Using a Clinical Data Repository to Estimate the Frequency and Costs of Adverse Drug Events

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ABSTRACT

As a result of increased attention to medical errors, many institutions are contemplating increased use of information technology and clinical decision support. We conducted a retrospective analysis to estimate the frequency and cost of adverse drug events (ADEs) for inpatients at the University of Virginia. Applying published criteria for the detection of potential adverse events, we used a clinical data warehouse to identify patients and cases with potential ADEs. Again using published criteria, we then estimated the actual number of adverse drug events and preventable adverse drug events, as well as their attributable costs and excess length of stay. Our results showed a higher estimate (10.4-11.5 events per 100 admissions) for ADEs than seen in the ADE Prevention Study, highlighting the importance of considering the generalizability of published ADE studies to other settings. Our analysis demonstrates that retrospective analysis can be an efficient and powerful technique to evaluate rules and criteria used to detect ADEs and to assess their impact.

BACKGROUND

The recent Institute of Medicine Report "To Err is Human" has focused increased attention on medical errors.[1] Citing studies from the Harvard Malpractice Study, the American Hospital Association, and the centers for Disease Control and Prevention, the authors estimate that medical errors occur in approximately 3% of hospitalizations, resulting in between 44,000 and 98,000 American deaths per year. Costs to society are estimated between $17 and 29 billion, of which one half can be attributed to healthcare.

Medication errors occur frequently and represent a significant portion of the above costs. The authors of the IOM report estimate increased hospital costs for preventable adverse drug events for inpatients at $2 billion nationally. These figures were extrapolated from results from studies at Brigham & Women's Hospital.

Following methods similar to those used at Brigham and Women's Hospital, we have derived estimates for the number of adverse drug events (ADEs) for University of Virginia (UVa) inpatients over the past four years. Our findings suggest that improving our ability to detect, characterize, and prevent adverse drug events represents a considerable opportunity for improving patient care and reducing costs.

METHODS

Investigators at Brigham and Women's Hospital and at the University of Utah have created automated monitors to screen for adverse drug events.[2,3] These monitors are computer programs that look for patterns in laboratory test results and/or medication ordering that may indicate adverse drug events. For example, a rising creatinine in a patient receiving a nephrotoxic medication may indicate an ADE. Likewise, the administration of antidote medications such as naloxone, flumazenil, or Digibind may be used to detect ADEs.

We performed a retrospective analysis, using the Clinical Data Repository (CDR), a relational data warehouse for the University of Virginia Health System, to estimate the frequency and costs of adverse drug events for UVa inpatients. The CDR extracts and links data from several UVa clinical and administrative computer systems.[4] The database is enriched with clinical details from additional internal and external sources, including Virginia Department of Health death certificate data.

Our study uses the rules published for the Brigham ADE monitor.[2] We programmed each of the 52 rules against the CDR to identify retrospectively instances where the ADE monitor would have indicated potential ADEs. We adhered as closely as possible to the published methods—accordingly, pediatric and obstetric cases were excluded. The

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ADE rules are based on medications and laboratory results— the CDR contains each recorded instance of a medication being administered and receives laboratory test results from a SunQuest laboratory information system. For inpatients, all medications are ordered via electronic physician order entry; nurses document their administration online.

After identifying these potential adverse drug events, detected with the automated criteria, we attempted to estimate the actual number of adverse drug events and preventable adverse drug events, as well as their attributable costs and excess length of stay. To derive these estimates, we also followed published studies from Bates and colleagues. [5] Classen has also published figures for estimating excess length of stay, costs, and mortality[6]; however, since we used the ADE screening criteria from Brigham & Women's, we chose to adopt Bates' methods for estimating the impact of ADEs.

RESULTS

We applied the screening criteria from Brigham and Women's Hospital to UVa data to identify patients and cases with potential ADEs (Table 1).

Year	*1996*	*1997*	*1998*	*1999*
Patients	17,053	16,480	16,287	15,949
Cases	19,625	18,792	18,756	18,139

Table 1. Potential ADEs identified with automated screening criteria.

Using an overall estimate for the positive predictive value of the ADE screening criteria of 0.17, we estimated the actual number of ADEs.[2] (Table 2)

Year	*1996*	*1997*	*1998*	*1999*
Patients	2899	2802	2769	2711
Cases	3336	3194	3188	3083

Table 2. Estimated number of actual ADEs. Based on positive predictive value for automated screening criteria of 0.17.

Using Bates' estimate that 31.6% of ADEs are preventable [2], as well as his figures for excess length of stay and costs associated with ADEs (Table 3), we derived estimates for the excess length of stay and costs resulting from ADEs at the University of Virginia. (Table 4) We did not adjust the cost or LOS figures for inflation or other secular trends.

	All ADEs	*Preventable ADEs*
Excess LOS	2.2 days	4.6 days
Excess Costs	$3244	$5857
Attributable Post-ADE Costs	$2595	$4865

Table 3. Estimates for excess LOS and costs associated with ADEs (after Bates et al. 1997).

DISCUSSION

We found that ADEs occurred more frequently than in published studies.

Our estimates suggest that between 1996 and 1999, ADEs occurred at a rate of 10.4 – 11.5 events per 100 admissions. (Table 5) The Adverse Drug Event Prevention Study found that ADEs occurred at rate of 6.5 per 100 admissions.[7] Thus, our findings suggest that ADEs may occur more frequently than in the ADE Prevention Study. Possible explanations include:

- This finding is true. ADEs are more common at UVa than in the ADE Prevention Study.
- Our estimates are too high implying that the screening criteria may not perform in the same way at UVa as at Brigham & Women's. For example, the positive predictive value may be less than 0.17. Of note, we did use cut-offs and ranges from the Brigham (e.g. digoxin level > 1.7) even when the "normal" range at UVa is different (e.g. 2.2 for digoxin), which might explain a portion of the excess frequency.
- One or more assumptions made in our analysis may not be accurate.

Year	*1996*	*1997*	*1998*	*1999*
Total # ADEs (patients)	2899	2802	2769	2711
# Preventable ADEs	916	885	875	857
Excess days (all)	6378	6164	6091	5965
Excess days (preventable)	4214	4072	4025	3941
Excess costs (all)	$ 9,404,388	$ 9,088,390	$ 8,981,955	$ 8,795,555
Excess costs (preventable)	$ 5,365,522	$ 5,185,235	$ 5,124,510	$ 5,018,162
Attributable post-ADE costs (all)	$ 7,522,931	$ 7,270,152	$ 7,185,010	$ 7,035,901
Attributable post-ADE costs (preventable)	$ 4,456,764	$ 4,307,012	$ 4,256,572	$ 4,168,236

Table 4. Estimates for excess length of stay and costs resulting from ADEs at UVa. Based on estimate that 31.6% of ADEs are preventable.

	1996	*1997*	*1998*	*1999*
# Admissions (total)	28,826	28,867	29,641	29,680
#Admissions (excluding Peds/OB)	25,148	25,188	26,113	26,122
#ADEs per 100 admits	11.5	11.1	10.6	10.4

Table 5. Number of ADEs per 100 admissions at UVa. The ADE Prevention Study found that ADEs occurred at a rate of 6.4 per 100 admissions.

We made several assumptions in our analysis that may affect our results.

Key assumptions that were used in our analysis include:

1. The adverse drug event screening criteria have similar predictive values at the University of Virginia as at Brigham and Women's. At the Brigham, the predictive value for each rule was evaluated using concomitant manual chart review for all cases.
2. Attributable costs and excess length of stay for each adverse event (and preventable adverse event) are similar at the University of Virginia and Brigham and Women's.
3. Attributable costs and excess length of stay for adverse events detected by the automated monitor are similar to those detected via manual chart review. The latter method was used to identify cases used to estimate attributable costs and excess length of stay. [5]

At Brigham and Women's, the automated ADE monitor significantly outperformed voluntary report for detecting ADEs and was comparable to manual chart review.[2] However, there was not very much overlap between ADEs detected by the automated monitor and those detected by chart review. The cost estimates were derived using ADEs detected by manual review.[5] In our analysis, we have assumed that costs for ADEs detected by automated criteria have similar costs to those detected by manual review. This may not be the case.

Retrospective analysis using the CDR is an efficient and convenient method of exploring the impact of ADEs. We believe that these assumptions are reasonable to estimate the magnitude of the ADE problem at the University of Virginia. Our estimate for the frequency of ADEs, within a factor of two of the ADE Prevention Study finding, suggests that these assumptions are not far off. Chart review of selected potential ADEs, as well as negative controls, would be useful to more precisely examine the generalizability of the assumptions and the predictive value of the screening criteria for UVa.

Significance of this study

Our findings are significant for three reasons:

1. The frequency of ADEs and their impact are substantial. Even if our estimates are off by a factor of two, there are still numerous opportunities for ADE prevention, improvement in patient care, and reduction in costs at UVa.
2. We have demonstrated the utility of routinely collected clinical and administrative data, stored in the Clinical Data Repository, for retrospective analysis of patient care at UVa.
3. Our findings suggest that the ADE screening criteria may be used prospectively to prevent future ADEs at UVa and add support to growing evidence that there is considerable potential to use information technology to reduce the cost of patient care.

Generalizability of published studies.
As a result of increased attention to medical errors, many institutions are contemplating increased use of information technology and clinical decision support. To estimate the incidence and cost of ADEs and to quantify the potential return on investment for clinical decision support systems, administrators and information technology professionals, like the authors of the IOM report, must rely on published studies such as the ones cited in this paper. It is therefore useful to consider and assess the generalizability of these analyses to other settings. In particular, how well can the attributable costs of an ADE be extrapolated, and how do these costs vary across different types of ADEs? For example, Raschke and colleagues implemented several rules to detect and prevent adverse drug events.[8] To estimate the savings generated by these rules, they used published estimates for costs per ADE. Our analysis, which produced a higher estimate for the frequency of ADEs, suggests that the assumptions behind published estimates may be somewhat generalizable, but not with a high degree of precision.

Usefulness of retrospective analysis.
A notable aspect of our study is that is was relatively easy and inexpensive to conduct. We used routinely collected clinical and administrative data, stored in a data warehouse, to generate rapid estimates about the frequency and costs of ADEs. While retrospective analysis cannot be used to directly prevent future adverse events, it can provide an efficient and non-resource-intensive way to conduct exploratory analyses and identify areas for further study. Our retrospective analysis has proven useful to highlight the magnitude of the problem of ADEs and the potential savings. In addition, retrospective analysis is very useful for testing potential rules prior to implementing them in a prospective manner. As more vendors and institutions make available decision support modules and rules, they can be rapidly and efficiently assessed against historical data.

Declining frequency of adverse drug events
The data in Table 5 appear to demonstrate a downward trend in the frequency of ADEs from 11.5 ADEs per 100 admissions in 1996 to 10.4 ADEs per 100 admissions in 1999. This decrease may represent a true decline in the frequency of ADEs at UVa, a secular trend, or decreased sensitivity of the ADE monitor rules over time. Some of the published rules are intended to detect ADEs related to medications that may be have been used less frequently, as practice patterns changed— for example, theophylline or quinidine. Other rules are targeted at specific medications (e.g. ranitidine, gentamicin) rather than classes of medications (H2-blockers, aminoglycosides). Over time, use of specific medications may change dramatically due to formulary substitutions (e.g. famotidine for ranitidine) and shifts in practice patterns (e.g. from H2-blockers to proton pump inhibitors). We have not yet analyzed our data more closely to understand how these changes may contribute to the apparent decline in ADEs. However, this observation does highlight the need to modify and update ADE rules in a production system.

Opportunities for future investigation
We have already suggested that chart review of selected potential ADEs, as well as negative controls, would be useful to more precisely examine the generalizability of the assumptions and the predictive value of the screening criteria for UVa. It would also be helpful to look more closely at the distribution of potential ADEs that we identified and examine how well our findings correlate with the published Brigham results. Similar distributions would provide additional evidence that the ADE rules can be generalized.

In addition, our methodology may also be extended to the outpatient setting to develop screening criteria for potential ADEs. Currently, there are no published rules for detecting ADEs for outpatients. Using existing laboratory and outpatient pharmacy data, we can begin to develop and validate automated rules to detect and prevent outpatient ADEs.

CONCLUSION

By applying published criteria for the detection of potential adverse events and for estimating their costs, we used a clinical data warehouse at the University of Virginia to estimate the frequency and costs of adverse drug events. Our analysis demonstrates that retrospective analysis can be an efficient and powerful technique to evaluate rules and criteria used to detect ADEs and to assess their impact. We derived an estimate for the frequency of ADEs that is greater than the one reported in the ADE Prevention Study, highlighting the importance of considering the generalizability of published ADE studies to other settings.

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