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RE Official information request CDHB 9980

We refer to your email dated 26 November 2018 requesting the following information under the Official Information Act from Canterbury DHB regarding hospital admissions related to adverse drug reactions. I note this was clarified as 'Prescription' drugs. We note that this request is for information for each of the 2015/16, 2016/17, and 2017/18 Financial Years:

1. **The total number of admissions to hospital each year.**
2. **The average (both mean and median) bed stay of patients admitted to hospital each year.**

Please refer to **Table one** (below) for the total number of admissions to hospital for calendar years 2016, 2017 and 2018 year to date, and the average (both mean and median) bed stay of these patients.

Table One:

	2016	2017	2018
Number of admissions	119,482	122,997	125,335
Average LOS	3.1 days	3.0 days	2.9 days
Median LOS	1 day	1 day	1 day

3. **The total number of admissions to hospital in relation to adverse (prescription) drug reactions each year. (Clarified: "adverse drug reactions" to be defined as an "unwanted or harmful reaction experienced following the administration of a drug or combination of drugs under normal conditions of use and is suspected to be related to the drug.")**

4. **The total cost of admissions in relation to adverse drug reactions each year.**

Please refer to **Table two** (overleaf) for the total number of admissions to hospital in relation to Adverse (prescription) Drug Reactions (ADR) each year for calendar years 2016, 2017 and 2018 year to date, and the cost of those admissions.

Table two: Number of admissions in relation to adverse drug reactions.

	2016	2017	2018
Number of admissions	3,149	2,987	3,390
Cost	$20,127,483.8	$18,673,806.6	$20,427,224.3
Average LOS	5.4 days	5.1 days	4.7 days
Median LOS	3 days	3 days	2 days

5. **The total number of admissions to hospital in relation to adverse drug reactions each year which were preventable. (Clarified as: "preventable ADR admission" to be defined as an "ADRs caused by medication errors, whether they be acts of omission or commission, incorrect medication/dose/timing, administration of a medication to a patient with a known allergy, inadequate monitoring, or other errors.")**

6. **The total cost of the preventable admissions.**

7. **The average (both mean and median) bed stay of patients admitted to hospital in relation to adverse drug reactions which were preventable.**

This information is not routinely collected.

A prospective observational study of patients admitted to General Medicine at Canterbury DHB in 2011/12 noted that we estimate 19.3% are caused by an Adverse Drug Event (ADE) and 9.2% are contributed to by an ADE. In 2017/18, General Medicine had 18,257 admissions and using this paper we would estimate there would have been 3,523 admissions due to an ADE. We actually had 3,390. The paper is attached as **Appendix 1.**

Differences in rates are more often due to differences in definitions of data collection than in differences in clinical events. These are hard to count for comparisons to other hospitals or health systems.

Canterbury though does have shared electronic records with HealthOne which can assist both primary and secondary care clinicians to understand and potentially help prevent ADEs specifically where they may have previous history of adverse drug reaction.

I trust that this satisfies your interest in this matter.

Please note that this response, or an edited version of this response, may be published on the Canterbury DHB website after your receipt of this response.

Yours sincerely

Carolyn Gullery
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INTERNAL MEDICINE JOURNAL

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ORIGINAL ARTICLES

Adverse drug events are a major cause of acute medical admission

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Key words
drug-related side effect and adverse reaction, patient admission, clinical coding, patient readmission, recreational drug.

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Background: Adverse drug events (ADE) contribute significantly to hospital admissions. Prospective New Zealand data are scant, and the ability of clinical coding to identify ADE associated admissions is uncertain. Outcomes after cessation of causative medications are unknown.

Aims: To assess the frequency, nature and causality of ADE associated with acute admissions to General Medicine at Christchurch Hospital.

Methods: Prospective observational study of patients admitted to our medical team over 20 weeks.

Results: Of 336 admissions, 96 (28.6%) were ADE related. Sixty-five (19.3%) were caused by an ADE, and 31 (9.2%) were contributed to by an ADE. The mean age of non-ADE patients was 64.3 years (range 16–91), which was similar to the mean age of ADE patients (65.9 years; 21–92). However, if intentional overdoses and recreational drug use were excluded, ADE patients were significantly older at 72.4 years (21–92) ($P = 0.0007$). ADE patients took more regular medications on admission (mean 6.6, range 0–22) than non-ADE patients (mean 5.0, 0–18), ($P = 0.003$). The average length of stay was similar. The commonest medications implicated were vasodilators, psychotropics and diuretics. The most common adverse effects were postural hypotension and/or vasovagal syncope (29% of ADE), intentional overdoses and recreational drug use (15%) and acute renal failure and/or clinical dehydration (10%). Seventy-six patients had culprit medications stopped or reduced, and this potentially contributed to six readmissions. Coding identified 61% of ADE associated admissions.

Conclusion: ADE are a common cause of hospital admission. The most frequent problems are postural hypotension and vasovagal syncope, intentional drug misuse and dehydration.

Introduction

Adverse drug events (ADE) cause a significant burden to individual patients and healthcare systems. Regular medication for the treatment or prevention of disease provides benefit in many situations, but should always be weighed against the potential for harm, particularly in the elderly. Published studies have shown large variation in the frequency of hospital admissions secondary to ADE. Much of this relates to study method and patient selection. Prospective observational studies using clinical chart review in Europe[1–6] have found between 3.4% and 20.9% of hospital admissions are caused or contributed to by ADE. A review of Australian studies published between 1988 and 1996 found a similar range of frequency: 2.4% to 22.0%.[7] In the elderly, the frequency has been reported to be even higher at 30.4%.[8] Retrospective studies usually report lower frequencies, for example, a retrospective chart review audit of acute geriatric admissions found that 5.7% of acute admissions were secondary to ADE.[9] Furthermore, studies using computer database codes to identify ADE related admissions report even lower frequencies: A review of the Netherlands' nationwide computer database found a frequency of 1.83%[10] and in England 0.31%.[11] Thus, it is recognised that retrospective studies using coding underestimate ADE frequency.[12] Other important sources of variation include acute versus arranged admissions and the nature of the admitting ward(s).[13] When considering prospective studies of acute admissions, a key factor affecting ADE frequency is causality, that is, the strength

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of the relationship between the patient's presentation and the suspected culprit drug. Causality has been assessed in a variety of ways[1,4,8,13,14] including what action is taken by the admitting doctors with regard to the drug(s). Methods using a scoring system such as the Naranjo adverse drug reaction probability scale demonstrate improved intra- and inter-observer reliability.[14] However, many of these scales include re-challenge, a placebo challenge and/or an assessment of dose response, which are often not possible or practicable. Classification of ADE as certain or probable therefore becomes difficult to achieve. Causality criteria are by no means universal. However, we aimed to assess causality for each ADE so that our data are transparent and therefore comparable with other studies.

There can be a reluctance to stop regular medications even after they have resulted in an ADE requiring hospital admission.[15] There is a lack of published data on outcomes such as readmission rates following alteration of regular medications due to an ADE related admission.

Aims

Our aim was to assess the frequency, nature and causality of ADE affecting medical patients admitted acutely to Christchurch Hospital. We also aimed to evaluate the accuracy of clinical coding for identifying ADE-related admissions, and to assess the frequency of readmission resulting from alteration of medications following an ADE.

Methods

Our department admits approximately 12 000 patients per year, divided among 12 teams. Acute cardiology and a small number of sub-specialty patients are not included. Our general medical team collected data on all patients admitted overnight or longer on our on-call days during two periods, 1 October to 11 November 2011 and 24 December 2011 to 4 April 2012 (20 weeks, 23 on-call days). On the post-take ward round the consultant and registrar assessed whether each admission was caused or contributed to by an ADE. An ADE was defined as any side effect or adverse reaction to a drug (prescribed or non-prescribed) or its withdrawal.[16] This comprises mainly adverse drug reactions (which occur at recommended doses) but also intentional or unintentional overdoses, alcohol use or withdrawal and recreational drug use as a separate subgroup. Therapeutic drug failures were excluded. For ADE-associated admissions, we collected the following data: age, gender, culprit medication(s), changes made to culprit medication during the admission, total number of regular medications on admission (including inhaled or topical treatments), past medical history, duration of admission in number of nights, the primary diagnosis for the admission and a secondary diagnosis if this related to an ADE. For non-ADE admissions, we collected data on age, gender, number of regular medications on admission and length of hospital stay. Data were collected from ward rounds, clinical notes and the electronic discharge summary at the time of discharge. One investigator assessed the strength of the causality of each ADE against the World Health Organization (WHO) Uppsala Monitoring Centre criteria[17] and against the Naranjo criteria.[14] Six months after the date of discharge, the electronic hospital record was reviewed to identify any readmissions relating to drugs that had been stopped, dose reduced or changed to an alternative. A relevant readmission was one that required one of the altered medications to be restarted or the dose increased, or that required an alternative medication started for the same indication. Clinical coding data were obtained for each ADE admission, and we assessed whether the contribution of an ADE was identified in the codes assigned to the admission. As this was an audit as defined by the Operational Standards for Ethics Committees, Ethics Committee approval was not required.

Data were analysed in Excel and R 2.14.1 with the assistance of a Canterbury District Health Board biostatistician. Student *t*-test (or Mann–Whitney test when normality assumption does not hold) was used to assess two-sample differences for continuous variables. Chi-squared test was used for categorical variables. Statistical significance was determined at 0.05. Both total ADE and ADE excluding the 'overdose subgroup' (see above) were compared with non-ADE patients.

Results

Over the 20 weeks, we admitted 336 patients for one or more nights. Adverse drug events were associated with 96 (28.6%) of these admissions. In 65 patients (19.3%) an ADE was the primary cause for admission, and in 31 (9.2%) an ADE contributed to admission. Common examples of 'contributing ADE' were dehydration, acute renal failure or postural hypotension exacerbated by continued diuretics or vasodilators during an acute illness. Out of the 65 patients admitted primarily due to an ADE, 16 were admitted following intentional overdoses, recreational drug use or alcohol or its withdrawal (4.8% of all admissions). Some patients experienced more than one ADE, and in many cases we identified multiple medications that contributed to a single ADE.

Of the 65 admissions for primary ADE, causal relationship was assessed as certain or probable in over 50%, whether the WHO criteria or the Naranjo criteria were

Table 1 Causality assessments of adverse drug events (ADE)

Causality criteria	WHO UMC†		Naranjo	
Primary ADE admissions	Certain	28%		
n = 65	Probable	43%	Probable	54%
	Possible	29%	Possible	46%
Contributing ADE	Certain	9%		
n = 31	Probable	36%	Probable	36%
	Possible	55%	Possible	64%

†World Health Organization Uppsala Monitoring Centre.

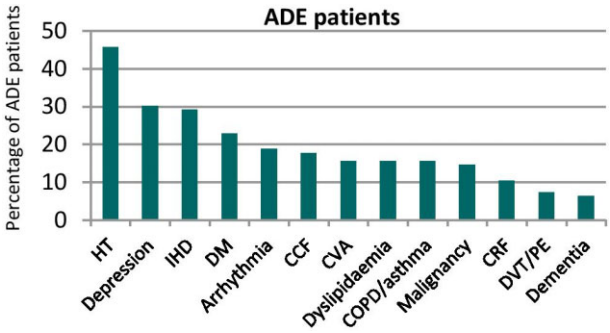

Figure 1 Prevalence of comorbidity in adverse drug events (ADE) patients. CCF, congestive cardiac failure; COPD, chronic obstructive pulmonary disease; CRF, chronic renal failure; CVA, cerebrovascular accident; DM, diabetes mellitus; DVT, deep vein thrombosis; HT, hypertension; IHD, ischaemic heart disease; PE, pulmonary embolism.

used. Causality was less secure for the ADE contributed admissions, with 36 to 45% assessed as certain or probable (Table 1). Therefore, if we include only primary ADE admissions with a certain or probable association, then the frequency of ADE drops to 10.4–13.7% of our acute general medical admissions.

The mean age of ADE patients was similar to non-ADE patients: 65.9 years (range 21–92 years) versus 64.3 years (range 16–91) (P = 0.54). However, when intentional overdoses and recreational drug use were excluded, the ADE patient group was significantly older: 72.4 years (range 21–92 years) (P = 0.0007) (Table 2). The ADE patient group tended to have a higher proportion of males: 41% versus 32% (P = 0.14).

ADE patients took significantly more regular medications on admission (median 6.5, range 0–22) than non-ADE patients (median 4.0, range 0–18) (P = 0.003). Some ADE were caused by non-regular medications, for example respiratory arrest following IV fentanyl and midazolam for an outpatient procedure, hence the inclusion of zero in the range for both groups. The median length of stay in nights for ADE patients was 4.0 (range 1–29) and for non-ADE patients was also 4.0 (range 1–29) (P = 0.24). ADE patients had a high burden of medical comorbidity (Fig. 1). Of the patients, 45.8% suffered hypertension, 30.2% depression, 29.2% ischaemic heart disease and 22.9% diabetes.

The most commonly implicated medications were vasodilators (23% of all culprit medications), followed by psychotropic medications (18%) and diuretics (16%). However, a wide range of medications was represented (Table 3).

The most common class of ADE was postural hypotension/vasovagal syncope, accounting for 29% of all ADE. Of the ADE, 15% of ADE were intentional overdoses, and a further 2% were due to recreational drug use or its withdrawal. Other common diagnoses included acute renal failure/clinical dehydration (10% of ADE) and confusion, delirium or drowsiness secondary to medication (6%). Other adverse effects were diverse (Fig. 2).

During the admission 59.5% of implicated medications were stopped, 22.8% were dose reduced, 3.7% were changed to an alternative medication and 14.0% were continued. Seventy-six patients had regular medications stopped, reduced or changed as a result of their ADE. Follow up at 6 months showed these medication changes may have contributed to six readmissions resulting in a readmission rate of 8% among patients whose medications were altered (Table 4).

Clinical coding data were obtained for nearly all (95/96) of the ADE patients. It correctly identified 61% of the ADE associated with the admission and partially identified a further 7% (one ADE identified but a significant second contributor omitted). In 32% of ADE admissions, no drug-related effect was included in the coding.

Table 2 Comparison of adverse drug event (ADE) admissions with non-ADE-associated admissions

	Non-ADE	All ADE-associated admissions		ADE admissions excluding recreational drugs and overdoses	
Age, mean (range) (years)	64.3 (16–91)	65.9 (21–92)	P = 0.54	72.4 (21–92)	P = 0.0007*
Gender (male)	32%	41%	P = 0.14	39%	P = 0.2748
No. medications on admission, median (range)	4.0 (0–18)	6.5 (0–22)	P = 0.003*	7.0 (0–22)	P < 0.0001*
Length of stay in nights, median (range)	2.0 (1–29)	2.5 (1–29)	P = 0.24	2.0 (1–29)	P = 0.4120

*Statistically significant at P < 0.05.

Table 3 Medications responsible for adverse drug event (ADE)-associated admissions

Class	Examples	Events	% of ADE
Vasodilators	ACE inhibitors, alpha receptor blockers, angiotensin receptor blockers, felodipine, isosorbide mononitrate	36	23%
Psychotropics	Benzodiazepines, bupropion, chlorpromazine, methylphenidate, phenytoin, quetiapine, selective noradrenaline reuptake inhibitors, selective serotonin reuptake inhibitors, sodium valproate, tricyclic antidepressants	28	18%
Diuretics	Furosemide, spironolactone, thiazide diuretics	25	16%
Chronotropes	Amiodarone, beta blockers, diltiazem, digoxin	18	11%
Opiates	Codeine, fentanyl, morphine, oxycodone	12	8%
Others	Adalimumab, alcohol, alendronate, amantidine, antibiotics, aspirin, carbidopa/levodopa, chemotherapy for malignancy, domperidone, ferrous fumarate, heroin, IV contrast, lisuride, omeprazole, paracetamol, phenylephrine, prednisone, promethazine, sulfasalazine, trial medication (MIS 416), unknown recreational drug, warfarin	39	25%

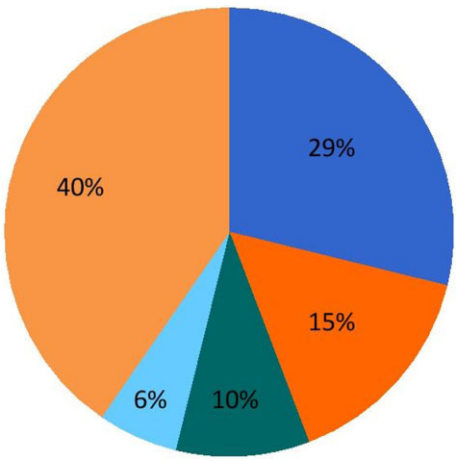

Figure 2 Adverse drug events. (■), Postural hypotension or vasovagal syncope; (■), intentional overdoses or recreational drugs; (■), acute renal failure or dehydration; (■), confusion or drowsiness; (■), other. Other (≤4 occurrences): opiate toxicity, symptomatic bradycardia, gastritis, urinary retention, aspiration, respiratory arrest, nausea, vomiting, anaemia, phenytoin toxicity, hypocalcaemia, epistaxis, INR > 8, hyponatraemia, headache, intracerebral haemorrhage, chemo-induced acute myeloid leukaemia, hypokalaemia, malaise, constipation, fever and myalgias, diarrhoea, seizures, alcohol withdrawal, opiate withdrawal, hypotension, rash, cerebellar toxicity.

Discussion

We found a very high proportion of acute general medical admissions (almost 30%) are attributable to, or contributed to, by an ADE. Even if we decrease the frequency (to 10.4–13.7%) by accepting only primary ADE admissions with certain or probable causality (see above) ADE still remains a common cause for medical admission. This is consistent with results from other prospective studies including patient interview and/or medical chart screening, which have been demonstrated to identify the highest frequency of ADE-associated admissions.[13,18] We also included intentional overdoses, recreational drug use, and alcohol effects, in order to capture the contribution of drugs in the widest definition, and this will have further increased our ADE associated admissions. However, we did not include therapeutic drug failure in our ADE total.

The most common ADE category we recognised was postural hypotension/vasovagal syncope, and this was consistent with the most frequent culprit medications (vasodilators, antidepressants and diuretics) and the relatively high frequency of hypertension in our patients. General practitioners and cardiologists are under pressure

Table 4 Readmissions within 6 months of discharge

ADE	Other diagnoses	Medication altered	Readmission diagnosis	Medication added during readmission
Spontaneous ICH	LV thrombus	Aspirin, warfarin stopped	NSTEMI	Aspirin restarted
Dehydration	COPD exac	Frusemide stopped	Heart failure	Frusemide restarted
Bradycardia	N/A	Digoxin stopped, metoprolol reduced	Fast AF	Digoxin restarted and metoprolol increased
Postural hypotension	N/A	Metoprolol stopped	CVA	Metoprolol restarted
Antibiotic assoc diarrhoea	N/A	Antibiotic stopped	COPD exac	Antibiotic restarted
Postural hypotension	N/A	ISMN, digoxin, frusemide stopped	Fast AF	Beta blocker started
			Angina	ISMN restarted

AF, atrial fibrillation; COPD, chronic obstructive pulmonary disease; CVA, cerebrovascular accident; ICH, intracerebral haemorrhage; exac, exacerbation; ISMN, isosorbide mononotrate; LV, left ventricular. N/A, not applicable; NSTEMI, non-ST elevation myocardial infarction.

from many sources to treat systolic hypertension aggressively in the elderly.[19] A consequence of this is that the incidence of iatrogenic postural hypotension and vasovagal syncope will increase. This trend may be underreported in some ADE studies. First, the history may not be clear, and is often non-specific (e.g. falls).[20] Second, junior doctors tend to defer the measurement of standing blood pressure to the nurses.[21] Third, postural hypotension is sometimes transient (and therefore hard to diagnose with intermittent manual BP measurements) but still severe enough to cause syncope.[22] It is very important that doctors make the diagnosis and are therefore confident enough to stop or adjust culprit medications in the knowledge that they are improving patient quality of life.

For 14% of the implicated medications, drugs and doses were not altered as we assessed that despite the adverse event, the benefit of that medication still outweighed the risk. Of the 76 patients who had medications stopped, altered or dose reduced, we identified only six who experienced a readmission that was potentially contributed to by that medication change. Given these medications had contributed to 76 admissions in the first place, and had been the primary cause of 49 of those admissions, we feel six readmissions (8%) is an acceptable rate.

We did not identify readmissions occurring elsewhere in New Zealand or overseas, and we did not collect data on medications that were subsequently restarted by the general practitioner or in the outpatient setting. However, as ours is the only acute admitting hospital in Christchurch, we will have identified all local presentations requiring readmission.

A further weakness of our study is that we only included general medical patients admitted to Christchurch Hospital, which is a tertiary centre with multiple subspecialty departments. Patients with a presentation related to a single organ system are frequently excluded from the population admitted under general medicine. As a rule, the subspecialty departments admit younger patients with a lower risk of ADE – local data from our 'Decision Support service' shows the mean age of patients admitted to our respiratory and cardiology services is 63 and 62 years respectively, compared to 75 years for general medicine. This has the dual effect of decreasing non-ADE admissions and increasing the average age of general medical patients. Both will tend to increase the ADE frequency in our department, as the elderly are known to have higher rates of ADE.[23,24] We also have not captured patients with gastrointestinal bleeding secondary to anticoagulants or anti-platelet drugs, as in our hospital upper gastrointestinal haemorrhage is admitted under general surgery or gastroenterology. Furthermore, patients admitted to orthopaedic, neurosurgical or general surgical wards with traumatic complications of ADE such as syncope resulting in fractured neck of femur were not identified, nor patients admitted under cardiology with medication-induced arrhythmia. Our study also excluded patients assessed in the emergency department or by the general medical team and discharged home the same day, and this group of patients may include a significant number of ADE. Despite these limitations, we have shown that ADE are a large burden on our general medicine department and on our patient population. In fact, of the diagnostic categories recorded by our information service (DRG coding), we estimate that ADE has become the commonest admission diagnosis in our service, well ahead of the traditional 'favourites' including acute respiratory illness, heart failure and stroke.

Other limitations on our study include the possibility of over-attribution of conditions to ADE and/or bias in the assessment of causality, which was determined prospectively by the medical team conducting the study, and then quantitatively by one investigator applying the Naranjo and WHO causality criteria. The accuracy of causality assessment is a limitation for all studies seeking to quantitate the frequency of ADE.[17] Our methods could have been made more objective by using an independent panel of investigators to apply causality criteria, but are at least transparent allowing comparisons with other studies.

The proportion of ADE that were identified by clinical coding was higher than has been found in previous studies.[12] Since the clinical team that was carrying out the study was also completing the discharge paperwork, we may have been more aware of and more likely to document ADE clearly on the discharge summary. It is possible that the proportion identified on coding at other times and by other teams is lower than our results suggest.

Strengths of our study include prospective data collection over a 5-month period, collected by a single medical team thereby ensuring consistency of methods. Our assessment of causality is transparent, and acknowledgement of uncertainty in causation allows for measurement of all possible ADE or alternatively inclusion of only probable/certain ADE. We have compared coding data with our identified rates of ADE, and have followed up all patients for a period of 6 months to identify readmission outcomes following cessation of medications implicated in ADE.

Conclusion

ADE are a common cause of acute general medical admission to Christchurch Hospital. Of the admissions,

28.6% were associated with an ADE, in 19.3% the primary reason for admission was an ADE, and up to 13.7% of admissions were caused by a probable or certain ADE. Patients with ADE-associated admissions tended to be older and are on more regular medications than the other patients. Vasodilating medications and diuretics accounted for 39% of all ADE-associated admissions, and the commonest adverse events were postural hypotension and vasovagal syncope.

Acknowledgements

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References

1 Mannesse CK, Derkx FHM, de Ridder MAJ, Man in't Veld AJ, van der Cammen TJM. Contribution of adverse drug reactions to hospital admission of older patients. *Age Ageing* 2000; **29**: 35–9.
2 Hallas J, Harvald B, Gram LF, Grodium E, Brosen K, Haghfelt T *et al*. Drug related hospital admissions: the role of definitions and intensity of data collection, and the possibility of prevention. *J Intern Med* 1990; **228**: 83–90.
3 Mjorndal T, Boman MD, Hagg S, Backstrom M, Wilholm B, Wahlin A *et al*. Adverse drug reactions as a cause for admissions to a department of internal medicine. *Pharmacoepidemiol Drug Saf* 2002; **11**: 65–72.
4 Somers A, Robays H, vander Stichele R, van Maele G, Bogaert M, Petrovic M. Contribution of drug related problems to hospital admission in the elderly. *J Nutr Health Aging* 2010; **14**: 477–82.
5 Alexopoulou A, Dourakis SP, Mantzoukis D, Pitsariotis T, Kandyli A, Deutsch M *et al*. Adverse drug reactions as a cause of hospital admissions: a 6-month experience in a single center in Greece. *Eur J Intern Med* 2008; **19**: 505–10.
6 Onder G, Pedone C, Landi F, Cesari M, Vedova CD, Bernabei R *et al*. Adverse drug reactions as a cause of hospital admissions: results from the Italian group of pharmacoepidemiology in the elderly (GIFA). *J Am Geriatr Soc* 2002; **50**: 1962–8.
7 Roughead EE, Gilbert AL, Primrose JG, Sansom LN. Drug-related hospital admissions: as review of Australian studies published 1988–1996. *Med J Aust* 1998; **168**: 405–8.
8 Chan M, Nicklason F, Vial JH. Adverse drug events as a cause of hospital admission in the elderly. *Intern Med J* 2001; **31**: 199–205.
9 Betteridge TM, Frampton CM, Jardine DL. Polypharmacy – we make it worse! A cross-sectional study from an acute admissions unit. *Intern Med J* 2012; **42**: 208–11.
10 van der Hooft CS, Sturkenboom MCJM, van Grootheest K, Kingma HJ, Stricker BHC. Adverse drug reaction-related hospitalisations. *Drug Saf* 2006; **29**: 161–8.
11 Waller P, Shaw M, Ho D, Shakir S, Ebrahim S. Hospital admissions for 'drug-induced' disorders in England: a study using the Hospital Episodes Statistics (HES) database. *Br J Clin Pharmacol* 2004; **59**: 213–19.
12 Houghland P, Xu W, Pickard S, Masheter C, Williams SD. Performance of international classification of diseases, 9th revision, clinical modification codes as an adverse drug event surveillance system. *Med Care* 2006; **44**: 629–36.
13 Leendertse AJ, Visser D, Egberts ACG, van den Bemt PMLA. The relationship between study characteristics and the prevalence of medication-related hospitalizations. A literature review and novel analysis. *Drug Saf* 2010; **33**: 233–44.
14 Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA *et al*. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981; **30**: 239–45.
15 Zhang M, Holman CDJ, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. *BMJ* 2009; **338**: 155–8.
16 Nebeker JR, Barach P, Samore MH. Clarifying adverse drug events: a clinician's guide to terminology, documentation and reporting. *Ann Intern Med* 2004; **140**: 795–801.
17 The Uppsala Monitoring Centre [homepage on the Internet]. The use of the WHO-UMC system for standardised case causality assessment. 2011. [cited 2013 Mar 4]. Available from URL: http://www.who-umc.org/graphics/24734.pdf
18 Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Ann Pharmacother* 2008; **42**: 1017–25.
19 Aronow WS. Treating hypertension in older adults. Safety considerations. *Drug Saf* 2009; **32**: 111–18.
20 Mendu ML, Lampert R, Stoehr J, Tinetti ME. Yield of diagnostic tests in evaluating syncopal episodes in older patients. *Arch Intern Med* 2009; **169**: 1299–305.
21 Naschitz JE, Rosner I. Orthostatic hypotension: framework of the syndrome. *Postgrad Med J* 2007; **83**: 568–74.
22 Wieling W, Krediet CTP, van Dijk N, Linzer M, Tschakovsky ME. Initial orthostatic hypotension: review of a forgotten condition. *Clin Sci* 2007; **112**: 157–65.
23 Beijer HJM, de Blaey CJ. Hospitalisations caused by adverse drug reactions (ADR): a meta-analysis of observational studies. *Pharm World Sci* 2002; **24**: 46–54.
24 Scott I, Jayathissa S. Quality of drug prescribing in older patients: is there a problem and can we improve it? *Intern Med J* 2010; **40**: 7–18.