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Title page

Title: Antimicrobial-related medication safety incidents: a regional retrospective study in West of Scotland hospitals

Running title: Antimicrobial-related safety incidents

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**Keywords:** Anti-infectives, medication errors, adverse events, Datix
**Summary**

**BACKGROUND:** Medication-related incidents are an important consideration in enhancing patient safety in hospital care. The wide utilisation of antimicrobial therapy in this population renders these medications particularly vulnerable to errors and adverse events.

**AIM:** To analyse the characteristics of antimicrobial therapy-related incident reports across a group of secondary care hospitals.

**METHODS:** Reports for antimicrobial-related incidents from April 2010 to December 2013 were obtained from a regional area of hospitals in National Health Service (NHS) Scotland. Reports were analysed at-large, with subset analyses of incidents resulting in patient harm/injury and those included in a multivariable regression adjusted by occupied bed days (OBD) and defined daily doses (DDD) to better ascertain areas to target for antimicrobial safety.

**FINDINGS:** A total of 1345 incidents were reported at a crude rate of 0.98 reports/day (95% CI: 0.93-1.03 reports/day). Penicillins (371 reports; 27.6%), aminoglycosides (358; 26.6%) and glycopeptides (210; 15.6%) were the most commonly involved classes of medications. Most incidents involved no injury/harm (514; 38.2%), but 72 reports (5.4%) did result in patient harm.

Rehabilitation/Assessment (RR: 2.61, 95% CI: 1.70-4.03) and Women/Childrens (RR: 2.61, 95% CI: 1.70-4.03) had higher incident reporting rates compared to other hospital services, likely as a function of at-risk patient populations. Among the types of incidents reported, those involving issues with administration/supply were most common (RR: 2.07, 95% CI: 1.51-2.84).
CONCLUSION: Incident reporting for antimicrobials identified several key areas for quality improvement in the hospital setting which can guide safety efforts.
INTRODUCTION:

Patient safety incident reporting is recognised as an important quality improvement measure and a focus for the delivery of healthcare. In 2005, it was estimated that patient safety incidents resulted in additional yearly costs to the National Health Service (NHS) in the United Kingdom (UK) of £2 billion in extra hospital bed days and £1 million in treating hospital-acquired infections; medication errors were found to be the second most commonly reported incident behind patient injury due to falls.\(^1\) The number of medication incident reports in England/Wales increased from approximately 42,000 in 2005 to over 132,000 in 2010.\(^2\)

Although reports indicate the presence of undesired incidents, increased reporting in itself can be considered a positive trend as it is known that the number of actual events greatly surpasses the reports made, and overcoming clinician barriers to making reports is a key step in improving medication use.\(^3\) For instance, reporting rates in the acute care setting have been positively correlated with hospital staff perceptions of positive safety culture at their institution.\(^4\) In the UK, two patient safety alerts were released regarding incident reporting for medications and medical devices and the formation of national networks to enhance understanding and prevention of these events.\(^5\)

Antimicrobial agents are some of the most widely prescribed medications in healthcare across the world.\(^6\) Due to their extensive utilisation across the clinical
spectrum, their prescribing is especially vulnerable to errors and adverse events. An analysis of over 21,000 adverse drug events in outpatients in the United States (USA) identified the top three responsible medications as insulin, warfarin and amoxicillin; antibiotics were responsible for 7 of the top 18 implicated medications. Two analyses of medication-related incidents in UK hospitals found that between 13.1 and 14.3% of incidents involved antimicrobials. Events involving antibiotics can occur across all stages of the medication use spectrum and have potential for serious consequences, particularly with regard to prescribing without consideration of allergy status, or delayed or missed administration in the case of life-threatening infections.

Traditionally, the focus on antimicrobial utilisation has been on limiting inappropriate use through stewardship to protect against the unnecessary development of resistance; however, this fails to fully capture the whole spectrum of utilisation. In depth analysis of medication errors associated with antimicrobials although limited is an important contributor to the understanding of this class of high-risk and widely utilised medications. Therefore, the objective of the present study was to analyse the characteristics of voluntary incident reporting relating to antimicrobial therapies across a regional group of secondary care hospitals in the West of Scotland.

METHODS:

Setting and data

The study was a retrospective analysis of Datix incident reports involving antimicrobials. Datix is a web-based software tool utilised for the collection, analysis
and dissemination of information related to patient safety and risk management; approximately three-quarters of the NHS in the UK utilises the software in this capacity.¹⁰ The tool is available for a variety of uses, including reporting of incidents by clinicians (medication-related or otherwise), or for patient experience/feedback, malpractice claims management or institutional self-assessment.¹⁰

The data extract from Datix was limited to medication-related incident reports submitted from a single regional health board in Scotland, serving a population of approximately 1.2 million people. Data were exported for a 15-quarter time period (April 2010 to December 2013) for participating institutions within the health board area. Reports were limited to include only those associated with systemic medications for infection listed in Chapter 5 of the British National Formulary (BNF), including sub-sections on antibacterial, antifungal, antiviral, antiprotozoal and anthelmintic medications." Data columns of interest included hospital directorate (a coordinated group of related clinical specialties), medication administered, and incident date, sub-category, stage, description, action taken, result and severity. All characteristic variables were categorical in nature (Table I) with the exception of the medication administered and incident description/action taken, which included subjective text from the reporter. Incident result was consolidated from 19 categories in Datix to 5 user-defined categories to facilitate analysis. No ethics approval was deemed necessary to conduct the present study.

**Overall analysis**

Data were first evaluated as a function of total raw reports from the complete data extract and were broadly described among available variables. Medications
administered during the incident were grouped into corresponding BNF sub-sections with the exception of 5.1.7 (‘Some other antibacterials’) for which vancomycin and teicoplanin were analysed separately as ‘glycopeptides’.\textsuperscript{11} A further in-depth analysis regarding incidents resulting in patient harm was conducted utilising incident sub-categories and narratives from the report submitter in the incident description. Specific clinical outcomes from incidents were not included to maintain patient confidentiality.

\textit{Adjusted analysis}

Data were secondarily analysed in an adjusted subset analysis to better assess relative prevalence of events; to achieve this, the Datix extract was supplemented with a second dataset of occupied bed day (OBD) to assess occupancy and defined daily dose (DDD) figures to assess medication utilisation for the regional area. Data for OBD and DDD (limited to BNF Chapter 5 medications for infection) were provided annually for calendar years 2010 through 2013, subdivided by hospital facility and directorate, although they were only available for a subset of the largest 10 hospitals and 6 hospital directorates. A negative binomial regression was applied using hospital directorate, incident year, incident stage and incident result as predictors of number of reports. The Datix extract was limited to the selected hospitals and hospital directorates available in the OBD/DDD dataset; this subset was subsequently matched to the secondary dataset, using DDDs/1000 OBDs as the offset variable. Pharmacy Services as a hospital unit did not have figures available for OBD/DDD, but as their services cover the entirety of the facility, the sum of other directorates was utilised. While OBD were available for 2010-2013 inclusive, reliable tracking of DDD was not available within the health board until 2011. Therefore,
DDD for calendar year 2010 were back-extrapolated using linear trend from 2011-2014. Lastly, a 25% adjustment applied to OBD/DDD figures for 2010 to account for the three quarters of Datix reporting in 2010.

Statistical analysis

The analysis was performed using IBM SPSS Statistics 21 (IBM; Armonk, NY, USA). The α-significance level for all tests was set at 0.05. Variables in the regression were assessed on a singular basis, followed by inclusion of significant variables within a final multivariable model. Results were displayed using relative rates (RR) and 95% confidence intervals (CI).

RESULTS:

Overall analysis

A total of 1345 Datix reports on incidents related to antimicrobials were recorded between April 2010 and December 2013 in our regional analysis, at a crude rate of 0.98 reports/day (95% CI: 0.93-1.03 reports/day). The number of reports each year was relatively stable at 1.04 reports/day (2010), 0.95 reports/day (2011), 0.93 reports/day (2012) and 1.01 reports/day (2013). Ten hospitals contributed reports within the timeframe: two of which contributed approximately 30% of reports and the rest were divided among the remaining 8 facilities. Three directorates accounted for approximately three-quarters of reports – Emergency/Medical (385; 28.6%), Women/Childrens (332; 24.7%) and Surgery/Anaesthetics (273; 20.3%) – with Rehabilitation/Assessment (145; 10.8%), Pharmacy Services (78; 5.8%) and Regional Services (76; 5.6%) constituting the majority of the remainder. Remaining
directorates (Diagnostics, Health/Community Care, Mental Health, and Sexual Health) represented less than 5% of reports collectively.

Reports concerning medication administration/supply (673; 50.0%) represented the largest group under incident stage, followed by prescribing (342; 25.4%). Preparation (97; 7.2%), monitoring (74; 5.5%) and advice (20; 1.5%) were less common; however, a total of 138 reports (10.3%) were classified as ‘other,’ which included multi-stage incidents, environmental hazards, patient-prompted events or those unable to be classified under the aforementioned categories by the reporter. Incident results were most frequently classified as resulting in no injury/harm (514; 38.2%), followed by change/delay in treatment (285; 21.3%), near miss (187; 13.9%), or harm (72; 5.4%); a total of 287 reports (21.3%) were classified as ‘other.’ Among the ‘other’ incident results, 274 (95.5%) reports were coded as ‘unable to assess outcome.’ The most common incident severity rating was minor (642; 47.7%), followed by negligible (443; 32.9%), moderate (223; 16.6%) and major (8; 0.6%). No severe errors were reported, and 29 reports (2.2%) had no severity rating attached.

A total of 1300 reports (96.7%) denoted a single class of antimicrobial involved in the incident, with the remainder involving 2 or 3 classes simultaneously; the most common combinations were aminoglycosides/penicillins (9 reports) and aminoglycosides/glycopeptides (6 reports). Overall, penicillins and aminoglycosides were the most commonly involved classes of medications at 371 reports (27.6%) and 358 reports (26.6%), respectively (Figure 1). Glycopeptides contributed a further 210 reports (15.6%). The most commonly identified agents in each of these classes were
amoxicillin (126 reports; 34.0% of class), gentamicin (344 reports; 96.1% of class) and vancomycin (189 reports; 90.0% of class).

Incidents associated with harm

A total of 72 reports involved harm/injury to the patient. Thirteen reports (18.1%) involved scenarios where antimicrobials were administered to patients with known/documentated allergies; almost all of these cases involved penicillins (10 reports; 76.9% of group). Nine reports (12.5%) noted omissions of antimicrobial therapy where it was felt to have contributed to prolonged infection or hospital stay. Twenty-two reports (30.5%) involved some type of ‘wrong’ event (e.g. dose, frequency, strength, patient, etc.), the most common of which was wrong dose (7 reports) or wrong drug (5 reports). Five reports (6.9%) were related to extravasation of intravenous medication. The most commonly involved medication classes were penicillins (45 reports; 62.5%) and aminoglycosides (13 reports; 18.1%).

Adjusted analysis

Using the available subset of reports (constraints applied to hospital, hospital directorate and incident stage) corresponding to OBD/DDD figures provided 1081 reports (80.4% of total) available for adjusted analysis with an overall adjusted rate of 1.83 reports per 10,000 OBDs (95% CI: 1.72-1.93) or 1.12 reports per 10,000 DDDs (95% CI: 1.05-1.19). Descriptive characteristics of this subset were largely similar to the full extract. Incidents regarding administration/supply (616; 57.0%) resulting in no harm/injury (435; 40.2%) and of minor severity rating (511; 47.3%) were again most common. Emergency/Medical (334; 30.9%), Women/Childrens (301; 27.8%) and Surgery/Aneasthetics (241; 22.3%) remained the top directorates.
reporting. When adjusted, Women/Childrens had a significantly higher reporting rate based on both occupancy (5.59 reports per 10,000 OBDs) and utilisation (4.43 reports per 10,000 DDDs) compared to other directorates, followed by Surgery/Anaesthetics (1.98 and 1.30 reports per 10,000 OBDs and DDDs, respectively). Emergency/Medical services had an elevated reporting rate driven by utilisation (1.89 vs. 0.61 reports per 10,000 OBDs and DDDs, respectively) while Rehabilitation had elevated reporting driven by occupancy (0.51 vs. 1.48 reports per 10,000 OBDs and DDDs, respectively).

The regression analysis (adjusted for both OBDs and DDDs) found that Rehabilitation/Assessment (RR: 2.61, 95% CI: 1.70-4.03) and Women/Childrens (RR: 2.61, 95% CI: 1.70-4.03) were most likely to report incidents on antimicrobials and that administration/supply incidents were most common (RR: 2.07, 95% CI: 1.51-2.84) (Table II). Incidents involving no harm to the patient were most likely and those resulting in some form of harm were least likely among all results (RR: 0.12, 95% CI: 0.07-0.19). Although the number of reports demonstrated a trend toward an increase from 2010 to 2013, this effect was not significant and was not included in the final model.

DISCUSSION:

This retrospective study on hospital medication incident reporting was the first study, to our knowledge, to report on the specific characteristics of antimicrobial incidents using an adjusted approach. This analysis also directly contributes to national goals
for identifying trends and actions in medication error incident reporting to improve patient safety.\textsuperscript{5}

Limited data are available on the extent of antimicrobials as a proportion of total medication incidents, but international estimates from Saudi Arabia (20.5\%)\textsuperscript{12}, Greece (16.5\%)\textsuperscript{13} and the USA (17.6\%)\textsuperscript{14} are broadly comparable to those found in the UK (14.3\%\textsuperscript{8} and 13.1\%\textsuperscript{9}) and indicate the importance of evaluating the characteristics of these reports more in depth. Characteristics of antimicrobial errors may not necessarily mirror those of medication errors at-large; a previous analysis of Datix reports across all medications in a separate group of Scottish hospitals associated prescribing with only 10.8\% of reports,\textsuperscript{15} whereas the rate among antimicrobials in this study was over twice that estimate at 25.4\%. Therefore, education and optimisation in prescribing practices (via clinician in-services and prescribing nomograms) may represent a specific focus for improvement in the use of antimicrobials compared to the overall spectrum of medication use.

A total of 5.4\% of reports on antimicrobials involved incidents causing harm/injury, similar to the 6\% identified among medications at-large in Scotland.\textsuperscript{15} A significant proportion of these errors involved administration of penicillins to patients with known allergies (13.9\% of harm-resulting events and 37.0\% of penicillin-related harm events), which is a highly preventable event. A survey of clinicians in England identified knowledge gaps as a significant contributor to medication errors in penicillin-allergic patients; only 55.9\% of respondents considered themselves knowledgeable about which antibiotics contain penicillin and 87.7\% consider a lack of knowledge an issue among ‘some’ or ‘most’ of their colleagues.\textsuperscript{16} Targeted efforts
in education after identification of problems through clinical audit have been shown to significantly improve practice and potentially reduce patient harm,\textsuperscript{17} demonstrating these incidents to be preventable. A recent initiative in the health board from this analysis produced an information poster highlighting which specific antibiotics are associated with penicillin allergies; the effects of this scheme will be measured using future incident data.

The regression model was utilised as both patient occupancy and medication utilisation may feasibly affect incident reporting rates, although not in linear or singular fashion. Rehabilitation/Assessment and Emergency Care/Medical had the similarly highest occupancy among the directorates assessed (approximately 1.8 million OBDs each over the study period); while Emergency Care/Medical had over 8 times the amount of antimicrobials used during this time period (5.5 million vs 650,000 DDDs), its reporting rate was only 3.5 times higher. However, Women/Childrens, which had similar antimicrobial use to Rehabilitation/Assessment (approximately 675,000 DDDs each), had 3 times as many reports submitted.

Women/Childrens services had the highest reporting rates among directorates as a function of both occupancy and utilisation. This is likely driven by the paediatric component of the service, which has been shown to have higher rates of incident reporting and prescribing errors in previous analyses from the UK\textsuperscript{9} and Spain.\textsuperscript{18} Indeed, post hoc exploration of the events in our analysis estimated that services for children represented 81\% of events from the combined Women/Childrens division (data not shown), in line with these previous data. Children are subject to a higher degree of risk in medication use due to complex dosing schemes/calculations and
Due to this heightened risk, reporting for these patients may also be better engrained in the clinician culture to promote safety or documentation for the purposes of potential litigation. Similarly, the regression model revealed a higher risk of reporting among the Rehabilitation/Assessment directorate, which includes services for rehabilitation, geriatric medicine and palliative care. The latter end of the age spectrum contributes a unique set of risk factors for medication-related incidents, including complexity of health/disability, polypharmacy, diminished or disrupted renal/hepatic function, and lack of standardised recommendations in this population. However, the directorate had the lowest overall utilisation of antimicrobials, suggesting this was not the primary contributor to the incident rate. The high patient occupancy reflected by the OBDs in this directorate is likely driven by longer lengths of stay (as opposed to high throughput seen in Emergency Care/Medical), which lend better opportunity for incident occurrence, recognition and reporting.

With regard to specific therapeutic agents, an estimate of most common antibiotics prescribed in Scottish hospitals identified the most common agents prescribed as amoxicillin (15.6%), co-amoxiclav (10.0%) and metronidazole (9.0%), of which only amoxicillin was involved in a high number of reports in this analysis (9.3%); in fact, gentamicin and vancomycin are estimated to represent 10.8% of antimicrobial prescribing in Scottish hospitals, but were involved in 39.6% of reports in this analysis. This is likely because gentamicin and vancomycin have narrow therapeutic windows, require therapeutic drug monitoring and have an enhanced environment of safety regarding their use.
As a retrospective study, this analysis is subject to limitations, such as lack of entry standardisation by multiple reporters and incomplete information for events. Additionally, the voluntary reporting of safety events is an important consideration. There is a complex interplay of reasons behind a clinician’s choice to contribute to voluntary incident reporting, including habit, social and cultural factors, perceived consequences, facilitating conditions and overall motivation. To complete an adjusted analysis, a subset of the data with corresponding OBD/DDD figures was utilised; although this subset appeared representative of the full extract, it has the potential to skew the results. Furthermore, there was no OBD/DDD estimate for Pharmacy Services because of its nature as a support service rather than an admitting patient service. Being that a pharmacy department provides services to the entire facility, the sum of all other OBD/DDD figures was utilised, resulting in an artificially low reporting rate. An alternative option would have been to exclude consideration of this service from the adjusted analysis; however, this would further limit the representativeness of the subset, and would almost entirely remove reports associated with preparation/dispensing, which were felt to be important to capture.

In summary, antimicrobials should be considered an important focus in improving medication safety due to their widespread use across the clinical spectrum and significant contribution to medication-related incidents. In this regional analysis, increased rates of event reporting were identified among Women/Childrens and Rehabilitation/Assessment services, which follow-up will be needed to determine if this is a function of increased awareness for reporting or higher overall risk within antimicrobial use. However, targeting at-risk paediatric and elderly patients may provide a useful focus for efforts to enhance medication safety. Allergy-induced harm
events were also identified as an important area for quality improvement, and educational efforts in the health board will be measured to determine any reductions in these events. It is hoped that this regional experience identifying areas for quality improvement in hospital antimicrobial use can inform and stimulate a wider audience toward safer use of these medications.

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Conflict of interest statement: The authors have nothing to declare.

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### TABLES

**Table I**: Selected variables and categories in the Datix extract

<table>
<thead>
<tr>
<th>Variable</th>
<th>Categories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hospital directorate</td>
<td>Diagnostics &lt;br&gt; Emergency/Medical † &lt;br&gt; Facilities/Estates &lt;br&gt; Health/Community Care &lt;br&gt; Mental Health &lt;br&gt; Pharmacy Services &lt;br&gt; Regional Services ‡ &lt;br&gt; Rehabilitation/Assessment § &lt;br&gt; Sexual Health &lt;br&gt; Specialist Childrens &lt;br&gt; Surgery/Anaesthetics &lt;br&gt; Women/Childrens</td>
</tr>
<tr>
<td>Incident stage</td>
<td>Prescribing &lt;br&gt; Preparation/dispensing &lt;br&gt; Administration/supply &lt;br&gt; Monitoring/follow-up &lt;br&gt; Advice &lt;br&gt; Supply/use of OTC medicine &lt;br&gt; Other</td>
</tr>
<tr>
<td>Incident result ¥</td>
<td>Change/delay to treatment &lt;br&gt; Change to treatment &lt;br&gt; Delay in treatment &lt;br&gt; Harm/injury &lt;br&gt; Critical condition &lt;br&gt; Ill health &lt;br&gt; Infection &lt;br&gt; Pain/prolonged pain &lt;br&gt; Patient distress &lt;br&gt; Personal injury &lt;br&gt; Prolonged stay in hospital &lt;br&gt; Supportive treatment required &lt;br&gt; Temporary deterioration &lt;br&gt; Near miss &lt;br&gt; Near miss by chance &lt;br&gt; Near miss by intervention &lt;br&gt; No harm &lt;br&gt; No injury, harm or adverse outcome &lt;br&gt; Other &lt;br&gt; Disruption to services &lt;br&gt; Financial loss &lt;br&gt; Loss of property &lt;br&gt; Referred to another service &lt;br&gt; Unable to assess outcome</td>
</tr>
<tr>
<td>Incident severity</td>
<td>Negligible &lt;br&gt; Minor &lt;br&gt; Moderate &lt;br&gt; Major &lt;br&gt; Severe</td>
</tr>
</tbody>
</table>
† includes general medical services: cardiology, endocrinology, gastroenterology, respiratory medicine, rheumatology, dermatology and accident/emergency (A&E)
‡ includes medical specialty services: plastics, nephrology, neurosurgery/neurology, haematology/oncology
§ includes rehabilitation, geriatric medicine and palliative care
¥ upper-level designations denote user-defined categories, lower-level designations denote original Datix categories
Table II: Regression results for antimicrobial reports

<table>
<thead>
<tr>
<th>Variable</th>
<th>Univariable model RR (95% CI)</th>
<th>Adjusted model RR (95% CI)</th>
<th>p-value (adjusted)</th>
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<tbody>
<tr>
<td>Hospital directorate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Emergency/Medical</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
<td></td>
</tr>
<tr>
<td>Regional Services</td>
<td>0.22 (0.14-0.34)</td>
<td>0.25 (0.16-0.41)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Pharmacy Services</td>
<td>0.35 (0.23-0.53)</td>
<td>0.62 (0.39-0.99)</td>
<td>0.046</td>
</tr>
<tr>
<td>Rehabilitation</td>
<td>2.59 (1.76-3.81)</td>
<td>2.61 (1.70-4.03)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Surgery/Anaesthetics</td>
<td>1.49 (1.04-2.11)</td>
<td>1.34 (0.91-1.98)</td>
<td>0.143</td>
</tr>
<tr>
<td>Women/Childrens</td>
<td>2.05 (1.45-2.90)</td>
<td>2.04 (1.39-2.99)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Year</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2010</td>
<td>1 (reference)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>2011</td>
<td>0.92 (0.67-1.27)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2012</td>
<td>0.87 (0.63-1.20)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2013</td>
<td>0.95 (0.69-1.31)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Incident stage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prescribing</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
<td></td>
</tr>
<tr>
<td>Preparation/dispensing</td>
<td>0.25 (0.17-0.35)</td>
<td>0.36 (0.24-0.54)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Administration/supply</td>
<td>2.04 (0.51-2.75)</td>
<td>2.07 (1.51-2.84)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Monitoring/follow-up</td>
<td>0.23 (0.16-0.33)</td>
<td>0.27 (0.19-0.40)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Incident result</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No harm</td>
<td>1 (reference)</td>
<td>1 (reference)</td>
<td></td>
</tr>
<tr>
<td>Near miss</td>
<td>0.34 (0.24-0.49)</td>
<td>0.45 (0.31-0.65)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Change/delay in treatment</td>
<td>0.45 (0.32-0.63)</td>
<td>0.47 (0.32-0.67)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Harm</td>
<td>0.09 (0.06-0.14)</td>
<td>0.12 (0.07-0.19)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other</td>
<td>0.52 (0.37-0.73)</td>
<td>0.54 (0.38-0.78)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

CI: confidence interval; N/A: not applicable; RR: relative rate
FIGURE LEGEND

Figure 1: Selected reports by medication class (with BNF classification)

* Glycopeptides includes only vancomycin and teicoplanin listed in BNF sub-section 5.1.7