Drugs associated with quality-related events reported by community pharmacies in Nova Scotia, Canada

Neil J MacKinnon, Adrian Boucher, James Barker, Certina Ho

INTRODUCTION
Twenty years since its publication, the Institute of Medicine’s report, *To Err is Human: Building a Safer Health System,* has generated much attention towards identifying safety issues in healthcare. Quality-related events (QREs) are those medication incidents that reach the patient as well as incidents that are intercepted prior to dispensing.

While considerable progress has been in documenting the magnitude of QREs in the inpatient setting, less is known about QREs in community pharmacy. In 2018, Campbell and colleagues coauthored a systematic review and meta-analysis of community pharmacy errors. Only nine studies met the inclusion criteria, the majority of which were of short duration (all but one were 40 weeks or less) and included a small number of prescriptions (all but one included less than 13,000 prescriptions). Significant heterogeneity was identified among the studies.

To address this knowledge gap, we analysed QREs reported by community pharmacies in one Canadian province over a 7-year period and identified the drugs associated with harm.

METHODS
Since 2010, all community pharmacies in Nova Scotia, Canada have been required by the provincial pharmacy regulator to report all QREs anonymously to a national incident data repository (housed by the Institute for Safe Medication Practices Canada). QREs reported by all Nova Scotia community pharmacies from 1 October 2010 to 30 June 2017 were included in this retrospective analysis. A descriptive analysis was performed on QREs with respect to the drugs involved and whether the QREs resulted in harm. The Anatomical Therapeutic Chemical Classification System was used to classify the active ingredients of the drugs and to group them into categories for the purpose of this analysis. Patients and the public were not involved in the design of this study. A complete methodology description has been previously published.

RESULTS
The 301 pharmacies in Nova Scotia reported 98,097 QREs during the 7-year period. Of these QREs, almost 1% (928) were associated with patient harm, where 90% (839 out of 928) were reported as mild harm. Levothyroxine sodium was the drug most commonly associated with a QRE, accounting for 2433 QREs or 2.34% of all QREs (table 1). It was closely followed by amoxicillin, which was reported in 2361 QREs or 2.27% of all QREs. Levothyroxine sodium was the drug most commonly associated with a QRE causing harm (46 cases). Regarding levothyroxine, of the 46 harm cases, 44 (96%) were reported as mild harm and 2 (4%) were reported as moderate harm. Citalopram (27 cases), hydromorphone (25 cases) and warfarin (22 cases) were also commonly associated with harm. Together, these four drugs were responsible for 11.3% (120 out of 1064 cases) of all QREs that resulted in harm.

Table 2 displays the top 20 medications by proportion of QREs with harm (minimum of 10 QREs reported with harm). One in 10 (10.33%) QREs reported with methadone resulted in harm, representing the greatest proportion of QREs with harm. Regarding methadone, of the 19 harm cases, 18 (95%) were reported as mild harm and 1 (5%) was reported as moderate harm. Methadone was followed by risperidone (3.51%), warfarin (2.95%) and morphine (2.82%) as far as QRE cases associated with harm.

DISCUSSION
This study presents the first large-scale, longitudinal analysis of drugs associated with community pharmacy QREs in one
entire jurisdiction over an extended period of time. By identifying the drugs most commonly associated with QREs that result in harm, proactive strategies can be developed to reduce future events. When planning and prioritising quality improvement interventions in community pharmacy, it is important to consider the frequency and the severity of harm associated with the QREs.

Strengths of this study include the large number of QREs collected (nearly 100 000) over a 7-year period from all pharmacy types (independent, chain and so on) in every setting (urban, rural and so on) in one jurisdiction. Limitations include the small number of QREs causing harm, which precluded testing for differences across types of pharmacies or locations. Finally, Nova Scotia is a small province. Recently, other provinces have begun implementing new requirements for medication incident reporting in community practice, which could facilitate the completion of a larger analysis in the future. Nevertheless, this analysis provides valuable insight into the drugs associated with QREs in community pharmacy practice.

Table 1 Top 20 medications with respect to the number of reported QREs

| Medication            | ATC classification | Number (%) of QREs |
|-----------------------|--------------------|--------------------|
| Levthyroxine sodium   | H03AA01            | 2433 (2.34)        |
| Amoxicillin           | J01CA04            | 2361 (2.27)        |
| Rosuvastatin          | C10AA07            | 1905 (1.84)        |
| Lorazepam             | N05BA06            | 1840 (1.77)        |
| Hydromorphone         | N02AA03            | 1826 (1.76)        |
| Metoprolol            | C07AB02            | 1786 (1.72)        |
| Salbutamol            | R03AC02            | 1745 (1.68)        |
| Metformin             | A10BA02            | 1568 (1.51)        |
| Rabeprazole           | A02BC04            | 1459 (1.41)        |
| Zopiclone             | N05CF01            | 1374 (1.32)        |
| Atorvastatin          | C10AA05            | 1290 (1.24)        |
| Citalopram            | N06AB04            | 1261 (1.21)        |
| Prednisone            | H02AB07            | 1254 (1.21)        |
| Naproxen              | M01AE02            | 1236 (1.19)        |
| Clonazepam            | N03AE01            | 1175 (1.13)        |
| Codeine, combinations excl. Psycholeptics | N02AA59 | 1163 (1.12) |
| Hydrochlorothiazide   | C03AA03            | 1158 (1.12)        |
| Venlafaxine           | N06A616             | 1143 (1.10)        |
| Cefalexin             | J01DB01            | 1127 (1.09)        |
| Pantoprazole          | A02BC02            | 1044 (1.01)        |
| Total                 |                    | 103 812*           |

*Total of all reported medications in QREs (excluding free-form entry of medication name). The reporter can input more than one medication per QRE; hence, the total number of QREs in this table is greater than what is shown in the results section.

Table 2 Top 20 medications by proportion of QREs with harm (minimum of 10 QREs reported with harm)

| Medication            | ATC classification | Number (%) of QREs with harm | Number (%) of QREs | Proportion of QREs with harm (%) |
|-----------------------|--------------------|------------------------------|--------------------|----------------------------------|
| Methadone             | N07BC02            | 19 (1.79)                    | 184 (0.18)         | 10.33                            |
| Risperidone           | N05A408            | 11 (1.03)                    | 313 (0.30)         | 3.51                             |
| Warfarin              | B01AA03            | 22 (2.07)                    | 746 (0.72)         | 2.95                             |
| Morphine              | N02AA01            | 16 (1.50)                    | 568 (0.55)         | 2.82                             |
| Atenolol              | C07AB03            | 14 (1.32)                    | 544 (0.52)         | 2.57                             |
| Citalopram            | N06AB04            | 27 (2.54)                    | 1261 (1.21)        | 2.14                             |
| Norgestrel and oestrogen | G03AB11          | 10 (0.94)                    | 528 (0.51)         | 1.89                             |
| Levthyroxine sodium   | H03AA01            | 46 (4.32)                    | 2433 (2.34)        | 1.89                             |
| Glucilazine           | A10BB09            | 13 (1.22)                    | 694 (0.67)         | 1.87                             |
| Ramipril              | C09AA05            | 14 (1.32)                    | 778 (0.75)         | 1.80                             |
| Sulmefamethoxazol and trimethoprim | J01E001 | 13 (1.22) | 808 (0.78) | 1.61 |
| Furosemide            | C03CA01            | 15 (1.41)                    | 1024 (0.99)        | 1.46                             |
| Hydromorphone         | N02AA03            | 25 (2.35)                    | 1826 (1.76)        | 1.37                             |
| Venlafaxine           | N06A616            | 14 (1.32)                    | 1143 (1.10)        | 1.22                             |
| Amlodipine            | C08CA01            | 12 (1.13)                    | 988 (0.95)         | 1.21                             |
| Sertraline            | N06AB06            | 10 (0.94)                    | 845 (0.81)         | 1.18                             |
| Naproxen              | M01AE02            | 13 (1.22)                    | 1236 (1.19)        | 1.05                             |
| Prednisone            | H02AB07            | 13 (1.22)                    | 1254 (1.21)        | 1.04                             |
| Pantoprazole          | A02BC02            | 10 (0.94)                    | 1044 (1.01)        | 0.96                             |
| Rosuvastatin          | C10AA07            | 18 (1.69)                    | 1905 (1.84)        | 0.94                             |
| Total                 |                    | 1064*                        | 103 812†           |                                  |

*Total of all reported medications in QREs with harm (excluding free-form entry of medication name); the reporter can input more than one medication per QRE; hence, the total number of QREs associated with patient harm in this table is greater than what is shown in the results section.

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ORCID iD Neil J MacKinnon http://orcid.org/0000-0001-8111-6651
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