

# Antipsychotic use in the intensive care unit for treatment of delirium and agitation

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## Background

- Delirium is associated with increased intensive care unit (ICU) mortality, prolonged length of stay, higher healthcare costs, and long-term cognitive dysfunction<sup>1</sup>
- The 2018 PADIS guideline suggests utilizing antipsychotics only in patients with significant signs of delirium.<sup>1</sup> However, antipsychotics are not without adverse effects, especially risk of QTc prolongation<sup>2</sup>
- The facility guidance for assessment, prevention, and management of delirium in the ICU recommends daily EKG and QTc assessment in the ICU for some of the antipsychotics used for delirium

## Objective

The goal of this medication use evaluation is to assess whether antipsychotics were safely used in the ICU to treat delirium and agitation and if they were discontinued prior to downgrade or discharge.

## Methods

- Study Period:** October 15th, 2021 to July 31st, 2022
- Study Design:** Single-center, retrospective chart review using clinical support software generated list

Inclusion Criteria	Exclusion Criteria
Admitted to ICU	Received as needed, on-call, and one-time orders of antipsychotic
Received ≥1 dose of scheduled antipsychotic	

- Primary Outcome:** To determine if QTc was obtained prior to initiating antipsychotics
- Secondary Outcomes:**
  - To evaluate how often QTc was documented
  - If antipsychotics initiated in the ICU for delirium and agitation were discontinued prior to ICU downgrade or hospital discharge\*
- Data collection included:**
  - The available QTc values prior to the first dose, within 48 hours, within 7 days, and prior to downgrade or discharge
  - The total number of QTc-prolonging\*\* agents received
  - Reported arrhythmias during antipsychotic therapy<sup>‡</sup>

\*Excluding patients that were expired during the ICU hospital stay  
\*\*Prolonged QTc is defined as QTc≥500 msec

## Results

- From the 216 patients that were screened, 50 patients met the inclusion criteria

Table 1. Demographics

Characteristics	Analysis Group (N=50)
Mean age —yr	63.5
Female — no. (%)	24 (48)
Race — no. (%)	
African American	11 (22)
Asian	1 (2)
Caucasian	27 (54)
Other	10 (20)
QTc≥ 500 msec — no. (%)	10 (20)
Pre-treatment <sup>†</sup> QTc≥ 500 msec — no. (%)	10 (20)
Most used antipsychotics — no. (%)	
Quetiapine	46 (92)
Olanzapine	4 (8)
Other antipsychotics <sup>‡</sup>	3 (6)
Prior to therapy — no. (%)	
History of arrhythmias	17 (34)

<sup>†</sup> Including ziprasidone haloperidol, and risperidone

Figure 1. Most Recent EKG Prior to Starting Antipsychotics

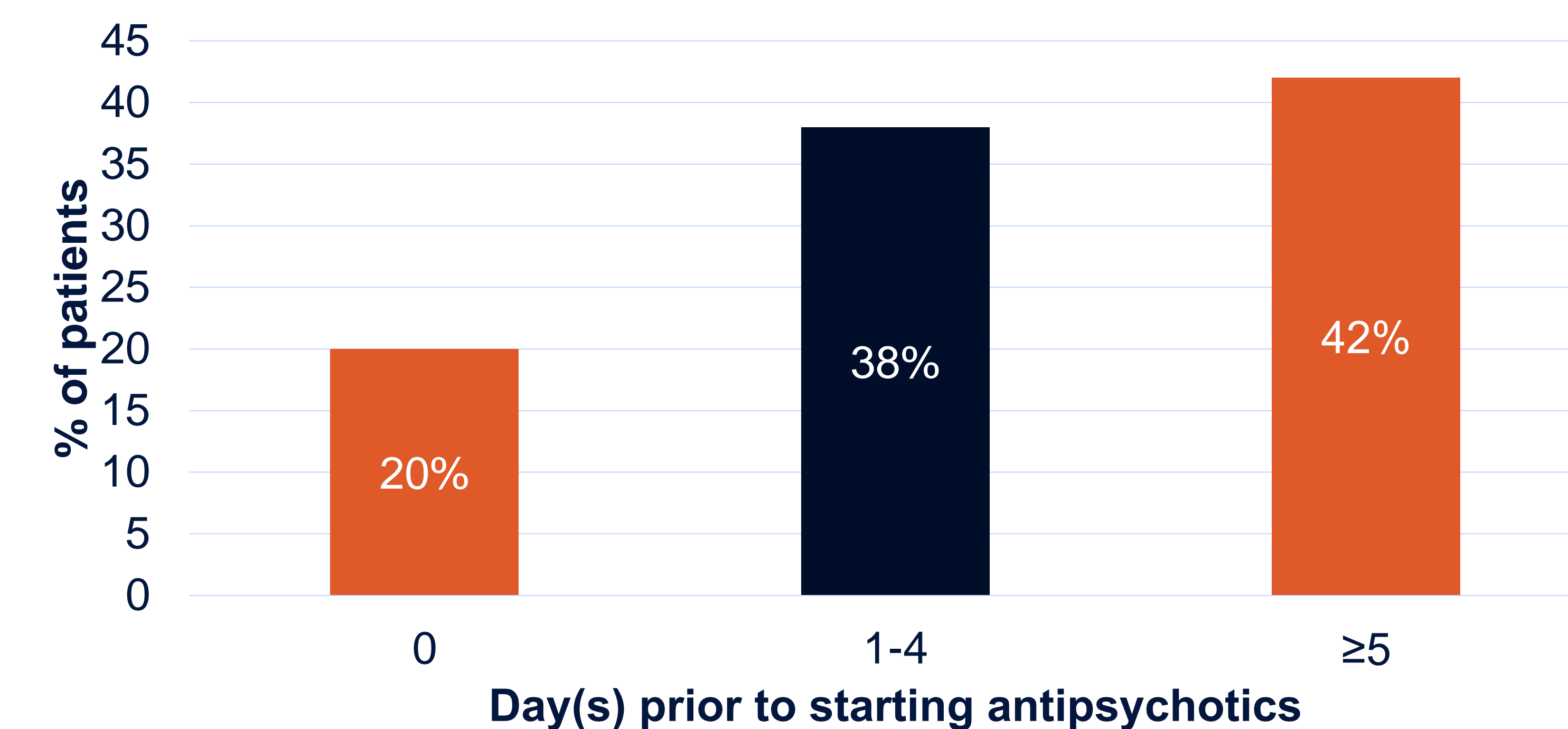


Table 2. Post-treatment Outcomes

Endpoint	Analysis Group (N=50)
EKG during treatment— no. (%)	
Daily	1 (2)
Within 48 hours	15 (30)
Within 7 days	20 (40)
Antipsychotic discontinuation rate — no. (%)	4 (100)
Concomitant use of QTc prolonging agents — no. (%)	30 (60%)
Amiodarone	16 (53%)
Azithromycin	12 (40%)
Fluconazole	9 (30%)
Other <sup>x</sup>	3 (10%)
Development of arrhythmias — no. (%)	4 (8%)

<sup>x</sup> Including quinolones, anti-depressants, and macrolides

## Discussion

- About half of the patients had a recent QTc reported that was within the timeframe of 4 days prior to starting an antipsychotic. However, only 1 patient received daily EKG and QTc monitoring; 30% had a QTc reported within 48 hours of treatment and 40% within 7 days
- One fifth of the patients had QTc prolongation prior to treatment and more than half of them were taking at least one additional QTc prolonging drug
- Although only 8% of the patients developed an arrhythmia during treatment, close monitoring of the QTc is necessary in these populations, especially those that are on multiple QTc prolonging agents, or have a history of arrhythmias
- The facility protocol does not specify which antipsychotic requires closer EKG and QTc monitoring. This should be addressed and clarified for safe medication use
- Limitations:
  - Only QTc-values from EKG were assessed, but the interdisciplinary team may have utilized continuous cardiac monitoring system to trend daily QTc
  - Evaluated pre-treatment QTc that was closest to the start of antipsychotic treatment, but some were from an EKG performed greater than 5 days ago
  - Excluded approximately 75% of the patients screened. Some excluded antipsychotics may have been initiated for the treatment of delirium and agitation

## Conclusion

- Despite noted baseline QTc prolongation, patients were initiated on antipsychotics
- The facility has an established protocol stating that daily EKG and QTc should be assessed in the ICU for some of the antipsychotics used for delirium. To reduce the risk of arrhythmias, the facility should specify the frequency of EKG and QTc monitoring for the most frequent used antipsychotics
- There are limitations noted to this evaluation, but that should not have affected the need for close monitoring of QTc in these populations, especially those that are at high risk.

## References

- Devlin JW, Skrobik Y, Gélinas C, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. Crit Care Med. 2018;46:e825–73.
- Stöllberger C, Huber JO, Finsterer J. Antipsychotic drugs and QT prolongation. Int Clin Psychopharmacol. 2005;20(5):243-251. doi:10.1097/01.yic.0000166405.49473.70