A systematic review of approaches for calculating the cost of medication errors

<table>
<thead>
<tr>
<th>Journal:</th>
<th>European Journal of Hospital Pharmacy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Manuscript ID</td>
<td>Draft</td>
</tr>
<tr>
<td>Article Type:</td>
<td>Review</td>
</tr>
<tr>
<td>Date Submitted by the Author:</td>
<td>n/a</td>
</tr>
</tbody>
</table>
| Complete List of Authors: | Patel, Krishan; University of Leicester College of Medicine Biological Sciences and Psychology, Medical Education  
Jay, Robery; University of Leicester College of Medicine Biological Sciences and Psychology, Medical Education  
Shahzad, Muhammad; University of Leicester School of Management  
Green, William; University of Leicester School of Management  
Patel, Rakesh; University of Leicester, Department of Medical and Social Care Education |
| Keywords: | MEDICAL ERRORS, CLINICAL PHARMACY, HEALTH ECONOMICS, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, QUALITATIVE RESEARCH |
EDITORIAL

An initiative to address medication errors in healthcare systems is gaining increased attention in the healthcare industry. Medication errors are costly and can have significant consequences for patients, ranging from minor side effects to life-threatening complications. Understanding the factors contributing to medication errors is crucial for improving patient safety. This editorial aims to summarize the current state of research on medication errors and propose strategies for reducing their incidence.

In recent years, research has highlighted various factors contributing to medication errors, such as drug interactions, patient compliance, and physician knowledge gaps. These factors can be addressed through education, technology integration, and policy changes. For instance, implementing electronic prescribing systems can reduce errors by automating the medication ordering process and improving medication reconciliation.

In conclusion, addressing medication errors requires a multifaceted approach that involves healthcare providers, patients, and policymakers. By focusing on education, technology, and policy changes, we can work towards reducing medication errors and improving patient safety.

References:

Conflict of Interest: None.

Keywords: medication errors, patient safety, healthcare systems, education, technology, policy changes.
ABSTRACT

Introduction:

Although medication errors may cause significant morbidity and mortality for patients, the true cost of avoidable harm from such errors is unclear. Whilst studies describe different methods for calculating a financial cost from an error, there remains variability in the way calculations are conducted and the final cost, depending on the clinical context. The aim of this review was to investigate the range of approaches used for calculating medication error costs across healthcare settings.

Methods:

Medline, Embase and Web of Science were searched for relevant studies published between 1993 and 2015. Papers that explicitly described a method for calculating medication error cost were included in the review. The variables used for the calculations and a description of the approach for calculating errors was also reported on.

Results:

21 papers were included in the final review. There was wide variation in the way calculations were undertaken, with some calculations using a single variable only and others using several variables in a multi-step approach. Few calculations included indirect costs, such as loss of earnings for the patient, and only one calculation considered opportunity cost. The majority of studies presented direct medication error costs whereas others approximated error costs from the savings made following an intervention.

Conclusion:

There are a wide range of methods used for calculating the cost of medication errors. The diversity arises from the number of variables used in calculations, the perspective from which the calculation is conducted from, and the degree of economic rigor applied by researchers.
KEY WORDS

Medical errors, clinical pharmacy, health economics, health and safety, quality in healthcare, qualitative research.

INTRODUCTION

A significant component of avoidable harm in any healthcare system can be attributed to medication errors [1]. Although there are a number of interventions for reducing medication errors such as pharmacy reconciliation or electronic prescribing systems, accurately estimating the degree of harm avoided or the overall benefit of the intervention to the healthcare system remains challenging. There is a lack of reliable methodologies for estimating the cost of medication errors and no consensus on how to apply them to different clinical contexts.

A number of methodologies have been described for estimating the cost of medication errors, however the descriptions suggest a wide degree of variation in approaches to the calculations and in their application across clinical contexts. Thus, as well as the difficulty of accurately calculating the true cost of a medication error, there is the additional challenge of making reliable cost comparisons for errors across care contexts. Furthermore, there is the problem of having many descriptions for the term medication error[2-4] yet there remains an absence of a formal consensus for the definition.

Difficulties arising around calculating the cost of a medication error stem from the possibility of the event taking place at any time in the patient journey. An error can occur at any point from the initial presentation of a condition, across care contexts and between different professionals. Furthermore, a medication error can alter the course of a clinical presentation for example the failure of dose adjustment and consequent inappropriate dosing of antibiotics in patients with kidney disease.
Therefore, deciphering the true outcomes or consequences independent of the natural history of a condition is difficult and can be subjective. Continuing the same example above this challenge would involve determining the additional number of nights a patient remained in hospital solely as a result of their medication error as opposed to the natural history of their underlying illness. Taking these factors into account, identifying and calculating each and every additional cost resulting from a medication error remains the main difficulty.

Other problems relate to the absence of matched patients to enable true comparison of outcomes and, as a result, different outcomes that may also result from the same medication error. This variation leads to sufficient subjectivity in the application of methods for calculating error across care contexts. Finally, some calculations use mainly direct costs, such as the increase in raw cost of a medication to treat a patient following an error[5], whereas others use specific indirect costs or equate the entire cost of the subsequent care incurred after an error[6-8] in the calculation for evaluating cost. This implies that some methods may incorrectly estimate the cost of medication errors but more importantly that setting the viewpoint from which the errors are calculated is essential.

This variation in methodologies has implications for how the consequent interventions, aimed at reducing medication errors, are evaluated in cost-benefit and effectiveness analyses. Aside all the problems that result from inconsistency in the use of different methods, few approaches are underpinned by methodologies used in health economics. Furthermore, there is also a lack of understanding around how to group different methodologies for calculating medication errors in a given clinical context or for a given type of medication error. The aim of this review is to identify the approaches used for calculating the cost of a medication error across healthcare settings to facilitate future research and evaluation of interventions.
METHODS

This review sourced papers from Medline, Embase and Web of Science. There was no review protocol that be identified for this particular subject area. The searches were carried out on 14th August 2015 and contained all publications from the preceding 22 years. The search string contained a number of key words and associated synonyms linking “medication” and “error” to “economics” and “cost”. See Appendix 1 for details of the search used in Medline and Embase. The titles and abstracts were read to exclude publications which did not mention medication errors and their potential economic impact. Publications were also excluded if they were not in the English language or if they did not originate from peer reviewed literature. After sourcing the articles, the full texts were analysed specifically for any methodologies for calculating the cost associated with a medication error. Those papers which did not specifically allude to how a cost was attributed to a medication error were excluded (See Figure 1). All papers were reviewed for any resulting bias from the way in which the calculations were performed or any bias resulting from the interpretation from the outputs of the calculations.

This review specifically looks at medication errors which are different to prescribing errors and adverse drug events. Medication error incorporates prescribing error[9] within its definition but is not as broad as the definition for adverse drug event[10] which also includes adverse drug reactions. The definition of medication errors used in this review is taken from the European Medicines Agency as “unintended mistakes in in the prescribing, dispensing and administration of a medicine that could cause harm to a patient.”[3]

An initial pilot search of the literature gave a broad overview of the methodologies surrounding the cost of a medication error. Reviewing a selection of relevant papers helped to set the context of the review and yielded a set of criteria against which the papers in the review would be compared.

These criteria are detailed below.
All eligible papers were fully reviewed by two researchers and data was extracted separately into spreadsheets. Any disparity over the interpretation and categorisation of the data was discussed with at least one additional reviewer present and an agreement was reached.

The publications were examined to identify factors such as setting, study design and length of study for the purposes of bringing greater context and clarity to the findings. The mode of prescription and the type of medications analysed were identified to find any association with the chosen methodology of calculating the cost of medication errors. It is beyond the scope of this review to analyse the severity of medication errors or their aetiology, therefore it was simply reported whether or not there was any evidence of consideration for these factors within the study designs.

The definition of medication errors covers a number of potential stages in the process from prescription to administration for an error to occur. Each paper was analysed to see which stages in the Medicines Use Pathway[11] were investigated to detect medication errors. This consists of four distinct stages: 1) prescribing of medication, 2) supply/dispensing of medication, 3) administration of medication and 4) review of the effects of medication.

From the pilot study, it was evident that some papers examined the impact of medication errors within the context of an intervention aimed at reducing the number or impact of those errors. Therefore, the nature of those interventions, where applicable, was also noted.

Finally and most importantly, the calculation of costs of medication errors was identified. Particular focus was given to the type of costs which were included in the calculation and whether the cost incurred was directly related to the patient’s treatment or otherwise.
RESULTS

The literature search heralded 1133 potentially relevant papers. Duplicate papers were filtered within the search command. After applying the exclusion criteria to the publication abstracts, the 48 potentially relevant abstracts were singled out. Reading the full articles and excluding those without explicit evidence of calculating cost of a medication error finally left 21 publications for the analysis (See Figure 1).

Figure 1 – Flow Chart of Study Selection

Database searched: Medline, Embase, Web of Science
Total number of papers: 1133

Titles and abstracts screened for potentially relevant papers

Papers excluded: 1085
Reasons for exclusion:
Not relevant
No mention of the cost of medication errors
Not in English language
Not peer reviewed (e.g. conference abstracts)

48 Papers read in full

Data extracted from 21 papers

Papers excluded: 27
Reasons for exclusion:
Does not specify methodology for finding the cost of a medication error

Description of Studies

As illustrated in Table 1, 11 publications originated from USA, 2 from France, 2 from Germany and one each from Iraq, Iran, Israel, Mexico, Holland and Switzerland. With respect to clinical areas, 16 publications focussed on secondary care (defined here as any inpatient hospital setting), 2 on both primary and secondary care and 3 papers on primary care alone.
<table>
<thead>
<tr>
<th>Study</th>
<th>Country</th>
<th>Clinical Area</th>
<th>Prescription</th>
<th>Study</th>
<th>Length of data collection</th>
<th>Intervention</th>
<th>Medication</th>
<th>Grading of MEs</th>
<th>Aetiology Considered</th>
<th>Medicines Use Pathway Stage</th>
<th>Components of Calculation for ME (indirect/opportunity costs in BOLD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Aceves-Avila et al. (2011)[6]</td>
<td>Mexico</td>
<td>Primary Care (Outpatients)</td>
<td>Paper</td>
<td>Prospective Cohort</td>
<td>6 months</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>1, 2, 3 &amp; 4</td>
<td>Medication cost + patient’s income foregone</td>
</tr>
<tr>
<td>2. Al-Ilea et al. (2012)[12]</td>
<td>Iraq</td>
<td>Primary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>Minimum of 2 days/50 doses 6 months</td>
<td>No</td>
<td>Vaccines</td>
<td>No</td>
<td>No</td>
<td>3</td>
<td>Medication cost + cost of labour</td>
</tr>
<tr>
<td>3. Bates et al. (1997)[13]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Paper</td>
<td>Nested case control in Prospective Cohort</td>
<td>6 months</td>
<td>No</td>
<td>Any</td>
<td>Yes</td>
<td>No</td>
<td>Unclear</td>
<td>Not specified</td>
</tr>
<tr>
<td>4. Cullen et al. (1997)[10]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>6 months</td>
<td>No</td>
<td>Any</td>
<td>Yes</td>
<td>Yes</td>
<td>1, 2, 3 &amp; 4</td>
<td>(Overall length of stay) + pharmacy cost + laboratory costs + surgical costs</td>
</tr>
<tr>
<td>5. Dennehy et al. (1996)[7]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>1 month</td>
<td>No</td>
<td>Any</td>
<td>Yes</td>
<td>Yes</td>
<td>1, 3 &amp; 4</td>
<td>Not specified (All direct and indirect costs for a hospital visit associated with a medication error)</td>
</tr>
<tr>
<td>6. Field et al. (2005)[8]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>6 months</td>
<td>No</td>
<td>Any</td>
<td>Yes</td>
<td>Yes</td>
<td>1</td>
<td>Cost of hospital stay + nursing facility stay + rehabilitation stay + ED visit + Ambulatory care + physician wage + diagnostic tests + therapies + laboratory tests + ambulances + medical equipment + home visits + medication</td>
</tr>
<tr>
<td>7. Gharekhani et al. (2014)[14]</td>
<td>Iran</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cross-Sectional</td>
<td>18 months</td>
<td>Yes</td>
<td>Any</td>
<td>Yes</td>
<td>Yes</td>
<td>1 &amp; 3</td>
<td>Medication cost</td>
</tr>
<tr>
<td>8. Glowacki et al. (2003)[15]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Paper</td>
<td>Prospective Cohort</td>
<td>23 non consecutive days in 3 months</td>
<td>Yes</td>
<td>Antibiotics</td>
<td>No</td>
<td>Yes</td>
<td>1 &amp; 3</td>
<td>Medication costs pre and post intervention (+ pharmacist wage to identify the ME)</td>
</tr>
<tr>
<td>9. Helling and Encinosa (2010)[16]</td>
<td>USA</td>
<td>Primary and Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>12 months</td>
<td>No</td>
<td>Anti-retrovirals</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>Medication cost</td>
</tr>
<tr>
<td>10. Hohl et al. (2011)[17]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>3 weeks</td>
<td>No</td>
<td>Any</td>
<td>No</td>
<td>No</td>
<td>1 &amp; 4</td>
<td>Costs of hospital admission + outpatient care + ED visit + surgical procedures</td>
</tr>
<tr>
<td>11. Hoornhout et al. (2010)[18]</td>
<td>Holland</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Retrospective Cohort</td>
<td>Not Specified</td>
<td>No</td>
<td>Any</td>
<td>Yes</td>
<td>Yes</td>
<td>1, 2, 3 &amp; 4</td>
<td>Cost of staff + drugs + equipment + overheads + beds + additional procedures</td>
</tr>
<tr>
<td>12. Lampert and Klaenhenbuehl (2008)[19]</td>
<td>Switzerland</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>32 weeks</td>
<td>Yes</td>
<td>Any</td>
<td>Yes</td>
<td>Yes</td>
<td>1</td>
<td>Medication cost</td>
</tr>
<tr>
<td>13. Meier et al. (2015)[20]</td>
<td>Germany</td>
<td>Primary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>3 x 1 months</td>
<td>No</td>
<td>Any</td>
<td>Yes</td>
<td>Yes</td>
<td>1</td>
<td>Not specified (cost of entire stay for ME related admission)</td>
</tr>
<tr>
<td>14. Meissner et al. (2009)[21]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Retrospective Cohort</td>
<td>2 x 12 months</td>
<td>No</td>
<td>Opioid PCA</td>
<td>No</td>
<td>Yes</td>
<td>1, 2, 3 &amp; 4</td>
<td>Medication cost + laboratory tests + radiology + hospital stay + medical supplies + labour + opportunity costs</td>
</tr>
<tr>
<td>15. Nerich et al. (2013)[9]</td>
<td>France</td>
<td>Secondary Care</td>
<td>Electronic</td>
<td>Prospective Cohort</td>
<td>11 months</td>
<td>Yes</td>
<td>Anti-neoplastic</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
<td>Medication cost + pharmacist wage + cost of hospital stay</td>
</tr>
<tr>
<td>16. Ojeniran et al. (2010)[5]</td>
<td>Israel</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Retrospective Cross-Sectional</td>
<td>6 months</td>
<td>No</td>
<td>Antibiotics</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
<td>Medication cost</td>
</tr>
<tr>
<td>17. Ranchon et al. (2011)[22]</td>
<td>France</td>
<td>Secondary Care</td>
<td>Paper</td>
<td>Prospective Cohort</td>
<td>12 months</td>
<td>No</td>
<td>Anti-neoplastic / Chemotherapy</td>
<td>Yes</td>
<td>Yes</td>
<td>1, 2 &amp; 4</td>
<td>Not specified (Overall cost of treating the complication)</td>
</tr>
<tr>
<td>18. Rottenkoiber et al. (2012)[23]</td>
<td>Germany</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Retrospective Cohort</td>
<td>12 months</td>
<td>No</td>
<td>Any</td>
<td>No</td>
<td>No</td>
<td>Unclear</td>
<td>Costs of personnel + non-personnel + infrastructure (Every resource consumed)</td>
</tr>
<tr>
<td>19. Samp et al. (2014)[24]</td>
<td>USA</td>
<td>Primary and Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cross-Sectional</td>
<td>2 weeks</td>
<td>Yes</td>
<td>Any</td>
<td>Yes</td>
<td>No</td>
<td>1</td>
<td>Medication cost + pharmacist + drug monitoring + estimated cost of permanent harm to patient</td>
</tr>
<tr>
<td>20. Schneider et al. (1995)[25]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>24 months</td>
<td>No</td>
<td>Any</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>Costs of laboratory + non-invasive procedures + invasive monitoring/ procedures + length of stay + intensive care</td>
</tr>
<tr>
<td>21. Waddell et al. (1998)[26]</td>
<td>USA</td>
<td>Secondary Care</td>
<td>Unclear</td>
<td>Prospective Cohort</td>
<td>8 months</td>
<td>Yes</td>
<td>Any</td>
<td>No</td>
<td>No</td>
<td>1</td>
<td>Medication cost</td>
</tr>
</tbody>
</table>
Within secondary care, 15 publications focussed on inpatient prescriptions and one on ambulatory care prescriptions. The majority (n=14) of papers did not specify particular groups of medications in their analysis and were therefore assumed to include all prescribed medications. There was a wide variation in the approach to grading medication errors. Some papers did not allude to any form of grading system for type or severity, whilst other papers discussed preventability (Meier et al., Cullen et al., Hoonhout et al., Bates et al.[10, 13, 18, 20]) or attributed a level of harm which ensued (Cullen et al., Schneider et al., Dennehy et al., Nerich et al., Field et al., Samp et al.[7, 8, 10, 24, 25, 27]). Only two papers used a previously validated methodology of measuring severity of a medication error (Ranchon et al., Lampert and Kraehenbuehl[19, 28]). With regards to the aetiology of medication errors, 11 papers showed at least some evidence of acknowledging or considering the factors contributing to or causing errors.

**Medicines Use Pathway**

Categorising studies by the medicines use pathway showed that most studies (n=17) focussed on medication errors in the prescribing phase, where the decision is made as to whether a medicine is needed. Fewer studies showed evidence of considering errors occurring at supply/dispensing (n=4), administration (n=8) and in the monitoring of the response to medicines (n=7). Noted was a variation in the terminology used to describe medication errors, with some studies reporting on Adverse Drug Events (ADEs) and other similar phrases.

**Calculation of Medication Errors**

As illustrated in Table 2, of the 21 identified studies which specifically outlined a strategy for calculating the cost of medication errors, 6 used an intervention aimed at reducing medication errors and then equated the resultant cost savings to the cost of medication errors. The remaining 15 studies observed medication errors and calculated the cost of the events occurring as a consequence.
There was a wide variety in the factors used to estimate the cost as a result of a medication error (Table 1 - Components of Calculation for ME). The review revealed eight types of factors used for calculating the cost of medication errors (Table 3).

### Direct costs:

Some studies used the raw pharmaceutical cost of a medication to estimate the cost of an error (Glowaki et al., Ojeniran et al., Lampert and Kraehenbuehl, Waddell et al., Hellinger and Encinosa, Gharekhani et al., Aceves-Avila et al.[6, 14-16, 19, 26, 29]) and this was the only single direct cost involved in the calculation. Others expanded on this basic methodology, adding in additional direct costs related to the cost of a hospital stay, laboratory tests and labour costs. Direct costs were defined as any costs incurred by the healthcare provider in order to deliver their services to patients.

### Indirect and opportunity costs:

Few papers assessed beyond direct costs; 3 papers mention indirect costs (costs incurred by other parties not directly involved in the delivery of healthcare) with Aceves-Avila et al.[6] including the cost of a patient’s wage for a day lost in their calculation and Samp et al.[24] including the cost of permanent harm to the patient in their costing. Meissner et al.[21] was the only paper to consider the true economic cost of medication errors by including opportunity cost in addition to just the accounting costs reported by all of the other studies.
Table 3 – Terminology used to describe components of calculations

<table>
<thead>
<tr>
<th>Classification of costs included in calculations</th>
<th>Glossary of terminology</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pharmaceutical</strong></td>
<td></td>
</tr>
<tr>
<td>Medication cost</td>
<td>Raw pharmaceutical cost of the drug involved in the error</td>
</tr>
<tr>
<td>Drug monitoring</td>
<td>Any procedures/investigations required to maintain a drug within its therapeutic range</td>
</tr>
<tr>
<td><strong>Investigations</strong></td>
<td></td>
</tr>
<tr>
<td>Laboratory</td>
<td>Any tests undertaken with therapeutic intent</td>
</tr>
<tr>
<td>Radiology</td>
<td>To include all pathology services</td>
</tr>
<tr>
<td><strong>Procedures</strong></td>
<td></td>
</tr>
<tr>
<td>Diagnostic</td>
<td>Any examination or intervention with a therapeutic intent</td>
</tr>
<tr>
<td>Invasive monitoring</td>
<td>Examination or interventions to determine a condition or disease</td>
</tr>
<tr>
<td>Surgical</td>
<td>Interventions which involve break of the skin to observe body functions</td>
</tr>
<tr>
<td>Therapies</td>
<td>Interventions which involve break of the skin with therapeutic intent</td>
</tr>
<tr>
<td><strong>Labour</strong></td>
<td></td>
</tr>
<tr>
<td>Pharmacist</td>
<td>The sum of all wages paid to employees</td>
</tr>
<tr>
<td>Physician</td>
<td>Wages paid to pharmacists</td>
</tr>
<tr>
<td><strong>Services</strong></td>
<td></td>
</tr>
<tr>
<td>Outpatient care</td>
<td>Cost of providing a particular facility for a patient’s care</td>
</tr>
<tr>
<td>Home visits</td>
<td>Cost of patient care in their own home</td>
</tr>
<tr>
<td>Transport/ambulance</td>
<td>Cost of patient transport</td>
</tr>
<tr>
<td>Ambulatory care</td>
<td>Cost of a hospital visit short of an admission</td>
</tr>
<tr>
<td>Rehabilitation stay</td>
<td>Cost of a stay at a rehabilitation centre</td>
</tr>
<tr>
<td>Nursing facility stay</td>
<td>Cost of a stay at a nursing facility</td>
</tr>
<tr>
<td>Emergency department visit</td>
<td>Cost of a visit to the emergency department</td>
</tr>
<tr>
<td>Intensive care stay</td>
<td>Cost of admission to an intensive care unit</td>
</tr>
<tr>
<td><strong>Infrastructure</strong></td>
<td></td>
</tr>
<tr>
<td>Bed</td>
<td>Cost of providing physical facilities for delivering healthcare</td>
</tr>
<tr>
<td>Overheads</td>
<td>Operating expenses not directly related to a single patient admission – typically a fixed cost</td>
</tr>
<tr>
<td>Equipment</td>
<td>Cost of consumables used to deliver patient care</td>
</tr>
<tr>
<td>Medical supplies</td>
<td>Cost of consumables used to deliver patient care</td>
</tr>
<tr>
<td>Hospital admission</td>
<td>Sum of all variable costs which can be attributed to a single patient</td>
</tr>
<tr>
<td><strong>Patient</strong></td>
<td></td>
</tr>
<tr>
<td>Cost of permanent harm</td>
<td>Any cost borne by the consumer of the service</td>
</tr>
<tr>
<td>Income</td>
<td>Estimation of the cost of living with any lasting consequence of a medication error</td>
</tr>
<tr>
<td><strong>Economic</strong></td>
<td></td>
</tr>
<tr>
<td>Opportunity costs</td>
<td>Accounting cost plus opportunity cost</td>
</tr>
<tr>
<td></td>
<td>The cost of an alternative that must be forgone in order to pursue a certain action</td>
</tr>
</tbody>
</table>
DISCUSSION

This systematic review was conducted to investigate approaches for calculating the cost of medication errors since there is a need to accurately quantify the impact of interventions for reducing avoidable harm. The findings demonstrate that a standardised approach for exploring the costs of medication errors was lacking, therefore, the development of valid and reliable methods for undertaking calculations are necessary before the impact of interventions for reducing medication errors can be known.

No previous systematic reviews were found in this area and the primary observation was a general inconsistency in the terminology and methods used by researchers for calculating medication error costs. Furthermore, no studies identified in the review were conducted within a NHS setting, confirming the calculation of true costs following medication errors remains unknown. The cost components within the calculations were also not explicitly defined and varied across studies, so understanding how calculations can be applied across clinical contexts is unclear. Meissner et al.[21] and Hoonhout et al.[18] described using labour costs in their calculations. Both studies were conducted in different countries and therefore the meaning of labour costs, in the absence of further clarification, was unknown. Similarly, Al-lela et al.[12] and Rottenkolber et al.[23] used a microcosting method but applied the approach differently in both studies. Al-lela et al.[12] added only medication costs to labour costs to derive a cumulative cost whereas Rottenkolber et al.[23] also included infrastructure, pharmaceutical and personnel costs as part of the calculation.

There was wide variation in the way similar calculations were conducted across studies since the number of inputs and stages within a given calculation was inconsistent. Lampert and Kraehenbuehl [19] used a single input cost for a single stage calculation to investigate the cost of medication errors whereas Rottenkolber et al.[23] used multiple inputs (“every resource consumed”) into a multi-stage calculation for costing medication errors. Aceves-Avila et al.[6] calculated medication errors using
Field et al. [8] generated multiple inputs by taking into account the wider costs within the clinical environment. Field et al. [8] inputted many costs including inpatient, outpatient and personnel costs and compared the difference 6 weeks before and after a medication error. The diversity among the various cost components used demonstrates the inherent difficulty for researchers in deciding upon and costing all the relevant costs into a given calculation.

The findings from this review also confirmed that the assignment of costs incurred following a medication error was heavily based on the subjective judgment of the researchers. There was no consensus or an accepted standard method for calculating the cost of medication errors. In the absence of a standard approach and with many types of factors used for calculating medication error costs, the findings from the studies are open to bias. Schneider et al. [25] inputted costs for inpatient stay, procedures, laboratory tests and intensive care into their calculation however, evidence or justification for how, if at all, all these outcomes were relevant or actual consequences from the medication error(s) was lacking. Dennehy et al. [7] used the entire cost of the hospital stay in the calculation to mitigate against any subjective decision-making. Conversely, Bates et al. [13] used a cohort of control patients who suffered no harm to compare costs with those patients who suffered from a medication error. Nerich et al. [27] justified the choices of inputs into their calculation by asking experts to judge the likelihood of clinical sequelae being attributable to a particular medication error. These various approaches demonstrate the difficulty and complexity in determining causality between a specific medication error and subsequent events following it.

A number of studies [9, 14, 15, 19, 24, 26] attempted to calculate the cost of a medication error indirectly by estimating the cost-reduction from preventing errors following an intervention. The cost of the medication errors calculated in this way varied depending on the nature and effectiveness of the intervention in a particular care context. Oftentimes, costs of the intervention

https://mc.manuscriptcentral.com/ejhpharm
were mixed into the calculations. Glowacki et al.[15] used a pharmacist led intervention for reducing medication error. In this calculation, the cost of the pharmacist’s time was included when estimating the cost reduction from reducing medication errors following the intervention. The validity for using such approaches is questionable. Including costs of an intervention into a calculation and measuring the resultant cost savings may underestimate the true cost of a medication error. Furthermore, other costs which were not influenced by the chosen intervention may be missed from the calculation, but this is beyond the scope of this study.

Although many studies utilised methods for calculating medication error derived from perspective of the healthcare provider, some studies took into account costs from the perspective of others. Aceves-Avila et al.[6] included a simple indirect cost into their calculation in the form of a single day’s wage forgone for the patient as a result of an error. Samp et al.[24] focussed more heavily on indirect cost by including into the calculation the cost of any permanent harm to the patient as a result of a medication error. Meissner et al.[21] took insight from health economics by combining the opportunity cost, or cost of missing out on an alternative, with the accounting cost of a medication error. Samp et al.[24] also takes an economic approach by using a decision tree analysis to model their data and probabilities of events occurring to structure potential scenarios for the calculation.

CONCLUSION

In conclusion, there is a wide variation in approaches to calculating the cost of medication errors. Some of the variation can be explained due to the different methods used for calculating medication error whilst other variation can be explained by the number of inputs or stages within the calculations. Methods also vary depending on the use of indirect costs which take into account the cost of medication errors from other sources, such as the patient. Finally, some variation is also attributable to the degree of economic rigor applied to calculations, such as the use of opportunity cost.
costs, which takes into account the loss of other treatment opportunities because of the costs resulting from a medication error.

This systematic review had particular strengths in its broad search criteria and subsequent stringent exclusion criteria. The selected papers were therefore of sufficient quality and detail to avoid making assumptions about the nature of methodologies for calculating medication errors. The review was conducted in a systematic approach and there were multiple reviewers involved in extracting the data. A significant weakness would be the number of databases included in the search. Furthermore, a limitation of the review could be the small sample size of 21 papers, reducing the generalisability of the findings. Finally, there is a lack of a standardised tool for measuring the quality of the individual studies.

The implications of this study will affect how people undertake economic evaluations of interventions aimed at reducing medication errors. Further research is required to determine the most appropriate context specific method for calculating medication error, since medication errors occur across all healthcare contexts and have costs which affect patients, institutions and wider economy/society.

ACKNOWLEDGEMENTS

All the authors would like to thank the University Hospital of Leicester NHS Trust Clinical Librarian Service at the Leicester Royal Infirmary for the tremendous support provided throughout this study.

COMPETING INTERESTS

All authors have completed the Unified Competing Interest form at http://www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and
declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous 3 years; no other relationships or activities that could appear to have influenced the submitted work.

CONTRIBUTORSHIP STATEMENT:

RSP, KP and RJ conceived the idea for conducting the review. KP and RJ conducted the database searches. All authors (RSP, KP, RJ, WG and MWS) extracted the data from the papers. The final manuscript was written and checked by all authors (RSP, KP, RJ, WG and MWS).

REFERENCES


Figure 1 – Flow Chart of Study Selection

Database searched: Medline, EMBASE, Web of Science
Total number of papers: 1133

Titles and abstracts screened for potentially relevant papers
Papers excluded: 1085
Reasons for exclusion:
Not relevant
No mention of the cost of medication errors
Not in English language
Not peer reviewed (e.g. conference abstracts)

48 Papers read in full
Papers excluded: 27
Reasons for exclusion:
Does not specify methodology for finding the cost of a medication error

Data extracted from 21 papers

756x578mm (120 x 120 DPI)
Appendix 1 – Search String – Medline and Embase

1. MEDLINE; exp MEDICATION ERRORS/

2. MEDLINE; exp DRUG PRESCRIPTIONS/

3. MEDLINE; prescrib*.ti,ab

4. MEDLINE; prescrip*.ti,ab

5. MEDLINE; medication*.ti,ab

6. MEDLINE; error*.ti,ab

7. MEDLINE; mistake*.ti,ab

8. MEDLINE; exp PHYSICIANS/

9. MEDLINE; physician*.ti,ab

10. MEDLINE; doctor*.ti,ab

11. MEDLINE; clinician*.ti,ab

12. MEDLINE; exp ECONOMICS/

13. MEDLINE; exp COSTS AND COST ANALYSIS/

14. MEDLINE; exp ECONOMICS, HOSPITAL/

15. MEDLINE; exp ECONOMICS, MEDICAL/

16. MEDLINE; exp ECONOMICS, PHARMACEUTICAL/

17. MEDLINE; exp ECONOMICS, NURSING/

18. MEDLINE; exp HEALTH CARE COSTS/

19. MEDLINE; economic*.ti,ab

20. MEDLINE; cost.ti,ab

21. MEDLINE; costs.ti,ab

22. MEDLINE; costly.ti,ab

23. MEDLINE; costing.ti,ab
24. MEDLINE; price.ti,ab
25. MEDLINE; prices.ti,ab
26. MEDLINE; pricing.ti,ab
27. MEDLINE; pharmacoeconomic*.ti,ab
28. MEDLINE; "value for money".ti,ab
29. MEDLINE; budget*.ti,ab
30. MEDLINE; exp HOSPITALS/
31. MEDLINE; hospital*.ti,ab
32. MEDLINE; 2 OR 3 OR 4 OR 5
33. MEDLINE; 6 OR 7
34. MEDLINE; 32 AND 33
35. MEDLINE; 1 OR 34
36. MEDLINE; 8 OR 9 OR 10 OR 11
37. MEDLINE; 30 OR 31
38. MEDLINE; 12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29
39. MEDLINE; 35 AND 36 AND 37 AND 38
40. EMBASE; exp MEDICATION ERROR/
41. EMBASE; exp PRESCRIPTION/
42. EMBASE; exp PRESCRIPTION DRUG/
43. EMBASE; prescrib*.ti,ab
44. EMBASE; prescrip*.ti,ab
45. EMBASE; medication*.ti,ab
46. EMBASE; error*.ti,ab
47. EMBASE; mistake*.ti,ab
48. EMBASE; exp PHYSICIAN/
49. EMBASE; physician*.ti,ab
50. EMBASE; doctor*.ti,ab
51. EMBASE; clinician*.ti,ab
52. EMBASE; exp ECONOMICS/
53. EMBASE; exp COST/
54. EMBASE; exp HOSPITAL COST/
55. EMBASE; exp HEALTH ECONOMICS/
56. EMBASE; exp HEALTH CARE COST/
57. EMBASE; exp PHARMACOECONOMICS/
58. EMBASE; economic*.ti,ab
59. EMBASE; cost.ti,ab
60. EMBASE; costs.ti,ab
61. EMBASE; costly.ti,ab
62. EMBASE; costing.ti,ab
63. EMBASE; price.ti,ab
64. EMBASE; prices.ti,ab
65. EMBASE; pricing.ti,ab
66. EMBASE; pharmacoeconomic*.ti,ab
67. EMBASE; "value for money".ti,ab
68. EMBASE; budget*.ti,ab
69. EMBASE; 41 OR 42 OR 43 OR 44 OR 45
70. EMBASE; 46 OR 47
71. EMBASE; 69 AND 70
72. EMBASE; 40 OR 71
73. EMBASE; 48 OR 49 OR 50 OR 51
74. EMBASE; exp HOSPITAL/
75. EMBASE; hospital*.ti,ab
76. EMBASE; 74 OR 75
77. EMBASE; 52 OR 53 OR 54 OR 55 OR 56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66 OR 67 OR 68
78. EMBASE; 72 AND 73 AND 76 AND 77
79. EMBASE; 78 [Limit to: Human]
80. MEDLINE; 39 [Limit to: Humans]
81. EMBASE; 79 [Limit to: Human and Publication Year 1993-Current]
82. MEDLINE; 80 [Limit to: Humans and Publication Year 1993-Current]
83. EMBASE; 81 [Limit to: Human and English Language and Publication Year 1993-Current]
84. MEDLINE; 82 [Limit to: English Language and Humans and Publication Year 1993-Current]
85. EMBASE,MEDLINE; Duplicate filtered: [81 [Limit to: Human and English Language and Publication Year 1993-Current]], [82 [Limit to: English Language and Humans and Publication Year 1993-Current]]
86. EMBASE,MEDLINE; Duplicate filtered: [81 [Limit to: Human and English Language and Publication Year 1993-Current]], [82 [Limit to: English Language and Humans and Publication Year 1993-Current]]