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The Adverse Drug Event Collaborative: a joint venture to measure medication-related patient harm

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Abstract

Aim To measure the extent of patient harm caused by medications (rate of Adverse Drug Events) in three New Zealand District Health Boards (DHBs), using a standardised trigger tool method.

Methods Counties Manukau, Capital & Coast and Canterbury DHBs decided to work collaboratively to implement the ADE Trigger Tool (TT). Definitions of ADE were agreed on and triggers refined. A random sample of closed charts (from March 2010 to February 2011) was obtained excluding patients who were admitted for <48 hours, children under the age of 18 and psychiatric admissions. In each DHB trained reviewers scanned these in a structured way to identify any of the 19 triggers. If triggers were identified, a more detailed, though time-limited review of the chart was done to determine whether an ADE had occurred. The severity of patient harm was categorised using the National Coordinating Council for Medication Error Reporting and Prevention Index. No attempt was made to determine preventability of harm and ADEs from acts of omission were excluded.

Results The ADE TT was applied to 1210 charts and 353 ADE were identified, with an average rate of 28.9/100 admissions and 38/1,000 bed days. 94.5% of the ADE identified were in the lower severity scales with temporary harm, however in 5 patients it was considered that the ADE contributed to their death, 9 required an intervention to sustain life and 4 suffered permanent harm. The most commonly implicated drugs were morphine and other opioids, anticoagulants, antibiotics, Non Steroidal Anti-Inflammatory Drugs (NSAIDs) and diuretics. Patients who suffered an ADE were more likely to be female, older with more complex medical illnesses, and have a longer length of stay.

Conclusion The rate of medication-related harm identified by the ADE TT is considerably higher than that identified through traditional voluntary reporting mechanisms. The ADE TT provides a standardised measure of harm over time that can be used to determine trends and the effect of medication safety improvement programmes. This study not only shows the problem of medication-related patient harm, but it also shows the utility of informal collaboratives as a mechanism for change.

The New Zealand Adverse Drug Event Collaborative (ADEC) was formed in October 2009, as a result of a fortuitous meeting between representatives of three New Zealand DHBs at a Health Roundtable meeting. The representatives of Counties Manukau, Capital & Coast and Canterbury DHBs all felt that there was a significant lack of knowledge around the rate and type of Adverse Drug Events (ADEs)

occurring in New Zealand. The group decided to use the Institute for Healthcare Improvement's (IHI) Trigger Tool (TT) methodology to develop a standardised approach to ADE measurement.

Adverse Drug Events are one of the most common adverse events found internationally.[1–4] A meta-analysis suggested that these events constituted between the fourth and sixth leading cause of death in the United States.[5] Also in the United States it has been estimated that each ADE increases the length of hospital stay by between 1.91 and 2.2 days, and significantly increases hospital costs.[6,7]

In the New Zealand Adverse Events study[2] drug events made up 15.4% of all adverse events[8] and 9.3% of permanent disability or death adverse events.[9] This local and international data reinforced the DHB collaborative view that measuring ADE was an important first step in improving medication safety.

The IHI introduced the ADE trigger tool in 2000.[3] Recognising that voluntary reporting of medication errors had a poor correlation with the actual number of ADEs, and that chart review, though better at detecting ADEs, was expensive and time consuming, the idea was to use triggers as an effective and efficient way to screen for ADEs. These triggers (19 in total) are clues that an ADE may have occurred and a reviewer then searches the relevant portion of the clinical notes for evidence that harm did in fact occur. For instance, trigger M5—administration of naloxone—may indicate an overdose of morphine with respiratory depression requiring resuscitation (an ADE).[10]

The strength of the ADE TT is that it uses a standard approach for the detection of ADEs over time and can therefore be used to determine trends and assess an organisation's medication safety improvement efforts. There are several key aspects that are standardised. The ADE TT includes all ADEs regardless of whether they are preventable. Although this is challenging, especially for clinicians, there is good reason for this decision. The ADE TT considers unintended physical harm to a patient from the patient's perspective, the important question is "was the patient harmed?" not could that harm have been prevented.

Furthermore some of the harms considered not to be preventable today, may in fact be preventable in the future—and a changing definition would negate the utility of a standard approach over time. The TT also includes only those adverse events related to the active delivery of care, and excludes issues related to substandard care or omission of evidence-based care.[11] Again this is to avoid the changes in what is considered evidence-based care over time. A maximum of 20 minutes is allocated for each chart review and this cut-off means that not all ADEs in a very complex chart would be identified, but this is sacrificed to ensure standardisation.

Here we report on both the collaborative process to develop the NZ Trigger Tool and the type of ADEs discovered.

Methods

Definitions—Firstly it was important to agree on what was being measured with the ADE TT. Harm was defined as "unintended physical injury resulting from, or contributed to, by medical care that required additional monitoring, treatment, hospitalisation, or that resulted in death."[1] The term ADE includes harm caused by the drug (adverse drug reactions) and harm from the use of the drug (including medication errors).[12] See Table 1.

Table 1. Summary of definitions relevant to medication-related harm

Variables	Definition	Example	Characteristics
Medication Error	Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer.[13]	Medication is given to the wrong patient	Most medication errors do not cause patient harm.[14] Voluntary reporting systems that measure medication error do not allow identification of trends over time.
Adverse Drug Reaction (ADR)	Response to a drug which is noxious and unintended and which occurs at doses normally used in man[13]	An allergic reaction to a medication	Primary focus of pharmacovigilance and regulatory agencies for post marketing surveillance. The ADR definition excludes medication errors[1,14]
Adverse Drug Event (ADE)	An injury resulting from the use of a drug[15]	Aspiration pneumonia after over-sedation secondary to morphine overdose	Includes both ADRs and medication errors that cause harm. Approximately 25% of ADEs are caused by medication errors)[1]

The harm resulting from an ADE was categorised using a modified index developed by the National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP).[16] The categories A - D are errors that do not cause harm and are not considered in the ADE TT. Categories E–I include harm caused by medication errors and ADRs:

Category E	Temporary harm to the patient and required intervention
Category F	Temporary harm to the patient and required initial or prolonged hospitalisation
Category G	Permanent patient harm
Category H	Intervention required to sustain life
Category I	Patient death

Trigger tool methodology—All patients admitted during the sample period (1 March 2010 to 28 February 2011) were identified and then a simple random sample was selected using Excel's Rand function. The list of randomised patient numbers was sent to Medical Records at each DHB for collection of the respective closed clinical records (i.e. discharge summary and coding completed). The first ten closed records were assessed retrospectively for each week of the year.

In order to be eligible for review, the admission had to be for a minimum of 48 hours, with neonatal, paediatric (<18 years) and psychiatric admissions excluded.

Each set of notes was screened for the presence of medication 'triggers' (Table 2). The triggers were modified only slightly from the original IHI template (to account for different medication names).[3] When a trigger was identified, the relevant section of the patient's file was reviewed to identify whether an ADE occurred, and if so, what degree of harm was caused.

Table 2. Triggers used to screen for potential ADEs

Trigger	Possible ADE suggested
M1 antihistamines	Allergic reaction to a medication
M2 vitamin K (phytomenadione)	Warfarin-related bleed
M3 flumazenil	Benzodiazepine overdose
M4 antiemetics	Medication-related nausea
M5 naloxone	Opiate-induced over-sedation
M6 antidiarrhoeal	Medication-related diarrhoea
M7 resonium	Medication-related hyperkalaemia
M8 serum glucose <3.0 mol/L	Insulin or oral diabetic therapy overdose
M9 *C. difficile* positive	Antibiotic-related *C. difficile* diarrhoea
M10 APTT >100 seconds	Heparin-related bleed
M11 INR >6	Warfarin-related bleed
M12 WBC $<3 \times 10^9$/L	Medication-related leukopenia and infection
M13 platelet count $<50 \times 10^9$/L	Medication-related bleeding
M14 digoxin level >2 nmol/L	Digoxin toxicity
M15 rising serum creatinine	Medication-related renal impairment
M16 over-sedation/ lethargy/fall/hypotension	Various medication toxicities
M17 rash	Allergic reaction to medications, often seen by the use of steroid creams & emollients on medication charts
M18 abrupt cessation of medication	Medication adverse effects requiring drug withdrawal
M19 transferred to a higher level of care	Medication adverse effects requiring transfer to specialist care area
O2-non-trigger ADE	Other triggers found in the process of the standard chart review, but which don't fit the standard trigger criteria.

The clinical notes were reviewed in a standard order, starting with the discharge summary and then reviewing all medication charts. From there the reviewer focused on the vital sign observation charts, laboratory reports and the patient management system to identify patients transferred to higher levels of care (e.g. ICU).

The collaborative had to define how to handle cases where there was debate as to whether an ADE had occurred. For example, nausea and vomiting are distressing symptoms to a patient, but do they constitute an ADE? Nausea and vomiting can be the result of drug toxicity or overdose, particularly in patients with impaired renal function.

Drugs such as morphine and theophylline frequently cause nausea and vomiting when plasma concentrations are elevated. Antiemetics are also commonly administered to patients postoperatively or to patients receiving chemotherapy. The IHI guidance is that chart reviewers must use professional judgment in these situations to differentiate brief side-effects from ADEs.

The collaborative decided that nausea and vomiting would only be counted as an ADE if they were not quickly relieved by a single dose of antiemetic, but were persistent and requiring further intervention. Similarly, constipation as an ADE was only counted if prolonged (>3 days) and required intervention. Each DHB had different staff and resources, but in all areas where there was a question of harm or the degree of harm, 2 reviewers were available.

Data analysis & reporting—The data was entered into a MS Access database developed by CMDHB.

As all three DHBs were using the same database, the data could be combined to create unified reports. Demographics, including case-weight were provided by the decision support team at each DHB. Case weights measure the relative complexity of the treatment given to each patient. For example, a cataract operation will receive a case weight of approximately 0.5, while a hip replacement will receive 4 case weights. This difference reflects the resources needed for each operation, in terms of theatre time, number of days in hospital, etc.[17]

Rates of ADEs (categories E–I) were calculated both by 1000 bed days and by 100 admissions.

Staff resources—Each of the DHBs had different resourcing setups, and a unique combination of reviewers.

- **DHB 1** had a Clinical Pharmacist (2 days per week), a Medication Safety Pharmacist and the Clinical Director overseeing the work
- **DHB 2** had a Clinical Pharmacist, a Medication Safety Pharmacist, and the active involvement of the CMO.
- **DHB 3** had a Clinical Pharmacist and Clinical Pharmacologist undertaking the ADE module. There was no specific budget for this work which forced costs to be absorbed into existing departmental budgets, with staff also donating a significant amount of their own time. DHB 3 were consequently unable to screen a large number of notes.

Staff training—The IHI on-line resource was used and there were six webinar interactive sessions.[11] CMDHB had also been involved in teleconferences and e-mail discussions with the IHI directly which clarified issues and aided the training process.

DHB collaboration—The utilisation of frequent e-mails and teleconferences allowed the work to run smoothly; knowledge to be shared; questions to be answered, and helped achieve consistency of chart assessments between sites.

Results

The data reported below covers the 12 month period from 1 March 2010 to 28 February 2011. The simple random sample of patients was similar to the overall patient mix, in terms of age, and length of stay in DHB 1 but the sample were younger in DHB 2 compared with their patient mix (61.4 in sample versus 65.9 in inpatient population) DHB three's sample was only 77 patients and this limits the utility of the sample for analysis.

In all three DHBs, the patients suffering ADEs were more likely than those without ADE, to be older, female, and with an increased length of stay. (see Table 3) Patients suffering an ADE were also more likely to have complex illnesses with higher case weights.

The overall rate of ADEs in the three DHBs combined was 28.9 ADE/100 admissions and 38 ADE/1,000 bed days (see Table 4) One in four patients (24.7%) in the sample had at least one ADE. Over 15% of the ADEs occurred in the community and precipitated admission.

The most common ADEs were in the least severe categories of harm (E and F), with a total of 94.5% (see Table 5). Boxes 1–5 give a real example of each category.

The most sensitive triggers were abrupt cessation of medications (20.1% of ADEs), antiemetics (19%), falls/hypotension (6.2%), raised creatinine (3.7%), naloxone (2.8%), antihistamines (2.8%) and Vitamin K (2.3%). Four triggers identified no ADEs—antidiarrhoeals charted, raised INR, decreased platelet count and digoxin level >2 nmol/L.

The 10 top medications associated with ADE are shown in Table 6, with morphine, warfarin, and tramadol taking out the top 3. The most common class of medications implicated were opioids (156 ADE, 32.9%), anticoagulants (48 ADE, 10.0%) antibiotics (42 ADE, 8,8%), NSAIDs (24 ADE, 5.0%), and diuretics (19 ADE, 4%). There were 6 ADE associated with insulin or oral hypoglycaemics.

A review of ADEs at DHB 1 showed that none of the 196 ADEs were present in the voluntary medication error reporting system.

Table 3. Characteristics of sample population compared with patients with ADE

Variables	Sample (minus ADE) N=916	ADE N=286	Difference	P value
LOS days (mean)	7.06	10.62	3.56	0.001
Age years (mean)	58.72	64.76	6.04	0.001
Gender (F)	53%	62%	9%	0.001
Case weight	1.68	2.14	0.46	0.001

Table 4. ADE rates March 2010–February 2011

Month 2010 & 2011	Charts Reviewed	Inpatient ADEs	Non-Inpatient ADEs	Total ADEs	ADEs per 100 Admissions	ADEs per 1000 Bed Days
Mar 2010	148	35	8	43	29.1	45.0
Apr	106	17	3	20	18.9	28.6
May	116	24	4	28	24.1	34.4
Jun	127	40	6	46	36.2	44.4
Jul	93	23	3	26	28.0	36.1
Aug	90	24	2	26	28.9	38.7
Sep	84	21	4	25	29.8	32.9
Oct	89	17	6	23	25.8	35.0
Nov	85	14	6	20	23.5	32.8
Dec	77	16	3	19	24.7	35.4
Jan 2011	91	24	4	28	30.8	40.3
Feb	104	44	5	49	47.1	52.9
Total	**1210**	**299**	**54**	**353**	**Average: 28.9**	**Average: 38.0**

Table 5. ADEs by harm category

Harm Category	Inpatient ADEs n (%)	Non-Inpatient ADEs n (%)	Total ADEs n (%)
E (Temporary harm to the patient and required intervention)	213 (60.3)	3 (0.8)	216 (61.0)
F (Temporary harm to the patient and required initial or prolonged hospitalisation)	68 (19.3)	50 (14.2)	118 (33.5)
G (Permanent patient harm)	4 (1.1)	0	4 (1.1)
H (Intervention required to sustain life)	9 (2.5)	0	9 (2.5)
I (Patient death)	5 (1.2)	1 (0.28)	6 (1.5)

Table 6. Top 10 medications implicated in ADE

Medication	Number of ADE	Percentage of total ADE
Morphine	83	17.4%
Warfarin	29	6.1%
Tramadol	25	5.2%
Aspirin	21	4.4%
Frusemide	20	4.2%
Oxycodone hydrochloride	20	4.2%
Enoxaparin	16	3.3%
Prednisone	15	3.1%
Fentanyl	14	2.9%
Codeine phosphate	13	2.7%

Box 1. Category I – ADE contributing to death

An 80-year-old woman was admitted to hospital following a fall the previous day. A CT scan revealed a large subdural haematoma. She was on warfarin (INR of 3.4), which contributed to her bleed. Vitamin K and prothrombinex were administered in the emergency department in order to reverse the effects of warfarin. However, she continued to deteriorate and died later that day.

Box 2. Category H – ADE requiring intervention to sustain life

A 46-year-old man was admitted to hospital with an exacerbation of congestive heart failure. Allopurinol and colchicine were stopped on a background of acute on chronic renal failure, resulting in an attack of gout whilst an inpatient. When treated with oxycodone and codeine, he suffered severe Type II respiratory failure, resulting in transfer to the respiratory ward for treatment with non-invasive ventilation. Naloxone was administered to reverse the effect of opiate analgesia.

Box 3. Category G – ADE causing permanent patient harm

A 78-year-old man presented to hospital with increasing shortness of breath and ongoing hypoxia. He had never smoked. Cause of shortness of breath thought to be due to pulmonary fibrosis secondary to amiodarone. He had been on amiodarone for more than 10 years for atrial fibrillation. Amiodarone was stopped and he was placed on home oxygen and prednisone.

Box 4. Example of Category F – ADE causing temporary harm to the patient and required initial or prolonged hospital stay

A 61-year-old man was recently discharged from hospital on a combination of warfarin and aspirin for atrial flutter. Ten days later, he was readmitted to hospital with a GI bleed and a high INR (4.5). Anticoagulants were stopped and the high INR was reversed with prothrombinex, fresh frozen plasma and Vitamin K. He was then treated with IV omeprazole twice daily and discharged on oral omeprazole.

Box 5. Category E – ADE causing temporary harm to the patient and required intervention

A 37 year old woman was admitted to hospital for an operation to correct a disc prolapse. Post-operatively, she suffered ongoing (> 3 episodes) nausea and vomiting secondary to a morphine PCA. This medication was stopped and regular antiemetics were prescribed and administered. Nausea and vomiting resolved with the above interventions.

Discussion

This work has demonstrated a successful collaboration between three DHBs, which has shown a reliable way to calculate Adverse Drug Event (ADE) rates using the ADE Trigger Tool. The combined data from the three DHBs showed an ADE rate of approximately 30 per 100 admissions. This is very much higher than the number identified by the usual voluntary hospital incident reporting systems—in fact in the DHB that looked at this issue, none of the ADE were identified in the hospital incident reporting system.

The most common harm was relatively mild and fleeting (category E), however more serious harm occurred in 5% with 5 deaths associated with ADEs. There were 54 patients with category F harms that occurred in the community and precipitated admission.

The most common drugs were those identified internationally as 'high-risk' – opioids, anticoagulants, NSAIDs and insulin. Antibiotics of various types were the third most common cause of patient harm. Patients suffering an ADE were more likely to be older, female and with an increased length of stay. This is consistent with other findings both in New Zealand and the United States.[8,18]

Rozich et al[3] published the first paper using the ADE Trigger Tool. This reviewed the tool in 86 US hospitals and the overall ADE rate was 2.68/1,000 medication doses. We were unable to measure medication doses and so we cannot directly compare these results. However, as in our paper, the authors found that M18 (abrupt cessation of medication) was the trigger with the highest yield of ADE, while antiemetics (M4) was the most frequent trigger found.

In a more recent study[19] the trigger tool was used in a pilot on one ward in a U.K. hospital. They applied the Trigger Tool to 207 patients of which 61% had positive triggers, however they identified only 7 ADE (7 ADE/1000 patient days). Some of the reasons why this result is lower than ours are: it was conducted only on a surgical ward, they excluded ADEs which caused admission, the tool was based on the original U.S. tool but was considerably modified, 25% of patients did not have their records available and were therefore excluded and another 17% did not have laboratory results available but they were still included in the study, and finally e-prescribing was introduced to the ward after the first 3 months of the study.

There are several limitations to our work. The three DHBs were new to the Trigger Tool method and it took some time to agree on definitions, randomisation techniques

and processes. One DHB excluded charts that were unavailable at the time of review, whereas another decided to continue to chase such charts. One DHB struggled with the demands of the Trigger Tool in terms of human resource and managed only a sample of 77 patients. Furthermore they struggled to get the database set up and this delayed their ability to undertake the ADE TT work.

We did not assess the inter-rater reliability of the assessors in each DHB, we focused instead on being internally consistent over time (the same assessor) and we also wrote a practical guide for assessors which outlined the approach to common areas of confusion/difference. A further limitation is that we did not compare the ADE rates identified with the trigger tool with those found using the gold standard chart review, but our aim was not to identify all ADE but rather to establish a standardised system that could be analysed over time.

The NZ health system has a strong history of innovation and improvement, but does not succeed well when it comes to generalisation or spread of ideas. The District Health Board structure provides a model for integrated funding decisions based on local need, but can lead to isolated or duplicated efforts on issues of interest to the whole sector. This is particularly evident when it comes to quality and patient safety where the needs are similar if not identical across DHBs. The 3 District Health Boards in this collaborative decided to work together and implement the IHI ADE Trigger Tool.

A “just do it” approach was agreed; a model with perhaps a touch of anarchy as no one planned to seek permission before embarking on this work. This voluntary initiation by key clinical leaders from each DHB, who had sufficient influence within their own organisation, provided the opportunity for such a constructive approach. The experience at DHB 3 however, showed the limits of clinical enthusiasm to overcome institutional barriers.

In order to make this collaborative a success we required a reliable, systematic way of working that would work despite the geographical distances. The regular teleconferencing enabled relatively rapid progress and the continued cooperative approach. This process created a form of distributed leadership with no central control and a degree of informality. Innovations and ways of working could be developed between meetings, the best ideas agreed, and then pursued. The team was able to move from a state of naive enthusiasm through to informed practice without a break in continuity of engagement and commitment.

With a modest investment of resources in terms of time commitment from clinical leaders and allocated time from clinical pharmacists it has been possible to achieve an application of the medication trigger tools in a way that we would expect to be sustainable across DHBs. The same approach could be used to extend the collaborative through a series of "cells" on a regional basis. One would expect this to be quicker, as there would be expertise available to support a new “cell” and the specific tools such as forms and databases would be available as a starting point.

All three DHBs plan to continue with the Trigger Tool, but will probably incorporate it into the more expansive Global Trigger Tool (GTT),[10] which looks at harms from medical care, not just medication-related harm. Of note the 4 ADE triggers that we found to have little value have been deleted from the medication section in the GTT.

In the future it is also likely that we will move to greater computer automation to identify triggers using the electronic databases that we already have: e-laboratory results, data from Pyxis administration machines (CCDHB and CMDHB), e-pharmacy systems and in the future electronic prescribing and medication repositories.

The group has continued to collaborate on using the TT data to decrease medication adverse events. This involves focusing on frequent ADEs (e.g. constipation and nausea/vomiting) and high risk medications - the top 10 medications was a useful place for DHBs to focus their education campaigns. To date, CCDHB have run a campaign around insulin ADEs and sent a national alert to other DHBs, CMDHB has focused on morphine-related ADE, and CDHB have a range of medication safety initiatives stemming from this work.

It is important to note that the ADE TT is not useful for benchmarking one hospital against another as patient populations and reviewer techniques are likely to differ; it is designed to assess trends over time in the same hospital (20)

Conclusion

This study shows the extent of medication-related patient harm in three DHBs, with 30% of patients suffering some medication-related harm, 5% of these were serious, with medications ADEs contributing to 5 deaths. It is over 10 years since the Institute of Medicine's report "To Err is Human"[21] showed the scale of medical harm, however, despite a mixture of central pressure, exhortation and local initiatives, progress to improve patient safety in New Zealand has been uncomfortably slow.

The required urgency dictates a new approach. Our suggestion would be the creation of more collaborative models across organisations, mimicking what has been achieved here.

Competing interests: Nil.

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