Identifying the contribution of admission order sets to deliriogenic medication prescribing in elderly patients admitted with delirium – a prevalence study

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Objectives: To determine the extent and patterns with which admission order set usage in a tertiary care setting contributes to deliriogenic medication prescribing in elderly patients admitted with delirium.

Design: Retrospective chart review.

Setting: Community-teaching hospital.

Participants: Two-hundred and fourteen (N = 214) patients aged 65 or older admitted with an admission order set and a diagnosis of delirium.

Measurements: Patients with an admission diagnosis of delirium were identified using hospital decision support coding. Deliriogenic medications were identified using the 2015 American Geriatrics Society Beers Criteria. The primary outcome was to determine the proportion of patients receiving at least one dose of a deliriogenic medication prescribed from an admission order set. Secondary objectives were to determine the proportion of patients prescribed at least one deliriogenic medication from an admission order set, and the proportion of orders that were (i) manually-checked versus pre-checked, (ii) as-needed versus scheduled, and (iii) stopped or held within 48 hours of prescription.

Results: Of 214 patients, 14% received at least one dose of a deliriogenic medication and 49.5% were prescribed at least one deliriogenic medication from an admission order set. Of the 145 deliriogenic medication orders, 96.6% were as-needed and 92.4% were manually-checked by the physician. A total 10.3% of orders were stopped or held within 48 hours. The most commonly prescribed deliriogenic medications were dimenhydrinate (67.6%) and zopiclone (15.2%).

Conclusion: This prevalence study provides a local baseline estimate of the impact of clinical order sets on deliriogenic medication prescribing in an at-risk population.

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**Key words:** medication; order set; delirium; elderly
INTRODUCTION

Delirium is common in hospitalized elders, with an estimated 10% to 31% presenting to the emergency department with the neuropsychiatric syndrome. Delirium in elderly patients has also been associated with poor outcomes, including increased risk of mortality and institutionalization. As significant modifiable risk factors, medications can negatively contribute to the development of an older adult’s delirium. A broad range of psychoactive medications and medication classes have been associated with precipitating or exacerbating delirium. In the perspective of prevention and management, the Canadian Coalition for Seniors Mental Health (CCSMH) therefore recommends withholding medications that may contribute to a patient’s delirium, whenever possible.

There are a number of validated tools that have been developed to help clinicians identify and manage potentially inappropriate medications (PIMs) in the elderly. One tool that provides explicit lists of PIMs is the 2015 Updated Beers Criteria, which includes a compilation of medications and medication classes that are recommended to be avoided in those with or at high-risk of delirium. Based on the Beers Criteria, the prescribing of multiple PIMs in hospitalized older adults have been associated with increased length of stay and healthcare costs. There is currently a lack of literature that specifically evaluates the prevalence deliriogenic medication prescribing in hospitalized elders.

Identifying patterns of deliriogenic medication prescribing can be valuable to determine an institution’s potential contribution to patient harm. Prescribing from clinical order sets is of particular interest in the hospital setting. Although the tools have been found to increase standardization to evidence-based treatment, their use does not replace clinical judgment.
Misuse can impede their role as a patient safety mechanism, and may instead provoke unintended consequences.\textsuperscript{14-15}

The objective of this prevalence study was to determine the extent and patterns with which order set usage at a community-teaching hospital contributes to deliriogenic medication prescribing in elderly patterns admitted with delirium.

**METHODS**

*Study Design and Setting*

The study was a retrospective chart review at the Mississauga Hospital site of Trillium Health Partners (THP). THP is a community-teaching hospital network that encompasses three main sites in Mississauga, Ontario. Mississauga Hospital is one of two acute care facilities, where order set usage approximates 70% of all inpatients. The study was approved by the Research Ethics Board of Trillium Health Partners.

*Study Population*

Eligible patients were older adults aged 65 years or older who were admitted with an admission order set and a diagnosis of delirium. An admission diagnosis of delirium was determined by diagnostic coding from the THP decision support department, indicated by a Type 1 Dx code for delirium. A Type 1 Dx code labels diagnoses that significantly affected length of stay or resources used, and were prevalent on admission. Patients were excluded if they were admitted with alcohol or benzodiazepine withdrawal syndrome, admitted or transferred to the intensive care unit (ICU) within 48 hours of admission, or had an ICU admission order set written within 24 hours of admission. The intent was to exclude neurological disorders where recommended treatment for delirium would commonly include deliriogenic medications. The
authors also acknowledged differences in the etiology of delirium for a critically ill, delirious patient.\textsuperscript{8,16}

\textit{Study Assessment}

Patients admitted to Mississauga Hospital between the period of April 1\textsuperscript{st}, 2015 to March 31\textsuperscript{st}, 2016 were screened for eligibility. A list of patients with an admission diagnosis of delirium was generated by the THP decision support department. The study investigators subsequently screened for inclusion and exclusion criteria. Patient data was collected electronically from Meditech and Sunrise Clinical Manager. The two electronic health records store patient information related to pharmacy, laboratory, diagnostic imaging, consult notes and discharge summaries, among other functions.

Deliriogenic medications were identified based on the AGS 2015 Beers Criteria. The validated tool is derived from systematic review and consensus opinion from a multidisciplinary expert panel, and provides explicit criteria concerning PIM use in older adults. The Beers Criteria includes a list of medications and medication classes that should be avoided in those with or at high risk of delirium (\textit{Supplementary Figure S1}). The tool also includes a list of medications with strong anticholinergic properties (\textit{Supplementary Figure S2}).\textsuperscript{10} With the exception of anticholinergics, the Anatomical Therapeutic Chemical (ATC) classification system was used to identify medications within individual drug classes that may induce or worsen delirium as per the Beers Criteria. The ATC classification system was developed by the World Health Organization to serve as a tool for drug utilization research.\textsuperscript{17}

\textit{Study Outcomes}

The primary outcome of the study was to determine the proportion of elderly patients admitted with delirium that received at least one dose of a deliriogenic medication prescribed
from an admission order set. Secondary outcomes quantified the extent and characteristics of deliriogenic medication prescribing, including the: (a) proportion of elderly patients admitted with delirium that were prescribed at least one deliriogenic medication from an admission order set, (b) proportion of total deliriogenic medications prescribed from an admission order set that were ordered as i. manual-check boxes ii. default boxes iii. as-needed orders or iv. scheduled orders, and (c) proportion of total deliriogenic medications that were stopped or held within 48 hours of prescription. The 48-hour timeframe for stopping or holding a deliriogenic medication acted as the study’s indicator for patient re-assessment. Medications that were handwritten by the clinician onto the order set and not part of the original template were excluded.

Patient data related to study outcomes were collected from Chartmaax 6.30, a software system that stores patient charts electronically. This includes physician orders and medication administration records.

Statistical Analysis

A target sample size of 216 patients was calculated based on a 95% level of confidence ($Z$), 15% expected prevalence of the primary outcome ($P$), and 5% precision of the prevalence estimate ($d$). The calculated sample size was multiplied by 10% to account for potential missing data. Due to a lack of current literature, the expected prevalence was based on expert opinion by the THP Delirium Working Group. Patient screening was completed chronologically until target sample size was reached or after all eligible records assessed, whichever came first.

Dichotomous variables were expressed as proportions, and continuous variables were expressed as means ± standard deviation.

RESULTS
Of 459 eligible patients extracted by Decision Support, 233 patients were screened by study investigators. Ten (n = 10) were excluded as they were not admitted by an admission order set. Seven (n = 7) were excluded as the patients had an ICU admission order set written within 24 hours of admission. Of the 216 remaining patients, two (n = 2) were excluded from data analysis. The exclusions were not pre-specified based on study methods. One patient was excluded due to imminent death upon admission, and another was excluded due to being admitted with uncontrolled seizures in the context of epilepsy. The second patient had a neurological disorder that was complicated by delirium. Benzodiazepines, or more specifically lorazepam, is recommended as first-line treatment for controlling status epilepticus.19

Patient baseline characteristics are outlined in Table 1. The study population was 47.7% male with a mean age of 84 years. Regarding neurological status, 56.5% of patients had baseline cognitive impairment, 38.3% had dementia, and 13.6% had a history of delirium. The most common admitting service was internal medicine (91.1%), followed by cardiology (3.3%) and respirology (2.3%).

Table 2 lists study outcomes related to the extent of deliriogenic medication prescribing in elderly patients admitted with delirium. Of 214 total patients, 14% received at least one dose of a deliriogenic medication prescribed from an admission order set, whereas 49.5% of patients were prescribed at least one deliriogenic medication from an admission order set.

Table 3 outlines the characteristics of deliriogenic medication orders prescribed from the admission order sets. Of 145 total orders, 92.4% were manually-checked and 96.6% were as-needed (or PRN) orders. Fifteen orders (n = 15) were stopped or held within 48 hours of prescription. The most common deliriogenic medication class prescribed were anticholinergics.
(76.6%), followed by sedative hypnotics (15.2%). The two most common deliriogenic medication prescribed were dimenhydrinate (67.6%) and zopiclone (15.2%).

**DISCUSSION**

This prevalence study provided a local baseline estimate of the impact of order sets on deliriogenic medication prescribing in elderly patients admitted with delirium. While a paucity of literature exists for comparison, CCSMH recommends withholding medications potentially contributing to delirium when possible.\textsuperscript{8} Study results showed that half of the population were prescribed at least one deliriogenic medication from an admission order set (49.5%, \(n = 106\)), and one-tenth received at least one dose of a deliriogenic medication prescribed (14%, \(n = 30\)).

Baseline risk for delirium in the population was high with the presence of multiple risk factors. Notably, advanced age and baseline cognitive impairment are the two most common predisposing risk factors for delirium in older adults.\textsuperscript{20} Our population had both, with a mean age of 84 years and more than half of patients with pre-existing cognitive dysfunction (56.5%).

This is the first study to quantify deliriogenic medication prescribing in an at-risk population. One recent prevalence study aimed to assess inappropriate medication prescribing in older adults before and during hospitalization; however, deliriogenic medications and delirious patients were not individually evaluated. Based on a subset of criteria from the 2012 Beers Criteria, 24% and 49% of older adults from that study were found to have at least one potentially inappropriate medication on admission and during hospitalization, respectively. The results illustrate in part an increase in PIM prescribing once hospitalized.\textsuperscript{21}

Our study showed high rates of older adults who received or were prescribed a deliriogenic medication from an admission order set. Results highlight that these findings may be
attributed to two factors: order set design and clinician assessment. Regarding order set design, over 90% of deliriogenic medication orders were as-needed regimens (96.6%). Compared to the proportion of patients who actually received a dose of their deliriogenic medication (14%), this raises the question as to whether the majority of orders were required. A similar point was raised in a 2015 retrospective chart review, which found an 18-fold increase in as-needed trazodone prescribing after its addition onto a general admission order set. Almost half of patients who were prescribed the sleep aid did not receive a dose during their hospital stay (48%).

Nevertheless, there has been recent literature demonstrating that optimizing order set content can positively impact delirium outcomes. A 2016 pragmatic, controlled trial found that the implementation of “delirium-friendly” pre-printed order sets significantly reduced postoperative delirium compared to routine care in older adults admitted for hip fracture. The revised order sets included orders for scheduled laxatives and analgesics, along with substituting non-deliriogenic options for sleep and nausea management.

Knowledge and assessment of deliriogenic medications may have also played a role on study results. Of 145 deliriogenic medication orders from admission order sets, over 90% were manually-checked by clinicians. These findings highlight that while order sets are advantageous for standardizing patient care, their use must be complemented by clinician judgement.

Explicit tools outlining criteria for prescribing in older adults may be one method to reduce inappropriate prescribing. A 2011 randomized, controlled trial (RCT) of 400 hospitalized older adults found that applying the STOPP/START criteria on discharge significantly increased prescribing appropriateness compared to standard care. Appropriateness was assessed using the Medication Appropriateness Index and was sustained on 6-month follow-up. A subsequent 2014 RCT of 359 nursing home residents found a significant reduction in
polypharmacy, drug costs, and falls after one year when comparing STOPP/START screening of medications versus standard care.25

According to our results, specific areas may warrant attention. The most commonly prescribed deliriogenic medication was dimenhydrinate (67.6%), and the most common medication class were anticholinergics (76.6%). The most common admitting service was internal medicine, admitting over 90% of study patients (91.1%). Quality-improvement initiatives should therefore focus on noted key areas.

There are some limitations to this study. The Confusion Assessment Method (CAM) tool is a validated diagnostic aid with high sensitivity and specificity used commonly in clinical practice to identify delirium.8 Due to a lack of current routine implementation at Trillium Health Partners, hospital-based diagnostic coding was used as an alternative. In principle, deliriogenic medications should be avoided in delirious patients; however, there may have been unidentified instances where such medications were appropriately indicated. This was not evaluated by investigators. Finally, this prevalence study did not evaluate whether an association existed between the prescribing of deliriogenic medications and the exacerbation of delirium.

In conclusion, this study provided a baseline estimate of the impact of admission order sets on deliriogenic medication prescribing in elderly patients admitted with delirium. This is the first known study to attempt to quantify inappropriate prescribing in this at-risk population. Study findings highlight that order sets are not fail-safe tools for patient safety, and local quality improvement strategies should target both order set development and education initiatives.

**Word Count:** 2112

**Table & Figures Count:** 3
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REFERENCES

1. Inouye SK. Delirium in older persons. NEJM 2006;354:1157-1165.


References count: 25
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Study Subjects, n = 214</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD</td>
<td>84.4 ± 7.8</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>102 (47.7%)</td>
</tr>
<tr>
<td>Charlson Comorbidity Index, mean ± SD</td>
<td>2.2 ± 1.8</td>
</tr>
<tr>
<td>Cognitive impairment, n (%)</td>
<td>121 (56.5%)</td>
</tr>
<tr>
<td>Dementia*, n (%)</td>
<td>82 (38.3%)</td>
</tr>
<tr>
<td>History of delirium, n (%)</td>
<td>29 (13.6%)</td>
</tr>
<tr>
<td>Functional impairment, n (%)</td>
<td>131 (61.2%)</td>
</tr>
</tbody>
</table>

Admitting service, n (%)

- Internal Medicine 195 (91.1%)
- Cardiology 7 (3.3%)
- Respirology 5 (2.3%)
- General Surgery 3 (1.4%)
- Other** 4 (1.9%)

*Patients with baseline dementia were also counted as having baseline cognitive impairment.

**Other specialities included neurology, gastroenterology, and oncology.
### Table 2. Outcomes Associated with Extent of Deliriogenic Medication Prescribing in Elderly Patients Admitted with Delirium

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Study Subjects, n = 214</th>
</tr>
</thead>
<tbody>
<tr>
<td>Received at least one dose of a deliriogenic medication prescribed from an admission order set, n (%)</td>
<td>30 (14%)</td>
</tr>
<tr>
<td>Prescribed at least one deliriogenic medication from an admission order set, n (%)</td>
<td>106 (49.5%)</td>
</tr>
</tbody>
</table>
Table 3. Outcomes Associated with Characteristics of Deliriogenic Medication Orders

Prescribed from Admission Order Sets

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Deliriogenic Medication Orders, n = 145</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manually-checked*, n (%)</td>
<td>134 (92.4%)</td>
</tr>
<tr>
<td>Pre-checked, n (%)</td>
<td>11 (7.6%)</td>
</tr>
<tr>
<td>As-needed, n (%)</td>
<td>140 (96.6%)</td>
</tr>
<tr>
<td>Scheduled, n (%)</td>
<td>5 (3.4%)</td>
</tr>
<tr>
<td>Orders stopped or held within 48 hours of prescription, n (%)</td>
<td>15 (10.3%)</td>
</tr>
</tbody>
</table>

*Manually-checked orders are those requiring a clinician to manually check off the order on the order set.
**Supplementary Figure S1:** 2015 American Geriatrics Society Beers Criteria – List of Potentially Inappropriate Medications in Older Adults with or at High Risk of Delirium

**Supplementary Figure S2:** 2015 American Geriatrics Society Beers Criteria – List of Drugs with Strong Anticholinergic Properties