

# LENGTH OF STAY BETWEEN PATIENTS WITH RAPID VERSUS STANDARD CLOZAPINE TITRATION IN A PSYCHIATRIC ACUTE INPATIENT FACILITY

## Introduction

Clozapine, FDA approved in 1989 for treatment of patients with refractory schizophrenia and bipolar disorder, remains one of the most efficacious drugs for treatment resistant schizophrenia. Due to its historic association with a variety of side effects, a standard titration dosing to 300 mg by day 14 has been most common, with higher dosing then left to the clinician's judgement. The standard titration results in a long delay in controlling symptoms, need for additional medications and a prolonged length of stay. Rapid titration has been demonstrated as safe and efficacious in two reports, but there is variability in dosing regimens. A newer rapid titration option of 450 mg by day 14 was instituted at Valleywise facilities in September 2018.

## Research Question

In this study, we compare rapid versus standard clozapine titration and its association with length of stay (LOS) for treatment resistant psychiatric inpatients. Secondary outcomes included discharge ready (DCR) status, primary diagnosis of patients, and post-discharge placement.

## Materials and Methods

This retrospective chart review study collected socio-demographics and clinical outcomes of psychiatric inpatients with clozapine order sets, including primary diagnosis, order initiation date, discharge readiness and post-discharge placement. An electronic health record report of psychiatric inpatients with clozapine orders between September 2016 and April 2018 yielded 93 separate admissions receiving either rapid titration protocol (RTP) or standard titration (STP) based upon the physician preference. Patients on maintenance dosage or whose orders were altered or stopped upon initiation of orders were excluded. Patients on RTP were compared to those on STP for overall length of stay (LOS) and time from admit to 'discharge ready' (DCR) status, in order to account for those stable enough for release but whose discharge date may be delayed due to lack of a discharge placement in the community. An additional variable of time from treatment initiation date to DCR date was also evaluated. The results were analyzed using Wilcoxon rank-sum test.

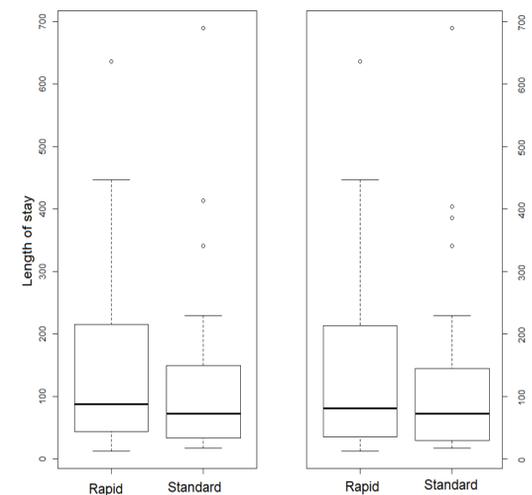
## Results

- There were 60 male and 33 female subjects in our sample, identifying racially as White (72), African American (12), Native American/Alaskan (5), and Asian/Pacific Islander (4). 14% claimed Hispanic ethnicity.
- Of the 93 patients who were prescribed clozapine, 37 were started on the rapid titration and 56 were on the standard titration schedule.
- Primary outcome: The LOS was calculated from the date of admission to date of discharge and for patients awaiting discharge, LOS was calculated up to date for analysis.
- The mean and median LOS for patients on the RTP (n = 37) was 120.43 and 81 days, while that for STP patients (n=56) was 111.98 and 81.5 days (p=0.866), respectively.
- Secondary outcome: days until discharge ready status. Median discharge ready (DCR) days were lower for RTP than STP inpatients (51.5 to 76.5 days, p=0.644).
- The primary diagnosis of patients in both RTP and STP groups was Schizoaffective disorder at 78.38% and 62.5%, respectively.
- In terms of post-discharge placement, 24.32% of RTP patients went to a 24 hr residential and 18.19% to home. In the STP group, 25% went to a 24 hr residential and 30.36% were discharged home.

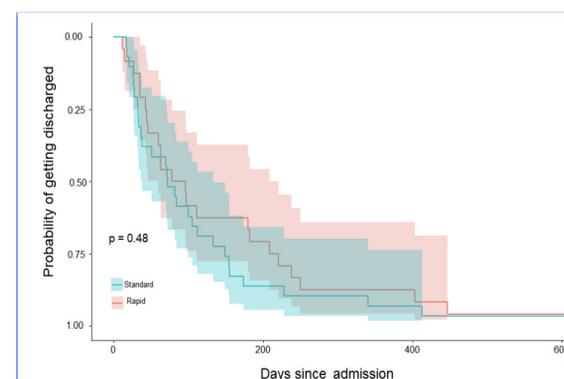
	N	LENGTH OF STAY(DAYS)		DAYS TO DC READY	
		MEAN	MEDIAN	MEAN	MEDIAN
RAPID TITRATION	37	120.43	81	93.38	51.5
STANDARD TITRATION	56	111.98	81.5	93.28	76.5
P			0.866		0.644

\*P value comparing accelerated vs standard titration GROUPS, Wilcoxon rank sum two tailed P, with t-approximation

**Table 1: Length of stay and days to discharge ready status in patients on the rapid titration as compared to the standard titration schedule.**



**Figure 1: Distribution of length of stay (left) and days until discharge ready (right) between rapid and standard clozapine titration schedule groups of inpatients. Minimum and maximum values for both RTP and STP group DCR days (13 to 366, and 18 to 404 days). Dots above the whiskers indicate extreme values.**



**Figure 2: Probability of getting discharged over time between patients in rapid and standard clozapine titration schedules (P=0.48)**

## Discussion

A shorter LOS among those on RTP was anticipated by the fact that RTP allows a minimally effective therapeutic dose range to be reached sooner than standard titration, hence presuming quicker stabilization. In fact, median LOS was essentially similar between patients on rapid and standard titrations, (81 to 81.5 days, P = 0.866). Median discharge ready (DCR) days were lower for RTP than STP inpatients (51.5 to 76.5 days, p=0.644), although this was not statistically significant. Any expected difference in LOS may be offset by clinical and system-level factors. Study limitations include small sample size and incomplete account of cofactors including comorbidities contributing to extended DCR. Future studies with a larger sample of patients and consistent recording of Discharge Ready status would improve the accuracy of results. Additionally, there continues to be a need for large, randomized, double blinded clinical trials to further assess the efficacy of rapid clozapine titration versus standard titration.

## Conclusion

- The median discharge ready (DCR) days were in fact lower for rapid titration protocol (RTP) than standard titration (STP) inpatients. Although this was not statistically significant, it may be clinically relevant.
- Ultimately, it was determined that the median LOS was similar between patients on rapid and standard titrations.

## Acknowledgements

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## References

Available upon Request.