REVIEW ARTICLE

Clinical Pharmacists and Inpatient Medical Care

A Systematic Review

Peter J. Kaboli, MD, MS; Angela B. Hoth, PharmD; Brad J. McClimon, MD, PharmD; Jeffrey L. Schnipper, MD, MPH

Background: The role of clinical pharmacists in the care of hospitalized patients has evolved over time, with increased emphasis on collaborative care and patient interaction. The purpose of this review was to evaluate the published literature on the effects of interventions by clinical pharmacists on processes and outcomes of care in hospitalized adults.

Methods: Peer-reviewed, English-language articles were identified from January 1, 1985, through April 30, 2005. Three independent assessors evaluated 343 citations. Inpatient pharmacist interventions were selected if they included a control group and objective patient-specific health outcomes; type of intervention, study design, and outcomes such as adverse drug events, medication appropriateness, and resource use were abstracted.

Results: Thirty-six studies met inclusion criteria, including 10 evaluating pharmacists' participation on rounds, 11 medication reconciliation studies, and 15 on drug-specific pharmacist services. Adverse drug events, adverse drug reactions, or medication errors were reduced in 7 of 12 trials that included these outcomes. Medication adherence, knowledge, and appropriateness improved in 7 of 11 studies, while there was shortened hospital length of stay in 9 of 17 trials. No intervention led to worse clinical outcomes and only 1 reported higher health care use. Improvements in both inpatient and outpatient outcome measurements were observed.

Conclusions: The addition of clinical pharmacist services in the care of inpatients generally resulted in improved care, with no evidence of harm. Interacting with the health care team on patient rounds, interviewing patients, reconciling medications, and providing patient discharge counseling and follow-up all resulted in improved outcomes. Future studies should include multiple sites, larger sample sizes, reproducible interventions, and identification of patient-specific factors that lead to improved outcomes.

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Author Affiliations: Center for Research in the Implementation of Innovative Strategies in Practice (CRIISP), Iowa City VA Medical Center (Drs Kaboli and Hoth); and Division of General Internal Medicine, Department of Internal Medicine, University of Iowa Carver College of Medicine, University of Iowa Hospitals and Clinics (Drs Kaboli and McClimon), Iowa City; and Division of General Internal Medicine, Brigham and Women's/Faulkner Hospitalist Service, Brigham and Women's Hospital and Harvard Medical School, Boston, Mass (Dr Schnipper).

CLINICAL PHARMACISTS ARE uniquely trained in therapeutics and provide comprehensive drug management to patients and providers (includes physicians and additional members of the care team). Pharmacist intervention outcomes include economics, health-related quality of life, patient satisfaction, medication appropriateness, adverse drug events (ADEs), and adverse drug reactions (ADRs). An ADE is defined as "an injury resulting from medical intervention related to a drug," and an ADR is defined as "an effect that is noxious and unintended and which occurs at doses used in man for prophylaxis, diagnosis, or therapy."[1(p20)] Reviews have been published about clinical pharmacy services in various settings, including ambulatory care,[2-5] geriatrics,[6] psychiatry,[7] critical care,[8] economic outcomes,[9,10] and health-related quality of life,[11] and a comprehensive review[12] was published in 1986. To our knowledge, no previous reviews have focused specifically on clinical pharmacist interventions in the inpatient setting. This type of review is of particular importance because most studies reporting medication errors and ADEs were in hospitalized patients, and with the growth of hospital medicine,[13] there is increased focus on interventions to improve the care of hospitalized patients. Benefits of clinical pharmacists have also been used to support expansion of their scope of practice.[14]

Two recent Institute of Medicine reports recognized that pharmacists are an essential resource in safe medication use, that participation of pharmacists on rounds improves medication safety, and that pharmacist-physician-patient collaboration is important.[15,16] In a recent survey, 30% of hospitals (74% of hospitals with >400 beds) reported that pharmacists attend

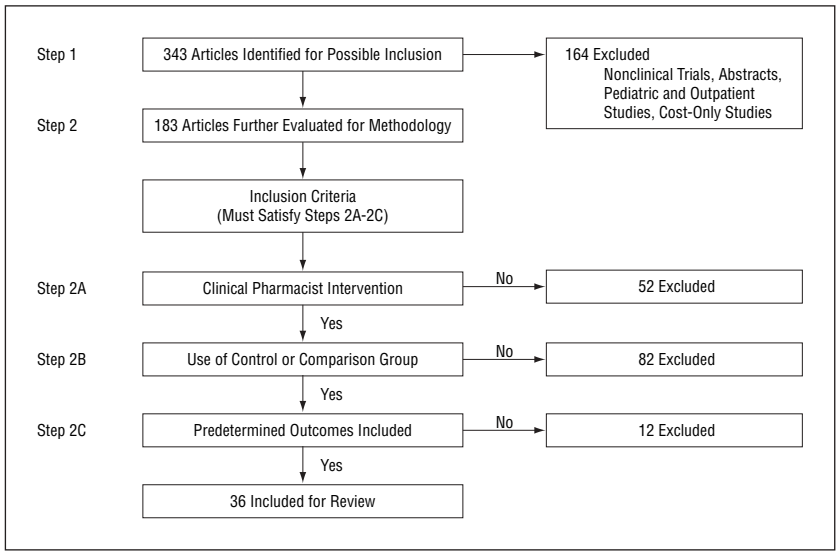

Figure. Search taxonomy and results.

rounds, and the rate is increasing.[17] The role of clinical pharmacists differs from that of traditional pharmacists in that they work directly with providers and patients to provide services not simply associated with dispensing of drugs. Many clinical pharmacists have completed residencies and are board certified in specialty areas such as pharmacotherapy, oncology, nutrition, and psychiatry. This qualitative systematic review evaluates the published literature on the effects of pharmacist interventions in controlled trials in hospitalized patients.

METHODS

A medical librarian–assisted search of English-language publications from January 1, 1985, through April 30, 2005, was conducted using the following MEDLINE and International Pharmaceutical Abstracts search terms: *clinical pharmacy, pharmaceutical care, pharmacy services, pharmacists, inpatient, hospitalization, intensive care unit, treatment outcome, outcome assessment, quality of health care, adverse drug reactions, medication errors, morbidity*, and *mortality*. Hand searches of bibliographies of relevant articles and authors' personal files were performed. Studies presented only in abstracts, letters to the editor, editorials, surveys, reviews, pediatric studies, and studies with the primary intervention occurring in an ambulatory setting were excluded from this review (**Figure**).

Methods of identified studies were reviewed for required criteria, including pharmacy service or intervention described, control group used, and objective patient-specific health outcomes reported. Pharmacist interventions consisted of cognitive services not routinely associated with activities of dispensing or compounding medications. Order review or order clarification was considered to accompany the act of dispensing. **Table 1** gives the elements of clinical pharmacist services acceptable for this review. Services or interventions occurring as a component of guideline or protocol implementation or provider education were excluded. Observational studies, descriptions of pharmacy interventions, and studies without a comparison or control group were also excluded. Studies reporting only pharmacoeconomic outcomes were excluded because these have been previously reviewed.[9] A single pharmacist (A.B.H.) performed the initial systematic search as described, with subsequent review by a physician (P.J.K.) of all included and excluded studies. One year later, the process was repeated by another pharmacist-physician (B.J.M.) with physician review (P.J.K.). The senior author (J.L.S.) reviewed the final selection and process for completeness.

RESULTS

Of 346 publications identified, 164 were excluded because of publication type or study population, 52 did not use an intervention unique to clinical pharmacy, 82 lacked a control or comparison group, and 12 did not report outcomes necessary for inclusion (Figure). The 36 studies[18-53] reviewed are categorized according to the primary type of clinical pharmacist service: patient care unit pharmacist participation on rounds, admission or discharge medication reconciliation, and drug class–specific pharmacist services (**Table 2**).

PATIENT CARE UNIT PHARMACIST PARTICIPATION ON ROUNDS

Two studies involved the intensive care unit (ICU). Leape et al[18] implemented a trial of pharmacist participation in a medical ICU, comparing ADE rates before and after intervention and with a control ICU. Preventable ADEs decreased by 66%, from 10.4 per 1000 patient-days before the intervention to 3.5 patient-days after the intervention ($P<.001$), with no change in the control ICU, from 10.9 per 1000 patient-days before the intervention to 12.4 per 1000 patient-days after the intervention ($P=.76$). Actual ADEs also decreased in the study ICU, from 33.0 to 11.6 per 1000 patient-days ($P<.001$), with an increase in the control ICU, from 34.7 to 46.6 per 1000 patient-days ($P<.001$). In a medical progressive care unit, Smythe et al[19] implemented a clinical pharmacist–structured evaluation of 131 patients during 8 weeks and reported fewer ADRs compared with baseline (1 vs 8 events; $P=.03$); ICU transfer, readmission rate, and hospital length of stay (LOS) did not differ between baseline and intervention.

Eight studies[20-27] assessed clinical pharmacists on general medicine, surgery and psychiatry services. Bjornson et al[20] evaluated a clinical pharmacist intervention involving medication reconciliation, drug therapy plans, and discharge counseling. Intervention teams had fewer patients transferred for more intensive care and their patients had shorter LOS, but hospital readmissions and mortality did not differ. There were more ADRs in the intervention group (1.7%) compared with the control group (0.5%), but no *P* value was reported. The authors attribute this to a higher propensity for pharmacists to document ADRs. Scarsi et al[21] compared results in patients when a pharmacist participated on rounds with an inpatient medicine team compared with patients who received pharmacist services only on the first day of

hospitalization or when requested. These authors reported reductions in medication errors, number of patients without a medication error during hospitalization, and duration that an error persisted once it occurred.

One of the first intervention trials of clinical pharmacists on patient care units by Clapham et al[22] involved regular interaction with physicians, patients, and nurses compared with the more traditional role of centralized pharmacy drug monitoring. The intervention reduced total average cost ($1293; $P<.05$) and produced nonsignificant reductions in LOS and drug costs, and pharmacists found working on the patient care area more professionally rewarding. In similar studies by Haig and Kiser[23] and Boyko et al,[24] inclusion of pharmacists on general medical teams resulted in reductions in LOS and in hospital and pharmacy costs. Kucukarslan et al[25] found that a clinical pharmacist on the medicine team reduced preventable ADEs by 78%, but the number of events was small (2 vs 9; $P=.02$). The intervention was well accepted by physicians, with 98% of pharmacist recommendations accepted.

Owens et al[26] assessed a geriatric team pharmacist and found that the intervention resulted in fewer medications by day 3 ($P<.05$), with the greatest reduction in patients in nursing homes. Medication use was increased by day 3 in 40% of subjects in the control group vs 18% of patients in the intervention group ($P<.005$), and control subjects received more medications without indications (19% vs 11%; $P<.025$) and inappropriate medications (37% vs 20%; $P<.005$), with no difference in number of medications at 6 weeks and 3 months. In the 1 inpatient psychiatry study, Canales et al[27] showed significant improvements in clinical response (measured by psychiatric scales) and extrapyramidal symptoms, with no difference in medication costs and LOS.

Table 1. Inclusion Criteria

- Clinical pharmacy activities and responsibilities
  - Patient interview
  - Medication profile and medical record review
  - Presentation of drug regimen recommendations to care team or physician
  - Participating on rounds with inpatient care team
  - Drug monitoring and recommendation follow-up
  - Drug therapy dosing or management
  - Documentation of clinical interventions or recommendations
  - Patient counseling before discharge
  - Telephone follow-up after discharge
- Study design
  - Concurrent control group (randomized, controlled, or quasi-experimental design)
  - Preintervention vs postintervention design (historical control)
  - Crossover design
- Outcome measures
  - Mortality
  - Adverse drug events/adverse drug reactions
    - Identification of frequency and severity of events
    - Prevention of events
    - Events requiring further treatment
  - Health services use
    - Admission and readmission rates because of complications
    - Transfer to more intensive care
    - Emergency department/urgent care use after discharge
    - Length of stay
  - Therapeutic management and professional practice process measures
    - Anticoagulation (time to therapeutic activated PTT or INR, time to the initiation of warfarin sodium therapy, time spent at therapeutic INR)
    - Pharmacokinetic dosing and drug monitoring (appropriateness of drug levels, time to therapeutic level, time spent at therapeutic level)
  - Changes in medication regimen
    - No. of medications
    - Medication appropriateness
    - Nonindicated medications
  - Other measures
    - Quality of life
    - Patient satisfaction
    - Medication adherence
    - Knowledge of medication regimen

Abbreviations: PTT, partial thromboplastin time; INR, international normalized ratio.

ADMISSION OR DISCHARGE MEDICATION RECONCILIATION

Medication review and reconciliation was the primary target of 11 studies.[28-38] In the 2 admission interventions, Nester and Hale[28] found that medication histories taken by pharmacists, as opposed to nurses, resulted in more accurate medication and allergy information, identified allergy history errors more frequently, and entered allergy information into the computer more quickly, with no difference in drug interactions or ADRs. In a study from Australia, Stowasser et al[29] implemented a medication liaison service to improve communication between outpatient physicians and pharmacists and the inpatient team at admission and discharge. The intervention group was more likely to have a pharmacist intervene or change at least 1 medication during hospitalization, with no effect on LOS or mortality. At 30 days, the intervention group had fewer health care visits, nonsignificant reduction in readmissions, and no overall change in health status.

Another 9 studies focused on discharge counseling. Smith et al[30] performed home visits and assessed pharmacist discharge counseling on patient medication-taking behavior and found significantly better levels of medication adherence ($P<.01$), although 75% of patients in the intervention group and 96% of patients in the control group were not taking medications as prescribed. Bolas et al[31] compared standard discharge planning with pharmacist discharge counseling coupled with a discharge letter from the inpatient physician to the patient's general practitioner. Significant improvement was noted in the correlation between discharge and home medications 10 to 14 days after discharge, as well as

Table 2. Studies Included for Review and Summary of Selected Outcomes

Reference, Service	Study Design and Sample Size	Major Selected Outcomes Reported	Results
		Patient Care Unit Pharmacist Participation on Rounds	
Leape et al,[18] Medical ICU	Pre-post (N = 275) Pre (I = 75, C = 50) Post (I = 75, C = 75)	Intervention group	
		ADEs, pre vs post, No.	33.0-11.6 per 1000 patient-days; $P<.001$
		Preventable ADEs, pre vs post, No.	10.4-3.5 per 1000 patient-days; $P<.001$
		Control group	
		ADEs, pre vs post, No.	34.7 vs 46.6 per 1000 patient-days; $P<.76$
		Preventable ADEs, pre vs post, No.	10.9 vs 12.4 per 1000 patient-days, $P<.001$
Smythe et al,[19] Medical Progressive Care Unit	Pre-post (N = 266) I = 131 C = 135	ADRs, No.	1 (I) vs 8 (C); $P = .03$
		ICU transfer, No.	11 (I) vs 13 (C)
		Readmission to Medical Progressive Care Unit, No.	6 (I) vs 3 (C)
		Length of stay, d	9.1 (I) vs 9.1 (C)
Bjornson et al,[20] General Medicine and Surgery	Quasi-experimental (N = 3081) I = 1201 C = 1880	ADRs documented, %	1.7 (I) vs 0.5 (C); P=NR
		ICU transfer, %	5.8 (I) vs 8.5 (C); $P = .02$
		Readmission at 30 d, %	10 (I) vs 11.1 (C); P = NS
		In-hospital mortality rate, %	1.75 (I) vs 2.45 (C); $P = .20$
		Length of stay, log-d	7.6 (I) vs 8.2 (C); $P = .03$
Scarsi et al,[21] General Medicine	Randomized (N = 70) I = 35 C = 35	Medication errors per patient, No.	1.3 (I) vs 2.6 (C); $P<.05$
		Patients with no medication errors, %	14 (I) vs 8 (C); $P<.05$
		Mean duration of errors, d	0.73 (I) vs 2.4 (C); $P<.001$
Clapham et al,[22] General Medicine and Surgery	Pre-post (N = 1155) I = 496 C = 659	Length of stay, d	10.02 (I) vs 11.53 (C); P = NS
		Hospital cost per patient, $	5997 (I) vs 7290 (C); $P<.05$
		Drug cost per patient, $	494 (I) vs 649 (C); P = NS
Haig and Kiser,[23] General Medicine	Randomized (N = 619) I = 332 C = 287	Length of stay, d	5.9 (I) vs 7.2 (C); $P = .004$
		Hospital charge per patient, $	6122 (I) vs 8187 (C); $P = .001$
		Pharmacy cost per patient, $	173 (I) vs 287 (C); $P = .01$
		Pharmacy charges per patient, $	652 (I) vs 1020 (C); $P = .001$
Boyko et al,[24] General Medicine	Randomized (N = 867) I = 414 C = 453	Length of stay, d	4.2 (I) vs 5.5 (C); $P<.001$
		Hospital cost per patient, $	4501 (I) vs 6155 (C); $P<.001$
		Pharmacy cost per patient, $	481 (I) vs 782 (C); $P<.001$
Kucukarslan et al,[25] General Medicine	Nonrandomized, single-blind (N = 165) I = 86 C = 79	Preventable ADEs per 1000 patient-days, No.	5.7 (I) vs 26.5 (C); P = NR
		ADEs, No.	2 (I) vs 9 (C); $P = .02$
		Length of stay, d	0.3 d shorter, I vs C; P = NS
Owens et al,[26] Geriatrics	Randomized (N = 436) I = 221 C = 215	Medications 3-d postrandomization, No.	5.3 (I) vs 5.9 (C); $P<.05$
		Medication increase at 3-d postrandomization, %	18% (I) vs 40% (C); $P<.005$
		Medications 6-wk postrandomization, No.	6.3 (I) vs 5.9 (C); P = NS
		Medications 3 mo postrandomization, No.	6.0 (I) vs 6.0 (C); P = NS
		Multiple unpaired indications, %	11 (I) vs 19 (C); $P<.03$
		Inappropriate medication choices, %	20 (I) vs 37 (C); $P<.005$
Canales et al,[27] Psychiatry	Pre-post (N = 93) I = 45 C = 48	Brief Psychiatric Rating Scale, % change in score	14.6 (C) vs 32.4 (I); $P<.001$
		Clinical Global Impression, % change in score	11.8 (C) vs 32.7 (I); $P<.10$
		Hamilton Psychiatric Depression Scale, % change in score	25.8 (C) vs 55.0 (I); $P<.001$
		Mini-Mental State Examination, % change in score	9.2 (C) vs 14.1 (I); P = NS
		Abnormal involuntary movement, % change in score	–0.9 (C) vs 3.5 (I); $P = .02$
		Drug-induced akathisia, % change in score	–6.8 (C) vs 27 (I); $P = .04$
		Drug-induced extrapyramidal symptoms, % change in score	–6.5 (C) vs 21.9 (I); $P = .002$

(*continued*)

knowledge of drug name, dosage, and frequency, with no difference in readmission rates. In a Veterans Administration hospital discharge counseling intervention, Williford and Johnson[32] reported that patients were no more knowledgeable or compliant at the 6-week follow-up.

In a study by Lipton and Bird,[33] pharmacists reviewed hospital records, consulted with physicians, provided discharge counseling, and made 4 follow-up telephone calls after discharge. At 2 months, patient medication knowledge was higher in the intervention group. At 3 months, patients in the intervention group compared with those in the control group received fewer medications (5.16 vs 6.75; $P<.001$) and fewer daily doses (8.30 vs 12.04; $P<.001$), and reported fewer missed doses (8% vs 22%; $P<.001$); resource use was not affected. From the same study, Lipton et al[34] evaluated a

Table 2. Studies Included for Review and Summary of Selected Outcomes (cont)

Reference, Service	Study Design and Sample Size	Major Selected Outcomes Reported	Results
		Admission or Discharge Medication Reconciliation Services	
Nester and Hale,[28] Admission	Randomized (N = 100) I = 50 C = 50	Herbal and nonprescription medications per patient, No.	5.1 (I) vs 1.5 (C); $P<.001$
		Patients with incorrect allergy information identified, No.	4/50 (I) vs 0/50 (C); $P<.001$
		Time from admission to entry of allergy information, min	68 (I) vs 156 (C); $P<.005$
		Medication histories clarified by community pharmacies, %	24 (I) vs 4 (C); $P<.001$
Stowasser et al,[29] Admission and discharge	Randomized (N = 240) I = 113 C = 127	Readmissions per subject at 30 d, No.	0.12 (I) vs 0.46 (C); $P = .06$
		Health care professional visits at 30 d, No.	7.54 (I) vs 9.94 (C); $P<.05$
		Patients with >1 pharmacist intervention, %	68 (I) vs 44 (C); $P<.05$
		Patients with >1 medication change, %	97 (I) vs 90 (C); $P<.05$
		Health status, SF-36	No change; $P>.05$
Smith et al,[30] Discharge	Randomized (N = 53) I = 18 C = 25	Medication adherence, I vs C	Better medication adherence; $P<.01$ Less counseling required; $P<.01$
		Discrepancies between discharge instructions and patients' medication behaviors, %	75 (I) vs 96 (C); P = NR
Bolas et al,[31] Discharge	Randomized (N = 162) I = 81 C = 81	Mismatch between discharge and home drug list	1.5 (I) vs 7 (C); $P<.005$
		Drug name, %	10 (I) vs 17 (C); $P<.07$
		Drug dose, %	11 (I) vs 18 (C); $P<.004$
		Dosage frequency, %	
		Errors in drug therapy knowledge	15 (I) vs 43 (C); $P<.001$
		Drug name, %	14 (I) vs 39 (C); $P<.001$
		Drug dose, %	15 (I) vs 39 (C); $P<.001$
		Dosage frequency, %	
		Readmission at 30 d	$P>.05$ (NS)
Williford and Johnson,[32] Discharge	Randomized (N = 60) I = 31 C = 29	Medication knowledge compliance score	90.7 (I) vs 75.4 (C); P = NS
Lipton and Bird,[33] Discharge and telephone follow-up	Randomized (N = 706) I = 350 C = 356	Medical care use (charges and hospital), d	P = NS
		Medication compliance score	94.4 (I) vs 91.4 (C); $P = .04$
		Assessment 1	94.4 (I) vs 92.3 (C); $P<.001$
		Assessment 2	
		Patient knowledge of purpose of medications, %	92.7 (I) vs 84.6 (C); $P = .02$
		Assessment 1	95.7 (I) vs 85.9 (C); $P<.001$
		Assessment 2	
		Polypharmacy at assessment 2 (12-14 wk), No.	5.16 (I) vs 6.75 (C); $P<.001$
		Long-term medications	8.30 (I) vs 12.04 (C); $P<.001$
		Total daily doses of medications	
		Length of stay, d	7.2 (I) vs 8.2, d (C); $P = .06$
Lipton et al,[34] Discharge and telephone follow-up	Randomized (N = 236) I = 123 C = 113	(Sample of 236 of 706 patients from 1994 study)	
		Medication appropriateness	$P = .02$
		Correct dosage	$P = .05$
		Fewer prescribing problems in any of 6 categories	$P = .05$
Johnston et al,[35] Discharge	Randomized (N = 27) I = 14 C = 13	Medication knowledge score, %	93 (I) vs 77 (C); $P = .02$
Nazareth et al,[36] Discharge and Outpatient Coordination	Randomized (N = 362) I = 181 C = 181	Readmission at 3 mo, %	39 (I) vs 39.2 (C); P = NS
		General practitioner visit at 3 mo, %	77.7 (I) vs 75 (C); P = NS
		Mortality at 3 mo, %	6.1 (I) vs 2.8 (C); P = NS
		Drug knowledge, %	57 (I) vs 55 (C); P = NS
Al-Rashed et al[37] Discharge and Outpatient Coordination	Randomized (N = 83) I = 43 C = 40	Readmission at 2-3 wk, %	11.6 (I) vs 32.5 (C); $P<.05$
		General practitioner visit at 2-3 wk, %	44.2 (I) vs 67.5 (C); $P<.05$
		Medication compliance, %	48.4 (I) vs 15.9 (C); $P<.001$
Schnipper et al[38] Discharge and telephone follow-up	Randomized (N = 176) I = 92 C = 84	ADEs, %	18 (I) vs 16 (C); $P = .99$
		Preventable ADEs, %	1 (I) vs 11 (C); $P = .01$
		Readmission or emergency department visit at 30 d, %	30 (I) vs 30 (C); $P = .99$
		Medication compliance score	88.9 (I) vs 87.5 (C); $P = .91$

(*continued*)

236-patient sample in 6 domains of medication appropriateness. Patients in the intervention group were less likely to have one or more prescribing problems in any category, in appropriateness or in dosage.

Johnston et al[35] evaluated the role of pharmacist discharge counseling on medication knowledge in older pa-

Table 2. Studies Included for Review and Summary of Selected Outcomes (cont)

Reference, Service	Study Design and Sample Size	Major Selected Outcomes Reported	Results
		Drug Class–Specific Pharmacist Service	
Mamdani et al[39] Anticoagulation	Prospective cohort (N = 100) I = 50 C = 50	Time to therapeutic PTT level, h	23.6 (I) vs 25.3 (C); *P* = .14
		Supratherapeutic level within 12 h of starting heparin, %	88 (I) vs 82 (C); *P* = .40
		Subtherapeutic PTT level, %	15.8 (I) vs 21.3 (C); *P* = .03
		Therapeutic PTT level, %	47.7 (I) vs 41.5 (C); *P* = .05
		Supratherapeutic PTT level, %	36.6 (I) vs 37.2 (C); *P* = .83
		PTT values per patient, n	9 (I) vs 9 (C); *P* = .78
		Warfarin sodium started within 2 d of heparin, %	82 (I) vs 63 (C); *P* = .05
		Therapeutic INR at discharge, %	71 (I) vs 58 (C); *P* = .21
		Length of stay, d	5.0 (I) vs 7.0 (C); *P* = .05
Dager et al,[40] Anticoagulation	Pre-post (N = 120) I = 60 C = 60	In-hospital bleeding complications or VTE, No. (%)	1 (2) (I) vs 6 (10) (C); *P* = .11
		Readmission at 3 mo because of bleeding or VTE, No.	7 (I) vs 15 (C); *P* = NR
		Drugs prescribed with warfarin sodium interactions, No.	6 (I) vs 13 (C); *P* = .02
		Time to therapeutic INR, d	3.0 (I) vs 3.0 (C); *P* = NS
		Patients with INR >3.5 at admission, %	27 (I) vs 62 (C); *P*<.002
		Patients with INR >6.0 at admission, %	3 (I) vs 33 (C); *P*<.001
		INR at discharge	2.6 (I) vs 3.3 (C); *P* = .07
		Days from start of warfarin until discharge, No.	6.8 (I) vs 9.5 (C); *P* = .009
		Length of stay, d	9.5 (I) vs 6.8 (C); *P* = .01
Ellis et al,[41] Anticoagulation	Pre-post (N = 157) I = 52 C = 97	Duration of warfarin sodium therapy, d	7.83 (I) vs 8.12 (C); *P* = .35
		PT measurements ordered per day, No.	1.34 (I) vs 1.56 (C); *P* = .02
		Therapeutic level at first outpatient appointment, %	69 (I) vs 46 (C); *P* = .001
		Supratherapeutic level at first outpatient appointment, %	2 (I) vs 18 (C); *P* = .002
Tschol et al,[42] Anticoagulation	Pre-post (N = 227) I = 97 C = 130	Major bleeding complications, %	6.2 (I) vs 5.1 (C); *P* = .72
		Days in therapeutic range, %	3.3 lower in I; *P* = .27
		Days with INR >4.0, %	5.9 lower in I; *P*<.001
		Days with INR <2.0, %	7 higher in I; *P* = .06
Fraser et al,[43] Antibiotics	Randomized (N = 225) I = 127 C = 98	Antibiotic charges per patient, $	1287 (I) vs 1673 (C); *P* = .05
		Daily doses of IV antibiotic per patient, n	10.16 (I) vs 13.59 (C); *P* = .09
		Clinical response, %	79.5 (I) vs 80.6 (C); *P* = NS
		Length of stay, d	20.0 (I) vs 24.7 (C); *P* = NS
		Readmission at 30 d, %	15.0 (I) vs 10.2 (C); *P* = NS
		In-hospital mortality, %	13.4 (I) vs 11.2 (C); *P* = NS
		Readministration of antibiotics within 7 d, %	4.7 (I) 13.3 (C); *P* = .01
Gentry et al,[44] Antibiotics	Pre-post (N = 7219) I = 3570 C = 3649	In-hospital mortality, %	6.61 (I) vs 8.28 (C); *P* = .01
		Readmission because of infection, %	10.42 (I) vs 10.96 (C); *P* = .46
		Length of stay, d	10.8 (I) vs 13.2 (C); *P*<.001
Bailey et al,[45] Antibiotics	Randomized (N = 102) Hospital A I = 41 C = 38 Hospital B I = 10 C = 13	Intravenous antibiotic, d	
		Hospital A	1.2 (I) vs 1.9 (C) 0.4 (I) vs 2.4 (C); *P* = .01, ANOVA
		Hospital B	
		Antibiotic cost	
		Hospital A, $	21.38 (I) vs 29.36 (C)
		Hospital B, $	13.40 (I) vs 54.79 (C); *P* = .03, ANOVA
		Length of stay, d	
		Hospital A	4.9 (I) vs 4.4 (C)
		Hospital B	4.8 (I) vs 4.8 (C); *P* = .95, ANOVA
		Readmission at 30 d, %	
		Hospital A	34 (I) vs 10 (C)
		Hospital B	10 (I) vs 7.7 (C); *P* = .02, ANOVA
		In-hospital mortality, %	
		Hospital A	4.9 (I) vs 5.3 (C)
		Hospital B	10 (I) vs 7.7 (C); *P* = .96, ANOVA

(*continued*)

tients. An evaluation immediately before discharge and a recall questionnaire found that the percentage of critical items correct for the pharmacist-counseled group was 93% compared with 77% in the control group (*P* = .02). Nazareth et al[36] reported no differences in hospital readmissions, outpatient visits, or mortality at 3 or 6 months for a discharge pharmacist intervention to coordinate care with outpatient pharmacists and provid-

Table 2. Studies Included for Review and Summary of Selected Outcomes (cont)

Reference, Service	Study Design and Sample Size	Major Selected Outcomes Reported	Results
Gums et al,[46] Antibiotics	Randomized (N = 252) I = 127 C = 125	In-hospital mortality, %	6.3 (I) vs 12.0 (C); $P = .17$
		Length of stay from randomization, d	5.7 (I) vs 9.0 (C); $P = .001$
		Overall length of stay, d	10.1 (I) vs 14.5 (C); $P = .001$
Destache et al,[47] TDM: aminoglycosides	Randomized (N = 145) I = 75 C = 70	Nephrotoxicity, %	8 (I) vs 14.4 (C); $P = .08$
		Febrile period, d	2.09 (I) vs 3.84 (C); $P < .05$
		In-hospital mortality, %	18.7 (I) vs 10.0 (C); $P > .05$
		Length of stay, d	13.4 (I) vs 18.4 (C); $P = .08$
		Hospital cost per patient, $	7102 (I) vs 13 758 (C); $P < .05$
Destache et al,[48] TDM: aminoglycosides	Retrospective (N = 46) I = 23 C = 23	Duration of aminoglycoside therapy, d	6.27 (I) vs 7.65 (C); P = NS
		Dosage changes, No.	1.5 (I) vs 1.1 (C); P = NS
		Temperature return to normal, d	1.76 (I) vs 3.18, d (C); $P < .05$
		Heart rate return to normal, d	1.0 (I) vs 3.75 (C); $P = .005$
		Respiratory rate return to normal, d	1.63 (I) vs 3.95 (C); $P = .05$
		Maximum peak, µg/mL	6.31 (I) vs 5.82 (C); P = NS
		Length of stay, d	13.09 (I) vs 19.08 (C); $P < .05$
Welty and Copa,[49] TDM: vancomycin	Prospective cohort (N = 116) I = 61 C = 55	Patients with decreased renal function, %	7 (I) vs 24 (C); $P < .05$
		Duration of therapy, d	11.1(I) vs 13.4 (C); P = NS
		Dose changes per patient, n	1.1 (I) vs 0.7 (C); $P < .05$
		Dosage, g/kg/d	20.9 (I) vs 22.8 (C); P = NS
		Length of stay, d	36.8 (I) vs 44.5 (C); P = NS
Burton et al,[50] TDM: aminoglycosides	Randomized (N = 147) I = 72 C = 75	Nephrotoxicity, %	5.1 (I) vs 9.7 (C); P = NS
		In-hospital mortality, %	1.4 (I) vs 4 (C); P = NS
		Max peak concentration, mg/L	5.3 (I) vs 4.4 (C); $P = .001$
		Patients with peak concentrations >4 mg/L, %	82.9 (I) vs 60.3 (C); P = NS
		Length of stay, d	16.0 (I) vs 20.3 (C); $P = .03$
Winter et al,[51] TDM: aminoglycosides and theophylline	Cross-sectional (N = 100) Phase 1 (C = 36) Phase 2A (I = 31) Phase 2B (I = 11) Phase 3 (C = 22)	Appropriate drug levels, %	54.2 (2A) vs 15.8 (1) vs 20.5 (3); $P < .05$
		Inappropriately labeled or drawn drug levels per patient-day, No.	0.14 (2A) vs 0.38 (1); $P < .05$
		Inappropriately used drug levels, %	7.1 (2A) vs 6.7 (1) vs 0 (3); P = NS
Leehey et al,[52] TDM: aminoglycosides	Randomized: (N = 243) Ia = 90 Ib = 80 C = 73	Nephrotoxicity, %	16 (C) vs 27 (Ia) vs 16 (Ib); $P = .31$
		Mean peak drug level, µg/mL	4.0 (C) vs 4.8 (Ia) vs 5.0 (Ib); $P = .003$
		Dose, mg	91(C) vs 97 (Ia) vs 107 (Ib); $P < .001$
		Doses per day, n	2.3 (C) vs 2.0 (Ia) vs 2.0 (Ib); $P = .001$
Wing and Duff,[53] TDM, phenytoin	Prospective, randomized, crossover (N = 122) Phase 1 (C = 28) Phase 2 (I = 28) Phase 3 (C = 27) Phase 4 (I = 39)	Seizure-related readmissions, phase 2 vs phase 3, No.	0 (I) vs 0.19 (C); $P < .02$
		Seizure-related readmissions, phase 4 vs phase 3, No.	0.03 (I) vs 0.19 (C); $P < .02$
		Assays performed per patient, phase 2 vs phase 1, No.	0.61 (I) vs 2.14 (C); $P < .02$
		Assays per patient not indicated, phase 2 vs phase 1, No.	0 (I) vs 0.61 (C); $P < .05$
		Assays per patient with blood drawn incorrectly, phase 2 vs phase 1, No.	0.39 (I) vs 1.57 (C); $P < .02$
		Assays per patient used inappropriately, phase 2 vs phase 1, No.	0.5 (I) vs 1.86 (C); $P < .02$

Abbreviations: ADE, adverse drug event; ADR, adverse drug reaction; ANOVA, analysis of variance; C, control group; I, intervention group; ICU, intensive care unit; INR, international normalized ratio; IV, intravenous; NR, not reported; NS, not significant; Pre-post, before or after intervention; PT, prothrombin time; PTT, partial thromboplastin time; SF-36, 36-Item Short-Form Health Survey; TDM, therapeutic drug monitoring; VTE, venous thromboembolism.

ers in patients older than 75 years. In a similar study, Al-Rashed et al[37] enrolled 83 elderly patients at discharge and reported improvements in knowledge, compliance, outpatient visits, and hospital readmissions. In the most recent study of pharmacist counseling at discharge with telephone follow-up after 3 to 5 days, Schnipper et al[38] reported fewer preventable ADEs (1% vs 11%; $P = .01$) and fewer preventable medication-

related emergency department visits or hospital readmissions (1% vs 8%; $P=.03$) at 30 days in the intervention group compared with the control group, with no difference in medication compliance.

DRUG CLASS–SPECIFIC PHARMACIST SERVICES

Of the 15 drug class–specific pharmacist services,[39-53] 4 studies[39-42] evaluated inpatient anticoagulation services. In a pharmacist-managed anticoagulation service in patients with venous thromboembolism, Mamdani et al[39] found no difference in time to therapeutic partial thromboplastin time (PTT), percentage of patients with supratherapeutic PTT levels, or number of blood samples drawn to measure PTT. However, the intervention group had a greater proportion of therapeutic PTT levels, shorter time from blood drawing to adjustment (2.8 vs 4.4 hours; $P<.001$), earlier initiation of warfarin sodium therapy, and shorter LOS. Dager et al[40] evaluated a clinical pharmacist anticoagulation service providing daily consultation and follow-up to patients beginning warfarin therapy compared with matched historical control subjects. The intervention was associated with reductions in excessive anticoagulation, major warfarin drug interactions, inpatient days receiving warfarin therapy, and less time spent at supratherapeutic international normalized ratios (INRs). In a study by Ellis et al,[41] consultation was provided to patients receiving warfarin therapy to evaluate laboratory results, warfarin dosages, drug interactions, and outpatient anticoagulation follow-up. Patients in the intervention group had fewer INR and PTT measurements, improved discharge INR stability, rate of therapeutic INRs, and fewer supratherapeutic INRs at clinical follow-up; bleeding and thromboembolism rates did not differ. Finally, Tschol et al[42] compared warfarin management by pharmacists and physicians after prosthetic valve insertion and found no difference in days in the therapeutic range, subtherapeutic INRs, or major bleeding, but pharmacists had 5.9% fewer days with an INR higher than 4.0 ($P<.001$).

Four studies[43-46] focused on antibiotic therapy and infectious disease consultation. Fraser et al[43] evaluated a clinical pharmacist–infectious disease fellow team receiving designated parenteral antibiotic therapy and reported that 62 (49%) of 127 patients in the intervention group received 74 suggestions, of which 85% were implemented. Changes in antibiotic choice, dosing, or administration route resulted in mean antibiotic cost savings of $400 ($P=.05$). Mortality, clinical response, antibiotic toxic effects, and LOS were similar. Gentry et al[44] evaluated the effects of an antimicrobial control program in which a pharmacist approved restricted and nonformulary antimicrobial agents and assisted the primary team with changes in therapy and culture report interpretation. A significant reduction in hospital mortality, LOS, and antimicrobial costs was observed, with no change in hospital readmissions. Bailey et al[45] studied a pharmacist intervention to contact the patient's physician with antibiotic recommendations and reported significant reductions in days with intravenous antibiotic therapy and antibiotic cost, no difference in mortality and LOS, but more readmissions. Finally, Gums et al[46] evaluated a team including a pharmacist, a microbiologist, and an infectious disease specialist for patients receiving intravenous antibiotic therapy. In 127 patients in the intervention group, LOS was shorter (5.7 vs 9.0 days; $P=.0001$), with no difference in mortality; 89% of pharmacist recommendations were accepted.

One of the first clinical services established by pharmacists involved therapeutic drug monitoring of aminoglycosides, vancomycin, anticonvulsant drugs, and theophylline. Seven studies[47-53] addressed the clinical value of providing therapeutic drug-monitoring services evaluating toxic effects, therapeutic effects, health care use, and appropriate drug concentration testing. Destache et al[47] reported shorter febrile periods, faster return to normal vital signs, and shorter LOS with aminoglycoside therapeutic drug monitoring.[48] Nephrotoxicity occurred less often in pharmacist-dosed patients in several studies, but was not statistically significant. In the vancomycin monitoring trial by Welty and Copa,[49] fewer patients developed vancomycin-related renal insufficiency. In other aminoglycoside trials, improvements were seen in peak concentrations and LOS,[50] appropriate aminoglycoside concentrations,[51] and improved pharmacokinetic parameters.[52] Wing and Duff[53] evaluated phenytoin therapeutic drug monitoring and reported significant reductions in number of assays performed or not indicated and blood samples drawn incorrectly and used inappropriately; the number of seizure-related readmissions was also reduced (all $P<.05$).

The results were further categorized by specific outcomes or process measures of interest. Twelve of 36 studies* evaluated ADEs, ADRs, or medication errors as an end point: preventable and actual ADEs,[18] preventable ADEs,[25,38] ADRs,[19,20] anticoagulation-associated complications,[40,42] medication errors,[21] and nephrotoxicity.[47,49,50,52] This lack of a uniform definition of ADEs, ADRs, and medication errors prevents systematic generalization to clinical practice or meta-analysis. However, 7 reported a reduction,[18-21,25,38,48] 5 reported no difference,[40,42,47,50,52] and no studies reported statistically higher rates compared with controls.

Health care use was assessed in 24 of 36 trials† by LOS, costs, laboratory testing, readmissions, ICU transfers, or health care visits. Hospital LOS was reduced in 9 of 17 trials, and readmission rates, ICU transfers, test use, and costs were either reduced or not affected. Only 1 trial[45] demonstrated an increase in use (hospital readmissions). Drug monitoring and process measures were evaluated in 15 trials,[28,29,39-43,45,47-53] with significant improvements in anticoagulation, medication history and allergy documentation, antibiotic use, treatment response, and therapeutic drug levels. In 4 trials, clinical pharmacist recommendations led to reductions in the number of unnecessary medications and number of daily doses,[26,33] improved medication appropriateness and medications lacking an indication or known ADRs,[26,34] and fewer drug interactions.[40]

References 18-21, 25, 38, 40, 42, 47, 49, 50, 52.

†References 19, 20, 22-25, 29, 31, 33, 36-41, 43-51, 53.

Mortality was evaluated in 8 studies. One study[44] showed a significant reduction; of the other 7 studies, 3 demonstrated lower mortality[20,46,50] and 4 demonstrated higher mortality in the intervention group[36,43,45,47] but these differences were not significant ($P>.05$). Nine studies[29-33,35-38] used patient measures of medication adherence and knowledge as outcomes, with improvements demonstrated in 5 studies.[30,31,33,35,37] Only 1 study[29] evaluated health-related quality of life, with no improvement in the 36-Item Short-Form Health Survey scores, and psychiatric scales showed improvement in 1 psychiatry intervention.[27]

COMMENT

Our review supports the use of clinical pharmacists in the inpatient setting to improve the quality, safety, and efficiency of care. The Institute of Medicine report *Crossing the Quality Chasm*[54] proposes that clinical pharmacists have a significant role in addressing quality issues in hospitalized patients, and the Joint Commission on Accreditation of Healthcare Organizations mandates medication reconciliation at the time of hospital admission and discharge.[55] By further developing collaborative health care, the clinical pharmacist can be an integral part of the inpatient care team. Our findings are supported by a large observational study by Bond et al[56] that identified 17 clinical pharmacy services in hospitals associated with improvement in mortality, drug costs, cost of care, and LOS. In a follow-up study, Bond et al[57] reported lower medication error rates as the number of clinical pharmacists increased per occupied bed.

Implementing new hospital programs is difficult, especially if they require allocation of new resources. One fundamental advantage to the pharmacist interventions discussed is that most can be implemented through reallocation of existing resources to increase clinical pharmacist services. Published studies evaluating the cost of incorporating clinical pharmacists have generally demonstrated a net hospital cost benefit in terms of cost avoidance and use.[9,58-60] In some settings, new pharmacy positions (eg, technicians) have been created to fill expanded clinical roles and pharmacist duties have been reorganized to enable more direct interaction with patients and physicians on rounds.

There are many limitations to this systematic review and included studies. Many pharmacist intervention studies have small sample size, and most are single-institution studies, limiting generalizability. Interventions are costly, limiting sample size and increasing the chance of a type II error. Different study designs were used (ie, randomized, cohort, case-control, preintervention vs postintervention), and each has limitations. It is difficult to standardize interventions; thus, reproducing them is challenging, limiting comparisons, and it is impossible to combine results, as in meta-analysis. Determining outcome measurements in pharmacist intervention trials is difficult. Many definitions for outcomes such as ADEs, ADRs, and medication errors are confusing and not consistent. Process measures (eg, drug levels) are frequently used and may not be related to outcomes. Health care use is often measured because it is easily quantified, is generalizable, and can be used to justify increased pharmacist personnel costs. Systematic reviews are subject to publication bias, although it is unlikely that the addition of a clinical pharmacist to a medical care team would adversely affect outcomes. This review is retrospective and observational, and, therefore, subject to systematic and random error, and it did not include studies before 1985 because of significant changes in pharmacy services that may make earlier studies less relevant.

More research is needed to better understand the role of clinical pharmacists, clinical areas most likely to benefit, and patient-specific factors associated with improvements. Cost-effectiveness can also be improved by identifying pharmacist duties most beneficial to patients and determining whether less skilled and costly personnel can perform other duties. Future studies should describe interventions in sufficient detail that they can be reproduced, and outcomes such as medication appropriateness and adherence should be measured using validated instruments. Last, larger, multicenter, randomized, controlled trials should be conducted to prove that benefits of pharmacist interventions are generalizable across institutions and to quantify the value to the health care system.

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Correspondence: Peter J. Kaboli, MD, MS, Division of General Internal Medicine, Department of Internal Medicine, University of Iowa Carver College of Medicine, University of Iowa Hospitals and Clinics, SE615GH, 200 Hawkins Dr, Iowa City, IA 52246 (peter-kaboli@uiowa.edu).
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