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# Economic Evaluations of Clinical Pharmacy Services: 2001–2005

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The objectives of this review were to (1) summarize and evaluate studies that measured the economic impact of clinical pharmacy services (CPSs) published between 2001 and 2005 (inclusive) and (2) provide guidance on methodological considerations to individuals performing such research in the future. A systematic literature search using MEDLINE and International Pharmaceutical Abstracts was conducted to identify published economic evaluations of CPSs. Studies were screened and then randomly assigned to reviewers, who reassessed inclusion/exclusion criteria and abstracted prespecified data from each study. Among the many characteristics examined in each study were study design and type of economic evaluation, setting and type of CPS, study quality, and results. Ninety-three articles were included in the final analysis. Included studies were published in 43 different journals, most of which (68 [73.1%]) were pharmacy-based. Most studies were performed in hospitals (40 [43.0%]), ambulatory care clinics or physician's offices (20 [21.5%]), or community pharmacies (16 [17.2%]). The most common types of CPSs evaluated were general pharmacotherapeutic monitoring services (32 [34.4%]), target drug programs (27 [29%]), and disease state management services (21 [22.6%]). Full economic evaluations were performed in just less than half (45 [48.4%]) of the studies, and a positive economic benefit associated with CPSs was noted in 69% (n=31) of these. Among studies reporting data necessary to determine a benefit-to-cost ratio (n=15), the pooled median value was 4.81:1—meaning that for every $1 invested in CPS, $4.81 was achieved in reduced costs or other economic benefits. The quality of studies varied widely, with less than one-half considered good to fair (40 [43.0%]), but the proportion of studies using appropriate study designs increased compared with previous reviews. Based on the evidence examined in this review, CPSs continue to provide a significant return on investment, but improvements are still needed in the methods used to evaluate the economic impact of these services.

**Key Words:** clinical pharmacy services, cost, cost-effectiveness, cost-benefit, cost-utility, outcomes, programs, economic evaluation.

**(Pharmacotherapy 2008:28(11):285e–323e)**

During the past decade, there has been continued progress in the transformation of the practice of pharmacy, with increasing emphasis on the patient and the provision of clinical pharmacy services (CPSs). This transformation is evidenced by the inclusion of medication therapy management (MTM) services in the Medicare Prescription Drug, Improvement, and Modernization Act of 2003[1]; the legislative efforts to grant provider status to pharmacists[2];

and the development of Current Procedural Terminology codes to allow pharmacists to bill for clinical services.[3]

The role that pharmacists can play in improving the quality and safety of medication use, and in reducing costs, is expected to increase in the future. The aging population and increased reliance on pharmaceuticals for improving health have resulted in greater per capita drug use,[4] yet at the same time, there are heightened concerns about the safety and costs of new and existing drugs and the processes by which drugs are procured, prescribed, dispensed, and administered.[5–11] These issues create new and expanded opportunities for pharmacists.

Although such opportunities bode well for the future of the profession, there are also threats to the continued expansion of clinical pharmacy practice. The U.S. health care system, which accounted for 16% of the U.S. gross domestic product and cost $2.1 trillion in 2006, has been characterized as both inefficient and ineffective.[12] Reform of the health care system was a major theme of the 2008 presidential debates,[13] and any such effort will certainly have the reduction of costs among its principal goals. Even though health care continues to use increasingly advanced technology, personnel costs remain the largest single component of health system expenditures, and these costs will undoubtedly be a primary target for cost-reduction efforts.[14]

Pharmacy leaders are constantly under pressure to justify both existing and expanded CPSs. Robotics, medication-dispensing cabinets, and other automated devices have reduced the pharmacy staff time required for order processing; computerized physician order entry and other advances in informatics have created efficiency in order processing. Even though these advances have been touted for their potential to allow pharmacists to spend more time in direct patient care,[15] not all health care administrators may fully appreciate the value of CPSs and may view automation and technology as an opportunity to reduce costs by eliminating pharmacist positions. Published evidence of the value of CPSs is an important resource that pharmacy leaders can use to justify pharmacist-led programs that maintain or improve clinical outcomes while also improving net revenue by reducing overall expenses or augmenting gross revenue.

The American College of Clinical Pharmacy (ACCP) is "a professional and scientific society that provides leadership, education, advocacy, and resources enabling clinical pharmacists to achieve excellence in practice and research."[16] Toward that end, the ACCP has been integral in efforts to chronicle the value of clinical pharmacists and CPSs. The ACCP previously commissioned three large reviews of studies that assessed the economic impact of CPSs. The first, printed in 1989, summarized the literature published before 1988[17]; the second reviewed economic evaluations of CPSs published between 1988 and 1995[18]; and the third spanned the period 1996–2000.[19] In 2006, the ACCP again charged a group of its members to conduct a systematic review of pharmacoeconomic evaluations of CPSs, this time from 2001 to 2005. This article is the product of that work.

The specific objectives of this review were (1) to summarize and evaluate studies that measure the economic impact of CPSs published during the 5-year period 2001–2005 and (2) to provide guidance on methodological considerations to individuals performing such research in the future.

## Methods

### Article Retrieval, Screening, and Data Collection

A systematic search of the literature databases MEDLINE and International Pharmaceutical Abstracts was conducted to identify economic evaluations of CPSs published between January 2001 and December 2005 (inclusive). The beginning date of January 2001 was selected

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because the previous ACCP review was inclusive through December 2000.[19] The ending date of December 2005 was selected to maintain the 5-year time interval of the previous review. Search terms used were "clinical pharmacy services," "cost," "cost-analysis," "cost-benefit," "cost-effectiveness," "cost-utility analysis," "economic evaluation," "outcomes analysis," "pharmacy services," "outcomes," and "programs." The search was filtered to exclude non-English articles, review articles, editorials, and other incomplete or unoriginal works.

In addition to the literature database search, several methods were used to find pertinent literature and ensure a comprehensive search of the literature. First, a search of the Science Citation database (Web of Science, Thomson Reuters, New York, NY) was conducted to identify articles that referenced previous reviews.[18, 19] Second, the authors examined their personal files for previously unidentified articles. Third, the authors examined the bibliographies of included articles and of review articles to identify cited works. Papers identified by these methods were added to the papers subjected to full review.

Similar to previous reviews, inclusion criteria were (1) original research, (2) assessment of a CPS (defined as a patient-level interaction), and (3) economic assessment (measurement of costs to provide the service, economic outcomes, or both). Unoriginal work (reviews, editorials, or letters) or studies published in abstract form only were excluded. Studies that evaluated only clinical or humanistic outcomes, without an economic assessment, were also excluded.

All citations identified in the electronic database search were screened for inclusion by two authors (P.D.M., J.M.H.). Articles without abstracts were collected manually and screened for inclusion. After title and abstract screening, an electronic copy of each full-text article was obtained for full review. In the full review process, each study was randomly assigned to two of seven reviewers for data abstraction. Data were recorded using a series of database forms designed for this purpose in Microsoft Access (Microsoft Office Access 2003, Microsoft Corp., Redmond, WA). The forms required entry of information on specific characteristics of each study. The following sections were included in the forms: citation, inclusion/exclusion criteria, objective, perspective, setting, methods, description of program costs, outcomes measured, description of site, patients, intervention, length of follow-up, structural characteristics (pharmacist autonomy, access to clinical data, and pharmacist training), type of economic evaluation, and economic results. A double data extraction approach was used because this method produces fewer errors in systematic reviews.[20] Discrepancies between reviewers were resolved through discussion and consensus among all authors, and a final consensus version of the database (with a single consensus record for each article) was created for subsequent data analysis.

### Study Classification and Data Analysis

Each article was assessed for the type of evaluation and categorized as shown in Table 1 using criteria adapted from Drummond.[21] Two factors were considered in determining the type of evaluation: the presence of two or more alternatives and both input cost(s) and outcome(s). Evaluations that included two or more alternatives (e.g., concurrent control group, historical control, pre/postdesign) were

**Table 1. Criteria for Assessment of Type of Analysis**

| | Were both costs and outcomes considered? | |
|---|---|---|
| | No | Yes |
| Were two or more alternatives considered? | | |
| No | Cost description or outcome description | Cost and outcome description |
| Yes | Cost analysis or outcome analysis | Full economic analysis<br>Subcategories:<br>Cost-minimization analysis<br>Cost-benefit analysis<br>Cost-effectiveness analysis<br>Cost-utility analysis |

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considered "analyses," whereas those that did not include a comparison were labeled "descriptions." Each evaluation was classified as one of the following: cost description, outcome description, cost and outcome description, cost analysis, outcome analysis, cost and outcome analysis, or full economic analysis. The articles considered full economic analyses were subcategorized by type; subcategories included cost-minimization analysis, cost-benefit analysis, cost-effectiveness analysis, and cost-utility analysis. In addition, information on the method of empirical data collection was abstracted to determine the archetypical study design, based on definitions shown in Table 2.

Articles were classified both by setting of evaluation and by type of CPS. The settings included hospital; ambulatory care clinic; physician's office; community pharmacy; long-term care, rehabilitation, or residential facility; clinic or hospital-based outpatient pharmacy; patient's home or telephone-based service; and Veterans Administration Health Care System.

The categories used to classify articles by type of CPS were as follows: (1) general pharmacotherapeutic monitoring—services that encompassed a broad range of activities based primarily on the needs of an assigned group of patients, with services provided such as patient drug regimen review and recommendation, adverse drug reaction monitoring, drug interaction assessment, formulary compliance, and rounding with physicians; (2) targeted drug program—services that primarily focused on a single drug or class of drugs and may have included predefined guidelines for the provision of alternative therapy or dosing recommendations, such as intravenous to oral switch recommendations for antibiotics; (3) disease management—services primarily directed at patients with a specific disease state or diagnosis, such as an asthma management program; (4) MTM (as stated by authors)—services provided by pharmacists as part of the Medicare Modernization Act; (5) wellness program or immunization service—services

**Table 2. Study Designs Used for Evaluations of Clinical Pharmacy Services**

| Design | Notation | | | | Strengths | Weaknesses |
|---|---|---|---|---|---|---|
| Experimental | | | | | Randomization reduces heterogeneity resulting from selection bias | Randomization may not be feasible; difficult and expensive to accomplish |
| Pretest-posttest | | | | | Repeated measures allows assessment of baseline equivalence of groups | Subject to multiple-group threats to internal validity |
| Intervention | R | O | X | O | | |
| Control | R | O | | O | | |
| Posttest only | | | | | Simplest of all experimental designs; does not use repeated measures; therefore, subject to less bias or measurement error | Subject to multiple-group threats to internal validity |
| Intervention | R | | X | O | | |
| Control | R | | O | | | |
| Quasi-experimental | | | | | More feasible to perform when randomization is not possible | Lacks benefit of random assignment (i.e., baseline group equivalence); may be expensive to accomplish |
| Pretest-posttest | | | | | Repeated measures allows assessment of equivalence of groups at baseline | Subject to multiple-group threats to internal validity |
| Intervention | N | O | X | O | | |
| Control | N | O | | O | | |
| Pre-experimental | | | | | May help in generating hypotheses | Cause and effect between the intervention and outcome cannot be established |
| Static group comparison | | | | | | Unable to assess and adjust for baseline differences in groups |
| Intervention | N | | X | O | | |
| Control | N | | | O | | |
| One-group pretest-posttest | | | | | Easy to perform | No comparison group |
| Intervention | O | | X | O | | |

"R" indicates that the groups are randomly assigned; "N" indicates that the groups are nonrandomized (nonequivalent groups); "O" denotes observations or measures (for example, costs and clinical measures); vertical alignment of "Os" shows that measurements occur at the same time; "X" denotes the intervention (program). When there are two lines, one denotes the intervention group, and the other represents the control group. Time sequence (temporality) of variables is designated by the position of the variable (e.g., "to the left" occur before, "to the right" occur after another variable in the sequence).

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focused on promotion or maintenance of good health rather than correction of poor health; (6) pharmacokinetic monitoring—services that primarily involved evaluation of anticipated or actual serum drug concentrations and provision of subsequent dosing recommendations; (7) health screening or laboratory testing service—services that offered routine screening for health issues such as hypercholesterolemia, blood pressure, or osteoporosis; and (8) patient education program or cognitive service—services that primarily instructed patients on the proper administration of drugs and/or identified drug-related problems. Services were also rated as either single level (i.e., one size fits all) or multilevel (i.e., customizable and needs-based) based on whether programs were structured to offer tailored services based on a patient's needs.

In addition to the type of CPS, information on specific aspects of the CPS was collected, including pharmacist work activities and characteristics of the pharmacist's work environment (i.e., level of autonomy, level of access to clinical data, and level of pharmacist training). For classification of work activities, the pharmacist practice activity scheme developed by the American Pharmacists Association was used to determine which of four activity categories were provided ([1] ensuring appropriate therapy and outcomes, [2] dispensing medications and devices, [3] health promotion and disease prevention, and [4] health systems management).[22] Level of autonomy was rated as low, medium, or high based on the need for oversight from another provider (e.g., [low] other providers had full control, and all pharmacist interventions required approval by a prescribing clinician before implementation; [high] pharmacists were able to intervene freely—collaborative practice agreements were in place). Level of access to clinical data was rated as low, medium, or high based on the number of clinical information sources available to the pharmacist (e.g., [low] pharmacists had access to information collected from a single source at the time of patient visit, or available from a medication profile; [high] pharmacists had access to information collected at the time of patient encounter or available from a medication profile in addition to a broad range of clinical data from multiple other sources [e.g., medical records, computerized clinical information systems]). Training or qualifications of pharmacists involved in the provision of services were classified as program-specific training, Pharm.D. degree, residency training, postgraduate training, board certification, work experience, or some combination of these qualifications.

Descriptive statistics were used to profile and characterize the articles within each data field abstracted by the reviewers. Study results were carefully scrutinized by the reviewers. Benefit-to-cost ratios (financial benefit per dollar invested to provide the service) were pooled from applicable articles to calculate an overall mean value. When the benefit-to-cost ratio was not provided but enough information was provided in the article for the reviewers to calculate a ratio, the reviewers did so. The benefit-to-cost ratio was calculated by dividing the reported total costs to provide the CPS by the reported gross economic benefit derived from the service for the same period.

### Study Quality Assessment

The quality of the economic methods used in each study included in this systematic review was assessed. Although several published approaches for assessment of study quality are available, none was designed specifically for economic evaluations of health care services.[21, 23, 24] Therefore, a new measure was developed using the relevant components from multiple sources,[21, 24] with the major intent of providing a statistic by which individuals could quickly determine the relative methodological rigor of the economic components of the study. A three-question assessment tool (see Table 3) was used during the abstraction process to rate the quality of each article as being of "good quality," "fair quality," or "poor quality" with respect to its economic methods. Studies that met all three criteria were rated as "good quality" studies. Studies that did not have a comparator or had multiple or fatal flaws received a "poor quality" rating. All other studies were rated as "fair quality." This rating relates only to the evaluation and description of economic outcomes. For example, a study that was well designed to evaluate clinical outcomes, such as a randomized controlled trial, that described the expense associated with offering the service but did not the evaluate economic benefits associated with the service would receive a rating of "fair quality."

## Results

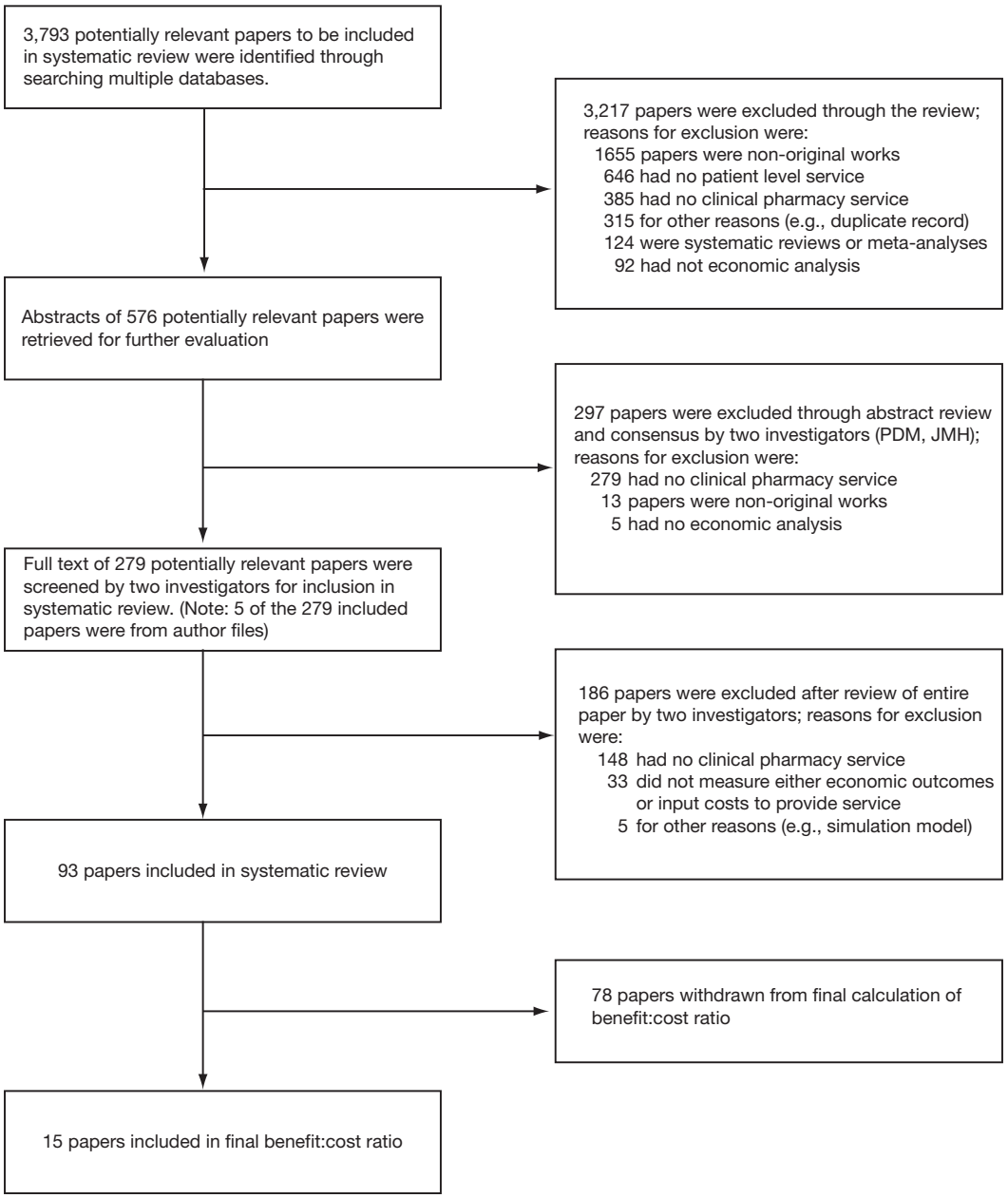
Figure 1 demonstrates the systematic process the authors used to identify, screen, and review

**Table 3. Quality Criteria Used to Examine Methodological Rigor of Studies Examining Economic Outcomes of Clinical Pharmacy Services**

| Item | Weight | Quality Score Calculation (start with a score of 2) |
|---|---|---|
| Comparator group used | | |
| -Concurrent or historical | 2 | Subtract 2 points if no comparator is used |
| Program costs evaluated and described | | |
| -Monetary or other (e.g., time requirements) | 1 | Subtract 1 point if costs are not described |
| Outcomes evaluated and described | | |
| -Economic or other (e.g., clinical outcomes) | 1 | Subtract 1 point if economic outcomes are not described |

Quality scores: A score of 2 represents "good quality," a score of 1 represents "fair quality," and a score of less than 1 represents "poor quality." Example: A nonrandomized trial using a historical comparator (pre-implementation period compared with post-implementation period at a single site) that describes institutional cost savings (economic outcome in monetary terms) but does not address program inputs (no description of pharmacist time/salary, equipment or software expense, etc.) would receive a score of 1 or "fair quality"; *calculation:* 2 (base value) – 0 (comparator present) – 1 (no description of costs) – 0 (description of economic outcomes present) = 1 (fair).

**Figure 1.** Literature search method and screening results.



the papers identified in the initial database search, including reasons for paper exclusion at each step. Almost 4000 papers were initially identified. After application of inclusion and exclusion criteria, 93 articles were considered in the final analysis.[25–117] Appendix 1 describes this final set of 93 studies, which were categorized by setting of CPS and then subcategorized by type of service or intervention. Each study is summarized with information describing the study objectives, study design (including the perspective), method of economic analysis, economic inputs (i.e., costs necessary to provide the service), economic outcomes (i.e., financial benefits of the service), sample size and study duration, results of the analysis, and year in which the costs or economic benefits were valued (currency year), which may have been different from the year of publication.

Studies were published in 43 different journals. Pharmacy journals published 68 (73.1%) of the 93 studies. The most common journal was the *American Journal of Health-System Pharmacy* (n=13 studies [14%]). Studies from the journals *Pharmacotherapy*, *The Journal of Managed Care Pharmacy*, and the *International Journal of Pharmacy Practice* were also common (10 [10.8%] of 93 studies, 7 [7.5%] of 93 studies, and 6 [6.5%] of 93 studies, respectively). Twenty-five studies (26.9%) were published in nonpharmacy journals. Just more than one-half of the studies (52 [55.9%] of 93 studies) were conducted in the United States, and other studies were conducted in Europe (19 [20.4%] of 93 studies), Australia (10 [10.8%] of 93 studies), Canada (8 [8.6%] of 93 studies), and Asia (3 [3.2%] of 93 studies); one study was conducted in Brazil. More studies were published in 2001 (25 [26.9%] of 93 studies) than in any other year, followed by 2003 (23 [24.7%] of 93 studies) and 2004 (18 [19.4%] of 93 studies).

Evaluations fell into 8 broad setting categories and 15 subcategories. Table 4 summarizes the broad settings of the studies included in this evaluation, and additional detail is provided in Appendix 1. Most studies (76 [81.7%] of 93) were performed in hospitals, ambulatory care clinics or physician's offices, or community pharmacies. Other settings (17 [18.3%] of 93) where CPSs were studied included long-term care, rehabilitation, or other residential facilities; clinic- or hospital-based outpatient pharmacies; telephone-based services; and patients' homes.

Table 5 shows a breakdown of CPS types across all studies. The most common type of service evaluated was general pharmacotherapeutic monitoring, followed by target drug programs and then by disease state management

**Table 4. Setting of Economic Evaluations of Clinical Pharmacy Services**

| Setting | No. of Studies (%) |
|---|---|
| Hospital | 40 (43.0) |
| Ambulatory care clinic or physician's office | 20 (21.5) |
| Community pharmacy | 16 (17.2) |
| Long-term care, rehabilitation, or residential facility | 6 (6.5) |
| Clinic or hospital-based outpatient pharmacy | 4 (4.3) |
| Patient's home or telephone-based service | 3 (3.2) |
| Various settings or setting unspecified | 3 (3.2) |
| Veterans Administration Health Care System | 1 (1.1) |

**Table 5. Types of Clinical Pharmacy Services or Interventions Studied**

| Type of Service or Intervention (n=93) | No. of Studies (%) |
|---|---|
| General pharmacotherapeutic monitoring | 32 (34.4) |
| Target drug program | 27 (29.0) |
| Disease state management | 21 (22.6) |
| Medication therapy management (as stated by authors) | 3 (3.2) |
| Wellness program or immunization service | 2 (2.2) |
| Pharmacokinetic monitoring | 1 (1.1) |
| Health screening or laboratory testing service | 1 (1.1) |
| Other | 6 (6.5) |
| Patient education program or cognitive service | 0 (0) |

Includes academic detailing/physician profiling service, dose optimization service, drug reconciliation service, and various other services.

services. The top three categories accounted for 80 (86%) of 93 studies. Medication therapy management and wellness or immunization programs were evaluated in 3 (3.2%) of 93 studies and 2 (2.2%) of 93 studies, respectively. Pharmacokinetic monitoring and health screening or laboratory testing services were evaluated in one study (1.1%) each. The services studied were rated as single level (one size fits all) or multilevel (customizable, needs-based approach) by the reviewers in 44 (47.3%) of 93 studies and 38 (40.9%) of 93 studies, respectively (service level was unknown in 11 [11.8%] of 93 studies). Regarding practice activities, pharmacists were most commonly involved in activities that aimed to ensure appropriate therapy and outcomes (84 [90.3%] of 93 studies) and manage medication use within health systems (40 [43%] of 93 studies). Dispensing activities (14 [15.1%] of 93 studies) and health promotion and disease prevention activities (5 [5.4%] of 93 studies) were much less commonly studied.

For each study, the authors evaluated the level of pharmacist autonomy, access to clinical data, and pharmacist training. The level of pharmacist autonomy was rated as low in 41 (44.1%) of 93 studies, medium in 29 (31.2%) of 93 studies, and high in 7 (7.5%) of 93 studies. The authors were unable to evaluate the level of pharmacist autonomy in 16 (17.2%) of 93 studies. Level of access by the pharmacists to clinical data was rated as low in 17 (18.3%) of 93 studies, medium in 26 (28%) of 93 studies, and high in 23 (24.7%) of 93 studies. No detail was provided on level of access to clinical data in 27 (29%) of 93 studies. For level of pharmacist training, program-specific training was provided in 16 (17.2%) of 93 studies, pharmacist work experience was noted in 6 (6.5%) of 93 studies, residency training was noted in 3 (3.2%) of 93 studies, and board certification was noted in only 1 (1.1%) of 93 studies. Four (4.3%) of 93 studies noted some combination of the Doctor of Pharmacy degree, work experience, board certification, and program-specific training as the pharmacist training qualifications. A description of pharmacist training was not provided in 63 (67.7%) of 93 studies.

The perspective of each study was also assessed and is provided in Appendix 1. Economic evaluations typically take one of several possible perspectives, which may include the patient, provider, payer, or societal perspective. The most common perspective in the studies reviewed was that of the provider (54 [58.1%] of 93 studies); the payer perspective was used in 22 (23.7%) of 93 studies. Multiple perspectives were used in only 9 (9.7%) of 93 studies, and perspective was not specified or was unable to be determined by the reviewers in 4 (4.3%) of 93 studies.

The evaluated studies used a variety of economic methods. Formal, complete economic evaluations were conducted in 45 (48.4%) of 93 studies. These included seven cost-minimization analyses (7.5% of studies), 18 cost-benefit analyses (19.6% of studies), 7 cost-effectiveness analyses (7.5% of studies), and 13 cost-and-outcome analyses with insufficient detail to calculate an economic ratio (14% of studies). A positive economic benefit associated with CPSs was noted in 69% (31 of 45 studies) of full economic analyses. Fourteen (15.1%) of 93 studies were classified as outcome analyses. Thirty-four (36.6%) of 93 studies were purely descriptive. Eleven (11.8%) of 93 studies included descriptions of both cost and outcome, whereas 23 (24.7%) of 93 studies focused exclusively on a description of outcomes associated with a CPS. Input costs, or the costs associated with actually conducting the CPS, were measured in only 56 (60.2%) of 93 studies.

Thirty (32.2%) of 93 studies used noncomparative designs, simply describing the observed outcomes associated with implementing a CPS. A static group comparison was used in 10 (10.8%) of 93 studies, and a before-after design was used in 23 (24.7%) of 93 studies. Twelve (12.9%) of 93 studies used a quasi-experimental design, and 18 (19.4%) of 93 studies used the most rigorous design, the randomized experimental design. Statistical analysis was conducted in a majority of the studies (58 [62.4%] of 93 studies), whereas in the remaining studies, this was either not performed or not described.

In just more than one-half of the studies evaluated, a single experimental site was involved in the analysis (49 [52.7%] of 93 studies). Multiple sites were involved in 42 (45.2%) of 93 studies, but the number of sites involved was not specified in 2 (2.2%) of 93 studies. The median sample size across all studies evaluated was 199 subjects. Four (4.3%) of 93 studies enrolled less than 50 subjects, 35 (37.6%) of 93 studies enrolled between 50 and 199 subjects, 12 (12.9%) of 93 studies enrolled between 200 and

499 subjects, 11 (11.8%) of 93 studies enrolled between 500 and 999 subjects, and 16 (17.2%) of 93 studies included more than 1000 subjects. In 15 (16.1%) of 93 studies, the number of subjects enrolled was not specified. The mean study duration was 15.8 months (± SD of 21.5 months), and the median study duration was 12 months.

## Discussion

Based on the evidence examined in this systematic review, CPSs continue to be economically viable. The number of articles published per year has increased since the first in this series of reviews, from 13.0 ± 5.4 in the first two reviews (1988–2000) to 18.6 ± 5.3 in the current review (2001–2005) (p=0.034). The proportion of papers describing a higher quality of study design and reporting has continued to increase. During the current review period, 26.9% (n=25) of studies included a comparator group and described both costs and economic outcomes, compared with 18.3% in the 1988–1995 review and 23.7% in the 1996–2000 review. Of these 25 studies in the current review, 17 evaluated a concurrent comparator group and 8 evaluated a historical comparator. Of the remaining studies, 22.1% (n=15 of 68) included a comparator group, and 42.6% (n=29) evaluated the cost of establishing and/or providing a service compared with 58.6% and 67.8%, respectively, in the 1988–1995 review and 31.7% and 47.4% in the 1996–2000 review.

### Study Design and Rigor

Ten papers (10.8% of all included studies) used prospective experimental designs with recommended methods for collecting and reporting economic information (see Tables 1 and 2).[25–34] One additional manuscript used a quasi-experimental design and good pharmacoeconomic methods.[37] The number and proportion of studies using strong methods in the current review is consistent with other recent systematic reviews of clinical interventions.[118–120] Twenty-five (27%) of the 93 articles were of good quality, 15 (16%) of 93 were of fair quality, and 53 (57%) of 93 were of poor quality in terms of the economic analysis conducted. Although the quality of study design and reporting is improving, the high proportion of studies that use less rigorous methods or do not report program costs suggests that improvement is still needed in the methods used to examine the economic impact of CPSs.

The authors strongly encourage investigators conducting future studies involving economic evaluations to use an experimental design when feasible and to conduct full economic analyses using the best costing methods available. When developing the economic portion, the authors strongly recommend following guidelines available for the design and reporting of economic evaluations.[121]

Important modifications can be made to the study design that can have a significant effect on the credibility of an economic evaluation of pharmacy services' conclusions. Calculation of sample size and enrollment of sufficient study subjects, inclusion of a concurrent control group (with randomization whenever possible), and use of best possible methods for estimation of all costs and consequences (including start-up and ongoing program costs) are examples of critical methodologies for improving internal validity. When randomization is not possible, quasi-experimental methods can often be used to improve the utility of the study's findings. For example, the choice of control patients requires thoughtful consideration, especially if the intervention is a referral service. When important differences exist between control and intervention subjects, statistical adjustment of baseline factors may improve the plausibility of any effects seen in the intervention group. Matching intervention and control patients on important potential confounding factors (instead of statistically adjusting for differences) may further improve the study's credibility. Additional measures to enhance internal and external validity have been previously presented.[19] Increasing the availability of funding and developing training programs for researchers interested in conducting this challenging type of research could also dramatically improve the quality and quantity of publications.[122, 123]

### Study Setting and Publication

Reporting of studies measuring the value of clinical services provided in the outpatient arena was similar to the last evaluation period (1996–2000). In this review, one-half of studies examined the economic impact of services in the outpatient setting. In 2006, the Medicare Modernization Act expanded the roles of pharmacists as health care providers in the community and other settings by legislating and

facilitating the development of MTM programs for eligible patients. In the current analysis, only two studies were found that directly addressed the economic impact of MTM. This is unfortunate, because various groups, including the Center for Medicare and Medicaid Services and the Pharmacy Quality Alliance, are currently struggling with ways to assess these programs. As methods of evaluating both the clinical and economic impact of MTM programs are developed and the results of clinical trials now under way are made available, it is expected that several studies will focus on this increasingly important area of pharmacy practice by the time of the next review.

A large proportion of the reviewed studies 60.2% (n=56 of 93) assessed broad-based CPSs, rather than services that focus on interventions related to a specific medication, class of medications, or clinical service. With the implementation of interdisciplinary clinics and MTM services, pharmacists' roles will continue to expand, and pharmacists will assume greater responsibility for patient care in the outpatient setting. Therefore, studies that examine broad-based pharmacist services in the ambulatory setting are expected to be published often in the future.

Interest in the economic evaluation of CPSs is growing substantially outside the United States. Studies conducted abroad have increased both in the number of articles published and the number of countries in which the studies were conducted. The *International Journal of Pharmacy Practice* published six articles that were included in this analysis, making it the fourth most-commonly included journal.

Pharmacist investigators have also been successful in publishing the results of their research in nonpharmacy journals. More than one-quarter of studies evaluated (n=25) were published outside the pharmacy literature, compared with 20% in the previous review.[19] This change illustrates both the increase in the quality of these studies and the increasing interest shown by other disciplines in expanding the role of CPSs.

## Context and Application of These Data

Benefit-to-cost ratios were pooled from applicable articles and summarized as overall mean and median values (Table 6). Pooled estimates of the median benefit-to-cost ratio increased (see Table 7) compared with the two previous study periods. Despite increases in pharmacists' salaries, the rising cost of fringe benefits (particularly health care insurance premiums), and the increasing complexity of the services provided, CPSs appear to continue to provide a positive return on investment.

Although the benefits associated with interventions in the inpatient setting may have substantial cost implications, they will necessarily be realized in a relatively short time (i.e., during the hospital admission). As more services are implemented in the ambulatory

**Table 6. Benefit-to-Cost Ratios from Selected Studies**

| Setting | Type of Service | Currency (Year) | Benefit:Cost Ratio |
|---|---|---|---|
| Ambulatory care clinic[40] | General pharmacotherapeutic monitoring | U.S. Dollar (2002) | 2.89[a] |
| Ambulatory care clinic[36] | Target drug program | British Pound (2001) | 1.02[a] |
| Community pharmacy[39] | Disease state management services | U.S. Dollar (2003) | 1.17[a] |
| Community pharmacy[35] | Disease state management services | Canadian Dollar (1998) | 9.47 |
| Community pharmacy[38] | Other, dose optimization service | British Pound (2004) | 7.67[a] |
| Facility (unspecified) [116] | General pharmacotherapeutic monitoring | U.S. Dollar (2002) | 2.05 |
| Hospital[46] | Disease state management services | U.S. Dollar (2002) | 4.81[a] |
| Hospital[53] | General pharmacotherapeutic monitoring | Malaysia RM (2001) | 7.28[a] |
| Hospital[43] | General pharmacotherapeutic monitoring | Australian Dollar (1998) | 22.99[a] |
| Hospital[51] | General pharmacotherapeutic monitoring | Euro (2000) | 34.61[a] |
| Hospital[48] | Other, various services | U.S. Dollar (2000) | 3.09 |
| Hospital[50] | Pharmacokinetic monitoring | U.S. Dollar (1999) | 4.89[a] |
| Hospital[41] | Target drug program | U.S. Dollar (2001) | 4.65[a] |
| Long-term care facility[30] | General pharmacotherapeutic monitoring | Australian Dollar (1999) | 1.33[a] |
| Long-term care facility[42] | General pharmacotherapeutic monitoring | U.S. Dollar (2002) | 11.78 |
| | | **Median (mean)** | **4.81 (7.98)** |

Values indicate benefit per unit of cost (i.e., "2.89" signifies "2.89:1").
[a]Benefit-to-cost ratios calculated by reviewers.

**Table 7. Benefit-to-Cost Ratios of Published Economic Evaluations of Clinical Pharmacy Services from Three Periods[a, b]**

| Statistic | 1988–1995 | 1996–2000 | 2001–2005 |
|---|---|---|---|
| n | 7 | 16 | 15 |
| Minimum | 1.1 | 1.7 | 1.0 |
| Maximum | 75.8 | 17.0 | 34.6 |
| Median | 4.1 | 4.7 | 4.8 |
| Mean | 16.7 | 5.5 | 8.0 |

Pooled benefit-to-cost ratios calculated by author(s) or reviewers.
[a]Values indicate benefit per unit of cost (i.e., "16.7" signifies "16.7:1").

setting, it will become increasingly important to consider the long-term consequences of various interventions. The median benefit-to-cost ratio was 2.89 in ambulatory settings (ambulatory clinics and community pharmacies) and 4.89 in hospital settings. As long-term benefits accrue and are evaluated after a clinical pharmacy intervention in the outpatient setting, it is reasonable to expect benefit-to-cost ratios to continue to improve.

Pharmacy leaders and clinicians will certainly not be surprised by these findings. During the past two decades, the role of the clinical pharmacist in many settings has expanded dramatically, yet justifying the investment in new pharmacy resources has also become increasingly challenging. It is critical that these data be communicated to the health care administrators responsible for allocating resources within the health care system. The findings described in this article should form the foundation for proposals for new services. Health care administrators often require estimates of potential return on investment in proposals for new services, and these data provide such information. Sufficient detail is provided to frame proposals in the context of the specific type of service provided and in the setting the proposed service is to be delivered. With care, these data can also be extrapolated to project the value of similar CPSs. For example, data from a study evaluating an anti-infective stewardship program in adult patients can be generalized to forecast the savings associated with a similar program provided in pediatrics.

It will be more challenging to use these data to justify novel CPSs such as granting pharmacists independent prescribing authority. As new, progressive clinical services are developed, measurement of the value of those investments will be necessary. In all cases, investigators should continue to improve the rigor of the study design and economic methods used in economic evaluations of CPSs.

## Limitations

This review had several important limitations that must be considered when interpreting the results. The primary search strategy used included papers referenced in MEDLINE and International Pharmaceutical Abstracts. To minimize the likelihood of missing relevant papers, bibliographies of identified manuscripts were searched. However, it is possible that not all of the relevant literature was captured by this strategy. No attempt was made to identify unpublished work. Therefore, this analysis may be subject to publication bias.

Unfortunately, many of the reviewed articles lacked data important to the analysis and were therefore either excluded from the analysis or included with only the information reported. No attempt to contact authors to obtain additional unreported data was made. This may result in a reporting bias if study results were different for studies in which economic outcomes were reported compared with studies in which they were not.

A final limitation was that the pooled benefit-to-cost ratio was derived from studies with various patient populations, practice settings, types of clinical services evaluated, and study designs. Many of the studies used to derive this ratio were not truly experimental in terms of study design, but instead were quasi-experimental or pre-experimental designs. The heterogeneity of these studies reduces the reliability of these pooled estimates, as does the pooled value not being weighted by the number of subjects in the study or any other factor.

## Conclusion

In general, positive returns continue to be realized from investments in CPSs. Despite recent, rapid increases in pharmacist salaries, the accompanying rapid increase in pharmaceutical and general health care expenditures allows maintained economic viability of CPSs. The scope of the practice of pharmacy continues to grow and diversify, as does the expertise of pharmacists. While this happens, the core responsibility of a pharmacist remains the same. The pharmacist's key function is pharmaceutical stewardship, ensuring that rational and effective use of medication therapy is provided to patients. Economic benefits associated with implementation of CPSs can be due to various sources, from direct medication expenditures to nonpharmaceutical health care costs.

Economic evaluations of CPSs in general, but especially in the outpatient setting, are becoming more common. This trend can be expected to continue as rising pharmaceutical expenses gain increased public awareness, as reports on recently implemented MTM services are published, and as pharmacists move into the management of high-cost injectable medications in outpatient clinics. The outpatient and clinic venues provide pharmacists the opportunity to have a significant effect on clinical outcomes and health care expenditures because pharmacist interventions are expected to have a long-term influence on or affect complex and expensive medication therapies. A recent white paper commissioned by the ACCP described the development process for business-practice models in the ambulatory setting, and regardless of the intent to publish the results, the white paper emphasized the need for an assessment of economic outcomes of services in addition to clinical and humanistic outcomes. Harris et al. suggested that "documentation of ... the economic value of [clinical pharmacy interventions] is absolutely vital" for ensuring the sustainability of a CPS.[124]

Despite increases in the volume of reports on the economic evaluation of CPSs, continued improvement in the breadth and quality of examinations is needed. Many of the articles examined in the current review were conducted to explore the clinical effects caused by implementation of these services and merely reported on the cost of the service or an economic outcome due to the service. A quality economic analysis of CPSs is necessary to ensure that health care administrators and payers understand the savings or benefits that can be achieved through the implementation of these services. Relatively minor changes in study design, such as adding a concurrent or historical comparator and ensuring that expenses and cost savings are both captured, will improve study rigor and may significantly improve the ability of other pharmacists to implement similar services in other health care venues.

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**Appendix 1. Ninety-three Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| AMBULATORY CARE CLINIC | | | |
| **Disease state management services** | | | |
| To compare clinical, economic, and humanistic outcomes of a pharmacist-managed hypertension clinic with physician-managed clinics[28] | Randomized experiment, concurrent control (group received usual [physician managed] care); Payer and provider perspectives | CEA | Total program costs (per visit) |
| To compare clinical outcomes of a hypertension management program by primary care physicians and clinical pharmacists vs. usual care[34] | Randomized experiment, concurrent control (group received standard care); Provider perspective | COA | Ongoing costs only, wages |
| To compare a pharmacist-managed anemia program in an outpatient hemodialysis clinic with U.S. averages[52] | Static group comparison, historical control (U.S. average); Provider perspective | OA | No input or ongoing costs measured |
| To describe the quality and costs associated with anticoagulation clinic services[47] | Noncomparative study; Provider perspective | COD | Ongoing costs only, wages, equipment (laboratory costs), overhead (space) |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate clinical and economic outcomes of pharmacotherapy consultation in patients receiving polypharmacy[115] | Randomized experiment, concurrent control (group received no intervention); Payer perspective | OA | No input or ongoing costs measured |
| To evaluate clinical and economic outcomes of pharmacist medication reviews in general practice of elderly patients[29] | Randomized experiment, concurrent control; Payer and provider perspective | COA | Ongoing costs only, wages |
| To evaluate the effect of pharmacist intervention in polypharmacy managed care patients in the area of drug safety[40] | Before-after study; Provider perspective | CBA | Ongoing costs only, wages, equipment (basic supplies) |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (total, pharmaceutical); number of medical encounters (emergency visits) | 330 patients (166 in control group) from one site [6-month study] | Total costs were nonsignificantly different between pharmacist group and physician group ($242 vs. $233 per patient), but cost-effectiveness ratios for systolic and diastolic blood pressure were lower in the pharmacist group, $1.18 and $2.51 per mm Hg. | 1999 |
| Direct medical costs (total) | 197 patients (99 in control group) from two sites [12-month study] | The average provider visit costs per patient were significantly higher in the usual care group than in the physician-pharmacist comanagement group, $195 and $160, respectively, during 12 months. | 2001 |
| Direct medical costs (pharmaceutical) | 278 patients from one site [5-month study] | The reduced epoetin doses used in the program resulted in an annual cost avoidance of $3000 per patient. | 2003 |
| Quality-based assessment (percentage of days with therapeutic international normalized ratio) | 600 patients from three sites [10.5-month (average) follow-up] | The mean annual per patient cost of warfarin monitoring was $288, $339, and $216 for sites A, B, and C, respectively. | 2003 |
| Direct medical costs (total, pharmaceutical); quality-based assessment (adverse drug events, patient and physician satisfaction) | 268 patients (144 in control group) from 19 sites [6-month study, with 6-month follow-up] | No significant differences were demonstrated in the changes or drug costs between the consult and control groups, during 6 months' time. | 2000 |
| Direct medical costs (pharmaceutical); number of interventions (medication changes); drug use (repeat medication); quality-based assessment (number of patients receiving a medication review, acceptance rate) | 1131 patients (550 in control group) from four sites [12-month study] | Cost savings in intervention group compared with control group were GBP4.75 per 28-day supply. Annual savings on net ingredient costs were GBP62 in the intervention group, and after accounting for pharmacist time, a net cost savings per patient per year was GBP54. | 1999 |
| Direct medical costs (total); drug use (number of prescriptions); quality-based assessment (rate of polypharmacy events) | 195,971 patients from 25 sites [2-year study, with 6-month follow-up] | Prescription costs per member per month were reduced by 49.1%, and the overall institution drug costs were reduced by $4.8 million. Similar effects were seen after the second intervention, having a combined net benefit of $4.5 million. [2.9:1 benefit:cost ratio[a]] | 2002 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Methoda | Input Costs |
|---|---|---|---|
| **General pharmacotherapeutic monitoring, MTM-like service** | | | |
| To measure the impact of a community-based geriatric pharmaceutical care model on drug-related issues[45] | Randomized experiment, concurrent control (usual care); Payer perspective | OA | Ongoing costs only (unspecified) |
| **Medication therapy management service (as stated by authors)** | | | |
| To assess economic outcomes of a pharmaceutical care program targeting patients with heart and lung diseases[44] | Quasi-experimental (randomized patients in selected pharmacies), concurrent control; Payer perspective | OA | No input or ongoing costs measured |
| **Other, academic detailing, and physician profiling service** | | | |
| To measure economic outcomes of a Pharmacist Review to Increase Cost-Effectiveness Clinic[49] | Before-after study; Provider perspective | CBA | Ongoing costs only, personnel time |
| To measure economic outcomes of pharmacist interventions in a primary care setting operating under a financial risk contract with a health plan[70] | Before-after study, historical control (before pharmacist intervention period, compared 1998 with 1999; intervention began in 1999); Provider perspective | OD | No input or ongoing costs measured |
| **Target drug program** | | | |
| To identify inappropriate diuretic prescribing and to describe protocol implementation[36] | Before-after study; Provider perspective | CBA | Initial and ongoing costs, wages, equipment (laboratory costs) |
| To determine clinical and economic outcomes in an anticoagulation center among patients with atrial fibrillation[54] | Noncomparative study (single-group design); Payer perspective | COD | Ongoing costs only, personnel time, equipment (laboratory and drug costs) |
| To evaluate clinical and economic outcomes of a perioperative bridge program[66] | Noncomparative study; Payer perspective | OD | No input or ongoing costs measured |
| To describe clinical and economic outcomes of a pharmacist-directed statin conversion project[56] | Noncomparative study; Payer perspective | OD | No input or ongoing costs measured |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (pharmaceutical); drug use (number of prescriptions); quality-based assessment (adverse drug events, medication adherence, patient's drug therapy knowledge, physician satisfaction) | 135 patients (66 in control group) from one site [24-month study] | The annual prescription drug costs for the test group at baseline were CAD881 and CAD809 at follow-up. The annual prescription drug costs for the control group at baseline were CAD944 and CAD874 at follow-up. The differences were not significant. | 1999 |
| Direct medical costs (inpatient and outpatient pharmacy charges); number of medical encounters (outpatient visits) | 1070 patients (444 in control group) from 149 sites [1-year study, with 2-year follow-up] | There was no significant difference between the two groups in the change in total number of clinic visits or total costs. | 1997 |
| Indirect costs (out-of-pocket payments by patient); drug use (number of prescriptions) | 520 patients from five sites [1-year study] | Out-of-pocket expenditures decreased 68%, from $185 to $60 per patient per month. | 2005 |
| Direct medical costs (pharmaceutical) | 23,317 patients from 24 sites [2-year study, with 1-year follow-up] | Per member per year expenditures . for drugs increased 31.2% nationally for all health plan types; the intervention group limited drug expenditures to 1.7%. The average cost per prescription claim increased by 31.2% nationally but decreased by 2.1% in intervention group | 2002 |
| Direct medical costs (pharmaceutical); quality-based assessment (adverse drug events) | 61 patients from two sites [12-month study, with 12-month follow-up] | There was a significant reduction in cost of diuretic prescriptions for reviewed patients of GBP1220. The cost per potential hyperkalemia case prevented, including protocol development, was GBP345. [1:1 benefit:cost ratiob] | 2001 |
| No economic outcome | 97 patients from nine sites [12-month study] | Medication, monitoring, and laboratory costs were $51 per patient per month. | 2002 |
| Mortality; direct medical costs (hospital) | 84 patients from one site [51-month study] | Cost savings produced were $212,475 per year in a health maintenance organization. | 1996 |
| Direct medical costs (expenditures); out-of-pocket payments by patient | 5046 patients from 16 sites [6-month study] | The annual cost savings was $4.14 per member per year. Patient savings in reduced copayments changed significantly to $145 per patient. | 2001 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| CLINIC OR HOSPITAL-BASED OUTPATIENT PHARMACY | | | |
| **Disease state management services** | | | |
| To assess the economic and humanistic outcomes of clinical pharmacist interventions for patients with asthma[57] | Before-after study (baseline controlled); Provider perspective | COD | No input or ongoing costs measured |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate the impact of a pharmacist consult of elderly outpatients based on the Health Belief Model[63] | Randomized experiment, concurrent control (randomization by Zelen's design); Provider perspective | OA | No input or ongoing costs measured |
| **Health Screening/Laboratory Testing service** | | | |
| To describe the cost savings of a pharmacy Chlamydia trachomatis detection program[69] | Noncomparative study; Payer perspective | CEA | Equipment (basic supplies) |
| **Target drug program** | | | |
| To assess the lipid-lowering efficacy, safety, and costs of a large-scale statin formulary conversion program[67] | Before-after study (single-group design); Payer perspective | COD | Ongoing costs only, wages, equipment (laboratory and drug costs), cost of adverse drug events |
| COMMUNITY PHARMACY | | | |
| **Disease state management services** | | | |
| To assess clinical and economic outcomes of a community pharmacist intervention program to improve cholesterol risk management[65] | Randomized experiment, concurrent control (group received usual pharmacy care); Payer and provider perspectives | COA | Initial and ongoing costs, wages, equipment |
| To evaluate economic and humanistic outcomes with skin condition advice of community pharmacists[64] | Noncomparative study; Payer and patient perspective | COD | Ongoing costs only, personnel time |
| To compare clinical, humanistic, and economic outcomes in asthma patients who received enhanced pharmaceutical care vs. usual care[27] | Randomized experiment (pharmacy as unit of randomization), concurrent control; Payer perspective | CMA | Ongoing costs only, fees paid |
| To describe the clinical and economic outcomes of a hypertension management program[35] | Quasi-experimental, contemporaneous control (group of patients in pharmacies where no intervention was provided); Societal perspective | CBA | Initial and ongoing costs, wages, equipment (computer + software), overhead (travel) |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (total); patient knowledge about asthma | 55 patients from one site [3-month study, with 3-month follow-up] | Total costs per patient were significantly reduced from TWD2880 to TWD1683 after 3 months. | 2002 |
| Drug use (number of prescriptions); cost avoidance; quality-based assessment (adverse drug events, medication adherence) | 126 patients (56 in control group) from one site [2-month study] | After 2 months, there was a cost avoidance of SGD387 and overall cost savings of SGD427, resulting in a net savings of SGD387. | 2002 |
| Direct medical costs (pharmaceutical) | 446 patients from one site [2-year study, with 2-year follow-up] | Net cost per pelvic inflammatory disease prevented ranged from cost savings of up to EUR3740 in a low complication rate/high testing cost situation. | 2002 |
| Direct medical costs (pharmaceutical, laboratory); quality-based assessment (adverse drug events); quality-based assessment (patient and physician satisfaction) | 942 patients from one site [6-week study, with 6-week follow-up] | Conversion of statin resulted in cost savings of $115 per patient treatment year. | 1999 |
| Direct medical costs (total); number of medical encounters (physician visits) | 675 patients (331 in control group) from > 50 sites [16-week study] | Incremental costs to a government payer and community pharmacy manager were CAD6.40 per patient and CAD21.76 per patient, respectively, during 4 months. | 1999 |
| Direct medical costs (total, physician, pharmaceutical); quality-based assessment (patient's drug therapy knowledge, satisfaction) | 181 patients from 126 sites [1-week study] | Total costs for 144 pharmacist consultations were AUD1232 for 1 week, potentially saving the government between AUD3024 and AUD5544 in physician management costs. | 1999 |
| Direct medical costs (pharmaceutical); number of medical encounters (hospitalization, physician visits, emergency visits); indirect costs (days off from school) | 224 patients (226 in control group) from 18 sites [1-year study] | Compared with usual care, the enhanced care group physician office visits, emergency visits, days off from work and school, and overall health costs were decreased by 75%, 75%, 61%, and 57%, respectively. | 2003 |
| Willingness to pay; cost savings | 100 patients (59 in control group), nine pharmacies (four received intervention) [study duration (unspecified, intervention provided in test pharmacies for 9 months)] | Between-group difference in savings was a significant CAD290 per patient in favor of the exposed group during 9 months. Total benefits were CAD295. Cost:benefit ratio (excluding fixed costs) was 1:9.6. | 1998 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| To assess short-term clinical, economic, and humanistic outcomes of pharmaceutical care services for patients with diabetes | Quasi-experimental, external control (control group from future [later in time at second site]); Payer perspective[60] | COA | Ongoing costs only, fees paid |
| To assess the 5-year clinical and economic outcomes of community pharmacy services for patients with diabetes[59] | Before-after study; Payer perspective | OD | No input or ongoing costs measured |
| To evaluate an asthma care model that would answer the societal need for improved asthma management[37] | Quasi-experimental, concurrent control (group of patients in alternative pharmacy who received standard care); Societal perspective | COA | Ongoing costs only, personnel time |
| To evaluate economic outcomes of a self-insured company's cardiovascular wellness program[39] | Noncomparative study (single-group design); Provider perspective | CBA | Ongoing costs only, wages, equipment (basic supplies), overhead (administrative) |
| **General pharmacotherapeutic monitoring** | | | |
| To measure clinical and economic outcomes of a pharmaceutical care program for elderly patients[26] | Randomized experiment of ongoing intervention (pharmacy as unit of randomization), concurrent control (group received standard care); Payer perspective | CMA | Ongoing costs only, personnel time |
| To describe a pharmacist domiciliary visiting program from a health center community pharmacy[58] | Noncomparative study; Provider perspective | COD | No input or ongoing costs measured |
| To describe the findings of an outcomes-based method of pharmacist reimbursement program for cognitive services[62] | Noncomparative study; Payer perspective | COD | Ongoing costs only, fees paid |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Health care use (number of diabetes claims per member per month); quality-based assessment (patient satisfaction) | 85 patients (47 in control group) from 12 sites [21-month study, with 9-month follow-up] | There was a significant increase of $52 per patient per month in diabetes costs for both groups. There was a nonsignificant 29% decrease in nondiabetes costs and 16% decrease in all diagnosis costs. | 2001 |
| Direct medical costs (total) | 194 patients from 12 sites [3.5-year study, with follow-up every 6 months for (average of) 5.8 years] | Mean insurance per patient per year decreased by $2704, $3609, $3908, $5480, and $6502 in the first through fifth follow-up years, respectively. Mean total prescription costs increased significantly by $656, $1487, $1932, $1942, and $2188 per patient per year for the same years. | 2001 |
| Direct medical costs (total, pharmaceutical); willingness to pay; drug use (dose); quality-based assessment (medication adherence, patientís drug therapy knowledge, satisfaction) | 102 patients (48 in control group) from three sites [6-month study, with 6-month follow-up] | Direct cost savings in the intervention group were AUD12.50 per month, and cost savings related to decrease in severity were AUD100,801 per year for the entire group. | 2001 |
| Revenue | 36 patients from one site [1-year study] | For the development and first year of the program, the net benefit to the pharmacy amounted to $2413. [1.1:1 benefit:cost ratio[a]] | 2003 |
| Direct medical costs (hospital, pharmaceutical); number of medical encounters (hospitalizations) | 2454 patients (1164 in control group) from 190 sites [18-month study (with evaluations every 6 months for 18 months)] | Between-group analysis showed no significant differences between the total cost for control and intervention patients in any country; but some countries showed a significant difference between intervention and control patients in relation to individual components. | 1999 |
| No economic outcome; quality-based assessment (patientís drug therapy beliefs and health beliefs) | 100 patients from one site [9-month study] | The estimated costs to the pharmacy were GBP5000 per year, equivalent to 33 working days. | 1999 |
| Direct medical costs (pharmaceutical); drug use (number of prescriptions); number of medical encounters (hospitalizations, emergency visits, physician visits); quality-based assessment (drug-related problems, drug-related problem severity level); cost avoidance | 8335 patients, number of sites (unspecified) [12-month study] | Return on investment was generally above target after implementation of $1 withholding in 2001. Additional physician visits, prescription orders, and emergency visits were avoided by identifying drug-related problems. | 2000 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| To evaluate a patient medication management service and a patient medication concordance service in three health care models[55] | Before-after study; Payer and provider perspective | CMA | Total costs (per year) |
| **General pharmacotherapeutic monitoring, MTM-like service** | | | |
| To measure the outcomes of a pharmaceutical care program provided to elderly patients by community pharmacists[32] | Randomized experiment (pharmacy as unit of randomization), concurrent control; Perspective unspecified | COA | Ongoing costs only, personnel time |
| **Other, dose optimization service** | | | |
| To compare two methods of dose optimization by community pharmacists[38] | Noncomparative study; Provider perspective | CBA | Initial and ongoing costs, wages |
| **Other, various services** | | | |
| To develop a cost analysis of a Wellness program/Immunization service Community Pharmacy Model Practices project[61] | Noncomparative study; Payer and provider perspective | CMA | Initial and ongoing costs, wages, equipment (computer + software), overhead (travel) |
| To assess a smoking cessation program in a community[68] | Noncomparative study (single-group design); Payer perspective | CEA | Ongoing costs only, wages, equipment (basic supplies and drug costs) |
| EMERGENCY DEPARTMENT | | | |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate economic outcomes of an efficient Personal Digital Assistant program that tracks pharmacist interventions[83] | Noncomparative study; Provider perspective | COD | Ongoing costs only, personnel time |
| HOSPITAL | | | |
| **Disease state management services** | | | |
| To examine the impact of immediate concurrent feedback on dose adjustments in patients with renal failure[73] | Static group comparison, historical control (before pharmacist began rounding); Provider perspective | OA | No input or ongoing costs measured |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Drug use (number of prescriptions); number of medical encounters (hospitalizations, physician visits); direct medical costs (pharmaceutical); quality-based assessment (medication management and appropriateness) | 168 patients from nine sites [3-month study] | There was a nonsignificant decrease in monthly medication costs per patient. | 2001 |
| Direct medical costs (pharmaceutical); number of medical encounters (hospitalizations); quality-based assessment (medication adherence, patientís drug therapy knowledge, satisfaction) | 191 patients (81 in control group) from 10 sites (five intervention and five control sites) [18-month study, with 18-month follow-up] | During the first 6 months, the intervention group had nonsignificantly lower mean costs of GBP558 compared with GBP865 in the control group. Mean costs in the second and third assessment periods were nonsignificantly different between the groups. | 1999 |
| Direct medical costs (pharmaceutical) | 207 interventions (60 by pharmacists) from 13 sites [8-month study] | For 8 months, the first phase annualized cost savings were GBP9592, whereas in the second phase, annualized cost savings were GBP23,883. [7.8:1 benefit:cost ratio[a]] | 2004 |
| Direct medical costs (pharmaceutical); health care use | 411 patients from 10 sites [11-month study, with 11-month follow-up] | Cost savings ranged from AUD87 to AUD1444 per patient. Most pharmacies were able to generate potential resource savings greater than total variable cost. | 1997 |
| Quality of life (QALY estimates from literature) | 48 patients from seven sites [12-month study] | The incremental cost of getting an additional patient to quit smoking using the pharmacological alternatives vs. a self-directed quit attempt was $236 for the "cold turkey" method, $936 for nicotine patch, $1232 for nicotine gum, and $1150 for bupropion. | 2000 |
| Direct medical costs (pharmaceutical); number of interventions (type); quality-based assessment (acceptance rate, adverse drug events, drug-related problem severity level); cost avoidance (adverse event costs) | 687 interventions from one site [study duration (unspecified)] | Total cost avoidance was estimated at $192,923 during 5 months. | 1999 |
| Direct medical costs (pharmaceutical); quality-based assessment (adverse drug events) | 1648 patients (70 in control group) from one site [12-month study] | There was a significant difference in the mean cost between standard and adjusted dose of drugs, CHF5.3 in the control group and CHF0.75 in the intervention group. | 1999 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| To evaluate clinical and economic outcomes in a *Helicobacter pylori* patient counseling program[25] | Randomized experiment, concurrent control (group received standard care); Provider perspective | CEA | Ongoing costs only, personnel time |
| To evaluate clinical and economic outcomes of pharmacist involvement on posttraumatic seizure prophylaxis in patients with head injury[71] | Static group comparison, historical control (before pharmacist joined health care team); Provider perspective | OA | Ongoing costs only, equipment (drug and laboratory costs) |
| To evaluate clinical and economic outcomes of a pharmacist-initiated intervention in a pediatric mental health setting[87] | Quasi-experimental, historical control (cost of care 12-months before pharmacist intervention period); Provider perspective | COA | Ongoing costs only, personnel time |
| To describe the role of a pharmacist on a medical telemetry unit in optimizing compliance of secondary prophylaxis of coronary artery disease[117] | Randomized experiment, concurrent control (group received usual [physician, nurse, or inpatient pharmacy] care); Perspective unspecified | OA | No input or ongoing costs measured |
| To evaluate economic outcomes of an aggressive hypercholesterolemia treatment program in patients with coronary heart disease[46] | Static group comparison, concurrent control (group received standard care); Provider perspective | CBA | Ongoing costs only, wages, equipment (basic supplies) |
| **General pharmacotherapeutic monitoring** | | | |
| To determine the effects of psychiatric pharmacy services on clinical outcomes of acute-care psychiatric inpatients[72] | Static group comparison, historical control (6 months before pharmacist intervention period); Provider perspective | CEA | Ongoing costs only, wages |
| To evaluate the effect of a discharge pharmacist in the discharge process[78] | Noncomparative study; Provider perspective | OD | No input or ongoing costs measured |
| To evaluate clinical and economic outcomes of a clinical pharmacist in a pediatric intensive care unit[80] | Noncomparative study; Provider perspective | CMA | Ongoing costs only, wages |
| To evaluate the costs and benefits of detecting prescribing errors by the hospital pharmacy staff[51] | Noncomparative study; Provider perspective | CBA | Ongoing costs only, wages |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (pharmaceutical, laboratory); additional course of drug therapy; additional laboratory test (urea breath test) | 76 patients (38 in control group) from one site [6-month study] | About GBP8402 per 100 patients would be spent using a treatment regimen plus counseling, whereas an additional GBP3026 per 100 patients would be spent with same regimen but no counseling. | 2000 |
| Drug concentration (phenytoin); drug use (length of treatment); cost savings | 109 patients (43 in control group) from one site [2-year study] | A cost savings of about $28,000 during 15 months was observed after the clinical pharmacist joined the service. | 2000 |
| Direct medical costs (pharmaceutical); number of interventions (type); quality-based assessment (acceptance rate) | 48 interventions from one site [24-month study, with 12-month follow-up] | There was a significant decrease in medication costs of CAD1.39 per patient-day, but there was a nonsignificant difference in the comparison of the year before and after pharmacist position implementation. | 2001 |
| Direct medical costs (pharmaceutical); drug use (target medications) | 110 patients (56 in control group) from one site [2-week duration] | The mean costs of the usual care group and the pharmacy care group were $107 and $116, respectively, and did not differ significantly. | 2002 |
| Mortality; direct medical costs (pharmaceutical, cost of adverse drug events); number of medical encounters (hospitalizations, physician visits); quality-based assessment (adverse drug events) | 612 patients (303 in control group) from one site [2-year study] | The total cost per patient for use of health care resources was $6497 in the control group and $5103 in the intervention group; the net savings associated with intervention was $1394 per patient during 2 years. [2:1 benefit: cost ratio[a]] | 2002 |
| Direct medical costs (total, hospital, pharmaceutical); length of hospital admission; cost-effectiveness ratio; quality-based assessment (patient satisfaction) | 93 patients (48 in control group) from one site [15-month study] | The cost-effectiveness ratios for the control and intervention groups were $35,536 and $10,596, respectively. The incremental cost per successful outcome was $2484 per 1000 patients. | 1999 |
| Direct medical costs (pharmaceutical); number of interventions (timely prescription transcription); quality-based assessment (patient counseling, physician and nurse satisfaction) | 244 patients from three sites [4-month study] | Discharge pharmacists were responsible for a cost savings of GBP2236 for 4 months. This is projected to save GBP6708 per year for the 36% of patients discharged by a pharmacist in 4 months and GBP20,124 per year if 100% of patients were to receive this service. | 1999 |
| Direct medical costs (pharmaceutical) | 215 patients from one site [24-week study] | The total direct cost savings was $1977 during 24 weeks for 0.73 hour per day in the pediatric intensive care unit, extrapolated to $9135 per year. | 1997 |
| Direct medical costs (pharmaceutical); quality-based assessment (prescribing errors) | 3540 orders (351 with errors) from two sites [1-week study] | During the 1-week study period, pharmacist time costs were EUR285, and estimated benefits were EUR9867. [34:1 benefit:cost ratio[a]] | 2000 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| To evaluate clinical and economic outcomes of pharmacist interventions in patient care in the hospital setting[53] | Noncomparative study; Provider perspective | CBA | Ongoing costs only, wages |
| To evaluate economic outcomes of pharmacist interventions in a hospital setting[43] | Noncomparative study; Provider perspective | CBA | Ongoing costs only, wages |
| To assess the impact of pharmacist interventions on posttake ward rounds[74] | Quasi-experimental, historical control (before pharmacist intervention period); Provider perspective | OA | No input or ongoing costs measured |
| **Other, drug reconciliation service** | | | |
| To assess the impact of medication reconciliation in preventable medication errors[76] | Noncomparative study; Provider perspective | CEA | Ongoing costs only, wages |
| **Other, various services** | | | |
| To assess the clinical and economic outcomes of a clinical staff pharmacist practice model[48] | Noncomparative study; Provider perspective | CBA | Ongoing costs only, wages + benefits, equipment (basic supplies) |
| To evaluate clinical and economic outcomes of pharmacist interventions in a hospital[75] | Noncomparative study; Provider perspective | OD | No input or ongoing costs measured |
| **Pharmacokinetic monitoring** | | | |
| To examine the impact of individualized pharmacokinetic monitoring on the development of aminoglycoside-associated nephrotoxicity[50] | Quasi-experimental (authors state that this is a "retrospective case-control study" using data from a randomized experiment), historical control (group received usual [physician managed] care); Provider perspective | CBA | Ongoing costs only, wages + benefits, equipment (basic supplies) |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (pharmaceutical) | 57 interventions from one site [1-month study] | During 1 month, the total net cost savings was MYR634 per patient. A pharmacist can save MYR507 per working day or MYR11166 per month in the hospital setting. [7.3:1 benefit:cost ratio[a]] | 2001 |
| Direct medical costs (medical procedures, pharmaceutical, laboratory); number of medical encounters (hospitalizations); length of hospital admission | 1399 interventions from eight sites [1-month study] | Cost savings of pharmacist interventions was AUD263,221 during an average of 22 days. The total annualized cost savings was AUD4,447,947, including AUD193,602 of pharmacist salary. [23:1 benefit:cost ratio[a]] | 1998 |
| Direct medical costs (pharmaceutical); quality-based assessment (accuracy of medication history, medication errors) | 103 patients (50 in control group) from one site [3-day follow-up] | Increases in drug costs between admission and discharge in the preintervention and intervention groups were 42% and 20%, respectively. The mean savings per patient per annum in the preintervention and intervention groups were GBP5.5 and GBP88, respectively. | 2003 |
| Number of interventions (type); quality-based assessment (category of potential harm, acceptance rate) | 2046 patients from one site [11-month study] | The estimated cost of potential harm avoided by pharmacists was almost $39,000, based on a cost of $2595 for any adverse drug effect. | 2002 |
| Number of interventions; cost savings; cost avoidance; quality-based assessment (adverse drug events) | 4959 interventions from one site [12-month study] | During 12 months, the cost savings was $92,076, and the cost avoidance was $488,436, for a total of $580,511. The cost to provide the service was $187,852. The net benefit was $392,660, and the benefit:cost ratio was 3.1:1. | 2000 |
| Direct medical costs (pharmaceutical) | 3136 interventions from one site [6-month study (collected pharmacist intervention data for 18 months)] | A total of 3136 interventions were analyzed, and they represented a cost savings of EUR129,058 during 6 months. | 2001 |
| Mortality; direct medical costs (hospital); quality-based assessment (adverse drug events) | 2405 patients (152 in control group) from two sites [study duration (unspecified)] | The total cost difference among patients receiving individualized pharmacokinetic monitoring ($135,635 per 100 patients) vs. those without monitoring ($226,630 per 100 patients) was $90,995 per 100 patients. [4.9:1 benefit:cost ratio[a]] | 1999 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| **Target drug program** | | | |
| To compare the effectiveness of an antimicrobial management team with that of usual care[77] | Static group comparison, concurrent control; Provider perspective | CBA | Ongoing costs only, wages + benefits, fees |
| To evaluate clinical and economic outcomes of a pharmacist-managed anemia program[85] | Before-after study (preintervention group); Provider perspective | COD | Ongoing costs only, personnel time |
| To describe clinical and economic outcomes of a protocol for oral ondansetron for the management of chemotherapy-induced nausea and vomiting[89] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| To determine whether a simple educational intervention can influence use of prescription medication and costs[86] | Before-after study, historical control; Provider perspective | OD | No input or ongoing costs measured |
| To assess economic outcomes of a pharmacist-managed levofloxacin conversion protocol[81] | Static group comparison, historical control; Provider perspective | CMA | Ongoing costs only, wages, equipment (drug and administration costs) |
| To evaluate the impact of a perioperative antibiotic prophylaxis protocol[84] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| To evaluate clinical and economic outcomes of an antibiotic review program[82] | Noncomparative study; Provider perspective | OD | No input or ongoing costs measured |
| To describe clinical and economic outcomes of an activated protein C protocol[79] | Static group comparison, concurrent control (group of patients not meeting protocol); Provider perspective | COA | Ongoing costs only, wages |
| To evaluate the impact of guidelines and pharmacist reinforcement for intravenous to oral antibiotic switch in the hospital setting[88] | Quasi-experimental, historical control (before pharmacist intervention period); Provider perspective | OA | No input or ongoing costs measured |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (pharmaceutical, laboratory) | 180 patients (93 in control group) from one site [study duration (unclear)] | These were nonsignificant differences of total hospital costs, antimicrobial costs, and costs attributable to infection between the antimicrobial management team and the infectious disease fellows of $1396, $43, and $695, respectively. | 1993 |
| Direct medical costs (pharmaceutical) | Sample size (unspecified), one site [4-year study, with 4-year follow-up] | The total cost avoidance for this program was $1,018,638 during 4 years. | 1999 |
| Direct medical costs (pharmaceutical) | 184 patients from one site [1-year follow-up] | Without protocol, the projected annual cost would have been $146,949; therefore, the projected annual savings was $37,703. | 1999 |
| Direct medical costs (pharmaceutical) | Sample size (unspecified), one site [1-year study, with 1-year follow-up] | There was a decrease in the use of the more costly anticoagulants, H2 antagonists, and nonsteroidal anti-inflammatory agents and an increase in the use of less costly alternatives. | 1999 |
| Direct medical costs (hospital, pharmaceutical); length of hospital admission; number of interventions (conversion to oral therapy) | 131 patients (49 in control group) from one site [4-month study] | Level 1, level 2, and level 3 costs were significantly less during the proactive conversion program than those in the prospective observational study during 2 months ($77 vs. $133, $91 vs. $151, and $13,931 vs. $17,198, respectively). | 2000 |
| Direct medical costs (pharmaceutical); quality-based assessment (medication appropriateness, medication timing) | 687 patients from one site [2-month study, with 1-month follow-up (two [2] 1-month periods in 2 different years)] | After protocol implementation, the median cost decreased to $4.40 per surgery, and the real median cost fell to $1232, projecting an annual expense of $14,784, a 40.5% reduction in the cost of the perioperative antibiotic prophylaxis. | 2000 |
| Direct medical costs (pharmaceutical) | 5370 interventions from one site [13-year study] | About $2,194,173 was saved during 13 years with 5334 antibiotic changes. This program appeared to promote an average savings of $168,782 per year at $411 per antibiotic change. | 2000 |
| Mortality; cost-avoidance | 34 patients (14 in control group) from one site [study duration (unspecified)] | Potentially avoidable costs included activated protein C therapy in control group patients totaling $46,626 during 12 months. | 2002 |
| Direct medical costs (pharmaceutical); length of hospital admission; quality-based assessment (time until conversion from intravenous to oral therapy) | 55 patients (29 in control group) from one site [12-week study, with 6-week follow-up] | There was a nonsignificant difference in mean costs of antibiotic therapy from the fulfillment of the switch criteria to discharge, EUR92 in group A and EUR44 in group B, 6 weeks after intervention. | 2001 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| To measure the effects of a pharmacist-based intervention when assessing redundant inpatient antibiotic combinations[95] | Noncomparative study; Provider perspective | COD | Ongoing costs only, wages |
| To evaluate clinical and economic outcomes of a multidisciplinary antibiotic management program[41] | Before-after study, historical control; Provider perspective | CBA | Total program costs (per year) |
| To evaluate an intervention to reduce inappropriate use of key antibiotics with an interrupted time-series analysis[90] | Before-after study; Provider perspective | CMA | Initial and ongoing costs, wages |
| To compare estimated vs. actual cost benefits of a therapeutic interchange program[92] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| To evaluate a pharmacist-managed intravenous to enteral proton pump inhibitor interchange program[100] | Noncomparative study; Provider perspective | OD | No input or ongoing costs measured |
| To develop and describe clinical and economic outcomes of a venous thromboembolism prophylaxis program[91] | Noncomparative study; Perspective unspecified | OD | No input or ongoing costs measured |
| To assess clinical and economic outcomes of a recombinant human erythropoietin protocol[99] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| To describe the implementation of an intravenous fluconazole restriction program[93] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| To evaluate the impact of antibiotic guidelines, with and without reinforcement by clinical pharmacists, in three hospitals[101] | Randomized experiment (randomized, pre-post experiment; hospital as unit of randomization), concurrent control (group of patients in sites with no pharmacist service); Provider perspective | OA | No input or ongoing costs measured |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (pharmaceutical); cost avoidance | 192 patients from one site [23-day study] | Redundant antibiotic combinations resulting from physician prescribing errors were administered on 173 inpatient antibiotic days, at a total drug cost of $36 per episode. This would provide an estimated net cost savings of $48,000 per year. | 2001 |
| Direct medical costs (pharmaceutical, antibiotic expenditures); cost avoidance (use of less costly drug) | One site [7-year study, with 10-year follow-up] | Comparison of the cost of antibiotic acquisition per 1000 patient-days with subsequent costs indicated that there had been a savings in acquisition costs of $200,000–$250,000 per year. [4.7 benefit:cost ratio[a]] | 2001 |
| Direct medical costs (pharmaceutical) | 794 patients from one site [48-month study, with 24-month follow-up] | The analysis of change in slope showed a reduction in cost of key antibiotics by GBP1908 per month in the 2 years after intervention. | 2001 |
| Direct medical costs (pharmaceutical); number of interventions (percentage of patients switched from intravenous to oral therapy) | 91 patients from one site [6-month study] | Conservatively estimated $30,000–50,000/year saved due to intravenous to oral interchange. 30% of doses were eligible for intravenous to oral conversion. Median was 2 days after it was identified that patient was switched. | 2000 |
| Direct medical costs (pharmaceutical) | 113 patients from one site [4-month study] | Daily acquisition cost savings ranged from $5 to $25 per patient. | 2001 |
| Direct medical costs (pharmaceutical) | 463 patients from one site [10-month study] | Program resulted in avoidance of 250 days of enoxaparin prophylaxis and $8495 of medical costs. | 2001 |
| Direct medical costs (pharmaceutical); drug use (iron replacement therapy and dose); quality-based assessment (medication appropriateness) | 103 patients from one site [6 months before (prephase) and 12-month follow-up (postphase)] | Program resulted in a 63% increase in the use of iron and a reduction of $121,672 in target drug spending during 12 months. | 2001 |
| Direct medical costs (pharmaceutical), quality-based assessment (medication appropriateness) | 68 patients from one site [2-month study, with 1-month follow-up] | Program achieved an annualized cost savings of $69,000. About $64,000 was spent on inappropriate therapy. | 2002 |
| Direct medical costs (total, pharmaceutical); length of hospital admission; drug use (duration) | 1200 patients (200 patients per site for each [pre- and post-] period) from three sites (two intervention hospitals [designated low and high intervention sites] and one control hospital) [6-month study] | Practice guidelines plus pharmacist reinforcement incurred the highest spending, followed by practice guidelines alone and the control group, but results were nonsignificantly different. | 2003 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| To assess the impact of guideline implementation on intravenous antibiotic prescribing on admission to a hospital[98] | Quasi-experimental, historical control (no pharmacist intervention unless requested); Provider perspective | COA | Total program costs (per year) |
| To assess the impact of a pharmacist-managed ciprofloxacin conversion service[96] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| To report the clinical and economic outcomes of a 5-year antimicrobial control program[97] | Noncomparative study; Provider perspective | OD | No input or ongoing costs measured |
| To assess the economic outcomes of a clinical pharmacy service in a coronary care unit[94] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| LONG-TERM CARE FACILITY | | | |
| **Disease state management services** | | | |
| To measure the impact of an antihypertensive drug substitution program[108] | Before-after study; Provider perspective | OD | No input or ongoing costs measured |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate clinical outcomes of a clinical pharmacy program in nursing home residents[30] | Randomized experiment, concurrent control (group of patients in nursing homes with no pharmacist service [3:1 ratio]); Payer and provider perspective | CBA | Ongoing costs only, personnel time |
| To determine the clinical and economic outcomes of the North Carolina Polypharmacy Initiative[42] | Before-after study; Payer perspective | CBA | Total costs (per intervention), overhead (administrative) |
| To determine the rates and drug costs of potential drug therapy problem alerts after intervention by a consultant pharmacist[113] | Quasi-experimental, concurrent control (group of patients in nursing homes who did not respond); Payer perspective | COA | Ongoing costs only, wages |
| PATIENT'S HOME | | | |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate the clinical, humanistic, and economic outcomes of a pharmacist-led medication review in the elderly[106] | Randomized experiment, concurrent control (group received standard care); Societal perspective | OA | No input or ongoing costs measured |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (pharmaceutical); quality-based assessment (time until conversion from intravenous to oral therapy) | 757 patients (282 in control group) from one site [40-week study, with 4-week follow-up] | Antibiotic costs per episode treated were reduced by 17%, GBP86 in group 1 and GBP71 in group 2. | 2003 |
| Direct medical costs (pharmaceutical); length of hospital admission | 200 patients from one site [365 days before (prephase) and 120 days follow-up (postphase)] | The proportional cost avoidance associated with pharmacist-preventable inappropriate ciprofloxacin use was reduced significantly from CAD3367/CAD16,517 (20%) to CAD1975/CAD17,919 (11%). | 2004 |
| Direct medical costs (pharmaceutical); drug use | Sample size (unspecified), one site [5-year study, with 5-year follow-up] | Pharmacy expenditures for all antimicrobials, including antiviral, antifungal, and antibacterial agents, decreased 24.7%, with a cumulative cost savings of $1,401,126 without inflation in drug costs, in 5 years' time. | 2003 |
| Direct medical costs (hospital, pharmaceutical) | Sample size (unspecified) [18-month follow-up] | Estimated reduction in drug costs associated with the clinical pharmacist interventions totaled $372,384 in 1 year. | 1999 |
| Direct medical costs (pharmaceutical); quality-based assessment (adverse drug events) | 119 patients from 17 sites [4-month study, with 2-month follow-up] | Drug costs decreased by $19 per patient per month when drug was substituted. | 2001 |
| Mortality; direct medical costs (pharmaceutical); drug use (number of prescriptions) | 3230 patients (2325 in control group) from 52 sites [34-month study, with 22-month follow-up] | There was a net savings of AUD16 per resident per year. [1.3:1 benefit:cost ratio[a]] | 1999 |
| Direct medical costs (pharmaceutical); number of interventions (recommendations made); quality-based assessment (acceptance rate) | 6344 patients from 253 sites [4-month study, with 1-month follow-up] | First-year cost savings was an estimated $1.7 million, and cost-minimization ratio was 12:1. The drug cost savings was $30.33 per patient per month. | 2002 |
| Direct medical costs (pharmaceutical); quality-based assessment (drug-related problems) | 7362 patients (2202 in control group) from 384 sites [6-month study] | Mean drug costs per patient in the intervention group decreased by $12.14 and increased in the control group by $44.98, creating a relative cost reduction of $19.04 per patient per month. | 2003 |
| Direct medical costs (pharmaceutical); number of medical encounters (hospitalizations, emergency visits) | 332 patients (164 in control group), number of sites (unspecified) [3-month study, with 3-month follow-up] | There were no significant differences between groups in the average monthly costs of prescribed medication per patient, either at initial interview or after intervention. | 1999 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| To evaluate the initial impact of in-home medication reviews for war veterans by accredited pharmacists[110] | Before-after study; Payer perspective | OD | No input or ongoing costs measured |
| PHYSICIAN'S OFFICE | | | |
| **General pharmacotherapeutic monitoring** | | | |
| To determine the effect of repeat prescription reviews in general practice through consultations with elderly patients[33] | Randomized experiment, concurrent control (group received standard care); Payer and provider perspective | COA | Ongoing costs only, wages |
| To determine the effect of a pharmacist consultation program on outpatient physician prescribing and medication costs[31] | Randomized experiment, concurrent control (group received usual care); Payer and provider perspectives | COA | Ongoing costs only, personnel time |
| To measure the cost outcomes of pharmacist interventions in the drug therapy of high-use patients in a managed care health plan[102] | Before-after study; Payer perspective | OD | No input or ongoing costs measured |
| **General pharmacotherapeutic monitoring, MTM-like service** | | | |
| To describe clinical and economic outcomes of a collaborative approach between a physician and a pharmacist in medication reviews[103] | Noncomparative study (single-group design); Payer perspective | COD | Ongoing costs only, wages |
| **Medication therapy management service (as stated by authors)** | | | |
| To evaluate clinical and economic outcomes of pharmacist face-to-face medication reviews in the primary care setting[109] | Randomized experiment, concurrent control (group of patients with no pharmacist service); Payer perspective | OA | No input or ongoing costs measured |
| REHABILITATION CENTER | | | |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate clinical and economic outcomes of pharmaceutical interventions among the elderly with a history of falls[114] | Static group comparison, historical control (before pharmacist intervention period); Payer perspective | OA | No input or ongoing costs measured |

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (pharmaceutical), quality-based assessment (medication appropriateness) | 92 patients from one site [48-week study, with 24-week follow-up] | There was an insignificant increase in the number of medications, from 12.6 to 13.9, and the mean health service cost, from AUD1818 to AUD2123 in the 24 weeks after intervention. | 2002 |
| Direct medical costs (pharmaceutical); drug use (dose); number of interventions (medication changes) | 1188 patients (550 in control group) from four sites [12-month study] | Monthly drug costs rose significantly in both groups from GBP7.04 to GBP2.41, but the rise was less in the intervention group. | 1999 |
| Direct medical costs (pharmaceutical); number of interventions; quality-based assessment (acceptance rate) | 132 patients (66 in control group) from four sites [6-month study] | Medication costs were not significantly different, CAD4.26 for the control group and CAD3.85 for the intervention group. Pharmacist costs for all intervention participants were CAD5537. | 1999 |
| Direct medical costs (total, pharmaceutical); number of interventions; quality-based assessment (acceptance rate, medication adherence, patient and physician satisfaction) | 80 patients from two sites [4-month follow-up] | 206 interventions were implemented, producing an average per member per month drug cost decrease of $17.04. | 2000 |
| Direct medical costs (pharmaceutical); number of interventions (therapeutic issues); quality-based assessment (acceptance rate) | 52 patients from one site [study duration (not stated)] | Medication regimen simplifications resulted in an annual cost savings of AUD4471 with no observed adverse effects on health status. | 1999 |
| Direct medical costs (total, pharmaceutical); health care use; drug use (number of prescriptions); quality-based assessment (drug-related problems, interventions, acceptance rate) | 889 patients (458 in control group) from 48 sites [8-month study] | After 5 months, the mean costs of health care resources per patient were nonsignificantly different, CAD1281 in the intervention group and CAD1299 in the control group. | 2001 |
| Cost estimate per patient fall; quality-based assessment (adverse drug events) | 400 patients (200 in control group) from one site [1-year follow-up] | The number of patient falls was reduced in the postintervention group by 47%; interventions can reduce the number of falls by 47%, resulting in a future savings of $7.74 per patient per day or an annualized savings of $308,000. | 2001 |

**Appendix 1. (continued)**

| Study Objective(s) | Study Design | Economic Method | Input Costs |
|---|---|---|---|
| RESIDENTIAL CARE CENTER | | | |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate economic outcomes of consultant pharmacist interventions among a multidisciplinary aged care assessment team[104] | Quasi-experimental, historical control (group received standard care with no pharmacist service); Societal perspective | CBA | Ongoing costs only, wages |
| TELEPHONE-BASED SERVICE | | | |
| **Wellness program/Immunization service** | | | |
| To compare a pharmacist-run travel medicine telephone service with an existing nurse-based travel medicine system[105] | Static group comparison, historical control; Payer perspective | COA | Ongoing costs only, wages, fees |
| VETERANS ADMINISTRATION HEALTH CARE SYSTEM | | | |
| **Target drug program** | | | |
| To assess clinical and economic outcomes of a cyclooxygenase-2 inhibitor therapeutic interchange protocol[112] | Noncomparative study; Provider perspective | OD | No input or ongoing costs measured |
| VARIOUS (COMMUNITY PHARMACY AND HOSPITAL-BASED PHARMACY) | | | |
| **Disease state management services** | | | |
| To conduct an economic evaluation of a community pharmacy-delivered disease state management service for patients with diabetes[111] | Quasi-experimental, concurrent control (group received standard care); Payer perspective | CEA | Ongoing costs only, personnel time, overhead (telephone) |
| VARIOUS (HOSPITAL, NURSING HOME, AND OUTPATIENT SETTING) | | | |
| **General pharmacotherapeutic monitoring** | | | |
| To evaluate clinical and economic outcomes of pharmacist recommendations in a Veterans Affairs Medical Center[107] | Noncomparative study; Provider perspective | OD | No input or ongoing costs measured |
| FACILITY (UNSPECIFIED) | | | |
| **General pharmacotherapeutic monitoring** | | | |
| To assess clinical and economic outcomes of pharmaceutical care services[116] | Noncomparative study; Perspective unspecified | CBA | Ongoing costs only, fees paid (methods unclear) |

CBA = cost-benefit analysis; CEA = cost-effectiveness analysis; CMA = cost-minimization analysis; COA = cost-and-outcome analysis; COD = cost-outcome description; OA = outcome analysis; OD = outcome description
$ = U.S. Dollar; AUD = Australian Dollar; CAD = Canadian Dollar; CHF = Swiss Franc; EUR = Euro; MYR = Malaysian Ringgit; SGD = Singapore Dollar.
[a]Not reported in paper—calculated by the reviewers.

**Appendix 1. (continued)**

| Economic Outcome | Sample [Duration] | Results | Currency Year |
|---|---|---|---|
| Direct medical costs (hospital, medical services, residential care, assisted living, pharmaceutical, over-the-counter drugs) | 759 patients from two sites [2-year study, with 6-month follow-up] | The study was not able to show a statistically significant reduction in overall costs associated with pharmacist review and advice. | 1996 |
| Direct medical costs (pharmaceutical) | Total patients, unspecified (40 in control group) from two sites [study duration (one-time intervention with no follow-up)] | The researchers estimated that they could save $47,000 annually in unnecessary vaccinations and medications. Program costs were $450,000 per year or $45– $50 per consultation. | 2002 |
| Direct medical costs (pharmaceutical); drug use (continuation of therapy); quality-based assessment (adverse drug events) | 32 patients from one site [3-month study] | Potential cost savings for 32 patients switched to valdecoxib was $8282 per year or $25,881 per year for every 100 patients. Successful interchange cost savings for 14 patients was $3504 per year or $10,641 per year for every 100 patients. | 2003 |
| Direct medical costs (hospital, physician, pharmaceutical) | 99 patients (46 in control group) from three sites [9-month study] | The cost of providing specialized care was AUD1821 per patient in the intervention group vs. AUD1437 for usual care during 9 months. The cost of diabetes-related health care resources was AUD155 for the intervention group and AUD197 for the control group. | 2001 |
| Direct medical costs (pharmaceutical) | 600 interventions from three sites [12-month study] | There was a cost avoidance of $700 per recommendation; the mean total cost avoidance for 600 recommendations was $420,155. | 2000 |
| Cost savings; quality-based assessment (drug-related problems) | 2985 patients from 36 practitioner sites [4-year study] | The total health care savings was $1,134,162 for 4 years, and the cost per patient visit was $47, yielding a cost:benefit ratio of 1:2. | 2002 |