

**PUBLISHED ABSTRACT**

# Using Technology to Enhance Clozapine Prescribing Guidelines

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## Background

Clozapine is the most effective antipsychotic for the management of treatment-resistant schizophrenia [1], however, it continues to be under prescribed [1]. Adverse-effects of Clozapine, are one of the contributing factors leading to its low prescription rate [1], due the significant morbidity and mortality related to Clozapine. In order to monitor and prevent these complications, evidence based practice guidelines recommend dietary modifications, stool softeners and scheduled absolute neutrophil counts (ANC) [2]. In this study, we explore the effectiveness of how a Clozapine provider order sets (CPOS) in an Electronic Medical Records (EMR) system, improves compliance to evidence based practice guidelines; to ensure prevention of Clozapine adverse drug events, and thus, possibility increasing Clozapine use.

## Methods

We utilized a multistep approach to explore the effectiveness of Clozapine order-sets. First, a Clozapine CPOS, which included: ordering ANC, stool softeners, and a high fiber diet, was implemented in Richmond University Medical Center's (RUMC) EMR Software (Meditech) (**Figure 1**). Second, training was provided to prescribing physicians in the psychiatric department.

A retrospective study was conducted to quantitatively analyze Clozapine EMR data over an 18-month period (June 2017–December 2018).

The screenshot displays the EMR interface for Clozapine order sets. At the top, a table titled 'New Orders (5)' lists five items:

Item ID	Description	Date	Quantity	Status	Priority	Alert
61	cloZAPine (CLOZARIL) 25 MG PO bid	3/14/19	1800	New		*
62	Lactulose (Lactulose) 30 ML PO daily PRN CONSTIPATION	3/14/19	1645	New		*
63	Docusate Sodium (Colace) 100 MG PO bedtime	3/14/19	2200	New		*
64	REGULAR DIET (HOUSE) (DIET)	R 3/15/19	B	New		*
65	COMPLETE BLOOD COUNT (LAB) QWEEK	R 3/15/19	0600	New		*

Below the table are navigation buttons: Orders, Meds, Sets, Favorites, Category, Name, Transfer, Notifications, Assoc Data, Cont from Amb, and Oncology. A search bar is present with the text 'Search |'. Below the search bar, it indicates '1 Selected Items.' and shows a list of 'Standard Order Sets' with the following items:

- Psychiatry
  - ADULT PSYCHIATRIC ADMISSION
  - CHILD PSYCHIATRIC ADMIT SET
  - CLOZAPINE INITIATION
- Pulmonary
- Surgery

**Figure 1:** Sample of the Clozapine Order Set implemented into the EMR System.

A total of 112 records were retrieved. Twenty-three did not meet study criteria and were excluded. The no order set group was n = 50, with a mean age of 44.4 years; (44% female and 56% male). The order set group was n = 39, with a mean age of 41.2 years (61.5% female and 38.5% male) (Table 1).

We compared compliance of “order set” vs. “no order set” groups using logistic regression to determine the benefits of CPOS in our patient population. Adverse drug events was measured by the incidence of gastrointestinal hypo-motility [3], defined by the Constipation Assessment Scale (CAS). Criteria for data analysis included patients in the psychiatric department and who received >1 dose of Clozapine.

**Results**

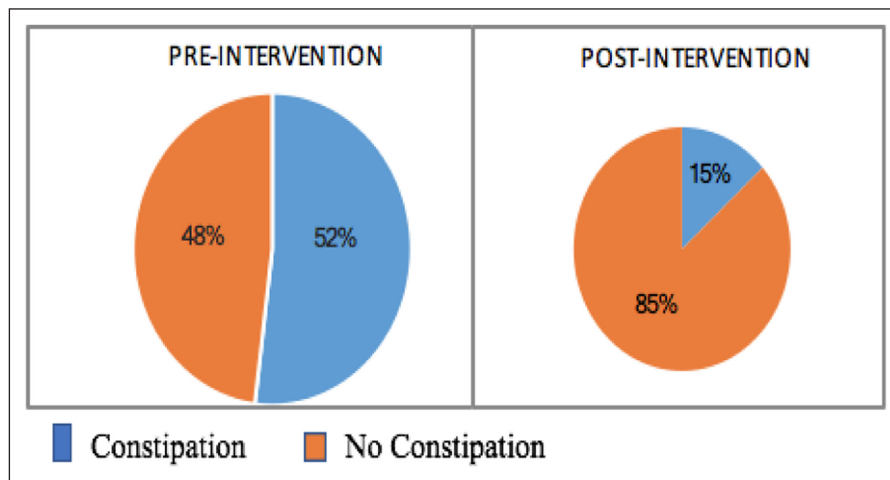
CPOS are effective in ensuring compliance with safe prescribing guidelines [95% CI 0.098–0.526, p = .0001].

Adverse drug events were reduced by 35.41% [95% CI 0.104–0.599; p = .005]. In the pre-intervention group, 52% of the patients experienced constipation while on the unit. Compared to only 15% in the post-intervention group (Figure 2).

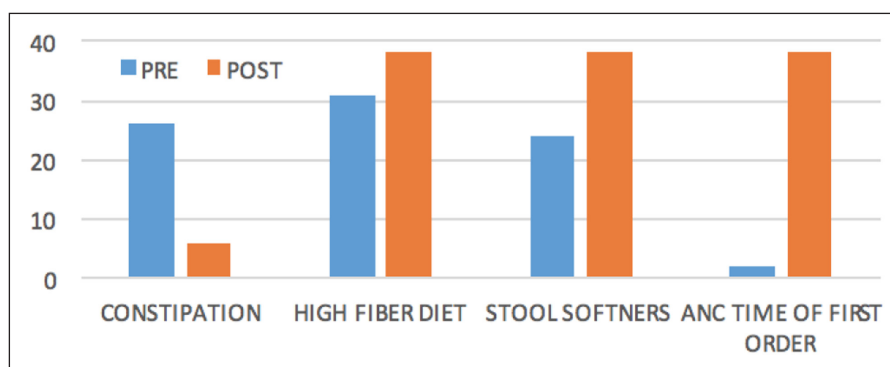
After the CPOS intervention, the compliance of ordering: stool softeners increased from 32% to 91% (p < .0001); high fiber diet increased from 46% to 68% (p < .0001). The percentage of ordering weekly ANCs at the time of the first Clozapine order increased from 18% to 98% (p < .001).

**Table 1:** Demographical information of Study Population.

	Pre-intervention group	Post-intervention	Total
Mean Age	44.4	41.2	42.8
Female (%)	22 (44%)	24 (61.5%)	46 (51.7%)
Male	28 (56%)	15 (38.5%)	43 (48.3%)
n-value	50	39	89



**Figure 2:** % of Constipation in Pre vs. Post Intervention Groups.



**Figure 3:** Comparing adverse side effects and compliance with evidence based guidelines in pre and post interventional groups.

## Discussion

Despite significant differences found when comparing the two groups, the current sample size remains small. Primarily, due to the implementation of the order set occurring less than a year ago. Future plans include conducting a similar study over a larger time period (+/-2 years from the intervention onset 2016–2020), about a 4-year span. In addition, future plans have been made to implement the CPOS order set throughout all departments at RUMC. Overall, including multiple departments, over a larger time period, will provide a larger sample size.

Compliance of the using the CPOS also varied. The highest occurrence of non-compliance happened in the first few months of new residency training (July–September). Efforts will be made to train incoming residents on the order-set during orientation and by email instructions; providing not only initial training of the PGY-1 class but retraining for senior classes (PGY 2–4) and attending prescribers.

## Conclusions

Clozapine CPOS improve compliance with safe prescription guidelines, patient outcome and subsequently have the prospect to increase Clozapine prescription rates. More awareness of CPOS availability and expansion on the use of Clozapine CPOS in different departments at RUMC should be encouraged. Further studies are required to explore effective implementation of medication order sets, in the context of a larger process of patient care practice standards.

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