Cross Sectional Study of Prescribing Error in Patients Admitted to Nine Hospitals Across North West England

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002036
Article Type:	Research
Date Submitted by the Author:	31-Aug-2012
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Primary Subject Heading:	Health services research
Secondary Subject Heading:	Health services research
Keywords:	EDUCATION & TRAINING (see Medical Education & Training), Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Cross Sectional Study of Prescribing Error in Patients Admitted to Nine Hospitals Across North West England

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Article Summary

1. Article Focus

- Some studies have reported lower error rates with more senior prescriber grades, and insufficient undergraduate prescriber training as a potential risk for prescribing errors
- Prescriptions frequently contain multiple medications, but data about errors on complete prescriptions, which give a better estimate of numbers of patients at risk of harm, are lacking
- We aimed to determine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge and type of medication prescribed

2. Key Messages

- We observed an error rate of 10.9% per prescribed item, with only 56.2% of 4238 complete prescriptions remaining error free.
- In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription.
- We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues.

3. Strengths and Limitations

- This was a large study across nine diverse hospital settings
- We determined the rate of errors on complete prescriptions rather than individually prescribed items, giving a better estimate of the numbers of patients affected by errors.
- We did not evaluate the impact of electronic prescribing on the prevalence and type of prescribing errors, however up to a quarter of the errors observed could potentially have been avoided through use of electronic prescribing and medicines administration systems

Abstract

Objective To evaluate the prevalence, type and severity of prescribing errors made by different categories of prescriber, and the prevalence, type and severity of prescribing errors occurring at admission compared with on discharge prescriptions.

Design Ward-based clinical pharmacists prospectively documented prescribing errors at the point of clinically checking admission or discharge prescriptions. Error categories and severities were assigned at the point of data collection, and verified independently by the study team

Setting Prospective study of nine diverse National Health Service (NHS) hospitals in North West England, including teaching hospitals, district hospitals and specialist services for paediatrics, women and mental health.

Results Of 4238 prescriptions evaluated, one or more error was observed in 1857 (43.8%) prescriptions, with a total of 3011 errors observed. Of these, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and 9 (0.30%) were potentially life-threatening. The majority of errors considered to be potentially lethal (n=9) were dosing errors (n=8), mostly relating to overdose (n=7). The rate of error was not significantly different between newly qualified doctors compared with junior, middle grade or senior doctors. Multivariable analyses revealed the strongest predictor of error was the number of items on a prescription (risk of error increased 14% for each additional item). We observed a high rate of error from medication omission, particularly amongst patients admitted acutely into hospital. Electronic prescribing systems could potentially have prevented up to a quarter of (but not all) errors.

Conclusions In contrast to other studies, prescriber experience did not impact on overall error rate (although there were qualitative differences in error category). Given that multiple drug therapies are now the norm for many medical conditions, health systems should introduce and retain safeguards which detect and prevent error, in addition to continuing training and education, and migration to electronic prescribing systems.

Introduction

Prescribing error is common, with systematic reviews suggesting that as many as 50% of hospital admissions and 7% of medication orders are affected.[1] In recent studies, prescribing errors have been found to affect approximately 9-15% of medication orders for hospital inpatients in the United Kingdom (UK).[2 3] Over one third of 651 patients were found to have a prescribing error occurring at hospital admission in the United States (US).[4] Prescribing errors are also prevalent in primary care, affecting 37% of 9385 prescriptions in the US,[5] and one in eight patients (one in 20 prescription items) in the UK.[6] In a UK study of 3695 inpatient episodes, 15% of patients experienced an adverse drug reaction (ADR), more than half of which were considered definitely or possibly avoidable. 59% of ADRs were linked to drug interactions, and ADRs were found to increase length of hospital stay in 27% of episodes.[7] A study evaluating medication omission errors in elderly patients admitted to hospital reported adverse consequences in 21% of 100 patients.[8]

Human error in healthcare may be considered in the context of individuals or health systems.[9-11] While personal factors such as forgetfulness, inattention, poor motivation, carelessness, negligence, and recklessness are important, a health systems approach more comprehensively addresses recurrent errors and organisation factors and processes which may give rise to that error. The person, the team, the task, the workplace and the institution as a whole are considered, [9] which identify weaknesses in the system's defences.[9] For example, higher hospital mortality at weekends may be associated with lower numbers of senior staff available outside of the normal working week.[12 13]

Data on causes of prescribing errors, for example differences between grades of prescriber, ward area, admission or discharge and type of medication prescribed are sparse.[3 14 15] Existing data suggest that newly qualified and junior doctors are twice as likely to make prescribing errors than senior doctors.[3] Provision of sufficient undergraduate training to allow medical students to become safe prescribers when they begin work as newly qualified doctors is widely recognised as an important factor in reducing prescribing errors.[14 16-18] Teaching in UK medical schools has changed considerably over the last decade, with the General Medical Council stipulating that medical students must be adequately prepared to prescribe drugs and manage risk at the point of graduation.[19 20]

Whilst previous studies have evaluated error for individual medications, few studies have systematically evaluated complete prescriptions to evaluate factors associated with prescribing error.[1-3] This is important as it gives a more accurate estimate of the numbers of patients who are potentially put at risk of harm by prescribing errors. We undertook a prospective survey of prescribing errors in nine diverse National Health Service (NHS) hospitals in the North West of England, to examine the prevalence, type and severity of errors made by different categories of prescriber, and also the prevalence, type and severity of prescribing errors at admission, discharge and in different ward areas. Specifically, we recorded only errors concerned with issuing of the prescription, excluding errors in clinical decision making, or 'downstream' errors in executing the prescription.

Methods

Data Collection

A total of nine NHS hospitals from the Merseyside and Cheshire region took part in the audit. These comprised large teaching hospitals, general hospitals, specialist centres for paediatrics, women's health and mental health. As this was a survey of unlinked anonymised prescriptions, Ethics approval was not required in accordance with local guidance.

A standard questionnaire collected data on error category and severity (based on EQUIP error classifications). The EQUIP study was a large prospective survey of prescribing errors affecting hospital inpatients in the UK,[3] and the error classifications were therefore considered relevant to our setting. Nominated ward-based clinical pharmacists prospectively documented prescribing errors at the point of checking admission or discharge prescriptions, during normal pharmacy working hours. Acute admission was defined as the first 24 hours in hospital. For all prescription sheets generated in acute admission settings, a separate form was completed (to allow for emergency prescribing in the absence of a full drug history without this being recorded as an error) and we sought to record only unintended medication omissions (e.g. following medicines reconciliation with general practices or primary healthcare databases). Hospitals were advised to complete the study over alternate days through the period of the audit, for example Monday in week one, Tuesday in week two, Wednesday in week three, in order to minimise inadvertent double auditing of the same patient on admission to hospital and subsequent admission to a ward.

Prescriber Category

Pharmacists were required to indicate the category of prescribers on data collection forms. For this analysis, prescribers were categorised as follows: newly qualified (Foundation Year 1, House officers), Junior (Foundation Year 2, specialist or 'core' training years 1 & 2), mid grade (specialist registrars, training Fellows), senior (Consultant), non-medical (nurse or pharmacist prescribers), other (for example locum doctors for whom grade was unclear or not recorded) and unknown (information not recorded).

Grading of prescribing errors

We modified EQUIP study criteria[3] for error categorisation and severity classification by adding or clarifying severity criteria for all error categories, and by grouping errors into distinct areas according to origin (see below and Table 1). 'Exclusion' and 'inclusion' of errors into EQUIP study error types were defined, in order to differentiate categories with potential overlap. Severity ratings were further defined and assigned to each error category based on modified EQUIP study criteria, the perceptions of the original pharmacist gradings, and reference to the licensing information of the relevant medication. In order to limit misclassification error, the original 29 EQUIP categories were batched into 10 different types of error groups as follows: (1) Dosing errors, (2) Writing errors, (3) Allergy status errors, (4) Duration of treatment wrong/not specified, (5) Drug interactions, (6) Omission of medication, (7) Excessive/unnecessary prescribing, (8) Safety errors, (9) Lack of clear directions for administration, (10) a new error category (Miscellaneous) was added (Table 1).

Despite using a standard set of definitions, we noted discrepancies across various hospitals in both error categorisation and severity rating. In particular there was a tendency to over-call errors and to overestimate their potential severity. This was confirmed by a *post-hoc* inter-rater agreement analysis. A set of six sample prescriptions was generated. A list of 14 standard errors was decided by the study team, including study error type and severity,

according to the criteria in Table 1 utilised for analysis of the main study. Six pharmacists from each participating hospital were asked to each screen the six prescription scenarios and to record errors, allocating error types and severities. The exact agreement percentages between category classification, severity classification and both combined were computed to measure the absolute concordances between pharmacist scores against the gold standard assessment. For all prescriptions, approximately 75% of error categories were correctly identified by pharmacists when compared to the standards. Only 47% of severity ratings were concordant with the standards, and 40% of pharmacists rated both error category and severity in concordance with the standards.

Therefore, in order to limit inter-observer bias, all grading and severity of errors identified in the main study were independently reassessed by two members of the study team (KS and SK), with discordant assessments collectively discussed with a third (TK) in order to agree a final categorisation for error type and severity. 143 errors were not considered true errors of the process of prescribing and were excluded. The error category was re-graded for 434 errors, and severity was re-graded for 724 errors, which was predominantly a down-grading.

Statistical Analyses

Data were analysed at the prescription level using complete case data. The prevalence and severity of errors observed were tabulated using percentage frequencies. A forest plot was produced to present the error incidence rate and 95% confidence interval (95% CI) for each hospital and grade of prescriber. For the formal statistical analysis, when there was more than one error on a prescription, only the most severe error was included. In this study, we assessed hospital, prescriber grade (newly qualified, junior, mid-grade, senior, non-medical, other), ward area (medical, surgical, A&E, mental health, critical care), number of prescribed medicines, an indicator to denote whether the prescription was prescribed on admission or on discharge and an indicator to denote whether the prescriber was Liverpool trained or not as potential risk factors. Univariate statistical analyses were performed using a chi-squared test except for continuous data, which were analysed using the Mann-Whitney U test. A multivariate logistic regression model for a prescription error was fitted to the data. Results are given in terms of an odds ratio (OR) and associated 95% CI. All risk factors that were statistically significant ($p<0.1$) in the univariate analysis were considered for inclusion in the multivariate model with the exception of ward area as a number of hospitals only reported a single specialty type.

All statistical analysis was carried out using the statistical software package SPSS (version 20) using a two-sided significance level of 0.05 (5%) throughout.

Results

Descriptive data and severity of errors

A total of 4238 prescriptions were evaluated; of these, 1857 (43.8%) prescriptions contained at least one error (Table 2). The overall incidence of prescribing errors (number of prescriptions with one or more error/prescriptions evaluated) ranged from 20% to 60% across the nine hospitals (Figure 1a).

A total of 3011 individual errors were observed within the 1857 prescriptions containing an error. Of these 3011 errors, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and nine (0.30%) were potentially life-threatening (Table 2). Details of all potentially life-threatening errors are listed in Table 3 and mainly comprised dosing errors (n=8), particularly overdose (n=7), with one incidence of under dose. A further error considered to be potentially lethal related to prescription of a medicine to which the patient had previously had a serious allergic reaction.

The proportion of errors categorised with severity as significant or higher by prescriber grade were as follows: all prescribers 58.0%, newly qualified 51.2%, junior 60.8%, mid grade 66.4%, senior 57.6% (Table 2).
Fewer errors were observed on discharge prescriptions than on prescriptions written on admission. More errors were observed in prescriptions containing antibiotics, insulin, warfarin and oxygen, although this does not take into account the number of items on each prescription. Whether doctors were Liverpool trained or not did not affect the number of errors observed (Table 2).

Error types

The most frequent error types for all prescribers were medication omission, accounting for 26.9%, writing errors accounting for (20.7%) and dosing errors accounting for (20.6%) of all errors recorded. There was little difference in the variability of error types across different prescriber grades (Figure 2).

Risk factor analysis

Results of the univariate analysis are shown in Table 4. All factors considered appeared to show a significant difference except for medical school training of doctors, which made no significant difference (p=0.91) to whether an error occurred on the prescription. Multivariate risk factor analysis showed that the likelihood of an error increased for every additional item included on the prescription (OR 1.14, 95% C 1.12, 1.17, p<0.001) (Table 4). Therefore, for each additional item on the prescription, the risk of an error occurring increased by about 14%. There was also a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16 (95% CI 0.70, 1.92, p=0.58), although this difference did not reach statistical significance (Table 5). No significant differences were found in error rates between different prescriber grades. (Figure 1b, Figure 2).

Discussion

In this large study, only 56.2% of 4238 prescriptions written had no reported errors. Of the errors recorded, 41.9% were minor, 54.1% significant, 3.6% serious and 0.3% potentially life threatening. It is important to note that severity ratings relate to the potential severity had the error been allowed to progress through to the patient - in fact the majority of errors were corrected prior to the point of administration. In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing error increasing by 14% for every additional medication item prescribed. Where data were available, prescriptions contained an average of 6.3 medication items, although this varied from 2.4 – 7.5 items according to medical specialty surveyed. Uncorrected analyses suggested that errors were frequent in prescriptions containing insulin (15.5%), antibiotics (18%), warfarin (9.2%) and oxygen (5.6%), although these patients were very likely to have been receiving multiple medications. Error rates were highest amongst specialties which prescribed a broad range of medications (e.g. acute medicine, compared to elective surgery), and also differed between different hospital Trusts, with hospitals specialising in paediatrics (Hospital I), maternal health (Hospital G) and mental health (Hospital D) exhibiting the lowest error rates. However, when corrected for number of medications, these differences did not remain significant.

The most frequent error encountered was unintended medication omission following acute hospital admission (0.97 errors/prescription written, versus 0.53 for discharge medications). When adjusted in multivariable analyses (Table 5) there was no statistically significant difference in error rates between admission and discharge. We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues. Although numbers were relatively small, we observed no difference in error rate amongst newly qualified doctors by undergraduate training, and doctors trained in Liverpool were neither more nor less likely to commit medication errors. The categories and severity of errors made by different prescriber grades were broadly similar (Table 2, Figure 2), however some differences were observed. For example, writing errors were more frequently observed with newly qualified doctors, medication omission was more frequently observed with junior and mid grade doctors, and dosing errors were more frequently observed with mid grade doctors.

These results are consistent with previously published studies. Both the EQUIP and PRACtICe Studies[3 6] reported error rates of approximately 1 in 10 medications prescribed (we observed a rate of 10.9%). Given the high number of medications prescribed (mean of 6.3 items/prescription) nearly half of all prescriptions contained at least one error. A systematic review found prescribing errors to be more common in adults than in children.[1] A study in Spain comparing paediatric wards with obstetrics found that paediatric patients had a fourfold higher risk of serious errors than the maternity population (2.3% vs 14.3%), which were mainly related to drug dosing, which is in keeping with our data.[21] Another study reported that prescribing errors were more common in primary care amongst men compared to women.[6]

In the EQUIP study, multivariate analysis showed that all grades of doctors were more likely to write a prescription containing an error than consultants.[3] A retrospective study which evaluated errors on discharge prescriptions found no significant difference in error rates between prescriber grades, although no senior (consultant) level prescribers were included.[15] In primary care, the grade of general practitioner was not associated with

prescribing errors.[6] EQUIP also reported that medication orders issued at acute admission were 70% more likely to be associated with a prescribing error.[3] Another study found lower error rates on discharge prescriptions than general inpatient prescribing, due a lower rate of medication omission, however these factors were not corrected for the number of items on each prescription.[2]

Our study was limited by missing data (one acute hospital failed to return data on number of items on each prescription), and although pharmacists had received some basic training in completing the evaluations, post-hoc analyses suggested significant variability between pharmacists' classification of errors, and especially in assignment of severity classification. Two of us independently revised each prescribing error and noted a tendency to over-call the severity of errors, and (in keeping with EQUIP criteria) included in our evaluations an assessment of whether or not a wrong dose was likely to have been actually administered based on tablet burden. We also refined EQUIP criteria to assign severity ratings to error categories where these had previously not been provided. Finally, by grouping errors into categories according to their origin and cause, we sought to reduce misclassification as far as possible. Since our data collection forms did not allow us to evaluate errors which had been missed, it is possible that our observed error rates may represent an under-estimate of the true burden of prescribing error.

Medication omission was the most prevalent error, representing 26.9% of all errors observed, which is consistent with previous reports. [2 15] Prescribing during acute admission in the absence of a full medication history may sometimes be unavoidable, and does not necessarily constitute an error. For this reason we discriminated between 'emergency' prescribing, and errors where a more complete or accurate medication history would have prevented omission of prescribed medications. Although we sought to capture only unintended medication omission, it is possible that there might still have been cases where the omission was intentional (for example, suspension of diuretics in a patient who was hypotensive or dehydrated on admission) but this intent had been missed by the pharmacist collecting the data. A sensitivity analysis showed that if all errors of medication omission either on discharge or admission were excluded, the number of errors totals 2249 (0.53 per prescription written); with 1471 (34.7%) prescriptions containing at least one error.

EQUIP error categories which could potentially be eliminated by introduction of electronic prescribing (Strength/dose missing, Product/formulation not specified, No signature, Start date incorrect/missing, incorrect route, IV instructions incorrect/missing) accounted for 357 (11.9%) of the 3011 errors observed. A further 376 (12.5%) errors could be reduced by electronic prescribing, via alerts, cautions and required fields at the patient entry/prescribing stage, although many of these can be over-ridden by the prescriber.[22] These include: administration times missing/incorrect, duplication, CD requirements incorrect/missing. The extent to which electronic prescribing can eliminate particular error types depends on the individual systems used. Importantly, whilst electronic prescribing systems could potentially have prevented up to a quarter of errors, these systems are best utilised alongside rather than instead of existing safeguards. Although one hospital (Hospital G) was utilising electronic prescribing systems, and many of the other hospitals were using electronically generated discharge summaries, we failed to observe any clear association with error rate, mainly because of the large variability in case mix which impacted directly on the number of items/prescription. In contrast, EQUIP reported that electronic prescriptions were 12% less likely to be associated with a prescribing error than handwritten prescriptions.[3] Although electronic discharge summaries may reduce error due to legibility, they do not eliminate the

transcription step from inpatient charts. One study which analysed 1808 handwritten and electronic discharge summaries found no difference in the number or types of errors observed.[15] It is also worth noting that electronic systems, while clearly offering an advantage over conventional medicines management and prescribing systems, have themselves been associated with new patterns of error. Studies in the UK and Australia found a significant reduction in prescribing errors detected after introduction of electronic prescribing systems, but also identified errors specific to the electronic prescribing system used, for example, incorrect product selected from drop-down menu, or incorrect dosing frequency selected.[23-25] These electronic systems will doubtless continue to improve through refinement.[22 26]

The Erice Medication Errors Research Group (EMERGE) recommendations for reducing prescribing errors, includes training and assessment of prescribers, ongoing monitoring, awareness and communication.[14] Health systems which may impact on likelihood of error occurring include European harmonisation of prescribing, introduction of integrated prescription forms, use of IT systems such as electronic prescribing, and standardisation, evaluation, and certification of such systems. Involvement of clinical pharmacists at all points of the medication process is also recommended.[14] The latter is important since all the hospital Trusts in our survey had evolved systems to safeguard patients from prescribing error (regardless of the adoption of electronic prescribing), and this involved use of ward-based pharmacists and dispensary staff to perform routine checks on all prescriptions issued [3 10 21 27]. This arguably represents the 'last line of defence' against prescribing error, and has greatest utility when deployed in clinical areas associated with highest risk. One fundamental role of clinical pharmacists during acute admission is medicines reconciliation, where a patient's full medication history is determined and recorded using all available sources of information. Our findings suggest that removing this safeguard (e.g. through service reconfiguration or in an effort to reduce costs) could potentially lead to higher numbers of medication error actually reaching the patient.

Acknowledgements

We gratefully acknowledge the contributions of pharmacists who participated in this study. This work was funded through an unrestricted educational grant from Mersey Deanery, although design, execution, analysis and reporting was carried out independently by the study team.

We thank the National Institute of Health Research (NIHR Department of Health) and the Northwest Development Agency (NWDA) for infrastructural and project support.

Declaration

All authors have completed the Unified Competing Interest form and declare that (1) SK has received research funding for website development from Merck, Bristol Myers Squibb, Gilead, ViiV, Tibotec, and Abbott, and honoraria, travel support for conference attendance from Roche, Tibotec, and Viiv in the past 3 years. All other authors have nothing to declare

TK and SHK developed the study concept, ML, SJ, AMc, AR, JS, AG, CC, BT co-ordinated data collection, KS, SHK analysed the data, JJK undertook the main statistical analysis with tabulations produced by KS. KS, SHK prepared the manuscript. JJK was involved in substantial revisions of the manuscript. TK, ML, SJ, AMc, AR, JS, AG, CC, BT reviewed the manuscript, SHK Is the guarantor for the project.

All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis

Data sharing: all requests for data sharing to Professor SH Khoo (khoo@liv.ac.uk)

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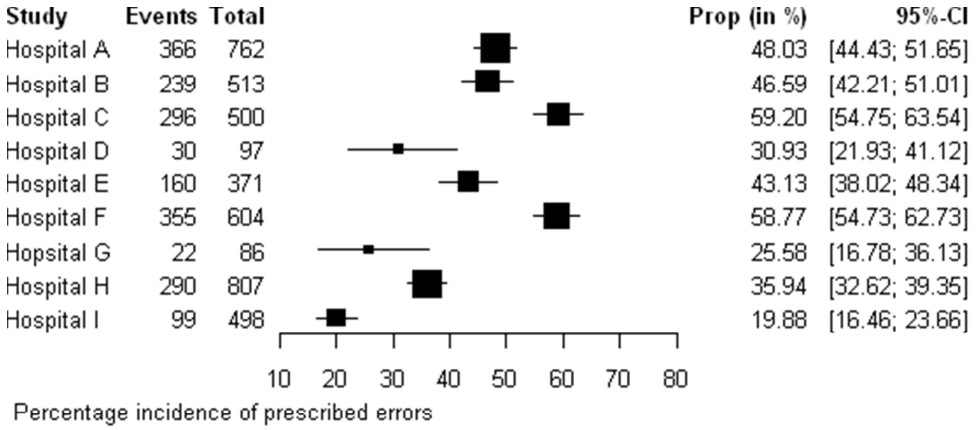

Figure 1a. Forest plot showing prescribing error rates in nine hospitals across North West England.

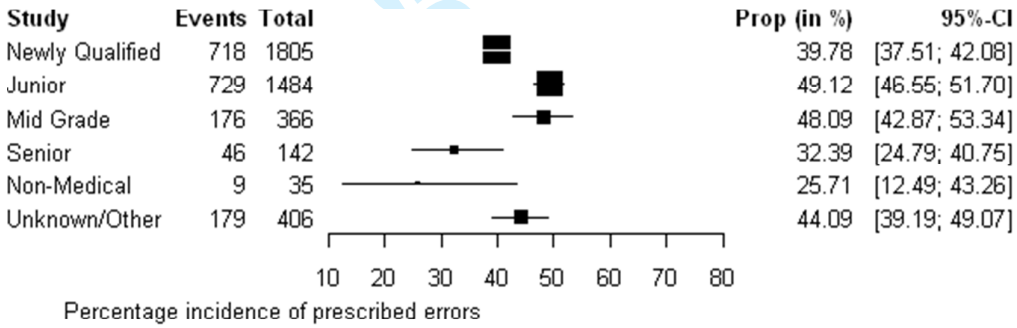

Figure 1b. Forest plot showing prescribing error rates made by different prescriber grades

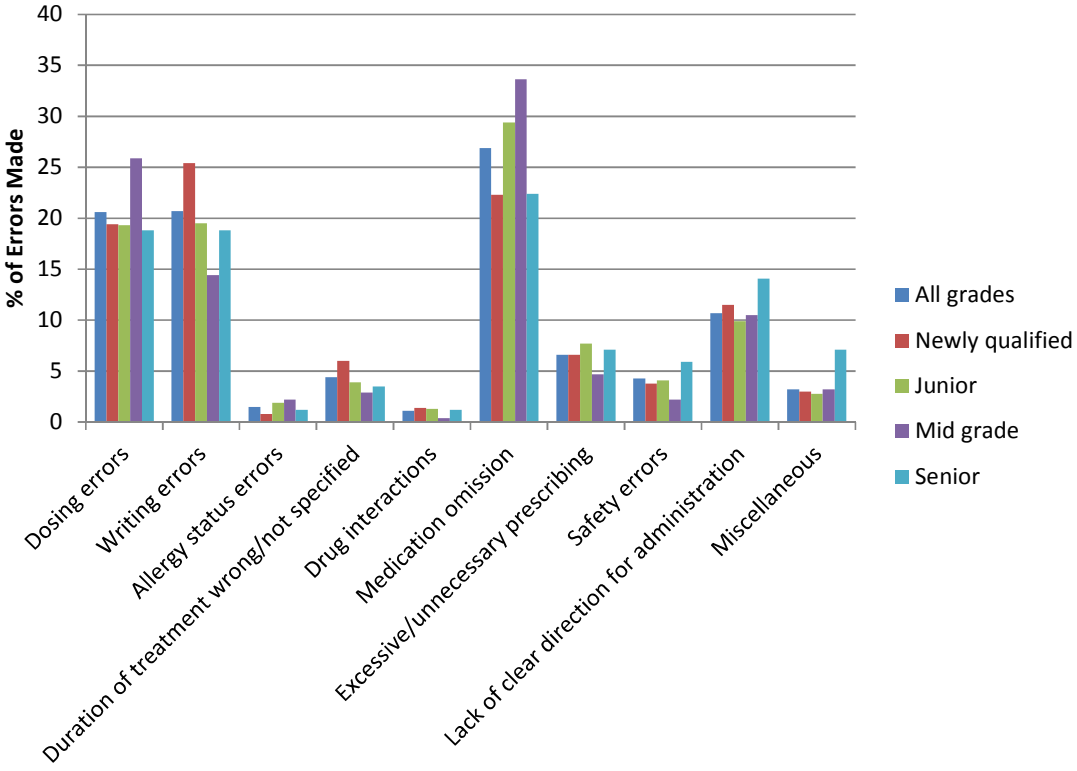

Figure 2. Categories of prescribing errors made by different grades of prescriber

Table 1. Application of error categories and severity ratings for the Mersey Deanery Prescribing Audit

Modified EQUIP Error Category	Original EQUIP Error Category	Includes/Excludes	Severity (EQUIP)	Severity Modification
1. Dosing Errors	2. Underdose		**Minor** if unable/unlikely to carry out (units); **Significant** if dose too low to treat the condition; **Serious** if patient in acute distress; **Pot. Lethal** if medication life saving	
	3. Overdose	Excludes overdoses caused by duplication eg. Paracetamol with co-codamol (7)	**Minor** if unable/unlikely to carry out (units); **Significant** - low TI, ½-4 times; **Serious**- Low TI, 4-10 times; errors in units if chance dose could be given; **Pot. Lethal** if v.low TI and dose 10 times normal dose, results in serum levels of drug in severe toxicity range, or has high potential to cause cardiopulmonary arrest	**Minor** if effect of dosing expected to be minimal
	29. Dose/rate mismatch		-	Judgement used based on Equip severity categories
2. Writing Errors	4. Strength/dose missing	Includes dose units missing	**Minor**	
	8. Product/formulation not specified		-	**Minor**
	9. Incorrect formulation		-	**Minor** unless formulation likely to have implication on treatment eg. Insulin, co-careldopa, in which case **significant/serious** based on potential consequence
	12. No signature		-	**Significant** (governance issue)
	20. Start date incorrect/missing		-	**Minor**
	21. CD requirements incorrect/missing		-	**Minor**
3. Allergy status missing/significant allergy	24. Significant allergy	Includes allergy status not completed, or where a drug has been prescribed despite an allergy to that drug/class	-	**Significant** allergy status/specific allergy missed off prescription; **Serious** if patient prescribed agent allergic to; **Pot. Lethal** if patient prescribed drug which previously had severe reaction to eg. oedema

4. Duration of treatment wrong/not specified	18. Continuation for longer than needed	Includes no stop/review date for antibiotics, steroids etc	-	**Minor** if continuation of the medicine or the duration represents little potential for harm; **Significant** if continued >3 days longer than needed for medication such as: antibiotics, oral steroids, LMWH, potassium; **Serious** if ongoing treatment could cause serious harm
	26. Premature discontinuation	Includes drugs stopped without appropriate reducing course	-	**Minor** if discontinuation is unlikey to have a significant clinical impact; **Significant** if duration of treatment insufficient to treat condition eg. Antibiotics, or if no reducing course eg. Oral steroids
5. Drug Interactions	22. Drug interaction	Excludes 2 items prescribed from same class e.g omeprazole with lansporazole (7-Duplication)	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-drug interaction	**Significant** if manufacturer advises the combination is contraindicated, should be avoided, or advises caution; **Serious** if adverse events highly probable
	27. Drug interaction not taken into account	As above: unable to differentiate 22 and 27 from available data		
6. Omission of medication	1. Omission on admission		**Significant** (regular medication)	-
	5. Omission on TTO		**Significant**	-
	17. Drug not prescribed but indicated		-	**Minor** if medication is unlikely to significantly impact patient care; **Significant** if medication would have significant impact on clinical course **Serious** if medication would alleviate a serious condition /patient is in acute distress; **Potentially lethal** if medication is potentially life saving
7. Excessive/ unnecessary prescribing	7. Duplication	Includes a second agent prescribed which contains an ingredient already being taken; 2 drugs prescribed from the same class/with same clinical effect eg. Lansoprazole + omeprazole	**Minor** if duplicate therapy prescribed without potential for increased adverse events	**Significant, Serious, Pot.lethal:** As for overdose when duplicated items co-administered (3)
	11. Unintentional prescription of	Drug prescribed was not that desired.		Judgement used based on Equip

	drug	Includes prescription of a discontinued drug, excluding discontinuation due to ADR (25), or course is too long (18)	-	severity categories
8. Safety Errors	10. No maximum dose	Excludes prescriptions with no frequency (6-administration times missing/incorrect)	**Minor**- order lacked specific drug, dose, strength, frequency or route information	**Significant** if no maximum dose stated for opioids
	13. Clinical contraindication	Contraindication according to summary of product characteristics	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-disease interaction	**Significant** if administration unlikely to have serious clinical consequences in the given situation
	25. Continuation after ADR		-	Judgement used based on Equip severity categories
	28. No dosage alteration after levels out of range		-	Judgement used based on Equip severity categories
9. Lack of clear directions for administration	6. Administration times incorrect/missing	No frequency/times of dosing incorrect eg. In relation to food, morning vs night.	**Minor**	**Significant** if administration time would be expected to affect treatment eg. Exenatide with meals, hypnotics at night
	14. Incorrect route		**Minor** if unlikely to be carried out/little chance of toxicity/therapeutic failure; **Significant** if wrong route to treat condition; **Serious** if potential for toxicity	-
	16. IV instructions incorrect/missing		-	Judgement used based on Equip severity categories
	19. Route missing		**Minor**- order lacked specific drug, dose, strength, frequency or route information	-
	23. Daily dose divided incorrectly	Number of dosing intervals incorrect. Excludes under/overdose (2/3)	-	**Minor** if dosing intervals are not standard, but are unlikely to significantly affect treatment; **Significant** if dosing intervals are inappropriate to treat the condition; **Serious** if medication has narrow therapeutic index and dosing intervals

				may affect toxicity/efficacy eg. Parenteral aminoglycosides
10. Miscellaneous	15. No indication	Includes PRN medications, where lack of indication on prescription could prevent administration. Excludes failure to write an indication when prescribing antibiotics	-	**Minor** if indication not written up for PRN medication; **Significant** if indication not written up for formulations which are licensed for specific conditions.
	30. Miscellaneous	Illegible drug details, non-standard abbreviations, patient details incorrect/missing, warfarin fixed dose prescribed.	-	Judgement used based on Equip severity categories

Table 2. Summary data showing prevalence and severity of errors observed

		Total Prescriptions	One or more error reported		Error Severity				Total errors
			No (%)	Yes (%)	Minor (%)	Significant (%)	Serious (%)	Pot. Lethal (%)	
All		**4238**	**2381 (56.2)**	**1857 (43.8)**	**1264 (42.0)**	**1629 (54.1)**	**109 (3.6)**	**9 (0.3)**	**3011**
Prescriber Grade	Newly Qualified	1805	1087 (60.2)	718 (39.8)	519 (48.8)	507 (47.7)	35 (3.3)	3 (0.3)	1064
	Junior	1484	755 (50.9)	729 (49.1)	496 (39.2)	725 (57.4)	41 (3.2)	2 (0.2)	1264
	Mid Grade	366	190 (51.9)	176 (48.1)	93 (33.6)	166 (59.9)	15 (5.4)	3 (1.1)	277
	Senior	142	96 (67.6)	46 (32.4)	36 (42.4)	43 (50.6)	6 (7.1)	0 (0)	85
	Non-medical	35	26 (74.3)	9 (25.7)	8 (57.1)	5 (35.7)	1 (7.1)	0 (0)	14
	unknown/other	406	227 (55.9)	179 (44.1)	112 (36.5)	183 (59.6)	11 (3.6)	1 (0.3)	307
Training	Liverpool	1290	787 (61.0)	503 (39.0)	270 (35.4)	456 (59.8)	36 (4.7)	1 (0.1)	763
	Non-Liverpool	922	478 (51.8)	444 (48.2)	342 (43.8)	420 (53.8)	19 (2.4)	0 (0)	781
	Unknown	2026	1118 (55.2)	908 (44.8)	652 (44.4)	753 (51.3)	54 (3.7)	8 (0.5)	1467
Admission/ Discharge	Discharge	2467	1615 (65.5)	852 (34.5)	685 (52.5)	584 (44.8)	32 (2.5)	4 (0.3)	1305
	Admission	1744	756 (43.4)	988 (56.7)	576 (34.2)	1030 (61.1)	75 (4.4)	5 (0.3)	1686
	Unknown	27	12 (44.44)	15 (55.55)	3 (15)	15 (75)	2 (10)	0 (0)	20
Ward Area	Medicine	2059	1083 (52.6)	976 (47.4)	634 (39.0)	921 (56.7)	64 (3.9)	6 (0.37)	1625
	Surgery	1395	836 (59.9)	559 (40.1)	448 (50.1)	417 (46.6)	27 (3.0)	2 (0.2)	894

	Mental health	96	66 (68.8)	30 (31.3)	24 (60)	16 (40)	0 (0)	0 (0)	40
	A&E	8	1 (12.5)	7 (87.5)	1 (9.1)	10 90.9	0 (0)	0 (0)	11
	Critical care	17	14 (82.4)	3 (17.7)	1 (25.0)	3 (75.0)	0 (0)	0 (0)	4
	Unknown	663	383 (57.8)	280 (42.2)	156 (35.7)	262 (60.0)	18 (4.1)	1 (0.2)	437
Prescription contains[#]	Antibiotic	724	301 (41.6)	423 (58.4) (**Antibiotic**: 130 (18.0))	57 (29.8)	118 (61.8)	16 (8.4)	0 (0)	191
	Insulin	129	42 (32.6)	87 (67.4) **Insulin**: 20 (15.5)	12 (37.5)	19 (59.4)	1 (3.1)	0 (0)	32
	Warfarin	196	71 (36.2)	125 (63.8) **Warfarin**: 18 (9.2)	6 (23.1)	16 (61.5)	4 (15.4)	0 (0)	26
	Oxygen	36	7 (19.4)	29 (80.6) **Oxygen**: 2 (5.6)	1 (14.3)	5 (71.4)	1 (14.3)	0 (0)	7

* Relates to errors per prescriptions written, not errors per number of items prescribed

Error severities, total errors and error rates relate to errors associated with Antibiotics/Insulin/Warfarin/Oxygen only

Table 3. Summary of the Errors Observed which were Considered to be Potentially Lethal

Error Description	Category	Prescriber Grade	Ward Area	Admission/ Discharge
Gliclazide 400mg prescribed when 40mg needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Digoxin 625micrograms prescribed when 62.5micrograms needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Oxycodone 500mg prescribed: overdose	1- Dosing Errors	Mid Grade	Surgery	Admission
Methotrexate prescribed daily, not weekly	1- Dosing Errors	Junior	Medicine	Admission
Doxazocin prescribed; had been stopped by GP due to angioedema	3. Allergy status missing/ significant allergy	Junior	Medicine	Admission
Phenytoin dose of 300mg daily incorrectly prescribed as 800mg	1- Dosing Errors	Newly Qualified	Medicine	Discharge
Midazolam IV for sedation: overdose	1- Dosing Errors	Mid Grade	Unknown	Admission
Amiodarone loading dose of 200mg three times daily continued as a regular dose	1- Dosing Errors	Other	Surgery	Discharge
Enoxaparin prescribed 1mg/kg once daily instead of 1mg/kg twice daily for a patient with acute coronary syndrome	1- Dosing Errors	Mid Grade	Medicine	Admission

Table 4. Univariate statistics showing the significance of explanatory variables in predicting error rates in prescriptions.

Variable	n	Error	No Error	Difference (95%CI)	p-value
		n (%)	n (%)		
Prescriber Grade (n=3850)		n=1689	n=2161		
Newly qualified	1803	716 (42%)	1087 (50%)	-8% (-11.2% to -4.8%)	<0.001
Junior	1482	727 (43%)	755 (35%)	8% (4.9% to 11.1%)	
Mid-grade	366	176 (10%)	190 (8.8%)	1.2% (-0.7% to 3.1%)	
Senior	142	46 (2.7%)	96 (4.4%)	-1.7% (-2.8% to -0.4%)	
Non-medical	35	9 (0.5%)	26 (1.2%)	-0.7% (-1.3% to -0.1%)	
Other	22	15 (0.9%)	7 (0.3%)	0.56% (0.1% to 1.1%)	
TTO/Admission (n=3065)		n=1135	n=1930		
TTO	2467	853 (75%)	1614 (84%)	-9% (-12.0% to -6.0%)	<0.001
Admission	598	282 (25%)	316 (16%)		
Liverpool trained (n=1325)		n=518	n=807		
Liverpool	35	14 (2.7%)	21 (2.6%)	0.1% (-1.7% to 1.9%)	0.911
Non-Liverpool	1290	504 (97%)	786 (97%)		
Hospital (n=4238)		n=1857	n=2381		
Hospital A	762	366 (20%)	396 (17%)	3% (0.6% to 5.4%)	<0.001
Hospital B	513	239 (12%)	274 (12%)	0% (-2.0% to 2.0%)	
Hospital C	500	296 (16%)	204 (8.6%)	7.4% (5.4% to 9.4%)	
Hospital D	97	30 (1.6%)	67 (2.8%)	-1.2% (-2.1% to -0.3%)	
Hospital E	371	160 (8.6%)	211 (8.9%)	-0.3% (-2.0% to 1.4%)	
Hospital F	604	355 (19%)	249 (10%)	9% (6.8% to 11.2%)	
Hospital G	86	22 (1.2%)	64 (2.7%)	-1.5% (-2.3% to -0.7%)	
Hospital H	807	290 (16%)	517 (22%)	-6% (-8.4% to -3.6%)	
Hospital I	498	99 (5.3%)	399 (17%)	-11.7% (-13.5% to -9.9%)	
Ward Area (n=3575)		n=1577	n=1998		
Medical	2059	977 (62%)	1082 (54%)	8% (4.8% to 11.2%)	<0.001
Surgical	1395	560 (36%)	835 (42%)	-6% (-9.2% to -2.8%)	
A & E	8	7 (0.4%)	1 (0.1%)	0.3% (-0.04% to 0.6%)	
Mental health	96	30 (1.9%)	66 (3.3%)	-1.4% (-2.4% to -0.4%)	
Critical care	17	3 (0.2%)	14 (0.7%)	-0.5% (-0.9% to -0.1%)	
Number of Medicines on Prescription (n=3386) Median (IQR)		8; (4,11) (n=1435)	4; (2,7) (n=1951)	-4 (-4.5, -3.5)	<0.001

Table 5. Multivariate logistic regression analysis for predicting error rates in prescriptions.

Variable	Odds ratio (95%CI)	p-value
Hospital		
Hospital H	1	
Hospital A	Not estimable*	
Hospital B	1.11 (0.78 to 1.58)	0.57
Hospital C	2.38 (1.63 to 3.46)	<0.001
Hospital D	0.64 (0.13 to 3.06)	0.57
Hospital E	1.39 (0.96 to 2.01)	0.08
Hospital F	3.53 (2.63 to 4.73)	<0.001
Hospital G	1.80 (1.03 to 3.12)	0.04
Hospital I	1.11 (0.73 to 1.70)	0.62
Prescriber Grade		
Newly qualified	1	
Junior	1.06 (0.85 to 1.32)	0.61
Mid-grade	0.96 (0.64 to 1.44)	0.83
Senior	0.97 (0.58 to 1.63)	0.92
Non-medical	0.59 (0.21 to 1.64)	0.31
Other	1.50 (0.53 to 4.23)	0.44
Discharge/Admission	1.16 (0.70 to 1.92)	0.58
Number of prescribed items	1.14 (1.12 to 1.17)	<0.001

Analysis contains only 2127 records (50.2%) where complete data was provided for all variables

* Trust provided no data on number of prescription items

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TO: Editor
BMJ Open

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31st August 2012.

Dear Editor

Re: Cross Sectional Study of Prescribing Error in Patients Admitted to Nine Hospitals Across North West England

Please find enclosed our manuscript for your consideration. The BMJ Group Journals have a long and honourable tradition of championing patient safety, and publishing research which seeks to characterise, understand and limit harms resulting from medication error. Earlier this year, Ingrid Torjesen's article highlighted findings from two of the UK's largest studies into prescribing error in primary and secondary care (the PRACtICe and EQUIP studies respectively) [*Torjesen I. BMJ 2 May 2012*]. Both studies have released study reports on the GMC website, but neither has yet been published in a peer-reviewed journal.

Our sample size is comparable to EQUIP, and larger than PRACtICe, and our observed error rate of ~10% of medication items prescribed is similar to EQUIP (9%) and PRACtICe (4%), using a modified version of EQUIP definitions. By analysing error within complete individual prescriptions (rather than individual medication items) we show that a significant proportion of patients were exposed to prescribing error, and that this risk increased by 14% for every medication item added to their prescription. Risk of error did not vary with hospital, seniority of prescriber or medical school training, but acute medical admission scenarios were associated with highest risk of error (mainly arising from unintended medication omission). Finally, electronic prescribing and medication administration systems could only have prevented up to a quarter of these errors, highlighting the important role of the ward pharmacist, particularly in high-pressure acute areas.

We believe these results are likely to accurately reflect the prevalence of prescribing error more generally throughout the UK, and to consequently inform health policy which seeks to minimise patient harms through improvements in health systems. Thank you for considering this for publication in BMJ Open.

With best wishes,

Professor S.H. Khoo
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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	√
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√
Objectives	3	State specific objectives, including any prespecified hypotheses	√
Methods			
Study design	4	Present key elements of study design early in the paper	√
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	√
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√
Bias	9	Describe any efforts to address potential sources of bias	√
Study size	10	Explain how the study size was arrived at	√
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	√
		(*b*) Describe any methods used to examine subgroups and interactions	√
		(*c*) Explain how missing data were addressed	√
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	√
		(*e*) Describe any sensitivity analyses	√
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	√
		(b) Indicate number of participants with missing data for each variable of interest	√
Outcome data	15*	Report numbers of outcome events or summary measures	√
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	√

		(*b*) Report category boundaries when continuous variables were categorized	√
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√
Discussion			
Key results	18	Summarise key results with reference to study objectives	√
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√
Generalisability	21	Discuss the generalisability (external validity) of the study results	√
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ open

Cross Sectional Study of Prescribing Errors in Patients Admitted to Nine Hospitals Across North West England

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002036.R1
Article Type:	Research
Date Submitted by the Author:	23-Oct-2012
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Primary Subject Heading:	Health services research
Secondary Subject Heading:	Health services research
Keywords:	EDUCATION & TRAINING (see Medical Education & Training), Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Cross Sectional Study of Prescribing Errors in Patients Admitted to Nine Hospitals Across North West England

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Article Summary

1. Article Focus

- Some studies have reported lower error rates with more senior prescriber grades, and insufficient undergraduate prescriber training as a potential risk for prescribing errors
- Prescriptions frequently contain multiple medications, but data about errors on complete prescriptions (all prescribed items on an inpatient chart or discharge prescription), which give a better estimate of numbers of patients at risk of harm, are lacking
- We aimed to determine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge and type of medication prescribed

2. Key Messages

- We observed an error rate of 10.9% per prescribed item, with only 56.2% of 4238 complete prescriptions remaining error free.
- In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription.
- We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues.

3. Strengths and Limitations

- This was a large study across nine diverse hospital settings
- We determined the rate of errors on complete prescriptions as well as for individually prescribed items, giving a better estimate of the numbers of patients affected by errors.
- We did not evaluate the impact of electronic prescribing on the prevalence and type of prescribing errors, however up to a quarter of the errors observed could potentially have been avoided through use of electronic prescribing and medicines administration systems

Abstract

Objective To evaluate the prevalence, type and severity of prescribing errors observed between grades of prescriber, ward area, admission or discharge and type of medication prescribed

Design Ward-based clinical pharmacists prospectively documented prescribing errors at the point of clinically checking admission or discharge prescriptions. Error categories and severities were assigned at the point of data collection, and verified independently by the study team

Setting Prospective study of nine diverse National Health Service (NHS) hospitals in North West England, including teaching hospitals, district hospitals and specialist services for paediatrics, women and mental health.

Results Of 4238 prescriptions evaluated, one or more error was observed in 1857 (43.8%) prescriptions, with a total of 3011 errors observed. Of these, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and 9 (0.30%) were potentially life-threatening. The majority of errors considered to be potentially lethal (n=9) were dosing errors (n=8), mostly relating to overdose (n=7). The rate of error was not significantly different between newly qualified doctors compared with junior, middle grade or senior doctors. Multivariable analyses revealed the strongest predictor of error was the number of items on a prescription (risk of error increased 14% for each additional item). We observed a high rate of error from medication omission, particularly amongst patients admitted acutely into hospital. Electronic prescribing systems could potentially have prevented up to a quarter of (but not all) errors.

Conclusions In contrast to other studies, prescriber experience did not impact on overall error rate (although there were qualitative differences in error category). Given that multiple drug therapies are now the norm for many medical conditions, health systems should introduce and retain safeguards which detect and prevent error, in addition to continuing training and education, and migration to electronic prescribing systems.

Introduction

Prescribing errors are common, with systematic reviews suggesting that as many as 50% of hospital admissions and 7% of medication orders are affected.[1] In recent studies, prescribing errors have been found to affect approximately 9-15% of medication orders for hospital inpatients in the United Kingdom (UK).[2 3] Over one third of 651 patients were found to have a prescribing error occurring at hospital admission in the United States (US).[4] Prescribing errors are also prevalent in primary care, affecting 37% of 9385 prescriptions in the US,[5] and one in eight patients (one in 20 prescription items) in the UK.[6] A study in the Netherlands evaluating medication omission errors in elderly patients admitted to hospital reported adverse consequences in 21% of 100 patients.[8]

Human error in healthcare may be considered in the context of individuals or health systems.[9-11] While personal factors such as forgetfulness, inattention, poor motivation, carelessness, negligence, and recklessness are important, a health systems approach more comprehensively addresses recurrent errors and organisation factors and processes which may give rise to that error. The person, the team, the task, the workplace and the institution as a whole are considered, [9] which identify weaknesses in the system's defences.[9] For example, higher hospital mortality at weekends may be associated with lower numbers of senior staff available outside of the normal working week.[12 13]

Data on factors which may contribute to prescribing errors, for example differences between grades of prescriber, ward area, admission or discharge and type of medication prescribed are sparse.[3 14 15] Existing data suggest that newly qualified and junior doctors are twice as likely to make prescribing errors than senior doctors, taking into account the larger volume of prescriptions written by more junior prescriber grades.[3] Provision of sufficient undergraduate training to allow medical students to become safe prescribers when they begin work as newly qualified doctors is widely recognised as an important factor in reducing prescribing errors.[14 16-18] Teaching in UK medical schools has changed considerably over the last decade, with the General Medical Council stipulating that medical students must be adequately prepared to prescribe drugs and manage risk at the point of graduation.[19 20]

Whilst previous studies have evaluated error for individual medications, few studies have systematically evaluated complete prescriptions (all items included on a single prescription chart or discharge prescription at the time of clinical pharmacist check) to evaluate factors associated with prescribing error.[1-3] This is important as it gives a more accurate estimate of the numbers of patients who are potentially put at risk of harm by prescribing errors. We undertook a prospective survey of prescribing errors in nine diverse National Health Service (NHS) hospitals in the North West of England, aiming to examine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge, hospitals and the type and number of medication prescribed. In order to further evaluate the role of undergraduate training, we also tested for a relationship between occurrence of error and medical school training of prescribers. Univariate analysis and multivariate logistic regression was used to evaluate factors associated with prescribing errors.

Methods

Setting

A total of nine NHS hospitals from the Merseyside and Cheshire region took part in the audit. These comprised large teaching hospitals, general hospitals, specialist centres for

paediatrics, women's health and mental health (Table 1). One hospital was using complete electronic prescribing systems (inpatient prescribing, medication ordering, discharge prescriptions) on some wards at the time of the audit. Eight of the hospitals were using paper prescription charts for inpatients and either handwritten or transcribed electronically generated discharge prescriptions. In this setting, ward-based clinical pharmacists check inpatient prescriptions at or soon after patient admission, when medicines reconciliation is undertaken. Inpatient prescription charts are then checked at least daily by the pharmacist. Discharge prescriptions are checked and authorised by a clinical pharmacist prior to supply of medication. Pharmacists may amend or clarify some aspects of prescribing, or discuss with the clinical team any recommendations or safety issues at these points of care. Clinical pharmacists may also participate in ward rounds and multidisciplinary team meetings, where prescribing may be discussed with clinicians, clarified or amended.

Data Collection

As this was an audit of unlinked anonymised prescriptions, Ethics approval was not required in accordance with local guidance. We aimed to capture data from all seven hospital trusts in the region. Two additional hospitals adjacent to and linked with healthcare provision in the Merseyside region were also audited. The number of prescriptions audited was empirically determined in order to generate a sample size equivalent to a large study recently undertaken in the UK.[3] In order to audit practice across the region, each hospital was asked to audit a minimum of 400 prescriptions.

We adopted the following definition of prescribing errors for the study, which excludes adherence to local prescribing policy and guidelines: "A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice".[21] A standard questionnaire collected data on error category and severity (based on EQUIP error classifications). The EQUIP study was a large prospective survey of prescribing errors affecting hospital inpatients in the UK,[3] and the error classifications were therefore considered relevant to our setting. Nominated ward-based clinical pharmacists prospectively documented prescribing errors at the point of checking inpatient or discharge prescriptions, during normal pharmacy working hours, therefore each audit form was a point prevalence of prescribing errors at the time of pharmacist clinical check. Acute admission was defined as the first 24 hours in hospital. For all prescription sheets generated in acute admission settings, a separate audit form was completed (to allow for emergency prescribing in the absence of a full drug history without this being recorded as an error) and we sought to record only unintended medication omissions (e.g. following medicines reconciliation with general practices or primary healthcare databases). Hospitals were advised to complete the study on different days of the week throughout the period of the audit, in order to capture an even spread of days. For example data collection would occur weekly, on Monday in week one, Tuesday in week two, Wednesday in week three, in order to minimise double auditing of the same patient on admission to hospital and subsequent admission to a ward. Therefore, if patients were audited twice, an interval of at least one week would separate each audit form, unless their acute admission/inpatient /discharge prescription were audited on the same day. If items on prescriptions had been previously screened, they would be counted again in any subsequent auditing , though there would be a one week interval since previous auditing, or the patient would be a different stage of hospital admission. All types of inpatient medication order were audited, including IV fluids, when required and once only medication.

Prescriber Category

Pharmacists were required to indicate the category of prescribers on data collection forms. For this analysis, prescribers were categorised as follows: newly qualified (foundation year 1, house officers), junior (foundation year 2, specialist or 'core' training years 1 & 2), mid grade (specialist registrars, training fellows), senior (consultant), non-medical (nurse or pharmacist prescribers), other (for example locum doctors for whom grade was unclear) and unknown (no information concerning prescriber recorded).

Grading of prescribing errors

We modified EQUIP study criteria[3] for error categorisation and severity classification by adding or clarifying severity criteria for all error categories, and by grouping errors into ten distinct areas according to stage of the prescribing process (see below and Table 2). 'Exclusion' and 'inclusion' of errors into EQUIP study error types were defined, in order to differentiate categories with potential overlap. Severity ratings were further defined and assigned to each error category based on modified EQUIP study criteria andtaking into account the perceptions of the original pharmacist gradings. Severity ratings related to the potential severity had the error been allowed to progress through to the patient, as the majority of errors were corrected prior to the point of administration. In order to limit misclassification error, the original 29 EQUIP categories were batched into 10 different types of error groups as follows: (1) Dosing errors, (2) Writing errors, (3) Allergy status errors, (4) Duration of treatment wrong/not specified, (5) Drug interactions, (6) Omission of medication, (7) Excessive/unnecessary prescribing, (8) Safety errors, (9) Lack of clear directions for administration, (10) a new error category (Miscellaneous) was added (Table 2). The modification and definition of error categories and severities was undertaken by two members of the study team (KS, SK) and agreed by a third (TK).

Despite using a standard set of definitions, we noted discrepancies across various hospitals in both error categorisation and severity rating. In particular there was a tendency to over-report errors and to overestimate their potential severity. This was confirmed by a *post-hoc* inter-rater agreement analysis. A set of six sample prescriptions was generated. A list of 14 sample errors was decided by the study team, including study error type and severity, according to the criteria in Table 2 utilised for analysis of the main study. The errors selected occurred frequently in the main study, and covered a broad range of error categories and severities. Six pharmacists from each participating hospital were asked to each screen the six prescription scenarios containing the 14 errors and to record any observed errors, allocating error types and severities. The exact agreement percentages between category classification, severity classification and both combined were computed to measure the absolute concordances between pharmacist scores against the gold standard assessment.

In order to limit inter-observer bias, all grading and severity of errors identified in the main study were independently reassessed by two members of the study team (KS and SK), with discordant assessments collectively discussed with a third (TK) in order to agree a final categorisation for error type and severity. For severity ratings, the summary of product characteristics for relevant medication was consulted, in order to determine potential implications of different degrees of overdose, underdose, of drug interactions, and also to confirm clinical contra-indications.

Statistical Analyses

Data were analysed at the prescription level using complete case data. The prevalence and severity of errors observed were tabulated using percentage frequencies. A Forest plot was produced to present the error prevalence rate and 95% confidence interval (95% CI) for

each hospital and grade of prescriber. For the formal statistical analysis, when there was more than one error on a prescription, only the most severe error was included. This approach was used to ensure that the errors included in the analysis were independent. In this study, we assessed hospital, prescriber grade (newly qualified, junior, mid-grade, senior, non-medical, other), ward area (medical, surgical, A&E, mental health, critical care), number of prescribed medicines, an indicator to denote whether the prescription was prescribed on admission or on discharge and an indicator to denote whether the prescriber was Liverpool trained or not as potential risk factors. Univariate statistical analyses were performed using a chi-squared test except for continuous data, which were analysed using the Mann-Whitney U test. A multivariate logistic regression model for a prescription error was fitted to the data. Results are given in terms of an odds ratio (OR) and associated 95% CI. All risk factors that were statistically significant ($p<0.1$) in the univariate analysis were considered for inclusion in the multivariate model with the exception of ward area as a number of hospitals only reported a single specialty type.

All statistical analysis was carried out using the statistical software package SPSS (version 20) using a two-sided significance level of 0.05 (5%) throughout.

Results

Error Classification

During the *post-hoc* inter-rater agreement analysis, , approximately 75% of error categories were correctly identified by pharmacists when compared to the standards. Only 47% of severity ratings were concordant with the standards, and 40% of pharmacists rated both error category and severity in concordance with the standards.

Re-assessment of errors by the study team resulted in exclusion of a total of 143 errors which were not considered true errors of the process of prescribing. The error category was re-graded for 434 errors, and severity was re-graded for 724 errors, which was predominantly a down-grading.

Descriptive data and severity of errors

A total of 4238 prescriptions were evaluated; of these, 1857 (43.8%) prescriptions contained at least one error (Table 3). The overall prevalence of prescribing errors (number of prescriptions with one or more error/prescriptions evaluated) ranged from 20% to 60% across the nine hospitals (Figure 1). The rate of errors per prescribed item was 10.9%.

A total of 3011 individual errors were observed within the 1857 prescriptions containing an error. Of these 3011 errors, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and nine (0.30%) were potentially life-threatening (Table 3). Details of all potentially life-threatening errors are listed in Table 3 and mainly comprised dosing errors (n=8), particularly overdose (n=7), with one incidence of under dose. A further error considered to be potentially lethal related to prescription of a medicine to which the patient had previously had a serious allergic reaction.

The proportion of errors categorised with severity as significant or higher by prescriber grade were as follows: all prescribers 58.0%, newly qualified 51.2%, junior 60.8%, mid grade 66.4%, senior 57.6% (χ^2_{trend} $p<0.001$ for univariate analysis, although this association disappeared when corrected for other potential confounders)(Table 3).
Fewer errors were observed on discharge prescriptions than on prescriptions written on admission. More errors were observed in prescriptions containing antibiotics, insulin, warfarin and oxygen, although this does not take into account the number of items on each prescription. Whether doctors were Liverpool trained or not did not affect the number of errors observed (Table 3).

Differences in error prevalence and error types were observed in individual participating hospitals. The lowest rates of errors were reported for the paediatrics specialty, with 0.07 errors observed per prescribed item, and 0.26 errors observed per prescription. However, in multivariate analysis, there was no significant reduction in error risk and it is likely that the effect could be due to lower number of items per prescription (mean 3.5, vs pooled data: 6.3). The most common error types were dosing errors (30%) and medication omission (23.1%).
Significantly lower risk of errors was observed in the hospital providing specialist services for women (p=0.04, Table 6) in multivariate analysis. One of the lowest error rates per prescription was observed (0.28), although the error rate per prescribed item (0.11) was

equal to that of the pooled data. The most common error type observed was excessive/unnecessary prescribing (50%). No errors of medication omission were observed. This hospital also had a low number of items per prescription (2.4), and was using electronic prescribing systems on some wards.

Error types

The most frequent error types for all prescribers were medication omission, accounting for 26.9%, writing errors accounting for (20.7%) and dosing errors accounting for (20.6%) of all errors recorded. There was little difference in the variability of error types across different prescriber grades (Figure 2).

Risk factor analysis

Results of the univariate analysis are shown in Table 5. Missing data limited inclusion of all reported prescriptions in risk factor analysis, notably as one acute hospital failed to return data on number of items on each prescription. All factors considered appeared to show a significant difference except for medical school training of doctors, which made no significant difference (p=0.91) to whether an error occurred on the prescription. Multivariate risk factor analysis showed that the likelihood of an error increased for every additional item included on the prescription (OR 1.14, 95% C 1.12, 1.17, p<0.001) (Table 5). Therefore, for each additional item on the prescription, the risk of an error occurring increased by about 14%. There was also a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16 (95% CI 0.70, 1.92, p=0.58), although this difference did not reach statistical significance (Table 6). No significant differences were found in error rates between different prescriber grades, when compared to newly qualified doctors (Figure 2, Figure 3) in multivariate analyses.

Discussion

In this large study, only 56.2% of 4238 prescriptions written had no reported errors. Of the errors recorded, 41.9% were minor, 54.1% significant, 3.6% serious and 0.3% potentially life threatening. It is important to note that severity ratings relate to the potential severity had the error been allowed to progress through to the patient - in fact the majority of errors were corrected prior to the point of administration. In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing error increasing by 14% for every additional medication item prescribed. Where data were available, prescriptions contained an average of 6.3 medication items, although this varied from 2.4 – 7.5 items according to medical specialty surveyed. Uncorrected analyses suggested that errors were frequent in prescriptions containing insulin (15.5%), antibiotics (18%), warfarin (9.2%) and oxygen (5.6%), although these patients were very likely to have been receiving multiple medications. Error rates were highest amongst specialties which prescribed a broad range of medications (e.g. acute medicine, compared to elective surgery), and also differed between different hospital Trusts, with hospitals specialising in paediatrics , maternal health and mental health exhibiting the lowest error

rates. However, when corrected for number of medications, these differences did not remain significant, with the exception of maternal health.

The most frequent error encountered was unintended medication omission following acute hospital admission (0.97 errors/prescription written, versus 0.53 for discharge medications). When adjusted in multivariable analyses (Table 6) there was no statistically significant difference in error rates between admission and discharge. We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues. Although numbers were relatively small, we observed no difference in error rate amongst newly qualified doctors by undergraduate training, and doctors trained in Liverpool were neither more nor less likely to commit medication errors. The categories and severity of errors made by different prescriber grades were broadly similar (Table 3, Figure 2), however some differences were observed. For example, writing errors were more frequently observed with newly qualified doctors, medication omission was more frequently observed with junior and mid grade doctors, and dosing errors were more frequently observed with mid grade doctors.

These results are consistent with previously published studies. Both the EQUIP and PRACtICe Studies[3 6] reported error rates of approximately 1 in 10 medications prescribed (we observed a rate of 10.9%). Given the high number of medications prescribed (mean of 6.3 items/prescription) nearly half of all prescriptions contained at least one error.
A systematic review found prescribing errors to be more common in adults than in children.[1] A study in Spain comparing paediatric wards with obstetrics found that paediatric patients had a fourfold higher risk of serious errors than the maternity population (2.3% vs 14.3%), which were mainly related to drug dosing..[22] This is in keeping with our data, as we observed a low error rate for the paediatrics specialty, although this was likely due to a low number of prescribed items. Dosing errors were the most common error type. Another study reported that prescribing errors were more common in primary care amongst men compared to women.[6] We observed a significantly lower risk for errors in specialist services for women.

In the EQUIP study, multivariate analysis showed that all grades of doctors were more likely to write a prescription containing an error than consultants.[3] A retrospective study which evaluated errors on discharge prescriptions found no significant difference in error rates between prescriber grades, although no senior (consultant) level prescribers were included.[15] In primary care, the grade of general practitioner was not associated with prescribing errors.[6] We observed no significant difference in prescribing error rates between prescriber grades, when compared to newly qualified prescribers. EQUIP also reported that medication orders issued at acute admission were 70% more likely to be associated with a prescribing error.[3] Another study found lower error rates on discharge prescription items than was observed with general inpatient prescribing, due to a lower rate of medication omission, however these factors were not corrected for the number of items on each prescription.[2] We observed a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16, although this did not reach significance in multivariate analysis.

Our study was limited by missing data (one acute hospital failed to return data on number of items on each prescription), and although pharmacists had received some basic training in completing the evaluations, post-hoc analyses suggested significant variability between pharmacists' classification of errors, and especially in assignment of severity classification. Two of us independently revised each prescribing error and noted a tendency to over-

estimate the severity of errors, and (in keeping with EQUIP criteria) included in our evaluations an assessment of whether or not a wrong dose was likely to have been actually administered based on tablet burden. We also refined EQUIP criteria to assign severity ratings to error categories where these had previously not been provided. Finally, by grouping errors into categories according to their origin, we sought to reduce misclassification as far as possible. Since our data collection forms did not allow us to evaluate errors which had been missed, it is possible that our observed error rates may represent an under-estimate of the true burden of prescribing error.

Medication omission was the most prevalent error, representing 26.9% of all errors observed, which is consistent with previous reports. [2 15] Prescribing during acute admission in the absence of a full medication history may sometimes be unavoidable, and does not necessarily constitute an error. For this reason we discriminated between 'emergency' prescribing, and errors where a more complete or accurate medication history would have prevented omission of prescribed medications. Although we sought to capture only unintended medication omission, it is possible that there might still have been cases where the omission was intentional (for example, suspension of diuretics in a patient who was hypotensive or dehydrated on admission) but this intent had been missed by the pharmacist collecting the data. A sensitivity analysis showed that if all errors of medication omission either on discharge or admission were excluded, the number of errors totals 2249 (0.53 per prescription written); with 1471 (34.7%) prescriptions containing at least one error, whichrepresents a significant reduction in overall prescribing error rate. A core role for clinical ward based pharmacists is medicines reconciliation for admitted patients. This involves detailed medication history taking, recording of full medication list in the patient's case notes, and discussion with the clinical team to ensure that all regular medicines are prescribed throughout the admission, if appropriate. Similarly, on discharge, pharmacists ensure that necessary regular medicines are continued, and that any medicines newly started during the admission are prescribed for discharge as appropriate. The majority of the omission errors reported will have been rectified during admission or prior to discharge, as a result of the pharmacist clinical check. This highlights the importance of medicines reconciliation as soon as practicable at hospital admission, in order to minimise the possibility of missed doses of essential medicines. The role of pharmacists in actue admission settings may therefore be of particular benefit.

EQUIP error categories which could potentially be eliminated by introduction of electronic prescribing (strength/dose missing, product/formulation not specified, no signature, start date incorrect/missing, incorrect route, IV instructions incorrect/missing) accounted for 357 (11.9%) of the 3011 errors observed. A further 376 (12.5%) errors could be reduced by electronic prescribing, via alerts, cautions and required fields at the patient entry/prescribing stage, although many of these can be over-ridden by the prescriber.[23] These include: administration times missing/incorrect, duplication, CD requirements incorrect/missing. The extent to which electronic prescribing can eliminate particular error types depends on the individual systems used. Importantly, whilst electronic prescribing systems could potentially have prevented up to a quarter of errors, these systems are best utilised alongside rather than instead of existing safeguards. We did not formally evaluate differences in error rates between electronic prescribing and paper-based prescribing systems. Although one hospital (Hospital G) was utilising complete electronic prescribing systems on some wards at the time of the study, and many of the other hospitals were using electronically generated discharge summaries, we failed to observe any clear association with error rate, mainly because of the large variability in case mix which impacted directly on the number of items/prescription. In

contrast, EQUIP reported that electronic prescriptions were 12% less likely to be associated with a prescribing error than handwritten prescriptions.[3] Although electronic discharge summaries may reduce error due to legibility, they do not eliminate the transcription step from inpatient charts. One study which analysed 1808 handwritten and electronic discharge summaries found no difference in the number or types of errors observed.[15] It is also worth noting that electronic systems, while clearly offering an advantage over conventional medicines management and prescribing systems, have themselves been associated with new patterns of error. Studies in the UK and Australia found a significant reduction in prescribing errors detected after introduction of electronic prescribing systems, but also identified errors specific to the electronic prescribing system used, for example, incorrect product selected from drop-down menu, or incorrect dosing frequency selected.[24-26] These electronic systems will doubtless continue to improve through refinement.[23 27]

The Erice Medication Errors Research Group (EMERGE) recommendations for reducing prescribing errors, includes training and assessment of prescribers, ongoing monitoring, awareness and communication.[14] Health systems which may impact on likelihood of error occurring include European harmonisation of prescribing, introduction of integrated prescription forms, use of IT systems such as electronic prescribing, and standardisation, evaluation, and certification of such systems. Involvement of clinical pharmacists at all points of the medication process is also recommended.[14] The latter is important since all the hospital Trusts in our survey had evolved systems to safeguard patients from prescribing error (regardless of the adoption of electronic prescribing), and this involved use of ward-based pharmacists and dispensary staff to perform routine checks on all prescriptions issued [3 10 22 28]. This likely represents the 'last line of defence' against prescribing error, and has greatest utility when deployed in clinical areas associated with highest risk. One fundamental role of clinical pharmacists during acute admission is medicines reconciliation, where a patient's full medication history is determined and recorded using all available sources of information. Our findings suggest that removing this safeguard (e.g. through service reconfiguration or in an effort to reduce costs) could potentially lead to higher numbers of medication error actually reaching the patient.

Acknowledgements

We gratefully acknowledge the contributions of pharmacists who participated in this study. This work was funded through an unrestricted educational grant from Mersey Deanery, although design, execution, analysis and reporting was carried out independently by the study team.

We thank Professor David Graham, Postgraduate Medical Dean, Mersey Deanery for supporting the project

We thank the National Institute of Health Research (NIHR Department of Health) and the Northwest Development Agency (NWDA) for infrastructural and project support.

Declaration

All authors have completed the Unified Competing Interest form and declare that (1) SK has received research funding for website development from Merck, Bristol Myers Squibb, Gilead, ViiV, Tibotec, and Abbott, and honoraria, travel support for conference attendance from Roche, Tibotec, and Viiv in the past 3 years. All other authors have nothing to declare

TK and SHK developed the study concept, ML, SJ, AMc, AR, JS, AG, CC, BT co-ordinated data collection, KS, SHK analysed the data, JJK undertook the main statistical analysis with tabulations produced by KS. KS, SHK prepared the manuscript. JJK was involved in substantial revisions of the manuscript. TK, ML, SJ, AMc, AR, JS, AG, CC, BT reviewed the manuscript, SHK Is the guarantor for the project.

All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis

Data sharing: all requests for data sharing to Professor SH Khoo (khoo@liv.ac.uk)

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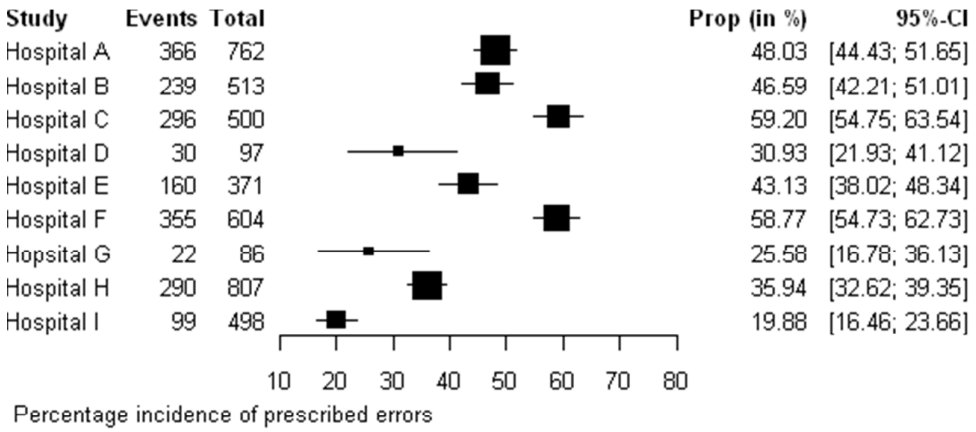

Figure 1a. Forest plot showing prescribing error rates in nine hospitals across North West England.

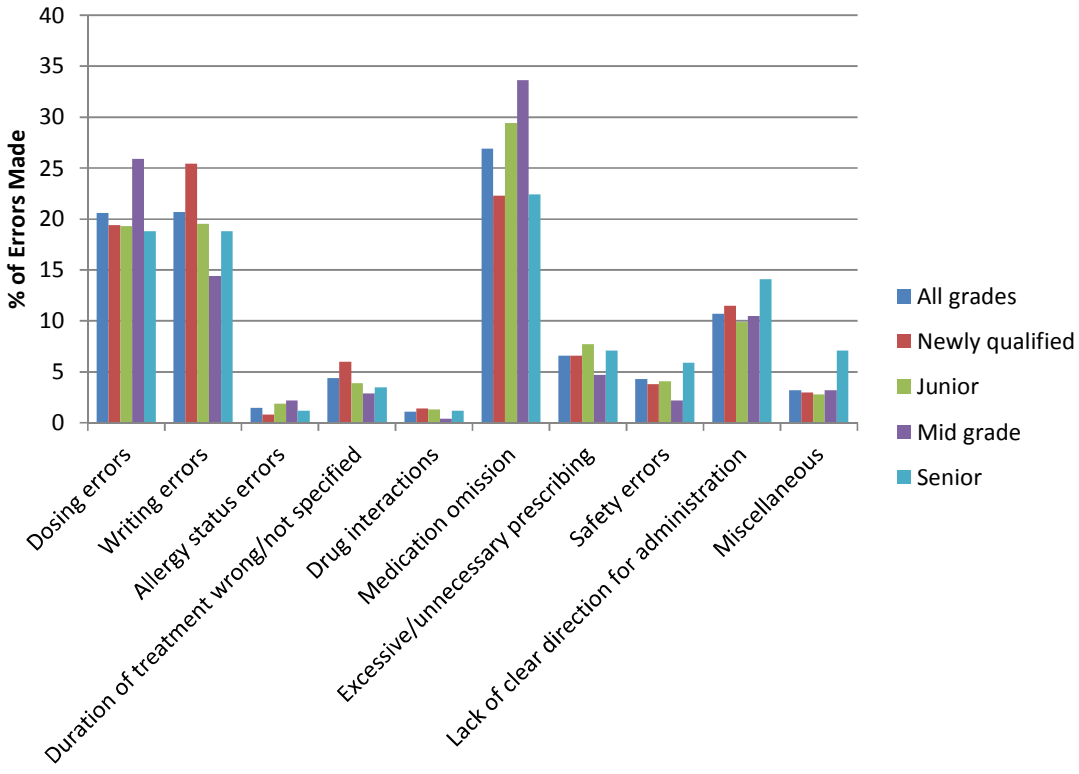

Figure 2. Categories of prescribing errors made by different grades of prescriber

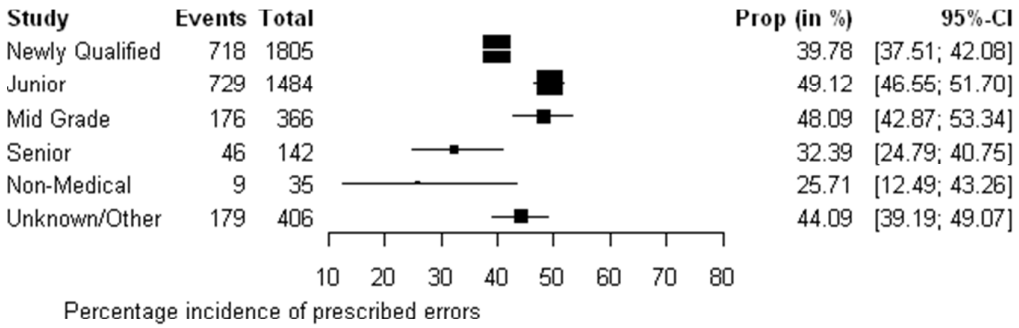

Figure 3~~1b~~. Forest plot showing prescribing error rates made by different prescriber grades

Table 1. Types of hospitals contributing prescription data

Teaching Hospitals	District Hospitals	Specialist Hospitals (Women, Paediatrics, Mental Health)
Hospital A	Hospital B	Hospital D
Hospital C	Hospital E	Hospital G
Hospital H	Hospital F	Hospital I

Table ~~1~~2. Application of error categories and severity ratings for the Mersey Deanery Prescribing Audit

Modified EQUIP Error Category	Original EQUIP Error Category	Includes/Excludes	Severity (EQUIP)	Severity Modification
1. Dosing Errors	Underdose		**Minor** if unable/unlikely to carry out (units); **Significant** if dose too low to treat the condition; **Serious** if patient in acute distress; **Potentially Lethal** if medication life saving	
	Overdose	Excludes overdoses caused by duplication eg. Paracetamol with co-codamol	**Minor** if unable/unlikely to carry out (units); **Significant** - low TI, ½-4 times; **Serious**- Low TI, 4-10 times; errors in units if chance dose could be given; **Potentially Lethal** if v.low TI and dose 10 times normal dose, results in serum levels of drug in severe toxicity range, or has high potential to cause cardiopulmonary arrest	**Minor** if effect of dosing expected to be minimal
	Dose/rate mismatch		-	Judgement used based on Equip severity categories
2. Writing Errors	Strength/dose missing	Includes dose units missing	**Minor**	
	Product/formulation not specified		-	**Minor**
	Incorrect formulation		-	**Minor** unless formulation likely to have implication on treatment eg. Insulin, co-careldopa, in which case **significant/serious** based on potential consequence
	No signature		-	**Significant** (governance issue)
	Start date incorrect/missing		-	**Minor**
	CD requirements incorrect/missing		-	**Minor**
3. Allergy status missing/significant allergy	Significant allergy	Includes allergy status not completed, or where a drug has been prescribed despite an allergy to that drug/class	-	**Significant** allergy status/specific allergy missed off prescription; **Serious** if patient prescribed agent allergic to; **Potentially Lethal** if patient prescribed drug which previously had severe

				reaction to eg. oedema
4. Duration of treatment wrong/not specified	Continuation for longer than needed	Includes no stop/review date for antibiotics, steroids etc	-	**Minor** if continuation of the medicine or the duration represents little potential for harm; **Significant** if continued >3 days longer than needed for medication such as: antibiotics, oral steroids, LMWH, potassium; **Serious** if ongoing treatment could cause serious harm
	Premature discontinuation	Includes drugs stopped without appropriate reducing course	-	**Minor** if discontinuation is unlikey to have a significant clinical impact; **Significant** if duration of treatment insufficient to treat condition eg. Antibiotics, or if no reducing course eg. Oral steroids
5. Drug Interactions	Drug interaction	Excludes 2 items prescribed from same class e.g omeprazole with lansporazole (Duplication)	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-drug interaction	**Significant** if manufacturer advises the combination is contraindicated, should be avoided, or advises caution; **Serious** if adverse events highly probable
	Drug interaction not taken into account	As above: unable to differentiate drug interaction and drug interaction not taken into account from available data		
6. Omission of medication	Omission on admission		**Significant** (regular medication)	-
	Omission on discharge		**Significant**	-
	Drug not prescribed but indicated		-	**Minor** if medication is unlikely to significantly impact patient care; **Significant** if medication would have significant impact on clinical course **Serious** if medication would alleviate a serious condition /patient is in acute distress; **Potentially lethal** if medication is potentially life saving
7. Excessive/ unnecessary	Duplication	Includes a second agent prescribed which contains an ingredient already being taken; 2 drugs prescribed from the same class/with same clinical	**Minor** if duplicate therapy prescribed without potential for increased adverse events	**Significant, Serious, Potentiallylethal:** As for overdose when duplicated items co-administered (3)

prescribing		effect eg. Lansoprazole + omeprazole		
	Unintentional prescription of drug	Drug prescribed was not that desired. Includes prescription of a discontinued drug, excluding discontinuation due to ADR , or course is too long	-	Judgement used based on Equip severity categories
8. Clinical Safety Errors	No maximum dose	Excludes prescriptions with no frequency (administration times missing/incorrect)	**Minor**- order lacked specific drug, dose, strength, frequency or route information	**Significant** if no maximum dose stated for opioids
	Clinical contraindication	Contraindication according to summary of product characteristics	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-disease interaction	**Significant** if administration unlikely to have serious clinical consequences in the given situation
	Continuation after ADR		-	Judgement used based on Equip severity categories
	No dosage alteration after levels out of range		-	Judgement used based on Equip severity categories
9. Lack of clear directions for administration	Administration times incorrect/missing	No frequency/times of dosing incorrect eg. In relation to food, morning vs night.	**Minor**	**Significant** if administration time would be expected to affect treatment eg. Exenatide with meals, hypnotics at night
	Incorrect route		**Minor** if unlikely to be carried out/little chance of toxicity/therapeutic failure; **Significant** if wrong route to treat condition; **Serious** if potential for toxicity	-
	IV instructions incorrect/missing		-	Judgement used based on Equip severity categories
	Route missing		**Minor**- order lacked specific drug, dose, strength, frequency or route information	-
	Daily dose divided incorrectly	Number of dosing intervals incorrect. Excludes under/overdose	-	**Minor** if dosing intervals are not standard, but are unlikely to significantly affect treatment; **Significant** if dosing intervals are inappropriate to treat the condition;

				Serious if medication has narrow TI and dosing intervals may affect toxicity/efficacy eg. Parenteral aminoglycosides
10. Miscellaneous	No indication	Includes PRN medications, where lack of indication on prescription could prevent administration. Excludes failure to write an indication when prescribing antibiotics	-	**Minor** if indication not written up for PRN medication; **Significant** if indication not written up for formulations which are licensed for specific conditions.
	Miscellaneous	Illegible drug details, non-standard abbreviations, patient details incorrect/missing, warfarin fixed dose prescribed.	-	Judgement used based on Equip severity categories

Abbreviations: TI- therapeutic index, CD- controlled drug, ADR- adverse drug reaction, PRN- when required

Table 32. Summary data showing prevalence and severity of errors observed

		Total Prescriptions	One or more error reported		Error Severity				Total errors
			No (%)	Yes (%)	Minor (%)	Significant (%)	Serious (%)	Potentially Lethal (%)	
All		**4238**	**2381 (56.2)**	**1857 (43.8)**	**1264 (42.0)**	**1629 (54.1)**	**109 (3.6)**	**9 (0.3)**	**3011**
Prescriber Grade	Newly Qualified	1805	1087 (60.2)	718 (39.8)	519 (48.8)	507 (47.7)	35 (3.3)	3 (0.3)	1064
	Junior	1484	755 (50.9)	729 (49.1)	496 (39.2)	725 (57.4)	41 (3.2)	2 (0.2)	1264
	Mid Grade	366	190 (51.9)	176 (48.1)	93 (33.6)	166 (59.9)	15 (5.4)	3 (1.1)	277
	Senior	142	96 (67.6)	46 (32.4)	36 (42.4)	43 (50.6)	6 (7.1)	0 (0)	85
	Non-medical	35	26 (74.3)	9 (25.7)	8 (57.1)	5 (35.7)	1 (7.1)	0 (0)	14
	unknown/other	406	227 (55.9)	179 (44.1)	112 (36.5)	183 (59.6)	11 (3.6)	1 (0.3)	307
Training	Liverpool	1290	787 (61.0)	503 (39.0)	270 (35.4)	456 (59.8)	36 (4.7)	1 (0.1)	763
	Non-Liverpool	922	478 (51.8)	444 (48.2)	342 (43.8)	420 (53.8)	19 (2.4)	0 (0)	781
	Unknown	2026	1118 (55.2)	908 (44.8)	652 (44.4)	753 (51.3)	54 (3.7)	8 (0.5)	1467
Admission/ Discharge	Discharge	2467	1615 (65.5)	852 (34.5)	685 (52.5)	584 (44.8)	32 (2.5)	4 (0.3)	1305
	Admission	1744	756 (43.4)	988 (56.7)	576 (34.2)	1030 (61.1)	75 (4.4)	5 (0.3)	1686
	Unknown	27	12 (44.44)	15 (55.55)	3 (15)	15 (75)	2 (10)	0 (0)	20
Ward Area	Medicine	2059	1083 (52.6)	976 (47.4)	634 (39.0)	921 (56.7)	64 (3.9)	6 (0.37)	1625

	Surgery	1395	836 (59.9)	559 (40.1)	448 (50.1)	417 (46.6)	27 (3.0)	2 (0.2)	894
	Mental health	96	66 (68.8)	30 (31.3)	24 (60)	16 (40)	0 (0)	0 (0)	40
	Accident & Emergency	8	1 (12.5)	7 (87.5)	1 (9.1)	10 90.9	0 (0)	0 (0)	11
	Critical care	17	14 (82.4)	3 (17.7)	1 (25.0)	3 (75.0)	0 (0)	0 (0)	4
	Unknown	663	383 (57.8)	280 (42.2)	156 (35.7)	262 (60.0)	18 (4.1)	1 (0.2)	437
Prescription contains[#]	Antibiotic	724	301 (41.6)	423 (58.4) (**Antibiotic**: 130 (18.0))	57 (29.8)	118 (61.8)	16 (8.4)	0 (0)	191
	Insulin	129	42 (32.6)	87 (67.4) **Insulin**: 20 (15.5)	12 (37.5)	19 (59.4)	1 (3.1)	0 (0)	32
	Warfarin	196	71 (36.2)	125 (63.8) **Warfarin**: 18 (9.2)	6 (23.1)	16 (61.5)	4 (15.4)	0 (0)	26
	Oxygen	36	7 (19.4)	29 (80.6) **Oxygen**: 2 (5.6)	1 (14.3)	5 (71.4)	1 (14.3)	0 (0)	7

* Relates to errors per prescriptions written, not errors per number of items prescribed

Error severities, total errors and error rates relate to errors associated with Antibiotics/Insulin/Warfarin/Oxygen only

Table 4. Summary of the Errors Observed which were Considered to be Potentially Lethal

Error Description	Category	Prescriber Grade	Ward Area	Admission/ Discharge
Gliclazide 400mg prescribed when 40mg needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Digoxin 625micrograms prescribed when 62.5micrograms needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Oxycodone 500mg prescribed: overdose	1- Dosing Errors	Mid Grade	Surgery	Admission
Methotrexate prescribed daily, not weekly	1- Dosing Errors	Junior	Medicine	Admission
Doxazocin prescribed; had been stopped by general practitioner due to angioedema	3. Allergy status missing/ significant allergy	Junior	Medicine	Admission
Phenytoin dose of 300mg daily incorrectly prescribed as 800mg	1- Dosing Errors	Newly Qualified	Medicine	Discharge
Midazolam IV for sedation: overdose	1- Dosing Errors	Mid Grade	Unknown	Admission
Amiodarone loading dose of 200mg three times daily continued as a regular dose	1- Dosing Errors	Other	Surgery	Discharge
Enoxaparin prescribed 1mg/kg once daily instead of 1mg/kg twice daily for a patient with acute coronary syndrome	1- Dosing Errors	Mid Grade	Medicine	Admission

Table 5. Univariate statistics showing the significance of explanatory variables in predicting error rates in prescriptions.

Variable	n	≥1 Error	No Error	Difference (95%CI)	p-value
		n (%)	n (%)		
Prescriber Grade (n=3850)		1689	2161		
Newly qualified	1803	716 (42%)	1087 (50%)	-8% (-11.2% to -4.8%)	<0.001
Junior	1482	727 (43%)	755 (35%)	8% (4.9% to 11.1%)	
Mid-grade	366	176 (10%)	190 (8.8%)	1.2% (-0.7% to 3.1%)	
Senior	142	46 (2.7%)	96 (4.4%)	-1.7% (-2.8% to -0.4%)	
Non-medical	35	9 (0.5%)	26 (1.2%)	-0.7% (-1.3% to -0.1%)	
Other	22	15 (0.9%)	7 (0.3%)	0.56% (0.1% to 1.1%)	
Discharge/Admission (n=3065)		1135	1930		
Discharge	2467	853 (75%)	1614 (84%)	-9% (-12.0% to -6.0%)	<0.001
Admission	598	282 (25%)	316 (16%)		
Liverpool trained (n=1325)		518	807		
Liverpool	35	14 (2.7%)	21 (2.6%)	0.1% (-1.7% to 1.9%)	0.911
Non-Liverpool	1290	504 (97%)	786 (97%)		
Hospital (n=4238)		1857	2381		
Hospital A	762	366 (20%)	396 (17%)	3% (0.6% to 5.4%)	<0.001
Hospital B	513	239 (12%)	274 (12%)	0% (-2.0% to 2.0%)	
Hospital C	500	296 (16%)	204 (8.6%)	7.4% (5.4% to 9.4%)	
Hospital D	97	30 (1.6%)	67 (2.8%)	-1.2% (-2.1% to -0.3%)	
Hospital E	371	160 (8.6%)	211 (8.9%)	-0.3% (-2.0% to 1.4%)	
Hospital F	604	355 (19%)	249 (10%)	9% (6.8% to 11.2%)	
Hospital G	86	22 (1.2%)	64 (2.7%)	-1.5% (-2.3% to -0.7%)	
Hospital H	807	290 (16%)	517 (22%)	-6% (-8.4% to -3.6%)	
Hospital I	498	99 (5.3%)	399 (17%)	-11.7% (-13.5% to -9.9%)	
Ward Area (n=3575)		1577	1998		
Medical	2059	977 (62%)	1082 (54%)	8% (4.8% to 11.2%)	<0.001
Surgical	1395	560 (36%)	835 (42%)	-6% (-9.2% to -2.8%)	
Accident & Emergency	8	7 (0.4%)	1 (0.1%)	0.3% (-0.04% to 0.6%)	
Mental health	96	30 (1.9%)	66 (3.3%)	-1.4% (-2.4% to -0.4%)	
Critical care	17	3 (0.2%)	14 (0.7%)	-0.5% (-0.9% to -0.1%)	
Number of Medicines on Prescription (n=3386) Median (IQR)		8; (4,11) (n=1435)	4; (2,7) (n=1951)	-4 (-4.5, -3.5)	<0.001

n= number of prescriptions

Table 6. Multivariate logistic regression analysis for predicting error rates in prescriptions.

Variable	Odds ratio (95%CI)	p-value
Hospital		
Hospital H	1	
Hospital A	Not estimable*	
Hospital B	1.11 (0.78 to 1.58)	0.57
Hospital C	2.38 (1.63 to 3.46)	<0.001
Hospital D	0.64 (0.13 to 3.06)	0.57
Hospital E	1.39 (0.96 to 2.01)	0.08
Hospital F	3.53 (2.63 to 4.73)	<0.001
Hospital G	1.80 (1.03 to 3.12)	0.04
Hospital I	1.11 (0.73 to 1.70)	0.62
Prescriber Grade		
Newly qualified	1	
Junior	1.06 (0.85 to 1.32)	0.61
Mid-grade	0.96 (0.64 to 1.44)	0.83
Senior	0.97 (0.58 to 1.63)	0.92
Non-medical	0.59 (0.21 to 1.64)	0.31
Other	1.50 (0.53 to 4.23)	0.44
Discharge/Admission	1.16 (0.70 to 1.92)	0.58
Number of prescribed items	1.14 (1.12 to 1.17)	<0.001

Analysis contains only 2127 records (50.2%) where complete data was provided for all variables

* Trust provided no data on number of prescription items

Cross Sectional Study of Prescribing Errors in Patients Admitted to Nine Hospitals Across North West England

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Article Summary

1. Article Focus

- Some studies have reported lower error rates with more senior prescriber grades, and insufficient undergraduate prescriber training as a potential risk for prescribing errors
- Prescriptions frequently contain multiple medications, but data about errors on complete prescriptions (all prescribed items on an inpatient chart or discharge prescription), which give a better estimate of numbers of patients at risk of harm, are lacking
- We aimed to determine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge and type of medication prescribed

2. Key Messages

- We observed an error rate of 10.9% per prescribed item, with only 56.2% of 4238 complete prescriptions remaining error free.
- In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription.
- We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues.

3. Strengths and Limitations

- This was a large study across nine diverse hospital settings
- We determined the rate of errors on complete prescriptions as well as for ~~rather than~~ individually prescribed items, giving a better estimate of the numbers of patients affected by errors.
- We did not evaluate the impact of electronic prescribing on the prevalence and type of prescribing errors, however up to a quarter of the errors observed could potentially have been avoided through use of electronic prescribing and medicines administration systems

Abstract

Objective To evaluate the prevalence, type and severity of prescribing errors observed between grades of prescriber, ward area, admission or discharge and type of medication prescribed~~prevalence, type and severity of prescribing errors made by different categories of prescriber, and the prevalence, type and severity of prescribing errors occurring at admission compared with on discharge prescriptions.~~

Design Ward-based clinical pharmacists prospectively documented prescribing errors at the point of clinically checking admission or discharge prescriptions. Error categories and severities were assigned at the point of data collection, and verified independently by the study team

Setting Prospective study of nine diverse National Health Service (NHS) hospitals in North West England, including teaching hospitals, district hospitals and specialist services for paediatrics, women and mental health.

Results Of 4238 prescriptions evaluated, one or more error was observed in 1857 (43.8%) prescriptions, with a total of 3011 errors observed. Of these, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and 9 (0.30%) were potentially life-threatening. The majority of errors considered to be potentially lethal (n=9) were dosing errors (n=8), mostly relating to overdose (n=7). The rate of error was not significantly different between newly qualified doctors compared with junior, middle grade or senior doctors. Multivariable analyses revealed the strongest predictor of error was the number of items on a prescription (risk of error increased 14% for each additional item). We observed a high rate of error from medication omission, particularly amongst patients admitted acutely into hospital. Electronic prescribing systems could potentially have prevented up to a quarter of (but not all) errors.

Conclusions In contrast to other studies, prescriber experience did not impact on overall error rate (although there were qualitative differences in error category). Given that multiple drug therapies are now the norm for many medical conditions, health systems should introduce and retain safeguards which detect and prevent error, in addition to continuing training and education, and migration to electronic prescribing systems.

Introduction

Prescribing errors are ~~is~~ common, with systematic reviews suggesting that as many as 50% of hospital admissions and 7% of medication orders are affected.[1] In recent studies, prescribing errors have been found to affect approximately 9-15% of medication orders for hospital inpatients in the United Kingdom (UK).[2 3] Over one third of 651 patients were found to have a prescribing error occurring at hospital admission in the United States (US).[4] Prescribing errors are also prevalent in primary care, affecting 37% of 9385 prescriptions in the US,[5] and one in eight patients (one in 20 prescription items) in the UK.[6] ~~In a UK study of 3695 inpatient episodes, 15% of patients experienced an adverse drug reaction (ADR), more than half of which were considered definitely or possibly avoidable. 59% of ADRs were linked to drug interactions, and ADRs were found to increase length of hospital stay in 27% of episodes.[7]~~ A study in the Netherlands evaluating medication omission errors in elderly patients admitted to hospital reported adverse consequences in 21% of 100 patients.[8]

Human error in healthcare may be considered in the context of individuals or health systems.[9-11] While personal factors such as forgetfulness, inattention, poor motivation, carelessness, negligence, and recklessness are important, a health systems approach more comprehensively addresses recurrent errors and organisation factors and processes which may give rise to that error. The person, the team, the task, the workplace and the institution as a whole are considered, [9] which identify weaknesses in the system's defences.[9] For example, higher hospital mortality at weekends may be associated with lower numbers of senior staff available outside of the normal working week.[12 13]

Data on factors which may contribute to ~~causes of~~ prescribing errors, for example differences between grades of prescriber, ward area, admission or discharge and type of medication prescribed are sparse.[3 14 15] Existing data suggest that newly qualified and junior doctors are twice as likely to make prescribing errors than senior doctors, taking into account the larger volume of prescriptions written by more junior prescriber grades.[3] Provision of sufficient undergraduate training to allow medical students to become safe prescribers when they begin work as newly qualified doctors is widely recognised as an important factor in reducing prescribing errors.[14 16-18] Teaching in UK medical schools has changed considerably over the last decade, with the General Medical Council stipulating that medical students must be adequately prepared to prescribe drugs and manage risk at the point of graduation.[19 20]

Whilst previous studies have evaluated error for individual medications, few studies have systematically evaluated complete prescriptions (all items included on a single prescription chart or discharge prescription at the time of clinical pharmacist check) to evaluate factors associated with prescribing error.[1-3] This is important as it gives a more accurate estimate of the numbers of patients who are potentially put at risk of harm by prescribing errors. We undertook a prospective survey of prescribing errors in nine diverse National Health Service (NHS) hospitals in the North West of England, aiming to examine the ~~-~~ differences in prescribing error rates between grades of prescriber, ward area, admission or discharge, hospitals and the type and number of medication prescribed. In order to further evaluate the role of undergraduate training, we also tested for a relationship between occurrence of error and medical school training of prescribers. Univariate analysis and multivariate logistic regression was used to evaluate factors associated with prescribing errors. ~~prevalence, type and severity of errors made by different categories of prescriber, and also the prevalence, type and severity of prescribing errors at admission, discharge and in different ward areas.~~

~~Specifically, we recorded only errors concerned with issuing of the prescription, excluding errors in clinical decision making, or 'downstream' errors in executing the prescription.~~

Methods

Setting

A total of nine NHS hospitals from the Merseyside and Cheshire region took part in the audit. These comprised large teaching hospitals, general hospitals, specialist centres for paediatrics, women's health and mental health (Table 1). One hospital was using complete electronic prescribing systems (inpatient prescribing, medication ordering, discharge prescriptions) on some wards at the time of the audit. Eight of the hospitals were using paper prescription charts for inpatients and either handwritten or transcribed electronically generated discharge prescriptions. In this setting, ward-based clinical pharmacists check inpatient prescriptions at or soon after patient admission, when medicines reconciliation is undertaken. Inpatient prescription charts are then checked at least daily by the pharmacist. Discharge prescriptions are checked and authorised by a clinical pharmacist prior to supply of medication. Pharmacists may amend or clarify some aspects of prescribing, or discuss with the clinical team any recommendations or safety issues at these points of care. Clinical pharmacists may also participate in ward rounds and multidisciplinary team meetings, where prescribing may be discussed with clinicians, clarified or amended.

Data Collection

~~A total of nine NHS hospitals from the Merseyside and Cheshire region took part in the audit. These comprised large teaching hospitals, general hospitals, specialist centres for paediatrics, women's health and mental health.~~ As this was an audit ~~survey~~ of unlinked anonymised prescriptions, Ethics approval was not required in accordance with local guidance. We aimed to capture data from all seven hospital trusts in the region. Two additional hospitals adjacent to and linked with healthcare provision in the Merseyside region were also audited. The number of prescriptions audited was empirically determined in order to generate a sample size equivalent to a large study recently undertaken in the UK.[3] In order to audit practice across the region, each hospital was asked to audit a minimum of 400 prescriptions.

We adopted the following definition of prescribing errors for the study, which excludes adherence to local prescribing policy and guidelines: "A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice".[21] A standard questionnaire collected data on error category and severity (based on EQUIP error classifications). The EQUIP study was a large prospective survey of prescribing errors affecting hospital inpatients in the UK,[3] and the error classifications were therefore considered relevant to our setting. Nominated ward-based clinical pharmacists prospectively documented prescribing errors at the point of checking inpatient~~admission~~ or discharge prescriptions, during normal pharmacy working hours, therefore each audit form was a point prevalence of prescribing errors at the time of pharmacist clinical check. Acute admission was defined as the first 24 hours in hospital. For all prescription sheets generated in acute admission settings, a separate audit form was completed (to allow for emergency prescribing in the absence of a full drug history without this being recorded as an error) and we sought to record only unintended medication omissions (e.g. following medicines reconciliation with general practices or primary healthcare databases). Hospitals were advised to complete the study on different days of the week~~ver alternate days~~ throughout the period of the audit, in order to capture an even spread of days. ~~f~~For example data collection would occur weekly, on Monday in week one, Tuesday in week two, Wednesday in week three, in order to minimise double auditing of the same patient on admission to hospital and subsequent

admission to a ward. Therefore, if patients were audited twice, an interval of at least one week would separate each audit form, unless their acute admission/inpatient /discharge prescription were audited on the same day. If items on prescriptions had been previously screened, they would be counted again in any subsequent auditing , though there would be a one week interval since previous auditing, or the patient would be a different stage of hospital admission. All types of inpatient medication order were audited, including IV fluids, when required and once only medication.

Prescriber Category

Pharmacists were required to indicate the category of prescribers on data collection forms. For this analysis, prescribers were categorised as follows: newly qualified (fFoundation yYear 1, hHouse officers), jJunior (fFoundation yYear 2, specialist or 'core' training years 1 & 2), mid grade (specialist registrars, training fFellows), senior (cConsultant), non-medical (nurse or pharmacist prescribers), other (for example locum doctors for whom grade was unclear ~~or not recorded~~) and unknown (no information ~~not~~ concerning prescriber recorded).

Grading of prescribing errors

We modified EQUIP study criteria[3] for error categorisation and severity classification by adding or clarifying severity criteria for all error categories, and by grouping errors into ten distinct areas according to ~~origin~~ stage of the prescribing process (see below and Table 2~~1~~). 'Exclusion' and 'inclusion' of errors into EQUIP study error types were defined, in order to differentiate categories with potential overlap. Severity ratings were further defined and assigned to each error category based on modified EQUIP study criteria and~~,~~ taking into account the perceptions of the original pharmacist gradings~~, and reference to the licensing information of the relevant medication~~.~~.~~ Severity ratings related to the potential severity had the error been allowed to progress through to the patient, as the majority of errors were corrected prior to the point of administration. In order to limit misclassification error, the original 29 EQUIP categories were batched into 10 different types of error groups as follows: (1) Dosing errors, (2) Writing errors, (3) Allergy status errors, (4) Duration of treatment wrong/not specified, (5) Drug interactions, (6) Omission of medication, (7) Excessive/unnecessary prescribing, (8) Safety errors, (9) Lack of clear directions for administration, (10) a new error category (Miscellaneous) was added (Table 2~~1~~). The modification and definition of error categories and severities was undertaken by two members of the study team (KS, SK) and agreed by a third (TK).

Despite using a standard set of definitions, we noted discrepancies across various hospitals in both error categorisation and severity rating. In particular there was a tendency to over-report~~call~~ errors and to overestimate their potential severity. This was confirmed by a *post-hoc* inter-rater agreement analysis. A set of six sample prescriptions was generated. A list of 14 ~~standard~~ sample errors was decided by the study team, including study error type and severity, according to the criteria in Table 2~~1~~ utilised for analysis of the main study. The errors selected occurred frequently in the main study, and covered a broad range of error categories and severities. Six pharmacists from each participating hospital were asked to each screen the six prescription scenarios containing the 14 errors and to record any observed errors, allocating error types and severities. The exact agreement percentages between category classification, severity classification and both combined were computed to measure the absolute concordances between pharmacist scores against the gold standard assessment. ~~For all prescriptions, approximately 75% of error categories were correctly identified by pharmacists when compared to the standards. Only 47% of~~

~~severity ratings were concordant with the standards, and 40% of pharmacists rated both error category and severity in concordance with the standards.~~

~~Therefore, i~~In order to limit inter-observer bias, all grading and severity of errors identified in the main study were independently reassessed by two members of the study team (KS and SK), with discordant assessments collectively discussed with a third (TK) in order to agree a final categorisation for error type and severity. For severity ratings, the summary of product characteristics for relevant medication was consulted, in order to determine potential implications of different degrees of overdose, underdose, of drug interactions, and also to confirm clinical contra-indications. ~~A total of 143 errors were not considered true errors of the process of prescribing and were excluded. The error category was re-graded for 434 errors, and severity was re-graded for 724 errors, which was predominantly a down-grading.~~

Statistical Analyses

Data were analysed at the prescription level using complete case data. The prevalence and severity of errors observed were tabulated using percentage frequencies. A ~~forest~~ Forest plot was produced to present the error prevalence~~incidence~~ rate and 95% confidence interval (95% CI) for each hospital and grade of prescriber. For the formal statistical analysis, when there was more than one error on a prescription, only the most severe error was included. This approach was used to ensure that the errors included in the analysis were independent~~For the formal statistical analysis, when there was more than one error on a prescription, only the most severe error was included~~. In this study, we assessed hospital, prescriber grade (newly qualified, junior, mid-grade, senior, non-medical, other), ward area (medical, surgical, A&E, mental health, critical care), number of prescribed medicines, an indicator to denote whether the prescription was prescribed on admission or on discharge and an indicator to denote whether the prescriber was Liverpool trained or not as potential risk factors. Univariate statistical analyses were performed using a chi-squared test except for continuous data, which were analysed using the Mann-Whitney U test. A multivariate logistic regression model for a prescription error was fitted to the data. Results are given in terms of an odds ratio (OR) and associated 95% CI. All risk factors that were statistically significant ($p<0.1$) in the univariate analysis were considered for inclusion in the multivariate model with the exception of ward area as a number of hospitals only reported a single specialty type.

All statistical analysis was carried out using the statistical software package SPSS (version 20) using a two-sided significance level of 0.05 (5%) throughout.

Results

Error Classification

During the *post-hoc* inter-rater agreement analysis, ~~For all prescriptions~~, approximately 75% of error categories were correctly identified by pharmacists when compared to the standards. Only 47% of severity ratings were concordant with the standards, and 40% of pharmacists rated both error category and severity in concordance with the standards.

~~,~~ RA~~a~~e-assessment of errors by the study team resulted in exclusion of a total of 143 errors which were not considered true errors of the process of prescribing ~~and were excluded~~. The error category was re-graded for 434 errors, and severity was re-graded for 724 errors, which was predominantly a down-grading.

Descriptive data and severity of errors

A total of 4238 prescriptions were evaluated; of these, 1857 (43.8%) prescriptions contained at least one error (Table 3~~2~~). The overall prevalence~~incidence~~ of prescribing errors (number of prescriptions with one or more error/prescriptions evaluated) ranged from 20% to 60% across the nine hospitals (Figure 1~~a~~). The rate of errors per prescribed item was 10.9%.

A total of 3011 individual errors were observed within the 1857 prescriptions containing an error. Of these 3011 errors, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and nine (0.30%) were potentially life-threatening (Table 3~~2~~). Details of all potentially life-threatening errors are listed in Table 3 and mainly comprised dosing errors (n=8), particularly overdose (n=7), with one incidence of under dose. A further error considered to be potentially lethal related to prescription of a medicine to which the patient had previously had a serious allergic reaction.

The proportion of errors categorised with severity as significant or higher by prescriber grade were as follows: all prescribers 58.0%, newly qualified 51.2%, junior 60.8%, mid grade 66.4%, senior 57.6% (χ^2_{trend} p<0.001 for univariate analysis, although this association disappeared when corrected for other potential confounders)(Table 3~~2~~).
Fewer errors were observed on discharge prescriptions than on prescriptions written on admission. More errors were observed in prescriptions containing antibiotics, insulin, warfarin and oxygen, although this does not take into account the number of items on each prescription. Whether doctors were Liverpool trained or not did not affect the number of errors observed (Table 3~~2~~).

Differences in error prevalence and error types were observed in individual participating hospitals. The lowest rates of errors were reported for the paediatrics specialty, with 0.07 errors observed per prescribed item, and 0.26 errors observed per prescription. However, in multivariate analysis, there was no significant reduction in error risk and it is likely that the effect could be due to lower number of items per prescription (mean 3.5, vs pooled data: 6.3). The most common error types were dosing errors (30%) and medication omission (23.1%).
Significantly lower risk of errors was observed in the hospital providing specialist services for women (p=0.04, Table 6) in multivariate analysis. One of the lowest error rates per prescription was observed (0.28), although the error rate per prescribed item (0.11) was

equal to that of the pooled data. The most common error type observed was excessive/unnecessary prescribing (50%). No errors of medication omission were observed. This hospital also had a low number of items per prescription (2.4), and was using electronic prescribing systems on some wards.

Error types

The most frequent error types for all prescribers were medication omission, accounting for 26.9%, writing errors accounting for (20.7%) and dosing errors accounting for (20.6%) of all errors recorded. There was little difference in the variability of error types across different prescriber grades (Figure 2).

Risk factor analysis

Results of the univariate analysis are shown in Table 5~~4~~. Missing data limited inclusion of all reported prescriptions in risk factor analysis, notably as one acute hospital failed to return data on number of items on each prescription. All factors considered appeared to show a significant difference except for medical school training of doctors, which made no significant difference (p=0.91) to whether an error occurred on the prescription. Multivariate risk factor analysis showed that the likelihood of an error increased for every additional item included on the prescription (OR 1.14, 95% C 1.12, 1.17, p<0.001) (Table 5~~4~~). Therefore, for each additional item on the prescription, the risk of an error occurring increased by about 14%. There was also a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16 (95% CI 0.70, 1.92, p=0.58), although this difference did not reach statistical significance (Table 6~~5~~). No significant differences were found in error rates between different prescriber grades, when compared to newly qualified doctors~~.~~ (Figure 2~~1b~~, Figure 3~~2~~) in multivariate analyses.

Discussion

In this large study, only 56.2% of 4238 prescriptions written had no reported errors. Of the errors recorded, 41.9% were minor, 54.1% significant, 3.6% serious and 0.3% potentially life threatening. It is important to note that severity ratings relate to the potential severity had the error been allowed to progress through to the patient - in fact the majority of errors were corrected prior to the point of administration. In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing error increasing by 14% for every additional medication item prescribed. Where data were available, prescriptions contained an average of 6.3 medication items, although this varied from 2.4 – 7.5 items according to medical specialty surveyed. Uncorrected analyses suggested that errors were frequent in prescriptions containing insulin (15.5%), antibiotics (18%), warfarin (9.2%) and oxygen (5.6%), although these patients were very likely to have been receiving multiple medications. Error rates were highest amongst specialties which prescribed a broad range of medications (e.g. acute medicine, compared to elective surgery), and also differed between different hospital Trusts, with hospitals specialising in paediatrics ~~(Hospital I)~~, maternal health ~~(Hospital G)~~ and mental health ~~(Hospital D)~~ exhibiting the lowest error rates. However, when corrected for number of

medications, these differences did not remain significant, with the exception of maternal health.

The most frequent error encountered was unintended medication omission following acute hospital admission (0.97 errors/prescription written, versus 0.53 for discharge medications). When adjusted in multivariable analyses (Table 65) there was no statistically significant difference in error rates between admission and discharge. We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues. Although numbers were relatively small, we observed no difference in error rate amongst newly qualified doctors by undergraduate training, and doctors trained in Liverpool were neither more nor less likely to commit medication errors. The categories and severity of errors made by different prescriber grades were broadly similar (Table 32, Figure 2), however some differences were observed. For example, writing errors were more frequently observed with newly qualified doctors, medication omission was more frequently observed with junior and mid grade doctors, and dosing errors were more frequently observed with mid grade doctors.

These results are consistent with previously published studies. Both the EQUIP and PRACtICe Studies[3 6] reported error rates of approximately 1 in 10 medications prescribed (we observed a rate of 10.9%). Given the high number of medications prescribed (mean of 6.3 items/prescription) nearly half of all prescriptions contained at least one error.
-A systematic review found prescribing errors to be more common in adults than in children.[1] A study in Spain comparing paediatric wards with obstetrics found that paediatric patients had a fourfold higher risk of serious errors than the maternity population (2.3% vs 14.3%), which were mainly related to drug dosing., which is in keeping with our data.[22] This is in keeping with our data, as we observed a low error rate for the paediatrics specialty, although this was likely due to a low number of prescribed items. Dosing errors were the most common error type. Another study reported that prescribing errors were more common in primary care amongst men compared to women.[6] We observed a significantly lower risk for errors in specialist services for women.

In the EQUIP study, multivariate analysis showed that all grades of doctors were more likely to write a prescription containing an error than consultants.[3] A retrospective study which evaluated errors on discharge prescriptions found no significant difference in error rates between prescriber grades, although no senior (consultant) level prescribers were included.[15] In primary care, the grade of general practitioner was not associated with prescribing errors.[6] We observed no significant difference in prescribing error rates between prescriber grades, when compared to newly qualified prescribers. EQUIP also reported that medication orders issued at acute admission were 70% more likely to be associated with a prescribing error.[3] Another study found lower error rates on discharge prescription items than was observed with general inpatient prescribing, due to a lower rate of medication omission, however these factors were not corrected for the number of items on each prescription.[2] We observed a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16, although this did not reach significance in multivariate analysis.

Our study was limited by missing data (one acute hospital failed to return data on number of items on each prescription), and although pharmacists had received some basic training in completing the evaluations, post-hoc analyses suggested significant variability between pharmacists' classification of errors, and especially in assignment of severity classification.

Two of us independently revised each prescribing error and noted a tendency to over-estimate~~call~~ the severity of errors, and (in keeping with EQUIP criteria) included in our evaluations an assessment of whether or not a wrong dose was likely to have been actually administered based on tablet burden. We also refined EQUIP criteria to assign severity ratings to error categories where these had previously not been provided. Finally, by grouping errors into categories according to their origin~~and cause~~, we sought to reduce misclassification as far as possible. Since our data collection forms did not allow us to evaluate errors which had been missed, it is possible that our observed error rates may represent an under-estimate of the true burden of prescribing error.

Medication omission was the most prevalent error, representing 26.9% of all errors observed, which is consistent with previous reports. [2 15] Prescribing during acute admission in the absence of a full medication history may sometimes be unavoidable, and does not necessarily constitute an error. For this reason we discriminated between 'emergency' prescribing, and errors where a more complete or accurate medication history would have prevented omission of prescribed medications. Although we sought to capture only unintended medication omission, it is possible that there might still have been cases where the omission was intentional (for example, suspension of diuretics in a patient who was hypotensive or dehydrated on admission) but this intent had been missed by the pharmacist collecting the data. A sensitivity analysis showed that if all errors of medication omission either on discharge or admission were excluded, the number of errors totals 2249 (0.53 per prescription written); with 1471 (34.7%) prescriptions containing at least one error, which~~.~~ represents a significant reduction in overall prescribing error rate. A core role for clinical ward based pharmacists is medicines reconciliation for admitted patients. This involves detailed medication history taking, recording of full medication list in the patient's case notes, and discussion with the clinical team to ensure that all regular medicines are prescribed throughout the admission, if appropriate. Similarly, on discharge, pharmacists ensure that necessary regular medicines are continued, and that any medicines newly started during the admission are prescribed for discharge as appropriate. The majority of the omission errors reported will have been rectified during admission or prior to discharge, as a result of the pharmacist clinical check. This highlights the importance of medicines reconciliation as soon as practicable at hospital admission, in order to minimise the possibility of missed doses of essential medicines. The role of pharmacists in actue admission settings may therefore be of particular benefit.

EQUIP error categories which could potentially be eliminated by introduction of electronic prescribing (s~~S~~trength/dose missing, p~~P~~roduct/formulation not specified, n~~N~~o signature, s~~S~~tart date incorrect/missing, incorrect route, IV instructions incorrect/missing) accounted for 357 (11.9%) of the 3011 errors observed. A further 376 (12.5%) errors could be reduced by electronic prescribing, via alerts, cautions and required fields at the patient entry/prescribing stage, although many of these can be over-ridden by the prescriber.[23] These include: administration times missing/incorrect, duplication, CD requirements incorrect/missing. The extent to which electronic prescribing can eliminate particular error types depends on the individual systems used. Importantly, whilst electronic prescribing systems could potentially have prevented up to a quarter of errors, these systems are best utilised alongside rather than instead of existing safeguards. We did not formally evaluate differences in error rates between electronic prescribing and paper-based prescribing systems. Although one hospital (Hospital G) was utilising complete electronic prescribing systems on some wards at the time of the study, and many of the other hospitals were using electronically generated discharge summaries, we failed to observe any clear association with error rate, mainly because of the

large variability in case mix which impacted directly on the number of items/prescription. In contrast, EQUIP reported that electronic prescriptions were 12% less likely to be associated with a prescribing error than handwritten prescriptions.[3] Although electronic discharge summaries may reduce error due to legibility, they do not eliminate the transcription step from inpatient charts. One study which analysed 1808 handwritten and electronic discharge summaries found no difference in the number or types of errors observed.[15] It is also worth noting that electronic systems, while clearly offering an advantage over conventional medicines management and prescribing systems, have themselves been associated with new patterns of error. Studies in the UK and Australia found a significant reduction in prescribing errors detected after introduction of electronic prescribing systems, but also identified errors specific to the electronic prescribing system used, for example, incorrect product selected from drop-down menu, or incorrect dosing frequency selected.[24-26] These electronic systems will doubtless continue to improve through refinement.[23 27]

The Erice Medication Errors Research Group (EMERGE) recommendations for reducing prescribing errors, includes training and assessment of prescribers, ongoing monitoring, awareness and communication.[14] Health systems which may impact on likelihood of error occurring include European harmonisation of prescribing, introduction of integrated prescription forms, use of IT systems such as electronic prescribing, and standardisation, evaluation, and certification of such systems. Involvement of clinical pharmacists at all points of the medication process is also recommended.[14] The latter is important since all the hospital Trusts in our survey had evolved systems to safeguard patients from prescribing error (regardless of the adoption of electronic prescribing), and this involved use of ward-based pharmacists and dispensary staff to perform routine checks on all prescriptions issued [3 10 22 28]. This ~~arguably~~ likely represents the 'last line of defence' against prescribing error, and has greatest utility when deployed in clinical areas associated with highest risk. One fundamental role of clinical pharmacists during acute admission is medicines reconciliation, where a patient's full medication history is determined and recorded using all available sources of information. Our findings suggest that removing this safeguard (e.g. through service reconfiguration or in an effort to reduce costs) could potentially lead to higher numbers of medication error actually reaching the patient.

Acknowledgements

We gratefully acknowledge the contributions of pharmacists who participated in this study. This work was funded through an unrestricted educational grant from Mersey Deanery, although design, execution, analysis and reporting was carried out independently by the study team.

We thank Professor David Graham, Postgraduate Medical Dean, Mersey Deanery for supporting the project

We thank the National Institute of Health Research (NIHR Department of Health) and the Northwest Development Agency (NWDA) for infrastructural and project support.

Declaration

All authors have completed the Unified Competing Interest form and declare that (1) SK has received research funding for website development from Merck, Bristol Myers Squibb, Gilead, ViiV, Tibotec, and Abbott, and honoraria, travel support for conference attendance from Roche, Tibotec, and Viiv in the past 3 years. All other authors have nothing to declare

TK and SHK developed the study concept, ML, SJ, AMc, AR, JS, AG, CC, BT co-ordinated data collection, KS, SHK analysed the data, JJK undertook the main statistical analysis with tabulations produced by KS. KS, SHK prepared the manuscript. JJK was involved in substantial revisions of the manuscript. TK, ML, SJ, AMc, AR, JS, AG, CC, BT reviewed the manuscript, SHK Is the guarantor for the project.

All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis

Data sharing: all requests for data sharing to Professor SH Khoo (khoo@liv.ac.uk)

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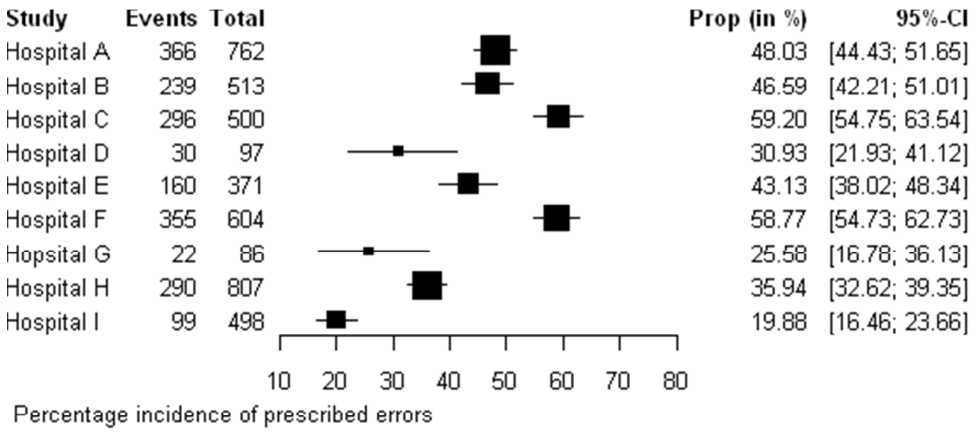

Figure 1a. Forest plot showing prescribing error rates in nine hospitals across North West England.

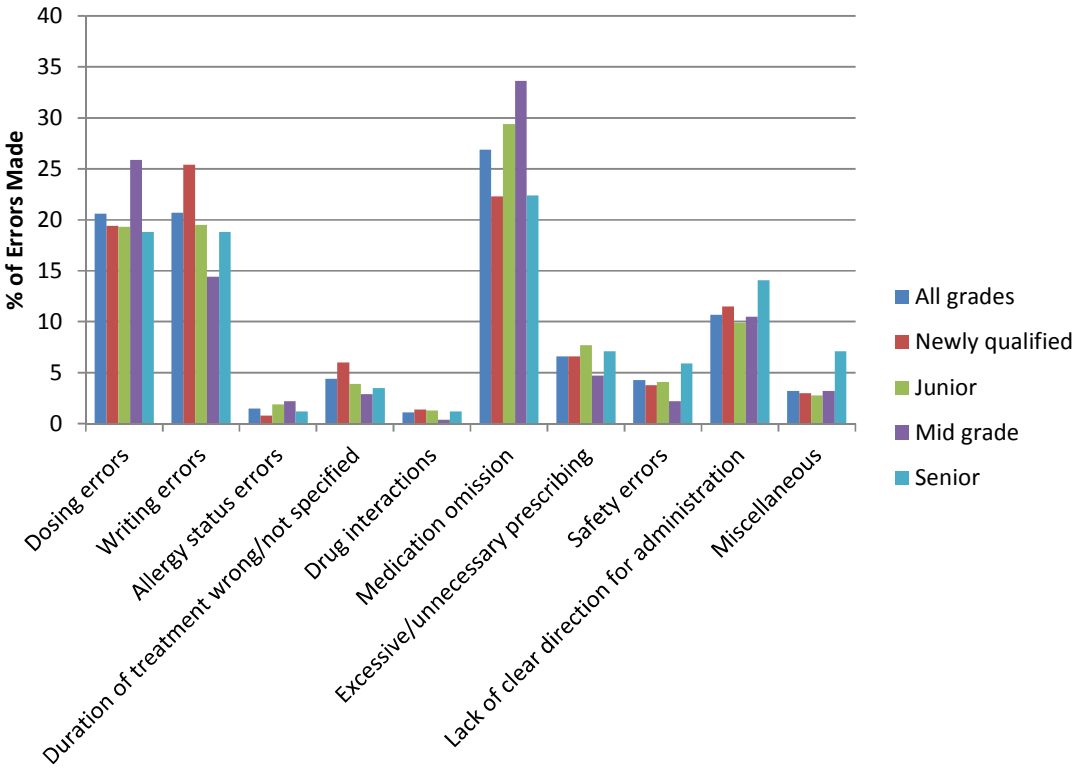

Figure 2. Categories of prescribing errors made by different grades of prescriber

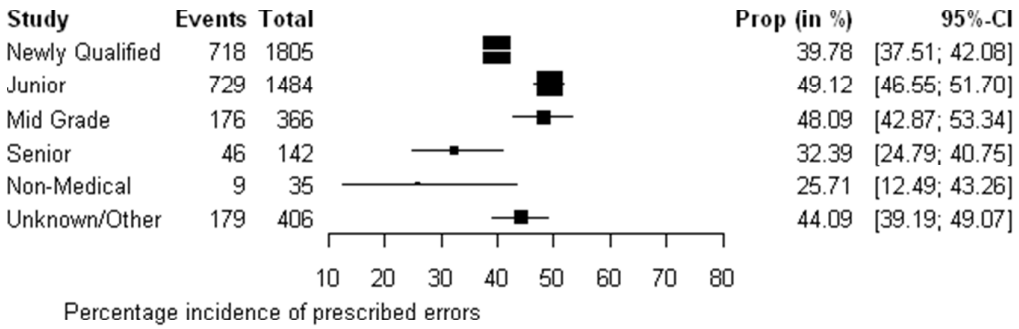

Figure 3~~1b~~. Forest plot showing prescribing error rates made by different prescriber grades

Table 1. Types of hospitals contributing prescription data

Teaching Hospitals	District Hospitals	Specialist Hospitals (Women, Paediatrics, Mental Health)
Hospital A	Hospital B	Hospital D
Hospital C	Hospital E	Hospital G
Hospital H	Hospital F	Hospital I

Table ~~1~~2. Application of error categories and severity ratings for the Mersey Deanery Prescribing Audit

Modified EQUIP Error Category	Original EQUIP Error Category	Includes/Excludes	Severity (EQUIP)	Severity Modification
1. Dosing Errors	~~2.~~ Underdose		**Minor** if unable/unlikely to carry out (units); **Significant** if dose too low to treat the condition; **Serious** if patient in acute distress; **Potentially~~,~~ Lethal** if medication life saving	
	~~3.~~ Overdose	Excludes overdoses caused by duplication eg. Paracetamol with co-codamol ~~(7)~~	**Minor** if unable/unlikely to carry out (units); **Significant** - low TI, ½-4 times; **Serious**- Low TI, 4-10 times; errors in units if chance dose could be given; **Potentially~~,~~ Lethal** if v.low TI and dose 10 times normal dose, results in serum levels of drug in severe toxicity range, or has high potential to cause cardiopulmonary arrest	**Minor** if effect of dosing expected to be minimal
	~~29.~~ Dose/rate mismatch		-	Judgement used based on Equip severity categories
2. Writing Errors	~~4.~~ Strength/dose missing	Includes dose units missing	**Minor**	
	~~8.~~ Product/formulation not specified		-	**Minor**
	~~9.~~ Incorrect formulation		-	**Minor** unless formulation likely to have implication on treatment eg. Insulin, co-careldopa, in which case **significant/serious** based on potential consequence
	~~12.~~ No signature		-	**Significant** (governance issue)
	~~20.~~ Start date incorrect/missing		-	**Minor**
	~~21.~~ CD requirements incorrect/missing		-	**Minor**
3. Allergy status missing/significant allergy	~~24.~~ Significant allergy	Includes allergy status not completed, or where a drug has been prescribed despite an allergy to that drug/class	-	**Significant** allergy status/specific allergy missed off prescription; **Serious** if patient prescribed agent allergic to; **Potentially~~,~~ Lethal** if patient

				prescribed drug which previously had severe reaction to eg. oedema
4. Duration of treatment wrong/not specified	~~18.~~ Continuation for longer than needed	Includes no stop/review date for antibiotics, steroids etc	-	**Minor** if continuation of the medicine or the duration represents little potential for harm; **Significant** if continued >3 days longer than needed for medication such as: antibiotics, oral steroids, LMWH, potassium; **Serious** if ongoing treatment could cause serious harm
	~~26.~~ Premature discontinuation	Includes drugs stopped without appropriate reducing course	-	**Minor** if discontinuation is unlikey to have a significant clinical impact; **Significant** if duration of treatment insufficient to treat condition eg. Antibiotics, or if no reducing course eg. Oral steroids
5. Drug Interactions	~~22.~~ Drug interaction	Excludes 2 items prescribed from same class e.g omeprazole with lansporazole (~~7~~ Duplication)	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-drug interaction	**Significant** if manufacturer advises the combination is contraindicated, should be avoided, or advises caution; **Serious** if adverse events highly probable
	~~27.~~ Drug interaction not taken into account	As above: unable to differentiate drug interaction~~22~~ and drug interaction not taken into account~~27~~ from available data		
6. Omission of medication	~~1.~~ Omission on admission		**Significant** (regular medication)	-
	~~5.~~ Omission on discharge~~TTO~~		**Significant**	-
	~~17.~~ Drug not prescribed but indicated		-	**Minor** if medication is unlikely to significantly impact patient care; **Significant** if medication would have significant impact on clinical course **Serious** if medication would alleviate a serious condition /patient is in acute distress; **Potentially lethal** if medication is potentially life saving
	~~7.~~ Duplication	Includes a second agent prescribed which contains an ingredient already	**Minor** if duplicate therapy prescribed without potential for	**Significant, Serious, Potentially~~.~~lethal:** As for overdose when duplicated items

7. Excessive/ unnecessary prescribing		being taken; 2 drugs prescribed from the same class/with same clinical effect eg. Lansoprazole + omeprazole	increased adverse events	co-administered (3)
	~~11.~~ Unintentional prescription of drug	Drug prescribed was not that desired. Includes prescription of a discontinued drug, excluding discontinuation due to ADR ~~(25)~~, or course is too long ~~(18)~~	-	Judgement used based on Equip severity categories
8. Clinical Safety Errors	~~10.~~ No maximum dose	Excludes prescriptions with no frequency (~~6.~~ administration times missing/incorrect)	**Minor**- order lacked specific drug, dose, strength, frequency or route information	**Significant** if no maximum dose stated for opioids
	~~13.~~ Clinical contraindication	Contraindication according to summary of product characteristics	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-disease interaction	**Significant** if administration unlikely to have serious clinical consequences in the given situation
	~~25.~~ Continuation after ADR		-	Judgement used based on Equip severity categories
	~~28.~~ No dosage alteration after levels out of range		-	Judgement used based on Equip severity categories
9. Lack of clear directions for administration	~~6.~~ Administration times incorrect/missing	No frequency/times of dosing incorrect eg. In relation to food, morning vs night.	**Minor**	**Significant** if administration time would be expected to affect treatment eg. Exenatide with meals, hypnotics at night
	~~14.~~ Incorrect route		**Minor** if unlikely to be carried out/little chance of toxicity/therapeutic failure; **Significant** if wrong route to treat condition; **Serious** if potential for toxicity	-
	~~16.~~ IV instructions incorrect/missing		-	Judgement used based on Equip severity categories
	~~19.~~ Route missing		**Minor**- order lacked specific drug, dose, strength, frequency or route information	-
	~~23.~~ Daily dose divided incorrectly	Number of dosing intervals incorrect. Excludes under/overdose ~~(2/3)~~	-	**Minor** if dosing intervals are not standard, but are unlikely to significantly affect treatment;

				Significant if dosing intervals are inappropriate to treat the condition; **Serious** if medication has narrow TI~~therapeutic index~~ and dosing intervals may affect toxicity/efficacy eg. Parenteral aminoglycosides
10. Miscellaneous	~~15.~~ No indication	Includes PRN medications, where lack of indication on prescription could prevent administration. Excludes failure to write an indication when prescribing antibiotics	-	**Minor** if indication not written up for PRN medication; **Significant** if indication not written up for formulations which are licensed for specific conditions.
	~~30.~~ Miscellaneous	Illegible drug details, non-standard abbreviations, patient details incorrect/missing, warfarin fixed dose prescribed.	-	Judgement used based on Equip severity categories

Abbreviations: TI- therapeutic index, CD- controlled drug, ADR- adverse drug reaction, PRN- when required

Table 32. Summary data showing prevalence and severity of errors observed

		Total Prescriptions	One or more error reported		Error Severity				Total errors
			No (%)	Yes (%)	Minor (%)	Significant (%)	Serious (%)	Pot-entially Lethal (%)	
All		**4238**	**2381 (56.2)**	**1857 (43.8)**	**1264 (42.0)**	**1629 (54.1)**	**109 (3.6)**	**9 (0.3)**	**3011**
Prescriber Grade	Newly Qualified	1805	1087 (60.2)	718 (39.8)	519 (48.8)	507 (47.7)	35 (3.3)	3 (0.3)	1064
	Junior	1484	755 (50.9)	729 (49.1)	496 (39.2)	725 (57.4)	41 (3.2)	2 (0.2)	1264
	Mid Grade	366	190 (51.9)	176 (48.1)	93 (33.6)	166 (59.9)	15 (5.4)	3 (1.1)	277
	Senior	142	96 (67.6)	46 (32.4)	36 (42.4)	43 (50.6)	6 (7.1)	0 (0)	85
	Non-medical	35	26 (74.3)	9 (25.7)	8 (57.1)	5 (35.7)	1 (7.1)	0 (0)	14
	unknown/other	406	227 (55.9)	179 (44.1)	112 (36.5)	183 (59.6)	11 (3.6)	1 (0.3)	307
Training	Liverpool	1290	787 (61.0)	503 (39.0)	270 (35.4)	456 (59.8)	36 (4.7)	1 (0.1)	763
	Non-Liverpool	922	478 (51.8)	444 (48.2)	342 (43.8)	420 (53.8)	19 (2.4)	0 (0)	781
	Unknown	2026	1118 (55.2)	908 (44.8)	652 (44.4)	753 (51.3)	54 (3.7)	8 (0.5)	1467
Admission/ Discharge	Discharge	2467	1615 (65.5)	852 (34.5)	685 (52.5)	584 (44.8)	32 (2.5)	4 (0.3)	1305
	Admission	1744	756 (43.4)	988 (56.7)	576 (34.2)	1030 (61.1)	75 (4.4)	5 (0.3)	1686
	Unknown	27	12 (44.44)	15 (55.55)	3 (15)	15 (75)	2 (10)	0 (0)	20
Ward Area	Medicine	2059	1083 (52.6)	976 (47.4)	634 (39.0)	921 (56.7)	64 (3.9)	6 (0.37)	1625

	Surgery	1395	836 (59.9)	559 (40.1)	448 (50.1)	417 (46.6)	27 (3.0)	2 (0.2)	894
	Mental health	96	66 (68.8)	30 (31.3)	24 (60)	16 (40)	0 (0)	0 (0)	40
	Accident & Emergency~~A&E~~	8	1 (12.5)	7 (87.5)	1 (9.1)	10 90.9	0 (0)	0 (0)	11
	Critical care	17	14 (82.4)	3 (17.7)	1 (25.0)	3 (75.0)	0 (0)	0 (0)	4
	Unknown	663	383 (57.8)	280 (42.2)	156 (35.7)	262 (60.0)	18 (4.1)	1 (0.2)	437
Prescription contains[#]	Antibiotic	724	301 (41.6)	423 (58.4) (**Antibiotic**: 130 (18.0))	57 (29.8)	118 (61.8)	16 (8.4)	0 (0)	191
	Insulin	129	42 (32.6)	87 (67.4) **Insulin**: 20 (15.5)	12 (37.5)	19 (59.4)	1 (3.1)	0 (0)	32
	Warfarin	196	71 (36.2)	125 (63.8) **Warfarin**: 18 (9.2)	6 (23.1)	16 (61.5)	4 (15.4)	0 (0)	26
	Oxygen	36	7 (19.4)	29 (80.6) **Oxygen**: 2 (5.6)	1 (14.3)	5 (71.4)	1 (14.3)	0 (0)	7

* Relates to errors per prescriptions written, not errors per number of items prescribed

Error severities, total errors and error rates relate to errors associated with Antibiotics/Insulin/Warfarin/Oxygen only

Table 43. Summary of the Errors Observed which were Considered to be Potentially Lethal

Error Description	Category	Prescriber Grade	Ward Area	Admission/ Discharge
Gliclazide 400mg prescribed when 40mg needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Digoxin 625micrograms prescribed when 62.5micrograms needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Oxycodone 500mg prescribed: overdose	1- Dosing Errors	Mid Grade	Surgery	Admission
Methotrexate prescribed daily, not weekly	1- Dosing Errors	Junior	Medicine	Admission
Doxazocin prescribed; had been stopped by general practitioner GP due to angioedema	3. Allergy status missing/ significant allergy	Junior	Medicine	Admission
Phenytoin dose of 300mg daily incorrectly prescribed as 800mg	1- Dosing Errors	Newly Qualified	Medicine	Discharge
Midazolam IV for sedation: overdose	1- Dosing Errors	Mid Grade	Unknown	Admission
Amiodarone loading dose of 200mg three times daily continued as a regular dose	1- Dosing Errors	Other	Surgery	Discharge
Enoxaparin prescribed 1mg/kg once daily instead of 1mg/kg twice daily for a patient with acute coronary syndrome	1- Dosing Errors	Mid Grade	Medicine	Admission

Table 54. Univariate statistics showing the significance of explanatory variables in predicting error rates in prescriptions.

Variable	n	≥1 Error	No Error	Difference (95%CI)	p-value
		n (%)	n (%)		
Prescriber Grade (n=3850)		~~n=~~1689	~~n=~~2161		
Newly qualified	1803	716 (42%)	1087 (50%)	-8% (-11.2% to -4.8%)	<0.001
Junior	1482	727 (43%)	755 (35%)	8% (4.9% to 11.1%)	
Mid-grade	366	176 (10%)	190 (8.8%)	1.2% (-0.7% to 3.1%)	
Senior	142	46 (2.7%)	96 (4.4%)	-1.7% (-2.8% to -0.4%)	
Non-medical	35	9 (0.5%)	26 (1.2%)	-0.7% (-1.3% to -0.1%)	
Other	22	15 (0.9%)	7 (0.3%)	0.56% (0.1% to 1.1%)	
Discharge~~TTO~~/Admission (n=3065)		~~n=~~1135	~~n=~~1930		
Discharge~~TTO~~	2467	853 (75%)	1614 (84%)	-9% (-12.0% to -6.0%)	<0.001
Admission	598	282 (25%)	316 (16%)		
Liverpool trained (n=1325)		~~n=~~518	~~n=~~807		
Liverpool	35	14 (2.7%)	21 (2.6%)	0.1% (-1.7% to 1.9%)	0.911
Non-Liverpool	1290	504 (97%)	786 (97%)		
Hospital (n=4238)		~~n=~~1857	~~n=~~2381		
Hospital A	762	366 (20%)	396 (17%)	3% (0.6% to 5.4%)	<0.001
Hospital B	513	239 (12%)	274 (12%)	0% (-2.0% to 2.0%)	
Hospital C	500	296 (16%)	204 (8.6%)	7.4% (5.4% to 9.4%)	
Hospital D	97	30 (1.6%)	67 (2.8%)	-1.2% (-2.1% to -0.3%)	
Hospital E	371	160 (8.6%)	211 (8.9%)	-0.3% (-2.0% to 1.4%)	
Hospital F	604	355 (19%)	249 (10%)	9% (6.8% to 11.2%)	
Hospital G	86	22 (1.2%)	64 (2.7%)	-1.5% (-2.3% to -0.7%)	
Hospital H	807	290 (16%)	517 (22%)	-6% (-8.4% to -3.6%)	
Hospital I	498	99 (5.3%)	399 (17%)	-11.7% (-13.5% to -9.9%)	
Ward Area (n=3575)		~~n=~~1577	~~n=~~1998		
Medical	2059	977 (62%)	1082 (54%)	8% (4.8% to 11.2%)	<0.001
Surgical	1395	560 (36%)	835 (42%)	-6% (-9.2% to -2.8%)	
Accident & Emergency~~A & E~~	8	7 (0.4%)	1 (0.1%)	0.3% (-0.04% to 0.6%)	
Mental health	96	30 (1.9%)	66 (3.3%)	-1.4% (-2.4% to -0.4%)	
Critical care	17	3 (0.2%)	14 (0.7%)	-0.5% (-0.9% to -0.1%)	
Number of Medicines on Prescription (n=3386) Median (IQR)		8; (4,11) (n=1435)	4; (2,7) (n=1951)	-4 (-4.5, -3.5)	<0.001

n= number of prescriptions

Table 6~~5~~. Multivariate logistic regression analysis for predicting error rates in prescriptions.

Variable	Odds ratio (95%CI)	p-value
Hospital		
Hospital H	1	
Hospital A	Not estimable*	
Hospital B	1.11 (0.78 to 1.58)	0.57
Hospital C	2.38 (1.63 to 3.46)	<0.001
Hospital D	0.64 (0.13 to 3.06)	0.57
Hospital E	1.39 (0.96 to 2.01)	0.08
Hospital F	3.53 (2.63 to 4.73)	<0.001
Hospital G	1.80 (1.03 to 3.12)	0.04
Hospital I	1.11 (0.73 to 1.70)	0.62
Prescriber Grade		
Newly qualified	1	
Junior	1.06 (0.85 to 1.32)	0.61
Mid-grade	0.96 (0.64 to 1.44)	0.83
Senior	0.97 (0.58 to 1.63)	0.92
Non-medical	0.59 (0.21 to 1.64)	0.31
Other	1.50 (0.53 to 4.23)	0.44
Discharge/Admission	1.16 (0.70 to 1.92)	0.58
Number of prescribed items	1.14 (1.12 to 1.17)	<0.001

Analysis contains only 2127 records (50.2%) where complete data was provided for all variables

* Trust provided no data on number of prescription items

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TO: Editor
BMJ Open

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31st August 2012.

Dear Editor

Re: Cross Sectional Study of Prescribing Error in Patients Admitted to Nine Hospitals Across North West England

Please find enclosed our manuscript for your consideration. The BMJ Group Journals have a long and honourable tradition of championing patient safety, and publishing research which seeks to characterise, understand and limit harms resulting from medication error. Earlier this year, Ingrid Torjesen's article highlighted findings from two of the UK's largest studies into prescribing error in primary and secondary care (the PRACtICe and EQUIP studies respectively) [*Torjesen I. BMJ 2 May 2012*]. Both studies have released study reports on the GMC website, but neither has yet been published in a peer-reviewed journal.

Our sample size is comparable to EQUIP, and larger than PRACtICe, and our observed error rate of ~10% of medication items prescribed is similar to EQUIP (9%) and PRACtICe (4%), using a modified version of EQUIP definitions. By analysing error within complete individual prescriptions (rather than individual medication items) we show that a significant proportion of patients were exposed to prescribing error, and that this risk increased by 14% for every medication item added to their prescription. Risk of error did not vary with hospital, seniority of prescriber or medical school training, but acute medical admission scenarios were associated with highest risk of error (mainly arising from unintended medication omission). Finally, electronic prescribing and medication administration systems could only have prevented up to a quarter of these errors, highlighting the important role of the ward pharmacist, particularly in high-pressure acute areas.

We believe these results are likely to accurately reflect the prevalence of prescribing error more generally throughout the UK, and to consequently inform health policy which seeks to minimise patient harms through improvements in health systems. Thank you for considering this for publication in BMJ Open.

With best wishes,

Professor S.H. Khoo
Institute of Translational Medicine
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STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	√
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√
Objectives	3	State specific objectives, including any prespecified hypotheses	√
Methods			
Study design	4	Present key elements of study design early in the paper	√
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	√
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√
Bias	9	Describe any efforts to address potential sources of bias	√
Study size	10	Explain how the study size was arrived at	√
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	√
		(*b*) Describe any methods used to examine subgroups and interactions	√
		(*c*) Explain how missing data were addressed	√
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	√
		(*e*) Describe any sensitivity analyses	√
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	√
		(b) Indicate number of participants with missing data for each variable of interest	√
Outcome data	15*	Report numbers of outcome events or summary measures	√
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	√

		(*b*) Report category boundaries when continuous variables were categorized	√
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√
Discussion			
Key results	18	Summarise key results with reference to study objectives	√
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√
Generalisability	21	Discuss the generalisability (external validity) of the study results	√
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

Cross Sectional Study of Prescribing Errors in Patients Admitted to Nine Hospitals Across North West England

Journal:	*BMJ Open*
Manuscript ID:	bmjopen-2012-002036.R2
Article Type:	Research
Date Submitted by the Author:	13-Dec-2012
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Primary Subject Heading:	Health services research
Secondary Subject Heading:	Health services research
Keywords:	EDUCATION & TRAINING (see Medical Education & Training), Quality in health care < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Risk management < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

Cross Sectional Study of Prescribing Errors in Patients Admitted to Nine Hospitals Across North West England

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Article Summary

1. Article Focus

- Some studies have reported lower error rates with more senior prescriber grades, and insufficient undergraduate prescriber training as a potential risk for prescribing errors
- Prescriptions frequently contain multiple medications, but data about errors on complete prescriptions (all prescribed items on an inpatient chart or discharge prescription), which give a better estimate of numbers of patients at risk of harm, are lacking
- We aimed to determine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge and type of medication prescribed

2. Key Messages

- We observed an error rate of 10.9% per prescribed item, with only 56.2% of 4238 complete prescriptions remaining error free.
- In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription.
- We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues.

3. Strengths and Limitations

- This was a large study across nine diverse hospital settings
- We determined the rate of errors on complete prescriptions as well as for individually prescribed items, giving a better estimate of the numbers of patients affected by errors.
- We did not evaluate the impact of electronic prescribing on the prevalence and type of prescribing errors, however up to a quarter of the errors observed could potentially have been avoided through use of electronic prescribing and medicines administration systems

Abstract

Objective To evaluate the prevalence, type and severity of prescribing errors observed between grades of prescriber, ward area, admission or discharge, and type of medication prescribed

Design Ward-based clinical pharmacists prospectively documented prescribing errors at the point of clinically checking admission or discharge prescriptions. Error categories and severities were assigned at the point of data collection, and verified independently by the study team

Setting Prospective study of nine diverse National Health Service (NHS) hospitals in North West England, including teaching hospitals, district hospitals and specialist services for paediatrics, women and mental health.

Results Of 4238 prescriptions evaluated, one or more error was observed in 1857 (43.8%) prescriptions, with a total of 3011 errors observed. Of these, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and 9 (0.30%) were potentially life-threatening. The majority of errors considered to be potentially lethal (n=9) were dosing errors (n=8), mostly relating to overdose (n=7). The rate of error was not significantly different between newly qualified doctors compared with junior, middle grade or senior doctors. Multivariable analyses revealed the strongest predictor of error was the number of items on a prescription (risk of error increased 14% for each additional item). We observed a high rate of error from medication omission, particularly amongst patients admitted acutely into hospital. Electronic prescribing systems could potentially have prevented up to a quarter of (but not all) errors.

Conclusions In contrast to other studies, prescriber experience did not impact on overall error rate (although there were qualitative differences in error category). Given that multiple drug therapies are now the norm for many medical conditions, health systems should introduce and retain safeguards which detect and prevent error, in addition to continuing training and education, and migration to electronic prescribing systems.

Introduction

Prescribing errors are common, with systematic reviews suggesting that as many as 50% of hospital admissions and 7% of medication orders are affected.[1] In recent studies, prescribing errors have been found to affect approximately 9-15% of medication orders for hospital inpatients in the United Kingdom (UK).[2 3] Over one third of 651 patients were found to have a prescribing error occurring at hospital admission in the United States (US).[4] Prescribing errors are also prevalent in primary care, affecting 37% of 9385 prescriptions in the US,[5] and one in eight patients (one in 20 prescription items) in the UK.[6] A study in the Netherlands evaluating medication omission errors in elderly patients admitted to hospital reported adverse consequences in 21% of 100 patients.[8]

Human error in healthcare may be considered in the context of individuals or health systems.[9-11] While personal factors such as forgetfulness, inattention, poor motivation, carelessness, negligence, and recklessness are important, a health systems approach more comprehensively addresses recurrent errors and organisation factors and processes which may give rise to that error. The person, the team, the task, the workplace and the institution as a whole are considered, [9] which identify weaknesses in the system's defences.[9] For example, higher hospital mortality at weekends may be associated with lower numbers of senior staff available outside of the normal working week.[12 13] Barriers which may prevent medication errors, or prevent errors from reaching the patient, may include electronic prescribing alerts, and prescription review by clinical pharmacists.

Data on factors which may contribute to prescribing errors, for example differences between grades of prescriber, ward area, admission or discharge and type of medication prescribed are sparse.[3 14 15] Existing data suggest that newly qualified and junior doctors are twice as likely to make prescribing errors than senior doctors, taking into account the larger volume of prescriptions written by junior prescriber grades.[3] Provision of sufficient undergraduate training to allow medical students to become safe prescribers when they begin work as newly qualified doctors is widely recognised as an important factor in reducing prescribing errors.[14 16-18] Teaching in UK medical schools has changed considerably over the last decade, with the General Medical Council stipulating that medical students must be adequately prepared to prescribe drugs and manage risk at the point of graduation.[19 20]

Whilst previous studies have evaluated error for individual medications, few studies have systematically evaluated complete prescriptions (all items included on a single inpatient prescription chart or discharge prescription at the time of clinical pharmacist check) to evaluate factors associated with prescribing error.[1-3] This is important as it gives a more accurate estimate of the numbers of patients who are potentially put at risk of harm by prescribing errors. We undertook a prospective survey of prescribing errors in nine diverse National Health Service (NHS) hospitals in the North West of England, aiming to examine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge, hospitals and the type and number of medicines prescribed. In order to further evaluate the role of undergraduate training, we also tested for a relationship between occurrence of error and medical school training of prescribers. As approximately 30% of the prescribers were trained at the local institution, the University of Liverpool, whether medical training was undertaken at this institution was included in the analysis. Univariate analysis and multivariate logistic regression was used to evaluate factors associated with prescribing errors.

Methods

Setting

A total of nine NHS hospitals from the Merseyside and Cheshire region took part in the audit. These comprised large teaching hospitals, general hospitals, specialist centres for paediatrics, women's health and mental health (Table 1). One hospital was using complete electronic prescribing systems (inpatient prescribing, medication ordering, discharge prescriptions) on some wards at the time of the audit. Eight of the hospitals were using paper prescription charts for inpatients and either handwritten or transcribed electronically generated discharge prescriptions. In this setting, ward-based clinical pharmacists check inpatient prescriptions at, or soon after patient admission, when medicines reconciliation is undertaken. Inpatient prescription charts are then checked at least daily by the pharmacist. Discharge prescriptions are checked and authorised by a clinical pharmacist prior to supply of medication. Pharmacists may amend or clarify some aspects of prescribing, or discuss with the clinical team any recommendations or safety issues at these points of care. Clinical pharmacists may also participate in ward rounds and multidisciplinary team meetings, where prescribing may be discussed with clinicians, clarified or amended.

Data Collection

As this was an audit of unlinked anonymised prescriptions, Ethics approval was not required in accordance with local guidance. We aimed to capture data from all seven hospital trusts in the region. Two additional hospitals adjacent to and linked with healthcare provision in the Merseyside region were also audited. The number of prescriptions audited was empirically determined in order to generate a sample size equivalent to a large study recently undertaken in the UK.[3] In order to audit practice across the region, each hospital was asked to audit a minimum of 400 prescriptions.

We adopted the following definition of prescribing errors for the study, which excludes adherence to local prescribing policy and guidelines: "A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant: (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice".[21] A standard questionnaire collected data on error category and severity (based on EQUIP error classifications). The EQUIP study was a large prospective survey of prescribing errors affecting hospital inpatients in the UK,[3] and the error classifications were therefore considered relevant to our setting. Nominated ward-based clinical pharmacists prospectively documented prescribing errors at the point of checking inpatient or discharge prescriptions, during normal pharmacy working hours, therefore each audit form was a point prevalence of prescribing errors at the time of pharmacist clinical check. Acute admission was defined as the first 24 hours in hospital. For all prescription sheets generated in acute admission settings, a separate audit form was completed (to allow for emergency prescribing in the absence of a full drug history without this being recorded as an error) and we sought to record only unintended medication omissions (e.g. following medicines reconciliation with general practices or primary healthcare databases). Hospitals were advised to complete the study on different days of the week throughout the period of the audit, in order to capture an even spread of days. For example data collection would occur weekly, on Monday in week one, Tuesday in week two, Wednesday in week three, in order to minimise double auditing of the same patient on admission to hospital and subsequent admission to a ward. Therefore, if patients were audited twice, an interval of at least one week would separate each audit form, unless their acute admission/inpatient /discharge prescription were audited

on the same day. If items on prescriptions had been previously screened, they would be counted again in any subsequent auditing, though there would be a one week interval since previous auditing, or the patient would be a different stage of hospital admission. All types of medication order were audited, including IV fluids, when required and once only medication.

Prescriber Category

Pharmacists were required to indicate the category of prescribers on data collection forms. For this analysis, prescribers were categorised as follows: newly qualified (foundation year 1, house officers), junior (foundation year 2, specialist or 'core' training years 1 & 2), mid grade (specialist registrars, training fellows), senior (consultant), non-medical (nurse or pharmacist prescribers), other (for example locum doctors for whom grade was unclear) and unknown (no information concerning prescriber recorded).

Grading of prescribing errors

We modified EQUIP study criteria[3] for error categorisation and severity classification by adding or clarifying severity criteria for all error categories, and by grouping errors into ten distinct areas according to stage of the prescribing process (see below and Table 2). 'Exclusion' and 'inclusion' of errors into EQUIP study error types were defined, in order to differentiate categories with potential overlap. Severity ratings were further defined and assigned to each error category based on modified EQUIP study criteria and taking into account the perceptions of the original pharmacist gradings. Severity ratings related to the potential severity, had the error been allowed to progress through to the patient, as the majority of errors were corrected prior to the point of administration. In order to limit misclassification of errors, the original 29 EQUIP categories were batched into 10 different types of error groups as follows: (1) Dosing errors, (2) Writing errors, (3) Allergy status errors, (4) Duration of treatment wrong/not specified, (5) Drug interactions, (6) Omission of medication, (7) Excessive/unnecessary prescribing, (8) Clinical safety errors, (9) Lack of clear directions for administration, (10) a new error category (Miscellaneous) was added (Table 2). The modification and definition of error categories and severities was undertaken by two members of the study team (KS, SK) and agreed by a third (TK).

Despite using a standard set of definitions, we noted discrepancies across various hospitals in both error categorisation and severity rating. In particular there was a tendency to over-report errors and to overestimate their potential severity. This was confirmed by a *post-hoc* inter-rater agreement analysis. A set of six sample prescriptions was generated. A list of 14 sample errors was decided by the study team, including study error type and severity, according to the criteria in Table 2 utilised for analysis of the main study. The errors selected occurred frequently in the main study, and covered a broad range of error categories and severities. Six pharmacists from each participating hospital were asked to each screen the six prescription scenarios containing the 14 errors and to record any observed errors, allocating error types and severities. The exact agreement percentages between category classification, severity classification and both combined were computed to measure the absolute concordances between pharmacist scores against the gold standard assessment.

In order to limit inter-observer bias, all grading and severity of errors identified in the main study were independently reassessed by two members of the study team (KS and SK), with discordant assessments collectively discussed with a third (TK) in order to agree a final categorisation for error type and severity. For severity ratings, the summary of product characteristics for relevant medication was consulted, in order to determine potential

implications of different degrees of overdose, underdose, of drug interactions, and also to confirm clinical contra-indications.

Statistical Analyses

Data were analysed at the prescription level using complete case data. The prevalence and severity of errors observed were tabulated using percentage frequencies. A Forest plot was produced to present the error prevalence rate and 95% confidence interval (95% CI) for each hospital and grade of prescriber. For the formal statistical analysis, when there was more than one error on a prescription, only the most severe error was included. This approach was used to ensure that the errors included in the analysis were independent. In this study, we assessed hospital, prescriber grade (newly qualified, junior, mid-grade, senior, non-medical, other), ward area (medical, surgical, A&E, mental health, critical care), number of prescribed medicines, an indicator to denote whether the prescription was prescribed on admission or on discharge and an indicator to denote whether the prescriber was Liverpool trained or not as potential risk factors. Univariate statistical analyses were performed using a chi-squared test except for continuous data, which were analysed using the Mann-Whitney U test. A multivariate logistic regression model for a prescription error was fitted to the data. Results are given in terms of an odds ratio (OR) and associated 95% CI. All risk factors that were statistically significant ($p<0.1$) in the univariate analysis were considered for inclusion in the multivariate model with the exception of ward area as a number of hospitals only reported a single specialty type.

All statistical analysis was carried out using the statistical software package SPSS (version 20) using a two-sided significance level of 0.05 (5%) throughout.

Results

Error Classification

During the *post-hoc* inter-rater agreement analysis, approximately 75% of error categories were correctly identified by pharmacists when compared to the standards. Only 47% of severity ratings were concordant with the standards, and 40% of pharmacists rated both error category and severity in concordance with the standards.

Re-assessment of errors by the study team resulted in exclusion of a total of 143 errors which were not considered true errors of the process of prescribing. The error category was re-graded for 434 errors, and severity was re-graded for 724 errors, which was predominantly a down-grading.

Descriptive data and severity of errors

A total of 4238 prescriptions were evaluated; of these, 1857 (43.8%) prescriptions contained at least one error (Table 3). The overall prevalence of prescribing errors (number of prescriptions with one or more error/prescriptions evaluated) ranged from 20% to 60% across the nine hospitals (Figure 1). The rate of errors per prescribed item was 10.9%.

A total of 3011 individual errors were observed within the 1857 prescriptions containing an error. Of these 3011 errors, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and nine (0.30%) were potentially life-threatening (Table 3). Details of all potentially life-threatening errors are listed in Table 4 and mainly comprised dosing errors (n=8), particularly overdose (n=7), with one incidence of under dose. A further error considered to be potentially lethal related to prescription of a medicine to which the patient had previously had a serious allergic reaction.

The proportion of errors categorised with severity as significant or higher by prescriber grade were as follows: all prescribers 58.0%, newly qualified 51.2%, junior 60.8%, mid grade 66.4%, senior 57.6% (χ^2_{trend} $p<0.001$ for univariate analysis, although this association disappeared when corrected for other potential confounders)(Table 3).
Fewer errors were observed on discharge prescriptions than on prescriptions written on admission. More errors were observed in prescriptions containing antibiotics, insulin, warfarin and oxygen, although this does not take into account the number of items on each prescription. Whether doctors were Liverpool trained or not did not affect the number of errors observed (Table 3).

Differences in error prevalence and error types were observed in individual participating hospitals. The lowest rates of errors was reported for the paediatrics specialty hospital, with 0.07 errors observed per prescribed item, and 0.26 errors observed per prescription. However, in multivariate analysis, there was no significant reduction in error risk and it is likely that the effect could be due to lower number of items per prescription (mean 3.5, vs pooled data: 6.3). The most common error types were dosing errors (30%) and medication omission (23.1%).
Significantly lower risk of errors was observed in the hospital providing specialist services for women (p=0.04, Table 6) in multivariate analysis. One of the lowest error rates per prescription was observed (0.28), although the error rate per prescribed item (0.11) was

equal to that of the pooled data. The most common error type observed was excessive/unnecessary prescribing (50%). No errors of medication omission were observed. This hospital also had a low number of items per prescription (2.4), and was using electronic prescribing systems on some wards.

Error types

The most frequent error types for all prescribers were medication omission, accounting for 26.9%, writing errors accounting for (20.7%) and dosing errors accounting for (20.6%) of all errors recorded. There was little difference in the variability of error types across different prescriber grades (Figure 2).

Risk factor analysis

Results of the univariate analysis are shown in Table 5. Missing data limited inclusion of all reported prescriptions in risk factor analysis, notably as one acute hospital failed to return data on number of items on each prescription. All factors considered appeared to show a significant difference except for whether doctors had trained in Liverpool, which made no significant difference (p=0.91) to whether an error occurred on the prescription. Multivariate risk factor analysis showed that the likelihood of an error increased for every additional item included on the prescription (OR 1.14, 95% C 1.12, 1.17, p<0.001) (Table 5). Therefore, for each additional item on the prescription, the risk of an error occurring increased by about 14%. There was also a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16 (95% CI 0.70, 1.92, p=0.58), although this difference did not reach statistical significance (Table 6). No significant differences were found in error rates between different prescriber grades, when compared to newly qualified doctors (Figure 2, Figure 3) in multivariate analyses.

Discussion

In this large study, only 56.2% of 4238 prescriptions written had no reported errors. Of the errors recorded, 41.9% were minor, 54.1% significant, 3.6% serious and 0.3% potentially life threatening. It is important to note that severity ratings relate to the potential severity had the error been allowed to progress through to the patient - in fact the majority of errors were corrected prior to the point of administration. In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing error increasing by 14% for every additional medication item prescribed. Where data were available, prescriptions contained an average of 6.3 medication items, although this varied from 2.4 – 7.5 items according to medical specialty surveyed. Uncorrected analyses suggested that errors were frequent in prescriptions containing insulin (15.5%), antibiotics (18%), warfarin (9.2%) and oxygen (5.6%), although these patients were very likely to have been receiving multiple medications. Error rates were highest amongst specialties which prescribed a broad range of medications (e.g. acute medicine, compared to elective surgery), and also differed between different hospital Trusts, with hospitals specialising in paediatrics, maternal health and mental health exhibiting the lowest error

rates. However, when corrected for number of medications, these differences did not remain significant, with the exception of maternal health.

The most frequent error encountered was unintended medication omission following acute hospital admission (0.97 errors/prescription written, versus 0.53 for discharge medications). When adjusted in multivariable analyses (Table 6) there was no statistically significant difference in error rates between admission and discharge. We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues. Although numbers were relatively small, we observed no difference in error rate amongst newly qualified doctors by undergraduate training, and doctors trained in Liverpool were neither more nor less likely to commit medication errors. The categories and severity of errors made by different prescriber grades were broadly similar (Table 3, Figure 2), however some differences were observed. For example, writing errors were more frequently observed with newly qualified doctors, medication omission was more frequently observed with junior and mid grade doctors, and dosing errors were more frequently observed with mid grade doctors.

These results are consistent with previously published studies. Both the EQUIP and PRACtICe Studies[3 6] reported error rates of approximately 1 in 10 medications prescribed (we observed a rate of 10.9%). Given the high number of medications prescribed (mean of 6.3 items/prescription) nearly half of all prescriptions contained at least one error.
A systematic review found prescribing errors to be more common in adults than in children.[1] A study in Spain comparing paediatric wards with obstetrics found that paediatric patients had a fourfold higher risk of serious errors than the maternity population (2.3% vs 14.3%), which were mainly related to drug dosing.[22] We observed a low error rate for the paediatrics specialty hospital, although this was likely due to a low number of prescribed items. Dosing errors were the most common error type. Another study reported that prescribing errors were more common in primary care amongst men compared to women.[6] We observed a significantly lower risk for errors in specialist services for women.

In the EQUIP study, multivariate analysis showed that all grades of doctors were more likely to write a prescription containing an error than consultants.[3] A retrospective study which evaluated errors on discharge prescriptions found no significant difference in error rates between prescriber grades, although no senior (consultant) level prescribers were included.[15] In primary care, the grade of general practitioner was not associated with prescribing errors.[6] We observed no significant difference in prescribing error rates between prescriber grades, when compared to newly qualified prescribers. EQUIP also reported that medication orders issued at acute admission were 70% more likely to be associated with a prescribing error.[3] Another study found lower error rates on discharge prescription items than was observed with general inpatient prescribing, due to a lower rate of medication omission, however these factors were not corrected for the number of items on each prescription.[2] We observed a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16, although this did not reach significance in multivariate analysis.

In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing error increasing by 14% for every additional medication item prescribed. Complex polypharmacy is becoming increasingly common, with patients potentially requiring management for multiple chronic conditions

simultaneously. In these patients, vigilance for prescribing errors and pharmacist review is of particular importance.

Our study was limited by missing data (one acute hospital failed to return data on number of items on each prescription), and although pharmacists had received some basic training in completing the evaluations, *post-hoc* analyses suggested significant variability between pharmacists' classification of errors, and especially in assignment of severity classification. Two of us independently revised each prescribing error and noted a tendency to over-estimate the severity of errors, and (in keeping with EQUIP criteria) included in our evaluations an assessment of whether or not a wrong dose was likely to have been actually administered based on tablet burden. We also refined EQUIP criteria to assign severity ratings to error categories where these had previously not been provided. Finally, in order to limit the impact of error misclassification on study findings, the original 29 error categories were batched into 10 different types of error groups relating to key components of prescribing. Since our data collection forms did not allow us to evaluate errors which had been missed, it is possible that our observed error rates may represent an under-estimate of the true burden of prescribing error.

Medication omission was the most prevalent error, representing 26.9% of all errors observed, which is consistent with previous reports. [2 15] Prescribing during acute admission in the absence of a full medication history may sometimes be unavoidable, and does not necessarily constitute an error. For this reason we discriminated between 'emergency' prescribing, and errors where a more complete or accurate medication history would have prevented omission of prescribed medications. Although we sought to capture only unintended medication omission, it is possible that there might still have been cases where the omission was intentional (for example, suspension of diuretics in a patient who was hypotensive or dehydrated on admission) but this intent had been missed by the pharmacist collecting the data. A sensitivity analysis showed that if all errors of medication omission either on discharge or admission were excluded, the number of errors totals 2249 (0.53 per prescription written); with 1471 (34.7%) prescriptions containing at least one error, which represents a significant reduction in overall prescribing error rate. A core role for clinical ward based pharmacists is medicines reconciliation for admitted patients. This involves detailed medication history taking, recording of full medication list in the patient's case notes, and discussion with the clinical team to ensure that all regular medicines are prescribed throughout the admission, if appropriate. Similarly, on discharge, pharmacists ensure that necessary regular medicines are continued, and that any medicines newly started during the admission are prescribed for discharge as appropriate. The majority of the omission errors reported will have been rectified during admission or prior to discharge, as a result of the pharmacist clinical check. This highlights the importance of medicines reconciliation as soon as practicable at hospital admission, in order to minimise the possibility of missed doses of essential medicines. The role of pharmacists in acute admission settings may therefore be of particular benefit.

EQUIP error categories which could potentially be eliminated by introduction of electronic prescribing (strength/dose missing, product/formulation not specified, no signature, start date incorrect/missing, incorrect route, IV instructions incorrect/missing) accounted for 357 (11.9%) of the 3011 errors observed. A further 376 (12.5%) errors could be reduced by electronic prescribing, via alerts, cautions and required fields at the patient entry/prescribing stage, although many of these can be over-ridden by the prescriber.[23] These include: administration times missing/incorrect, duplication, CD requirements incorrect/missing. The

extent to which electronic prescribing can eliminate particular error types depends on the individual systems used. Importantly, whilst electronic prescribing systems could potentially have prevented up to a quarter of errors, these systems are best utilised alongside rather than instead of existing safeguards. We did not formally evaluate differences in error rates between electronic prescribing and paper-based prescribing systems. Although one hospital (Hospital G) was utilising complete electronic prescribing systems on some wards at the time of the study, and many of the other hospitals were using electronically generated discharge summaries, we failed to observe any clear association with error rate, mainly because of the large variability in case mix which impacted directly on the number of items/prescription. In contrast, EQUIP reported that electronic prescriptions were 12% less likely to be associated with a prescribing error than handwritten prescriptions.[3] Although electronic discharge summaries may reduce error due to legibility, they do not eliminate the transcription step from inpatient charts. One study which analysed 1808 handwritten and electronic discharge summaries found no difference in the number or types of errors observed.[15] It is also worth noting that electronic systems, while clearly offering an advantage over conventional medicines management and prescribing systems, have themselves been associated with new patterns of error. Studies in the UK and Australia found a significant reduction in prescribing errors detected after introduction of electronic prescribing systems, but also identified errors specific to the electronic prescribing system used, for example, incorrect product selected from drop-down menu, or incorrect dosing frequency selected.[24-26] These electronic systems will doubtless continue to improve through refinement.[23 27]

The Erice Medication Errors Research Group (EMERGE) recommendations for reducing prescribing errors, includes training and assessment of prescribers, ongoing monitoring, awareness and communication.[14] Health systems which may impact on likelihood of error occurring include European harmonisation of prescribing, introduction of integrated prescription forms, use of IT systems such as electronic prescribing, and standardisation, evaluation, and certification of such systems. Involvement of clinical pharmacists at all points of the medication process is also recommended.[14] The latter is important since all the hospital Trusts in our survey had evolved systems to safeguard patients from prescribing error (regardless of the adoption of electronic prescribing), and this involved use of ward-based pharmacists and dispensary staff to perform routine checks on all prescriptions issued [3 10 22 28]. This likely represents the 'last line of defence' against prescribing error, and has greatest utility when deployed in clinical areas associated with highest risk, for example patients with complex polypharmacy, and hospital admission settings. One fundamental role of clinical pharmacists during acute admission is medicines reconciliation, where a patient's full medication history is determined and recorded using all available sources of information. We found that prescribing errors in secondary care are prevalent, regardless of prescriber grade. Our findings therefore suggest that removing this safeguard (e.g. through service reconfiguration or in an effort to reduce costs) could potentially lead to higher numbers of medication errors actually reaching the patient.

Acknowledgements

We gratefully acknowledge the contributions of pharmacists who participated in this study. This work was funded through an unrestricted educational grant from Mersey Deanery, although design, execution, analysis and reporting was carried out independently by the study team.

We thank Professor David Graham, Postgraduate Medical Dean, Mersey Deanery, for supporting the project

We thank the National Institute of Health Research (NIHR Department of Health) and the Northwest Development Agency (NWDA) for infrastructural and project support.

Declaration

All authors have completed the Unified Competing Interest form and declare that (1) SK has received research funding for website development from Merck, Bristol Myers Squibb, Gilead, ViiV, Tibotec, and Abbott, and honoraria, travel support for conference attendance from Roche, Tibotec, and Viiv in the past 3 years. All other authors have nothing to declare

TK and SHK developed the study concept, ML, SJ, AMc, AR, JS, AG, CC, BT co-ordinated data collection, KS, SHK analysed the data, JJK undertook the main statistical analysis with tabulations produced by KS. KS, SHK prepared the manuscript. JJK was involved in substantial revisions of the manuscript. TK, ML, SJ, AMc, AR, JS, AG, CC, BT reviewed the manuscript, SHK Is the guarantor for the project.

All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis

Data sharing: all requests for data sharing to Professor SH Khoo (khoo@liv.ac.uk)

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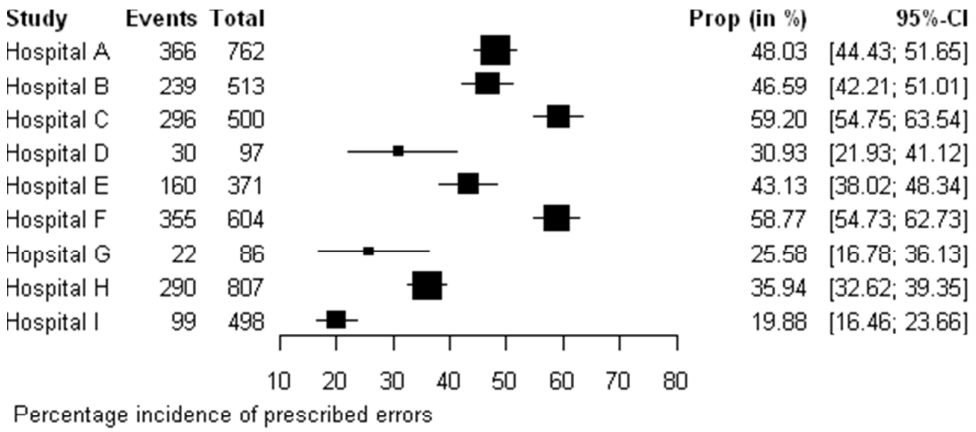

Figure 1. Forest plot showing prescribing error rates in nine hospitals across North West England.

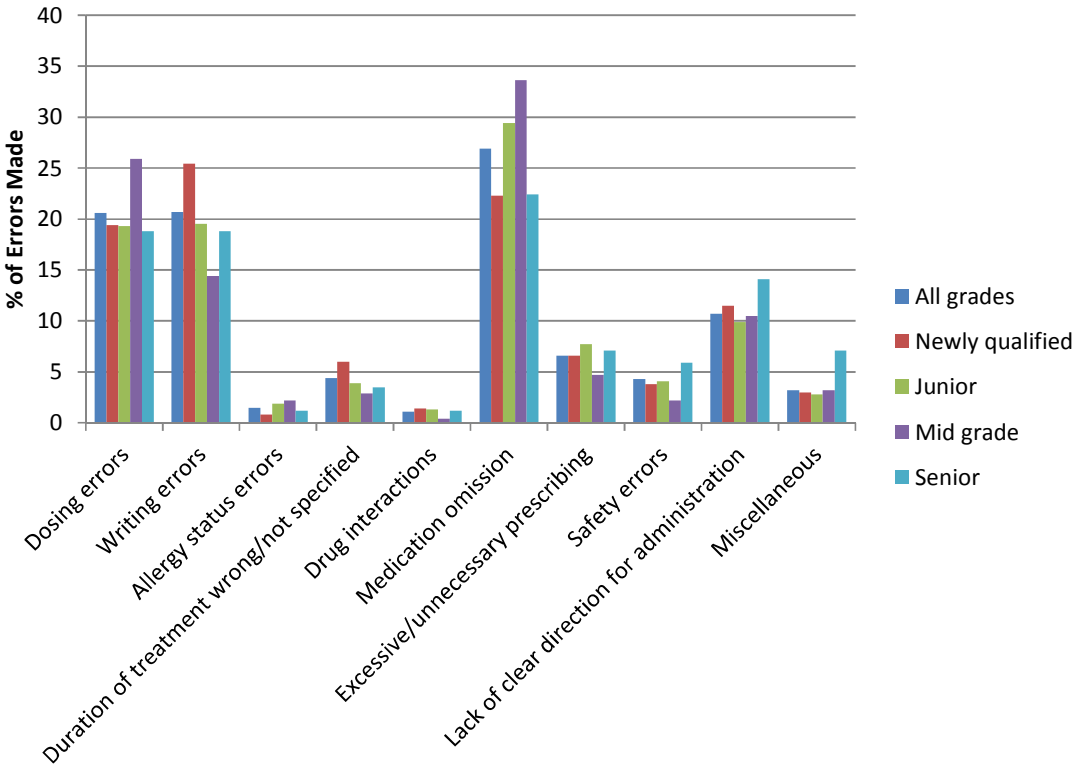

Figure 2. Categories of prescribing errors made by different grades of prescriber

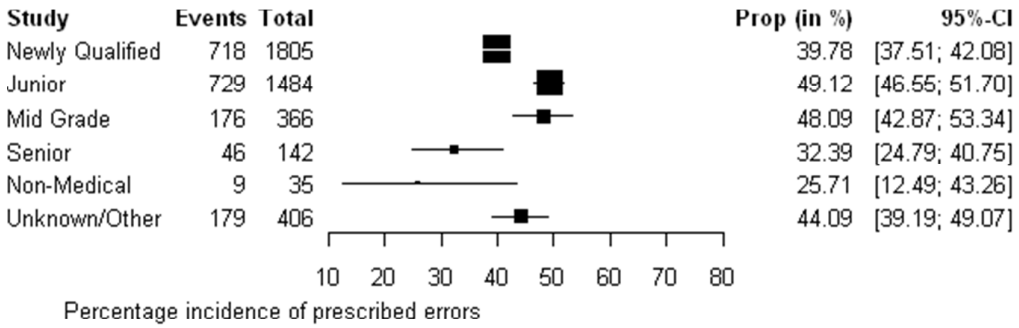

Figure 3. Forest plot showing prescribing error rates made by different prescriber grades

Table 1. Types of hospitals contributing prescription data

Teaching Hospitals	District Hospitals	Specialist Hospitals (Women, Paediatrics, Mental Health)
Hospital A	Hospital B	Hospital D
Hospital C	Hospital E	Hospital G
Hospital H	Hospital F	Hospital I

Table 2. Application of error categories and severity ratings for the Mersey Deanery Prescribing Audit

Modified EQUIP Error Category	Original EQUIP Error Category	Includes/Excludes	Severity (EQUIP)	Severity Modification
1. Dosing Errors	Underdose		**Minor** if unable/unlikely to carry out (units); **Significant** if dose too low to treat the condition; **Serious** if patient in acute distress; **Potentially Lethal** if medication life saving	
	Overdose	Excludes overdoses caused by duplication eg. Paracetamol with co-codamol	**Minor** if unable/unlikely to carry out (units); **Significant** - low TI, ½-4 times; **Serious**- Low TI, 4-10 times; errors in units if chance dose could be given; **Potentially Lethal** if v.low TI and dose 10 times normal dose, results in serum levels of drug in severe toxicity range, or has high potential to cause cardiopulmonary arrest	**Minor** if effect of dosing expected to be minimal
	Dose/rate mismatch		-	Judgement used based on Equip severity categories
2. Writing Errors	Strength/dose missing	Includes dose units missing	**Minor**	
	Product/formulation not specified		-	**Minor**
	Incorrect formulation		-	**Minor** unless formulation likely to have implication on treatment eg. Insulin, co-careldopa, in which case **significant/serious** based on potential consequence
	No signature		-	**Significant** (governance issue)
	Start date incorrect/missing		-	**Minor**
	CD requirements incorrect/missing		-	**Minor**
3. Allergy status missing/significant allergy	Significant allergy	Includes allergy status not completed, or where a drug has been prescribed despite an allergy to that drug/class	-	**Significant** allergy status/specific allergy missed off prescription; **Serious** if patient prescribed agent allergic to; **Potentially Lethal** if patient prescribed drug which previously had severe

				reaction to eg. oedema
4. Duration of treatment wrong/not specified	Continuation for longer than needed	Includes no stop/review date for antibiotics, steroids etc	-	**Minor** if continuation of the medicine or the duration represents little potential for harm; **Significant** if continued >3 days longer than needed for medication such as: antibiotics, oral steroids, LMWH, potassium; **Serious** if ongoing treatment could cause serious harm
	Premature discontinuation	Includes drugs stopped without appropriate reducing course	-	**Minor** if discontinuation is unlikey to have a significant clinical impact; **Significant** if duration of treatment insufficient to treat condition eg. Antibiotics, or if no reducing course eg. Oral steroids
5. Drug Interactions	Drug interaction	Excludes 2 items prescribed from same class e.g omeprazole with lansporazole (Duplication)	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-drug interaction	**Significant** if manufacturer advises the combination is contraindicated, should be avoided, or advises caution; **Serious** if adverse events highly probable
	Drug interaction not taken into account	As above: unable to differentiate drug interaction and drug interaction not taken into account from available data		
6. Omission of medication	Omission on admission		**Significant** (regular medication)	-
	Omission on discharge		**Significant**	-
	Drug not prescribed but indicated		-	**Minor** if medication is unlikely to significantly impact patient care; **Significant** if medication would have significant impact on clinical course **Serious** if medication would alleviate a serious condition /patient is in acute distress; **Potentially lethal** if medication is potentially life saving
7. Excessive/ unnecessary	Duplication	Includes a second agent prescribed which contains an ingredient already being taken; 2 drugs prescribed from the same class/with same clinical	**Minor** if duplicate therapy prescribed without potential for increased adverse events	**Significant, Serious, Potentiallylethal:** As for overdose when duplicated items co-administered (3)

prescribing		effect eg. Lansoprazole + omeprazole		
	Unintentional prescription of drug	Drug prescribed was not that desired. Includes prescription of a discontinued drug, excluding discontinuation due to ADR , or course is too long	-	Judgement used based on Equip severity categories
8. Clinical Safety Errors	No maximum dose	Excludes prescriptions with no frequency (administration times missing/incorrect)	**Minor**- order lacked specific drug, dose, strength, frequency or route information	**Significant** if no maximum dose stated for opioids
	Clinical contraindication	Contraindication according to summary of product characteristics	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-disease interaction	**Significant** if administration unlikely to have serious clinical consequences in the given situation
	Continuation after ADR		-	Judgement used based on Equip severity categories
	No dosage alteration after levels out of range		-	Judgement used based on Equip severity categories
9. Lack of clear directions for administration	Administration times incorrect/missing	No frequency/times of dosing incorrect eg. In relation to food, morning vs night.	**Minor**	**Significant** if administration time would be expected to affect treatment eg. Exenatide with meals, hypnotics at night
	Incorrect route		**Minor** if unlikely to be carried out/little chance of toxicity/therapeutic failure; **Significant** if wrong route to treat condition; **Serious** if potential for toxicity	-
	IV instructions incorrect/missing		-	Judgement used based on Equip severity categories
	Route missing		**Minor**- order lacked specific drug, dose, strength, frequency or route information	-
	Daily dose divided incorrectly	Number of dosing intervals incorrect. Excludes under/overdose	-	**Minor** if dosing intervals are not standard, but are unlikely to significantly affect treatment; **Significant** if dosing intervals are inappropriate to treat the condition;

				Serious if medication has narrow TI and dosing intervals may affect toxicity/efficacy eg. Parenteral aminoglycosides
10. Miscellaneous	No indication	Includes PRN medications, where lack of indication on prescription could prevent administration. Excludes failure to write an indication when prescribing antibiotics	-	**Minor** if indication not written up for PRN medication; **Significant** if indication not written up for formulations which are licensed for specific conditions.
	Miscellaneous	Illegible drug details, non-standard abbreviations, patient details incorrect/missing, warfarin fixed dose prescribed.	-	Judgement used based on Equip severity categories

Abbreviations: TI- therapeutic index, CD- controlled drug, ADR- adverse drug reaction, PRN- when required

Table 3. Summary data showing prevalence and severity of errors observed

		Total Prescriptions	One or more error reported		Error Severity				Total errors
			No (%)	Yes (%)	Minor (%)	Significant (%)	Serious (%)	Potentially Lethal (%)	
All		**4238**	**2381 (56.2)**	**1857 (43.8)**	**1264 (42.0)**	**1629 (54.1)**	**109 (3.6)**	**9 (0.3)**	**3011**
Prescriber Grade	Newly Qualified	1805	1087 (60.2)	718 (39.8)	519 (48.8)	507 (47.7)	35 (3.3)	3 (0.3)	1064
	Junior	1484	755 (50.9)	729 (49.1)	496 (39.2)	725 (57.4)	41 (3.2)	2 (0.2)	1264
	Mid Grade	366	190 (51.9)	176 (48.1)	93 (33.6)	166 (59.9)	15 (5.4)	3 (1.1)	277
	Senior	142	96 (67.6)	46 (32.4)	36 (42.4)	43 (50.6)	6 (7.1)	0 (0)	85
	Non-medical	35	26 (74.3)	9 (25.7)	8 (57.1)	5 (35.7)	1 (7.1)	0 (0)	14
	unknown/other	406	227 (55.9)	179 (44.1)	112 (36.5)	183 (59.6)	11 (3.6)	1 (0.3)	307
Training	Liverpool	1290	787 (61.0)	503 (39.0)	270 (35.4)	456 (59.8)	36 (4.7)	1 (0.1)	763
	Non-Liverpool	922	478 (51.8)	444 (48.2)	342 (43.8)	420 (53.8)	19 (2.4)	0 (0)	781
	Unknown	2026	1118 (55.2)	908 (44.8)	652 (44.4)	753 (51.3)	54 (3.7)	8 (0.5)	1467
Admission/ Discharge	Discharge	2467	1615 (65.5)	852 (34.5)	685 (52.5)	584 (44.8)	32 (2.5)	4 (0.3)	1305
	Admission	1744	756 (43.4)	988 (56.7)	576 (34.2)	1030 (61.1)	75 (4.4)	5 (0.3)	1686
	Unknown	27	12 (44.44)	15 (55.55)	3 (15)	15 (75)	2 (10)	0 (0)	20
Ward Area	Medicine	2059	1083 (52.6)	976 (47.4)	634 (39.0)	921 (56.7)	64 (3.9)	6 (0.37)	1625

	Surgery	1395	836 (59.9)	559 (40.1)	448 (50.1)	417 (46.6)	27 (3.0)	2 (0.2)	894
	Mental health	96	66 (68.8)	30 (31.3)	24 (60)	16 (40)	0 (0)	0 (0)	40
	Accident & Emergency	8	1 (12.5)	7 (87.5)	1 (9.1)	10 90.9	0 (0)	0 (0)	11
	Critical care	17	14 (82.4)	3 (17.7)	1 (25.0)	3 (75.0)	0 (0)	0 (0)	4
	Unknown	663	383 (57.8)	280 (42.2)	156 (35.7)	262 (60.0)	18 (4.1)	1 (0.2)	437
Prescription contains[#]	Antibiotic	724	301 (41.6)	423 (58.4) (**Antibiotic**: 130 (18.0))	57 (29.8)	118 (61.8)	16 (8.4)	0 (0)	191
	Insulin	129	42 (32.6)	87 (67.4) **Insulin**: 20 (15.5)	12 (37.5)	19 (59.4)	1 (3.1)	0 (0)	32
	Warfarin	196	71 (36.2)	125 (63.8) **Warfarin**: 18 (9.2)	6 (23.1)	16 (61.5)	4 (15.4)	0 (0)	26
	Oxygen	36	7 (19.4)	29 (80.6) **Oxygen**: 2 (5.6)	1 (14.3)	5 (71.4)	1 (14.3)	0 (0)	7

* Relates to errors per prescriptions written, not errors per number of items prescribed

Error severities, total errors and error rates relate to errors associated with Antibiotics/Insulin/Warfarin/Oxygen only

Table 4. Summary of the Errors Observed which were Considered to be Potentially Lethal

Error Description	Category	Prescriber Grade	Ward Area	Admission/ Discharge
Gliclazide 400mg prescribed when 40mg needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Digoxin 625micrograms prescribed when 62.5micrograms needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Oxycodone 500mg prescribed: overdose	1- Dosing Errors	Mid Grade	Surgery	Admission
Methotrexate prescribed daily, not weekly	1- Dosing Errors	Junior	Medicine	Admission
Doxazocin prescribed; had been stopped by general practitioner due to angioedema	3. Allergy status missing/ significant allergy	Junior	Medicine	Admission
Phenytoin dose of 300mg daily incorrectly prescribed as 800mg	1- Dosing Errors	Newly Qualified	Medicine	Discharge
Midazolam IV for sedation: overdose	1- Dosing Errors	Mid Grade	Unknown	Admission
Amiodarone loading dose of 200mg three times daily continued as a regular dose	1- Dosing Errors	Other	Surgery	Discharge
Enoxaparin prescribed 1mg/kg once daily instead of 1mg/kg twice daily for a patient with acute coronary syndrome	1- Dosing Errors	Mid Grade	Medicine	Admission

Table 5. Univariate statistics showing the significance of explanatory variables in predicting error rates in prescriptions.

Variable	n	≥1 Error	No Error	Difference (95%CI)	p-value
		n (%)	n (%)		
Prescriber Grade (n=3850)		1689	2161		
Newly qualified	1803	716 (42%)	1087 (50%)	-8% (-11.2% to -4.8%)	<0.001
Junior	1482	727 (43%)	755 (35%)	8% (4.9% to 11.1%)	
Mid-grade	366	176 (10%)	190 (8.8%)	1.2% (-0.7% to 3.1%)	
Senior	142	46 (2.7%)	96 (4.4%)	-1.7% (-2.8% to -0.4%)	
Non-medical	35	9 (0.5%)	26 (1.2%)	-0.7% (-1.3% to -0.1%)	
Other	22	15 (0.9%)	7 (0.3%)	0.56% (0.1% to 1.1%)	
Discharge/Admission (n=3065)		1135	1930		
Discharge	2467	853 (75%)	1614 (84%)	-9% (-12.0% to -6.0%)	<0.001
Admission	598	282 (25%)	316 (16%)		
Liverpool trained (n=1325)		518	807		
Liverpool	35	14 (2.7%)	21 (2.6%)	0.1% (-1.7% to 1.9%)	0.911
Non-Liverpool	1290	504 (97%)	786 (97%)		
Hospital (n=4238)		1857	2381		
Hospital A	762	366 (20%)	396 (17%)	3% (0.6% to 5.4%)	<0.001
Hospital B	513	239 (12%)	274 (12%)	0% (-2.0% to 2.0%)	
Hospital C	500	296 (16%)	204 (8.6%)	7.4% (5.4% to 9.4%)	
Hospital D	97	30 (1.6%)	67 (2.8%)	-1.2% (-2.1% to -0.3%)	
Hospital E	371	160 (8.6%)	211 (8.9%)	-0.3% (-2.0% to 1.4%)	
Hospital F	604	355 (19%)	249 (10%)	9% (6.8% to 11.2%)	
Hospital G	86	22 (1.2%)	64 (2.7%)	-1.5% (-2.3% to -0.7%)	
Hospital H	807	290 (16%)	517 (22%)	-6% (-8.4% to -3.6%)	
Hospital I	498	99 (5.3%)	399 (17%)	-11.7% (-13.5% to -9.9%)	
Ward Area (n=3575)		1577	1998		
Medical	2059	977 (62%)	1082 (54%)	8% (4.8% to 11.2%)	<0.001
Surgical	1395	560 (36%)	835 (42%)	-6% (-9.2% to -2.8%)	
Accident & Emergency	8	7 (0.4%)	1 (0.1%)	0.3% (-0.04% to 0.6%)	
Mental health	96	30 (1.9%)	66 (3.3%)	-1.4% (-2.4% to -0.4%)	
Critical care	17	3 (0.2%)	14 (0.7%)	-0.5% (-0.9% to -0.1%)	
Number of Medicines on Prescription (n=3386) Median (IQR)		8; (4,11) (n=1435)	4; (2,7) (n=1951)	-4 (-4.5, -3.5)	<0.001

n= number of prescriptions

Table 6. Multivariate logistic regression analysis for predicting error rates in prescriptions.

Variable	Odds ratio (95%CI)	p-value
Hospital		
Hospital H	1	
Hospital A	Not estimable*	
Hospital B	1.11 (0.78 to 1.58)	0.57
Hospital C	2.38 (1.63 to 3.46)	<0.001
Hospital D	0.64 (0.13 to 3.06)	0.57
Hospital E	1.39 (0.96 to 2.01)	0.08
Hospital F	3.53 (2.63 to 4.73)	<0.001
Hospital G	1.80 (1.03 to 3.12)	0.04
Hospital I	1.11 (0.73 to 1.70)	0.62
Prescriber Grade		
Newly qualified	1	
Junior	1.06 (0.85 to 1.32)	0.61
Mid-grade	0.96 (0.64 to 1.44)	0.83
Senior	0.97 (0.58 to 1.63)	0.92
Non-medical	0.59 (0.21 to 1.64)	0.31
Other	1.50 (0.53 to 4.23)	0.44
Discharge/Admission	1.16 (0.70 to 1.92)	0.58
Number of prescribed items	1.14 (1.12 to 1.17)	<0.001

Analysis contains only 2127 records (50.2%) where complete data was provided for all variables

* Trust provided no data on number of prescription items

Cross Sectional Study of Prescribing Errors in Patients Admitted to Nine Hospitals Across North West England

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Article Summary

1. Article Focus

- Some studies have reported lower error rates with more senior prescriber grades, and insufficient undergraduate prescriber training as a potential risk for prescribing errors
- Prescriptions frequently contain multiple medications, but data about errors on complete prescriptions (all prescribed items on an inpatient chart or discharge prescription), which give a better estimate of numbers of patients at risk of harm, are lacking
- We aimed to determine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge and type of medication prescribed

2. Key Messages

- We observed an error rate of 10.9% per prescribed item, with only 56.2% of 4238 complete prescriptions remaining error free.
- In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription.
- We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues.

3. Strengths and Limitations

- This was a large study across nine diverse hospital settings
- We determined the rate of errors on complete prescriptions as well as for individually prescribed items, giving a better estimate of the numbers of patients affected by errors.
- We did not evaluate the impact of electronic prescribing on the prevalence and type of prescribing errors, however up to a quarter of the errors observed could potentially have been avoided through use of electronic prescribing and medicines administration systems

Abstract

Objective To evaluate the prevalence, type and severity of prescribing errors observed between grades of prescriber, ward area, admission or discharge, and type of medication prescribed

Design Ward-based clinical pharmacists prospectively documented prescribing errors at the point of clinically checking admission or discharge prescriptions. Error categories and severities were assigned at the point of data collection, and verified independently by the study team

Setting Prospective study of nine diverse National Health Service (NHS) hospitals in North West England, including teaching hospitals, district hospitals and specialist services for paediatrics, women and mental health.

Results Of 4238 prescriptions evaluated, one or more error was observed in 1857 (43.8%) prescriptions, with a total of 3011 errors observed. Of these, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and 9 (0.30%) were potentially life-threatening. The majority of errors considered to be potentially lethal (n=9) were dosing errors (n=8), mostly relating to overdose (n=7). The rate of error was not significantly different between newly qualified doctors compared with junior, middle grade or senior doctors. Multivariable analyses revealed the strongest predictor of error was the number of items on a prescription (risk of error increased 14% for each additional item). We observed a high rate of error from medication omission, particularly amongst patients admitted acutely into hospital. Electronic prescribing systems could potentially have prevented up to a quarter of (but not all) errors.

Conclusions In contrast to other studies, prescriber experience did not impact on overall error rate (although there were qualitative differences in error category). Given that multiple drug therapies are now the norm for many medical conditions, health systems should introduce and retain safeguards which detect and prevent error, in addition to continuing training and education, and migration to electronic prescribing systems.

Introduction

Prescribing errors are common, with systematic reviews suggesting that as many as 50% of hospital admissions and 7% of medication orders are affected.[1] In recent studies, prescribing errors have been found to affect approximately 9-15% of medication orders for hospital inpatients in the United Kingdom (UK).[2 3] Over one third of 651 patients were found to have a prescribing error occurring at hospital admission in the United States (US).[4] Prescribing errors are also prevalent in primary care, affecting 37% of 9385 prescriptions in the US,[5] and one in eight patients (one in 20 prescription items) in the UK.[6] A study in the Netherlands evaluating medication omission errors in elderly patients admitted to hospital reported adverse consequences in 21% of 100 patients.[8]

Human error in healthcare may be considered in the context of individuals or health systems.[9-11] While personal factors such as forgetfulness, inattention, poor motivation, carelessness, negligence, and recklessness are important, a health systems approach more comprehensively addresses recurrent errors and organisation factors and processes which may give rise to that error. The person, the team, the task, the workplace and the institution as a whole are considered, [9] which identify weaknesses in the system's defences.[9] For example, higher hospital mortality at weekends may be associated with lower numbers of senior staff available outside of the normal working week.[12 13] Barriers which may prevent medication errors, or prevent errors from reaching the patient, may include electronic prescribing alerts, and prescription review by clinical pharmacists.

Data on factors which may contribute to prescribing errors, for example differences between grades of prescriber, ward area, admission or discharge and type of medication prescribed are sparse.[3 14 15] Existing data suggest that newly qualified and junior doctors are twice as likely to make prescribing errors than senior doctors, taking into account the larger volume of prescriptions written by junior prescriber grades.[3] Provision of sufficient undergraduate training to allow medical students to become safe prescribers when they begin work as newly qualified doctors is widely recognised as an important factor in reducing prescribing errors.[14 16-18] Teaching in UK medical schools has changed considerably over the last decade, with the General Medical Council stipulating that medical students must be adequately prepared to prescribe drugs and manage risk at the point of graduation.[19 20]

Whilst previous studies have evaluated error for individual medications, few studies have systematically evaluated complete prescriptions (all items included on a single inpatient prescription chart or discharge prescription at the time of clinical pharmacist check) to evaluate factors associated with prescribing error.[1-3] This is important as it gives a more accurate estimate of the numbers of patients who are potentially put at risk of harm by prescribing errors. We undertook a prospective survey of prescribing errors in nine diverse National Health Service (NHS) hospitals in the North West of England, aiming to examine the differences in prescribing error rates between grades of prescriber, ward area, admission or discharge, hospitals and the type and number of medicines prescribed. In order to further evaluate the role of undergraduate training, we also tested for a relationship between occurrence of error and medical school training of prescribers. As approximately 30% of the prescribers were trained at the local institution, the University of Liverpool, whether medical training was undertaken at this institution was included in the analysis. Univariate analysis and multivariate logistic regression was used to evaluate factors associated with prescribing errors.

Methods

Setting

A total of nine NHS hospitals from the Merseyside and Cheshire region took part in the audit. These comprised large teaching hospitals, general hospitals, specialist centres for paediatrics, women's health and mental health (Table 1). One hospital was using complete electronic prescribing systems (inpatient prescribing, medication ordering, discharge prescriptions) on some wards at the time of the audit. Eight of the hospitals were using paper prescription charts for inpatients and either handwritten or transcribed electronically generated discharge prescriptions. In this setting, ward-based clinical pharmacists check inpatient prescriptions at, or soon after patient admission, when medicines reconciliation is undertaken. Inpatient prescription charts are then checked at least daily by the pharmacist. Discharge prescriptions are checked and authorised by a clinical pharmacist prior to supply of medication. Pharmacists may amend or clarify some aspects of prescribing, or discuss with the clinical team any recommendations or safety issues at these points of care. Clinical pharmacists may also participate in ward rounds and multidisciplinary team meetings, where prescribing may be discussed with clinicians, clarified or amended.

Data Collection

As this was an audit of unlinked anonymised prescriptions, Ethics approval was not required in accordance with local guidance. We aimed to capture data from all seven hospital trusts in the region. Two additional hospitals adjacent to and linked with healthcare provision in the Merseyside region were also audited. The number of prescriptions audited was empirically determined in order to generate a sample size equivalent to a large study recently undertaken in the UK.[3] In order to audit practice across the region, each hospital was asked to audit a minimum of 400 prescriptions.

We adopted the following definition of prescribing errors for the study, which excludes adherence to local prescribing policy and guidelines: "A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescription writing process, there is an unintentional significant: (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice".[21] A standard questionnaire collected data on error category and severity (based on EQUIP error classifications). The EQUIP study was a large prospective survey of prescribing errors affecting hospital inpatients in the UK,[3] and the error classifications were therefore considered relevant to our setting. Nominated ward-based clinical pharmacists prospectively documented prescribing errors at the point of checking inpatient or discharge prescriptions, during normal pharmacy working hours, therefore each audit form was a point prevalence of prescribing errors at the time of pharmacist clinical check. Acute admission was defined as the first 24 hours in hospital. For all prescription sheets generated in acute admission settings, a separate audit form was completed (to allow for emergency prescribing in the absence of a full drug history without this being recorded as an error) and we sought to record only unintended medication omissions (e.g. following medicines reconciliation with general practices or primary healthcare databases). Hospitals were advised to complete the study on different days of the week throughout the period of the audit, in order to capture an even spread of days. For example data collection would occur weekly, on Monday in week one, Tuesday in week two, Wednesday in week three, in order to minimise double auditing of the same patient on admission to hospital and subsequent admission to a ward. Therefore, if patients were audited twice, an interval of at least one week would separate each audit form, unless their acute admission/inpatient /discharge prescription were audited

on the same day. If items on prescriptions had been previously screened, they would be counted again in any subsequent auditing, though there would be a one week interval since previous auditing, or the patient would be a different stage of hospital admission. All types of medication order were audited, including IV fluids, when required and once only medication.

Prescriber Category

Pharmacists were required to indicate the category of prescribers on data collection forms. For this analysis, prescribers were categorised as follows: newly qualified (foundation year 1, house officers), junior (foundation year 2, specialist or 'core' training years 1 & 2), mid grade (specialist registrars, training fellows), senior (consultant), non-medical (nurse or pharmacist prescribers), other (for example locum doctors for whom grade was unclear) and unknown (no information concerning prescriber recorded).

Grading of prescribing errors

We modified EQUIP study criteria[3] for error categorisation and severity classification by adding or clarifying severity criteria for all error categories, and by grouping errors into ten distinct areas according to stage of the prescribing process (see below and Table 2). 'Exclusion' and 'inclusion' of errors into EQUIP study error types were defined, in order to differentiate categories with potential overlap. Severity ratings were further defined and assigned to each error category based on modified EQUIP study criteria and taking into account the perceptions of the original pharmacist gradings. Severity ratings related to the potential severity, had the error been allowed to progress through to the patient, as the majority of errors were corrected prior to the point of administration. In order to limit misclassification of errors, the original 29 EQUIP categories were batched into 10 different types of error groups as follows: (1) Dosing errors, (2) Writing errors, (3) Allergy status errors, (4) Duration of treatment wrong/not specified, (5) Drug interactions, (6) Omission of medication, (7) Excessive/unnecessary prescribing, (8) Clinical safety errors, (9) Lack of clear directions for administration, (10) a new error category (Miscellaneous) was added (Table 2). The modification and definition of error categories and severities was undertaken by two members of the study team (KS, SK) and agreed by a third (TK).

Despite using a standard set of definitions, we noted discrepancies across various hospitals in both error categorisation and severity rating. In particular there was a tendency to over-report errors and to overestimate their potential severity. This was confirmed by a *post-hoc* inter-rater agreement analysis. A set of six sample prescriptions was generated. A list of 14 sample errors was decided by the study team, including study error type and severity, according to the criteria in Table 2 utilised for analysis of the main study. The errors selected occurred frequently in the main study, and covered a broad range of error categories and severities. Six pharmacists from each participating hospital were asked to each screen the six prescription scenarios containing the 14 errors and to record any observed errors, allocating error types and severities. The exact agreement percentages between category classification, severity classification and both combined were computed to measure the absolute concordances between pharmacist scores against the gold standard assessment.

In order to limit inter-observer bias, all grading and severity of errors identified in the main study were independently reassessed by two members of the study team (KS and SK), with discordant assessments collectively discussed with a third (TK) in order to agree a final categorisation for error type and severity. For severity ratings, the summary of product characteristics for relevant medication was consulted, in order to determine potential

implications of different degrees of overdose, underdose, of drug interactions, and also to confirm clinical contra-indications.

Statistical Analyses

Data were analysed at the prescription level using complete case data. The prevalence and severity of errors observed were tabulated using percentage frequencies. A Forest plot was produced to present the error prevalence rate and 95% confidence interval (95% CI) for each hospital and grade of prescriber. For the formal statistical analysis, when there was more than one error on a prescription, only the most severe error was included. This approach was used to ensure that the errors included in the analysis were independent. In this study, we assessed hospital, prescriber grade (newly qualified, junior, mid-grade, senior, non-medical, other), ward area (medical, surgical, A&E, mental health, critical care), number of prescribed medicines, an indicator to denote whether the prescription was prescribed on admission or on discharge and an indicator to denote whether the prescriber was Liverpool trained or not as potential risk factors. Univariate statistical analyses were performed using a chi-squared test except for continuous data, which were analysed using the Mann-Whitney U test. A multivariate logistic regression model for a prescription error was fitted to the data. Results are given in terms of an odds ratio (OR) and associated 95% CI. All risk factors that were statistically significant ($p<0.1$) in the univariate analysis were considered for inclusion in the multivariate model with the exception of ward area as a number of hospitals only reported a single specialty type.

All statistical analysis was carried out using the statistical software package SPSS (version 20) using a two-sided significance level of 0.05 (5%) throughout.

Results

Error Classification

During the *post-hoc* inter-rater agreement analysis, approximately 75% of error categories were correctly identified by pharmacists when compared to the standards. Only 47% of severity ratings were concordant with the standards, and 40% of pharmacists rated both error category and severity in concordance with the standards.

Re-assessment of errors by the study team resulted in exclusion of a total of 143 errors which were not considered true errors of the process of prescribing. The error category was re-graded for 434 errors, and severity was re-graded for 724 errors, which was predominantly a down-grading.

Descriptive data and severity of errors

A total of 4238 prescriptions were evaluated; of these, 1857 (43.8%) prescriptions contained at least one error (Table 3). The overall prevalence of prescribing errors (number of prescriptions with one or more error/prescriptions evaluated) ranged from 20% to 60% across the nine hospitals (Figure 1). The rate of errors per prescribed item was 10.9%.

A total of 3011 individual errors were observed within the 1857 prescriptions containing an error. Of these 3011 errors, 1264 (41.9%) were minor, 1629 (54.1%) were significant, 109 (3.6%) were serious and nine (0.30%) were potentially life-threatening (Table 3). Details of all potentially life-threatening errors are listed in Table 4 and mainly comprised dosing errors (n=8), particularly overdose (n=7), with one incidence of under dose. A further error considered to be potentially lethal related to prescription of a medicine to which the patient had previously had a serious allergic reaction.

The proportion of errors categorised with severity as significant or higher by prescriber grade were as follows: all prescribers 58.0%, newly qualified 51.2%, junior 60.8%, mid grade 66.4%, senior 57.6% (χ^2_{trend} $p<0.001$ for univariate analysis, although this association disappeared when corrected for other potential confounders)(Table 3).
Fewer errors were observed on discharge prescriptions than on prescriptions written on admission. More errors were observed in prescriptions containing antibiotics, insulin, warfarin and oxygen, although this does not take into account the number of items on each prescription. Whether doctors were Liverpool trained or not did not affect the number of errors observed (Table 3).

Differences in error prevalence and error types were observed in individual participating hospitals. The lowest rates of errors wasere reported for the paediatrics specialty hospital, with 0.07 errors observed per prescribed item, and 0.26 errors observed per prescription. However, in multivariate analysis, there was no significant reduction in error risk and it is likely that the effect could be due to lower number of items per prescription (mean 3.5, vs pooled data: 6.3). The most common error types were dosing errors (30%) and medication omission (23.1%).
Significantly lower risk of errors was observed in the hospital providing specialist services for women (p=0.04, Table 6) in multivariate analysis. One of the lowest error rates per prescription was observed (0.28), although the error rate per prescribed item (0.11) was

equal to that of the pooled data. The most common error type observed was excessive/unnecessary prescribing (50%). No errors of medication omission were observed. This hospital also had a low number of items per prescription (2.4), and was using electronic prescribing systems on some wards.

Error types

The most frequent error types for all prescribers were medication omission, accounting for 26.9%, writing errors accounting for (20.7%) and dosing errors accounting for (20.6%) of all errors recorded. There was little difference in the variability of error types across different prescriber grades (Figure 2).

Risk factor analysis

Results of the univariate analysis are shown in Table 5. Missing data limited inclusion of all reported prescriptions in risk factor analysis, notably as one acute hospital failed to return data on number of items on each prescription. All factors considered appeared to show a significant difference except for ~~medical school training of doctors~~whether doctors had trained in Liverpool, which made no significant difference (p=0.91) to whether an error occurred on the prescription. Multivariate risk factor analysis showed that the likelihood of an error increased for every additional item included on the prescription (OR 1.14, 95% C 1.12, 1.17, p<0.001) (Table 5). Therefore, for each additional item on the prescription, the risk of an error occurring increased by about 14%. There was also a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16 (95% CI 0.70, 1.92, p=0.58), although this difference did not reach statistical significance (Table 6). No significant differences were found in error rates between different prescriber grades, when compared to newly qualified doctors (Figure 2, Figure 3) in multivariate analyses.

Discussion

In this large study, only 56.2% of 4238 prescriptions written had no reported errors. Of the errors recorded, 41.9% were minor, 54.1% significant, 3.6% serious and 0.3% potentially life threatening. It is important to note that severity ratings relate to the potential severity had the error been allowed to progress through to the patient - in fact the majority of errors were corrected prior to the point of administration. In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing error increasing by 14% for every additional medication item prescribed. Where data were available, prescriptions contained an average of 6.3 medication items, although this varied from 2.4 – 7.5 items according to medical specialty surveyed. Uncorrected analyses suggested that errors were frequent in prescriptions containing insulin (15.5%), antibiotics (18%), warfarin (9.2%) and oxygen (5.6%), although these patients were very likely to have been receiving multiple medications. Error rates were highest amongst specialties which prescribed a broad range of medications (e.g. acute medicine, compared to elective surgery), and also differed between different hospital Trusts, with hospitals specialising in paediatrics, maternal health and mental health exhibiting the lowest error

rates. However, when corrected for number of medications, these differences did not remain significant, with the exception of maternal health.

The most frequent error encountered was unintended medication omission following acute hospital admission (0.97 errors/prescription written, versus 0.53 for discharge medications). When adjusted in multivariable analyses (Table 6) there was no statistically significant difference in error rates between admission and discharge. We found no overall difference in error rate amongst different grades of prescriber, and newly qualified doctors were not more likely to make errors than their senior colleagues. Although numbers were relatively small, we observed no difference in error rate amongst newly qualified doctors by undergraduate training, and doctors trained in Liverpool were neither more nor less likely to commit medication errors. The categories and severity of errors made by different prescriber grades were broadly similar (Table 3, Figure 2), however some differences were observed. For example, writing errors were more frequently observed with newly qualified doctors, medication omission was more frequently observed with junior and mid grade doctors, and dosing errors were more frequently observed with mid grade doctors.

These results are consistent with previously published studies. Both the EQUIP and PRACtICe Studies[3 6] reported error rates of approximately 1 in 10 medications prescribed (we observed a rate of 10.9%). Given the high number of medications prescribed (mean of 6.3 items/prescription) nearly half of all prescriptions contained at least one error.
A systematic review found prescribing errors to be more common in adults than in children.[1] A study in Spain comparing paediatric wards with obstetrics found that paediatric patients had a fourfold higher risk of serious errors than the maternity population (2.3% vs 14.3%), which were mainly related to drug dosing.[22] ~~This is in keeping with our data, as w~~We observed a low error rate for the paediatrics specialty hospital, although this was likely due to a low number of prescribed items. Dosing errors were the most common error type. Another study reported that prescribing errors were more common in primary care amongst men compared to women.[6] We observed a significantly lower risk for errors in specialist services for women.

In the EQUIP study, multivariate analysis showed that all grades of doctors were more likely to write a prescription containing an error than consultants.[3] A retrospective study which evaluated errors on discharge prescriptions found no significant difference in error rates between prescriber grades, although no senior (consultant) level prescribers were included.[15] In primary care, the grade of general practitioner was not associated with prescribing errors.[6] We observed no significant difference in prescribing error rates between prescriber grades, when compared to newly qualified prescribers. EQUIP also reported that medication orders issued at acute admission were 70% more likely to be associated with a prescribing error.[3] Another study found lower error rates on discharge prescription items than was observed with general inpatient prescribing, due to a lower rate of medication omission, however these factors were not corrected for the number of items on each prescription.[2] We observed a trend towards errors being more likely to occur on admission prescriptions than on discharge prescriptions, with an odds ratio (OR) of 1.16, although this did not reach significance in multivariate analysis.

In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing error increasing by 14% for every additional medication item prescribed. Complex polypharmacy is becoming increasingly common, with patients potentially requiring management for multiple chronic conditions

simultaneously. In these patients, vigilance for prescribing errors and pharmacist review is of particular importance.

Our study was limited by missing data (one acute hospital failed to return data on number of items on each prescription), and although pharmacists had received some basic training in completing the evaluations, *post-hoc* analyses suggested significant variability between pharmacists' classification of errors, and especially in assignment of severity classification. Two of us independently revised each prescribing error and noted a tendency to over-estimate the severity of errors, and (in keeping with EQUIP criteria) included in our evaluations an assessment of whether or not a wrong dose was likely to have been actually administered based on tablet burden. We also refined EQUIP criteria to assign severity ratings to error categories where these had previously not been provided. Finally, in order to limit the impact of error misclassification on study findings, the original 29 error categories were batched into 10 different types of error groups relating to key components of prescribing.~~Finally, by grouping errors into categories according to their origin, we sought to reduce misclassification as far as possible.~~ Since our data collection forms did not allow us to evaluate errors which had been missed, it is possible that our observed error rates may represent an under-estimate of the true burden of prescribing error.

Medication omission was the most prevalent error, representing 26.9% of all errors observed, which is consistent with previous reports. [2 15] Prescribing during acute admission in the absence of a full medication history may sometimes be unavoidable, and does not necessarily constitute an error. For this reason we discriminated between 'emergency' prescribing, and errors where a more complete or accurate medication history would have prevented omission of prescribed medications. Although we sought to capture only unintended medication omission, it is possible that there might still have been cases where the omission was intentional (for example, suspension of diuretics in a patient who was hypotensive or dehydrated on admission) but this intent had been missed by the pharmacist collecting the data. A sensitivity analysis showed that if all errors of medication omission either on discharge or admission were excluded, the number of errors totals 2249 (0.53 per prescription written); with 1471 (34.7%) prescriptions containing at least one error, which represents a significant reduction in overall prescribing error rate. A core role for clinical ward based pharmacists is medicines reconciliation for admitted patients. This involves detailed medication history taking, recording of full medication list in the patient's case notes, and discussion with the clinical team to ensure that all regular medicines are prescribed throughout the admission, if appropriate. Similarly, on discharge, pharmacists ensure that necessary regular medicines are continued, and that any medicines newly started during the admission are prescribed for discharge as appropriate. The majority of the omission errors reported will have been rectified during admission or prior to discharge, as a result of the pharmacist clinical check. This highlights the importance of medicines reconciliation as soon as practicable at hospital admission, in order to minimise the possibility of missed doses of essential medicines. The role of pharmacists in acute admission settings may therefore be of particular benefit.

EQUIP error categories which could potentially be eliminated by introduction of electronic prescribing (strength/dose missing, product/formulation not specified, no signature, start date incorrect/missing, incorrect route, IV instructions incorrect/missing) accounted for 357 (11.9%) of the 3011 errors observed. A further 376 (12.5%) errors could be reduced by electronic prescribing, via alerts, cautions and required fields at the patient entry/prescribing stage, although many of these can be over-ridden by the prescriber.[23] These include:

administration times missing/incorrect, duplication, CD requirements incorrect/missing. The extent to which electronic prescribing can eliminate particular error types depends on the individual systems used. Importantly, whilst electronic prescribing systems could potentially have prevented up to a quarter of errors, these systems are best utilised alongside rather than instead of existing safeguards. We did not formally evaluate differences in error rates between electronic prescribing and paper-based prescribing systems. Although one hospital (Hospital G) was utilising complete electronic prescribing systems on some wards at the time of the study, and many of the other hospitals were using electronically generated discharge summaries, we failed to observe any clear association with error rate, mainly because of the large variability in case mix which impacted directly on the number of items/prescription. In contrast, EQUIP reported that electronic prescriptions were 12% less likely to be associated with a prescribing error than handwritten prescriptions.[3] Although electronic discharge summaries may reduce error due to legibility, they do not eliminate the transcription step from inpatient charts. One study which analysed 1808 handwritten and electronic discharge summaries found no difference in the number or types of errors observed.[15] It is also worth noting that electronic systems, while clearly offering an advantage over conventional medicines management and prescribing systems, have themselves been associated with new patterns of error. Studies in the UK and Australia found a significant reduction in prescribing errors detected after introduction of electronic prescribing systems, but also identified errors specific to the electronic prescribing system used, for example, incorrect product selected from drop-down menu, or incorrect dosing frequency selected.[24-26] These electronic systems will doubtless continue to improve through refinement.[23 27]

The Erice Medication Errors Research Group (EMERGE) recommendations for reducing prescribing errors, includes training and assessment of prescribers, ongoing monitoring, awareness and communication.[14] Health systems which may impact on likelihood of error occurring include European harmonisation of prescribing, introduction of integrated prescription forms, use of IT systems such as electronic prescribing, and standardisation, evaluation, and certification of such systems. Involvement of clinical pharmacists at all points of the medication process is also recommended.[14] The latter is important since all the hospital Trusts in our survey had evolved systems to safeguard patients from prescribing error (regardless of the adoption of electronic prescribing), and this involved use of ward-based pharmacists and dispensary staff to perform routine checks on all prescriptions issued [3 10 22 28]. This likely represents the 'last line of defence' against prescribing error, and has greatest utility when deployed in clinical areas associated with highest risk, for example patients with complex polypharmacy, and hospital admission settings. One fundamental role of clinical pharmacists during acute admission is medicines reconciliation, where a patient's full medication history is determined and recorded using all available sources of information. We found that prescribing errors in secondary care are prevalent, regardless of prescriber grade. Our findings therefore suggest that removing this safeguard (e.g. through service reconfiguration or in an effort to reduce costs) could potentially lead to higher numbers of medication errors actually reaching the patient.

Acknowledgements

We gratefully acknowledge the contributions of pharmacists who participated in this study. This work was funded through an unrestricted educational grant from Mersey Deanery, although design, execution, analysis and reporting was carried out independently by the study team.

We thank Professor David Graham, Postgraduate Medical Dean, Mersey Deanery, for supporting the project

We thank the National Institute of Health Research (NIHR Department of Health) and the Northwest Development Agency (NWDA) for infrastructural and project support.

Declaration

All authors have completed the Unified Competing Interest form and declare that (1) SK has received research funding for website development from Merck, Bristol Myers Squibb, Gilead, ViiV, Tibotec, and Abbott, and honoraria, travel support for conference attendance from Roche, Tibotec, and Viiv in the past 3 years. All other authors have nothing to declare

TK and SHK developed the study concept, ML, SJ, AMc, AR, JS, AG, CC, BT co-ordinated data collection, KS, SHK analysed the data, JJK undertook the main statistical analysis with tabulations produced by KS. KS, SHK prepared the manuscript. JJK was involved in substantial revisions of the manuscript. TK, ML, SJ, AMc, AR, JS, AG, CC, BT reviewed the manuscript, SHK Is the guarantor for the project.

All authors, external and internal, had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis

Data sharing: all requests for data sharing to Professor SH Khoo (khoo@liv.ac.uk)

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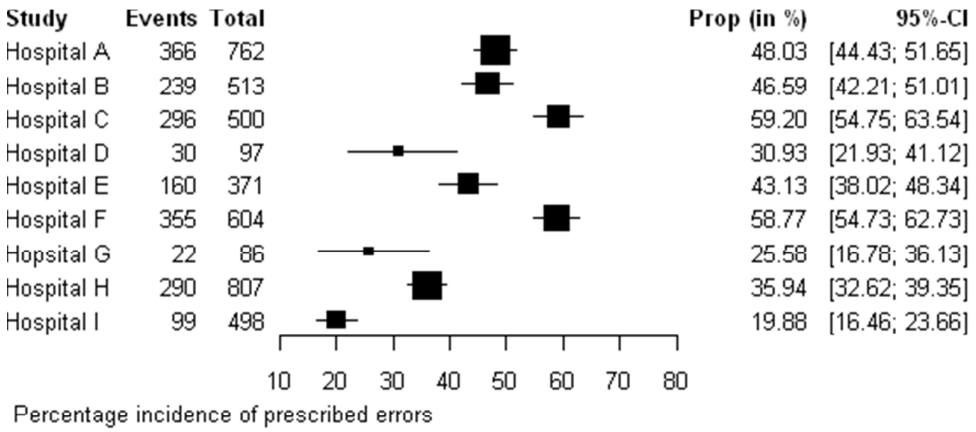

Figure 1. Forest plot showing prescribing error rates in nine hospitals across North West England.

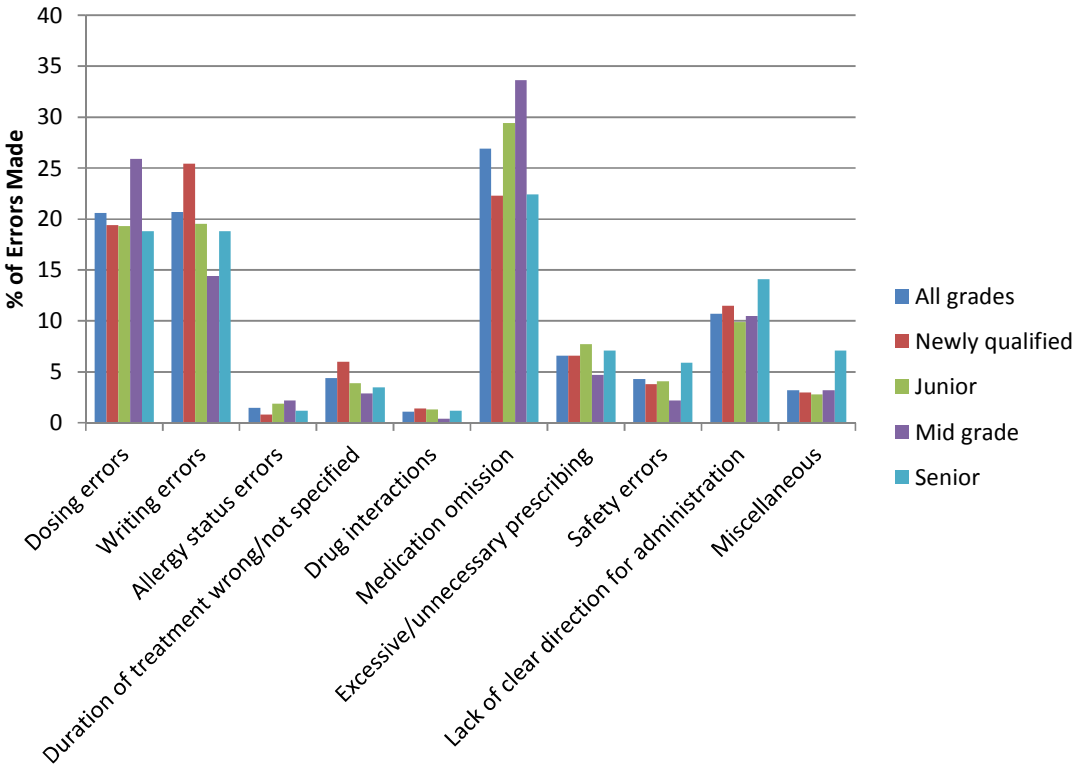

Figure 2. Categories of prescribing errors made by different grades of prescriber

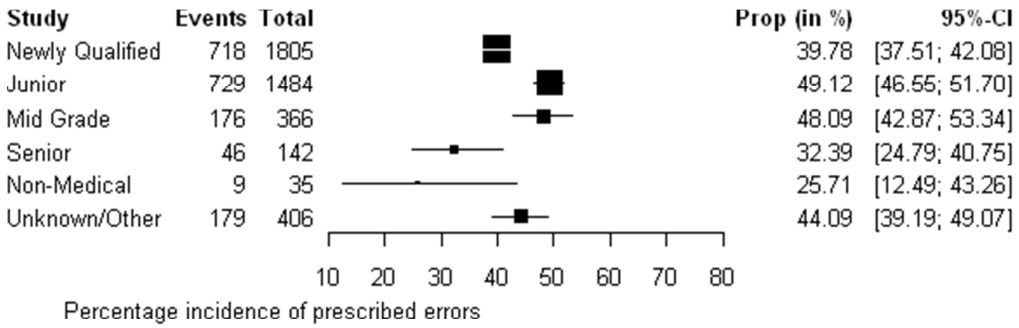

Figure 3. Forest plot showing prescribing error rates made by different prescriber grades

Table 1. Types of hospitals contributing prescription data

Teaching Hospitals	District Hospitals	Specialist Hospitals (Women, Paediatrics, Mental Health)
Hospital A	Hospital B	Hospital D
Hospital C	Hospital E	Hospital G
Hospital H	Hospital F	Hospital I

Table 2. Application of error categories and severity ratings for the Mersey Deanery Prescribing Audit

Modified EQUIP Error Category	Original EQUIP Error Category	Includes/Excludes	Severity (EQUIP)	Severity Modification
1. Dosing Errors	Underdose		**Minor** if unable/unlikely to carry out (units); **Significant** if dose too low to treat the condition; **Serious** if patient in acute distress; **Potentially Lethal** if medication life saving	
	Overdose	Excludes overdoses caused by duplication eg. Paracetamol with co-codamol	**Minor** if unable/unlikely to carry out (units); **Significant** - low TI, ½-4 times; **Serious**- Low TI, 4-10 times; errors in units if chance dose could be given; **Potentially Lethal** if v.low TI and dose 10 times normal dose, results in serum levels of drug in severe toxicity range, or has high potential to cause cardiopulmonary arrest	**Minor** if effect of dosing expected to be minimal
	Dose/rate mismatch		-	Judgement used based on Equip severity categories
2. Writing Errors	Strength/dose missing	Includes dose units missing	**Minor**	
	Product/formulation not specified		-	**Minor**
	Incorrect formulation		-	**Minor** unless formulation likely to have implication on treatment eg. Insulin, co-careldopa, in which case **significant/serious** based on potential consequence
	No signature		-	**Significant** (governance issue)
	Start date incorrect/missing		-	**Minor**
	CD requirements incorrect/missing		-	**Minor**
3. Allergy status missing/significant allergy	Significant allergy	Includes allergy status not completed, or where a drug has been prescribed despite an allergy to that drug/class	-	**Significant** allergy status/specific allergy missed off prescription; **Serious** if patient prescribed agent allergic to; **Potentially Lethal** if patient prescribed drug which previously had severe

				reaction to eg. oedema
4. Duration of treatment wrong/not specified	Continuation for longer than needed	Includes no stop/review date for antibiotics, steroids etc	-	**Minor** if continuation of the medicine or the duration represents little potential for harm; **Significant** if continued >3 days longer than needed for medication such as: antibiotics, oral steroids, LMWH, potassium; **Serious** if ongoing treatment could cause serious harm
	Premature discontinuation	Includes drugs stopped without appropriate reducing course	-	**Minor** if discontinuation is unlikey to have a significant clinical impact; **Significant** if duration of treatment insufficient to treat condition eg. Antibiotics, or if no reducing course eg. Oral steroids
5. Drug Interactions	Drug interaction	Excludes 2 items prescribed from same class e.g omeprazole with lansporazole (Duplication)	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-drug interaction	**Significant** if manufacturer advises the combination is contraindicated, should be avoided, or advises caution; **Serious** if adverse events highly probable
	Drug interaction not taken into account	As above: unable to differentiate drug interaction and drug interaction not taken into account from available data		
6. Omission of medication	Omission on admission		**Significant** (regular medication)	-
	Omission on discharge		**Significant**	-
	Drug not prescribed but indicated		-	**Minor** if medication is unlikely to significantly impact patient care; **Significant** if medication would have significant impact on clinical course **Serious** if medication would alleviate a serious condition /patient is in acute distress; **Potentially lethal** if medication is potentially life saving
7. Excessive/ unnecessary	Duplication	Includes a second agent prescribed which contains an ingredient already being taken; 2 drugs prescribed from the same class/with same clinical	**Minor** if duplicate therapy prescribed without potential for increased adverse events	**Significant, Serious, Potentiallylethal:** As for overdose when duplicated items co-administered (3)

prescribing		effect eg. Lansoprazole + omeprazole		
	Unintentional prescription of drug	Drug prescribed was not that desired. Includes prescription of a discontinued drug, excluding discontinuation due to ADR , or course is too long	-	Judgement used based on Equip severity categories
8. Clinical Safety Errors	No maximum dose	Excludes prescriptions with no frequency (administration times missing/incorrect)	**Minor**- order lacked specific drug, dose, strength, frequency or route information	**Significant** if no maximum dose stated for opioids
	Clinical contraindication	Contraindication according to summary of product characteristics	**Serious** if drug orders could exacerbate a patient's condition eg. Drug-disease interaction	**Significant** if administration unlikely to have serious clinical consequences in the given situation
	Continuation after ADR		-	Judgement used based on Equip severity categories
	No dosage alteration after levels out of range		-	Judgement used based on Equip severity categories
9. Lack of clear directions for administration	Administration times incorrect/missing	No frequency/times of dosing incorrect eg. In relation to food, morning vs night.	**Minor**	**Significant** if administration time would be expected to affect treatment eg. Exenatide with meals, hypnotics at night
	Incorrect route		**Minor** if unlikely to be carried out/little chance of toxicity/therapeutic failure; **Significant** if wrong route to treat condition; **Serious** if potential for toxicity	-
	IV instructions incorrect/missing		-	Judgement used based on Equip severity categories
	Route missing		**Minor**- order lacked specific drug, dose, strength, frequency or route information	-
	Daily dose divided incorrectly	Number of dosing intervals incorrect. Excludes under/overdose	-	**Minor** if dosing intervals are not standard, but are unlikely to significantly affect treatment; **Significant** if dosing intervals are inappropriate to treat the condition;

				Serious if medication has narrow TI and dosing intervals may affect toxicity/efficacy eg. Parenteral aminoglycosides
10. Miscellaneous	No indication	Includes PRN medications, where lack of indication on prescription could prevent administration. Excludes failure to write an indication when prescribing antibiotics	-	**Minor** if indication not written up for PRN medication; **Significant** if indication not written up for formulations which are licensed for specific conditions.
	Miscellaneous	Illegible drug details, non-standard abbreviations, patient details incorrect/missing, warfarin fixed dose prescribed.	-	Judgement used based on Equip severity categories

Abbreviations: TI- therapeutic index, CD- controlled drug, ADR- adverse drug reaction, PRN- when required

Table 3. Summary data showing prevalence and severity of errors observed

		Total Prescriptions	One or more error reported		Error Severity				Total errors
			No (%)	Yes (%)	Minor (%)	Significant (%)	Serious (%)	Potentially Lethal (%)	
All		**4238**	**2381 (56.2)**	**1857 (43.8)**	**1264 (42.0)**	**1629 (54.1)**	**109 (3.6)**	**9 (0.3)**	**3011**
Prescriber Grade	Newly Qualified	1805	1087 (60.2)	718 (39.8)	519 (48.8)	507 (47.7)	35 (3.3)	3 (0.3)	1064
	Junior	1484	755 (50.9)	729 (49.1)	496 (39.2)	725 (57.4)	41 (3.2)	2 (0.2)	1264
	Mid Grade	366	190 (51.9)	176 (48.1)	93 (33.6)	166 (59.9)	15 (5.4)	3 (1.1)	277
	Senior	142	96 (67.6)	46 (32.4)	36 (42.4)	43 (50.6)	6 (7.1)	0 (0)	85
	Non-medical	35	26 (74.3)	9 (25.7)	8 (57.1)	5 (35.7)	1 (7.1)	0 (0)	14
	unknown/other	406	227 (55.9)	179 (44.1)	112 (36.5)	183 (59.6)	11 (3.6)	1 (0.3)	307
Training	Liverpool	1290	787 (61.0)	503 (39.0)	270 (35.4)	456 (59.8)	36 (4.7)	1 (0.1)	763
	Non-Liverpool	922	478 (51.8)	444 (48.2)	342 (43.8)	420 (53.8)	19 (2.4)	0 (0)	781
	Unknown	2026	1118 (55.2)	908 (44.8)	652 (44.4)	753 (51.3)	54 (3.7)	8 (0.5)	1467
Admission/ Discharge	Discharge	2467	1615 (65.5)	852 (34.5)	685 (52.5)	584 (44.8)	32 (2.5)	4 (0.3)	1305
	Admission	1744	756 (43.4)	988 (56.7)	576 (34.2)	1030 (61.1)	75 (4.4)	5 (0.3)	1686
	Unknown	27	12 (44.44)	15 (55.55)	3 (15)	15 (75)	2 (10)	0 (0)	20
Ward Area	Medicine	2059	1083 (52.6)	976 (47.4)	634 (39.0)	921 (56.7)	64 (3.9)	6 (0.37)	1625

	Surgery	1395	836 (59.9)	559 (40.1)	448 (50.1)	417 (46.6)	27 (3.0)	2 (0.2)	894
	Mental health	96	66 (68.8)	30 (31.3)	24 (60)	16 (40)	0 (0)	0 (0)	40
	Accident & Emergency	8	1 (12.5)	7 (87.5)	1 (9.1)	10 90.9	0 (0)	0 (0)	11
	Critical care	17	14 (82.4)	3 (17.7)	1 (25.0)	3 (75.0)	0 (0)	0 (0)	4
	Unknown	663	383 (57.8)	280 (42.2)	156 (35.7)	262 (60.0)	18 (4.1)	1 (0.2)	437
Prescription contains[#]	Antibiotic	724	301 (41.6)	423 (58.4) (**Antibiotic**: 130 (18.0))	57 (29.8)	118 (61.8)	16 (8.4)	0 (0)	191
	Insulin	129	42 (32.6)	87 (67.4) **Insulin**: 20 (15.5)	12 (37.5)	19 (59.4)	1 (3.1)	0 (0)	32
	Warfarin	196	71 (36.2)	125 (63.8) **Warfarin**: 18 (9.2)	6 (23.1)	16 (61.5)	4 (15.4)	0 (0)	26
	Oxygen	36	7 (19.4)	29 (80.6) **Oxygen**: 2 (5.6)	1 (14.3)	5 (71.4)	1 (14.3)	0 (0)	7

* Relates to errors per prescriptions written, not errors per number of items prescribed

Error severities, total errors and error rates relate to errors associated with Antibiotics/Insulin/Warfarin/Oxygen only

Table 4. Summary of the Errors Observed which were Considered to be Potentially Lethal

Error Description	Category	Prescriber Grade	Ward Area	Admission/ Discharge
Gliclazide 400mg prescribed when 40mg needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Digoxin 625micrograms prescribed when 62.5micrograms needed	1- Dosing Errors	Newly qualified	Medicine	Discharge
Oxycodone 500mg prescribed: overdose	1- Dosing Errors	Mid Grade	Surgery	Admission
Methotrexate prescribed daily, not weekly	1- Dosing Errors	Junior	Medicine	Admission
Doxazocin prescribed; had been stopped by general practitioner due to angioedema	3. Allergy status missing/ significant allergy	Junior	Medicine	Admission
Phenytoin dose of 300mg daily incorrectly prescribed as 800mg	1- Dosing Errors	Newly Qualified	Medicine	Discharge
Midazolam IV for sedation: overdose	1- Dosing Errors	Mid Grade	Unknown	Admission
Amiodarone loading dose of 200mg three times daily continued as a regular dose	1- Dosing Errors	Other	Surgery	Discharge
Enoxaparin prescribed 1mg/kg once daily instead of 1mg/kg twice daily for a patient with acute coronary syndrome	1- Dosing Errors	Mid Grade	Medicine	Admission

Table 5. Univariate statistics showing the significance of explanatory variables in predicting error rates in prescriptions.

Variable	n	≥1 Error	No Error	Difference (95%CI)	p-value
		n (%)	n (%)		
Prescriber Grade (n=3850)		1689	2161		
Newly qualified	1803	716 (42%)	1087 (50%)	-8% (-11.2% to -4.8%)	<0.001
Junior	1482	727 (43%)	755 (35%)	8% (4.9% to 11.1%)	
Mid-grade	366	176 (10%)	190 (8.8%)	1.2% (-0.7% to 3.1%)	
Senior	142	46 (2.7%)	96 (4.4%)	-1.7% (-2.8% to -0.4%)	
Non-medical	35	9 (0.5%)	26 (1.2%)	-0.7% (-1.3% to -0.1%)	
Other	22	15 (0.9%)	7 (0.3%)	0.56% (0.1% to 1.1%)	
Discharge/Admission (n=3065)		1135	1930		
Discharge	2467	853 (75%)	1614 (84%)	-9% (-12.0% to -6.0%)	<0.001
Admission	598	282 (25%)	316 (16%)		
Liverpool trained (n=1325)		518	807		
Liverpool	35	14 (2.7%)	21 (2.6%)	0.1% (-1.7% to 1.9%)	0.911
Non-Liverpool	1290	504 (97%)	786 (97%)		
Hospital (n=4238)		1857	2381		
Hospital A	762	366 (20%)	396 (17%)	3% (0.6% to 5.4%)	<0.001
Hospital B	513	239 (12%)	274 (12%)	0% (-2.0% to 2.0%)	
Hospital C	500	296 (16%)	204 (8.6%)	7.4% (5.4% to 9.4%)	
Hospital D	97	30 (1.6%)	67 (2.8%)	-1.2% (-2.1% to -0.3%)	
Hospital E	371	160 (8.6%)	211 (8.9%)	-0.3% (-2.0% to 1.4%)	
Hospital F	604	355 (19%)	249 (10%)	9% (6.8% to 11.2%)	
Hospital G	86	22 (1.2%)	64 (2.7%)	-1.5% (-2.3% to -0.7%)	
Hospital H	807	290 (16%)	517 (22%)	-6% (-8.4% to -3.6%)	
Hospital I	498	99 (5.3%)	399 (17%)	-11.7% (-13.5% to -9.9%)	
Ward Area (n=3575)		1577	1998		
Medical	2059	977 (62%)	1082 (54%)	8% (4.8% to 11.2%)	<0.001
Surgical	1395	560 (36%)	835 (42%)	-6% (-9.2% to -2.8%)	
Accident & Emergency	8	7 (0.4%)	1 (0.1%)	0.3% (-0.04% to 0.6%)	
Mental health	96	30 (1.9%)	66 (3.3%)	-1.4% (-2.4% to -0.4%)	
Critical care	17	3 (0.2%)	14 (0.7%)	-0.5% (-0.9% to -0.1%)	
Number of Medicines on Prescription (n=3386) Median (IQR)		8; (4,11) (n=1435)	4; (2,7) (n=1951)	-4 (-4.5, -3.5)	<0.001

n= number of prescriptions

Table 6. Multivariate logistic regression analysis for predicting error rates in prescriptions.

Variable	Odds ratio (95%CI)	p-value
Hospital		
Hospital H	1	
Hospital A	Not estimable*	
Hospital B	1.11 (0.78 to 1.58)	0.57
Hospital C	2.38 (1.63 to 3.46)	<0.001
Hospital D	0.64 (0.13 to 3.06)	0.57
Hospital E	1.39 (0.96 to 2.01)	0.08
Hospital F	3.53 (2.63 to 4.73)	<0.001
Hospital G	1.80 (1.03 to 3.12)	0.04
Hospital I	1.11 (0.73 to 1.70)	0.62
Prescriber Grade		
Newly qualified	1	
Junior	1.06 (0.85 to 1.32)	0.61
Mid-grade	0.96 (0.64 to 1.44)	0.83
Senior	0.97 (0.58 to 1.63)	0.92
Non-medical	0.59 (0.21 to 1.64)	0.31
Other	1.50 (0.53 to 4.23)	0.44
Discharge/Admission	1.16 (0.70 to 1.92)	0.58
Number of prescribed items	1.14 (1.12 to 1.17)	<0.001

Analysis contains only 2127 records (50.2%) where complete data was provided for all variables

* Trust provided no data on number of prescription items

The authors wish to thank the reviewers for the opportunity to further improve this paper.

Reviewer(s)' Comments to Author:

Reviewer: Dr Penny Lewis, Clinical Lecturer, University of Manchester

I have no competing interests

Thank you for responding to my comments. I think that the paper has improved significantly. However, there are a few comments I would like to make regarding this version.

- *I am not sure that you provided a sufficient explanation as to why differences between Liverpool graduates were explored versus other university graduates. Is there something unique to this course? If you were to explore other universities might the results be different?*

This has been clarified in the introduction. A large proportion of evaluated prescribers (30%) received undergraduate training at the University of Liverpool. The study was funded by the Mersey Deanery.

- *In the results it is stated that the lowest rates of errors were reported for the paediatrics speciality – in table 4 this speciality was not explored individually so I take it you are referring to the paediatric hospital as oppose to paediatric patients from across the different hospitals? Or was this data collected from all paediatric patients seen across all hospitals?*

This refers to the error rate observed for the paediatrics specialty hospital; this has been clarified in the text

- *Risk factor analysis: 'All factors considered appeared to show a significant difference except for medical school training'. Perhaps this should be 'except for whether a doctor was trained at Liverpool medical school or not' as the study only tested for a difference between Liverpool graduates and other medical school graduates.*

The wording has been changed as suggested

- *One of the main findings of this study, as stated in the key messages, was that prescribing errors increased by 14% for every additional medication item prescribed but there is no discussion as to what this might mean for practice.*

The following has been added to the discussion: 'In multivariate analysis, the strongest predictor for prescribing error was the number of medicines on each prescription, with risk for prescribing errors increasing by 14% for every additional medication item prescribed. Complex polypharmacy is becoming increasingly common, with patients potentially requiring management for multiple chronic conditions simultaneously. In these patients, vigilance for prescribing errors and pharmacist review is of particular importance.'

- *It is stated that 'A study in Spain compared paediatric wards with obstetrics found the paediatric patients had a fourfold higher risk of serious errors then maternity population' – and then stated that this is in line with own findings but I didn't see anything in the results regarding severity of errors across different patient groups. I think is a simple misconception due to the way the paragraph is phrased.*

The paragraph has been rephrased and now reads: 'A study in Spain comparing paediatric wards with obstetrics found that paediatric patients had a fourfold higher risk of serious errors than the maternity population (2.3% vs 14.3%), which were mainly related to drug dosing. We observed a low error rate for the paediatrics specialty hospital, although this was likely due to a low number of prescribed items.'

- *Finally by grouping errors into categories according to the origin we sought to reduce misclassification as far as possible – could you explain this further as I'm not sure what is meant by this.*

This sentence has been altered and now reads: 'Finally, in order to limit the impact of error misclassification, the original 29 error categories were batched into 10 different types of error groups relating to key components of prescribing.'

- *The final conclusion of the paper states that removing safeguards such as pharmacists could lead to higher numbers of errors but the 'key messages' of the paper are that you found no difference in error rate by grade and the strongest predictor for prescribing error was the number of medicines. So I am not sure of the link between this and the overall aims/key messages. If this is the main conclusion then maybe there should be some mention of these safeguards in the introduction.*

The following sentence has been added to the introduction, in the paragraph relating to the background of error. 'Barriers which may prevent medication errors, or prevent errors from reaching the patient, may include electronic prescribing alerts, and prescription review by clinical pharmacists.'

The conclusion now states that as prescribing errors are prevalent in secondary care and are made by all grades of prescribers, removing safeguards (ie pharmacists) could lead to more errors actually reaching patients. We referred to the particular importance of pharmacists in clinical areas associated with high risk; patients with polypharmacy and admission areas are now given as examples. This now relates our key findings to the importance as pharmacists as 'safeguards'.

- *Overall, the study presents some very interesting data but I believe that the paper could be improved upon further, linking the key findings, introduction and discussion better and clarifying the important findings e.g. is the main message of the work that pharmacists should never be removed from their role or that there is no link between experience and number of errors made.*

The main message links both aspects. Our key findings are that grade of prescriber does not affect error rate and that increased number of prescribed items increases risk of errors. We conclude that prescribing errors are prevalent, regardless of the grade of prescriber, therefore a key role of clinical pharmacists is to ensure that errors are less likely to reach patients. Potential barriers to prescribing errors have now been mentioned in the introduction. Further comment on number of prescribed items conferring higher risk for prescribing errors has been added to the discussion.

STROBE Statement—Checklist of items that should be included in reports of ***cross-sectional studies***

	Item No	Recommendation	
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	√
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	√
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	√
Objectives	3	State specific objectives, including any prespecified hypotheses	√
Methods			
Study design	4	Present key elements of study design early in the paper	√
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	√
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants	√
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	√
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	√
Bias	9	Describe any efforts to address potential sources of bias	√
Study size	10	Explain how the study size was arrived at	√
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	√
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	√
		(*b*) Describe any methods used to examine subgroups and interactions	√
		(*c*) Explain how missing data were addressed	√
		(*d*) If applicable, describe analytical methods taking account of sampling strategy	√
		(*e*) Describe any sensitivity analyses	√
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	n/a
		(b) Give reasons for non-participation at each stage	n/a
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	√
		(b) Indicate number of participants with missing data for each variable of interest	√
Outcome data	15*	Report numbers of outcome events or summary measures	√
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	√

		(*b*) Report category boundaries when continuous variables were categorized	√
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	√
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	√
Discussion			
Key results	18	Summarise key results with reference to study objectives	√
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	√
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	√
Generalisability	21	Discuss the generalisability (external validity) of the study results	√
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	√

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

TO: Editor
BMJ Open

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31st August 2012.

Dear Editor

Re: Cross Sectional Study of Prescribing Error in Patients Admitted to Nine Hospitals Across North West England

Please find enclosed our manuscript for your consideration. The BMJ Group Journals have a long and honourable tradition of championing patient safety, and publishing research which seeks to characterise, understand and limit harms resulting from medication error. Earlier this year, Ingrid Torjesen's article highlighted findings from two of the UK's largest studies into prescribing error in primary and secondary care (the PRACtICe and EQUIP studies respectively) [*Torjesen I. BMJ 2 May 2012*]. Both studies have released study reports on the GMC website, but neither has yet been published in a peer-reviewed journal.

Our sample size is comparable to EQUIP, and larger than PRACtICe, and our observed error rate of ~10% of medication items prescribed is similar to EQUIP (9%) and PRACtICe (4%), using a modified version of EQUIP definitions. By analysing error within complete individual prescriptions (rather than individual medication items) we show that a significant proportion of patients were exposed to prescribing error, and that this risk increased by 14% for every medication item added to their prescription. Risk of error did not vary with hospital, seniority of prescriber or medical school training, but acute medical admission scenarios were associated with highest risk of error (mainly arising from unintended medication omission). Finally, electronic prescribing and medication administration systems could only have prevented up to a quarter of these errors, highlighting the important role of the ward pharmacist, particularly in high-pressure acute areas.

We believe these results are likely to accurately reflect the prevalence of prescribing error more generally throughout the UK, and to consequently inform health policy which seeks to minimise patient harms through improvements in health systems. Thank you for considering this for publication in BMJ Open.

With best wishes,

Professor S.H. Khoo
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University of Liverpool