

Chapter 7. The Clinical Pharmacist's Role in Preventing Adverse Drug Events

Rainu Kaushal, MD, MPH

David W. Bates, MD, MSc

Harvard Medical School

Background

A large literature documents the multiple roles clinical pharmacists can play in a variety of health care settings.¹⁻⁸ Much of this literature focuses on measures of impact not directly relevant to this Report – eg, economic benefits,^{4,8} patient compliance,⁶ and drug monitoring.^{2,3} More recently, systems-based analyses of medication errors and adverse drug events (ADEs) have drawn attention to the impact clinical pharmacists can exert on the quality and safety of medication use.⁹⁻¹² In this chapter, we review the evidence supporting the premise that direct participation of pharmacists' in clinical care reduces medication errors and ADEs in hospitalized and ambulatory patients.

Practice Description

Clinical pharmacists may participate in all stages of the medication use process, including drug ordering, transcribing, dispensing, administering, and monitoring. The specific activities of clinical pharmacists vary substantially in the studies reviewed in this chapter. In the hospital setting, one study evaluated the role of a senior pharmacist participating fully in intensive care unit rounds and available throughout the day in person or by page for questions.¹³ Another study evaluated a ward pharmacy service that examined order sheets for new therapies and carried out checks that were formerly performed in the pharmacy.¹⁴

Pharmacists may also play a role at the time of discharge. One study reported the impact of clinical pharmacists' consultation for geriatric patients at the time of discharge,¹⁵ with pharmacists serving as consultants to physicians and reinforcing patients' knowledge of their medication regimen. The roles of clinical pharmacists are similarly diverse in studies of ambulatory settings. Here they include the provision of consultative services,¹⁶⁻¹⁸ patient education,¹⁶⁻¹⁸ therapeutic drug monitoring,³ and even follow-up telephone calls to patients.^{3,16-18}

Prevalence and Severity of the Target Safety Problem

It is estimated that over 770,000 people are injured or die in hospitals from adverse drug events (ADEs) annually.¹⁹⁻²¹ The few hospitals that have studied incidence rates of ADEs have documented rates ranging from 2 to 7 per 100 admissions.^{11,19,22,23} A precise national estimate is difficult to calculate due to the variety of criteria and definitions used by researchers.²⁴ One study of preventable inpatient ADEs in adults demonstrated that 56% occurred at the stage of ordering, 34% at administration, 6% at transcribing, and 4% at dispensing.²² In this study, the drug class most commonly associated with preventable ADEs was analgesics, followed by sedatives and antibiotics. Even fewer studies have been conducted in the outpatient setting. One recent cross-sectional chart review and patient care survey found an ADE rate of 3% in adult primary care outpatients.²⁵

Opportunities for Impact

Although many hospital pharmacy departments offer clinical pharmacy consultation services,²⁶ the degree to which these services include rounding with clinicians¹³ is unclear.

Hospital pharmacies provide support to a variable degree in different ambulatory settings (clinics, nursing homes, adult daycare),²⁶ but the precise nature of clinical pharmacists' activities in these settings is not uniformly characterized.

Study Designs

We identified 3 systematic reviews of clinical pharmacists in the outpatient setting.^{5,17,18} We included only the most recent review,¹⁸ as it followed the most rigorous methodology and included the bibliographies of the previous reviews.^{5,17} We identified only one study¹⁶ of the impact of clinical pharmacists on patient outcomes in the ambulatory setting that had not been included in this systematic review.¹⁸ This study, a randomized controlled trial evaluating clinical pharmacists' participation in the management of outpatients with congestive heart failure,¹⁶ was therefore also included.

For studies of clinical pharmacists in the hospital setting, an older review² did not meet the characteristics of a systematic review, but was a very thorough summary of the relevant literature. It included 8 studies evaluating pharmacists' roles in detecting and reporting ADEs in the hospital setting. Preliminary review of these studies revealed that the measured outcomes were Level 3 (detection of ADEs as an end in itself). Consequently, we did not include them. One older retrospective before-after analysis (Level 3)¹⁴ did meet our inclusion criteria, as did 2 more recent studies of clinical pharmacists' roles in the inpatient setting: a prospective, controlled before-after study (Level 2)¹³ and a randomized controlled trial (Level 1).¹⁵

We included an additional meta-analysis focusing on therapeutic drug monitoring by clinical pharmacists in the hospital and ambulatory settings.³ The studies included in this meta-analysis consisted predominantly of controlled observational studies (Level 3) and non-randomized clinical trials (Level 2), but one randomized controlled trial was also included (Level 1-3A).

Table 7.1 lists the studies reviewed in this chapter and briefly describes their salient features. All of the listed studies involved adult patients, as the single pediatric study⁹ identified by our literature search had no control group (Level 4 design) and was therefore excluded.

Study Outcomes

Level 1 outcomes reported in the included studies consisted of ADEs¹³ and clinical events related to heart failure, including mortality.¹⁶ One study used telephone interviews to solicit patient self-reports of adverse drug reactions.^{13,27} This study was excluded since the systematic review of clinical pharmacists' roles in ambulatory settings¹⁸ incorporated its findings in several of its analyses.

The distinction between Level 2 and 3 outcomes can be somewhat ambiguous in studies of prescribing practice, as the exact point at which choices of therapeutic agents or dosing patterns become not just sub-optimal but actually represent "errors" is difficult to define precisely. Even for objective outcomes, such as serum drug concentrations, the connection to patient outcomes is weak in some cases (eg, monitoring vancomycin levels^{28,29}), and therefore more appropriately designated as Level 3 rather than Level 2. Acknowledging the subjectivity of this judgment in some cases, we included studies that contained a mixture of Level 2 and 3 outcomes, including "prescribing problems," (which included inappropriate choice of therapy, dosage errors, frequency errors, drug-drug interactions, therapeutic duplications, and allergies¹⁵), and serum drug concentrations for a broad range of medications.³

Evidence for Effectiveness of the Practice

In the inpatient setting, Leape's study¹³ demonstrated a statistically significant 66% decrease in preventable ADEs due to medication ordering. The study of geriatric patients at the time of discharge demonstrated clinically and statistically significant decreases in medication errors.¹⁵ The meta-analysis of the effect of clinical pharmacokinetics services on maintaining acceptable drug ranges indicated only modest effect sizes for the outcomes measured, and only 2 of the main results achieved statistical significance.³

The comprehensive review of clinical pharmacist services in ambulatory settings reported positive impacts for patients with hypertension, hypercholesterolemia, chronic heart failure, and diabetes.¹⁸ However, the authors identify important limitations: these studies are not easily generalizable, only 2 studies compared pharmacist services with other health professional services, and both studies had important biases. Consequently, they emphasized the need for more rigorous research to document the effects of outpatient pharmacist interventions.¹⁸ The additional study of outpatients demonstrated significant decreases in mortality and heart failure events,¹⁶ but these results may reflect closer follow-up and monitoring (including telemetry) for the intervention group or the higher doses of angiotensin-converting enzyme (ACE) inhibitors the patients received. Generalizing this benefit to other conditions is difficult since most conditions do not have a single medication-related process of care that delivers the marked clinical benefits as do ACE inhibitors in the treatment of congestive heart failure.³⁰

Potential for Harm

Introducing clinical pharmacists might potentially disrupt routine patient care activities. However, the 2 studies that assessed physician reactions to clinical pharmacists^{13,27} found excellent receptivity and subsequent changes in prescribing behavior.

Costs and Implementation

Two studies examined resource utilization and cost savings in the inpatient setting. The intensive care unit study indicated that there could be potential savings of \$270,000 per year for this hospital if the intervention involved re-allocation of existing pharmacists' time and resources.¹³ McMullin et al studied all interventions made by 6 hospital pharmacists over a one-month period at a large university hospital and estimated annual cost savings of \$394,000.³¹

A systematic review of outpatient pharmacists indicated that pharmacist interventions could lead to increased scheduled service utilization and decreased non-scheduled service utilization, specialty visits, and numbers and costs of drugs.¹⁸

Comment

At present, one study provides strong evidence for the benefit of clinical pharmacists in reducing ADEs in hospitalized intensive care unit patients.¹³ One additional study provides modest support for the impact of ward-based clinical pharmacists on the safety and quality of inpatient medication use.¹⁴ The evidence in the outpatient setting is less substantial, and not yet convincing. 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.

Table 7.1. Studies of clinical pharmacists' impact on ADEs and medication errors*

| Study | Study Design | Study Outcomes | Results |
|--|---|---|--|
| Beney, 2000. ¹⁸ Systematic review of the roles and impacts of pharmacists in ambulatory settings; reviewed studies included 16,000 outpatients and 40 pharmacists | Level 1A (systematic review) | Levels 1-3 (variety of patient outcomes, surrogate outcomes, impacts on physician prescribing practices and measures of resource use) | Improvement in outcomes for patients with hypertension, hypercholesterolemia, chronic heart failure, and diabetes |
| Gattis, 1999. ¹⁶ 181 patients with heart failure due to left ventricular dysfunction followed in a general cardiology clinic | Level 1 (RCT) | Level 1 (mortality and other clinical outcomes related to heart failure) | 16 versus 4 deaths or other heart failure events (p<0.005) |
| Leape, 1999. ¹³ Medical and cardiac intensive care unit patients at Massachusetts General Hospital, a tertiary care hospital in Boston | Level 2 (prospective before-after study with concurrent control) | Level 1 (ADEs) | 66% decrease in the rate of preventable ADEs (p<0.001) |
| Leach, 1981. ¹⁴ 315 patients at Queen Elizabeth Hospital in Birmingham, England | Level 3 (retrospective before-after analysis) | Level 2 (various types of medication errors) | 40-50% overall reduction in medication errors All 8 of the targeted error types decreased (results achieved statistical significance for 5 error types) |
| Lipton, 1992. ¹⁵ 236 geriatric patients discharged from the hospital on three or more medications | Level 1 | Levels 2 & 3 ("prescribing problems") | Less likely to have a "prescribing problem" (p=0.05) |
| Ried, 1989. ³ Pooled patient population not reported, but review of articles indicates predominance of studies of (mostly adult) hospitalized patients | Level 1A-3A (meta-analysis predominantly included controlled observational studies and non-randomized trials) | Levels 2 & 3 (measures of peak, trough and toxic serum drug concentrations for a variety of medications) | More likely to have therapeutic peak and trough and less likely to have toxic peak and trough, but modest effect sizes (results achieved statistical significance for only 2 measures) |

* ADE indicates adverse drug event; and RCT, randomized controlled trial.

References

1. Dyer CC, Oles KS, Davis SW. The role of the pharmacist in a geriatric nursing home: a literature review. *Drug Intell Clin Pharm.* 1984;18:428-433.
2. Hatoum HT, Catizone C, Hutchinson RA, Purohit A. An eleven-year review of the pharmacy literature: documentation of the value and acceptance of clinical pharmacy. *Drug Intell Clin Pharm.* 1986;20:33-48.
3. Ried LD, McKenna DA, Horn JR. Meta-analysis of research on the effect of clinical pharmacokinetics services on therapeutic drug monitoring. *Am J Hosp Pharm.* 1989;46:945-951.
4. Willett MS, Bertch KE, Rich DS, Ereshefsky L. Prospectus on the economic value of clinical pharmacy services. A position statement of the American College of Clinical Pharmacy. *Pharmacotherapy.* 1989;9:45-56.
5. Carter BL, Helling DK. Ambulatory care pharmacy services: the incomplete agenda. *Ann Pharmacother.* 1992;26:701-708.
6. Tett SE, Higgins GM, Armour CL. Impact of pharmacist interventions on medication management by the elderly: a review of the literature. *Ann Pharmacother.* 1993;27:80-86.
7. Jenkins MH, Bond CA. The impact of clinical pharmacists on psychiatric patients. *Pharmacotherapy.* 1996;16:708-714.
8. Schumock GT, Meek PD, Ploetz PA, Vermeulen LC. Economic evaluations of clinical pharmacy services—1988-1995. The Publications Committee of the American College of Clinical Pharmacy. *Pharmacotherapy.* 1996;16:1188-1208.
9. Folli HL, Poole RL, Benitz WE, Russo JC. Medication error prevention by clinical pharmacists in two children's hospitals. *Pediatrics.* 1987;79:718-722.
10. Lesar TS, Briceland LL, Delcours K, Parmalee JC, Masta-Gornic V, Pohl H. Medication prescribing errors in a teaching hospital. *JAMA.* 1990;263:2329-2334.
11. Bates DW, Boyle DL, Vander Vliet MB, Schneider J, Leape L. Relationship between medication errors and adverse drug events. *J Gen Intern Med.* 1995;10:199-205.
12. Kaushal R, Bates DW, Landrigan C, McKenna J, Clapp MD, Federico F, et al. medication errors and adverse drug events in pediatric inpatients. *JAMA.* 2001;285:2114-2120.
13. Leape LL, Cullen DJ, Clapp MD, Burdick E, Demonaco HJ, Erickson JI, et al. Pharmacist participation on physician rounds and adverse drug events in the intensive care unit. *JAMA.* 1999;282:267-270.
14. Leach RH, Feetam C, Butler D. An evaluation of a ward pharmacy service. *J Clin Hosp Pharm.* 1981;6:173-182.
15. Lipton HL, Bero LA, Bird JA, McPhee SJ. The impact of clinical pharmacists' consultations on physicians' geriatric drug prescribing. A randomized controlled trial. *Med Care.* 1992;30:646-658.
16. Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. *Arch Intern Med.* 1999;159:1939-1945.
17. Hatoum HT, Akhras K. 1993 Bibliography: a 32-year literature review on the value and acceptance of ambulatory care provided by pharmacists. *Ann Pharmacother.* 1993;27:1106-1119.

18. Beney J, Bero LA, Bond C. Expanding the roles of outpatient pharmacists: effects on health services utilisation, costs, and patient outcomes. In: *The Cochrane Library*, Issue 2, 2000. Oxford: Update Software.
19. Classen DC, Pestotnik SL, Evans RS, Lloyd JF, Burke JP. Adverse drug events in hospitalized patients. Excess length of stay, extra costs, and attributable mortality. *JAMA*. 1997;277:301-306.
20. Cullen DJ, Bates DW, Small SD, Cooper JB, Nemeskal AR, Leape LL. The incident reporting system does not detect adverse drug events: a problem for quality improvement. *Jt Comm J Qual Improv*. 1995;21:541-548.
21. Cullen DJ, Sweitzer BJ, Bates DW, Burdick E, Edmondson A, Leape LL. Preventable adverse drug events in hospitalized patients: a comparative study of intensive care and general care units. *Crit Care Med*. 1997;25:1289-1297.
22. Bates DW, Cullen DJ, Laird N, Petersen LA, Small SD, Servi D, et al. Incidence of adverse drug events and potential adverse drug events: Implications for prevention. *JAMA*. 1995;274:29-34.
23. Jha AK, Kuperman GJ, Teich JM, Leape L, Shea B, Rittenberg E, et al. Identifying adverse drug events: development of a computer-based monitor and comparison with chart review and stimulated voluntary report. *J Am Med Inform Assoc*. 1998;5:305-314.
24. Adverse drug events: the magnitude of health risk is uncertain because of limited incidence data. Washington, DC: General Accounting Office; 2000.
25. Gandhi TK, Burstin HR, Cook EF, Puopolo AL, Haas JS, Brennan TA, et al. Drug complications in outpatients. *J Gen Intern Med*. 2000;15:149-154.
26. Ringold DJ, Santell JP, Schneider PJ. ASHP national survey of pharmacy practice in acute care settings: dispensing and administration—1999. *Am J Health Syst Pharm*. 2000;57:1759-1775.
27. Hanlon JT, Weinberger M, Samsa GP, Schmader KE, Uttech KM, Lewis IK, et al. A randomized, controlled trial of a clinical pharmacist intervention to improve inappropriate prescribing in elderly outpatients with polypharmacy. *Am J Med*. 1996;100:428-437.
28. Freeman CD, Quintiliani R, Nightingale CH. Vancomycin therapeutic drug monitoring: is it necessary? *Ann Pharmacother*. 1993;27:594-598.
29. Cantu TG, Yamanaka-Yuen NA, Lietman PS. Serum vancomycin concentrations: reappraisal of their clinical value. *Clin Infect Dis*. 1994;18:533-543.
30. Flather MD, Yusuf S, Kober L, Pfeffer M, Hall A, Murray G, et al. Long-term ACE-inhibitor therapy in patients with heart failure or left-ventricular dysfunction: a systematic overview of data from individual patients. ACE-Inhibitor Myocardial Infarction Collaborative Group. *Lancet*. 2000;355:1575-1581.
31. McMullin ST, Hennenfent JA, Ritchie DJ, Huey WY, Lonergan TP, Schaiff RA, et al. A prospective, randomized trial to assess the cost impact of pharmacist-initiated interventions. *Arch Intern Med*. 1999;159:2306-2309.

