**Background**

- Drug-drug interactions (DDIs) can result in preventable adverse events and consumption of scarce healthcare resources.
- Pharmacists are in a unique position to prevent and monitor these adverse drug events, with the knowledge and capability to reduce DDIs.
- Tertiary drug information resources are limited in their ability to capture novel, evidence-based DDIs associated with an increased risk of hospitalization.
- Pharmacoepidemiologic evidence on drug use in the real world can be used to remedy this gap.

The Pharmacological Opinion Program (POP) (http://www.health.gov.on.ca/en/pro/programs/drugs/pharmacopinion/) supports pharmacists for preventing drug therapy problems such as DDIs.

<table>
<thead>
<tr>
<th>Drug-Drug Interaction Pairs</th>
<th>Potential Adverse Event</th>
<th>Adjusted Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACEIs / ARBs + TMP-SMX*</td>
<td>Hyperkalemia</td>
<td>6.7</td>
</tr>
<tr>
<td>CCBs + Clonidine</td>
<td>Hypertension</td>
<td>3.70</td>
</tr>
<tr>
<td>CCBs + Erythromycin</td>
<td></td>
<td>5.80</td>
</tr>
<tr>
<td>Dipyridamole + Mexiletine</td>
<td>Dipyridamole</td>
<td>16.83</td>
</tr>
<tr>
<td>Diltiazem + Lisinopril</td>
<td>Diltiazem</td>
<td>3.71</td>
</tr>
<tr>
<td>Glibenclamide + T-PKSMX</td>
<td>Hypoglycemia</td>
<td>5.7</td>
</tr>
<tr>
<td>Phenytoin + T-PKSMX*</td>
<td>Phenytoin toxicity</td>
<td>2.72</td>
</tr>
<tr>
<td>Sulfamethoxazole + Nitrofurantion</td>
<td></td>
<td>2.4</td>
</tr>
<tr>
<td>Sulfamethoxazole + T-PKSMX</td>
<td>Hyperkalemia</td>
<td>12.4</td>
</tr>
<tr>
<td>Warfarin + Clopidogrel</td>
<td>Hemorrhagic complications</td>
<td>1.94</td>
</tr>
<tr>
<td>Warfarin + T-PKSMX*</td>
<td></td>
<td>3.94</td>
</tr>
</tbody>
</table>

**Methods**

- Recruit pharmacists (or pharmacies) (Figure 2) and obtain informed consent.
- Collect pre-intervention POP data from the previous six months (Sept 2013 - Feb 2014).
- Review ISMP Canada Safety Alert outlining selected DDIs with an associated increased risk of hospitalization (Table 1).
- Incorporate customized POP forms from ISMP Canada to standardize communication with prescribers.
- Intervene on drug therapy problems such as DDIs via a pharmaceutical opinion to the prescriber.
- Collect post-intervention POP data on a monthly basis for six months (May-Jun-Nov-Dec 2014).
- Conduct focus groups to seek qualitative information and feedback from participants.

**Results**

**Figure 3.** Total number of pharmacologic opinion submissions pre- and post-intervention, broken down by prescriber response. Although there was an overall decrease, the difference was not statistically significant (p = 0.204).

**Figure 4.** The difference in total number of pharmacologic opinion submissions pre- and post-intervention per pharmacy, highlighting two outliers. The 16 pharmacies with a net increase in POP submissions exceeded the 15 pharmacies with a net decrease.

**Table 1.** Impact of the ISMP Canada Safety Alert on specific DDIs (POP submissions, and the resultant theoretical cost avoidance from 67 potentially averted hospitalizations).

**Discussion**

- The focus groups confirmed the value of the ISMP Canada Safety Alert, as it provided evidence and support to empower pharmacists to communicate DDI interventions to prescribers.
- The ISMP Canada Safety Alert prompted 67 interventions on DDIs – extrapolated to a potential, theoretical cost avoidance of approximately $16 million to the health care system if all pharmacies in Ontario participated in this study for one year.

**Limitations**

- Six-month pre- and post-intervention periods did not align with yearly trends in antibiotic use and staffing.
- The targeted DDIs included medications less commonly prescribed due to emerging evidence of undesirable safety profile or more effective alternatives.
- Additional evidence-based DDIs of common medications would better impact patient health.
- Total number of POP submissions was too broad to reflect impact of the Safety Alert, which targeted specific DDIs (only 9% of POP submissions).
- Obtaining the number of POP submissions related to the Safety Alert pre- and post-intervention would permit quantitative determination of the safety alert’s value.
- ~50% loss to follow-up (Figure 2) reduced the clinical impact of the ISMP Canada Safety Alert.

**Conclusion**

- DDIs are pervasive issues faced by health care practitioners and patients, and pharmacists are most well-suited to identify and address DDIs.
- The ISMP Canada Safety Alert successfully:
  - educated pharmacists on DDIs associated with an increased risk of hospitalization;
  - encouraged pharmacists to intervene on 67 DDIs (with potential costs avoided to the healthcare system (Table 2));
  - motivated pharmacists to continue to implement the POP for reimbursement of cognitive services.

The authors would like to acknowledge support from the Canadian Foundation for Pharmacy’s Innovation Fund Grant and dedication from the study participants.