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Understanding adverse drug-related emergency department visits: development of a conceptual model through a systematic review

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Abstract

Background: The burden of adverse drug event (ADE)-related emergency department (ED) visits is increasing despite several preventive measures. The objective of this paper was to develop and validate a conceptual model for a better understanding of ADE-related ED visits and to guide the design and implementation of effective interventions.

Methods: The development of the model involved a systematic review of the literature using PubMed and Embase databases. Studies reporting the risk factors associated with ADE-related ED visits were included. The methodological qualities of the included studies were assessed using the Mixed Methods Appraisal Tool (MMAT). The model was mapped and validated using face and content validity by an expert panel. Deficiencies and targeted interventions were identified, and steps for the design and implementation were recommended.

Results: The literature search generated 1361 articles, of which 38 were included in the review; 41 risk factors associated with ADE-related ED visits were identified. All factors were mapped, and the model was validated through face and content validity. The model consisted of six concepts related to sociodemographic factors, clinical factors, ADE-related to ED visits, ADE while in the ED, outcomes, and consequences. Interventions could be targeted at the factors identified in each concept to prevent ADE-related ED burden.

Conclusion: A conceptual model to guide the successful design and implementation of strategies to prevent ADE-related ED visits and the occurrence of ADE at ED was developed. Clinicians should take these factors into consideration to prevent untoward events, especially when treating high-risk patients.

Keywords: adverse drug events, drug-related problem, emergency department, pharmacoepidemiology

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Background

The trend for the use of medications in the treatment and prevention of acute and chronic disease conditions is increasing among the general population globally.[1] This may be partly related to the continuous introduction of new drugs, an ageing population, and overall population growth. In the United States alone, 81% of adults >18 years had used at least one medication during the previous week, and 50% take at least one prescription drug.[2] However, according to the World Health Organization's world medicines situation report, it was estimated that approximately 50% of all medicines were inappropriately prescribed, dispensed, or sold, and half of all patients receiving medications were unable to take their medicines

properly.[1] Thus, these circumstances may lead to many adverse drug events (ADEs) that may result in hospitalization and an increase in healthcare costs.

Recently, the increasing ADE-related healthcare burden has emerged as a public health concern. It is estimated to be responsible for over 100,000 deaths annually, and represents an estimated increase in healthcare costs of US $201.4 billion.[3] ADEs are responsible for many hospital emergency department (ED) visits and admissions. ADEs account for 2–3% hospital admissions in Australia,[4] and 30.6% contributed to ED visits in Malaysia.[5] ADE-related hospitalization continues to increase despite interventions to minimize the occurrence of ADEs. A fundamental step toward prevention of the increasing ADE-related healthcare burden is continuous identification and investigation of the contributions of ADE-related hospitalizations, including the associated risk factors for ADE-related events, within the general population. This is a sequel to the published report '*To err is human: Building a Safer Health System*' by the Institute of Medicine in 2000.[6] Since then, many studies have been conducted in clinical care settings such as hospital wards and EDs in order to determine the contribution of ADEs in these settings.[5,7]

A previous study has shown that 3 out of 10 ED visits were related to ADE.[5] It has been reported that patients presenting to the ED due to an ADE are more likely to have a longer hospital stay and additional healthcare costs compared to patients with non-ADE visits.[8] Patients with ADE-related ED visits may be discharged directly after seeing the ED physician, admitted to the ED ward, or, in many cases, transferred to an intensive care unit (ICU) or hospital ward.[5] In addition, ADEs can be moderate or severe and often lead to death or disability.[9,10] Moreover, an ADE can also occur in the ED while the patient is receiving care.[11] A study reported an incidence rate of 13% for ADE among patients admitted to ED.[11] However, ADE-related ED visits are potentially preventable with appropriate interventional measures.[12] Factors associated with ADE-related ED visits and ADE occurring in the ED setting can be identified and targeted with interventions that could prevent future occurrences. While these preventive interventions are of public health significance, their successful implementation depends largely on robust theoretical and evidence-based conceptual frameworks that will identify gaps in the targeted interventions.[13] The United Kingdom (UK) Medical Research Council guidelines recommend that appropriate existing evidence, theories, modelling processes, and outcomes should be identified in order to facilitate the development of an intervention.[13] To prevent ADE-related ED visits, public health interventions based on sound theoretical evidence are therefore needed to address this growing problem.

To our knowledge, there is no available conceptual model concerning ADE-related ED visits in the published literature. Therefore, the aim of the current study was to develop and validate a conceptual model of ADE-related ED visits that can be applied in the identification of ADE-related healthcare burdens in the ED, and to guide the design of preventative interventional measures.

Methods

The design of the model involved the identification of factors associated with ADE-related ED visits through a systematic review of the literature followed by mapping and validation of the identified factors in a conceptual model, and, finally, subjecting the model to a face validity test by an independent expert panel.

Operational definitions

ADE: Is any unfavourable occurrence related to the use or misuse of medications.[13]
ADE-related ED visit: Is any visit to an ED with chief presenting complaints related to an ADE.[13]
ADE occurring in the ED: Is any ADE occurring at an ED setting while the patient is under ED care.[12]

Development of the model

Systematic review. Literature search: A systematic literature search regarding the factors associated with ADE-related ED visits was performed using PubMed and Embase databases for articles published from January 2000 to March 2018. The two databases were selected based on their relevance in biomedical research. A search strategy using pertinent search terms such as medical subject heading (MeSH) and free text as title abstract (tiab) was developed. The search terms include 'risk factors (MeSH)' OR risk factor (tiab)'

'factor (tiab)' AND 'adverse drug event (MeSH)' OR 'drug-related problem (tiab)' AND 'drug-related visits (tiab)' AND 'emergency department (tiab)'. Only original articles published in English were included in the review. Relevant studies were also identified manually from the reference lists of the included articles. Additional information was also retrieved from Google Scholar and ED experts were contacted for relevant unpublished work. Google Scholar was searched using the following term 'factors associated with adverse drug-related emergency department visit'. Based on the previous recommendations, the first 200 search results from Google scholar were considered for study selection.[14]

Study selection: The inclusion criteria included article with the following characteristics: reporting factors associated with drug (ADE)-related ED visits; prevalence of ADE studies that reported ADE-related risk factors; and evaluating risk factors associated with a specific category of ADE (e.g. adverse drug reactions, therapeutic failures). Studies were excluded if they examined only ADE-related ED visit incidences or prevalence; investigated ADE-related admissions to other hospital settings such as wards, ambulatory units, and intensive care units; are review articles, editorials, letter to the editor, or conference abstracts. Figure 1 shows the study selection process for the systematic review.

Quality assessment of the included studies. The methodological qualities of the included studies were assessed using the mixed-methods appraisal tool (MMAT), version 2018.[15] Studies were ranked from one to five stars based on meeting the five-item MMAT criteria. Similarly, included studies were also rated based on the National Health Medical Research Council (NHMRC) hierarchy of evidence.[16] The quality assessment of the studies was undertaken by two reviewers and all disagreements were resolved through consensus.

Mapping of identified factors into the concepts. Factors associated with ADE-related ED visits identified from the literature were mapped into two concept groups: sociodemographic and clinical factors. The other subgroups in the clinical factor group represented ADEs encountered while in EDs, outcomes of ADE-related ED visits, and the consequences of these visits.

Validation

A table of the mapped variables was presented to an independent expert panel consisting of pharmacists and physicians with specialization and or research experience in pharmacoepidemiology research in emergency medicine. The panel reviewed the relevance of each of the identified factors and checked that each factor was appropriately mapped into each concept group, and included a review of the relationships among the concept groups/subgroups in the model. The model was revised based on feedback from the expert panel. Discrepancies were resolved through consensus by panel members. The final model was presented to the same expert panel for face validity. The panel was asked to give a judgement regarding the appropriateness, and whether the model made any sense, as well as to the relevance of the recommended interventions.

Results

The literature search from the electronic databases generated 1361 articles. Out these, 647 articles were excluded during the title and abstract screening, while 679 were excluded for reasons stated in Figure 1. Five articles were identified from a manual search of articles that were electronically retrieved. A total of 38 articles were included in the review for identifying factors associated with ADE-related ED visits. From the reviewed studies, 41 risk factors were reported to be associated with ADE-related ED visits. The factors were mapped as falling into one of the two concept groups: sociodemographic or clinical.

Quality assessment of the included studies

Of the 38 included studies, 8 met all five MMAT criteria of methodological quality; 16 studies were rated as four-star, 13 as three-star, and 1 study as a two-star rating of methodical quality. In terms of NHMRC hierarchy level of evidence, 10 of the studies were prospective cohorts with level II evidence, 14 were retrospective cohorts (III-2), 4 were case-control, and 10 were cross-sectional studies with level IV evidence (Table 1).

Mapping of the factors

Six concepts were developed, and factors identified from the studies were mapped to one of

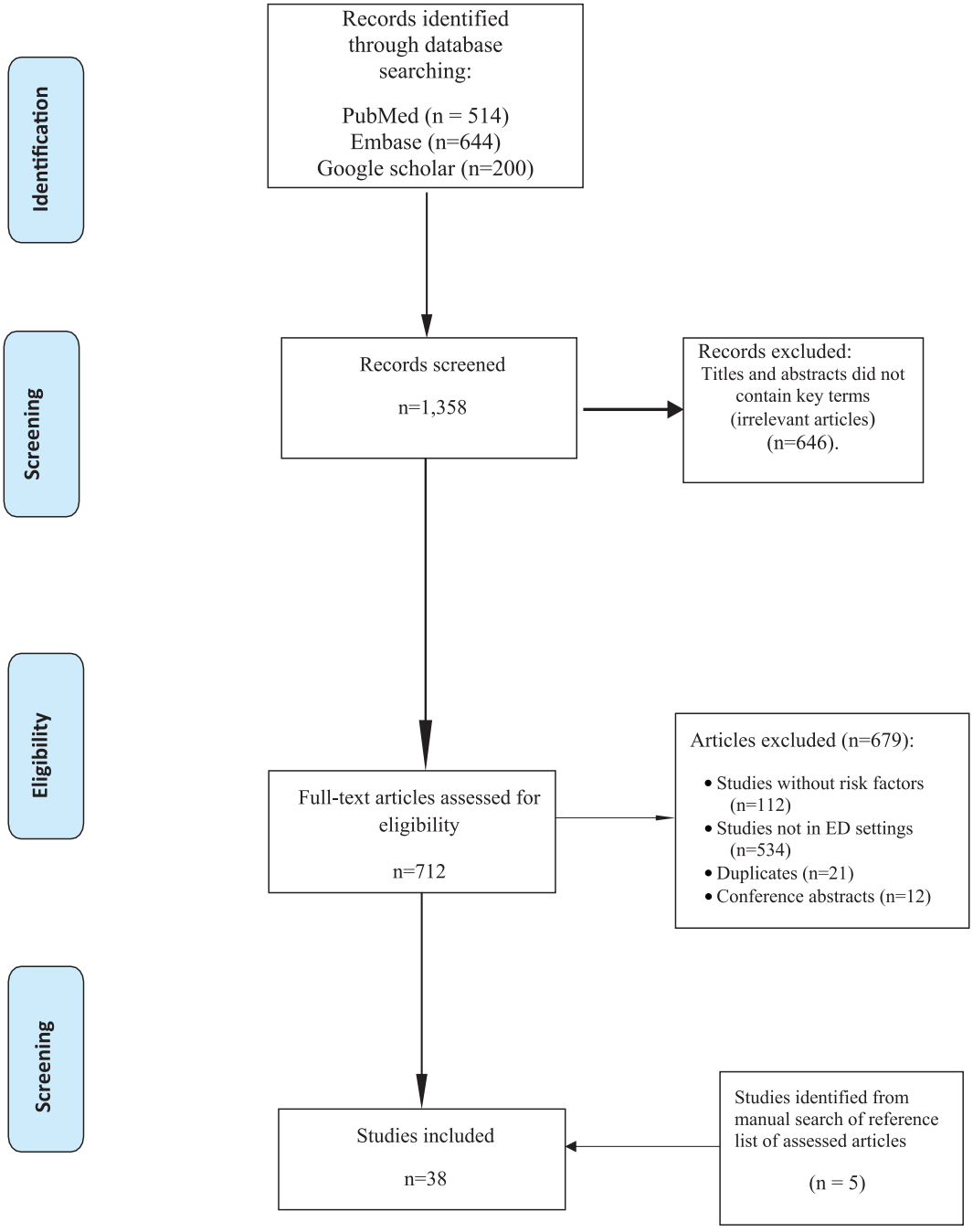

Figure 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow: study selection.

two concept groups: sociodemographic or clinical concept groups (Table 2). The remaining factors fell under one of four other subgroups: ADE-related ED visits, ADEs occurring while in ED, outcomes of ADE-related ED visits, and consequences from these visits. From the face validity, five factors initially mapped under the sociodemographic concept group were later moved to clinical factors, and two boxes were added to indicate 'general population' and 'ED' based on the expert panel's consensus.

Table 1. Summary of the included studies and quality assessment results.

Authors	Settings	Study period	Sample size	Study design	Risk factors identified	NHMRC Level of evidence[a]	MMAT Scoring [b]
Ab Fatah *et al*, 2017[44]	Teaching hospital, Malaysia	7 weeks	144	Case-control	Female sex, currently taking medication, comorbidity, a history of drug allergy and recent hospital admission	III-3	4
Salvi *et al.*, 2017[17]	Geriatric hospital, Italy	6 months	4042	Observational cohort study	Polypharmacy	IV	5
Chen *et al.*, 2015[18]	General Hospital, Taiwan	12 months	452	Prospective cohort study	Older population ⩾65 years	II	5
De Pepe *et al.*, 2013[19]	University hospital, Belgium	3 weeks	87	Prospective cohort study	Number of medications and age	II	3
Perrone *et al.*, 2014[20]	16 General hospitals, Italy	24 months	8862	Retrospective cohort study	Older age, Yellow and Red triage, number of medications, previous ED visit for the same ADE	III-2	3
Chen *et al.*, 2014[21]	Tertiary medical center, Taiwan	12 months	20,628	Case-control	Number of medications and increased serum creatinine.	III-3	4
Asseray *et al.*, 2013[22]	11 French academic hospitals, France	8-week period	3027	Prospective observational study	Age, gender, use of nervous system drugs, polypharmacy	II	4
Roulet *et al.*, 2013[23]	Tertiary care hospital, France	2 months	433	Cross sectional	Involuntary intoxication, hospitalized patients, poly-pathological condition, endocrine pathology and daily prescription of CVS drugs	IV	5
Pedros *et al.*, 2013[51]	Tertiary medical center, Spain	120 days	4098	Cross sectional	Old age and number of medications	IV	4
Nickel *et al.*, 2013[24]	University hospital, Basel, Switzerland	24 months	633	Cross-sectional	Comorbidities and number of medications	IV	4
Castro *et al.*, 2013 [52]	University hospital, Barcelona, Spain	3 months	652	Cross-sectional study	Number of medications taken	IV	3

(Continued)

Table 1. (Continued)

Authors	Settings	Study period	Sample size	Study design	Risk factors identified	NHMRC Level of evidence[a]	MMAT Scoring [b]
Heaton *et al.*, 2012[25]	NHAMCS, US	3 years	456,209	Retrospective cohort study	Mental illness, type II diabetes, nondependent abuse of drug and essential hypertension	III-2	4
Jayarama *et al.*, 2012[26]	Tertiary hospital, Kola, India	12 months	133	Prospective observational studies	Comorbidity, multiple prescribers, visiting many pharmacies and number of medications	II	3
Chen *et al.*, 2012[75]	Academic hospital, Taiwan	12 months	452	Prospective cohort study	Elderly age, severity of ADE, higher Charlson comorbidity index scores	II	4
Wu *et al.*, 2012[27]	Ontario, Canada	5 years		Retrospective cohort study	Female gender, old age, comorbidity, Number of medications, newly prescribed drugs, recent ED visit, multiple-pharmacies, recent -admission, and long-term care	III-2	4
Marcum *et al.*, 2012[53]	152 Veterans Affairs Medical Centers US	NR	778	Retrospective cohort study	Polypharmacy	III-2	4
Hohl *et al.*, 2011[8]	2 Tertiary hospitals. Vancouver, Canada	6 months	1591	Prospective observational studies	Comorbidity, antibiotic use within 7 days, medication changes within 28 days, age 80 years, arrival by ambulance, triage acuity, recent hospital admission, renal failure, and use of three or more prescription medications	II	5
Harduar-Morano, *et al.*, 2011[28]	Florida AHCA	NR	3024	Retrospective cohort study	Old age, white patients, and female gender	III-2	3
Vila-de-Muga *et al*, 2011[29]	Academic tertiary care children's hospital	1 week	1906	Retrospective cohort study	ED shift on weekends, holidays and between 0000 and 0800 hours	III-2	3
Perron *et al.*, 2011[30]	NESARC, US	NR	43,093	Retrospective cohort study of survey database	Heroine, inhalant and marijuana dependence. Pyschopathological factors: personality and mood disorder, socially connected has a protective factor	III-2	3

Table 1. (Continued)

Authors	Settings	Study period	Sample size	Study design	Risk factors identified	NHMRC Level of evidence[a]	MMAT Scoring [b]
Budnitz *et al.*, 2011[31]	NEISS-CADES US	2 years	177,504	Retrospective cohort study	Drugs with narrow therapeutic index; digoxin, insulin and warfarin	III-2	4
Braden *et al.*, 2002[32]	HealthCore and Arkansas Medicaid, US	NR	48,650	Retrospective cohort study	Use of short acting Drug Enforcement Agency Schedule II opioids	III-2	3
Sikdar *et al.*, 2011[33]	Two tertiary hospitals, Canada	12 months	1458	Retrospective chart review	Comorbidities and number of medications.	III-2	5
Ramos *et al.*, 2010[34]	University hospital, Spain	3 months	888	Cross sectional study	Number of drugs, female gender and health practice index	IV	4
Maria *et al.*, 2010[35]	3 hospitals, Italy	3 years	2644	Cross-sectional	Comorbidity, multiple drug regimens	IV	3
Backmund *et al.*, 2009[36]	Tertiary care hospital, Germany	NR	1049	Retrospective cohort study	Not living with a significant other, drug user, history of suicide attempt, daily use of barbiturates and cannabis	III-2	4
Olivier *et al.*, 2009[37]	University Hospital Toulouse, France	4 nonconsecutive weeks	789	Prospective cohort study	Number of medications taken, self-medication, use of antithrombotic and antibacterial drugs	II	4
Capuano *et al.*, 2009[38]	10 general hospitals in Regione Campania, Italy	10 days/ED in two study period	7861	Prospective cohort and nested case control study	Female gender and age category (30–39 and 60–69), patients taking RAS, NSAIDS, antibiotics, β-adrenoceptors agonist and β-lactam antibiotics	II	5
Zed *et al.*, 2008[12]	General hospital, Vancouver Canada	12 weeks	1017	Prospective observational study	Comorbidities, number of medications and multiple prescribers	II	5
Sauer *et al.*, 2007[39]	Administrative data, Florida, US	24 months	37,063	Retrospective cohort study	Age, male sex, number of medical conditions, and number of medications	III-2	2

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Table 1. (Continued)

Authors	Settings	Study period	Sample size	Study design	Risk factors identified	NHMRC Level of evidence[a]	MMAT Scoring [b]
Baena *et al.*, 2006[40]	University hospital, Granada, Spain	12 months	2261	Two-stage probabilistic sampling	Age, number of medications, and combined effect of the two	III-3	4
Tipping *et al.*, 2006[41]	Tertiary hospital, Cape Town, South Africa	4 months	517	Cross-sectional	Number of medications, patients taking NSAIDS, ACE- inhibitor, and warfarin	IV	3
Budnitz *et al.*, 2006[76]	9 NEISS, US	77 days	598	Retrospective cohort study	Use of warfarin and insulin	II-2	5
Trifiro *et al.*, 2005[45]	22 hospitals, Italy	10 days at intervals of 3 months	629	Prospective cohort study	Older age, male gender	II	4
Caterino *et al.*, 2004[77]	EDs of uninstitutionalised general hospital, US	NR	16.1 million	Retrospective cohort study	Number of medications at ED	III-2	4
Franceschi, *et al.*, 2004[78]	University hospital, Italy	10 days	607	Cross-sectional	Age and number of medications consumed	IV	3
Hafner *et al.*, 2002[42]	Teaching hospital, US	3 months	13,004	Case control	Old age, female gender, and polypharmacy	III-3	3
Malhotra *et al.*, 2011[9]	Referral hospital, India	7 months	578	Cross-sectional	Diabetes, patient living alone, poor recall of medication regimen, seeing multiple physicians, female gender, polypharmacy	IV	3

ADE: adverse drug event; ED: emergency department; NHAMCS: National Hospital Ambulatory Medical Care Survey; NESARC: National Epidemiology Survey on Alcohol and Related Conditions; NEISS-CADES: National Electronic Injury Surveillance System–Cooperative Adverse Drug Event Surveillance project; CVS: cardiovascular system; AHCA: Agency for Health Care Administration; RAS: renin-angiotensin system; NSAIDS: nonsteroidal anti-inflammatory drugs; ACE: angiotensin-converting-enzyme; NEISS: National Electronic Injury Surveillance System; US United States; NR: not reported.

[a]National Health and Medical Research Council level of evidence.

[b]Mixed Methods Appraisal Tool score.

Table 2. Concepts, mapped factors, gaps identified, and targeted interventions.

Concepts	Factors/ADEs	Gaps in drug-related knowledge	Targeted intervention
Sociodemographic characteristics	Old age, female, being white, low health practice index, social disconnection, nondependent drug abuse, Involuntary intoxication, Long-term care, Self-medication, Level of education.	Inadequate awareness of ADEs in the public.[55] Inappropriate of use medications among elderly. Inappropriate use of medications among pregnant women. Inadequate patient's knowledge on appropriate medication use. Lack of ADE screening tool in the public[56] high rate of drug abuse, self-medication, inadequate of patient information.	Use Beer's list at inappropriate medications for elderly[63] Improved awareness on rational medicines use in the society Availability of screening tool for detecting ADE in the community.[64]
Clinical characteristics	Drug allergy, comorbidity, chronic disease, consulting many prescribers, recent hospital admission, current medication, use of CAM, visiting many pharmacies, Use of multiple medications, Yellow and Red triage, Drugs with narrow therapeutic index; mental illness, personality and mood disorder, medication nonadherence.	Inadequate pharmacogenetic studies on drug effects. Inadequate prospective cohort studies on drugs use in chronic diseases and drug-related ED visits and ED readmission. Paucity of information on CAM use among ED patients (including CAM occurring at ED).[57]	More studies on pharmacogenetic to identify the genetic variations in drug effects.[66] More studies on drug including CAM-related ED visits particularly in developing countries.[57] Implementation Beer's list of appropriate when prescribing drugs to elderly.[63] Improve patient education and counselling at healthcare settings. More intervention to improve patient's medication adherence. More seminars and lectures to HCP on appropriate use of medication in the ED.

(Continued)

Table 2. (Continued)

Concepts	Factors/ADEs	Gaps in drug-related knowledge	Targeted intervention
ADE leading to ED visits	ADEs (1) Adverse drug reaction (2) Medication nonadherence (3) Drug treatment failure (4) Medication error (5) Drug over dosage (6) Drug under dose (7) Untreated indication (8) Treatment without indication	Inadequate studies on ADE-related ED visits and ADE occurring at ED[58] Lack of valid causality assessment of adverse events related to drug treatment failure, medication errors and drug abuse/misuse[59]	More studies to be conducted on ADE-related ED visits More studies on contribution of CAM at ED ED-based brief interventions[69] Provision of validated ADE screening tool at ED[56]
ADE encountered at the ED	(1) Adverse drug reaction (2) Medication error (3) Drug treatment failure	Inadequate studies on ADE occurring at ED[58] Inadequate patient-HCP communication,[60] inadequate counselling time, busy and overcrowded and multitasking nature of ED environment[61] Lack of decision and screening tools to guide the HCP on ADE in the ED[56] Lack of clinical pharmacy unit in some ED settings[62]	More studies should be conducted to identify ADE occurring at ED[58] Strategies to improved patient-HCP communication for adequate patient education and shared decision making[71] Training and improved collaborative communication among HCP in ED setting[72] Presence of a clinical pharmacy at ED for adequate ADE surveillance[73] Strategies to prevent to reduce ADEs in the ED such as computerized provider-order entry systems, automated dispensing cabinets, bar-coding systems[61] Implementation of Screening tool of Older People's Prescriptions and Screening Tool to Alert to Right Treatment criteria to detect ADE-related ED visits[67]Nauta *et al.*, 2017)

ADE: adverse drug event; ED: emergency department; CAM: complementary and alternative medicine; HCP: health care professionals.

Analysis of the conceptual model for understanding ADE-related ED visits and ADEs encountered at the ED

An ADE-related ED visit can be best explained using pharmacoepidemiological concepts. Pharmacoepidemiology is the study of the clinical use of drugs and ADEs in large numbers of people, and thus, provides an estimate of the probability of beneficial drug effects in a general population in addition to ADEs.[43] People use drugs for either therapeutic purposes such as disease management and prevention, or for illicit reasons, including ecstasy, recreational, to fit in with their peers, or for performance-enhancement such as in athletics. ADEs occur as a result of the use of drugs for all these purposes, leading to hospitalization, including unplanned visits to an ED. Empirical evidence from the reviewed studies reveals several factors as predictors of ED visits following drug use. Interventions can be targeted to these factors to prevent the increased healthcare burden of ADE-related ED visits.

The model starts with the general population. People in the community represent different socio-demographic characteristics. Some of these characteristics, such as old age,[18,19,40] female gender,[19,44] ethnic disparity (white),[28] low health practice index,[34] social disconnection (living alone),[30] long-term care,[27] and history of suicidal attempt, were all found to be associated with ADE-related ED visits. In addition, some individuals in the community will be involved in other use of drugs associated with ADE-related visits to the ED, such as nondependent drug abuse,[45] involuntary intoxication (e.g., unintentional poisoning),[23] self-medication,[37] use of short-acting Drug Enforcement Agency Schedule II opioids,[32] and use of cannabis and barbiturates[36] – all of which were found to be associated with ADE-related ED visits (see box on left side of general population in Figure 2).

People in the community also develop illnesses and require medications; thus, being exposed to many risk factors (termed clinical factors; see box on right side of general population in Figure 2). These factors increase the likelihood of visiting an ED due to an ADE from medication use, and include a history of drug allergies,[44] chronic illness,[25] type II diabetes, essential hypertension and other comorbid conditions,[24,39, 45–47] psychopathology (personality and mood disorder),[30,48] mental illness,[25] recent hospital admission,[27] consulting multiple prescribers,[12] and pharmacies.[26] Other clinical factors include failure to correctly use, or not use, prescription medicines after being prescribed by a physician,[49] use of complementary and alternative medicine (CAM),[50] current medication use,[44] use of multiple medications,[17,21,33,35,51–53] yellow and red triage,[20] and use of drugs with narrow therapeutic indices.[31] Drugs such as nonsteroidal anti-inflammatory drugs (NSAIDs) used in the management of chronic diseases,[41] antihypertensive medications,[38] antidiabetics,[45] antibiotics,[38] benzodiazepines, antidepressants, anticonvulsants,[54] and use of nervous system drugs[22] were also identified as factors contributing to ED visits due to an ADE. People with an increased serum creatinine level were also found to be at a higher risk of ED visits due to an ADE.[21]

Socio-demographic and clinical factors, such as drug abuse/misuse, medication errors, medication nonadherence, and medication under/overdose, are also known as exposure variables, and these predispose an individual to many types of ADEs. The manifestation of these events results in acute clinical conditions leading to an unplanned ED visit (Figure 2). Different outcomes (box in Figure 2) may arise from these visits: the patient may be discharged immediately after seeing an ED physician; admission to the ED observation ward; transfer to the hospital ward or ICU; permanent disability; death.

In some instances, an individual may visit an ED with other nondrug related conditions. Due to the busy nature of the ED environment, many ADEs occur in the ED, leading to complications of pre-existing disease conditions (Figure 2). Commonly encountered ADEs while in the ED environment includes adverse drug reactions, medication errors, drug overdoses, and therapeutic failures.[42] Similarly, working hours and day in the ED have been identified by ED healthcare personnel to be independent predictors of an ADE in the ED setting. Muga and colleagues reported working at an ED between 0000 to 0800 hours, and on weekends and holidays as predictors of medication error occurring in ED settings.[29]

Some consequences of ADE-related ED visits and ADEs encountered while in the ED are an increase in drug-related morbidity, mortality, and healthcare costs, prolonged hospital stay,

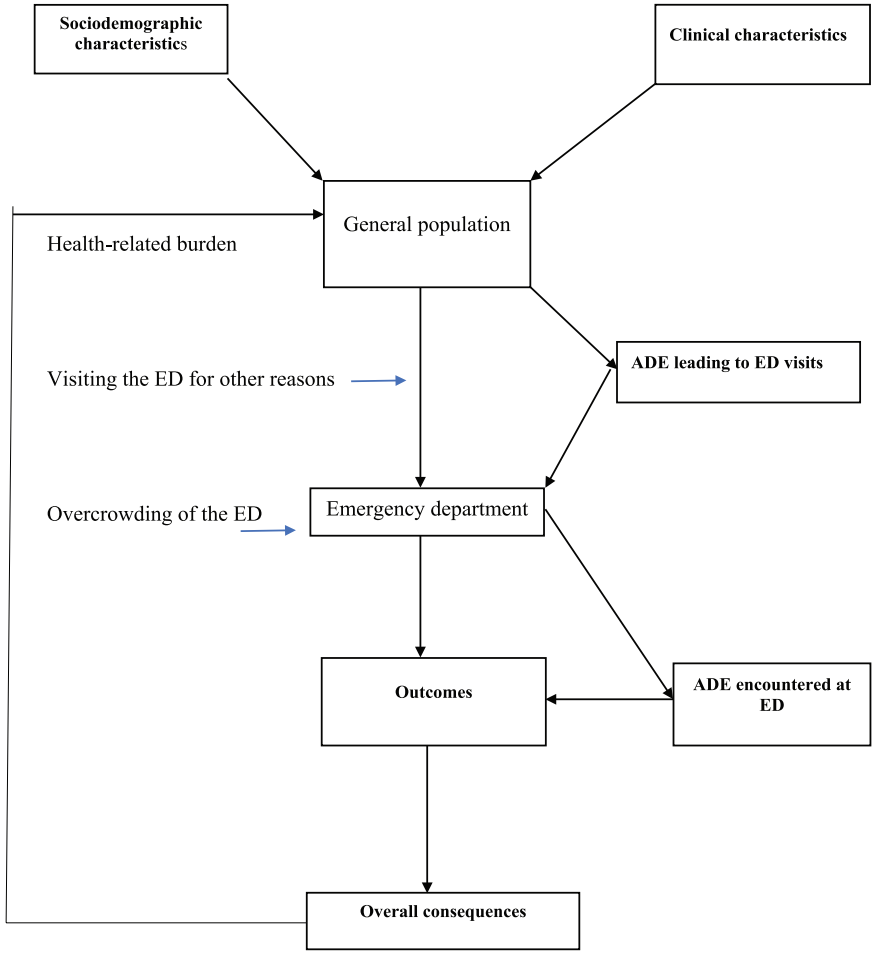

Figure 2. Conceptual framework for understanding drug-related emergency department (ED) visits.

decreased productivity and lost work hours (overall consequences box in Figure 2).[8] These consequences have negative effects on the general population (Figure 2) by increasing the socio-economic burden and ED overcrowding. This will directly or indirectly influence the occurrence of exposure variables, and increase the likelihood of ED visits due to drug use and its continuous cycle. Gaps in knowledge for targeted interventions can thus be identified and applied to any of these concepts in order to prevent or minimize future occurrences of ADE-related ED visits.

Identified gaps for intervention

Table 2 shows the gaps identified in the different concepts, including sociodemographic, clinical factors, ADE, and ADEs encountered while in the ED.

Sociodemographic factors. Previous studies have identified sociodemographic factors associated with people experiencing ADEs in the general population. These included inadequate awareness of ADE by the public,[56] high use of inappropriate medications among elderly people,[46] and absence of ADE screening tools in the community.[56] There are also a high rate of drug abuse, self-medication, and inadequate patient education concerning drug use.

Clinical factors. Identified gaps under clinical factors include inadequate pharmacogenetic and prospective cohort studies on drug use in chronic diseases. There is a minimal number of published studies concerning ADE-related ED visits and readmissions. Information on CAM use among ED patients (including CAM occurring while in the ED) has not been adequately studied or reported.[57]

ADE leading to ED visits. Published information on ADE-associated ED visits is limited. There are no adequate studies concerning ADE-related ED visits and ADE occurring while in ED.[58] Furthermore, there is a lack of validated causality ADE assessment tools such as objective tools or algorithms for the causality assessment of drug treatment failure, medication errors, and drug abuse/misuse.[59]

ADE occurring while in the ED. There are no adequate studies concerning ADE occurring while in ED.[58] Inadequate patient–healthcare provider (HCP) communication was identified as one cause of this problem.[60] The busy, overcrowded nature of the ED environment, coupled with inadequate counselling time with a patient, are some of the identified gaps in the ED-associated ADEs.[61] Furthermore, there is a lack of decision support tools such as computerized physician order entry systems (CPOE), barcodes, and/or screening tools to guide the HCP at ED.[56] ADEs are prevalent due to lack of clinical pharmacy units to oversee the pharmacotherapy in some ED settings.[62]

Targeted interventions (population and patient-centered)

A fundamental step in preventing drug-related ED visits is to continue identifying the prevalence/incidence of healthcare burden in the ED. More studies are needed to determine the contribution of drugs in ADE-related ED visits, including those ADEs that occur while in the ED. Unfortunately, information regarding this occurrence is limited in the published literature. More published studies are needed to provide comprehensive knowledge of the healthcare burden in order to design and recommend appropriate interventions.

The developed model has identified some areas for targeted interventions. Preventive measures can be targeted from the identified concepts:

Sociodemographic factors: Improving the level of awareness among the population with respect to the rational use of medicines will assist in reducing the occurrence of ADE-related ED visits. The use of Beer's list of inappropriate medications for older patients in healthcare settings will reduce ADEs among elderly population.[63] Availability of ADE screening tools in community pharmacy and primary healthcare settings will detect people at high-risk of experiencing ADEs that may lead to ED visits.[64] Thus, one of the most fundamental issues for addressing sociodemographic disparities that contribute to ED visits is to improve primary healthcare systems to allow more access to general practitioners. Therefore, providing appropriate information to patients regarding their medications and improved awareness of drug and substances abuse-associated dangers, especially illicit drugs, indiscriminate smoking, and alcohol consumption, will go a long way towards curbing drug-related ED visits.[65]

Clinical factors: Risk factors related to the clinical use of medications and disease conditions can be targeted for interventions and other strategies to prevent ADE-related ED visits. To effectively intervene with respect to patients' clinical characteristics, further studies are required on pharmacogenetic factors as this will help to identify patients' genetic variations that contribute to drug effects and the possibility of personalized medicines use.[66] Furthermore, more studies are required with respect to the use of CAMs among patients in the ED, including ED visits related to CAM toxicities and CAM-related ADEs occurring while a patient is in ED.[57] Such studies should be stressed in developing countries. More interventions such as implementation of Beer's list of inappropriate medications for the elderly,[63] Screening Tool of Older People's Prescriptions, the Screening Tool to Alert to Right Treatment (STOPP/START) criteria to detect ADE-related ED visits,[67] and provision for CPOEs will drastically reduce the occurrences of ADE-related ED visits. Telemedicine enables HCPs to prioritize their workloads and support people with long-term conditions in order to play a key role in managing healthcare.[68] Telemedicine is another healthcare technology relevant to elderly and physically challenged patients. It promotes safety and security, using at-home sensor monitoring devices that provide alerts for prompt action.[68]

ADEs leading to ED visits: To reduce the rate of ADEs, more studies are needed to evaluated the burden of ED visits related to ADE, including those associated with CAM use.[69] Provisions of interventions such as for validated ADE screening tools in the ED could assist in detecting more

ADE-related cases.[56] Adequate pharmacovigilance surveillance ADE-related ED visits. The advent of personalized therapy, tailored to an individual patient based on the patient's diagnosis, medical history, and genetic information, for the purpose of improving therapeutic outcomes minimizing and ADEs could go a long way in preventing ED visits associated with drug use.[70]

ADEs occurring in the ED: To provide a clear view of the event, more studies need to be conducted on ADEs occurring in the ED setting. ADEs occurring in the ED can be reduced by implementing strategies to improved patient–HCP communication for adequate patient education and shared decision-making.[71] Training and improvement of effective communication among HCPs in ED settings will improve patient safety.[72] The presence of a dedicated pharmacy unit in the ED that renders full clinical pharmacy services will help in ADE surveillance and provide more patient counselling, and other pharmaceutical care activities.[73] Other strategies such as informatics-based hospital interventions in the ED, including CPOE systems, automated dispensing cabinets, and bar-coding systems, have the potential to detect and prevent ADEs in ED settings.[61]

Role of clinical pharmacists in preventing ADE in the ED: Clinical pharmacists remain the professionals best entrusted with all aspects of pharmacotherapy. The success of therapeutic interventions depends largely on the clinical pharmacist's commitment to preventing ADEs, particularly in ED.[70] Most importantly, the pharmacist must ensure appropriate medication storage conditions in the ED pharmacy unit. Another critical role for a pharmacist is that of screening and scrutinizing prescriptions prior to dispensing them in order to identify any potential drug–drug interaction; drug-disease interaction; inappropriate dosing; or inappropriate dosing frequencies, errors, and ADE reporting. Other roles include identification of patients for enrollment of investigational drug study participants while these potential participants are in the ED, participation on interdisciplinary research committees that review ED-related research protocols, patient counselling and education, toxicology investigation recommendations, and targeted disease state counselling such as anticoagulation, anaphylaxis reactions, medication therapy updates, and education on optimal medical therapy for ED team members.[74]

Implications of the conceptual model in public health and clinical practice

To our knowledge, this conceptual model is the first to provide an in-depth understanding of ADE-related ED visit by identifying gaps in knowledge and suggesting interventions for preventative measures. The model could guide interventionists, and public health and clinical practice policymakers in identifying areas that need intervention, in addition to planning and implementation of intervention strategies.

Limitations

The current study may be limited to the inclusion only of studies published in the English language; thus, relevant information from studies published in other languages may have been excluded.

Conclusion

A validated conceptual model for better understanding of ADE-related ED visits was developed. We identified gaps in knowledge and clinical practice as well as targeted interventions that can be used to guide implementation of strategies for preventing ADE-related ED visits, including ADEs that occur while in an ED setting. This study underscores the need for the proactive role of clinical pharmacists to ensure optimal use of medicines and minimization of ADE-related ED visits. In elderly patients, consideration of the Beers Criteria for Potentially Inappropriate Medications and Screening Tool of Older Persons' Potentially Inappropriate Prescriptions/Screening Tool to Alert to Right Treatment Criteria would play a critical role in the prevention of ADE-related ED visits.

Highlights

(1) Drug use in the general population may lead to an ED visit with chief presenting complaints related to an ADE.
(2) An ADE may occur while in the ED from non-ADE related visits, leading to increased morbidity, mortality, and healthcare costs.

(3) The absence of an evidence-based model may lead to an intervention being less successful than anticipated.
(4) A conceptual model can guide the successful design of interventions to prevent ADE-related ED visits.
(5) A successful intervention based on a conceptual model will reduce morbidity, mortality, and healthcare costs.

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Authors contribution

We declared that this work was conducted by the authors named in this article and all liabilities relating to the content of this article will be borne by them. All authors meet the criteria for authorship outlined by the Uniform Requirements for Manuscripts Submitted to Biomedical Journals.

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Conflict of interest statement

The authors declare that there is no conflict of interest.

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