Title: Which poisoned patients require treatment in the intensive care unit? External Validation of the INTOXICATE Clinical Decision Rule

Background: Approximately 1 in 10 poisoned patients in the United States is admitted to the Intensive Care or Stepdown Units (collectively, ICU) for observation, meaning currently clinically stable but with anticipated respiratory or cardiovascular collapse. If we could predict which poisoned patients will not decompensate, we could simultaneously accelerate the care of some poisoned patients and improve ICU utilization. INTOXICATE (ex-TOXIC-Europe study) is a clinical decision rule developed in the Netherlands to predict which poisoned patients will require ventilatory or hemodynamic support for more than 24 hours. A retrospective study demonstrated that INTOXICATE could have decreased admissions to Dutch ICUs by 32%. Our objective in this project is to determine the performance of INTOXICATE in the U.S. healthcare system.

Methods: We conducted a retrospective study of toxicology consultations from Jan 2023 to Apr 2024 at one urban tertiary care center with a 24/7 bedside toxicology service. We used the methodology described by Brandenburg et al. (2017). Our outcome measure was the inter-rater reliability between the INTOXICATE’s prediction disposition and the treating physician's decision. To detect an inter-rater reliability of at least 0.6 with power 0.8 and 95% confidence, we needed to include 94 patients. We evaluated return visits by searching for encounters throughout the health system affiliated with this medical center and with the local health information exchange ('CareEverywhere'). This study was granted an exemption from review by the Institutional Review Board.

Results: We included 112 patients aged 28.5 [16 to 43] years, expressed as median [interquartile range]; 46% male, 53% female. We excluded 2 patients due to incomplete information. Of the remaining 110 patients, 21 (19%) were admitted to the ICU, 16 (14%) to a general medical floor, and 75 (68%) were discharged or transferred directly to psychiatry. INTOXICATE recommended ICU admission for 14/21 (67%) of patients for whom the toxicologist recommended ICU admission, ICU admission for 12 of the 16 (75%) patients for whom admission the toxicologist recommended a general medical floor, and ICU admission for and 37 of the 44 (84%) patients for whom the toxicologist recommended discharge. No patients for whom toxicology recommended a floor admission were admitted to a floor and then transferred to the ICU. No patients who were discharged but for whom INTOXICATE recommended admission returned to any hospital in the metropolitan area in 48 hours. The interrater agreement (Cohen's kappa) between INTOXICATE and the actual disposition was 0.045 (p=0.474).

Conclusions: INTOXICATE did not recommend ICU admission in 33% of patients for whom the bedside toxicologist recommended ICU admission and recommended ICU admission in 57% of the patients for whom the bedside toxicologist recommended discharge. This increased ICU utilization by approximately 200% (from 21 to 44). There was no more than chance agreement between INTOXICATE and the recommendation of the patient on the bedside, suggesting that the two approaches use different criteria, which can reflect geographic variation in the type of poisoning and variation in care practices across health care systems.