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Preventable adverse drug events causing hospitalisation: identifying root causes and developing a surveillance and learning system at an urban community hospital, a cross-sectional observational study

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ABSTRACT

Objectives To identify root causes of preventable adverse drug events (pADEs) contributing to hospital admission; to develop key messages which identify actions patients/families and healthcare providers can take to prevent common pADEs found; to develop a surveillance learning system for the community.

Methods Cross-sectional observational study; 120 patients and families, 61 associated healthcare providers were interviewed then root cause analysis was performed to develop key learning messages and an electronic reporting tool was designed. Most common pADE-related medical conditions and their root causes and most common pADE root causes of entire cohort are reported.

Results Most common pADE-related medical conditions: chronic obstructive pulmonary disease/asthma (13.3%), bleeding (12.5%), hypotension (12%), heart failure (10%), acute kidney injury (5%) and pneumonia (5%). Most common root causes were: providers not confirming that the patient/family understands information given (29.2%), can identify how a medication helps them/have their concerns addressed (16.7%), can identify if a medication is working (14.1%) or causing a side effect (23.3%); can enact medication changes (7.5%); absence of a sick day management plan (12.5%), and other action plans to help patients respond to changes in their clinical status (10.8%); providers not assessing medication use and monitoring competency (19.2%). Ten key learning messages were developed and a pADE surveillance learning system was implemented.

Conclusions To prevent pADEs, providers need to confirm that patients/families understand information given, how a medication helps them, how to recognise and respond to side effects, how to enact medication changes and follow action plans; providers should assess patient's/families' medication use and monitoring competency.

INTRODUCTION

Adverse drug events (ADEs) are responsible for 15% of hospital admissions in patients 65 years or older and up to 20% of patients admitted to acute medical units.[1–9] ADE refers to harm that occurs as a result of taking or not taking a medication or treatment that is below the expected standard of care.[9–11] Up to 50% of ADEs are potentially preventable, most commonly due to suboptimal prescribing or monitoring and patient self-management issues (30% of cases each).[7 10–17] The need to reduce severe avoidable medication-related harm is recognised by the WHO which is leading a 5-year global effort to halve it by 2022.[18] In the USA, the National Action Plan for Adverse Drug Event Prevention aims to develop strategies to reduce ADEs through surveillance and research.[19] Despite recognition that public health could be improved by preventing preventable ADEs (pADEs), few studies have performed root cause analysis (RCA) of pADEs on a case-by-case basis with interviews of patients and providers to find out why they occurred.[20] Such analysis is necessary to design effective strategies to prevent or mitigate pADEs. Therefore, in this study, we aimed to identify root causes of pADEs that caused or contributed to hospital admission, translate findings into actions that care providers and patients/families can take to prevent them. In addition, we set out to design a routine surveillance and reporting system to share root causes of pADEs with community providers. This shared learning system for the community could help prevent pADE recurrence in individual patients and their incidence in future patients. This programme is unique in its emphasis on searching for the root causes of pADEs and systematic sharing of that learning with community providers.

The study objectives were to develop and evaluate a system to report, monitor, mitigate and prevent pADEs by (1) identifying root causes of pADEs causing or contributing to hospitalisation, (2) developing learning messages to translate identified root causes into actions that providers, patients and families could take to prevent pADEs, and (3) developing a surveillance learning system to capture, report and share pADE root causes with providers to prevent their recurrence.

METHODS

Setting

The study was conducted at an urban community hospital in British Columbia with patient recruitment between November 2016 and December 2017.

Design

This was a cross-sectional observational study of pADEs that caused or contributed to a patient's hospital admission. Results were synthesised into learning messages for community care providers, patients and families, and used to inform development of an electronic pADE surveillance system. Reporting follows the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for cross-sectional studies.[21]

Participants

Admitted patients were eligible to participate if they were deemed to have at least a possible ADE by Nebeker or Naranjo criteria that caused or contributed to hospital admission and was deemed to be at least potentially preventable using the Hallas criteria.[22–27] Patients admitted due to intentional self-harm were excluded. Screening for pADEs was performed on all patients admitted to the medical or critical care unit and on patients in the emergency department (ED) who were 65 years or older and admitted to the hospitalist service, medical unit or critical care unit.

If necessary, the patient's family member/carer and healthcare providers were interviewed if deemed relevant to understanding the root cause of the possible pADE.

An ADE was defined as harm resulting from either (1) taking or not taking a medication or (2) therapeutic failure as a result of treatment not in accordance with current evidence and (3) an intervention was required to manage the resulting harm.[7 10 11]

Data collection

pADE screening and assessment was performed on weekdays by specially trained pharmacists. The online supplemental appendix contains more explanation of the pharmacist training process. Emergency and hospital physicians were also encouraged to report patients with potential pADEs to a pharmacist, using a reporting form which was already in routine use.

Informed consent or assent was sought from eligible patients, and consent was sought from families and providers as applicable. We conducted interviews with patients and all potentially relevant providers (eg, family doctors, specialists, pharmacists, nurses and so on) and family members using a semistructured format designed to identify potential environmental or self-management issues involving medication or monitoring that may have contributed to the suspected pADE.

Structured chart abstracts containing all relevant information about the case were produced. Community healthcare providers were interviewed by telephone, hospital providers in person. Routinely collected data extracted included at a minimum, age, gender, presenting symptoms, treatment in ED, list of verified medications taken preadmission and changes to medications considered involved in the potential pADE, cognitive and physical deficits, and the patient's living situation. Results of imaging and the eventual discharge summary were obtained from the patient's electronic health record.

Patient and family interviews were conducted by a research nurse after first discussing with the research pharmacist potential avenues to explore in the context of the pADE suspected. The research nurse also received training in qualitative interview techniques and the nature of various anticipated pADEs.[28] Other data collected during interviews preferred languages spoken, whether their family doctor speaks the same language, medication adherence aids used, use of action plans, understanding of purpose of medication and how to identify if is working or causing a side effect.

Interviews with family doctors, community pharmacists, specialists and nurse practitioners reflected the context of the suspected pADE and sought to identify and understand events leading up to the ADE. The online supplemental appendix contains further detail on family doctor engagement prior to the start of the study. When applicable, these providers were also asked if they could think of any actions that, if taken, could have avoided or mitigated the pADE, including system-level changes. Physicians and pharmacists were interviewed by a research physician (AD) or research pharmacist (prinicipal investigator (PI) JdL), respectively.

Health literacy was assessed by the Rapid Evaluation of Adult Literacy in Medicine REALM-65 Revised (if English preferred) or the Chinese Health Literacy Scale Short Form and the 3 Brief Questions test.[29–31] Patient's medication adherence was assessed by the Morisky score (when relevant).[32–34] Where relevant, inhaler technique was assessed using a checklist.[35] At the time of the study more than 90% of admitted patients had their best possible medication history verified in the ED, supported by dedicated ED pharmacy technicians, using a jurisdictional pharmacy dispensing record.

All content of interviews was captured by audio recording and/or detailed note-taking for later verification and content analysis. Certified translators were used to interview non-English-speaking participants in person or on the telephone as needed.

All collected data and assessments were summarised in a standardised electronic case summary for review

by the investigator committee using REDCap electronic data capture tools hosted at the University of British Columbia.[36 37]

Data analyses

To assess preventability and perform RCA, pairs of raters from the investigator committee (three internists, one emergency physician, two family physicians and three PharmD-trained pharmacists) independently reviewed all the case summaries. Each rater completed the following instruments as applicable: Naranjo and WHO algorithms for causality, Hallas and Thornton preventability assessments, and Pirmohahmed seriousness assessment.[7 23 24 26 27] Raters then used a Hishikawa process (ie, fishbone diagram) to identify all causal factors and associated root causes using a systems perspective.[38] Root causes were considered to be reasons why the causal factors existed.[38] Reviews were performed independently to reduce bias.

After cases were assessed, each was adjudicated at an all-investigator meeting to, by consensus, resolve discordances, reclassify causality or preventability, and identify additional root causes.[39] The PI (JdL) reviewed all interview transcripts with the research nurse to identify potential themes (inductively then deductively) that could represent the causal factors or root causes, and presented these at investigator meetings for discussion if not previously identified.[40] Participant recruitment and case adjudication occurred in parallel.

Following adjudication of all recruited patients, the PI sorted the root causes identified for each patient into mutually exclusive categories, which were subsequently reviewed by the investigator committee (see online supplemental table 1).

For reporting, we categorised participants by pADE-related medical conditions (eg, 'bleeding') and expressed this as a percentage of the cohort, then described the root causes of that type of pADE. We also expressed the root causes contributing to pADEs as a percentage of all root causes found. Statistical analysis was descriptive. Agreement between case reviewers for causality and seriousness was assessed using Cohen's weighted kappa, and seriousness with Cohen's unweighted kappa.[41]

Developing and sharing key learning messages, surveillance system

Using the RCA aggregate results, the committee synthesised root causes across cases into actionable key messages for community-based care providers and for patients and families. These were developed collaboratively with local experts in the hospital and community. See online supplemental table 1 for further detail on how these messages were developed and shared.

Finally, using the study results, we constructed an electronic pADE surveillance and reporting system for use in routine care (see online supplemental table 2).

Study size

No formal sample size calculation was performed, as the research questions were not hypothesis driven. Instead, we estimated a target of 120 patients would provide a reasonable number of pADEs to provide a range of representative root causes. We anticipated a study duration of 6 months to enrol 120 participants based on an average of 25 admissions per day, an anticipated 15% ADE incidence, 30% capture of patients with ADEs in non-acute medical areas and a 30% anticipated rate of ADEs being preventable. Study recruitment was extended to 9 months to recruit 120 patients with pADEs.

Patient and public involvement

Our data gathering process involved interviewing patients and their families to understand potential causal factors of the pADE to permit subsequent root cause identification. In addition, for the learning messages for patients and families, volunteer members of the public who work with our institution's community engagement group reviewed for clarity and provided input to message style and formatting.

RESULTS

Over 9 months (November 2016–December 2017), 136 patients with a possible pADE were identified and 134 were recruited. Ninety per cent were identified by pharmacist screening and 10% were referred by physicians. Case review resulted in no cases having the ADE downgraded to below 'possible', and 13 cases having the ADE's preventability downgraded to below 'possibly', leaving 121 eligible pADE cases. One case was removed from the analysis due to a readmission with a diagnosis refuting the previously confirmed pADE. Thus, 120 patients with a pADE provided data for RCA. During the final 3 months of the study, the PI rather than a research nurse interviewed the 34 patients recruited and did not perform formal tests of health literacy or adherence. Study flow is depicted in figure 1.

Seventy patients were interviewed alone, 23 were interviewed with a family member and 28 family members were interviewed alone. A total of 61 healthcare provider interviews pertaining to 47 pADE cases occurred, with 4 providers declining to participate and 12 non-responsive to interview requests.

Demographics of the participants and other study measures are shown in table 1.

Of the patients assessed for health literacy, 69% failed either the REALM-65 or the 3 Brief Questions test; 61% of these patients were unilingual English speakers.

Table 2 shows the post-adjudication assessments of causality, preventability and seriousness of included pADEs.

Two participant deaths attributed to pADEs occurred. Pre-adjudication agreement between research investigators' assessment was 'moderate' for causality (Cohen's weighted kappa 0.48 (95% CI 0.36 to 0.61)), 'substantial'

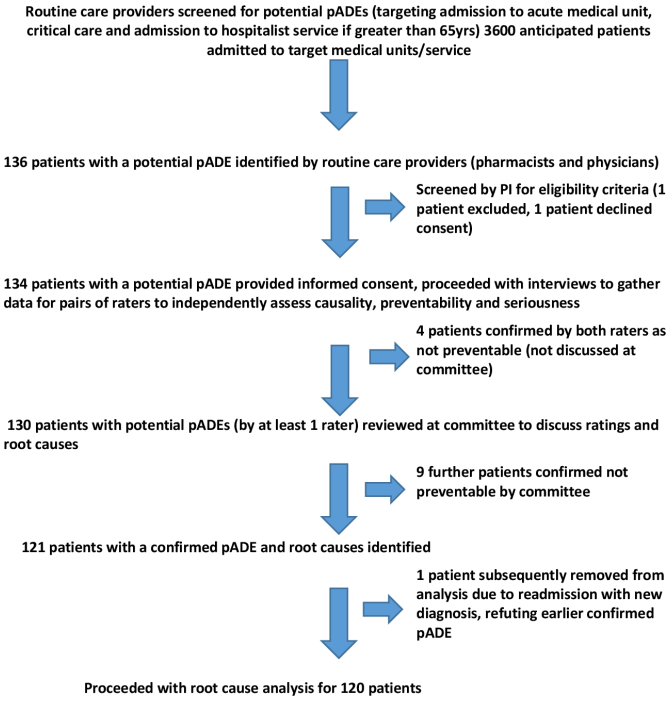

Figure 1 Flow diagram of exclusion criteria for study cohort. pADE, preventable adverse drug event; PI, principal investigator.

for seriousness (Cohen's weighted kappa 0.76 (95% CI 0.62 to 0.91)) and 'fair' for preventability (Cohen's unweighted kappa 0.38 (95% CI 0.20 to 0.55)).

The most common pADEs by type of presentation are shown in table 3.

Overall, 33 categories of root causes were identified (online supplemental table 2), with 281 root causes involved in all 120 patients. The most common causal factors and root causes of included pADEs are shown in table 4.

Table 1 Description of the study cohort

Variable	Cohort, n=120 (unless specified)
Mean (SD) age, years	77 (11)
Female, n (%)	65 (54)
Language spoken, n (%)	
English, unilingual	65 (54)
Cantonese, unilingual	16 (13)
English/Cantonese/Mandarin, bilingual	14 (12)
Mandarin, unilingual	7 (6)
Punjabi, unilingual	7 (6)
Other (various)	7 (6)
Tagalog, unilingual	4 (3)
Health literacy	
REALM-65 score 6 or less, failed	19/40 (48%)
3 Brief Questions, failed	36/45 (80%)
STIHLS 13/15 or less, failed	0/5 (0%)
Medication adherence, Morisky Medication Adherence Score (MMAS-8)*	
Less than 6, low adherence	16/45 (36%)
6 to less than 8, medium adherence	15/45 (33%)
Lives alone and 70 years or more	34/101 (34%)
Picks up prescriptions themselves	36/61 (59%)

*The MMAS, Morisky Medication Adherence Scale and Morisky are trademarks of Donald E Morisky, and may be used only with permission. All rights reserved. Use of the MMAS-8 is protected by US copyright laws. Permission to use the MMAS scales is required. Reproduction and distribution of the MMAS is protected by US copyright laws, A license agreement to use the scale is available from: Donald E Morisky, ScD, ScM, MSPH, Professor, 2020 Glencoe Ave, Venice, California 90 291-4007, dmorisky@gmail.com 2007 Donald E Morisky.

Key learning messages

Six key messages were identified and developed for community-based providers (table 4) and four for the public (table 5).

In total, in-person knowledge translation activities reached a total of 82 physicians, 24 community nurses and 62 community pharmacists (with some providers attending two sessions).

Surveillance system

This system is organised around common pADE-related adverse outcomes; populated with drop-down menus for root causes, informed from our findings, with expected actions required to prevent recurrence. Once information is entered, a PDF letter is generated for relevant community providers (see figure 2). In addition, since December 2019, as part of a national adverse drug reaction (ADR) surveillance programme, it became mandatory for hospitals to report ADRs. Therefore, in collaboration with the relevant provincial agency, we developed a process to share with them reports of pADEs that meet the criteria for an ADR (harm resulted from taking a medication).

CONCLUSIONS

Summary of findings

We are unaware of similar programmes designed to prevent or mitigate pADEs by finding and translating root causes into learning messages for providers, patients and families and by implementing a pADE surveillance system for community feedback. Providers are encouraged to ask patient/families open-ended questions to confirm their understanding of how taking a medication will help them, how to recognise and respond to side effects, how to know if a medication is working (why monitoring helps them), and understanding of medication changes and how to enact them.[42] Such conversations would identify patients with reduced medication use or monitoring competency who need additional supports (eg, referral to community resources or in-home services).

Table 2 Adjudicated assessments of ADE causality (certain, probable or possible), preventability (definitely or possibly) and seriousness (mild, moderate, severe, death)

ADE causality	Definitely preventable	Death	Severe	Moderate	Mild	Possibly preventable	Death	Severe	Moderate	Mild	Total
Certain (31/120, 25.8%)	22	0	4	18	0	9	0	5	4	0	**31 (25.8%)**
Probable (51/120, 42.5%)	9	0	1	8	0	42	0	2	40	0	**51 (42.5%)**
Possible (38/120, 31.7%)	5	1	0	4	0	33	1	7	24	1	**38 (31.7%)**
Total	**36/120 (37.5%)**	**1 (0.08%)**	**5 (0.04%)**	**30 (25%)**	**0**	**84/120 (62.5%)**	**1 (0.08%)**	**14 (11.7%)**	**68 (56.7%)**	**1 (0.08%)**	**120**

ADE, adverse drug event.

In addition to the learning messages developed, system-level changes as a result of our root cause findings included an update to our multisite hospital pharmacy drug–drug interaction alert system (carvedilol–amiodarone) and a change to our provincially based private laboratory reporting system (phenytoin–albumin reminder). Further work is planned and ongoing to address root causes found related to provider culture in our hospital.

Implications

Our findings provide insights that that could help to reduce the burden of pADEs. First, our results suggest that many ADEs involving anticoagulants, antihyperglycaemic agents, antihypertensive and cardiovascular drugs could be prevented by providers confirming that patients can follow the actions in our learning messages. Previous studies report that these drugs cause 40% of hospital admissions, but because patients/providers were not interviewed to identify root causes, the true opportunity for preventability was likely missed.[15] Second, chronic obstructive pulmonary disease (COPD) and heart failure are top reasons for recurrent hospitalisations.[43] Yet, we found that their root causes are also present in hospital. In the current culture, hospital providers take over the care of the patient and tend not to use the hospitalisation as an opportunity to engage the patient and family to confirm their understanding and impart skills needed to manage, monitor and respond to changes in their condition. Consequently, as this is not a current goal of care, hospital providers often miss opportunities to confirm the patient or family's ability to perform certain tasks (eg, correct inhaler technique or daily weighing) or ensure understanding of information by the most competent family member. As a result, hospital providers fail to identify the need to arrange appropriate supports for patients/families with reduced medication use/monitoring competency.

The concept and process of identifying root causes of ADEs could also be integrated into mandatory adverse drug reporting programmes. If the root cause is not considered, the ADR may be misattributed to the drug itself, the role the patient and provider played may be ignored, and thus potentially modifiable causes may be overlooked.

Finally, these findings highlight an important opportunity to reduce healthcare burden if systems of care and healthcare provider training address identified gaps. At an individual patient level, in order to prevent pADE recurrence, first requires that care providers recognise the presence of the pADE and then identify and address the root causes. This does require a change in thinking, to spend time analysing, for example, why the patient had a COPD/asthma or heart failure exacerbation, a bleeding event or a fall, then incorporate managing the root causes within the treatment plan (rather than limiting treatment to the symptoms or consequences related to the medical condition diagnosed). It has been previously shown that the risk of ADE non-recognition is higher when the ADE

Table 3 Type of pADE-related admissions, causal factors and associated root causes: presentations with more than five cases AND at least one root cause addressed by a learning message

Type of presentation	Causal factors and identified key root causes
COPD/asthma 16 cases (13.3%)	Intentional non-adherence due to patient lack of understanding of how medication helps them; provider not confirming how medication helps patient; poor technique; lack of provider assessment; lack of action plan provision
Bleeding, 15 cases (12.5%)	Concomitant NSAIDs due to providers not asking screening questions for NSAIDS; not confirming if patient can identify red flag symptoms; eligibility for PPI (lack of referral to guideline)
Hypotension 14 cases (11.7%)	Patient not recognising side effects; provider not ensuring that patient can confirm red flag symptoms or not asked to measure BP; lack of provision of sick day medication plan
Heart failure 12 cases (10%)	Lack of daily weighing; provider not confirming that patient understands fluid-weight concept; how medication helps patient; lack of action plan
Hyponatraemia 6 cases (5%)	Lack of provision of sick day medication plan, prescribing; provider not confirmed that patient can identify side effect
Pneumonia/*Clostridioides difficile* colitis 6 cases (5%)	Suboptimal antibiotic choice for pneumonia not identified at dispensing due to lack of referral to a guideline; unclear indication (*C. difficile* colitis)
Various types of presentation 6 cases (5%)	Medication mix-ups due to lack of confirming patient/family understands medication changes and need to implement them
Acute kidney injury 6 cases (5%)	Lack of provision of sick day medication plan (2 cases); provider deferring to specialist clinic (lack of expected monitoring frequency of serum creatinine; unidentified action able root cause, other than possible lack of reminder system); lack of adjustment (lapse) in response to abnormal serum creatinine

BP, blood pressure; COPD, chronic obstructive pulmonary disease; NSAIDs, non-steroidal anti-inflammatory drugs; pADE, preventable adverse drug event; PPI, patient and public involvement.

is part of a presenting illness rather than a direct drug effect.[44] Additionally, our findings suggest a need for healthcare providers to fundamentally alter how they may speak to patients to ensure they understand how to take medications safely and increase the likelihood that they will adhere to an agreed on regimen. At an institutional level, a rethink of the goals of care while the patient is in hospital should be broadened to include the patient/families' ability to demonstrate competency in managing tasks that can help them stay at home longer. This will require training of all healthcare providers to have more skilful conversations with patients and robust care processes developed to incorporate patient/family demonstration of competency to perform required tasks into the goals of care (eg, daily weighing, inhaler technique).

Related research

Previous reports have described the development of a prospective surveillance system to detect adverse events (not specifically drug related) in a multisite hospital setting.[45] The motivations underpinning that work mirror our intent to identify ways we can prevent pADEs. The authors developed trigger methodology, reflecting the medical context of certain patient care areas and used trained observers to screen for potential adverse events that were then peer reviewed to identify preventability and areas for quality improvement. Elements of this approach (trigger methodology, prompts to consider root causes at admission) could be explored for inclusion in our pADE surveillance programme.

Although studies have described the epidemiology of pADEs, we suggest that to view the full scope of preventability requires a lens focused on identifying root causes to purposefully learn how pADEs could be prevented.[11 16 17 39 46] Therefore, differences in types of pADEs reported across studies, will in part, likely reflect differences in study objectives, design, ADE definition and identification process, and whether patient and provider interviews were conducted and RCA was performed.

Generalisability and further research

Although the type of pADEs may differ across communities, we suggest that the process of considering whether a medical illness is caused by a pADE, identifying the root causes, addressing them, then sharing with relevant community providers is a worthwhile means to try to prevent ADEs given their expected incidence and public health impact. Further research is needed to assess whether providers can identify pADE root causes on hospital presentation, can incorporate actions from our learning messages into practice and whether providing feedback to community providers can reduce pADEs.

Limitations

Our study population of 34% of predominantly elderly patients being non-English speaking was reflective of our local demographics but may not be of other communities,

Table 4 Top 10 causal factors and associated root causes of included pADEs

Causal factor due to associated root cause	Example of type of pADE	% of all root causes	% of patients impacted by root cause
Patient had not understood information (possibly) previously provided due to provider not confirming patient understanding	Many different pADEs (except antibiotic related)	35/281 (12.4)	35/120 (29.2)
Unable to recognise medication side effect due to providers not confirming ability to do this	Bleeding, orthostatic hypotension, constipation	28/281 (10.0)	28/120 (23.3)
Prescribing (and not identified or managed at dispensing) antibiotics for CAP 25% of pADEs due to lack of referral to guideline	Unresolved pneumonia	24/281 (8.5)	24/120 (20)
Intentional non-adherence due to mainly not understanding purpose/benefit of medication±having concerns about taking it; provider not confirming that patient understands benefits/not identifying or addressing concern	Stroke, MI, aortic dissection, COPD, asthma, heart failure exacerbations	20/281 (7.1)	20/120 (16.7)
Medication monitoring provider (no actionable root cause identified: lack of system reminder, healthcare provider lapse, community pharmacy not routinely asking patient about bloodwork, except for lack of reminder on laboratory report to calculate phenytoin for low albumin n,1)	Acute kidney injury, hypothyroidism, phenytoin toxicity (n,1)	18/281 (6.4)	18/120 (15.0)
Could not identify if medication was working due to provider not confirming that patient can identify how medication is working and providing specific parameters (daily weighing, measuring BP)	Heart failure exacerbations, intracranial haemorrhage, hypertensive urgency	17/281 (6.0)	17/120 (14.1)
Patient did not have a sick day medication plan; due to lack of locally available resource in use, incorporation into routine practice; recognition of this as root cause in affected pADEs	Hypotension, acute kidney injury, elevated INR, bleeding, hypoglycaemia	15/281 (5.3)	15/120 (12.5)
Lack of provision of action plans for COPD, asthma or heart failure	COPD, asthma, heart failure	13/281 (4.6)	13/120 (10.8)
Provider not assessing medication use competency (ability to safely and reliably take medications)	Bleeding, drug toxicity, stroke	12/281 (4.3)	12/120 (10)
Provider had not adjusted medication based on laboratory parameters (actionable root cause not identified, presumed lapse by providers, laboratory results not available to community pharmacists)	Acute kidney injury, bleeding, stroke (due to hyperthyroidism)	11/281 (3.9)	11/120 (9.2)
Provider not assessing medication monitoring competency (ability to monitor for side effects or lack of effectiveness)	Bleeding, weakness, hypotension, heart failure, myxoedema	11/281 (3.9)	11/120 (9.2)

BP, blood pressure; CAP, community-acquired pneumonia; COPD, chronic obstructive pulmonary disease; INR, international normalised ratio; MI, myocardial infarction; pADE, preventable adverse drug event.

limiting our study's generalisability. Our reliance on pharmacist screening of pADEs may have resulted in unknown biases in the types of patients and pADEs identified compared with another type of healthcare professional screening, although pharmacist screening is common in hospital-based ADE surveillance programmes.[22]

Limitations of RCA as a method to improve healthcare have recently been reviewed.[47] Broadly, limitations can relate to poorly conducted data gathering and analysis. RCA can fail to yield improvements if strong solutions (described as controls) are not identified or implemented. The RCA process itself can be impaired by a weak political mandate. Finally, RCA needs to be followed by some means of measurement to know whether the implemented control is working and to provide feedback to relevant actors to complete the learning process.

We believe our study aims, objectives and methods address these known weaknesses of RCA. Our data gathering process started with interviewing patients and their families. Understanding derived from these interviews is central to our study findings. A wide system view was taken to identify root causes, which were required to be actionable issues that providers or patients could change. We performed aggregated review of potential pADE cases, as each research committee meeting

Table 5 Provider and public learning messages developed

Healthcare provider message (release date)	Content addressing root causes; accessed at https://www.vchri.ca/richmond/pADE
Sick Day Medication Management (March 2018)	Hold SADMANS drugs while decreased fluid intake (to avoid hypotension, acute kidney injury or other side effect); hold sulfonylureas while decreased caloric intake (to avoid hypoglycaemia); hold warfarin for 1 day if eating 50% less and or severe diarrhoea. Dialogue is provided for how to confirm patient's understanding, what they will do, when, why and how they will remember. S, sulfonylureas; A, ACE inhibitors; D, diuretics or direct renin inhibitor; M, metformin; A, angiotensin receptor blocker; N, non-steroidal anti-inflammatory drugs; S, SGLT2 inhibitors
Community and Nursing Home Acquired Pneumonia (May 2018)	Avoid macrolide monotherapy; use amoxicillin 1 g three times per day or alternate to target *Streptococcus pneumoniae* unless risk factors (provided) for other pathogens.
How to write an asthma action plan (April 2019)	Provides instructions to increase steroid dose ×4; confirm patient's ability to identify yellow level symptoms; understanding of purpose of steroid inhaler for prevention of flare-up; assess inhaler technique; provide action plan.
How to identify and address intentional non-adherence (April 2019)	Provides suggested dialogue to explore patient's current understanding/beliefs about medicines and condition, address gaps to help patient make an informed decision about the value of the medication, expected benefit.
Prevention of bleeding related pADEs (February 2019)	Describes how to ask screening questions to rule out NSAIDs in patients taking anticoagulants; how to confirm a patient can recognise red flag symptoms (side effects) and what they need to do; provides eligibility criteria for primary prevention.
Medication Mix Ups (May 2019)	Relates to situations where patients have resumed taking medications (existing supply at home) that were intended to be stopped; resumed old doses of medications, intended to be changed, did not fill prescription as unaware of a new medication. Provides suggested dialogue to confirm that patient and family can correctly identify what they need to do to successfully implement a medication change.
Public learning message	**Content addressing root causes; accessed at https://vch.eduhealth.ca/**
Your Medication Plan for Sick days BA.505.S53 (March 2018)	Identifies which medications to not take while not drinking as much fluid, during an illness or not eating or severe diarrhoea and why this is important.
COPD Flare Up Plan FN.510. F66 (February 1019)	How to recognise symptoms of flare-up, what to do; why it is important to regularly use long-acting inhalers, how regular use of these would help them stay out of hospital and feel better and improve other symptoms of COPD not just breathing.
How to prevent worsening of heart failure symptoms. FD.780. H434 (March 2019)	Describes connection between fluid gain and weight gain and how this leads to symptoms; provides explanation for purpose and expected benefit of daily weighing; what to do if weight gain.
Measuring BP at home (and recognising orthostatic hypotension) BD.820.W74 (April 2019)	Explains purpose of taking antihypertensive medications; explains need to measure BP to know if medication is working. Describes specific symptoms of orthostatic hypotension and what to do.

BP, blood pressure; COPD, chronic obstructive pulmonary disease; NSAIDs, non-steroidal anti-inflammatory drugs; pADEs, preventable adverse drug events.

built on previous thoughts and discussion to identify themes and key learning messages. Together this framework allowed us to identify an overarching root cause related to the culture of care in the hospital. This culture underpins our failure to seek and confirm competency of patients on medication-related issues. Our RCA was performed within the context of a research study, providing free political mandate to generate purposeful learning for sharing. Our active surveillance system, by providing a means to give feedback and monitor future pADEs, closes the learning loop.

For learning to occur, the surveillance system does need to be used by providers. We therefore measure the performance of our system by tracking a key performance indicator, a target pADE reporting rate of 5% of medical admissions, (reflecting 50% of expected pADEs, assuming an incidence of 10%). Currently, we are reporting 2%–3% of medical admissions as pADEs. Further work is planned to improve reporting of pADEs by providers. We also implemented a reporting structure to share aggregated reports of pADEs with hospital leadership and the local family physician network. Such engagement is important if the burden of pADEs is to be fully understood, and increases the likelihood that we can find appropriate solutions and build support for any required organisational change to be levied to resolve them.

A study limitation is selection of relatively weak corrective solutions. Potential solutions may be viewed as a hierarchy, with changes to processes inferior to systems.[47] Our solutions, mainly relate to changes in processes, as they aim to help providers do things differently, for example, asking patients questions around non-steroidal anti-inflammatory drug use, or asking a patient to demonstrate how they use their inhaler. This requirement for a conversation is unavoidable, but by taking a systems view led us to develop an organisational change to address a root cause of provider culture. Patients admitted with COPD or who visit the ED with asthma will be assessed by providers using a checklist to standardise

(Name of Hospital) Preventable Adverse Drug Event Program

This letter is sent to share actions taken after assessment by the healthcare team at (name of hospital, to address root causes of a possible preventable adverse drug event (pADE) with the aim to help mitigate or prevent recurrence and facilitate continuity of care.

Date:

Name of recipient (s):

Patient name, provincial health number, date of birth

Dear healthcare provider (s):

Patient (name) presented to hospital with *hypotension, acute kidney injury*.

Events leading up to presentation:

- *The patient had continued taking medications from the SADMANS group, despite decreased fluid intake these past few days due to gastroenteritis, SBP < gommHg at presentation (free text).*

Drug(s) involved:

- Captopril
- Empagliflozin
- Furosemide

Patient Admitted? Yes

This was presentation/admission was attributable in part to the following possible preventable adverse drug event (s):

- Needs a Sick Day Medication plan.

The patient will be provided the following action(s) from the hospital:

- Sick day medication plan will be provided and patient and family understanding confirmed.

Further follow-up requested:

- Community pharmacist to please continue to confirm patient's ability to follow the medication sick day plan at dispensing of future related medications.

Signed, (Profession)

***** This letter contains confidential information, please call XXX XXX XXXX if received in error ******

Figure 2 Example of letter to community providers showing output from pADE electronic reporting tool related to pADE due to absence of sick day medication plan (italicised text selected by user, prepopulated drop-down menu options unless stated). SADMANS, S=sulfonylureas A=ACE inhibitors D=diuretics or direct renin inhibitor M=metformin A=angiotensin receptor blocker N=non-steroidal anti-inflammatory drugs S=SGLT2 inhibitors; SBP, systolic blood pressure.

assessment of inhaler technique, non-adherence risk and action plan use. An electronic learning module has been developed to support training for hospital providers. These processes are incorporated into paper-based systems of admission and ED treatment orders. We expect to do the same to support our approach to care for patients with heart failure.

However, more organisational change is needed to embed learning from our study into a system of care. Avoiding medication mix-ups is an example of a pADE that needs a systems-based solution to ensure a provider confirms that the patient and family understands and can manage medication changes. We are developing a checklist to support hospital providers have that conversation. In tandem, we are collaborating with our national medication safety organisation and local community pharmacists to develop a conversational checklist for community pharmacists. This type of pADE is a problem with many actors involved.[47] However, with increased scrutiny to identify pADEs on admission and report them in our surveillance system, we now have a means to identify future recurrence of this pADE to make visible the gaps in the system that causes it, and provide feedback to providers and hospital leadership.

To date, our work has resulted in two system level changes (a change in reporting of phenytoin assays provincially and a health authority change in a drug interaction alert), and development and exploration of two organisational changes (for COPD/asthma and managing medication changes, respectively). Key learning messages specify actions that providers and patients need to take to avoid a pADE. Although it is hard to systematise this process, we hope our findings will allow others to identify stronger solutions that enable and ensure providers have good quality conversations with patients.

CONCLUSION

We identified 33 root causes of pADEs resulting in hospitalisation, most commonly in cases of COPD/asthma exacerbation, bleeding, hypotension, heart failure, hyponatraemia, pneumonia and acute kidney injury. The root causes identified suggest that providers should confirm: patient's/families' understanding of information, how a medication helps them, how to know if it is working or causing a side effect, how they plan to enact medication changes, whether they can follow action plans for variations in their clinical status, and if needed, arrange additional supports in context of medication use and monitoring competency. The process also allowed us to identify system-level and organisational changes that could reduce the risk of future pADEs and the surveillance system provides an ongoing means to identify new learning messages as needs arise.

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Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Our university, University of British Columbia (UBC), Clinical Research Ethics Board (CREB) reviewed our ethics submission, and recommended to us that the study be conducted instead under the auspices of our local quality committee. This was largely due to the ability of this review framework to allow Section 51 of the Evidence Act to be extended to family MDs and providers in the community who are not hospital employees. To permit this, our health authority (Vancouver Coastal Health), risk management department, consulted with the British Columbia Ministry of Health to confirm that for the purposes of this study, this extension of Section 51 would apply. This was done to increase the likelihood of a full and frank discussion of the reasons why pADEs may have occurred with these providers. Our Quality and Patient Safety Committee took this on with full knowledge of the rationale and UBC CREB's recommendation. Since we had already developed consent and assent forms (reviewed by UBC CREB), we felt it was best practice to continue to conduct the study as if it was a research study in all aspects. This was also the arrangement made with our Quality and Safety Committee that patients/family members would continue to be required to provide informed consent or assent.

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Data availability statement Data are available in a public, open access repository. Data are available upon reasonable request. The study protocol, consent forms and the case report form template will be shared immediately on publication, on Scholars Portal Dataverse at https://dataverse.scholarsportal.info/dataset.xhtml?persistentId=doi:10.5683/SP2/X9NOOU). In addition, de-identified individual-level participant-derived data that underlie the main results can be requested. These data will be: medical presentation, ADE causality, preventability and seriousness, all root causes identified, age <70 years, categories of health literacy, medication adherence, picks up prescription by themselves, lives alone. Individual data will be shared on provision of: an analysis plan, an institutional ethics certificate endorsing the proposed reuse of data as per the analysis plan and completion of a data sharing agreement. Evidence of the appropriate licensing agreement would be required before certain data can be shared (see page 14). These de-identified individual-level derived data will be available after 3 months and up to 3 years post-publication by contacting the corresponding author (https://orcid.org/0000-0003-0088-6895).

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REFERENCES

1 Phillips AL, Nigro O, Macolino KA, *et al*. Hospital admissions caused by adverse drug events: an Australian prospective study. *Aust Health Rev* 2014;38:51–7.
2 Jolivot P-A, Hindlet P, Pichereau C, *et al*. A systematic review of adult admissions to ICUs related to adverse drug events. *Crit Care* 2014;18:643–60.
3 Franceschi M, Scarcelli C, Niro V, *et al*. Prevalence, clinical features and avoidability of adverse drug reactions as cause of admission to a geriatric unit: a prospective study of 1756 patients. *Drug Saf* 2008;31:545–56.
4 Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Ann Pharmacother* 2008;42:1017–25.
5 Klopotowska JE, Wierenga PC, Smorenburg SM, *et al*. Recognition of adverse drug events in older hospitalized medical patients. *Eur J Clin Pharmacol* 2013;69:75–85.
6 Pedrós C, Quintana B, Rebolledo M, *et al*. Prevalence, risk factors and main features of adverse drug reactions leading to hospital admission. *Eur J Clin Pharmacol* 2014;70:361–7.
7 Pirmohamed M, James S, Meakin S, *et al*. Adverse drug reactions as cause of admission to hospital: prospective analysis of 18 820 patients. *BMJ* 2004;329:15–19.
8 Hamilton H, Gallagher P, Ryan C, *et al*. Potentially inappropriate medications defined by STOPP criteria and the risk of adverse drug events in older hospitalized patients. *Arch Intern Med* 2011;171:1013–9.
9 Salvi F, Marchetti A, D'Angelo F, *et al*. Adverse drug events as a cause of hospitalization in older adults. *Drug Saf* 2012;35 Suppl 1:29–45.
10 Howard RL, Avery AJ, Howard PD, *et al*. Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study. *Qual Saf Health Care* 2003;12:280–5.
11 Howard RL, Avery AJ, Slavenburg S, *et al*. Which drugs cause preventable admissions to hospital? A systematic review. *Br J Clin Pharmacol* 2007;63:136–47.
12 Chen Y-C, Fan J-S, Chen M-H, *et al*. Risk factors associated with adverse drug events among older adults in emergency department. *Eur J Intern Med* 2014;25:49–55.
13 Chan A, Soh D, Ko Y, *et al*. Characteristics of unplanned hospital admissions due to drug-related problems in cancer patients. *Support Care Cancer* 2014;22:1875–81.
14 Dalleur O, Beeler PE, Schnipper JL, *et al*. 30-Day potentially avoidable readmissions due to adverse drug events. *J Patient Saf* 2017. doi:10.1097/PTS.0000000000000346. [Epub ahead of print: 17 Mar 2017].
15 Budnitz DS, Lovegrove MC, Shehab N, *et al*. Emergency hospitalizations for adverse drug events in older Americans. *N Engl J Med* 2011;365:2002–12.
16 Perrone V, Conti V, Venegoni M, *et al*. Seriousness, preventability, and burden impact of reported adverse drug reactions in Lombardy emergency departments: a retrospective 2-year characterization. *Clinicoecon Outcomes Res* 2014;6:505–14.
17 Winterstein AG, Sauer BC, Hepler CD, *et al*. Preventable drug-related hospital admissions. *Ann Pharmacother* 2002;36:1238–48.
18 The third who global safety challenge: medication without harm. Geneva, 2020. Available: https://www.who.int/patientsafety/medication-safety/en/ [Accessed March 2020].
19 U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion. *National action plan for adverse drug event prevention*. Washington, DC: U.S. Department of Health and Human Services, Office of Disease Prevention and Health Promotion, 2014.
20 Gertler SA, Coralic Z, López A, *et al*. Root cause analysis of ambulatory adverse drug events that present to the emergency department. *J Patient Saf* 2016;12:119–24.
21 von Elm E, Altman DG, Egger M, *et al*. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol* 2008;61:344–9.
22 Olsen S, Neale G, Schwab K, *et al*. Hospital staff should use more than one method to detect adverse events and potential adverse events: incident reporting, pharmacist surveillance and local real-time record review may all have a place. *Qual Saf Health Care* 2007;16:40–4.
23 Naranjo CA, Busto U, Sellers EM, *et al*. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30:239–45.
24 Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: a clinician's guide to terminology, documentation, and reporting. *Ann Intern Med* 2004;140:795–801.
25 Hakkarainen KM, Andersson Sundell K, Petzold M, *et al*. Methods for assessing the preventability of adverse drug events: a systematic review. *Drug Saf* 2012;35:105–26.
26 Hallas J, Harvald B, Gram LF, *et al*. Drug related hospital admissions: the role of definitions and intensity of data collection, and the possibility of prevention. *J Intern Med* 1990;228:83–90.
27 Schumock GT, Thornton JP. Focusing on the preventability of adverse drug reactions. *Hosp Pharm* 1992;27:538.

28 Patton MQ, Interviewing Q. In:Patton MQ editor. In: *Qualitative research and evaluative methods: integrating theory and practice*. 4th ed.2015. Thousand Oaks: Sage Publications Inc, 2012: 423–516.
29 Bass PF, Wilson JF, Griffith CH. A shortened instrument for literacy screening. *J Gen Intern Med* 2003;18:1036–8.
30 Pan F. A short form of the Taiwan health literacy scale (THLS) for Chinese speaking adults. *International Journal of Social, Behavioural, Educational, Economic, Business and Industrial Engineering* 2010;4:40–5.
31 Chew LD, Bradley KA, Boyko EJ. Brief questions to identify patients with inadequate health literacy. *Fam Med* 2004;36:588–94.
32 Morisky DE, Green LW, Levine DM. Concurrent and predictive validity of a self-reported measure of medication adherence. *Med Care* 1986;24:67–74.
33 Morisky DE, Malotte CK, Choi P, *et al*. A patient education program to improve adherence rates with antituberculosis drug regimens. *Health Educ Q* 1990;17:253–66.
34 Morisky DE, DiMatteo MR. Improving the measurement of patient self-reported medication non-adherence. *J Clin Epidemiol* 2001;64:258–63.
35 Batterink J, Dahri K, Aulakh A, *et al*. Evaluation of the use of inhaled medications by hospital inpatients with chronic obstructive pulmonary disease. *Can J Hosp Pharm* 2012;65:111–8.
36 Harris PA, Taylor R, Thielke R, *et al*. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377–81.
37 Harris PA, Taylor R, Minor BL, *et al*. The REDCap Consortium: building an international community of software platform partners. *J Biomed Inform* 2019;95:103208.
38 Rooney J, Van den Heuvel L. Root cause analysis for beginners. *Quality Progress* 2004:45–53.
39 Zed PJ, Abu-Laban RB, Balen RM, *et al*. Incidence, severity and preventability of medication-related visits to the emergency department: a prospective study. *CMAJ* 2008;178:1563–9.
40 Patton MQ. Chapter 8, Qualitative Analysis and Interpretation. In: *Qualitative research and evaluative methods: integrating theory and practice*. 4th ed. Thousand Oaks: Sage Publications, 2015: 518–651.
41 Cohen J. A coefficient of agreement for nominal scales. *Educ Psychol Meas* 1960;20:37–46.
42 Always use TeachBack! National Institute of healthcare improvement. Boston, Massachusetts, 2020. Available: http://www.ihi.org/resources/Pages/Tools/AlwaysUseTeachBack!.aspx [Accessed March 2020].
43 Canadian Institute for Health Information. *All-Cause readmission to acute care and return to the emergency department*. Ottawa, ON: Canadian Institute Health Information, 2012.
44 Roulet L, Ballereau F, Hardouin J-B, *et al*. Assessment of adverse drug event recognition by emergency physicians in a French teaching hospital. *Emerg Med J* 2013;30:63–7.
45 Forster AJ, Huang A, Lee TC, *et al*. Study of a multisite prospective adverse event surveillance system. *BMJ Qual Saf* 2020;29:277–85.
46 Woo SA, Cragg A, Wickham ME, *et al*. Preventable adverse drug events: descriptive epidemiology. *Br J Clin Pharmacol* 2020;86:291–302.
47 Peerally MF, Carr S, Waring J, *et al*. The problem with root cause analysis. *BMJ Qual Saf* 2017;26:417–22.