Economic Evaluations of Clinical Pharmacy Services: 2006–2010

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Studies have consistently evidenced the positive clinical, economic, and humanistic benefits of pharmacist-directed patient care in a variety of settings. Given the vast differences in clinical outcomes associated with evaluated clinical pharmacy services (CPS), more detail as to the nature of the CPS is needed to better understand observed differences in economic outcomes. With the growing trend of outpatient pharmacy services, these economic evaluations serve as viable decision-making tools in choosing the most effective and cost-effective pharmacy programs. We previously conducted three systematic reviews to evaluate the economic impact of CPS from 1988 to 2005. In this systematic review, our objectives were to describe and evaluate the quality of economic evaluations of CPS published between 2006 and 2010, with the goal of informing administrators and practitioners as to their cost-effectiveness. We searched the scientific literature by using the Medline, International Pharmaceutical Abstracts, Embase, and Cumulative Index to Nursing and Allied Health Literature databases to identify studies describing CPS published from 2006 to 2010. Studies meeting our inclusion criteria (original research articles that evaluated CPS and described economic and clinical outcomes) were reviewed by two investigators. Methodology used, economic evaluation type, CPS setting and type, and clinical and economic outcome results were extracted. Results were informally compared with previous systematic reviews. Of 3587 potential studies identified, 25 met inclusion criteria. Common CPS settings were hospital (36%), community (32%), and clinic or hospital-based ambulatory practices (28%). CPS types were disease state management (48%), general pharmacotherapeutic monitoring (24%), target drug programs (8%), and patient education (4%). Two studies (8%) listed CPS as medication therapy management. Costs were evaluated in 24 studies (96%) and sufficiently described in 13 (52%). Clinical or humanistic outcomes were evaluated in 20 studies (80%) and were sufficiently described in 18 (72%). Control groups were included in 16 (70%) of 23 studies not involving modeling. Study assumptions and limitations were stated and justified in eight studies (32%). Conclusions and recommendations were considered justified and based on results in 24 studies (96%). Eighteen studies (72%) involved full economic evaluation. The mean ± SD study quality score for full economic evaluations (18 studies) was 60.4 ± 22.3 of a possible 100 points. Benefit-cost ratios from three studies ranged from 1.05:1 to 25.95:1, and incremental cost-effectiveness ratios of five studies were calculated and reported. Fewer studies documented the economic impact of CPS from 2006–2010 than from 2001–2005, although a higher proportion involved controlled designs and were full economic evaluations. Evaluations of ambulatory practices were increasingly common. CPS were generally considered cost-effective or provided a good benefit-cost ratio.

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Health care costs in the United States have continued to rise for decades, requiring health care institutions to identify and adopt efficient means of controlling these costs. Although the positive economic value of inpatient-based clinical pharmacy services (CPS) is already well established, recent changes to health care policy and the transition of CPS to ambulatory care settings require the evaluation of the effectiveness and costs.[1–4] Evidence evaluating CPS can lead to improvements in and justification for the delivery of such services, decreasing costs as well as improving health outcomes.

Within the past few decades, pharmacy services have undergone an immense transformation from solely focusing on medication dispensing and delivery to involving pharmacists in delivering individualized specialized care as part of health care teams. Clinical pharmacists are experts in promoting safe and rational medication use.[5] CPS improve disease management, use of rational drug therapy, health promotion, and disease prevention through the use of applied knowledge, gathered experience, formed judgment, and evidence-based practices, as well as continuing education.[5, 6]

Recently, two major changes in policy have played an essential role in molding the provision of CPS. First, the Medicare Prescription Drug, Improvement and Modernization Act (MMA) of 2003 recognized the pharmacist's role in managing medication therapy by establishing reimbursement for medication therapy management (MTM) services delivered to Medicare patients under Medicare Part D.[7, 8] Second, the Patient Protection and Affordable Care Act of 2010 supported the integration of pharmacists within multidisciplinary health teams in Patient-Centered Medical Homes (PCMHs) in which reimbursements are on a fee-for-service basis.[9] These two policies demonstrate the steady and sustained evolvement of CPS.

A recent policy paper published by the AARP (formerly known as the American Association of Retired Persons) Public Policy Institute is proposing changes in Medicare Part D to heighten patient participation in MTM programs and to require Part D plans to increase coverage for MTM services.[10] Additionally, the Patient Protection and Affordable Care Act of 2010 Health Care Reform has introduced the implementation of Accountable Care Organizations (ACOs) that extend the interprofessional model of PCMHs in enhancing patient-centered care.[9] Studies have also consistently evidenced the positive clinical, economic, and humanistic benefits of pharmacist-directed patient care in a variety of settings; however, many of these studies used less than optimal economic assessments of CPS.[2–4, 11] Additionally, given the vast differences in clinical outcomes associated with evaluated CPS services, more detail as to the nature of the CPS is needed to better understand observed differences in economic outcomes.

We previously conducted three systematic reviews to evaluate the economic impact of CPS from 1988–2005.[2–4] With the American Recovery and Reinvestment Act of 2004 (ARRA) requesting further implementation of comparative effectiveness research, and with the growing trend of outpatient pharmacy services, these economic evaluations serve as viable decision-making tools in choosing the most effective and cost-effective pharmacy programs.[1, 12, 13] Thus the objectives of this study were to describe and evaluate the quality of economic evaluations of CPS published between 2006 and 2010, with the goal of informing administrators and practitioners as to their cost-effectiveness.

Methods

Article Retrieval, Screening, and Data Collection

A systematic review of scientific literature databases, including Medline, International Pharmaceutical Abstracts (IPA), Embase, and Cumulative Index to Nursing and Allied Health Literature (CINAHL), for the years 2006–2010 inclusive was conducted to determine potential

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economic evaluations for review. Search terms used for the initial Medline and CINAHL searches were as follows: "cost and cost analysis," "cost benefit analysis," "economics, pharmaceutical" combined with "pharmaceutical services," "delivery of health care," "interdisciplinary communication," "interdisciplinary," "patient care team," "pharmacy service," and "hospital." Search terms used for the Embase database were as follows: "health economics," "health care cost," "economic evaluation," "cost benefit analysis," "cost effectiveness analysis," "drug cost," "pharmacoeconomics," "cost utility analysis," "cost minimization analysis," "cost," "drug cost," "hospital cost," "hospitalization cost" combined with "pharmaceutical care," "clinical pharmacy," "pharmacy," "interdisciplinary," "interdisciplinary communication," and "health care delivery." Searches were further refined to include only clinical trials, guidelines, and systematic reviews or meta-analyses, and to exclude non-English articles, review articles, editorials, and incomplete or unoriginal articles. In addition, the individual authors of this review contributed any articles within their personal collections, and ClinicalTrials.gov and references of relevant articles were searched to identify additional potentially eligible manuscripts.

Each abstract was evaluated by two authors. For inclusion, each study was required to be original research; to assess a CPS, defined as a patient-level interaction by a clinical pharmacist, whether as a sole clinician or as part of a team; and to include an economic assessment (measurement of costs to provide the service, economic outcomes, or both). Studies involving team-based care were included only when the pharmacist was part of the evaluative team for most or all patients and was not included as part of the team on a solely consultative basis. Studies that were only published in abstract form or only reported clinical or humanistic outcomes, with no accompanying economic assessment, were excluded. When the abstract had insufficient detail to assess inclusion, the text of the full article was reviewed.

After the review of abstracts for inclusion criteria, full-text articles were obtained for all accepted abstracts and were assigned to two authors for review.[14] The data obtained from each article were recorded in a structured database designed in REDCap application (REDCap v.4.3.11; Vanderbilt University, Nashville, TN, USA, 2011), a secure Web-based application for building and managing online surveys and databases. The categories of data included in the abstraction form were citation details; article classification, including type of pharmacist interaction (e.g., with patient, with physician); inclusion and exclusion criteria; objective; perspective; setting; study design; descriptions of sites, patients, and intervention; structure of CPS including the degree of pharmacist autonomy, pharmacist training, access to clinical data by the pharmacists involved; program costs; outcomes measured; type of economic evaluation; results; and quality assessment. If discrepancies arose between the two reviewers with respect to any area of the data abstraction, the article was subjected to a third reviewer. Continued discrepancies or uncertainty was discussed among the entire group of reviewers until consensus was achieved.

Study Classification and Data Analysis

Articles for the review were categorized by using a modified version of the structure in this study.[15] This classification involved denoting whether the article compared alternative interventions and whether the study collected information on both costs and outcomes of the differing arms. The studies were also subcategorized based on the type of empirical study design and type of economic evaluation performed. Studies were also evaluated on whether they were a partial evaluation, such as a cost description or outcomes description, or a full economic evaluation.

Where possible, the perspectives of studies were classified as societal, health care payer, provider, or patient. Setting was categorized as affiliated with a university, academic medical center, or other teaching institution, as well as according to location and type.

The type of CPS provided was described. Specifically, CPS were categorized as disease state management, a CPS primarily directed at patients with a specific disease state or diagnosis; general pharmacotherapeutic monitoring, CPS that encompasses a broad range of activities based primarily on the needs of a specific clinic or panel of patients; pharmacokinetic monitoring, target drug program, patient education, wellness program or immunization service, MTM, and health screening or laboratory testing service.

The structure of the CPS included the degree of pharmacist autonomy, pharmacist training, and access to patient clinical data. Degree of

autonomy was rated as "low" if others, such as physicians, had full control and all interventions required approval prior to implementation; "medium" if pharmacists could intervene freely in some aspects of the CPS but required approval for other areas; and "high" if the pharmacists were able to intervene freely in the CPS, such as when collaborative agreements were in place. The level of pharmacist training was categorized as a pharmacy residency, board certification, number of years of work experience, or completion of program-specific training. Access to clinical data, such as medical records or computerized clinical information for those involved in the CPS, was rated as "low" if the data were limited to information collected at the time of patient visit and a medication profile only, "medium" if pharmacists had access to information collected at the time of the patient encounter or medication profile in addition to a limited set of clinical data from one other source, and "high" if pharmacists had access to information collected at the time of the patient encounter or information available from a medication profile in addition to a comprehensive set of clinical data from multiple other sources.

The quality of every article was evaluated by using five questions addressing the presence or absence of a comparator and the degree to which economic, clinical, and humanistic outcomes were evaluated and described. For full economic evaluations, the Quality of Health Economics Studies instrument was applied.[16]

Results

Search Results

Using the specified search criteria, 3587 potentially relevant papers were initially identified from the search. The full text of 317 potentially relevant manuscripts was reviewed. Twenty-five unique economic evaluations evaluating 24 different studies that met all inclusion criteria were included. One study, the MEDMAN study, was represented by two distinct economic evaluations.[17, 18] Figure 1 shows the numbers of studies excluded at each step of the review.

Evaluations were published in 17 different journals. In 12 of 25 cases (48%), evaluations were published pharmacy journals, with 13 of 25 (52%) published in nonpharmacy journals. The most common journals in which publications appeared were *The Journal of the American Pharmacists Association* (4 of 25 [16%]) and *Family Practice*, *International Journal of Pharmacy Practice*, *Pharmacy World & Science*, and *Pharmacoeconomics*, each publishing two manuscripts (8%). In contrast to previous systematic reviews of this topic, none of the evaluations were published in the *American Journal of Health-System Pharmacy* or *Pharmacotherapy*, and only one evaluation was published in *The Journal of Managed Care Pharmacy*.

Objectives and Setting

Economic evaluation was included as a primary or secondary objective in 22 of 25 studies (88%). The study perspective was either stated or identifiable in all but 5 of 25 (20%) of the reports. Studies were conducted from the perspective of the health care payer (11 of 25), provider (11 of 25), and patient (1 of 25); two of the studies were conducted from two perspectives.[17, 19] No studies used the societal perspective.

With regard to where the study was conducted, the origins of the studies were Europe (13 of 25 [52%]), United States (9 of 25 [36%]), Canada (2 of 25 [8%]), and Australia (1 of 25 [4%]). None of the identified studies were conducted in Asia or Africa. Seven studies (28%) involved an academic faculty member or resident to provide the clinical service or were conducted at an academic medical center, 13 of 25 (52%) were conducted in nonacademic settings, and 5 of 25 (20%) were unclear.

Clinical pharmacist services were delivered in an extended and acute care setting in 13 studies (Table 1). Extended and acute care settings included the hospital setting in nine studies (36%) and long-term care facility in four studies (16%). CPS were provided in ambulatory and community settings in 13 studies. Ambulatory and community settings included community pharmacy (8 [32%]), clinic or hospital-based independent ambulatory pharmacy practices (7 [28%]), physician-run ambulatory care clinics (4 [16%]), and the patient's home or work (2 [8%]). None of the evaluated studies claimed to be part of a medical home.

Methods Used

A variety of study designs were used, with 8 studies (32%) using a randomized posttest experimental design, 5 (20%) a quasi-experimental design, 4 (16%) a preexperiment design (i.e., nonrandomized posttest without pretesting), 3 (12%) a before-and-after design (i.e.,

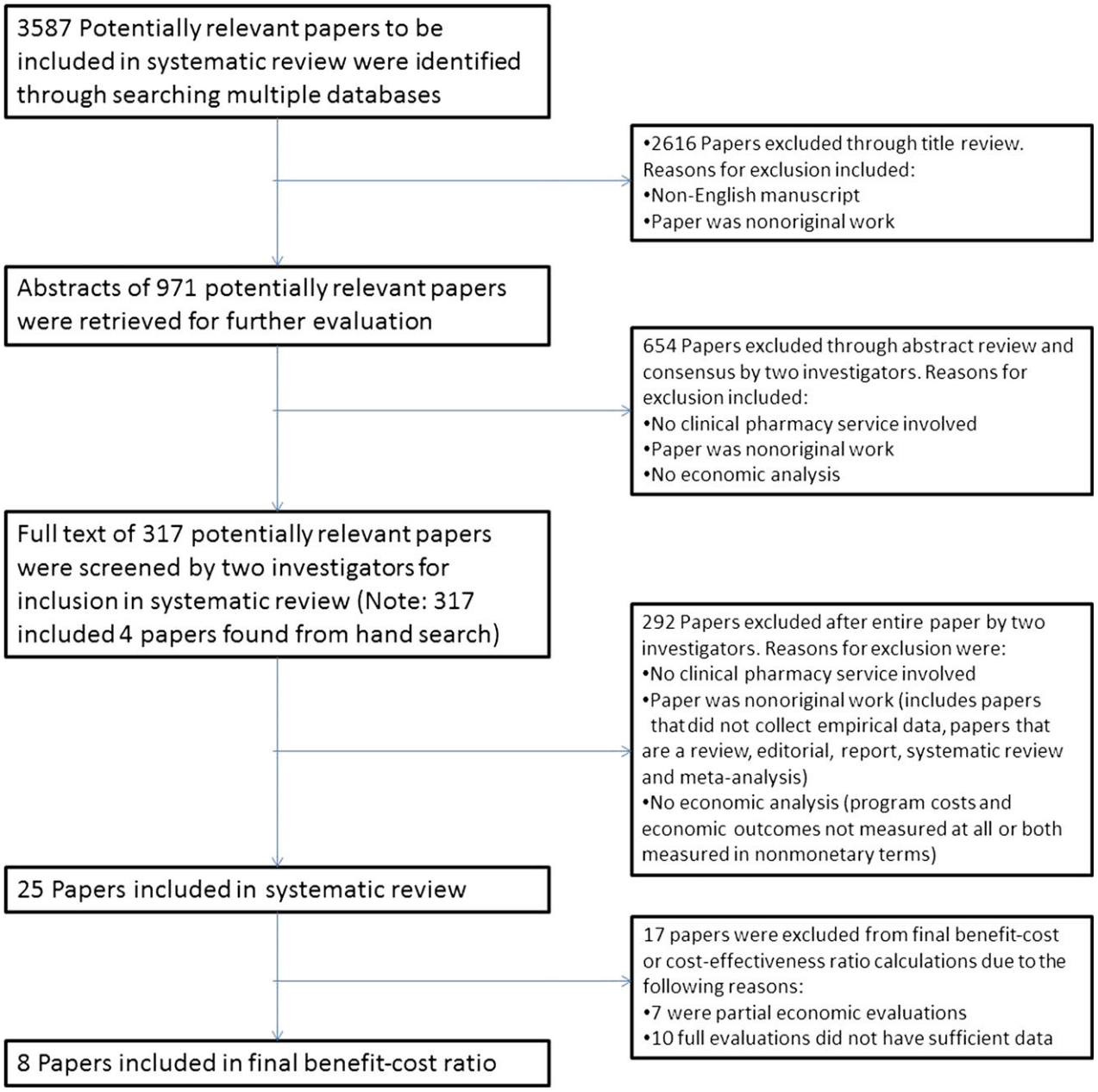

Figure 1. Schematic of the literature search methods and screening results.

historical control), 3 (12%) a noncomparative (i.e., single group) posttest design, and 2 (8%) solely used decision modeling. Of these, 16 of 23 studies (70%) had a concurrent or historical control, and 15 of 16 studies (94%) with a control group applied statistics to compare the two groups. Although seven of the studies incorporated some type of model, two of the studies exclusively used a modeling methodology. Most studies collected primary data (24 of 25 studies [96%]), whereas five studies used data from previously published sources (one exclusively and four augmenting primary empirical data).

With the exception of two modeling studies and one study that evaluated prescriptions and not people, the number of intervention subjects could be determined in 22 of 25 studies (88%). The median number of intervention study subjects enrolled was 293 (range: 58–1452). The median number of study sites was 2 (range: 1–44).

Pharmacist Practice Activities

Additional training, certification, or experience was required in 13 of 14 studies (93%)

Table 1. Settings of Economic Evaluations of Clinical Pharmacy Services[a]

Setting	No. (%) of studies (n=25)
Extended care facility	
Hospital	9 (36)
Long-term care facility	4 (16)
Other extended care facility	0 (0)
Not stated or could not be determined	0 (0)
Non–extended care facility	
Community pharmacy	8 (32)
Clinic or hospital-based outpatient pharmacy	7 (28)
Ambulatory care clinic	4 (16)
Urgent care clinic	0 (0)
Emergency department	0 (0)
Other non–extended care facility	2 (8)
Not stated or could not be determined	0 (0)

[a]Some studies evaluated clinical pharmacy services in more than one setting.

Table 2. Types of Clinical Pharmacy Services or Interventions Studied[a]

Type of service or intervention	No. (%) of studies (n=25)
Disease state management	12 (48)
General pharmacotherapeutic monitoring	6 (24)
Pharmacokinetic monitoring	0 (0)
Target drug program	2 (8)
Patient education program or cognitive service	1 (4)
Wellness program or immunization service	1 (4)
Health screening or laboratory testing service	0 (0)
Medication therapy management (as stated)	2 (8)
Other services	3 (12)

[a]Some studies evaluated more than one type of clinical pharmacy service.

where training was sufficiently described. Program-specific training was required in 11 studies, and board certification was required in two studies. Pharmacists were described as having had residency training in one study and had a number of years of work experience in one study.

Clinical pharmacist services were primarily categorized as disease state management (12 of 25 [48%]), general pharmacotherapeutic monitoring (6 [24%]), target drug program (2 [8%]), patient education only (1 [4%]), wellness program or immunization service (1 [4%]), and other or not sufficiently described (3 [12%]) (Table 2). None were described as pharmacokinetic monitoring or health screening or laboratory testing service. Although six (four of which were conducted in the United States) of the studies met at least six of nine criteria defining MTM,[20] only two studies (8%) stated that the program was "medication therapy management."

A sufficient description of clinical pharmacist services to classify the degree of pharmacist autonomy was provided in 21 of 25 studies (84%) (Table 3). In 1 of 21 studies (5%), pharmacist autonomy was classified as low (i.e., all interventions required approval prior to implementation), 18 of 21 studies (86%) were classified as medium (pharmacists could intervene freely in some aspects of the CPS, but other aspects required approval from others [e.g., physicians] prior to implementation), and 2 of 21 (10%) were classified as high (pharmacists were able to intervene freely [e.g., collaborative practice agreements were in place]), with one other study classified as "possibly high."

Next we provide a detailed description of the studies by type of CPS. Table 4 presents a summary of these studies.

Disease State Management

Twelve studies described 11 disease state management programs. Seven studies (evaluating six CPS programs) used controlled, patient-randomized, or cluster-randomized designs. One study randomized 314 heart failure patients (122 of whom received the intervention) to a community medication management program.[21] After 9 months, medication adherence was improved in the intervention program but not at 12 months. Annual direct costs of care were $2960 lower in the intervention group. Another study enrolled 134 heart failure patients (70 of whom received the intervention) in the hospital setting.[22] Pharmacists provided recommendations about diet and drug therapy at the time of discharge, and patients were followed up monthly for 6 months, then every 2 months. Patients in the intervention group had better medication compliance, lower 12-month mortality, and fewer hospital readmissions and hospital days. A third study included 1480 patients (980 of whom received the intervention) with coronary heart disease and evaluated the impact of pharmaceutical and lifestyle reviews by pharmacists through in-person interviews with patients.[17] The Community Pharmacy Medicines Management Project Evaluation Team, in a study of the same CPS but involving a different

Table 3. Description of Pharmacist Training, Role, and Autonomy for Clinical Pharmacy Services

Pharmacist training	Pharmacist role	Level of pharmacist autonomy
United Kingdom: Community pharmacist training occurred over a series of three events. Pharmacists received training designed and delivered by the Centre for Pharmacy Post-Graduate Education[17, 18]	The medicines management service was delivered from community pharmacy premises by community pharmacists. Pharmacists performed an initial consultation informed by the extracted medical data supplied by the researchers. Further consultations were provided according to pharmacist-determined patient need. Consultations included assessments of the following: therapy, medication compliance, lifestyle (e.g., smoking cessation, exercise, and diet) and social support (e.g., difficulties in collecting prescriptions and opening bottles). Recommendations were recorded on a referral form that was sent to the GP who returned annotated copies to the pharmacists	Medium. Pharmacists could make recommendations but not direct changes
United States: None described[21]	Protocol-driven medication history of all prescription and OTC drugs and assessment of patient medication knowledge and skills. Patient-centered verbal instructions and written materials about medications were provided to patients. Pharmacist monitored patients' medication use, health care encounters, and body weight. Communication with physicians and clinic nurses was on an as-needed basis	Medium. Pharmacists provided verbal and written advice to patients but did not appear to have prescriptive authority
Spain: None described[22]	Pharmacists were involved with giving information on disease, diet, and therapy on the day of hospital discharge. Patients were provided with the contact number and name of the pharmacist in case questions arose. In addition, the pharmacist called the patient monthly for the first 6 mo of therapy and then once every 2 mo	Medium. The pharmacist could intervene and make recommendations about diet and drug therapy but could not prescribe medications
United Kingdom: 20 pharmacists attended a 1-wk training course including lectures and workshops on the following topics: cardiovascular disease, Scottish Prescribing Analysis data, prescribing indicators, repeat prescribing systems, drug information, formularies, evidence-based medicine, communication, implementing guidelines, and an orientation to the study. An additional 1-day workshop was held after 1 wk, and a feedback session was held after 6 mo once all pharmacists had started work in practice to share experiences and to answer any logistical or clinical queries[23]	Pharmacists were asked to conduct a single review of the patient's medical records and recommend to the GP changes for action. Recommendations were communicated to GPs by using a study referral form and were not systematically followed up. Medication reviews were conducted by using a form adapted from a national template, and compliance assessment was conducted	Medium. The pharmacists could make recommendations to the physician but not prescribe

(continued)

Table 3. (continued)

Pharmacist training	Pharmacist role	Level of pharmacist autonomy
United Kingdom: Pharmacists had extensive experience of community pharmacy practice[24, 25]	An enhanced pharmacy review was carried out in general practice surgeries. The intention was that patients would receive between three and six consultations with the pharmacist over a period of 10–12 wks. The pharmacist had access to patient notes. At the consultation, the pharmacist explored prescription and OTC medications being used by the patient, including alternative and complementary therapies. All patients were assessed for NSAID safety and suitability based on medical and medication history. The pharmacist addressed knee pain control and provided recommendations to continue, add, or change medications, or provided a GP referral. The pharmacist also discussed relevant self-help measures that the patient could take	Medium. Pharmacists could make recommendations to the physician but not prescribe
Australia: Training was provided to intervention pharmacists only. Pharmacists undertook a wound management training course developed and delivered by the Department of Pharmacy Practice at Monash University, Australia. The course covered wound etiology, physiology of wound healing, pathophysiology of chronic wounds, factors impacting on wound healing, and wound management. The course also included case studies and practical hands-on sessions. Course participants were not formally assessed[26]	Nurses and the pharmacist met at least weekly to identify new wounds and discuss treatment options within the protocol. Between face-to-face meetings, pharmacists and nurses discussed case management by telephone. Pharmacists in the control arm did not participate in wound management	Medium. Pharmacists had some autonomy to work with the nurses to suggest wound management techniques
United States: Participating pharmacists received cardiovascular certificate training recognized by the North Carolina Center for Pharmaceutical Care, a service of the North Carolina Association of Pharmacists[27]	Medication assessments were provided by care managers including a comparison of the patient's treatment regimen with those recommended in national guidelines. Blood pressure was checked at baseline as well as during care manager visits. Lipid panels were measured at baseline and at least annually. Recommendations were made to patients' physicians, most commonly through faxes, when potential improvements in therapy were identified	Medium. Pharmacists could make recommendations to the physician but not prescribe

(continued)

Table 3. (continued)

Pharmacist training	Pharmacist role	Level of pharmacist autonomy
United States: Participating pharmacists received asthma certificate training recognized by the North Carolina Center for Pharmaceutical Care, a service of the North Carolina Association of Pharmacists[28]	Patients received education by a certified asthma educator and regular long-term follow-up by pharmacists (reimbursed for medication therapy management by health plans) including scheduled consultations, monitoring, and recommendations to physicians. Patients were provided an asthma action plan. Medication assessments were provided including a review of patterns of reliever and controller medication use. Inhaler technique, symptom frequency, and triggers were assessed	Medium. Recommendations were made to patients' physicians, most commonly through faxes, when problems or the potential for improvements in therapy were identified
United States: Participating pharmacists completed a training program in diabetes offered by a provider of continuing pharmacy education accredited by the Accreditation Council on Pharmacy Education or had otherwise been certified for diabetes care (e.g., Certified Diabetes Educator, certified in a specialty approved by the Board of Pharmaceutical Specialties)[29]	Community-based pharmacists provided patient self-management care services through scheduled consultations within a collaborative care management model. During regularly scheduled visits, pharmacists applied a prescribed process of care that focused on clinical assessments and progress toward clinical goal and worked with each patient to establish self-management goals. In addition, they worked with other health care providers and could recommend adjustments in the patients' treatment plans when appropriate	Medium. Pharmacists could make recommendations to the physician but not prescribe
Germany: None described[30]	The clinical pharmacist attended surgical intensive care unit ward rounds once/week. Orders for select antifungal agents were supervised by the clinical pharmacist, and interventions were made when necessary	High. The pharmacist attended rounds and was approved the use of certain drugs. Pharmacists could change prescriptions as needed
United States: Critical care–trained pharmacist with a doctor of pharmacy degree. No additional training specified[31]	The pharmacist evaluated and monitored medication therapy for all adult patients on the neurosurgical service, regardless of location within the institution. Prior to rounds, the pharmacist reviewed all patient profiles, laboratory data, and microbiologic cultures. During rounds, the pharmacist participated in patient care plan development and evaluated necessary changes to the medication regimen. After rounds, the pharmacist entered medication orders into the computerized provider order entry system. The pharmacist subsequently monitored pharmacologic changes initiated on morning rounds	Medium. The pharmacist attended rounds and provided input regarding therapy but did not appear to have prescriptive authority
United States: None described[32]	One clinical pharmacist provided the patients' physicians with written recommendations to optimize medication therapy in the intervention group. For the comparison group, the same pharmacist proposed recommendations that remained concealed from the physicians but were documented in a study database	Medium. The pharmacist could make recommendations to the physician but not prescribe

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Table 3. (continued)

Pharmacist training	Pharmacist role	Level of pharmacist autonomy
United States: Postgraduate qualification in pharmacy practice or recent continuing professional development in therapeutics. Pharmacists also attended a 2-day training course that included lectures on prescribing for the elderly, adverse drug reactions, improving adherence, and communication skills[33]	Pharmacists visited patient homes twice to educate them about their drugs, remove out-of-date drugs, inform GPs of drug reactions or interactions, and inform the local pharmacist if an adherence aid was needed	Medium. Pharmacists could make recommendations to the physician but not prescribe
Switzerland: Senior clinical pharmacist. No additional training specified[34]	Pharmacists participated in clinical ward rounds and reviewed daily all nonformulary prescriptions and case notes	Medium. Pharmacists could make recommendations to the physician but not prescribe
United Kingdom: Two training sessions covered the theory and practice of pharmaceutical care, practical exercises in collaborating with GPs, and involving patients and caregivers to construct, implement, and monitor a pharmaceutical care plan[35]	All recruited patients received pharmaceutical care adapted to British primary care	Not described
United States: Board-certified geriatric pharmacist. No study-specific training was described[36]	The pharmacist was included on an interprofessional team. The pharmacist provided drug information to unit nursing staff, nurse practitioners, and physicians for all of the transitional care unit patients. Other provided services included consultations on medically complex patients and those experiencing potential medication-related problems, routine drug regimen review for all patients on the unit, improving geriatric transitional care, and in-services on relevant topics. The pharmacist provided formal and informal education on geriatric pharmacology and evolving pharmacotherapy literature to all faculty	Medium. Pharmacists could make recommendations to the physician but not prescribe
Switzerland: Hypothetical service[37]	The hypothetical "clinical pharmacist" was not described	Not described
Canada: None described. Used pharmacists in an existing clinic[38]	The pharmacist-managed anticoagulation services pharmacist met patients once to review medical history and to discuss treatment objectives, possible adverse events, the need for frequent INR tests, and drug and food interactions. Warfarin was initiated according to an institution-approved protocol, and follow-up was conducted by telephone. Laboratory results were available through a networked computer system	Not described. Although not stated, it is inferred that pharmacists had autonomy to adjust warfarin dose according to a protocol, which would be consistent with a high level of autonomy
Denmark: No additional training was described[39]	Patients' medical records were screened once\week for suboptimal prescriptions within the 10 target intervention areas. If justified, the clinical pharmacist would discuss the prescription with the ward physician	Medium. Pharmacists could make recommendations to the physician but not prescribe

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Table 3. (continued)

Pharmacist training	Pharmacist role	Level of pharmacist autonomy
Canada: None described[40]	Patients were given the opportunity to discuss questions regarding natural health products. Pharmacists followed a stepwise counseling approach on a telephonic follow-up interview	Low. Pharmacists answered patient questions only
United States: Vaccination service implemented by the pharmacy resident, resident preceptor, and the residency program director[19]	The pharmacy resident conducted a chart review on the day before the vaccination service to identify and screen for potential contraindications for vaccination among the participants based on Centers for Disease Control and Prevention recommendations, such as documented hypersensitivity to eggs or components of the influenza vaccine, documented current acute febrile illness, or documented past severe adverse reactions to flu vaccination	Medium. Pharmacists administered vaccines
United States: Not described. Existing clinic[41]	The intensive care unit pharmacy staff evaluated creatinine clearance and patient medication profiles daily. Pharmacists recommended medication dosing to the medical team in accordance with institutional guidelines	Medium. Pharmacists could make recommendations to the physician but not prescribe
United Kingdom: "Suitably trained." Qualification required, but not described[42]	Supplementary prescribing	High. Does not require physician oversight. Pharmacists have prescriptive authority
United Kingdom: Hypothetical service[43]	The hypothetical service with "additional pharmacists" was not described	Not described

GP = general practitioner; INR = international normalized ratio; NSAID = nonsteroidal antiinflammatory drug; OTC = over the counter.

economic evaluation, found no significant differences in primary clinical outcomes, but patient satisfaction was better in the intervention group.[18] The total British National Health Service cost was statistically significantly higher in the intervention group (mean difference: £147). A fourth study evaluated the impact of pharmacists' reviews of the medical records of patients in 43 general practices in Scotland involving 706 angina patients (340 of whom received the intervention) and 1308 hypertensive patients (656 of whom received the intervention).[23] A 7.6% increase in antiplatelet drug use was found, with no significant cost differences at 1 year. A fifth study evaluated enhanced pharmacy review, community physiotherapy, or usual care involving 325 adults 55 years or older with knee pain in 15 general practices in North Staffordshire, United Kingdom.[24, 25] Improvements in the global assessment were observed at 3 months in the pharmacist review group, but 12-month clinical outcomes were not affected.[25] Monthly medication costs were decreased by £0.89 per person between the first and final consultation. A sixth study involved 21 Australian nursing homes and 342 uncomplicated leg and pressure ulcers in 176 patients.[26] The proportion of healed wounds was higher in the intervention arm versus the control arm (61.7% vs 52.5%), and wounds healed faster (mean 82 vs 101 days). Treatment resulted in decreased nursing time and a reduction in the cost of care by $358 (Australian dollars) (p=0.006).

Three studies used quasi-experimental or pre-post study designs. The first study evaluated a hypertension and dyslipidemia clinical pharmacist service provided at 12 community and hospital and pharmacy clinics in a cohort of 620 patients.[27] Mean blood pressure and low-density lipoprotein-cholesterol (LDL-C), high-density lipoprotein-cholesterol, and triglyceride levels were improved, and the cardiovascular event rate declined from 77 to 38 per 1000 person-years during the study period. A second study, in a similar program of 207 patients with asthma, found that objective and subjective measures of asthma control were improved, and emergency and hospital visits decreased.[28] Direct and indirect costs were decreased by $725/patient/year and $1230/patient/year, respectively. The third involved 573 patients with diabetes mellitus from 10 employer sites.[29] Glycosylated hemoglobin, LDL-C level, and blood pressure were improved at 12 months, and total health

Table 4. Summary of Studies of Economic Evaluations of Clinical Pharmacy Services and Their Outcomes

Study design	No. of patients	No. of patient visits	Clinical outcomes	Economic outcomes	Humanistic outcomes
United Kingdom: Cost-minimization analysis alongside multicenter, randomized, controlled trial with 12-mo follow-up[17, 18]	1480 (980 intervention and 500 control)	Initial consultation at study start, with further consultations based on pharmacist-determined need	Significant differences were not found in any of the clinical outcomes including appropriate medications as defined by the National Service Framework and self-reported medication compliance	Total NHS cost increased between baseline and follow-up in both groups (from £1243 to £1286 [3%] in the control group and from £1410 to £1433 [2%] in the intervention group). Cost of pharmaceuticals was higher in the intervention group (£769.20 vs £742.3, p=0.04). Intervention subject costs were higher, controlling for baseline differences (p=0.001)	Satisfaction with care was higher in intervention subjects
United States: Randomized prospective controlled trial with 12-mo follow-up[21]	314 heart failure patients (122 intervention)	9 mo of CPS were provided; number of visits were not provided	Significant difference in adherence of 10.9% favoring CPS at 9 mo. Nonsignificant difference of 3.9% favoring CPS at 12 mo	19.4% fewer emergency department and hospital admissions. Annual direct health care costs were $2960 lower in CPS group	None reported
Spain: Randomized prospective open clinical trial in the hospital setting. Enrollees were followed up for 1 yr[22]	134 (70 intervention and 64 control)	3 (follow-up visits were performed at 2, 6, and 12 mo after admission)	Compliance was better in intervention subjects (85% vs 74%) at 1 yr Mortality rate higher in the control group at 12 mo (30% vs 13% in the intervention group, p<0.05)	Intervention subjects were readmitted less frequently (difference = 32% at 12 mo). Control subjects used more hospital resources (mean 9.6 vs 5.9 hospital days per person) at 12 mo	No significant differences in quality of life. Satisfaction with care higher in intervention subjects
United Kingdom: Randomized controlled trial with 12-mo follow-up[23]	706 angina patients (340 intervention) and 1308 hypertensive patients (656 intervention)	Single review of patient medical records without systematic follow-up	7.6% improvement in prescribing of antiplatelet drugs. Fewer cardiovascular disease–related visits by angina patients	Adjusted costs were higher for intervention subjects at all time points	None reported
United Kingdom: Randomized controlled trial with 12 mo follow-up. Economic evaluation only evaluated pharmacist interventions[24, 25]	325 in three groups. 106 pharmacist intervention subjects evaluated in economic report	Mean of 3.2 consultations per patient over 12 mo	Improvement in 3-mo pain scores but not at 6 or 12 mo	Total monthly prescribing cost was £575 (mean £5.42 per person). Total monthly cost of prescribing at the final consultation was £480 (mean £4.53 per person)	None reported

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Table 4. (continued)

Study design	No. of patients	No. of patient visits	Clinical outcomes	Economic outcomes	Humanistic outcomes
Australia: Pseudo-randomized, pragmatic cluster trial with 20-wk follow-up in 21 nursing homes[26]	176 (342 with uncomplicated leg and pressure ulcers)	Weekly meetings between pharmacists and nurses	Percentage of healed wounds higher in the intervention arm (61.7% vs 52.5%). Intervention patients' wounds healed faster (mean time to healing 82 vs 101 days)	Reduction (unadjusted) in mean treatment costs of AUS$357.70 (p=0.006) when training costs included	None reported
United States: Quasi-experimental, longitudinal, pre-post study. Twelve community and hospital pharmacy clinics in Asheville, NC, over a 6-yr period from 2000 through 2005[27]	620 patients in the financial cohort and 565 patients in clinical cohort	30-min session every 3 mo	Mean systolic blood pressure decreased from 137.3 to 126.3 mmHg; mean diastolic blood pressure decreased from 82.6 to 77.8 mm Hg; percentage of patients at blood pressure goal increased from 40.2% to 67.4%; mean LDL-C level decreased from 127.2 to 108.3 mg/dl; percentage of patients at LDL-C goal increased from 49.9 to 74.6%; mean total cholesterol decreased from 211.4 to 184.3 mg/dl; mean serum triglyceride level decreased from 192.8 to 154.4 mg/dl; mean HDL-C level decreased from 48 to 46.6 mg/dl. The cardiovascular event rate of 77/1000 person-years during the historical period declined to 38/1000 person-years	Mean cost per cardiovascular event was $9931 compared with $14,343 during the historical period. Cardiovascular medication use increased nearly 3-fold; cardiovascular-related medical costs decreased by 46.5%. A 53% decrease in risk of a cardiovascular event and > 50% decrease in risk of a cardiovascular-related emergency department or hospital visit were also observed	None reported

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Table 4. (continued)

Study design	No. of patients	No. of patient visits	Clinical outcomes	Economic outcomes	Humanistic outcomes
United States: Quasi-experimental, longitudinal pre-post study in 12 pharmacy locations in Asheville, NC[28]	207	30-min session every 3 mo	Sustained improvement in asthma control. Proportion of patients with asthma action plans increased from 63 to 99%. Proportion of patients with emergency department visits decreased from 9.9 to 1.3%, and hospitalizations decreased from 4.0 to 1.9%	Spending on asthma medications increased. Asthma-related medical claims decreased. Total asthma-related costs significantly lower compared with projections. Direct cost savings averaged $725/patient/year and indirect cost savings $1230/patient/year	None reported
United States: Quasi-experimental observational analysis, pre-post comparison[29]	573 patients with diabetes mellitus	Two or more documented visits	Mean glycosylated hemoglobin decreased from 7.5 to 7.1% ($p=0.002$), LDL-C level decreased from 98 to 94 mg/dl ($p<0.001$), and systolic blood pressure decreased from 133 to 130 mm Hg ($p<0.001$) over a mean of 14.8 mo of participation in the program. Influenza vaccination rate increased from 32 to 65%, eye examination rate increased from 57 to 81%, and foot examination rate increased from 34 to 74%	Average total health care costs/patient/year were reduced by $1079 (7.2%) compared with projected costs	None reported
Germany: Before-and-after study evaluating cost of antifungal agents[30]	Not applicable	Pharmacist attends rounds once/week	None reported	Intervention associated with a significant decrease in antifungal agent use. Costs reduced by 50% in "post" period	None reported

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Table 4. (continued)

Study design	No. of patients	No. of patient visits	Clinical outcomes	Economic outcomes	Humanistic outcomes
United States: Patients admitted to neurosurgical service 2 yrs before and 2 yrs after CPS implementation[31]	2156 (1079 post-implementation)	Daily monitoring by pharmacist	Average hospital stay decreased from 8.56 to 7.24 days (p=0.003). Early hospital mortality decreased from 3.34 to 1.95% (p=0.06). Significantly lower postimplementation readmission rate (p=0.05)	Average pharmacy and intravenous therapy cost/patient decreased from pre- to post-implementation (from $4833 to $3239)	None reported
United States: Prospective controlled study in two internal medicine practices over 1 yr[32]	243 (127 intervention)	Single medical record review, although pharmacist available for physician questions	Between-group difference in the change in ER visits per 1000 patients approached statistical significance (p=0.054). CPS group patients more likely to have medication nonadherence, untreated indication, and medication choice issues addressed	Change in mean per patient per year medical (excluding pharmacy) cost did not differ significantly between the groups (p=0.711)	None reported
United Kingdom: Pragmatic, randomized, controlled trial with 6-mo follow-up[33]	855 patients (415 intervention)	Pharmacists were paid for two home visits	Statistically significant increase in emergency readmissions and nonsignificant reduction in deaths in the CPS group	Average cost per intervention group patient was £1695 compared with £1424 for control patients	Gain of 0.0075 QALY with CPS in 698 patients for whom QALY data were available. Incremental cost per QALY gained in the intervention was £54,454
Switzerland: Prospective, observational study in a tertiary 700-bed university hospital setting over 32 wks[34]	1444 patients	CPS conducted for 70 of 224 days	213 pharmaceutical interventions recorded	51 interventions (24%) considered to be directly cost saving without affecting care with a mean per person saving of €10.11 (extrapolated to €1158 for a year). Cost-relevant interventions estimated to equal €10,731 in cost avoidance, not counting the effect on length of stay, adverse drug event rate and possible litigation costs	None reported

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Table 4. (continued)

Study design	No. of patients	No. of patient visits	Clinical outcomes	Economic outcomes	Humanistic outcomes
United States: Randomized multiple interrupted time-series design analysis of pharmaceutical care at 2-mo intervals. Modeled cost-utility analysis[35]	Of 760 subjects recruited, 673 reached baseline and 563 had medication reviewed	Mean of 8.3 reviews per person	Reduction in U.K.-MAI score over time. Reduction in number of drugs over time	On average, pharmaceutical care costs an estimated £192/yr more than usual care but yields slightly greater benefits, namely 0.019 of a QALY. Incremental cost-effectiveness ratio estimated at ~£10,000/QALY gained	None reported
United States: Retrospective controlled analysis[36]	339 (163 intervention)	One or two visits per week by team of geriatric doctor, nurse practitioner, and geriatric pharmacist. One member of team is on site 5 days/wk	None reported	Significantly shorter lengths of stay (unadjusted difference = 6.5 days), fewer patient days, and lower total charges (unadjusted difference = $2297)	None reported
Switzerland: Ten possible interventions were modeled for their estimated potential impact on failures[37]	Not applicable	Not applicable	Gains in qualis (1 quali = reduction of the criticality index by one point) of 1292 for ready-to-use syringes, 1201 by employing clinical pharmacists, and 996 from double checks by nurses were predicted	Cost–efficacy ratios of €0.54 per quali gained by employing clinical pharmacists, €0.71 per quali gained from double checks by nurses, and €0.72 per quali gained for ready-to-use syringes were predicted	None reported
Canada: Randomized controlled open pragmatic clinical trial[38]	250 (128 intervention)	As frequent as necessary by telephone. Mean follow-up was 14.9 wks in PMAS	No difference in time in therapeutic range. PMAS patients were more frequently supratherapeutic (INR $\geq$ 5). Family physician visits per patient year were lower in PMAS patients	Maintaining PMAS cost was ~$123.80 per patient for first year. Family physician visits per patient year were lower (difference = 0.4 visits per year) in PMAS patients	No difference in QOL outcomes observed (SF-12 and EuroQOL EQ-5D)

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Table 4. (continued)

Study design	No. of patients	No. of patient visits	Clinical outcomes	Economic outcomes	Humanistic outcomes
Denmark: Comparative, prospective, crossover design involving two parallel groups[39]	2500 (1452 clinical pharmacy patients screened); 8362 control and 9654 CPS prescriptions screened	Patient medical records screened once weekly	Significant reduction in number of days from 10–5 with a suboptimal prescription	The cost of practicing clinical pharmacy service was €7360. Estimated direct cost savings (medicine and nursing time) for four of seven intervention areas of program was €3442	None reported
Canada: Before-and-after study. Subjects recruited over 8 mo period for "before" phase and 11 mo for "after" phase[40]	265 (123 intervention)	Single visit	None reported	Increased counseling time from a mean of 9–18 min. Mean additional cost of CDN$7.49 per patient	Increased patient satisfaction with routine counseling on natural health products
United States: Retrospective descriptive report[19]	58	Two 2-hr vaccination sessions	Immunization rate increased from 64% in the previous year to 83% with CPS	Net income of $13 per vaccination was realized after making adjustments for costs	Patients and staff were highly satisfied with the service
United States: Single-group retrospective analysis of a renal dosing program in the pediatric cardiac ICU[41]	131 patients with 140 admissions	Daily	Pharmacist recommendations were responsible for 96% of medication adjustments for renal dysfunction	CPS estimated to result in ~$12,000 in doses saved	None reported
United States: Retrospective data analysis to examine volume, cost, and trends of pharmacist prescribing[42]	Total number of pharmacist prescriptions were 2706 in 2004 and 11,458 in 2005	Not applicable	None reported	323% increase in the number of items prescribed between 2004 and 2005 and 170% increase in the number prescribed between 2005 and 2006. Net ingredient cost of items prescribed by pharmacists increased from £25,348 in 2004 to £278,634 in 2006	None reported

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Table 4. (continued)

Study design	No. of patients	No. of patient visits	Clinical outcomes	Economic outcomes	Humanistic outcomes
United Kingdom: Model comparing three hypothetical programs to reduce medication errors in hospitals[43]	Not applicable	Not applicable	None reported	Predicted mean monetary CPS cost £0.21–0.37 million and resulted in a net benefit of £27.25 million over a 5-yr time horizon. By comparison, computerized physician order entry and bar coding prescriptions resulted in a net benefit of £31.5 and £13.1 million, respectively	None reported

CPS = clinical pharmacy services; EuroQOL EQ-5D = five-dimension quality-of-life scale developed by the EuroQOL Group; HDL-C = high-density lipoprotein-cholesterol; INR = international normalized ratio; LDL-C = low-density lipoprotein-cholesterol; NHS = National Health Service; PMAS = pharmacist-managed anticoagulation services; QALY = quality-adjusted life-year; SF-12 = 12-Item Short Form Survey; U.K.-MAI = medication appropriateness index adapted for use in the United Kingdom.

care costs were reduced by $1080 compared with projected costs but were increased by $698 compared with baseline.

Two studies used before-and-after study designs. The first evaluated the implementation of practice guidelines for the treatment of fungal infections enforced by a clinical pharmacist in an unspecified number of patients.[30] The clinical pharmacist service was associated with an approximate reduction in the cost of antifungal agents of over 50%. The second evaluated 2156 neurology patients (1079 of whom received the clinical pharmacist-managed program) and 11,250 clinical pharmacist interventions.[31] Average hospital stay, mortality, and pharmacy and intravenous therapy costs decreased by 1.3 days, 1.4%, and $1594, respectively, after program implementation.

General Pharmacotherapeutic Monitoring

Six studies were classified as having provided general pharmacotherapeutic monitoring. Two of these studies used a prospective randomized trial design. The first evaluated 243 adult patients, 127 of whom received medication therapy optimization by a clinical pharmacist, from two internal medicine practices.[32] Intervention group patients were more likely to have medication nonadherence, untreated conditions, suboptimal medication choice, and cost issues addressed. Medical care costs were not significantly different between groups. The second evaluated the impact of pharmacist home visits after hospital discharge in 872 subjects (437 of whom received the intervention).[33] A statistically significant increase in emergency readmissions occurred in the intervention group, along with a nonsignificant reduction in deaths. The average calculated difference in total cost of care was £407 per person favoring the control group, whereas a difference of 0.0075 quality-adjusted life-year (QALY) favored the intervention, resulting in an incremental cost-effectiveness ratio (ICER) of £54,454 per QALY gained.

Another group conducted a prospective observational study assessing clinical pharmacist interventions on two wards of a single tertiary hospital involving 1444 patients.[34] In all, 148 interventions concerning drug therapy were made, with 83% adopted by physicians, 6% rejected, and 11% with unknown outcomes. Of these, 51 interventions were considered to be cost saving, with an estimated 1-year cost avoidance of €10,731.

A group of researchers conducted a randomized multiple interrupted time-series study evaluating pharmaceutical care in 760 subjects.[35] The number of drugs used declined over time, with a corresponding increase in costs (£192) and QALYs (0.019) and a calculated ICER of ~ £10,000/QALY gained. A second group conducted a retrospective controlled analysis of an interprofessional team including a pharmacist in 339 transitional care patients.[36] The care team patients had significantly shorter lengths of stay, fewer patient days, and lower total charges. Finally, a third group conducted a modeling study evaluating therapy failures and the criticality of those failures by the hypothetical addition of a pharmacist compared with nine other potential interventions.[37] Employment of a clinical pharmacist was expected to result in 1201 additional qualis (1 quali was defined as a reduction of the criticality index by 1 point), second only to the use of ready-to-use syringes. The best cost-efficacy ratios were obtained for adding a clinical pharmacist (1 quali = 0.54 euros), followed by double-checking medications by nurses (1 quali = 0.71 euros) and ready-to-use syringes (1 quali = 0.72 euros).

Target Drug Programs

Two studies evaluated target drug programs. The first conducted a randomized controlled open pragmatic clinical trial involving 250 subjects, 128 of whom received pharmacist-managed anticoagulation services.[38] No significant differences were observed in time in therapeutic international normalized ratio (INR) range or quality of life. First-year service costs were $123.80 per patient, and the number of family physician visits was reduced. The second evaluated 2500 subjects (1452 of whom received the CPS) and 18,016 prescriptions (9654 of which were prescriptions for patients receiving the CPS) in four orthopedic surgical wards in two hospitals using a modified prospective crossover design.[39] A significant reduction in the number of days with a suboptimal prescription (difference = 5 days) was observed in patients receiving the pharmacist service. Although service costs were €7360, the program was estimated to save €3442.

Patient Education Programs

A before-and-after study evaluated the impact of routine structured counseling on natural health products in 265 patients visiting the pharmacy of a comprehensive cancer center.[40] Patients were provided the opportunity to ask questions about natural health products, and pharmacists followed up with patients in a telephonic interview. The program increased patient satisfaction with routine natural health product counseling at an additional cost of $7.49 (Canadian dollars) per patient.

Wellness Program or Immunization Service

Another group conducted a retrospective descriptive evaluation of a screening initiative to identify potential vaccine recipients in a senior housing complex.[19] The immunization rate improved from 64–83%, with a net income of $4.55 per vaccination provided.

Other Services

Three studies evaluated programs that could not be grouped into one of the previously described classifications. The first retrospectively evaluated 140 admissions from 131 pediatric cardiac surgery patients at risk for renal insufficiency by using a noncontrolled posttest design.[41] Pharmacists made 74 renal dosing adjustments at an estimated drug cost savings of $12,482.54. The second evaluated the volume, patterns, and costs associated with pharmacist prescribing in England in a noncontrolled posttest design study.[42] Prescription costs increased 10-fold from 2004 to 2006; the clinical impact of this increased prescribing by pharmacists was not evaluated. The third, by using a decision model, evaluated the impact of hypothetical pharmacist participation on ward rounds to reduce adverse drug events.[43] In this model, when monetary valuations of the health impact of preventable adverse drug events were included, ward pharmacists were anticipated to cost £0.21–0.37 million and result in ~£27 million in net benefits over a 5-year timeline.

Economic Analysis Quality

Included costs were well described (i.e., all important and relevant costs were identified) in 13 of 25 studies (52%). Clinical or humanistic outcomes were evaluated in 20 of 25 studies (80%) and were well described in 18 of 25 studies (72%). Studies were considered full economic evaluations in 18 of 25 cases (72%). Objectives were considered clearly presented in

22 of 25 studies (88%), whereas perspectives were presented in 9 of 25 (36%). Uncertainty was adequately addressed in 12 of 25 studies (48%). Incremental analysis was conducted in 7 of 25 studies (28%). Methodologies for data abstraction were stated in 17 of 25 studies (68%) and time horizons were stated in 9 of 25 studies (36%). Study assumptions and limitations were stated and justified in 8 of 25 studies (32%) studies, whereas biases were adequately discussed in 9 of 25 studies (36%). Conclusions and recommendations were considered justified and based on results in 24 of 25 studies (96%). The funding source was disclosed in 17 of 25 studies (68%). A Quality of Health Economic Studies (QHES) score was calculated for the 18 full economic analyses evaluated in our review. The mean ± SD QHES score was 60.4 ± 22.3 of a possible 100 points (more than 75 points indicates high quality).

Benefit-Cost and Incremental Cost-Effectiveness Ratios

Benefit-cost (B:C) ratio or ICER could be calculated for eight of the studies. B:C ratios were not reported directly in any of the studies, but they could be calculated in three studies and ranged from 1.05:1–25.95:1. Although many studies did not report benefits in monetary terms, five studies did sufficiently report effectiveness or utility so that an ICER could be calculated. The ICERs and their denominators' unit of measurement are reported in Table 5.

Discussion

This article is a continuation of a series of systematic reviews of the economic value of clinical pharmacist services.[2–4] With the exception of a more exhaustive search strategy by including the Embase and CINAHL databases and an increased reporting of the nature and clinical outcomes of the CPS, our methods have remained consistent. In this latest analysis, the proportion of studies with full pharmacoeconomic evaluations increased from 48% during 2001–2005 to 72% in this review (2006–2010). In addition, the quality of published studies improved. For example, in the last review, 37% of all studies were purely descriptive,[2] with 16% descriptive in the current review. In this review, studies frequently had a comparison group (84% of studies), a vast improvement over our previous article in which only 43% of studies used a comparison group. Among the full economic analyses, studies scored 60.4 points on the QHES scale for study quality. These results are similar to the QHES results of 30 economic analyses of care strategies for gastroesophageal reflux disease (mean ± SD score: 63.6 ± 14.7) identified in another systematic review.[16]

Despite the improvement in study quality, the total number of full and partial economic evaluations decreased compared with previous periods (104 articles during 1988–1995, 59 during 1996–2000, 93 during 2001–2005,[2–4] and 25 during 2006–2010). Given our more comprehensive search strategy for the current period, the decline in the number of articles is real, but the reasons for this overall decline are unclear. The decline may be due to any or all of the following: decline in research funding or in the number of studies funded evaluating CPS; changes in journal review or publication patterns, requiring a higher standard for publishing economic analyses; fewer "novel" clinical pharmacist services being initiated; or a perception that the justification of clinical pharmacist services is no longer necessary. The

Table 5. Studies Evaluating Clinical Pharmacy Services with Calculable Benefit-Cost or Incremental Cost-Effectiveness Ratios[a]

Benefit-cost ratio	ICER	ICER denominator	Reported by authors or calculated
1.05:1			Calculated[22]
15.4:1			Calculated[21]
14.73–25.95:1			Calculated[43]
	Dominant	Wound prevented	Calculated[39]
	CDN $8.33	VC	Reported[40]
	€0.54	Quali	Reported[37]
	£10,000	QALY	Reported[35]
	£54,454	QALY	Reported[33]

ICER = incremental cost-effectiveness ratio; QALY=quality-adjusted life-years gained; Quali = reduction of the criticality index by 1 point; VC = satisfaction with complementary therapies subscale score.

[a]Seven studies were considered partial economic evaluations. Benefit-cost or cost-effectiveness ratios could not be calculated for 10 full economic evaluations.

dramatic decline in economic evaluations of CPS in the United States was particularly surprising, given recent policy changes that allowed for the payment of certain CPS.[8, 44]

Shifts in the type of journal published also occurred compared with the previous analysis. In this review, studies were published in 18 different journals; the most common was the *Journal of the American Pharmacists Association* (16% of studies). In the previous systematic reviews, articles were commonly published in the *American Journal of Health-System Pharmacy* and *Pharmacotherapy,* but no publications were included in these journals from 2006 to 2010. A higher proportion of studies were published in nonpharmacy journals (52%) compared with 26.9% in the systematic review covering 2001–2005.

In most cases, CPS were either considered cost-effective or had a favorable B:C ratio. When calculable, the B:C ratio ranged from 1.05:1 to 25.95:1. However, notable exceptions were three large prospective multicenter studies conducted in the United Kingdom that showed no or minimal benefits in clinical outcomes and an added cost with community-based CPS.[17, 18, 33]

As anticipated, we observed a continued shift from CPS addressing targeted drug therapy and pharmacokinetic monitoring services to those addressing general pharmacotherapy and disease state management. Compared with the previous reviews in this series, there was also a continued shift from inpatient hospital-based services to outpatient clinic- or community-based services. For the first time since we began this review, comprehensive economic evaluations were primarily conducted in countries outside the United States and were often conducted at a national or regional level, involved multiple sites, and were more frequently conducted in nonacademic community settings. This represents a dramatic shift from previous reviews, where the vast majority of studies were conducted in U.S. academic hospital settings.[2–4] This shift may also reflect a change in the management of patients from the inpatient to the outpatient setting and an increased focus on optimizing medication use in patients with chronic conditions.[45]

Surprisingly, there were still few full economic evaluations of MTM services. Only two of the programs were identified as MTM,[27, 28] although several others met criteria for being considered MTM.[20] Neither of the MTM studies included a concurrent control group. Without evidence supporting the effects and value of MTM, support for these programs by insurers may wane. Furthermore, the expansion of MTM services from targeted interventions without follow-up to more comprehensive services is unlikely to occur in the absence of evidence supporting more comprehensive programs.

There were no studies published that evaluated clinical pharmacist services in a medical home. Given the time frame of this review relative to the introduction of the Patient Protection and Affordable Care Act of 2010,[44] this finding was not surprising. However, we were anticipating some published studies supporting the inclusion of clinical pharmacists in care teams, conducted in a setting similar to a medical home. This is likely to be a fruitful area for research in the near future.

For the first time since we began publishing this series, we saw more studies conducted in countries other than the United States. In particular, 8 of 25 studies were conducted by investigators primarily based in the United Kingdom, and these studies accounted for five of the eight randomized controlled trials included in our review.[17, 18, 23, 25, 33] All five studies received federal funding from the U.K. government. In contrast, five European studies, conducted in Switzerland,[34, 37] Spain,[22] Germany,[30] and Denmark,[39] included just one randomized controlled trial[22] and two studies of quasi-experimental design.[30, 39] Funding was acknowledged for just two of the studies and were from nonfederal sources.[22, 39] Of the nine U.S. studies, just one was a randomized controlled trial,[21] and three used quasi-experimental designs.[27, 28, 32] The randomized controlled trial was the only federally funded study,[21] three were cofunded by industry and/or professional pharmacy organizations,[27, 28, 32] one was funded by an internal academic grant,[36] and four were not funded.[19, 31, 32, 41] From these data, there appears to be a strong association between high-quality trial designs and competitive adequately funded federal funding opportunities. Also notable is the lack of published economic evaluations of CPS receiving federal funding outside the United Kingdom.

Important limitations of this systematic review must be outlined. Although a comprehensive search strategy was used, it is possible that not all CPS economic evaluations were identified. A publication bias may also be present. In addition, due to the decrease in the number of published studies, we were unable to provide a pooled B:C ratio estimate as we did in our previous reviews.

Conclusion

A higher proportion of economic evaluations of CPS used controlled designs and better methodologies, although overall fewer studies were published during the 2006–2010 period. Evaluations of ambulatory practices were increasingly common. In general, CPS were cost-effective or provided a good B:C ratio. However, variability exists in both clinical outcomes achieved and the subsequent cost-effectiveness of CPS. Future studies should focus on identifying specific aspects of CPS that contribute to improved clinical outcomes and efficiency.

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