



## King's Research Portal

DOI:

[10.1016/j.sapharm.2018.11.010](https://doi.org/10.1016/j.sapharm.2018.11.010)

*Document Version*

Peer reviewed version

[Link to publication record in King's Research Portal](#)

*Citation for published version (APA):*

Härkänen, M., Vehviläinen-Julkunen, K., Murrells, T., Rafferty, A. M., & Franklin, B. D. (2018). Medication administration errors and mortality: Incidents reported in England and Wales between 2007–2016. *Research In Social & Administrative Pharmacy*. <https://doi.org/10.1016/j.sapharm.2018.11.010>

### **Citing this paper**

Please note that where the full-text provided on King's Research Portal is the Author Accepted Manuscript or Post-Print version this may differ from the final Published version. If citing, it is advised that you check and use the publisher's definitive version for pagination, volume/issue, and date of publication details. And where the final published version is provided on the Research Portal, if citing you are again advised to check the publisher's website for any subsequent corrections.

### **General rights**

Copyright and moral rights for the publications made accessible in the Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognize and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the Research Portal

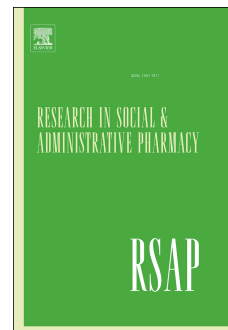
### **Take down policy**

If you believe that this document breaches copyright please contact [librarypure@kcl.ac.uk](mailto:librarypure@kcl.ac.uk) providing details, and we will remove access to the work immediately and investigate your claim.

# Accepted Manuscript

Medication administration errors and mortality: Incidents reported in England and Wales between 2007- 2016

Marja Härkänen, Katri Vehviläinen-Julkunen, Trevor Murrells, Anne Marie Rafferty, Bryony Dean Franklin



PII: S1551-7411(18)30635-1

DOI: <https://doi.org/10.1016/j.sapharm.2018.11.010>

Reference: RSAP 1179

To appear in: *Research in Social & Administrative Pharmacy*

Received Date: 28 June 2018

Revised Date: 15 November 2018

Accepted Date: 20 November 2018

Please cite this article as: Härkänen M, Vehviläinen-Julkunen K, Murrells T, Rafferty AM, Franklin BD, Medication administration errors and mortality: Incidents reported in England and Wales between 2007- 2016, *Research in Social & Administrative Pharmacy* (2018), doi: <https://doi.org/10.1016/j.sapharm.2018.11.010>.

This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

## Medication administration errors and mortality: incidents reported in England and Wales between 2007–2016

**Marja Härkänen**, Post-doctoral researcher, PhD, RN, Corresponding author  
University of Eastern Finland: Department of Nursing Science; Academy of Finland,  
Yliopistoranta 1c, Kuopio, Finland, marja.harkanen@uef.fi

**Katri-Vehviläinen-Julkunen**, Professor, PhD, RN, RM  
University of Eastern Finland: Department of Nursing Science; Kuopio University Hospital,  
Yliopistoranta 1c, Kuopio, Finland, katri.vehvilainenjulkunen@uef.fi

**Trevor Murrells**, BSc, MSc, Statistician (Nursing & Midwifery)  
King's College London: Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care,  
James Clerk Maxwell Building, 57 Waterloo Road, London, SE1 8WA, UK,  
trevor.murrells@kcl.ac.uk

**Anne Marie Rafferty**, Professor, PhD, RN  
King's College London: Florence Nightingale Faculty of Nursing, Midwifery & Palliative Care,  
James Clerk Maxwell Building, 57 Waterloo Road, London, SE1 8WA, UK,  
anne\_marie.rafferty@kcl.ac.uk

**Bryony Dean Franklin**, Professor, PhD, Pharmacist  
Centre for Medication Safety and Service Quality, Imperial College Healthcare NHS Trust,  
Charing Cross Hospital, Fulham Palace Road, / UCL School of Pharmacy, London, UK  
bryony.franklin@nhs.net

**Declarations of interest:** Bryony Dean Franklin supervises a PhD student part funded by Cerner, a supplier of hospital electronic health record systems, and has received funding from Pfizer for delivering teaching at a one-off symposium on medication safety unrelated to this study.

## 1 ABSTRACT

2 **Background:** Medication administration errors may contribute to patient mortality, thus  
3 additional understanding of such incidents is required.

4 **Objectives:** To analyse medication administration errors reported in acute care as resulting  
5 in death, to identify the drugs concerned, and to describe medication administration error  
6 characteristics (location of error, error type, patient's age) by drug group.

7 **Methods:** Medication administration errors reported in acute care in 2007– 2016  
8 (n=517,384) were obtained from the National Reporting and Learning System for England  
9 and Wales. Incidents reported as resulting in death (n=229) were analysed. Drugs were  
10 classified by two researchers using the British National Formulary. Drug categories were  
11 described by medication administration errors' year, location, patient age, and error  
12 category based on the incidents' original classification.

13 **Results:** Errors were most often reported on wards (66.4%, n=152), and in patients aged  
14 over 75 years (41.5%, n=95). The most common error category was omitted medicine or  
15 ingredient (31.4%, n=72); most common drug groups were cardiovascular (20.1%, n=46) and  
16 nervous system (10.0%, n=23). Most errors in patients under 12 years concerned drugs to  
17 treat infection; cardiovascular drugs were most common among other age groups.

18 **Conclusions:** In order to prevent these most serious of medication administration errors,  
19 interventions should focus on avoiding dose omissions, and administration of drugs for  
20 patient over 75 years old, as well as safe administration of parenteral anticoagulants and  
21 antibacterial drugs.

22  
23 **Keywords:** adverse event, death, drug, incident reporting, medication administration,  
24 patient safety

## 25 Abbreviations

26 ADE = adverse drug event

27 BNF = British National Formulary

28 ISMP = Institute for Safe Medication Practices

29 MAE = medication administration error

30 NHS = National Health Service

31 NRLS = National Reporting & Learning System

## 32 INTRODUCTION

33 In 2017, The World Health Organization (WHO) launched a third global patient safety  
34 challenge “Medication Without Harm”, aimed at improving medication safety, on the basis  
35 that medication errors are a leading cause of injury and avoidable harm in health care  
36 systems globally generating costs that has been estimated at 42 billion USD annually.<sup>1</sup> In  
37 February 2018, the report of the prevalence and burden of medication errors in England  
38 was published in response to the WHO challenge, estimating that 237 million medication  
39 errors at all stage of medication process occur in England per annum.<sup>2</sup>

40 The United States National Coordinating Council for Medication Error Reporting and  
41 Prevention<sup>3</sup> defines medication error as “any preventable event that may cause or lead to  
42 inappropriate medication use or patient harm while the medication is in the control of the  
43 health care professional, patient, or consumer”. The medication administration stage of the  
44 medication process is known to be prone to errors. Half or more of all medication incidents  
45 are medication administration errors (MAEs).<sup>2 4 5</sup> MAEs can be defined as “a deviation from  
46 the prescriber’s medication order as written on the patient’s chart, manufacturers’  
47 preparation/administration instructions, or relevant institutional policies”.<sup>6</sup> Direct  
48 observations of the inpatient medication process produce the most rigorous data on the  
49 prevalence of medication errors, and suggest that MAEs occur in 5% of non-intravenous and  
50 35% of intravenous doses<sup>7</sup> or up to 20% of all doses given.<sup>8 9</sup> Fortunately, the majority of  
51 MAEs do not result in harm<sup>2 10</sup>, but some are serious or even fatal. An adverse drug event  
52 (ADE) is defined as “an injury resulting from medical intervention related to a drug”.<sup>11</sup>

53 Medication errors as well as ADEs during hospitalization are more likely in the presence of  
54 co-morbidity and polypharmacy,<sup>2 12</sup> and among older people.<sup>2 13</sup> Some drugs are more likely  
55 to cause significant patient harm when used in error. These are listed as high-alert  
56 medications by the US Institute for Safe Medication Practices (ISMP).<sup>14</sup> In acute care  
57 settings, these drug classes include anaesthetics, anti-arrhythmics, anti-thrombotics,  
58 chemotherapeutics, dialysis solutions, epidural or intrathecal medications, insulin,  
59 narcotics/opioids, and parenteral nutrition.<sup>14</sup> The UK’s high risk drug list includes  
60 administration of methotrexate, diamorphine and morphine injections, low molecular  
61 weight heparins, anticoagulants, insulin, lithium, midazolam injection, opioids, injectable  
62 medicines, and liquid medicines as well as omitted doses.<sup>15</sup> Additionally, a systematic review

63 revealed that 47 % of all serious medication errors were caused by seven drugs / drug  
64 classes. Those were methotrexate, warfarin, nonsteroidal anti-inflammatory drugs (NSAIDs),  
65 digoxin, opioids, acetylic salicylic acid, and beta-blockers.<sup>16</sup>

66 Analysis of reported medication errors have traditionally included all medication incidents,  
67 whether or not they result in harm<sup>4 5</sup>. By focussing on the most serious MAEs, the aim was  
68 to specifically study the characteristics of MAEs reported as resulting in patient death. This  
69 study's objectives were 1) to analyse medication administration errors reported in acute  
70 care as resulting in death, 2) to identify the drugs concerned, 3) to describe MAE  
71 characteristics by drug group, and 4) to identify potential areas for intervention.

72

## 73 **METHODS**

### 74 **Design & setting**

75 This was a retrospective study of MAEs reported to the National Reporting & Learning  
76 System (NRLS) for England and Wales. The NRLS collects national data on all patient safety  
77 incidents that are voluntarily and anonymously reported by staff employed in the National  
78 Health Services (NHS) and other health care organisations. Incidents (including near misses  
79 and incidents causing harm) can also be reported directly to the NRLS. Data reported for  
80 incidents include both categorical data (e.g. type, severity of incident) and a free text  
81 description of what happened.

82 The original classification of the NRLS incidents were used. Based on this classification,  
83 location of error included: ward, intensive care unit, operating theatre, recovery room,  
84 anaesthetic room, therapy department, pharmacy, mortuary, hospital buildings, other, or  
85 the information was missing. Types of errors were: omitted medicine / ingredient, wrong /  
86 unclear dose or strength, wrong drug / medicine, wrong frequency, wrong quantity, wrong  
87 route, adverse drug reaction (when used as intended), patient allergic to treatment, contra-  
88 indication to the use of the medicine in relation to drugs or conditions, mismatching  
89 between patient and medicine, wrong storage, wrong method of preparation / supply,  
90 wrong / omitted verbal patient directions, wrong / omitted / passed expiry date, other, or  
91 unknown.

92

93

**94 Data acquisition**

95 A data sharing agreement was signed after applying and receiving acceptance from NRLS for  
96 data access. NRLS extracted the data (medication administration errors reported to the  
97 NRLS between 1 January 2007 and 31 December 2016) in December 2017. Inclusion criteria  
98 were that the incident was documented as involving: 1) medication, 2) administration /  
99 supply of a medicine from a clinical area, and 3) acute NHS trust (either a specialist or non-  
100 specialist organisation). Of all incidents (n=517,384), 94.3% concerned an acute non-  
101 specialist Trust, and only 5.7% acute specialist Trust. The total number of incidents extracted  
102 was 517,384. Of these, only MAEs reported as resulting in death caused by a patient safety  
103 incident (n=229, 0.04%) were analysed. Only the categorical data fields within the NRLS data  
104 were acquired.

105

**106 Data analysis**

107 Descriptive statistics of the data (n=229 MAEs reported as resulting in death) were  
108 calculated using IBM SPSS (version 23.0). Characteristics of the data were described using  
109 frequencies and percentages, and relationships amongst factors explored via cross-  
110 tabulation. Reports including the name of the drug were classified using the British National  
111 Formulary (BNF) classification.<sup>17</sup> The BNF classification's main groups are divided under the  
112 following sections: 1. Gastro-intestinal system, 2. Cardiovascular system, 3. Respiratory  
113 system, 4. Nervous system, 5. Infection, 6. Endocrine system, 7. Genito-urinary system, 8.  
114 Malignant disease, 9. Blood and nutrition, 10. Musculoskeletal system, 11. Eye, 12. Ear,  
115 nose, and oropharynx, 13. Skin, 14. Vaccines, 15. Anaesthesia, and 16. Emergency treatment  
116 of poisoning. MH classified the drugs into BNF groups which were then verified by BDF. Drug  
117 categories were cross-tabulated by MAEs' year, location, patients' age, and error category.  
118 The age bands used within the NRLS were amalgamated into six broader groups: 1) under 12  
119 years, 2) 12-17 years, 3) 18-25 years, 4) 26-55 years, 5) 56-75 years, and 6) over 75 years.

120

121

122

**123 Ethics**

124 King's College London ethics committee approved the study (LRS-17/18-5150). The data did  
125 not include any personal or organisational identifiers, thus anonymity of the reporters,  
126 patients, other involved persons, and organisations could be guaranteed.

127

**128 RESULTS****129 Characteristics of MAEs resulting in death**

130 MAEs resulting in death (n=229) occurred most often in 2008 (n=28, 12.2% of all MAEs  
131 reported as causing death) and 2016 (n=28, 12.2%), and less often 2012 (n=13, 5.7%).  
132 Overall 66.4% of MAEs were reported as occurring on non-critical care wards, and 41.5%  
133 (n=95) occurred amongst patients aged over 75 years. The most common error category  
134 was omitted medicine or ingredient (n=72, 31.4%). (Table 1.)

135

**136 Drugs related to MAEs**

137 The name of the related drug was mentioned in 58.1% (n=133) of all MAEs. The most  
138 common group of drugs in MAEs reported as resulting in death were cardiovascular drugs  
139 (20.1%, n=46). Of these 26 involved parenteral anticoagulants, six oral anticoagulants, and  
140 six sympathomimetics. The second most common were drugs of the central nervous system  
141 (10.0%, n=23). Of those, analgesics (n=10) were most common. Other common drug groups  
142 were antibacterials (n=20), cytotoxic drugs (n=8), and insulin (n=7). (Tables 2.) More specific  
143 information by name of drugs concerned (as written in the reports) is presented in Table 3.

144

**145 MAE characteristics by drug groups**

146 MAEs reported as resulting in death in general ward areas were most often reported for  
147 cardiovascular drugs (34 cases of 152 incidents at ward) followed by nervous systems drugs



148 (19 of 152). MAEs occurring in intensive care units most commonly concerned drugs used in  
149 blood and nutrition (4 of 18 incidents in intensive care units) and infection (3 of 18). Most  
150 MAEs in patients under 12 years were drugs to treat infection (3 of 10 incidents in patients  
151 under 12 years) whereas for patient's aged 26-55 years cardiovascular drugs (6 of 29  
152 incidents in patients aged 26-55 years) were the most common. Cardiovascular drugs (9 of  
153 58 of incidents in patients aged 56-75) or drugs to treat infection (10 of 58) featured most  
154 often for patients aged 56-75, and cardiovascular drugs (23 of 95 incidents in patients aged  
155 over 75 years) and nervous system drugs (11 of 95) for patients aged over 75. (Online  
156 appendix.)

157 The most common error categories for cardiovascular drugs were omitted medicine /  
158 ingredients (18 of 46 incidents with cardiovascular drugs), followed by wrong / unclear dose  
159 or strength (6 of 46). For nervous system drugs the most commonly reported errors were  
160 wrong / unclear dose or strength (4 of 23 incidents with nervous system drugs), wrong  
161 quantity (3 of 23), and wrong drug / medicine (3 of 23). For drugs to treat infection the most  
162 commonly reported errors were omitted medicine /ingredient (5 of 21 incidents with drugs  
163 to treat infection), adverse drug reaction (4 of 21), and patient allergic to treatment (4 of  
164 21). (Online appendix.)

165

## 166 **DISCUSSION**

167 In this study, MAEs most commonly reported as causing mortality in acute care Trusts over  
168 the 10-year period 2007 to 2016 were omissions of drugs. They occurred more often on  
169 hospital wards than other locations and amongst patients aged over 75 years. The drugs  
170 most commonly involved were parenteral anticoagulants followed by antibacterial drugs.  
171 Interventions to reduce MAEs, should therefore focus on those areas.

172 Almost one third of MAEs were related to omissions of drug doses. A previous study  
173 analysing all medication errors reported to the NRLS between 2005 and 2010 also found  
174 that omissions were the most commonly reported type, accounting for around 15% of  
175 incidents,<sup>4</sup> which is much lower than in the present study. In addition, a previous systematic  
176 review using observational evidence demonstrated that omission errors are the most  
177 common MAE type internationally.<sup>18</sup> More attention is needed on omissions since the

178 consequences can be serious. The risks of delay or omission of drugs have been categorised  
179 by the English National Patient safety Agency (NPSA),<sup>19</sup> which suggests that omission of  
180 anticoagulants, insulins, and cytotoxic agents, as identified in this study, can cause  
181 significant or catastrophic long-term patient impact. Reasons for medication omissions are  
182 manifold, such as staff shortages and delays in medication dispensing,<sup>20</sup> patients' inability to  
183 take the medicine, or medication unavailability.<sup>21</sup> More active solutions for problems related  
184 to medication omissions should be implemented with the development of technology,  
185 improving work processes, flow of information, verification systems and availability of  
186 drugs. Still, it is challenging to recommend any specific interventions, as a previous  
187 systematic review and meta-analysis demonstrated that interventions developed to  
188 decrease MAEs, including nurse training and education, automated delivery systems and  
189 barcode-assisted medication administration systems, did not find clear effect of the  
190 interventions.<sup>22</sup>

191 Cardiovascular drugs, particularly parenteral anticoagulants, were the most common drug  
192 group involved in MAEs reported as resulting in death. Many of those were omitted or  
193 administered in the wrong dose, strength, frequency, or quantity. Cardiovascular drugs  
194 were associated with the highest median proportion of preventable adverse drug reactions  
195 (PADR) also in a previous review of systematic reviews of inpatients' PADRs<sup>23</sup>. Those were  
196 also found to be the most frequent types of drugs involved in preventable ADEs<sup>24</sup>, and  
197 commonly related to observed MAEs<sup>18</sup>. Similarly, heparin and low molecular weight  
198 heparin were amongst the most common drugs reported as causing death in other previous  
199 studies,<sup>4 5</sup> demonstrating that the consequences of an error are more devastating for  
200 patients receiving these types of drugs as there is only a narrow difference between an  
201 effective and a toxic dose.<sup>5</sup> In addition, omission of such drugs may have a significant or  
202 catastrophic long-term impact<sup>19</sup> and the risk of ADEs has been found to increase especially for  
203 inpatients with coronary disease and using related drugs.<sup>12</sup> Thus, efforts to avoid dose  
204 omissions should focus on these patients.

205 Antibacterial drugs were also a common group of drugs identified in the present study.  
206 Most MAEs related to these drugs were omissions, adverse drug reactions, and  
207 administration to patients with a documented allergy. These drugs have been previously  
208 found to be related to medication errors causing death,<sup>4</sup> but are not amongst ISMP's list of

209 high-alert medications.<sup>14</sup> The data in the present study show that patients' allergies and  
210 other adverse reactions of drugs may not be verified as carefully as required. Other  
211 common drugs related to patients' deaths were opioids, insulins, and cytotoxic drugs, all in  
212 ISMP's list of high-alert medications<sup>14</sup>. The most common error types for nervous systems  
213 drugs (including opioids) were wrong or unclear dose or strength, wrong drug, or wrong  
214 quantity. Further research is needed to understand the reasons for these error types.

215 Each death caused by medication error is one death too many. There should also be some  
216 focus on rare and unusual MAEs. For example two MAEs resulting in death were caused by  
217 the administration of potassium permanganate (orally instead of topically). An NPSA Patient  
218 Safety Alert produced in 2014 was based on death caused by a patient ingesting potassium  
219 permanganate.<sup>25</sup> One incident in our data occurred before this alert and another  
220 afterwards, in 2016. More knowledge and competence in handling drugs and administration  
221 of drugs should be provided to all health professionals, especially nurses, as they are usually  
222 the final step in the medication use process. Educating patients about the medications they  
223 are receiving may help to reduce MAEs.

224

### 225 **Strengths and limitations**

226 This study was of a sufficient size to be able to identify rare MAEs that result in death. Drugs  
227 were classified into BNF category by two researchers, which supports reliability and validity.  
228 It is known that reported incidents do not represent all those that occur, and it is assumed  
229 that self-reporting systems (such as the NRLS) detect only a very small proportion of all  
230 medication incidents<sup>2</sup>. The incident reporting system has further possible weaknesses in  
231 that reporters may evaluate the consequences of incidents incorrectly such that some of the  
232 MAEs reported as resulting in death incidents may allude to possible rather than actual  
233 consequences. It was only possible to identify the name of the drug for 56% of all reports  
234 and only the categorical fields from the NRLS data were used in this analysis. In addition, the  
235 original classification of NRLS incidents was used, and it is thus impossible to evaluate what  
236 error types are hidden under the 'other' category. A further issue is whether an 'adverse  
237 drug reaction' may be an MAE when medication is administered for the first time to the  
238 patient, but descriptions of reported incidents did not include enough information to allow

239 re-classification. The free text descriptions could have provided a more detailed  
240 understanding of each incidents and further information about the drugs involved.

241

242

243

## 244 **CONCLUSION**

245 In order to prevent the most serious MAEs, additional studies and interventions should  
246 focus on dose omissions and administration of drugs to patients over 75 years old, as well as  
247 safe administration of parenteral anticoagulants and antibacterial drugs. Checking patient  
248 allergies and undertaking required verification procedures before medication  
249 administration, as well as additional education for safe handling and administration of drugs  
250 should be mandatory. Additional studies using observational research methods are  
251 important for exploring further the dynamics of serious MAEs.

252

## 253 **Acknowledgements**

254 We want to thank Philip Salter from NHS Improvement for his patience in helping the  
255 authors through the data acquisition process and refining the data extraction.

256

## 257 **Funding**

258 This work was financially supported by the post-doctoral research funding for the first  
259 author of this paper by the Academy of Finland. The last author is supported by the National  
260 Institute for Health Research (NIHR) Imperial Patient Safety Translational Research Centre,  
261 and the NIHR Health Protection Research Unit in Healthcare Associated Infections and  
262 Antimicrobial Resistance at Imperial College London, in partnership with Public Health  
263 England (PHE). The views expressed are those of the authors and not necessarily those of  
264 the NHS, the NIHR, PHE or the Department of Health and Care.

265

266 **REFERENCES**

- 267 1. WHO. Medication Without Harm: WHO's Third Global Patient Safety Challenge.  
268 <http://www.who.int/patientsafety/medication-safety/en/> 2018 Accessed 06.06.18
- 269 2. Elliott RA, Camacho E, Campbell F, Jankovic D, Martyn St James M, Kaltenthaler E, Wong  
270 R, Sculpher MJ, Faria R. Prevalence and economic burden of medication errors in the NHS in  
271 England. Rapid evidence synthesis and economic analysis of the prevalence and burden of  
272 medication error in the UK. Policy Research Unit in Economic Evaluation of Health & Care  
273 Interventions (EEPRU). [http://www.eepru.org.uk/wp-content/uploads/2018/02/eepru-](http://www.eepru.org.uk/wp-content/uploads/2018/02/eepru-report-medication-error-feb-2018.pdf)  
274 [report-medication-error-feb-2018.pdf](http://www.eepru.org.uk/wp-content/uploads/2018/02/eepru-report-medication-error-feb-2018.pdf) 2018 Accessed 14.06.18
- 275 3. NCCMERP. The National Coordinating Council for Medication Error Reporting and  
276 Prevention. Medication errors – Definition. [http://www.nccmerp.org/about-medication-](http://www.nccmerp.org/about-medication-errors)  
277 [errors](http://www.nccmerp.org/about-medication-errors) 2018 Accessed 18.05.18
- 278 4. Cousins DH, Gerrett D, Warner B. A review of medication incidents reported to the  
279 National Reporting and Learning System in England and Wales over 6 years (2005-2010). *Br J*  
280 *Clin Pharmacol.* 2012;74:597-604.
- 281 5. ISMP Canada. Ontario Hospital Critical Incidents Related to Medications or IV Fluids  
282 Analysis Report. October 2011 to December 2012. [http://www.ismp-](http://www.ismp-canada.org/download/ocil/ON_Critical_Incidents_Analysis_Report_31May2013.pdf)  
283 [canada.org/download/ocil/ON\\_Critical\\_Incidents\\_Analysis\\_Report\\_31May2013.pdf](http://www.ismp-canada.org/download/ocil/ON_Critical_Incidents_Analysis_Report_31May2013.pdf) 2018  
284 Accessed 06.06.18
- 285 6. Keers RN, Williams SD, Cooke J, Ashcroft DM. Prevalence and Nature of Medication  
286 Administration Errors in Health Care Settings: A systematic Review of Direct Observational  
287 Evidence. *Ann Pharmacother.* 2013;47:237-256.
- 288 7. McLeod MC, Barber N, Franklin BD. Methodological variations and their effects on  
289 reported medication administration error rates. *BMJ Qual & Saf.* 2013;22:278-89
- 290 8. Keers RN, Williams SD, Cooke J, Ashcroft DM. Causes of medication administration errors  
291 in hospitals: a systematic review of quantitative and qualitative evidence. *Drug Saf.*  
292 2013;36:1045-67.
- 293 9. Härkänen M, Ahonen J, Kervinen M, Turunen H, Vehviläinen-Julkunen K. The factors  
294 associated with medication errors in adult medical and surgical inpatients: a direct  
295 observation approach with medication record reviews. *Scand J Caring Sci.* 2015;29:297-306.
- 296 10. Maaskant J, Bosman D, van Rijn-Bikker P, van Aalderen W, Vermeulen H. Preventable  
297 errors with non-opioid analgesics and antiemetic drugs may increase burden in surgical  
298 pediatric patients. *Eur J Pediatr Surg.* 2014;24:381-8.
- 299 11. Kohn LT, Corrigan JM, Donaldson MS, editors. *To Err is Human: Building a Safer Health*  
300 *System.* Institute of Medicine (US) Committee on Quality of Health Care in America;. Washington (DC): National Academies Press (US); 2000.

- 302 12. Härkänen M, Kervinen M, Ahonen J, Voutilainen A, Turunen H, Vehviläinen-Julkunen K.  
303 Patient-specific risk factors of adverse drug events in adult inpatients – evidence detected  
304 using the Global Trigger Tool method. *J Clin Nurs*. 2015;24(3-4):582-91.
- 305 13. Haukland EC, von Plessen C, Nieder C, Vonon B. Adverse events in hospitalised cancer  
306 patients: a comparison to a general hospital population. *Acta Oncol*. 2017;56:1218-1223.
- 307 14. ISMP. High-Alert Medications in Acute Care Settings. July 25, 2014.  
308 [https://www.ismp.org/sites/default/files/attachments/2018-](https://www.ismp.org/sites/default/files/attachments/2018-01/highalertmedications%281%29.pdf)  
309 [01/highalertmedications%281%29.pdf](https://www.ismp.org/sites/default/files/attachments/2018-01/highalertmedications%281%29.pdf) 2018 Accessed 06.06.18
- 310 15. National Patient Safety Agency: High Risk Drugs List.  
311 [http://www.sssft.nhs.uk/images/pharmacy/documents/high\\_risk\\_drugs\\_list/High-Risk-](http://www.sssft.nhs.uk/images/pharmacy/documents/high_risk_drugs_list/High-Risk-Drugs-List.pdf)  
312 [Drugs-List.pdf](http://www.sssft.nhs.uk/images/pharmacy/documents/high_risk_drugs_list/High-Risk-Drugs-List.pdf) 2018 Accessed 29.10.18
- 313 16. Saedder EA, Brock B, Nielsen LP, Bonnerup DK, Lisby M. Identifying high-risk medication:  
314 a systematic literature review. *Eur J Clin Pharmacol*. 2014;70(6):637-45.
- 315 17. BNF 70. September 2015 - March 2016.  
316 [file:///C:/Users/marhar/Documents/Data%20mining%20-%20incidents/british-national-](file:///C:/Users/marhar/Documents/Data%20mining%20-%20incidents/british-national-formulary-2015.pdf)  
317 [formulary-2015.pdf](file:///C:/Users/marhar/Documents/Data%20mining%20-%20incidents/british-national-formulary-2015.pdf) 2018 Accessed 15.06.18
- 318 18. Keers RN, Williams SD, Cooke J, Ashcroft DM. Prevalence and nature of medication  
319 administration errors in health care settings: a systematic review of direct observational  
320 evidence. *Ann Pharmacother*. 2013;47(2):237-56.
- 321 19. NPSA Rapid Response Report: Reducing Harm from omitted and delayed medicines in  
322 hospital A tool to support local implementation.  
323 <http://www.ukmi.nhs.uk/filestore/ukmiaps/RRR09-UKMItool.pdf> 2018 Accessed 06.06.18
- 324 20. Leite B, Mistro S, Carvalho C, Mehta SR, Badaro R. Cohort study for evaluation of dose  
325 omission without justification in a teaching general hospital in Bahia, Brazil. *Int J Qual Health*  
326 *Care*. 2016;28:288-93.
- 327 21. Shandilya S, Nizamuddin K, Faisal MW, Noor S, Abraham S. Omitted medications: a  
328 continuing problem. *Clin Med (Lond)*. 2015;15:12-4.
- 329 22. Berdot S, Roudot M, Schramm C, Katsahian S, Durieux P, Sabatier B. Interventions to  
330 reduce nurses' medication administration errors in inpatient settings: A systematic review  
331 and meta-analysis. *Int J Nurs Stud*. 2016;53:342-50.
- 332 23. Wolfe D, Yazdi F, Kanji S, Burry L, Beck A, Butler C, Esmailisaraaji L, Hamel C, Hersi M,  
333 Skidmore B, Moher D, Hutton B. Incidence, causes, and consequences of preventable  
334 adverse drug reactions occurring in inpatients: A systematic review of systematic reviews.  
335 *PLoS One*. 2018;13(10): e0205426.

336 24. Jolivot PA, Pichereau C, Hindlet P, Hejblum G, Bigé N, Maury E, Guidet B, Fernandez C.  
337 An observational study of adult admissions to a medical ICU due to adverse drug events.  
338 Ann Intensive Care. 2016;6(1):9.

339 25. NHS. Patient Safety Alert. Stage One: Warning. Risk of death or serious harm from  
340 accidental ingestion of potassium permanganate preparations. 22 December 2014  
341 <https://www.england.nhs.uk/wp-content/uploads/2014/12/psa-potass-prmangant.pdf>  
342 2018 Accessed 03.06.18

343

344

345

346

347 Table 1. Characteristics of medication administration incidents resulting in death (n=229)

Variable	No.	%
<b>Year</b>		
- 2007	23	10.0
- 2008	28	12.2
- 2009	19	8.3
- 2010	22	9.6
- 2011	26	11.4
- 2012	13	5.7
- 2013	25	10.9
- 2014	24	10.5
- 2015	21	9.2
- 2016	28	12.2
<b>Location</b>		
- Ward	152	66.4
- Intensive care unit / high dependency unit	18	7.9
- Operating theatre	10	4.4
- Other	4	1.7
- Recovery room	2	0.9
- Hospital buildings (inside)	2	0.9
- Therapy department	2	0.9
- Pharmacy	1	0.4
- Anaesthetic room	1	0.4
- Mortuary	1	0.4
- Missing information	36	15.7
<b>Patient's age</b>		
- under 12	10	4.4
- 12-17	0	0.0
- 18-25	2	0.9
- 26-55	29	12.7
- 56-75	58	25.3
- over 75	95	41.5
- Missing	35	15.2
<b>Medication error category</b>		
- Omitted medicine / ingredient	72	31.4
- Other	37	16.2
- Wrong / unclear dose or strength	24	10.5
- Adverse drug reaction (when used as intended)	21	9.2
- Wrong drug / medicine	16	7.0
- Wrong frequency	13	5.6
- Wrong quantity	13	5.6
- Wrong route	8	3.5
- Patient allergic to treatment	7	3.1
- Contra-indication to the use of the medicine in relation to drugs or conditions	5	2.2
- Mismatching between patient and medicine	3	1.3
- Unknown	3	1.3
- Wrong storage	2	0.9
- Wrong method of preparation / supply	2	0.9
- Wrong / omitted verbal patient directions	2	0.9
- Wrong / omitted / passed expiry date	1	0.4

348

349



350 Table 2. Classified drugs related to death causing medication administration incidents  
 351 (n=229)

<b>BNF Drug classes</b>	<b>No.</b>	<b>%</b>
<b>1. Gastro-intestinal system</b>	0	0.0
<b>2. Cardiovascular system</b> - 2.2 (n=1) Diuretics - 2.3 (n=2) Anti-Arrhythmic Drugs - 2.5 (n=2) Hypertension and Heart Failure - 2.7 (n=6) Sympathomimetic - 2.8 (n=26) Parenteral Anticoagulants, (n=6) Oral Anticoagulants - 2.10 (n=1) Stable Angina, Acute/Coronary Synd&Fibrin - 2.11 (n=2) Antifibrinolytic Drugs & Haemostatics	46	20.1
<b>3. Respiratory system</b> - 3.6 (n=2) Oxygen	2	0.9
<b>4. Nervous system</b> - 4.1 (n=3) Hypnotics And Anxiolytics - 4.2 (n=1) Drugs Used In Psychoses & Rel.Disorders - 4.3 (n=1) Antidepressant Drugs - 4.6 (n=1) Drugs Used In Nausea And Vertigo - 4.7 (n=10) Analgesics - 4.8 (n=6) Antiepileptic Drugs - 4.9 (n=1) Drugs Used In Parkinsonism/Related Disorders	23	10.0
<b>5. Infection</b> - 5.1 (n=20) Antibacterial Drugs - 5.3 (n=1) Antiviral Drugs	21	9.2
<b>6. Endocrine system</b> - 6.1.1 (n=7) Insulin - 6.3 (n=1) Corticosteroids (Endocrine)	8	3.5
<b>7. Genito-urinary system</b>	0	0.0
<b>8. Malignant disease</b> - 8.1 (n=8) Cytotoxic Drugs - 8.2 (n=1) Drugs Affecting The Immune Response	9	3.9
<b>9. Blood and nutrition</b> - 9.1 (n=1) Anaemias + Other Blood Disorders - 9.2 (n=4) Fluids And Electrolytes - 9.3 (n=2) Intravenous Nutrition - 9.5 (n=4) Minerals	11	4.8
<b>10. Musculoskeletal system</b> - 10.2 (n=1) Drugs Used In Neuromuscular Disorders	1	0.4
<b>11. Eye</b> - 11.8 (n=1) Miscellaneous Ophthalmic Preparations	1	0.4
<b>12. Ear, nose, and oropharynx</b>	0	0.0
<b>13. Skin</b> - 13.11 (n=3) Skin Cleansers, Antiseptics & Desloughing	3	1.3
<b>14. Vaccines</b>	0	0.0
<b>15. Anaesthesia</b> - 15.1 (n=1) General Anaesthesia	1	0.4
<b>16. Emergency treatment of poisoning</b>	2	0.9
Multiple	2	0.9
Other	3	1.3
Missing	96	41.9
<b>Total</b>	<b>229</b>	<b>100</b>

352

Table 3. Names of the drugs related to death causing incidents (as written in reports)

BNF code	Drug names (as written in incident reports)
<b>2. Cardiovascular system</b>	
2.2 Diuretics	bumetanide
2.3 Anti-Arrhythmic Drugs	Digoxin [digitalis], amiodarone
2.5 Hypertension and Heart Failure	doxazosin and ramipril, verapamil
2.7 Sympathomimetic	noradrenaline x6, adrenaline x2, isoprenaline, metaraminol
2.8 Parenteral Anticoagulants & Oral Anticoagulants	enoxaparin x 7, Clexane [enoxaparin] x 6, heparin x 6, tinzaparin x 3, Fragmin [dalteparin sodium] x 4, warfarin x 3, rivaroxiban x 2, apixaban
2.10 Stable Angina, Acute/Crnry Synd&Fibrin	alteplase
2.11 Antifibrinolytic Drugs & Haemostatics	factor VIII, vitamin K
<b>3. Respiratory system</b>	
3.6 Oxygen	oxygen x 2
<b>4. Nervous system</b>	
4.1 Hypnotics And Anxiolytics	midazolam x 2, lorazepam
4.2 Drugs Used In Psychoses & Rel.Disorders	haloperidol
4.3 Antidepressant Drugs	mirtazapine
4.6 Drugs in Nausea And Vertigo	prochlorperazine / cyclizine,
4.7 Analgesics	aspirin, oxycodone x 3, fentanyl, remifentanyl, morphine x 2, diamorphine, buprenorphine
4.8 Antiepileptic Drugs	phenytoin x 4, phenobarbital, thiopentone
4.9 Park'ism/Related Disorders	co-careldopa
<b>5. Infection</b>	
5.1 Antibacterial Drugs	co-amoxiclav x 4, gentamicin x 3, Augmentin [amoxicillin and clavulanate] x 3, Tazocin [piperacillin sodium /tazobactam sodium] x 2, cefuroxime, flucloxacillin x2, daptomycin, benzylpenicillin, rifampicin, trimethoprim, levofloxacin, linezolid
5.3 Antiviral Drugs	abacavir
<b>6. Endocrine system</b>	
6.1.1 Insulin	insulin x 7
6.3 Corticosteroids (Endocrine)	hydrocortisone
<b>8. Malignant disease</b>	
8.1 Cytotoxic Drugs	chemotherapy x 2, cyclophosphamide x 2, eribulin, vinorelbine, ifosfamide, bleomycin
8.2 Immune Response Drugs	alemtuzumab
<b>9. Blood and nutrition</b>	
9.1 Anaemias + Blood Disorders	iron dextran
9.2 Fluids And Electrolytes	potassium chloride x2, 0.9% normal saline 1000ml, sando K
9.3 Intravenous Nutrition	glucose, Vamin [amino acids]
9.5 Minerals	magnesium x2, calcium chloride x 2
<b>10. Musculoskeletal system</b>	
10.2 Drugs In Neuromusc. Disord.	pyridostigmine
<b>11. Eye / Miscellaneous Ophthalmic Preparations</b>	fluorescein
<b>13. Skin</b>	
13.11 Clean., Antisep. & Desloughing	chlorhexidine, potassium permanganate
<b>15. Anaesthesia</b>	
15.1 General Anaesthesia	atropine
<b>16. Emerg. treatment of poisoning</b>	flumazenil, protamine sulphate

## Online appendix. Medication administration incidents (n=229) characteristics by drug groups

BNF Drug classes	2. Cardio-vascular system	3. Respi-ratory system	4. Nervous system	5. Infec-tion	6. Endocrine system	8. Malignant disease	9. Blood and nutrition	10. Musculo-skeletal system	11. Eye	13. Skin	15. Anaest-hesia	16. Emergency treatment	Missing / other multiple	TOTAL
<b>Charecteristics</b>														
<b>Incidents' location</b>														
Ward	34	1	19	11	6	5	5	1	0	2	1	2	65	152
Intensive care unit	3	0	1	3	1	0	4	0	0	0	0	0	6	18
Operating theatre	0	0	1	2	0	0	0	0	0	1	0	0	6	10
Other	2	0	0	1	0	0	0	0	0	0	0	0	1	4
Recovery room	0	0	1	0	0	0	0	0	0	0	0	0	1	2
Hospital buildings	0	0	0	0	0	2	0	0	0	0	0	0	0	2
Therapy depart.	0	0	0	0	0	0	0	0	0	0	0	0	2	2
Pharmacy	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Anaesthetic room	0	0	0	0	0	0	0	0	0	0	0	0	1	1
Mortuary	1	0	0	0	0	0	0	0	0	0	0	0	0	1
Missing	6	1	1	4	1	2	2	0	1	0	0	0	18	36
<b>TOTAL</b>	<b>46</b>	<b>2</b>	<b>23</b>	<b>21</b>	<b>8</b>	<b>9</b>	<b>11</b>	<b>1</b>	<b>1</b>	<b>3</b>	<b>1</b>	<b>2</b>	<b>101</b>	<b>229</b>
<b>Patient's age</b>														
under 12	2	0	1	3	0	0	2	0	0	0	0	0	2	10
18-25	0	0	1	0	0	0	0	0	0	0	0	0	1	2
26-55	6	0	3	1	0	2	1	0	0	0	0	1	15	29
56-75	9	1	3	10	0	5	4	0	0	1	1	0	24	58
over 75	23	1	11	4	5	1	3	1	0	2	0	1	43	95
Missing	6	0	4	3	3	1	1	0	1	0	0	0	16	35
<b>TOTAL</b>	<b>46</b>	<b>2</b>	<b>23</b>	<b>21</b>	<b>8</b>	<b>9</b>	<b>11</b>	<b>1</b>	<b>1</b>	<b>3</b>	<b>1</b>	<b>2</b>	<b>101</b>	<b>229</b>
<b>Error Category</b>														
Omitted medicine / ingredient	18	0	2	5	2	1	5	1	0	0	0	1	37	72
Other	4	0	2	0	3	2	1	0	0	0	1	1	23	37
Wrong / unclear dose or strength	6	1	4	0	1	2	2	0	0	0	0	0	8	24
Adverse drug reaction (when used as intended)	2	0	1	4	0	1	1	0	1	1	0	0	10	21
Wrong drug / medicine	4	0	3	1	1	0	0	0	0	0	0	0	7	16
Wrong frequency	3	0	1	1	0	1	1	0	0	0	0	0	6	13

Wrong quantity	4	1	3	1	0	0	1	0	0	0	0	0	3	13
Wrong route	2	0	1	0	0	1	0	0	0	2	0	0	2	8
Patient allergic to treatment	0	0	0	4	0	0	0	0	0	0	0	0	3	7
Contra-indication ..	1	0	1	2	0	1	0	0	0	0	0	0	0	5
Mismatching	1	0	1	1	0	0	0	0	0	0	0	0	0	3
Unknown	0	0	3	0	0	0	0	0	0	0	0	0	0	3
Wrong storage	0	0	0	1	0	0	0	0	0	0	0	0	1	2
Wrong preparation	0	0	0	0	1	0	0	0	0	0	0	0	1	2
Wrong verbal patient directions	0	0	1	1	0	0	0	0	0	0	0	0	0	2
Wrong / omitted / passed expiry date	1	0	0	0	0	0	0	0	0	0	0	0	0	1
TOTAL	46	2	23	21	8	9	11	1	1	3	1	2	101	229