Handbook for a Pilot Study to Reduce Potential Hospitalizations due to Preventable Drug-Drug Interactions

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Background

- Hospital reports on medication incidents suggest 37-51% of reported adverse drug events may have been prevented with appropriate interventions.[1,2]
- Community pharmacists are in a unique position to monitor and prevent adverse drug reactions, including drug-drug interactions.
- By identifying and offering recommendations to prescribers, community pharmacists can be reimbursed through the Pharmaceutical Opinion Program[3] offered by the Ontario Ministry of Health and Long-term Care (MOHLTC).
- The Institute of Clinical Evaluative Sciences (ICES) conducted population-based studies examining the association between specific drug-drug interactions and hospitalizations (Table 1).[4-11]

Objective

- To compile a list of evidence-based drug-drug interactions with association to an increased risk of hospitalizations (Table 1).
- To develop a Treatment Algorithm Handbook* that helps community pharmacists identify and communicate therapeutic alternatives to prescribers in situations involving evidence-based drug-drug interactions (Table 1).
- To implement a pilot study in community pharmacies that applies medication safety principles to integrate cognitive services and reimbursement of professional services.

Methodology

Identification of evidence-based drug-drug interactions

- A literature search was conducted using MEDLINE, and EMBASE. Medical subject heading (MeSH) terms used to search the database included "drug interaction", "elderly-patients", "nested-case control", "population-based", "pharmacoepidemiology", and "patient safety".
- Publications were also found by reviewing references contained within articles.
- Eight articles were selected based on relevant evidence-based drug-drug interactions associated with increased risk of hospitalization that could be easily screened by community pharmacies.

Development of treatment algorithms to resolve evidence-based drug-drug interactions

- Treatment algorithms were created to suggest alternative antibiotics for three community infections: Group A β-hemolytic *Streptococcus* pharyngitis, outpatient community-acquired pneumonia, and uncomplicated lower urinary tract infections.
- Published literature was searched using MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and through bibliographic review.
- Articles were selected based on appropriate trial design (including use of clinical and bacteriological outcomes), comparators, and inclusion of adult patients older than 65 years of age.

Table 1 Drug-drug interactions leading to potential hospitalizations identified from primary literature[4-11]

Drug Interaction Pairs		Patient Information	Adverse Outcome	Number of cases identified from Ontario Drug Benefit database	Adjusted odds ratio based on hospitalization within two weeks of exposure to antibiotic
Chronic Medication	Added Antibiotic				
Glyburide	Trimethoprim-sulfamethoxazole (TMP-SMX) or Co-trimoxazole	Older than 65 years treated with glyburide	Hypoglycemia	909	5.7
Digoxin	Clarithromycin	Older than 65 years treated with digoxin	Digoxin toxicity	1051	9.2
Digoxin	Azithromycin	Older than 65 years treated with digoxin	Digoxin toxicity	1659	3.71
	Erythromycin				3.69
Angiotensin Converting Enzyme Inhibitors (ACEIs) / Angiotensin Receptor Blocker (ARBs)	TMP-SMX	Older than 65 years treated with ACEIs or ARBs	Hyperkalemia	204	6.7
Warfarin	TMP-SMX	Older than 65 years treated with warfarin	Hemorrhagic complications	2151	3.84
Calcium Channel Blockers (CCBs)	Clarithromycin	Older than 65 years treated with non-dihydropyridine (DHP) CCBs	Hypotension	7100	3.7
	Erythromycin				5.8
Phenytoin	TMP-SMX	Older than 65 years treated with phenytoin	Phenytoin toxicity	796	2.11
Spironolactone	TMP-SMX	Older than 65 years treated with spironolactone	Hyperkalemia	248	12.4

Results

- Evidence-based drug-drug interactions in Table 1 involved either a macrolide or trimethoprim-sulfamethoxazole (TMP-SMX). In all cases, the evidence supports an alternative to either antibiotic for selected community infections (Figure 1).
- Older persons are underrepresented in trials evaluating antibiotic therapy for community infections. Selecting an appropriate antibiotic requires applying data derived primarily from children and adults.
- A Treatment Algorithm Handbook* was created for community pharmacies to resolve evidence-based drug-drug interactions.

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*Please contact Atsushi Kawano (akawano@uwaterloo.ca) to obtain more information about the Treatment Algorithm Handbook.

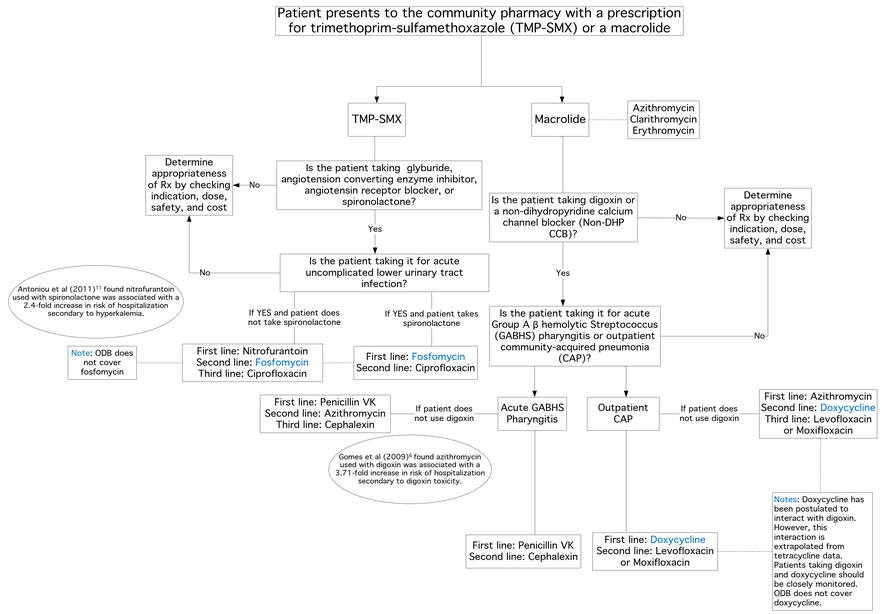

Figure 1 Treatment Algorithm Handbook* summary to prevent evidence-based drug-drug interactions for selected community infections

Conclusion / Next Steps

- The list of evidence-based drug-drug interactions with association to an increased risk of hospitalizations (Table 1) was made available to community pharmacists via ISMP Canada *Community Pharmacy Incident Reporting Newsletter* and Ontario College of Pharmacists quarterly publication, *Pharmacy Connection*.[12]
- Community pharmacists will have the option of using the Treatment Algorithm Handbook* to help resolve evidence-based drug-drug interactions (Table 1).
- Treatment Algorithm Handbook* content will be converted in difficult multimedia formats to increase accessibility to information by community pharmacists.
- Community pharmacies can participate in this pilot study to proactively initiate clinical interventions to prevent drug-drug interactions. More specifically, the information from this pilot study can be used as a catalyst to initiate cognitive services to support a financially sustainable business model.

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