Chapter 4. Clinical Pharmacist’s Role in Preventing Adverse Drug Events: Brief Update Review

Peter Glassman, M.B.B.S., M.Sc.

Introduction

In our original report, “Making Health Care Safer” 2001, Kaushal and Bates noted that over 770,000 people were harmed or died in hospitals annually from adverse drug events (ADE), \(^1\) with incidence rates in hospital-based studies ranging from 2 to 7 per 100 admissions. \(^1\) In the outpatient setting, as they also noted, one study on adults estimated the ADE incidence rate at 3 percent. \(^8\) The purpose of this review is to update the data on the incidence of ADEs in hospital settings and to review measures aimed at preventing these events, including the role of the clinical pharmacist. We searched the literature from 2001 to 2011 and included studies most relevant to clinical pharmacist interventions on medication errors and adverse drug events in various health care settings. Our focus was on studies that to some degree addressed the possible association between clinical pharmacist activities and improved prescribing practices and/or assessed whether such activities might lead to reduced medication errors and adverse drug events.

What is the Role of the Clinical Pharmacist in Preventing Adverse Drug Events?

There have been various patient safety initiatives implemented that involve pharmacists with the goal of reducing ADEs. These initiatives are often based on the premise that clinical pharmacists can play an important role in intercepting and acting on possible prescribing errors and/or recognizing drug-related problems before injury, or further injury, can occur. This concept has been tested in a variety of settings in a variety of ways.

In the original report, Kaushal and Bates \(^4\) noted that in a seminal study by Leape and colleagues, \(^9\) a clinical pharmacist participating in an intensive care unit team led to “a statistically significant 66% decrease in preventable ADEs due to medication ordering.” Another study suggested that ward-based clinical pharmacists may benefit inpatient medication use safety and quality. \(^10\) A single study in a geriatric population found a decrease in medication errors at the time of inpatient discharge when clinical pharmacists were involved. \(^11\) Based on a meta-analysis, clinical pharmacists were considered to have a modest effect on maintaining acceptable drug ranges. \(^12\) In the ambulatory setting, the authors noted that clinical pharmacists may have positive impacts on a variety of chronic diseases (hypertension, hypercholesterolemia, chronic heart failure, and diabetes). \(^13\) However, these ambulatory studies had significant limitations and potential biases, making generalizations problematic. \(^4\)

At the time of the first review, \(^4\) the authors noted that, in two studies, physicians were receptive to and often acted on clinical pharmacist interventions \(^9,14\) attesting to the often collaborative relationship between the two groups. Overall, Kaushal and Bates concluded that, “Given the other well-documented benefits of clinical pharmacists and the promising results in the inpatient setting, more focused research documenting the impact of clinical pharmacist interventions on medication errors and ADEs is warranted.” \(^4\)
What Have We Learned About the Role of Clinical Pharmacists?

Recent Reviews and Systematic Evaluations Suggest Clinical Pharmacists Improve Medication Management

Since the 2001 report, several new systematic reviews, have addressed the role of clinical pharmacists in different clinical settings. The largest such review was Kaboli and colleagues (AMSTAR score 7 positive of 9 relevant domains). This review included studies from 1985 to 2005 that assessed clinical pharmacists’ interventions in inpatient care. Eligible studies were those using concurrent controls or time series design, and measuring a number of different outcomes.

Thirty six studies contributed evidence to the review, including 10 studies of pharmacists’ participation on rounds, 11 studies of their participation in medication reconciliation, and 15 studies of drug-specific services (e.g. coumadin, antibiotics). The review was narrative, and concluded that the evidence “supports the use of clinical pharmacists in the inpatient setting to improve the quality, safety and efficiency of care,” although noting that the evidence base is still limited by small sample size, many studies were conducted at only a single institution, and most studies have differing measures of outcome.

Three other reviews dealt with clinical pharmacists benefit in the care of elderly adults, in nursing homes, and pediatric patients. Hanlon and colleagues found a number of benefits for elderly adults, in a variety of settings, in optimizing prescribing (i.e., improving quality of pharmaceutical care) and reducing drug-related problems. While there was scant evidence on reducing adverse drug events, they commented on the difficulty in designing a study that would show ADR reduction, noting that to detect a 25% decrease in adverse effects, due to a pharmacist intervention, would require randomizing at least 800 to 1400 elderly patients. This review scored 4 of 9 relevant AMSTAR domains. In a narrative review of interventions in nursing homes, Marcum and colleagues included five randomized controlled studies assessing the impact of clinical pharmacists on various outcomes, including drug-related adverse events; they also included two studies with a pharmacist or pharmacologist as part of a multidisciplinary approach. While some studies showed significant differences in the numbers and/or choices of (or changes in) drugs, clinical outcomes—measured in various ways—were mixed, tending overall to show inconsistent and/or nominal impacts. This review scored 6 of 9 relevant AMSTAR domains. Sanghera and colleagues noted that pharmacists provide important improvements on drug therapy for children. Many of the 18 studies in the review were older, and methodologies differed (e.g., measuring outcomes in various ways, by various designs and definitions), but an overall positive impact was consistently seen in the studies reviewed. Most of the studies were in the inpatient setting, and only three were in the outpatient area. Even so, the review highlighted that pharmacists play a crucial role in detecting and correcting medication errors, such as dosing mistakes, sometimes potentially lethal ones. The authors concluded, “…pharmacists reviewing medication charts is very important in identifying medication-related problems; hence it is likely to be the most effective factor in improving drug therapy in children.” It should be kept in mind that many of the studies pre-dated the electronic era. This review scored 7 of 9 relevant AMSTAR domains.

Another review, by Cohen and colleagues, included 16 studies of pharmacist activities in the Emergency Department (AMSTAR score 6 positive of 9 relevant domains). Again noted was the wide diversity of tasks in which pharmacists were engaged, including (but not limited to)
providing drug information, patient counseling, precepting, toxicology case assistance and various forms of therapeutic consultations, interventions and managements, including medication error prevention (though included studies were limited in this latter regard).

By and large, these reviews support clinical pharmacist activities in improving medication management. In general, three issues emerge from the literature. First, clinical pharmacists are engaged in a multitude of patient level activities, including recognizing, intercepting, and documenting drug-related problems, as well as assisting in optimizing pharmaceutical choices for patients and, in some cases, engaging in specific interventions or in specific disease management practices. Second, it is problematic to accurately capture all that pharmacists do at either an individual patient level or at an organization level, which makes it that much more difficult to assess their impact, especially since clinical pharmacists do not work in isolation but rather with other clinicians and, frequently, within hospitals or health care systems or settings. Third, studies that attempt to show the benefit of pharmacists engaged in various activities from a larger vantage point (e.g., assessing whether adding a pharmacist to a ward team reduces medication errors or adverse drug events) often have challenges in their interpretation, including lack of concurrent control groups, indeterminate definitions of suboptimal prescribing, varying definitions of medication errors and preventable adverse drug events, different methods of error and event capture and reporting, and varying clinical outcome assessments. Even so, while individual studies do not always demonstrate benefits from an organizational perspective, the body of work suggests that pharmacists provide substantial value to patient care, clinical teams, institutions, and health care organizations.

Original Studies Not Included in the Systematic Reviews Show that Interventions With Clinical Pharmacists Tend to Reduce Adverse Events

As with the systematic reviews we again focused on studies that attempted to address the relationship between clinical pharmacist activities and improved prescribing and/or a reduction in adverse events. We identified eight new studies not included in the systematic reviews already discussed. Of note, many of the more recent studies have had limited success in overcoming some of those methodological issues seen in some of the older studies. As above, we focused on studies from the United States and other English speaking countries. The studies are summarized in Table 1, Chapter 4.

<table>
<thead>
<tr>
<th>Study, Year</th>
<th>Population and Controls</th>
<th>Intervention</th>
<th>Outcomes Measured and Timing</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Kaushal, 2008††</td>
<td>Pediatric ICU or general ward with paper charting; matched units did not receive intervention</td>
<td>Part or full-time clinical pharmacist rounding and monitoring drug dispensing, storage, and administration</td>
<td>Medication errors and adverse events pre/post, identified by nurse and reviewed by 2 blinded physician reviewers; 6-8 weeks baseline, 3-month intervention period</td>
<td>Full-time clinical pharmacist decreased medication errors (29 to 6 per 1000 patient days); increase in medication errors in controls; part-time pharmacists did not decrease error rate.</td>
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<td>Wang, 2007</td>
<td>Pediatrics unit of a community teaching hospital</td>
<td>Addition of CPOE to existing clinical pharmacist system</td>
<td>Medication errors, near misses, and adverse events over a 3-month period</td>
<td>Clinical pharmacist intercepted 78% of 111 potentially serious prescribing errors but none of 32 harmful administrative errors and few of the transcribing (6/25) or monitoring errors (3/7)</td>
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<td>Rivkin, 2011</td>
<td>General medical ICU</td>
<td>Inclusion of clinical pharmacist in rounding</td>
<td>Clinically important drug-drug interactions pre/post over a 10-week period</td>
<td>Drug interaction rates decreased significantly (65%) when compared retrospectively (historically) to a 10-week period earlier in the year</td>
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<td>LaPointe, 2003</td>
<td>Cardiac ICU</td>
<td>Rounding and participation in patient-oriented activities (e.g., taking medication histories, discharge counseling), and provider level activities (e.g., giving in-service talks to house staff and communicating with physician and nursing staff)</td>
<td>Medication error interventions (e.g., dose or medication changes, missing medications, allergy-drug contraindications) pre/post over 5 years</td>
<td>Incidence of medication errors increased from around 15 to nearly 24 per 100 admissions, and a higher trend was seen during times of house staff transition</td>
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<td>Stoner, 2000</td>
<td>Outpatient psychiatric setting (235 sets of evaluations in 83 patients on antipsychotics)</td>
<td>Pharmacist testing/recommendations regarding patients on antipsychotics who had movement disorder complaints or who were taking drugs to counter movement disorders</td>
<td>Movement disorder (extrapyramidal) symptoms</td>
<td>A majority of recommendations (82% of 130 evaluations) were followed by clinicians; of these, 93% led to a resolution or reduction in extrapyramidal symptoms</td>
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<td>Simpson, 2004</td>
<td>Neonatal ICU</td>
<td>Pharmacist-run education program on medication orders and IV fluid review implemented at month 4 of 12 months plus other process changes</td>
<td>Medication errors pre/post; case finding by incident reporting</td>
<td>Significant decrease in medication errors (from 24 to 5 per 1,000 neonatal activity days/month); error rate increased during summer staffing change</td>
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<td>Bond, 2006&lt;sup&gt;17&lt;/sup&gt;</td>
<td>584 hospitals encompassing &gt;35,000 Medicare patient stays</td>
<td>Pharmacy staffing and presence or absence of various pharmacy services</td>
<td>Adverse drug reactions (ADRs)</td>
<td>Pharmacist involvement in 8 services (in-service education, drug information services, adverse drug reaction management, drug protocol management, cardiopulmonary resuscitation teams, medical rounds and completing admission drug histories) as well as higher staffing rates decreased ADRs; however, pharmacist participation in total parenteral nutrition teams increased ADRs</td>
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<td>Bond, 2007&lt;sup&gt;18&lt;/sup&gt;</td>
<td>885 U.S. hospitals with data on 2.8 million Medicare patients</td>
<td>14 different clinical pharmacy services and several staffing models</td>
<td>Severity-adjusted mortality rates</td>
<td>In-service education, drug information, adverse drug reaction monitoring; participation in drug protocol management, cardiopulmonary resuscitation teams and medical rounds; and completing admission drug histories were associated with reduced mortality as were two staffing variables</td>
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<td>Brown, 2008&lt;sup&gt;19&lt;/sup&gt;</td>
<td>Large rural hospital Emergency Department</td>
<td>Review of medication orders and identification of errors via retrospective review by an independent reviewer. Pharmacists also documented their interventions.</td>
<td>Medication Errors, 1 month when pharmacist was not present to check medication orders versus 1 month when pharmacist (s) was (were) present; time periods for assessment were one year apart</td>
<td>Pre-post analysis showed significant decrease (66.6%) from error rates of approximately 16 to 5 per one hundred medications orders</td>
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**Table 1, Chapter 4. Summary of studies (continued)**

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<tr>
<th>Study, Year</th>
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<th>Intervention</th>
<th>Outcomes Measured and Timing</th>
<th>Findings</th>
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<tbody>
<tr>
<td>Rothschild, 2010&lt;sup&gt;30&lt;/sup&gt;</td>
<td>Four academic Emergency Departments</td>
<td>Observational study in which pharmacy residents conducted 226 sessions (787 hours) of observing pharmacist activities; the study included over 17,000 medications ordered or administered to nearly 6,500 patients</td>
<td>Identification of medication errors at various stages of prescribing or administration by unblinded, continuous observation. Data collection was via templated forms. Captured elements included errors of interest, ranging from those intercepted before reaching the patient to caught after reaching the patient but before harm could occur to ameliorated adverse events (collectively these together were known as recovered medication errors). Case reviewers independently assessed suspected error interventions.</td>
<td>Pharmacists identified over 500 recovered medication errors, with an overall rate of about 3 per 100 medications or about 8 per 100 patients. Approximately 90% were intercepted before reaching the patient.</td>
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<tr>
<td>Cesarz, 2012&lt;sup&gt;31&lt;/sup&gt;</td>
<td>An academic medical center’s 32-bed Emergency Department, serving pediatric and adult populations</td>
<td>Prospective observational study looking at activities of four pharmacists during relevant shifts in reviewing discharge prescriptions. Data collection was over a 3 week period and used standardized forms for reporting interventions. All recommendations were provided to the ordering physician who made the determination to change a prescription</td>
<td>Self-report of interventions on discharge prescriptions. An independent reviewer determined whether the intervention was categorized as error prevention or therapeutic optimization</td>
<td>Of 674 discharge prescriptions reviewed, ED pharmacists intervened on about 10%; roughly half of the 68 interventions (54%) concerned error prevention.</td>
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A number of the studies contained design flaws that prevented ruling out the contribution of other process modifications or even secular changes to the observed results. Nevertheless, overall, these newer studies continue to support the important roles of clinical pharmacists in reducing prescribing mishaps as well as in improving several patient-level outcomes in various
settings. With the exception of one study, studies in which pharmacists participated in a greater number of clinical processes seemed to show stronger effects.

**Clinical Pharmacist Interventions Show Little Potential for Harm**

Virtually no study has shown an outright potential for harm, apart from an occasional isolated finding such as an ADR rate increase with pharmacist participation on total parenteral nutrition teams (a result that, given its oddity, must remain questionable). Theoretically speaking, as noted in the original report, involvement of clinical pharmacists and implementation of their review processes may result in some delays in dispensing medications. But if these interventions reduce errors (and/or clarify prescribing), this outcome cannot truly be considered a harm, though perhaps it is bothersome and time consuming for patients or providers.

**Benefits of Implementation May Outweigh Costs**

In terms of resource utilization and costs, the decrease in ADRs that should result from improved prescribing practices should lead to financial savings and/or mitigations in the costs of care. However, information in that regard is limited and generally unclear. Of the two primary studies noted in the 2001 report that estimated annual savings, one based on interventions in an intensive care unit and another based on pharmacist activities in a large university hospital, estimated savings ranged from $270,000 to almost $400,000 per year. Because differences in outcomes and how they are measured, true costs and/or savings are hard to gauge and, not surprisingly, vary widely. For example, in a review of economic benefits from hospital-based interventions by De Rijdt and colleagues, financial outcomes, generally stated in estimated annualized savings, ranged anywhere from less than $10,000 to over $500,000, depending on the study and the clinical or interim outcome measured as well as the method of financial evaluation and whether pharmacist costs were included. From another perspective, Bond and Raehl estimated that the legal settlement costs avoided by the reduction in preventable deaths in the patient population they studied (Medicare) would be nearly $2.4 billion for hospitals that incurred adverse events. While cost or savings estimates depend on a set of assumptions as well as the financial costs of pharmacists’ time and effort, these widely varying estimations bring home the point that reduction in medication errors or preventable ADEs can have subsequent “down the line” effects and that financial changes may accrue at a variety of levels depending on the intervention and the seriousness of clinical outcomes (or outcomes avoided). A major driver of the cost-effectiveness of a clinical pharmacist intervention is whether new pharmacists need to be hired or if the program can be implemented by reallocation of existing resources and/or the use of lower cost pharmacy technicians for some roles, and thus increase the availability of clinical pharmacists to directly interact with patients and physicians.

**Conclusions and Comment**

Clinical pharmacists play important roles in a variety of health care settings, and their activities appear to benefit individual patients as well as health care organizations in a multitude of ways, many of which are difficult to isolate when studying whether these interventions objectively lower medication errors or ADEs. Many of the studies are not methodologically strong, and the literature lacks consistency and comparability. Nevertheless, systematic reviews and recent evidence generally supports that pharmacist involvement in intensive care units, particularly when engaging in bedside rounds improves medication management and/or reduces
medication errors and preventable ADEs. The existing data for other inpatient and for outpatient care settings are also supportive of a role for pharmacists but less robust than in intensive care units. Data from nursing homes are not as clear as for other settings, but, logically speaking, since medication and prescribing errors occur in this setting, and patients are elderly and more prone to polypharmacy, it is likely by analogy that drug safety in nursing homes will be improved by clinical pharmacist interventions. Similarly, evidence from emergency departments is limited but given the high intensity of care activities and of prescription utilization, it is logical that benefits will accrue from pharmacist interventions. More and better designed studies should help determine the magnitude of the benefit(s), to the extent that such benefits exist, in various health care settings. A summary table is located in Table 2, Chapter 4.

### Table 2, Chapter 4. Summary table

<table>
<thead>
<tr>
<th>Scope of the Problem Targeted by the PSP (Frequency/Severity)</th>
<th>Strength of Evidence for Effectiveness of the PSPs</th>
<th>Evidence or Potential for Harmful Unintended Consequences</th>
<th>Estimate of Cost</th>
<th>Implementation Issues: How Much do We Know?/How Hard Is it?</th>
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<tbody>
<tr>
<td>Common/Low</td>
<td>Moderate-to-high</td>
<td>Low</td>
<td>High</td>
<td>Little/Moderate</td>
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### References


