**ORIGINAL ARTICLE**

Investigation into the reasons for preventable drug related admissions to a medical admissions unit: observational study

R L Howard, A J Avery, P D Howard, M Partridge

Objectives: To describe the drugs and types of medicine management problems most frequently associated with preventable drug related admissions to an acute medical admissions unit.

Design: Observation study.

Setting: Medical admissions unit in a teaching hospital in Nottingham, UK.

Participants: 4093 patients seen by pharmacists on the medical admissions unit between 1 January and 30 June 2001.

Main outcome measures: Proportion of admissions that were drug related and preventable, classification of the underlying causes of preventable drug related admissions, and identification of drugs most commonly associated with preventable drug related admissions.

Results: Of the admissions seen by pharmacists, 265 (6.5%) were judged to be drug related and 178 (67%) of these were judged to be preventable. Preventable admissions were mainly due to problems with prescribing (63 cases (35%)), monitoring (46 cases (26%)), and adherence to medication (53 cases (30%)). The drugs most commonly implicated were NSAIDs, antiplatelets, antiepileptics, hypoglycaemic, diuretics, inhaled corticosteroids, cardiac glycosides, and beta-blockers.

Conclusions: Potentially preventable drug related morbidity was associated with 4.3% of admissions to a medical admissions unit. In 91% of cases these admissions were related to problems with either prescribing, monitoring, or adherence.

**METHODS**

Selection of participants

The local research ethics committee approved the study. All patients admitted to the medical admissions unit (box 1) and seen by a pharmacist between 1 January and 30 June 2001 were included in the study. The pharmacists saw patients as part of their routine work Mondays to Fridays. They recorded details of all patients seen and reported patients with any suspected drug related morbidity to the principal investigator.

**Box 1 Description of the Medical Admissions Unit at Queens Medical Centre, Nottingham**

The medical admissions unit at Queens Medical Centre (QMC), Nottingham is a 30 bed unit which receives acute medical admissions from general practitioners and the A&E department. A small number of admissions come from other hospitals or wards within the QMC (these were not included in the study). The ward is covered Monday to Friday by three admissions ward pharmacists (all have a clinical diploma) between 07.00 and 19.00 hours. The pharmacists are responsible for checking the medication histories of patients admitted (by reviewing patients’ own medication, questioning patients, contacting general practice surgeries and nursing homes, etc), as well as supplying medication and ensuring the safety of the prescribing on the unit. Part of this role inevitably involves identifying drug related morbidity.

There are two consultant-led multidisciplinary ward rounds each day (morning and evening) which are attended by one of the admissions unit pharmacists.

Overnight and at weekends the admissions unit is covered by a limited pharmacy service.
8781 admissions between 1 January 2001 and 30 June 2001
4688 admissions not screened by the admissions ward pharmacists
3784 admissions screened by the admissions ward pharmacists and
309 by the principal investigator (total 4093 admissions screened)
3512 admissions screened as not drug related by the
admissions ward pharmacists and principal investigator
581 admissions screened as possibly drug related by the admissions
ward pharmacists and principal investigator
170 possible drug related admissions excluded after follow
up by the principal investigator
411 admissions assessed by the panel
146 admissions classified as not drug related
265 admissions classified as drug related
87 admissions classified as drug related and not
preventable
178 admission classified as drug related and preventable

Figure 1 Flow of patients through the study.

Box 3 Criteria used to review possible drug related admissions cases

Amended Hallas criteria for causality
(1) Known adverse drug reaction, toxic reaction, response to
omission of treatment or inadequate treatment.
(2) Reasonable temporal relationship between commence-
ment or cessation/omission of treatment and onset of
problem.
(3) Risk of further problems likely to be reduced by dose
reduction or increase, discontinuation, closer monitoring or
commencement of treatment.
(4) Not explained by any other known condition of predispo-
sition to the patient, or this condition/predisposition is likely to
be exacerbated by the presence/absence of the drug.
(5) For drug toxicity:
• symptoms re-appeared upon re-exposure;
• laboratory tests showed toxic drug levels or drug
induced metabolic disturbances that explained the
symptom;
• symptoms resolved on dose reduction or discontinuation
of the drug.
For drug omission:
• symptoms resolved upon re-introduction of the drug or
dose increase.
If 5 criteria fulfilled then definite.
If 4 criteria fulfilled then probable
If 3 criteria fulfilled then possible
If 2 or less criteria fulfilled then either, not drug related or
unevaluable

Haller criteria for preventability
(1) Drug related morbidity (DRM) preceded by a recognis-
able drug therapy problem (DRP).
(2) Given the DRP, the DRM would have been reasonably
foreseeable.
(3) The cause of DRM would have been identifiable with rea-
sonable probability (Hallas criteria probable or definite for
causality).
(4) The cause of the DRM could have been reasonably
controllable within the context and objectives of treatment.
All four criteria must be fulfilled to confirm preventability.

Contribution of drug related problem to hospital
admission
Score = 3 (dominant): the suspected symptoms were the main
reason for admission and no other symptoms contributed sig-
nificantly.
Score = 2 (partly contributing): the suspected symptoms
played a substantial role in admission, but other factors also
contributed significantly.
Score = 1 (less important): the suspected symptoms played a
minor or uncertain role, and the patient would probably have
been admitted without them.
Score = 0 (not contributing): other symptoms/circumstances
were the reason for hospitalisation.

Hepler definitions for classification of drug related
admissions
Score = 1: inappropriate prescribing.
Score = 2: inappropriate delivery (unavailable when needed,
inappropriate formulation, failure to administer, dispensing
error).
Score = 3: inappropriate behaviour by the patient
(non-compliance).
Score = 4: patient idiosyncrasy (response to drug, mistake, or
accident).
Score = 5: inappropriate monitoring.
Score = 6*: potentially preventable with interventions which
are not standard care at present.

*Category 6 is additional to the original Hepler classification

Box 2 Details included in the case summaries

• Unique identifier
• Patient’s age
• Sex
• Date of admission
• Date of discharge
• Presenting complaint
• Medication history (before admission to hospital)
• Medication on discharge
• Events leading up to the admission
• Summary of hospital treatment
• Test results
• Diagnosis made by the physicians caring for the patient in
hospital

(RH). Similar methods have been used successfully in at least
five previous studies.19

The principal investigator assessed possible cases using a combination of:
• medical note review (throughout the admission and on dis-
charge);
• contact with general practitioners, where necessary, to
obtain medication histories, test results, and information
regarding the management of patients in primary care;
• interviewing patients, where possible, about the type and
duration of symptoms and medication use, using an inter-
view schedule. Those not interviewed included patients
discharged home before being seen by the principal investi-
gator, patients too unwell to be interviewed, and patients
unable to speak English.

Following assessment by the principal investigator, some
cases were excluded from further review (fig 1). These included
cases where further investigation suggested that drug related
morbidity was unlikely—for example, a low probability VQ scan
in a case of suspected pulmonary embolism in a woman taking a
combined oral contraceptive. In order to ensure that some
patients were included in the study who had been admitted
at weekends, the principal investigator identified patients with
potential drug related morbidity through medical note review
and patient interview on alternate weekends (fig 1).

Classification of potential drug related admissions
Following discharge from hospital, the principal investigator
prepared detailed case summaries on patients with suspected

Preventable drug related admissions
Drug related morbidity (box 2). These summaries provided reviewers with information on temporal relationships between medications and symptoms, the nature of patients’ symptoms, medication changes resulting from the admission, and the diagnoses made by physicians caring for the patients. The case summaries were independently scored by a hospital physician (PH), an academic general practitioner with a special interest in prescribing (AA), and a clinical pharmacist (RH). Each reviewer scored the cases using explicit criteria for causality,13 preventability,13 contribution to the admission,13 and classification of the underlying cause of the drug related morbidity13 (box 3). All the criteria were validated in pilot study work where 46 possible cases of drug related morbidity were reviewed to ensure the criteria were reliable and gave reasonable agreement between the reviewers. After scoring the cases the reviewers met up and, in keeping with standard practice in this field,13 a majority decision was used to classify the cases where there was disagreement on any of the review criteria.

Admissions were classified as drug related if two or more reviewers scored 4 or 5 using the amended Hallas criteria and judged the drug to have made a dominant or partial contribution to the admission. Admissions were classified as potentially preventable if the above criteria were fulfilled and two or more reviewers scored 4 using the Hepler criteria for preventability.

Recording of data
For all admissions to the medical admissions unit age, sex, and date of admission were recorded on an ACCESS 97 database. The hospital routinely records details of primary diagnoses of patients admitted, classified according to the International Classification of Diseases and Related Health Problems, 10th revision.14 These data were available for 7962 (91%) of the patients admitted to the medical admissions unit (Table 1). The hospital routinely records details of primary diagnoses of patients admitted, classified according to the International Classification of Diseases and Related Health Problems, 10th revision.14 The proportion of patients considered to have a drug related admission was calculated as the percentage of patients seen by a pharmacist who were judged to have a preventable drug related admission.

Table 1 Primary diagnoses of patients admitted to the medical admissions unit where there was a statistically significant difference between the numbers of patients seen and not seen by a pharmacist.

<table>
<thead>
<tr>
<th>Primary diagnoses classified by ICD-10 chapter heading</th>
<th>Patients seen by pharmacist (n=3799)</th>
<th>All patients admitted (n=7962)</th>
<th>p value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Certain infectious and parasitic diseases</td>
<td>101 (2.7)</td>
<td>172 (2.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>Diseases of the nervous system</td>
<td>153 (4.0)</td>
<td>283 (3.6)</td>
<td>0.029</td>
</tr>
<tr>
<td>Mental and behavioural disorders</td>
<td>84 (2.2)</td>
<td>151 (1.9)</td>
<td>0.049</td>
</tr>
<tr>
<td>Diseases of the respiratory system</td>
<td>702 (18.5)</td>
<td>1305 (16.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diseases of the skin and subcutaneous tissue</td>
<td>51 (1.3)</td>
<td>163 (2.0)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Diseases of the musculoskeletal system and connective tissue</td>
<td>106 (2.8)</td>
<td>410 (5.1)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Values are no (%). *Based on χ^2 tests (1 degree of freedom).

Table 2 Reviewer agreement in scoring case summaries calculated using kappa and intraclass correlation coefficients

<table>
<thead>
<tr>
<th></th>
<th>Kappa for RH*TA</th>
<th>Kappa for RH*PH</th>
<th>Kappa for TA*PH</th>
<th>Intraclass correlation coefficient (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Causality</td>
<td>0.81</td>
<td>0.81</td>
<td>0.77</td>
<td>0.88 [0.86 to 0.90]</td>
</tr>
<tr>
<td>Preventability</td>
<td>0.77</td>
<td>0.77</td>
<td>0.69</td>
<td>0.74 [0.70 to 0.78]</td>
</tr>
<tr>
<td>Contribution to admission</td>
<td>0.74</td>
<td>0.87</td>
<td>0.76</td>
<td>0.80 [0.78 to 0.83]</td>
</tr>
<tr>
<td>Cause of suboptimal outcome</td>
<td>0.78</td>
<td>0.71</td>
<td>0.67</td>
<td>0.75 [0.71 to 0.78]</td>
</tr>
</tbody>
</table>

Analysis of data
Data were exported to SPSS version 10.0 for statistical analysis. To assess differences between the groups of patients seen and not seen by a pharmacist, patient characteristics were compared using an independent t test for age on admission and χ^2 tests for sex, day of admission, and primary diagnosis (available for 7962 (91%) of all patients admitted). To assess inter-reviewer reliability, case review scores were compared using Cohen’s kappa and intraclass correlation coefficients (moderate to substantial agreement is indicated by kappa 0.41–0.80).15 The proportion of patients considered to have a drug related admission was calculated as the percentage of patients seen by a pharmacist who were classified as having definite or probable drug related morbidity that had made a dominant or partial contribution to the admission. We also calculated the proportion of drug related admissions that were considered potentially preventable. The proportion of patients considered to have a potentially preventable drug related admission was calculated as the percentage of patients seen by a pharmacist who were judged to have a preventable drug related admission.

RESULTS
Patient characteristics
The flow of patients through the study is shown in box 2. Of the 8781 patients admitted to the medical admissions unit, 4093 (47%) were seen by a pharmacist. The mean (SD) age of patients seen was 62.6 (20.7) years and the mean (SD) age of patients not seen by a pharmacist was 62.0 (20.6) years. Of the patients seen by a pharmacist 2002 (49%) were female and 2289 (49%) were male.

Comparing patients who were either seen or not seen by a pharmacist, there were no significant differences in age...
In recent years there have been calls for researchers to move beyond simply reporting preventable adverse events to finding ways of improving patient safety through avoidance of these events. It has been suggested that an approach focusing on systems failures is likely to be most effective. The key to starting this process is to find out which types of problem are controllable in terms of the treatment (Box 4). Nevertheless, our results could be questioned in terms of the extent to which they reflect the true preventability of the observed outcomes. For example, a recent study of hospital deaths that were attributed to medical error suggested that in many cases the error made relatively little difference to expected fatal outcomes in seriously ill patients. While these results are not directly comparable to our study, we recognise that some of the patients in our study were at very high risk of hospital admission regardless of any preventable medication related adverse event.

In our study we reviewed only those patients seen by a pharmacist on the admissions unit. This means that our estimates of the proportion of admissions that were drug related and preventable need to be treated with some caution. The patients we studied were not fully representative of all patients admitted. However, the differences between the groups seen and not seen by a pharmacist were relatively small and, had we studied all the admissions, it is unlikely that the results would have been substantially different. In addition, our findings were similar to median figures from a recent systematic review.

In order to minimise the risk of misclassifying cases, we used a methodology which compares well with the most rigorous studies previously reported. We used explicit criteria to guide the assessment of cases and a three member panel of reviewers to independently classify each case. Despite the varied backgrounds of the reviewers, kappa and intraclass correlation coefficients showed good to excellent levels of agreement. Only those admissions where the drug related morbidity was judged to be the dominant cause, or partially contributing, to the admission were included as drug related admissions. Also, when we classified drug related admissions as preventable, it was our view that the problems identified were predictable and controllable in terms of the treatment (Box 4). Nevertheless, our results could be questioned in terms of the extent to which they reflect the true preventability of the observed outcomes. For example, a recent study of hospital deaths that were attributed to medical error suggested that in many cases the error made relatively little difference to expected fatal outcomes in seriously ill patients. While these results are not directly comparable to our study, we recognise that some of the patients in our study were at very high risk of hospital admission regardless of any preventable medication related adverse event.

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Almost 60% of the preventable drug related admissions that we found are shown in tables 3–5. These data describe the drugs most commonly associated with admissions. We have recently completed a systematic review of interventions aimed at reducing adverse drug events.

### Table 3

<table>
<thead>
<tr>
<th>Drug class</th>
<th>Adverse drug event</th>
<th>Prescribing problem</th>
<th>Number of cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-steroidal anti-inflammatory drugs</td>
<td>Gastrointestinal toxicity</td>
<td>Prescription in patients with two or more risk factors without gastrointestinal prophylaxis</td>
<td>21</td>
</tr>
<tr>
<td>Antiplatelet drugs</td>
<td>Gastrointestinal toxicity</td>
<td>Concurrent prescription of two full dose non-steroidal anti-inflammatory drugs without monitoring renal function</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>Renal tubular necrosis</td>
<td>Subtotal</td>
<td>22</td>
</tr>
<tr>
<td></td>
<td>Thrombotic event</td>
<td>Failure to prescribe in patients needing secondary prevention</td>
<td>4</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtotal</td>
<td>17</td>
</tr>
<tr>
<td>Beta-adrenoceptor blocking drugs</td>
<td>Congestive cardiac failure</td>
<td>Prescription of standard dose beta-blocker in patient with known congestive cardiac failure</td>
<td>2</td>
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<tr>
<td></td>
<td></td>
<td>Co-prescription of atenolol with verapamil</td>
<td>1</td>
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<tr>
<td></td>
<td></td>
<td>Sudden cessation</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Failure to maximise anti-arrhythmic therapy despite ongoing symptoms over a period of time</td>
<td>2</td>
</tr>
<tr>
<td>Antiplatelet drugs</td>
<td>Tachycardia</td>
<td>Cessation without prescription of alternative</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtotal</td>
<td>7</td>
</tr>
<tr>
<td>Antiepileptics</td>
<td>Bleeding oesophageal varices</td>
<td>Subtherapeutic prescription</td>
<td>4</td>
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<tr>
<td></td>
<td></td>
<td>Inappropriate cessation</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Subtotal</td>
<td>6</td>
</tr>
<tr>
<td>Other</td>
<td>Fitting</td>
<td></td>
<td>38†</td>
</tr>
</tbody>
</table>

*If a drug related admission involves more than one causative drug it may be recorded more than once in the table. †Further details on “other” drug categories are available on the QSHC website (www.qshc.com/supplemental).
Combining evidence from this review with results from the study presented here means that we are able to suggest the types of interventions that may be most successful in reducing medication related morbidity in primary care. Combining evidence from this review with results from the study presented here means that we are able to suggest the types of interventions that may be most successful in reducing medication related morbidity in primary care.

In terms of monitoring, some of the best evidence for improvements in primary care relate to the monitoring of warfarin. The results of these studies may not be applicable to other drugs, but they suggest that nurse led monitoring clinics, computerised decision support systems, patient education and involvement, and patient self-management may help to improve control through improved monitoring. In our systematic review we did not find many other studies that looked at medication monitoring in primary care, and we believe that there is a need for further research in this area.

In terms of patient adherence, a number of studies have shown that improved education and approaches that provide greater involvement of patients in decision making improve patient adherence and may reduce drug related admissions. However, few studies have attempted to show clinical benefits. Our study suggests that priority should be given to patients taking the drugs listed in Table 5.

Many of the problems identified in this study arise from medicines management in primary care, but it should be recognised that drug related admissions are relatively rare from the primary care perspective. For example, while NSAIDs were responsible for 12.4% of potentially preventable admissions in

<table>
<thead>
<tr>
<th>Table 5 Drug classes most frequently associated with preventable drug related admissions due to adherence problems.</th>
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<tbody>
<tr>
<td>British National Formulary class</td>
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<tr>
<td>Loop diuretics</td>
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<tr>
<td>Antiepileptics</td>
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<td>Corticosteroids</td>
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<tr>
<td>Nitrites</td>
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<td>Insulins</td>
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<tr>
<td>Other</td>
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<table>
<thead>
<tr>
<th>Table 4 Drug classes most frequently associated with preventable drug related admissions due to monitoring problems.</th>
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<tbody>
<tr>
<td>British National Formulary class</td>
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<tr>
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<tr>
<td>Loop diuretics</td>
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<tr>
<td>Potassium sparing diuretics</td>
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<tr>
<td>Sulphonylureas</td>
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<tr>
<td>Cardiac glycosides</td>
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<tr>
<td>Thiazide and related diuretics</td>
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<tr>
<td>Antiepileptics</td>
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Preventable drug related admissions

Key messages

- Drug related morbidity was responsible for 6.5% of admissions screened by a pharmacist and 69% were considered preventable.
- The drugs most commonly associated with the preventable drug related admissions were NSAIDs, antplatelets, antiepileptics, hypoglycaemics, diuretics, inhaled corticosteroids, cardiac glycosides and beta-blockers.
- The majority of preventable drug related admissions were caused by problems with prescribing (35%), monitoring (26%), or adherence (30%).

References


AA conceived the study and was responsible for the design along with RH and MP. RH collected all the data and produced all the case summaries needed for the study. RH, AA and PH reviewed all of the cases, RH processed the data, entered it on to computer and analysed it with help from AA. All of the authors were involved in the interpretation of the results. RH and AA wrote the paper with PH and MP providing critical comments.

Expanded versions of tables 3, 4 and 5 are available on the QSHC website at www.qshc.com/supplemental.