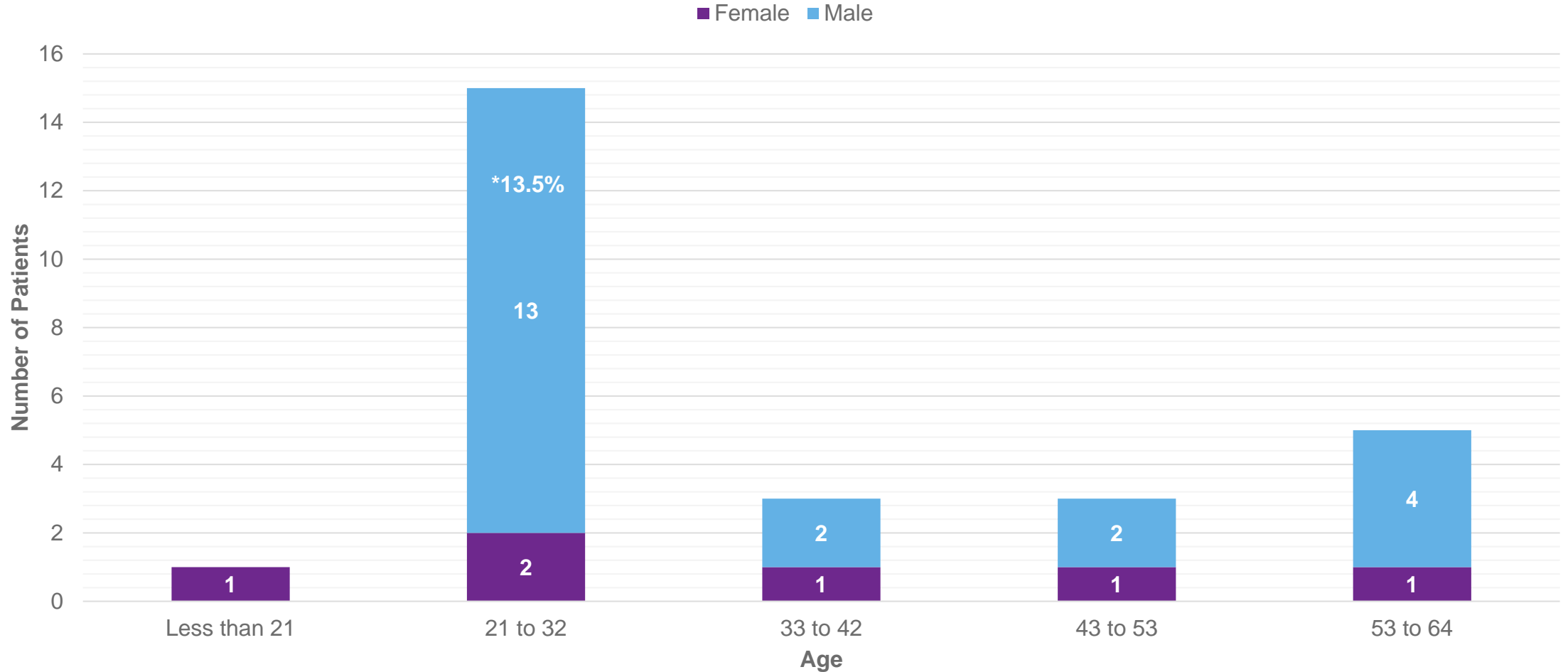
## Post-Implementation Outcome Data

Number of patients discontinued from Clozapine due to suspected Myocarditis



## Discontinued Patient Demographics

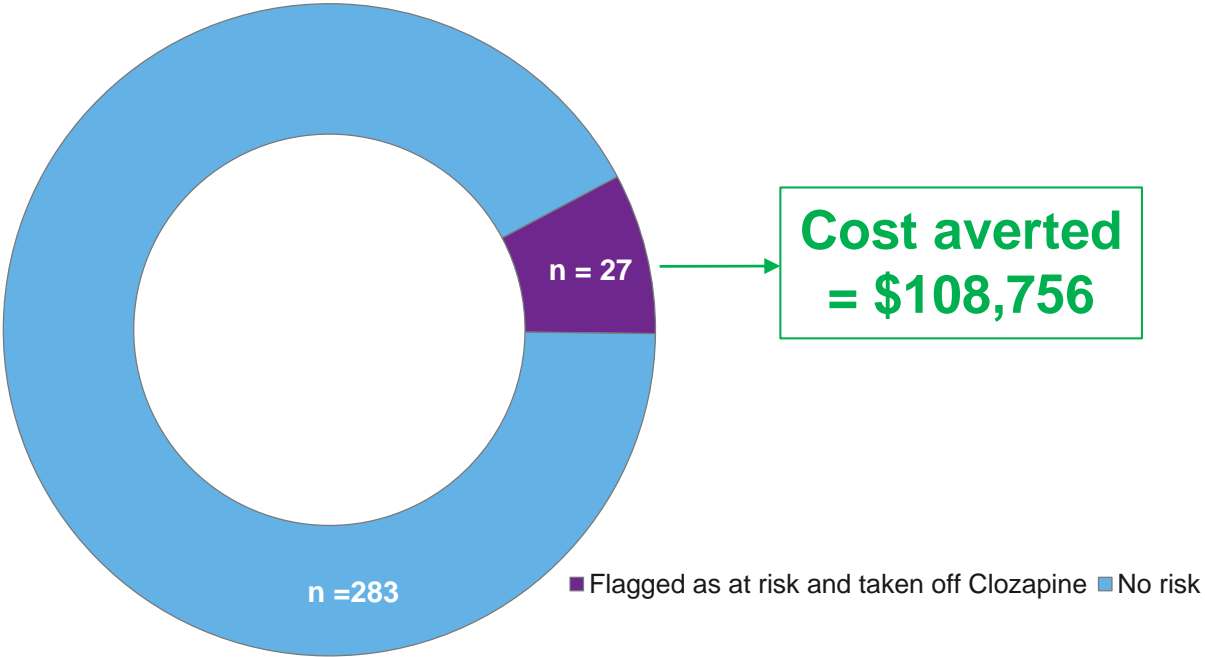
### Number of Clozapine Patients with Myocarditis Risk by Age and Sex



\*13 / 96 (13.5%) of males aged 21 to 32 discontinued

# Return on Investment


## Patients on Clozapine with Myocarditis Monitoring




Twenty-seven Clozapine-naïve patients had suspected myocarditis detected in early stages.  
Savings = (Cost of adverse event \* # of patients detected)

# Return on Investment


27 patients removed from Clozapine due to myocarditis warning signs (3 lives saved)




Able to measure the true incidence (8.6%) of Clozapine-induced myocarditis; 27 patients removed from Clozapine due to warning signs



Clinicians are able to more easily screen for Clozapine associated Myocarditis



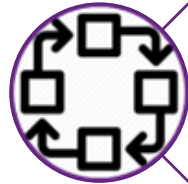
Developed guidelines for Clozapine cessation and reintroduction



CAMH is locally leading the way for Clozapine-induced myocarditis monitoring and we expect uptake on a regional and national level after publishing



## Lessons Learned



Policy change can be supported by health IT to support adoption and enforcement



Order sets are effective at driving adoption of mandatory protocols



Data sharing with clinicians is an effective method for practice awareness

# Thank You

camh