A C C P

Evidence of the Economic Benefit of Clinical Pharmacy Services: 1996–2000

Glen T. Schumock, Pharm.D., M.B.A., Melissa G. Butler, Pharm.D., Patrick D. Meek, Pharm.D., Lee C. Vermeulen, M.S., Bhakti V. Arondekar, M.S., and Jerry L. Bauman, Pharm.D., FCCP, for the 2002 Task Force on Economic Evaluation of Clinical Pharmacy Services of the American College of Clinical Pharmacy

We sought to summarize and assess original evaluations of the economic impact of clinical pharmacy services published from 1996–2000, and to provide recommendations and methodologic considerations for future research. A systematic literature search was conducted to identify articles that were then blinded and randomly assigned to reviewers who confirmed inclusion and abstracted key information. Results were compared with those of a similar review of literature published from 1988–1995. In the 59 included articles, the studies were conducted across a variety of practice sites that consisted of hospitals (52%), community pharmacies and clinics (41%), health maintenance organizations (3%), and long-term or intermediate care facilities (3%). They focused on a broad range of clinical pharmacy services such as general pharmacotherapeutic monitoring (47%), target drug programs (20%), disease management programs (10%), and patient education or cognitive services (10%). Compared with the studies of the previous review, a greater proportion of evaluations were conducted in community pharmacies or clinics, and the types of services evaluated tended to be more comprehensive rather than specialized. Articles were categorized by type of evaluation: 36% were considered outcome analyses, 24% full economic analyses, 17% outcome descriptions, 15% cost and outcome descriptions, and 8% cost analyses. Compared with the studies of the previous review, a greater proportion of studies in the current review used more rigorous study designs. Most studies reported positive financial benefits of the clinical pharmacy service evaluated. In 16 studies, a benefit:cost ratio was reported by the authors or was able to be calculated by the reviewers (these ranged from 1.7:1–17.0:1, median 4.68:1). The body of literature from this 5-year period provides continued evidence of the economic benefit of clinical pharmacy services. Although the quality of study design has improved, whenever possible, future evaluations of this type should incorporate methodologies that will further enhance the strength of evidence of this literature and the conclusions that may be drawn from it.
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In 1979, the first, to our knowledge, cost-benefit analysis of a clinical pharmacy service was published.[1] At the time, the authors' rationale for the study was that "evaluating the benefits and costs of clinical pharmacy services may be one solution to increasing acceptance of such services by the medical profession, third-party payers, and consumers." In the subsequent

25 years, the profession has made tremendous gains, not only in acceptance on the part of the medical profession, third-party payers, and consumers, but also in establishing clinical pharmacy as an independent, value-added component of the health care system. Yet, the need to provide evidence of the economic benefit of clinical pharmacy services has not lessened with these advances. To the contrary, ever-present efforts to reduce health care spending have required the near continuous evaluation of these programs.

Articles on the economic impact of clinical pharmacy services represent a unique resource for the pharmacy manager or clinician who may be in the position of initiating, defending, or expanding such programs. Still, the volume of published literature, along with diversity of methods and quality of analysis, makes it difficult to identify applicable articles and interpret the findings. As a result, efforts have been made to summarize the literature in a format that is easier for the busy practitioner to access. The American College of Clinical Pharmacy (ACCP) has been integral to these efforts by sponsoring two key reviews of the literature. The first, printed in 1989, summarized the literature published before 1988.[2] The second ACCP-sponsored work reviewed economic evaluations of clinical pharmacy services published between 1988 and 1995.[3] Other similar reviews that cover differing time ranges also have been published.[4–6]

Since the publication of these reviews, additional primary articles have continued to appear in the pharmacy literature. In fact, some very large and important studies have been conducted over the past 5 years that have advanced our understanding of issues pertinent to the economic impact of clinical pharmacy services.[7, 8] Because a need exists for a comprehensive review of these recent studies, the ACCP Board of Regents again charged a group of individuals, in this case the 2002 Task Force on Economic Evaluation of Clinical Pharmacy Services, to summarize and interpret this literature. Objectives for the group were to summarize and evaluate the literature published from 1996–2000 that assessed the economic impact of clinical pharmacy services and to provide guidance on methodologic considerations to individuals performing such research, as well as recommendations for future research.

From the Center for Pharmacoeconomics Research and Department of Pharmacy Practice (Drs. Schumock, Butler, and Bauman, and Ms. Arondekar), University of Illinois at Chicago, Chicago, Illinois; the Department of Pharmacy Practice, University of Wisconsin–Madison (Dr. Meek and Mr. Vermeulen), and the Center for Drug Policy and Clinical Economics, University of Wisconsin Hospital and Clinics (Mr. Vermeulen), Madison, Wisconsin.

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Address reprint requests to the American College of Clinical Pharmacy, 3101 Broadway, Suite 680, Kansas City, MO 64111.

Methods

A search of two literature databases (MEDLINE and International Pharmaceutical Abstracts) was conducted to identify articles published between January 1996 and December 2000 (inclusive). The beginning date of January 1996 was selected because the previous ACCP review was inclusive through December 1995.[3] Both medical subject headings and free text search terms were used to identify original economic evaluations of clinical pharmacy services. Search terms were clinical pharmacy services, cost, cost analysis, cost benefit, cost-effectiveness, cost-utility analysis, economic evaluation, outcomes analysis, pharmacy services, outcomes, and programs. Where possible, the search was filtered to exclude non-English articles, review articles, editorials, and other incomplete or unoriginal works.

All citations identified were screened for inclusion by reviewing titles and abstracts. Those articles for which abstracts were not available from the electronic databases or that did not have abstracts were collected manually and screened for inclusion. Inclusion criteria were English language, original evaluation, publication date between January 1996 and December 2000 inclusive, assessment of a clinical pharmacy service (defined as a patient-level interaction, and not including policy-type interventions unless accompanied by a patient-level interaction), and some form of economic assessment (measurement of either costs to provide the service or economic outcomes, or both). Not included were unoriginal work (reviews, editorials, letters) or studies published only in abstract form. Studies that evaluated only clinical or humanistic outcomes, without an economic assessment, were excluded. After reviewing titles and abstracts, a hard copy of each article that met the inclusion criteria was obtained for full review.

In addition to the articles identified by the literature database search, several other methods were used to find pertinent literature. First, the authors examined personal files for yet

Table 1. Criteria for Assessment of Type of Analysis

Were Two or More Alternatives Considered?	Were Both Costs and Outcomes Considered?	
	No	Yes
No	Cost description, or cost and outcome description	Outcome description
Yes	Cost analysis, or outcome analysis	Full economic analyses: Cost-minimization Cost-benefit Cost-effectiveness Cost-utility

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unidentified articles. Second, the authors examined the bibliographies of included articles and of review articles to identify cited works. Third, the authors sent an e-mail message to members of all ACCP practice research networks (by means of the listserves for those groups) requesting that members "nominate" articles that met the inclusion criteria. Fourth, a search of a science citation database (Web of Science) was conducted to identify articles that referenced previous reviews.[2–6] Articles identified through these methods again were collected and screened for inclusion, and added to the set of articles subjected to full review.

In the full review process, each paper was randomly assigned to at least two of six reviewers who were to confirm inclusion criteria, abstract key information, and assess the quality of each article. Reviewers were blinded to authors' names and affiliations, and journal of publication. Reviews were recorded on a standard report form and entered into a database for analysis. Discrepancies between reviewers were arbitrated by group consensus. Major categories of data abstracted were study setting, service type, objective(s), methods, and results.

Each article was assessed for the type of evaluation and categorized as shown in Table 1 by using criteria previously adapted.[9] Two factors were considered in determining the type of evaluation: the presence of two or more alternatives and the consideration of both input cost(s) and outcome(s). Evaluations that included two or more alternatives (i.e., concurrent control group, historical control, and a before and after design) were considered "analyses," whereas those that did not include a comparison were labeled "descriptions." Before and after designs were differentiated from historical control designs in the temporal relationship to the intervention under study. If a study compared measurements taken immediately before an intervention and immediately after, it was coded as a before and after design. If a longer period of time elapsed between comparison groups (e.g., comparing data from the study period to the same month 1 year earlier), the study was defined as a historical control. Some studies used a before and after or a historical design in addition to a concurrent control group. Each evaluation was classified as one of the following: cost description, outcome description, cost analysis, outcome analysis, cost and outcome description, or full economic analysis. Those articles considered full economic analyses were subcategorized by type; the subcategories were cost-minimization analysis, cost-benefit analysis, cost-effectiveness analysis, and cost-utility analysis.

Articles were classified both by setting of evaluation and by type of clinical pharmacy service. Five major categories used to classify articles by type of clinical pharmacy service were defined as follows: disease management—a clinical pharmacy service primarily directed at patients with a specific disease state or diagnosis, such as an asthma management program; general pharmacotherapeutic monitoring—a clinical pharmacy service 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; pharmacokinetic monitoring—a clinical pharmacy service that primarily involved evaluation of anticipated or actual serum drug concentrations and provision of subsequent dosing recommendations; targeted drug program—a clinical pharmacy service that primarily focused on a single drug or class of drugs and may have included predefined guidelines for provision of alternative therapy or

dosing recommendations, such as intravenous to oral switch recommendations for antibiotics; and patient education program or cognitive service—a clinical pharmacy service that primarily instructed patients on the proper administration of drugs and/or identified drug-related problems.

Descriptive statistics were used to profile and characterize the articles within each data field abstracted by the reviewers. Study results were scrutinized carefully by the reviewers. Benefit:cost ratios were calculated by the reviewers if not provided by the author(s) and if appropriate to do so. The benefit:cost ratio (financial benefit/dollar invested to provide the service) was calculated by dividing reported total costs to provide the clinical pharmacy service described by the reported gross economic benefits derived from the service for the same time period. Benefit:cost ratios were pooled from applicable articles to calculate an overall mean value. The median benefit:cost ratio from the pooled studies also was identified.

Results

Figure 1 illustrates the results of the search and screening process: 1465 citations were identified through the initial electronic literature database search, 3 articles were added from the files of the authors, 2 were obtained through requests of ACCP members, 5 were added through the secondary search of the bibliographies of included articles, and 46 were added from a search of a science citation database, for a total of 1521 articles. A preliminary review of the titles and abstracts of these articles identified 1435 that did not meet the primary inclusion criteria. The most common reason for exclusion was failure to meet the definition of a clinical pharmacy service. Many citations that were published only in abstract form were also excluded. Thus, 86 articles were subjected to full review. During full review, 20 articles were identified as not meeting the inclusion criteria. In addition, one article was removed because it was based on the same data as a previously included study.[10] Further, six articles[11–16] were excluded from the final group because these studies were based on secondary data (three articles) or derived from modeling techniques where data evaluated were not from an actual practice site (three articles); however, these articles were deemed important and are summarized separately.

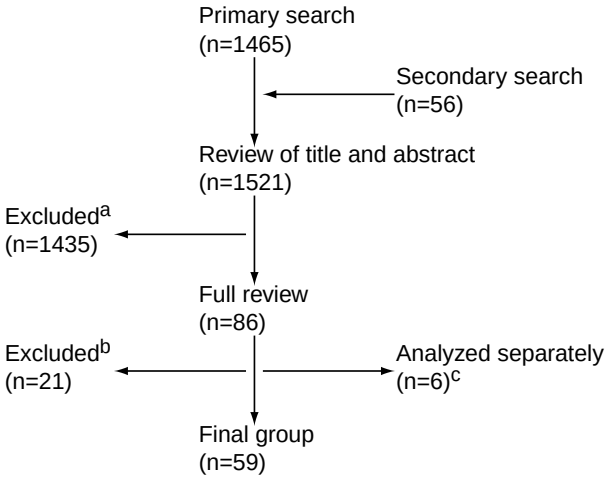

Figure 1. Literature search method and screening results.
[a]Articles excluded based on failure to meet primary inclusion criteria.
[b]Articles excluded based on failure to meet primary inclusion criteria (20 articles) or duplicate publication of same data (1 article).
[c]Articles excluded based on use of modeling or secondary data. These articles are discussed separately in Results.

Table 2. Settings of Economic Evaluations of Clinical Pharmacy Services

Setting	No. (%) of Studies (n=59)
Community hospital	16 (27)
University hospital	13 (22)
Government or VA clinic	10 (17)
Community pharmacy	6 (10)
Hospital-associated clinic	6 (10)
Government or VA hospital	2 (3)
Free-standing clinic or physician's office	2 (3)
Long-term or intermediate care facility	2 (3)
Health maintenance organization	2 (3)

VA = Veterans Affairs.

Included Articles

Appendix 1 describes the final set of 59 included articles.[17–75] These articles are sorted first by the setting of the evaluation and then by the type of clinical pharmacy service described in the evaluation. Articles from pharmacy-based journals dominated the set of included studies. The most common journal source was *American Journal of Health-System Pharmacy* (19 articles, 32%). *Pharmacotherapy* (8 articles, 14%), *Annals of Pharmacotherapy* (5 articles, 8%), and *Hospital Pharmacy* (4 articles, 7%) also were common. Twelve articles were published in nonpharmacy journals. Most studies (51 articles, 86%) were conducted in the United States. Studies also were conducted in Australia (2 articles) and in Canada, Greece, Japan, the Netherlands, Spain,

Table 3. Types of Clinical Pharmacy Services or Interventions Studied

Type of Service or Intervention	No. (%) of Studies (n=59)
General pharmacotherapeutic monitoring	28 (47)
Target drug program	12 (20)
Disease management	6 (10)
Patient education or cognitive service	6 (10)
Other[a]	6 (10)
Pharmacokinetic monitoring	1 (2)

[a]Includes patient allergy history taking, academic detailing, case management, drug information, vaccination administration, and telephone triage service.

Table 4. Analytic Methods Used in Economic Evaluations of Clinical Pharmacy Services

Method	No. (%) of Studies (n=59)
Outcome analysis	21 (36)
Full economic analysis	14 (24)
Outcome description	10 (17)
Cost and outcome description	9 (15)
Cost analysis	5 (8)
Cost description	0 (0)

and the United Kingdom (1 article each).

Evaluations fell into 10 categories based on setting (Table 2). The setting of most studies was either a community or a university hospital. Veterans Affairs or government clinics, community pharmacies, and hospital-associated clinics also were common. Other settings were freestanding clinics, physicians' offices, health maintenance organizations, long-term or intermediate care facilities, and Veterans Affairs or government hospitals.

The most common type of pharmacy service evaluated was general pharmacotherapeutic monitoring, followed by target drug programs (Table 3). Disease management and patient education or cognitive services were evaluated in 10% of studies each.

Table 4 summarizes the analytic methods used in the included articles. Fourteen studies (24%) included both an alternative or comparison group and measurement of both costs and outcomes (i.e., full economic analysis). The remaining articles consisted of less rigorous analytic methods. The most common of these, and the most common overall, was outcomes analyses (36%).

The study design of the included articles was further analyzed by considering the use of a comparison group(s) (or alternatives) and by the types of input costs and economic end points measured. Most studies (40 articles, 68%) included a comparison group, whereas 19 (32%) did not and therefore were considered to be descriptive in nature. Articles with study designs that included a comparison group used a concurrent control group (25 articles, 42%), a before and after design (11 articles, 19%), or a historical control group (9 articles, 15%).

Most studies (31 articles, 52%) did not evaluate the cost of providing the clinical service as part of the economic evaluation of that service, whereas some (28 articles, 47%) did consider the cost to provide the service. Of studies that did consider some input costs, the most common costs assessed were those of personnel. On the other side of the equation, most studies did evaluate the economic outcomes or consequences of the service evaluated. Most commonly, this was done in terms of drug costs avoided or reduced health care expenditures. Many studies also measured clinical or humanistic outcomes. When measured, clinical and humanistic outcomes tended to be positive or neutral; those results are not provided here.

Most studies (50 articles, 85%) described a beneficial economic impact of the clinical pharmacy service evaluated. More notable, of the studies that included both investment costs and economic benefits, as well as an alternative, 100% demonstrated positive findings. Findings from these studies often were expressed as net savings over the study period (or annualized), as net savings adjusted/patient, and/or as a benefit:cost ratio.

In only five articles did authors report a benefit:cost ratio; however, in an additional 11 articles the reviewers were able to calculate a benefit:cost ratio from the results provided (Table 5). The benefit:cost ratios ranged from 1.74:1–17.0:1, with the median being 4.68:1 and the mean being 5.54:1. Although the mean and medians are similar, the median was considered more representative of the group based on the distribution of the benefit:cost ratios from the different studies.

Other Relevant Articles

The six articles analyzed separately from those listed in Appendix 1 represent important contributions to the literature on the economic impact of clinical pharmacy services, and the current review would be remiss if these studies were not included. All six studies were conducted by using United States data sources,

Table 5. Benefit:Cost Ratios from Included Studies

Setting	Clinical Service	Benefit:Cost Ratio[a]
VA or government clinic[56]	General pharmacotherapeutic monitoring	1.74:1[b]
Hospital-associated clinic[52]	Target drug program	1.60:1[b]
Hospital-associated clinic[48]	General pharmacotherapeutic monitoring	2.06:1[b]
Physician's office[65]	Academic detailing	2.13:1[b]
Community hospital[34]	General pharmacotherapeutic monitoring	2.66:1
Community hospital[31]	General pharmacotherapeutic monitoring	2.72:1[b]
Community hospital[38]	General pharmacotherapeutic monitoring	3.50:1[b]
Community hospital[36]	General pharmacotherapeutic monitoring	4.25:1[b]
University hospital[27]	Target drug program	5:1
Free-standing clinic[64]	Disease state management	5.31:1[b]
VA or government clinic[62]	Patient education	5.73:1[c]
VA or government clinic[58]	General pharmacotherapeutic monitoring	5.8:1
University hospital [24]	Target drug program	8:1
Community hospital[39]	General pharmacotherapeutic monitoring	9.09:1[b]
University hospital[29]	Drug information	11.89:1[b]
University hospital[21]	Disease state management	17.01:1[b]
Median (mean)		4.68:1 (5.54:1)

VA = Veterans Affairs.
[a]Values are provided to the number of decimals as reported in the original article, or if calculated by reviewers, to two decimals.
[b]Calculated by reviewers.
[c]Value reported by authors replaced by that calculated by reviewers.

and together they span the key health care settings, including ambulatory or outpatient settings, hospitals, and nursing facilities.

Two articles, based on widely cited cost-of-illness studies, assessed the potential national impact of clinical pharmacy services on reducing drug-related problems.[11, 12] One article evaluated pharmaceutical care in the U.S. ambulatory population, and the other evaluated consultant pharmacist services in U.S. nursing facilities. Data for the analyses came from previously published studies that used decision models to estimate the cost of drug-related problems.[76, 77] An expert panel was used to determine conditional probabilities, and health care utilization and associated costs were estimated and/or derived from available statistical reports.

Providing clinical pharmacy services in these environments was estimated to be economically beneficial. The authors estimated that if all patients received pharmaceutical care in the ambulatory care setting, $45.6 billion (in 1995 U.S. dollars) in direct health care costs would be avoided. Even when the fee associated with the provision of pharmaceutical care was increased 4-fold, the estimated cost avoidance changed only slightly. In the nursing facility study, the annual cost of drug-related problems/resident decreased from an estimated $235 without consultant pharmacists to $162 with consultant pharmacists (in 1994 U.S. dollars). For all nursing facility residents in the United States, the total cost of managing drug-related morbidity and mortality was $6.64 billion and $9.64 billion with and without consultant pharmacists, respectively.

In another study that used a modeling methodology (Markov modeling),[13] the evaluation was designed to assess the impact of academic detailing by clinical pharmacists in an outpatient practice setting in three hypothetical cohorts of patients with comorbid disease (diabetic nephropathy, myocardial infarction, or left ventricular dysfunction). Drug utilization rates, quality-of-life utility values, and probabilities were derived from previously published articles. Charges were used in lieu of costs and were estimated by professional coders based on usual and customary rates derived from Medicare diagnosis-related groups and other sources. Compared with usual practice, the presence of an academic detailing clinical pharmacist netted a cost savings/quality-adjusted life year.

One group of authors conducted three important cross-sectional studies of clinical pharmacy services in U.S. hospitals.[14–16] In each study, data from hospitals across the country were obtained from secondary sources (American Hospital Association Abridged Guide to the Health Care Field, National Survey of Clinical Pharmacy Services, and/or Medicare) and analyzed by means of multiple regression for associations between the presence of clinical pharmacy

services and clinical and economic variables. Cost estimates were provided in 1992 U.S. dollars.

The first of these studies demonstrated an association between four specific types of clinical pharmacy services (clinical research, drug information, admission drug histories, and cardiopulmonary resuscitation team participation) and reduced mortality. Cost-effectiveness ratios for these services also were estimated; these ranged from $28.92 (clinical research) to $192.58 (drug information) per death avoided. The second study demonstrated an association between clinical pharmacy services (in-service education, drug information, drug protocol management, and admission drug histories) and hospital drug costs. Reductions in drug costs/occupied bed for hospitals with versus those without these services ranged from $490.96 for in-service education to $1961.55 for drug information. The benefit:cost ratios for each service also were estimated; these ranged from $23.80:1 (drug histories) to $83.23:1 (drug protocol management). The third study by these authors demonstrated an association between six different clinical pharmacy services and reductions in the total cost of hospital care (drug therapy evaluation, drug information, adverse drug reaction monitoring, drug protocol management, medical rounds participation, and admission drug histories). Benefit:cost ratios were estimated for each service; these ranged from $31.92:1 (drug therapy evaluation) to $2988.57:1 (adverse-reaction monitoring). Although the benefit:cost values from these studies are impressive, they should be interpreted in the context of the study design, which was not to determine causation but rather to determine association between clinical pharmacy services and cost reduction.

Discussion

Assessment of the Literature

This review provides evidence of the continued economic value of clinical pharmacy services. The number of articles published on this topic has remained constant over the past 13 years (mean ± SD of 13.0 ± 6.1 articles/yr from 1996–2000 based on the 59 included articles and 6 additional studies in the current review and a mean of 13.0 ± 5.4 articles/yr from 1988–1995), but the quality of these studies has improved somewhat compared with those of the previous review. A greater percentage of studies in the current review included a comparison group and measured both costs and outcomes compared with those in the previous review (23.7% vs 18.3%). Further, of those that used less rigorous designs, researchers were more likely than in the past to include a comparison group (67.8% vs 58.6%), a key factor in the ability to prove the effect of an intervention. More studies also included the cost or investment required to provide clinical pharmacy services compared with the studies in the previous review (47.4% vs 31.7%). Inclusion of input costs is required to determine the true net benefit of a clinical service. These improvements may reflect adoption of specific recommendations made in the previous review regarding the design of such studies, or may reflect a greater general understanding on the part of the profession of study designs relevant to the discipline of pharmacoeconomics and outcomes research as recommend by other authors.[78, 79] However, despite these advances, there remains ample opportunity for continued improvement in the quality of studies of clinical pharmacy services. Further recommendations with respect to study design are provided later.

Changes have occurred in the setting in which economic evaluations of clinical pharmacy services are being conducted. The current review identified a substantial shift toward the outpatient setting and practice sites other than hospitals. A greater percentage of studies were conducted in community pharmacies and clinics, compared with the studies in the previous review (40.7% vs 18.3%). The current review also identified studies conducted in health maintenance organizations and in long-term and intermediate care facilities. Conducting studies in settings other than the traditional hospital site was a recommendation made in the previous review. Furthermore, this shift likely reflects a general movement in the profession. Clinical pharmacy services first developed in the hospital setting and have moved gradually to other settings. However, in the past decade especially, a great deal of effort has been directed toward the expansion of clinical services in the ambulatory care and community pharmacy settings.

Also, a shift was noted in the type of clinical pharmacy services evaluated. A greater percentage of studies in this review were of general or comprehensive pharmacotherapeutic services (47.7% vs 36.5%) or disease management programs (10.2% vs 3.8%), whereas a decrease was noted in evaluations of specialized

or targeted types of interventions, such as pharmacokinetic services (1.7% vs 12.5%) or targeted drug programs (20.3% vs 47.1%). Reflective of the shift toward community pharmacy, this review also included evaluations of "cognitive pharmacy services," not seen in the previous review. These changes may be attributable to the profession-wide movement toward greater responsibility for outcomes of drug therapy (or pharmaceutical care) and are likely interrelated with the shift toward nonhospital practice sites.[80]

Most studies identified in this review were conducted in the United States. However, compared with the studies in the previous review, a greater proportion of studies in the current review were conducted in other countries (though, except for the United States, only Australia is represented by more than one study). This is a positive finding that may portend a greater diversity of studies in the future. It also likely reflects a general trend of expansion of clinical pharmacy services outside the United States. Clinical pharmacy services first developed in the United States but gradually have been adopted by other countries, first by Canada, then Europe and Australia, and more recently Asia.

Most studies identified in the current review reported a positive economic impact of clinical pharmacy services, and in all cases those studies using better economic methodologies demonstrated positive results. The benefit:cost ratios of applicable articles included in Appendix 1 are comparable to those of the previous review. Although the mean benefit:cost ratio in the previous review (16.70:1) was much higher than that reported in the current review, the median values are similar (4.68:1 for the current review vs 4.09:1 for the previous review). The mean value reported in the previous review was skewed upward by a single study.[81] Regardless, the economic benefit of clinical pharmacy services across a variety of practice sites and types of clinical pharmacy services reviewed here is well in excess of the costs required to provide those services. For every $1 invested in clinical pharmacy services in the studies reviewed, more than $4 in benefit is expected.

The ability of readers to generalize these results is dependent on many factors, including the way in which results are expressed, comparability of the patient population, and the type of service evaluated. Clinical pharmacy services are highly dependent on internal factors, such as the characteristics of the practice setting or skill of the individual practitioner(s). Nevertheless, pharmacy managers and clinicians should use the results of previously published evaluations and benefit from the positive experience of others.

Limitations

This review in which economic assessments of clinical pharmacy services were evaluated provides a resource for readers to access the primary literature on this subject. However, the limitations of this review should be considered and the findings interpreted correspondingly. Several limitations are noteworthy.

First, the articles identified represent only those published in the standard literature. We did not consider unpublished papers; therefore, our results may be subject to publication bias (the tendency to publish only positive results). The large number of studies on this topic that were presented in abstract form and never published as complete articles may be evidence of this type of bias.

Second, the literature databases used to identify potential articles for this review, along with the search strategy, may have affected the quantity and types of articles identified. Every effort was made to ensure that the search strategy was as comprehensive as possible.

Third, in some cases, the included articles lacked description of data important to our analysis (reporting bias) and thus may have altered our results. No effort was made to contact authors regarding missing data.

Fourth, many of the articles we reviewed had objectives in addition to or other than that of economic evaluation, and although economic impact may have been part of the study, the evaluation may not have been designed specifically for that purpose. Our assessment of studies was restricted to the economic evaluation conducted. We did not report clinical and/or humanistic outcomes measured in the studies reviewed; more thorough analyses of these outcomes can be found elsewhere.[82, 83]

Fifth, in this review, we classified cost savings resulting from clinical pharmacy services as economic outcomes or benefits. Because the main purpose of this evaluation was to investigate the economic impact of clinical pharmacy services, we chose to include the investment required to provide services but to separate that investment from the economic effect of those services. This approach is consistent with that used by many of the authors

Table 6. Study Designs Used for Evaluations of Clinical Pharmacy Services

Design	Notation[a]	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 as a result or measurement error	Subject to multiple-group threats to internal validity
Intervention	R X O		
Control	R O		
Quasiexperimental		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		
Preexperimental		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 = groups are randomly assigned; O = observations or measures (e.g., costs and clinical measures); X = the intervention (program); N = groups are nonrandomized (nonequivalent groups).

[a]Vertical alignment of Os shows that measurements occur at the same time. Time sequence (temporality) of variables is designated by the position of the variable (i.e., those to the left occur before and those to the right occur after another variable in the sequence).

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of the studies we reviewed, though it may differ from more traditional cost-effectiveness analyses in which economic outcome variables are considered costs.[84]

Last, the mean benefit:cost ratio from pooled studies reported here should be considered cautiously. Studies from which benefit:cost ratios were derived varied in terms of patient population, practice setting, type of clinical service evaluated, and study design. Further, the studies used to derive this ratio were not truly experimental in terms of study design, but instead were quasiexperimental or preexperimental designs. The heterogeneity of these studies reduces the reliability of the mean value.

Recommendations for Future Research

Although significant gains have been made in the quality of economic assessments of clinical pharmacy services, opportunities still exist to improve the study designs used in these evaluations. Studies of this type are dependent on the ability of the particular design to establish a relationship between the intervention(s) and the resultant observed outcome(s). Several archetypical study designs (experimental, quasiexperimental, and preexperimental) have been described and are illustrated in Table 6.[85] Future efforts to contribute in a meaningful way to the body of evidence surrounding the value of clinical pharmacy services should be made with an appreciation of the strengths and weaknesses of these study designs. Several recommendations for future research deal with considerations of study design.

Studies that aim to establish a causal relationship (e.g., evaluate whether a program has made a difference) must address the issue of internal validity. The key question of internal validity is whether observed changes can be attributed to the program (or intervention) and not to other possible causes or alternative explanations. Several conditions need to be met to establish a causal relationship, including temporal precedence (shows that the program happened before the effect), covariation of cause and effect (when program is present, effect is present and

when program is absent, effect is absent), and exclusion of other plausible explanations.

Potential threats to internal validity may arise from multiple sources. Threats that apply to studies when a single group receives a program with no comparator include history (events that take place during the study that might have an effect on the outcome), maturation (changes that subjects being studied undergo during the course of the study that might have an effect on the outcome), and regression to the mean (a statistical phenomenon that occurs whenever a nonrandom sample from a population is studied with two measures that are imperfectly correlated). These threats can be avoided by using a comparison (or control) group, but this leads to other threats. In studies with a control group, selection bias is the primary threat and may exist when any factor other than the program leads to posttest differences between groups. Randomization is done to reduce the possibility of selection bias.

Incorporating all desired elements of a proper study design into an evaluation of a clinical pharmacy service is often difficult. Selection of an appropriate control group and randomization in particular may be problematic. One study included in our review provides a good model for study design. In this study, the authors used a quasiexperimental design to evaluate pharmaceutical care in a Medicaid population.[48] Baseline data were measured for two groups (intervention and control) before the intervention, which was applied to only one cohort (intervention group), followed by another period of observation and measurement. The primary outcome evaluation was conducted between the two cohorts on the difference in relative change between baseline and postintervention periods. Though not randomized, this study is a good example of the use of a control and sequence of observation.

Whereas a rigorous study design may be considered ideal, there are disadvantages to consider. Such a design requires the availability of two distinct cohorts, does not preclude the possibility that the nonintervention group may become "contaminated" by the changes made in the intervention group, and may be relatively expensive and time-consuming to conduct. As investigators make study design decisions, they are forced to compromise on various design elements, often choosing less rigorous designs in the interest of feasibility and practicality.

Once the study is complete, investigators should consider additional factors that increase the credibility of their results. Articulating the purpose of the analysis in explicit terms (both when proposing the study and reporting its results) will assist the investigator in ensuring that the study is designed appropriately and will allow readers to more easily understand and apply the results. Also, greater attention must be paid to measures of cost, both in terms of the resources needed to conduct the clinical pharmacy intervention and the measure of cost as a consequence. Surprisingly, the investment required to provide clinical pharmacy services (e.g., personnel) was not included in just over 50% of the studies we reviewed. This is a critical component in the determination of net benefits and must be included in all future studies.

With regard to the measurement of economic consequences of clinical pharmacy services, many evaluations are based on the "cost of what might have been" had the intervention not occurred. For example, if an intervention is performed that discontinues a potentially harmful or costly therapy, this method assumes that the change would not have been made otherwise and therefore the service should be credited with improving outcomes or reducing cost. However, the impact of these assumptions is rarely measured (with sensitivity analysis) and may be the single most important vulnerability in the results of these studies. In these situations, investigators should either conduct sensitivity analysis on such assumptions, or preferably, use comparator cohorts (which avoids the need to make such assumptions).

Further, in measuring economic outcomes that result from clinical pharmacy services, researchers must take into account the inflationary changes that occur over time. Health care costs, and especially pharmaceuticals, have seen exponential increases in recent years. For example, drug costs have risen 10%–20%/year over the past decade (from both price inflation and increased utilization). Interventions that produce absolute reductions in expenditures over long periods also might be credited with avoiding costs associated with inflation.

Future research should continue to be conducted in alternative practice sites and of contemporary types of pharmacy services. For example, a paucity of evidence exists on the economic impact of collaborative practice models, though clearly this is an important direction for the profession and should be addressed by future research. Also, relatively few articles exist on the interface between technology and clinical pharmacy services. As technology is

implemented (either in drug distribution or to assist in provision of clinical services), the premise is that time is freed up for pharmacists to provide more patient care. However, few evaluative studies have been conducted to demonstrate this. Finally, it would be useful if a national or international agenda for this type of research were promoted by a representative group of pharmacy organizations to ensure that studies are conducted in practice sites and of the types of pharmacy services for which data are lacking. This effort would facilitate the availability of information that might support coordinated efforts to seek reimbursement of clinical pharmacy services.

The future success of pharmaceutical care models is increasingly dependent on our ability to provide compelling evidence of the value of clinical pharmacy services and to articulate that value to financial decision makers. The rising rate of inflation for pharmaceuticals, driven by the increasing age of our population and dramatic advances in pharmaceutical technology, has made drug resource consumption the most common cost containment target for health care systems. As across-the-board cuts are demanded of pharmacy departments, pharmacy leaders often are faced with the choice of reducing drug expenses or labor costs. Whereas limiting inefficient drug use may partially achieve the required cost containment, pharmacy managers must both articulate and provide evidence of the value of clinical pharmacy services so as to protect, or even expand, existing positions. The impact that clinical pharmacy services have by reducing overall health care expenses and improving patient outcomes should be fundamental to this message.

Studies of the cost impact of clinical pharmacy services have provided encouraging results, but we must continue to remain prepared to defend our participation in the care delivery process. We must improve both the quantity and quality of studies examining the value of clinical pharmacy services, raise the level of awareness and understanding of that research, and continue to find new ways to contribute to the health and well-being of patients; and this should be done in a manner that is convincing to health care decision makers.

Conclusion

The summarized data provide evidence of the economic benefit of clinical pharmacy services based on literature published between 1996 and 2000. The body of evidence on this topic has become more diverse, includes more contemporary practice sites and types of services, and has improved in the strength of study design and methodology. The information described in this article will assist pharmacy practitioners and managers in assessing both the costs to provide clinical pharmacy services and the anticipated economic benefits of such services. Our recommendations for future research may further enhance the strength of evidence of this literature and the conclusions that may be drawn from it.

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Appendix 1. Fifty-nine Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service

Objective	Analytic Method	Comparison Group	Input Costs Included in the Study	Resource Use or Economic Outcomes Included in the Study	Economic Results[a]	Comments by Reviewers
University hospital						
Disease management						
To evaluate the contribution of pharmaceutical care on improvement of disease and cost of asthma treatment[17]	OA	Control group	None	Change in emergency department and outpatient visits, drug costs for asthma agents	Over the 16-mo study period, drug costs were higher in the pharmaceutical care group than in the control group ($166 vs $79/patient/mo); however, frequency of emergency department and outpatient visits was lower.	Clinical outcomes also measured, conducted in Japan, monetary units expressed as U.S. dollars, small sample size (n=15) in intervention group, no consideration of costs to provide service, effect of emergency department and office visits not costed out, no mention of discounting, methodology and results not well described.
General pharmacotherapeutic monitoring						
To confirm that a reduction in LOS, and pharmacy and hospital costs can be achieved with direct pharmacist participation in a patient care team[18]	OA	Control group	None	Change in LOS, health care costs, and drug costs	Over the 9-mo study period, pharmacist participation reduced LOS by 1.3 days, prescription costs by $301/admission, and hospital costs by $1654/admission.	No consideration of costs to provide service.
To identify differences in the rate and cost of pharmacotherapeutic interventions performed for HIV-positive and HIV-negative patients[19]	OA	Control group	None	Drug cost reduction/intervention, LOS	Over the 2-mo study period, in HIV-positive and HIV-negative patients, $134 and $27 was saved/pharmacist intervention, respectively; there was no difference in LOS.	Clinical outcomes also measured, no consideration of costs to provide service, not necessarily designed to evaluate impact of clinical pharmacy services but rather difference between HIV-positive and HIV-negative patients.
To assess the impact of pharmacist initiated interventions on cost savings[20]	OA	Control group, randomized	None	LOS, change in drug costs	During the 30-day study period, the group randomized to pharmacist intervention had drug costs that were 41% lower than those of the control group; annualized savings was estimated to be $394,000.	Clinical outcomes also measured, no consideration of costs to provide service.
To describe a method used to collect data on cost savings and cost avoidance achieved through pharmacist intervention[21]	COD	None	Personnel time and benefits	LOS, drug costs savings, drug cost avoidance, change in hospital stay costs	Over the 10-mo period, 4050 interventions were documented, which represented a therapy cost savings of $487,833 and a cost avoidance of $158,563 in prevention of additional hospital days; costs for personnel were $38,000, B:C ratio was 17.01:1[b].	Lack of control group was a limitation in the study design.
To develop, implement, and assess the outcomes of a system for providing care to patients in a medical progressive care unit[22]	OA	Before and after intervention	None	Hospital readmissions, LOS, change in drug costs	Net drug costs were reduced by $6535 over the 2-mo intervention period, annualized savings were estimated to be $39,207,[b] and no difference was noted in readmissions or LOS.	Clinical outcomes also measured, no consideration of costs to provide service.
To describe the consequences of providing clinical pharmacy services[23]	OA	Historical group	None	Drug cost difference	Over the 9-mo period, drug costs were reduced by 50% (antibiotics, 998,299 drachmae savings/mo) and 36% (respiratory agents, 35,832 drachmae savings/mo) when compared with historical time point.	Conducted in Greece, monetary units in Greek drachmae, very little information provided on the method used to quantify savings associated with the program, no consideration of costs to provide service.
Target drug program						
To determine the effect of daily consultation by a team of hospital pharmacists, compared with physician management, on the accuracy and rapidity of optimizing warfarin therapy[24]	CBA	Historical group (physician managed)	Personnel time and benefits	Reduced LOS, heath care costs	Pharmacist group lowered LOS significantly (2.6 days), cost to provide the program was $107,000 and costs avoided were $824,000, and the B:C ratio was 8:1.	Clinical outcomes also measured, financial impact provided at the end of the article (after Discussion).
To evaluate the clinical and economic impact of guidelines for G-CSF and pharmacist intervention in HIV-positive patients[25]	OA	Historical group	None	Doses of G-CSF, charges for G-CSF, LOS	G-CSF utilization decreased, charges decreased from $200 to $112/patient day, and the estimated annual savings was $90,040.	Clinical outcomes also measured, no consideration of costs to provide service, used charges rather than costs.

Appendix 1. Fifty-nine Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service (continued)

Objective	Analytic Method	Comparison Group	Input Costs Included in the Study	Resource Use or Economic Outcomes Included in the Study	Economic Results[a]	Comments by Reviewers
To evaluate the impact of a computer-assisted pharmacy program on the number of days of antibiotics and the number of adverse effects[26]	OA	Before and after intervention	None	Antibiotic use and drug costs, health care costs avoided owing to decreased adverse drug reactions	Inappropriate antibiotic use decreased 6%, treatment duration decreased by 1.8 days, fewer adverse drug reactions occurred, and drug costs decreased by $30/patient; total costs avoided were $100,000 over 12 mo.	Clinical outcomes also measured, no consideration of costs to provide service.
To evaluate clinical and economic end points achieved by a pharmacist-managed anticoagulation consult service vs usual care[27]	CBA	Control group (usual care)	Personnel time, opportunity costs	LOS, health care costs	Total hospital costs/patient were lower in the pharmacist group than in the control group (median $1594 vs $2014), LOS was significantly shorter (median 5 vs 7 days), opportunity costs for pharmacist time was $82/patient, net savings/patient was $338, and B:C ratio was 5:1.	Clinical outcomes also measured, well-designed study, conducted at two sites.
Patient education or cognitive service						
To determine if drug discharge counseling by inpatient pharmacists is cost-effective[28]	CEA	Control group	Personnel and benefits, opportunity costs	None	The incremental cost to increase satisfaction from 79% to 91% was $190/satisfaction point gained; it would cost $84,000 for all eligible patients to receive program.	Cost-effectiveness analysis (all costs considered as inputs, outcome was patient satisfaction), level of patient satisfaction obtained from a mailed survey.
Other						
To determine potential cost avoidance resulting from a drug information service that responds to drug information requests[29]	COD	None	Personnel, subscriptions, telephone and other related expenditures	Health care costs avoided, LOS	Forty-nine percent of drug information responses resulted in cost avoidance totaling $190,000 over the 30-day study period; annualized cost avoidance of $1,735,585 estimated, whereas cost to provide service was $145,950 for 1 year; in sensitivity analysis, the B:C ratio was 2.9:1–13.2:1, and base case B:C ratio was 11.89:1[b].	Clinical outcomes also measured, used a model with cost-avoidance values based on published literature, no comparison group.
Community hospital						
General pharmacotherapeutic monitoring						
To prospectively analyze clinical pharmacy intervention for an acute-care adult psychiatric inpatient population[30]	OD	None	None	Reduced inpatient days and associated costs	Over the 6-mo period, 91% of the 204 interventions were accepted; the estimated cost avoidance was $24,700 (Australian dollars) as a result of 38 fewer hospital days.	Conducted in Australia, monetary units in Australian dollars, financial analysis described in the Discussion, costing methods not well described, lack of control group was a limitation in the study design, no consideration of costs to provide service.
To prospectively evaluate the impact of a clinical pharmacist rounding in a medical intensive care unit[31]	COD	None	Personnel time	Drug costs avoided	Over the 8-wk study period, 193 interventions were documented, 62% resulted in decreased costs, 3% cost avoidance, and 15% increased expenditures; a net benefit of $3218 was realized ($101/pharmacist day), extrapolated to $25,140/yr/pharmacist (based on an assumed 250 days/yr, 10 hrs/day, 5 days/wk spent in clinical activities); B:C ratio was 2.72[b].	Costing methodology not well-described, lack of control group a limitation in the study design.
To describe the revision of a transitional care unit pharmacy consultation program and to compare key outcomes[32]	OA	Historical group	None	LOS, drug costs avoided	LOS was reduced from 11.14 to 7.54 days; cost savings were estimated to be $15,000 in the first yr and $23,000 in the second yr.	No consideration of costs to provide service, discounting not performed.
To measure the effect of pharmacist participation in intensive care unit rounds on the rate of preventable adverse drug events caused by prescribing errors[33]	OA	Before and after intervention, and control group	None	Costs avoided by preventing adverse drug events	Preventable adverse drug events decreased by 66% in the postintervention period; extrapolated costs avoided were $270,000/yr.	Clinical outcomes also measured, cost to provide service not considered, cost of adverse drug events derived from literature.
To assess the costs and economic benefits of a clinical pharmacy service resulting from departmental reengineering[34]	CBA	Before and after intervention	Personnel time and benefits, drug information resources	Drug cost/patient day, cost avoidance	Drug costs decreased by $358,056 after 1 yr ($7/patient day); the cost to provide the service was $140,505, thus net benefit was $217,551; inflation-adjusted B:C ratio was 2.66:1.	Includes projected economic impact of clinical pharmacy services as well as actual economic impact after implementation.

Appendix 1. Fifty-nine Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service (continued)

Objective	Analytic Method	Comparison Group	Input Costs Included in the Study	Resource Use or Economic Outcomes Included in the Study	Economic Results[a]	Comments by Reviewers
To document the financial impact of pharmacists providing pharmaceutical care[35]	OD	None	None	LOS, drug and drug supply costs avoided, nursing time saved	Over the 1-mo period, there were 120 interventions resulting in a total of $4269 in costs avoided.	Methods not well described, no control group, no consideration of costs to provide service.
To demonstrate pharmacist contributions to patient care and cost avoidance[36]	CBA	Historical group	Personnel time	Drug costs avoided	Cost avoidance due to clinical pharmacy interventions was $6310 over 2 mo, investment required to perform the service was $1485, projected annual cost avoidance was $37,757, and B:C ratio was 4.25:1.	Costing methodology not well described.
To describe the influence of pharmacy faculty, residents, and students attributed to their involvement in patient care activities[37]	OD	None	None	Hospital and drug costs avoided	Over the 21-mo study period, 2873 interventions were documented from which the estimated costs avoided were $172,655.	No consideration of cost to provide service, no control group, dollar values (savings) for each type of intervention were arbitrarily set, no discounting.
To evaluate the cost impact and clinical benefit of a pharmacist rounding in a cardiac intensive care unit[38]	COD	None	Personnel time	Drug costs avoided	For the 23-day study period, drug costs avoided totaled $3106, whereas pharmacist time was 35.5 hrs or $887; the net savings was $2219, and the B:C ratio was 3.50:1[b].	No control group, costing methodology not well described.
To describe the contribution of managed care pharmacists who participate in clinical rounds at a contract hospital[39]	COD	None	Personnel time	Drug cost savings, hospital days avoided	Over 14 mo, the program saved $523,907 ($149,907 in drug cost savings and $374,000 in hospital days); the cost to provide the program was $57,643, thus the net was $466,264, and the B:C ratio was 9.09:1[b].	No control group.
To compare different levels of clinical services (drug order review only, basic pharmacotherapeutic monitoring, concurrent pharmacotherapeutic monitoring)[40]	OA	Control group	None	Drug cost savings	Pharmacists submitted 4559 recommendations; based on a sample of cases, drug costs were reduced an average 40%/recommendation (equivalent to a mean of $4.75 [Canadian dollars] savings/case/24 hrs of drug therapy).	Conducted at 17 sites (hospitals) in Canada, monetary units in Canadian dollars, no consideration of cost to provide service.
Pharmacokinetic drug monitoring						
To determine the benefits of proactive pharmacokinetic service on aminoglycoside therapy outcomes[41]	CEA	Before and after intervention	Personnel time, additional laboratory tests	None	The pharmacokinetics service decreased monitoring, therapy duration, LOS, and costs (total costs in the intervention vs control group were 13,125 guilders and 16,862 guilders, respectively); there was a trend toward higher mortality in the control patients.	Cost-effectiveness analysis (all costs considered inputs, outcomes were lives saved); in results, costs were less and effects (lives saved) were greater for the intervention group; conducted in the Netherlands, monetary unit expressed as guilders.
Target drug program						
To measure the clinical and economic impact of a pharmacist and infectious disease fellow team antibiotic optimization program[42]	OA	Control group	None	LOS, days of antibiotic therapy, antibiotic charges	Antibiotics charges/patient were $386 less in the intervention group, and the intervention group spent 1.6 fewer days taking intravenous antibiotics.	Clinical outcomes also measured, no consideration of costs to provide service.
To evaluate the clinical and economic impact of pharmacy interventions to promote switching from intravenous to oral clindamycin[43]	CMA	Before and after intervention	Personnel time, drug costs, costs to treat adverse drug reactions	None	The intervention reduced the costs/patient of clindamycin by 5246 pesetas, mainly from less utilization of intravenous drug and fewer days of therapy; there was no change in LOS, and pharmacist time/patient was reduced.	Started as CEA, clinical outcomes were not statistically different, so final analysis was CMA, conducted in Spain, monetary unit expressed as Spanish pesetas also converted to Euros, conducted at two sites (hospitals).
Other						
To describe the successful addition of a pharmacist to the case management department[44]	OD	None	None	LOS, decrease in drug costs	During the 6-mo period, cost savings were $13,483 and averaged $13/patient; LOS decreased from 4.3 to 4.0 days.	No consideration of costs to provide program, no control group.
To assess the accuracy of patient reports of drug allergies and to determine the cost-effectiveness of pharmacists efforts to clarify and document allergies[45]	COD	None	Personnel time	LOS, no economic outcomes	Over 3-mo study period, 27 interventions were documented and resulted in a 4.4-day reduction in LOS; the cost to provide the service was $750.	Included both inpatients and outpatients, did not cost out economic impact of reduced LOS (economic benefit), no control group.

Appendix 1. Fifty-nine Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service (continued)

Objective	Analytic Method	Comparison Group	Input Costs Included in the Study	Resource Use or Economic Outcomes Included in the Study	Economic Results[a]	Comments by Reviewers
Veterans Affairs or government hospital						
General pharmacotherapeutic monitoring						
To determine the number, type, and drug cost avoidance of interventions made by pharmacy personnel (pharmacists and technicians) in hematology or oncology patients[46]	OD	None	None	Drug costs avoided	During the 8-mo intervention period, 503 interventions were made, resulting in $23,051 in avoided drug costs.	Included both inpatients and outpatients, no consideration of costs to provide program, no control group.
Target drug program						
To compare clinical and economic outcomes of a pharmacist-run antibiotic control program[47]	OA	Historical	None	LOS, hospital readmissions, costs of antibiotics and other drugs	Total acquisition cost of intravenous antibiotics was reduced by 30.8% ($291,885) during the postintervention period (2 yrs), the intervention group reduced LOS by 2.4 days, and no change occurred in readmission rates.	Clinical outcomes also measured, discounting not performed, no consideration of costs to provide program.
Hospital-associated clinic						
General pharmacotherapeutic monitoring						
To evaluate the economic impact of a pharmaceutical care services program for a state Medicaid population[48]	CBA	Before and after intervention, and control group	Fixed budget for program	Change in health care utilization and costs, prescription drug costs	The cost to provide the program was $84,363 (1 yr), the direct benefit of the program was $173,651, so the net present value was $89,288 or $204/patient; thus, the B:C ratio was 2.06:1[b]; extrapolation to all of the state Medicaid patients could result in $22 million in savings in the next fiscal yr.	Well-designed and -conducted study, conducted at four hospitals.
Target drug program						
To compare clinical and economic outcomes in newly anticoagulated patients treated with usual care vs those treated at a pharmacist-run anticoagulation clinic[49]	OA	Control group	None	Hospital and emergency department visits and associated costs	Hospital and emergency department visits related to anticoagulation were 73% lower in the pharmacist-managed group (visits unrelated to anticoagulation were also lower), cost savings for both anticoagulation-related and unrelated hospital and emergency department visits were estimated to be $162,058/100 patients/yr.	Clinical outcomes also measured, no consideration of costs to provide program.
To test whether angiotensin-converting enzyme inhibitor dosage adjustment by a clinical pharmacist could improve rehospitalization rates and cost of care in heart failure[50]	OA	Control group	None	Hospital readmissions and associated charges; charges for outpatient visits, laboratory tests, and procedures	Hospital readmissions and mean total charges were significantly higher for patients whose physicians did not accept pharmacists' recommendations than for patients whose physicians did accept recommendations ($9848 vs $3808, respectively, at 180 days).	Clinical outcomes also measured, no consideration of costs to provide service.
To evaluate the effectiveness and outcomes of clinical pharmacists' recommendations on oral H_2 antagonists[51]	OA	Control group and historical control, randomized	None	Cost savings due to therapeutic interchange	There was a 30% reduction in annual costs due to the intervention ($28,104 vs $19,703), resulting in a projected annual cost savings of $8400 to the hospital.	Clinical outcomes also measured, no consideration of costs to provide service.
To measure emergency department visits and humanistic outcomes of a pharmacist-run anticoagulation clinic[52]	CBA	Before and after intervention	Personnel time, start-up costs, disease management software	Hospital costs avoided	Projected savings (benefit) over 2 yrs was $484,200, and the cost to provide the service over the same period was $250,720; thus, the net benefit was $182,103 and the B:C ratio was 1.60:1[b].	Clinical outcomes also measured, savings estimates were based on expected patient volume and results from previously published studies, no discounting.
Patient education or cognitive service						
To describe the experience with a pharmacist-run counseling service in an obstetrics and gynecology clinic[53]	OD	None	None	Physician services costs avoided	Over 10 mo, the estimated cost avoidance was $59,000 based on obstetrics and gynecology physician costs at a rate of $300/hr.	No consideration of costs associated with the pharmacist time or other costs associated with providing the service, methods not well described, no control group.

Appendix 1. Fifty-nine Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service (continued)

Objective	Analytic Method	Comparison Group	Input Costs Included in the Study	Resource Use or Economic Outcomes Included in the Study	Economic Results[a]	Comments by Reviewers
Veterans Affairs or government clinic						
Disease management						
To determine if routine follow-up with an ambulatory care clinical pharmacist improves the percentage of patients achieving lipid goals[54]	CA	Control group	Hospital and clinic visits and cost, laboratory and drug costs	None	No significant difference in overall costs despite increased number of pharmacist visits.	Clinical outcomes also measured, cost to provide program (i.e., pharmacist time) accounted for in cost of clinic visit, multiple site study, separate analysis of a subgroup of patients from a previous study.[59]
To evaluate the impact of a pharmacist-run *Helicobacter pylori* clinic[55]	OD	None	None	Drug costs avoided	Estimated cost avoidance of $9585 associated with the intervention ($95/patient).	Clinical outcomes also measured, no consideration of costs to provide service, no control group.
General pharmacotherapeutic monitoring						
To determine the effectiveness of a pharmacist in recognizing and resolving drug therapy problems, decreasing drug therapy costs, and maintaining positive clinical outcomes in a geriatric ambulatory clinic[56]	CBA	Control group	Personnel time, laboratory tests	Change in drug costs, change in laboratory costs	Cost to provide program for 1 yr was $10,470 ($7250 personnel, $142 laboratory tests, $3080 new therapy started), economic benefit from discontinuing unnecessary drugs was $18,260 over same period, net savings was $7788, and B:C ratio was 1.74:1[b].	Clinical outcomes also measured, well-designed study.
To evaluate the effectiveness of a pharmacist intervention program in elderly patients[57]	CEA	Control group	Personnel time (training and intervention), beeper, educational supplies, health care utilization costs	None	The incremental cost of the program was $120/patient, the drug appropriateness index increased by 4 points due to the intervention, the incremental cost-effectiveness ratio was $30/1-unit improvement in drug appropriateness index.	Cost-effectiveness analysis with drug appropriateness index as outcome, all economic variables were considered costs.
To determine the impact of a pharmacotherapy consult clinic on outcomes and cost avoidance[58]	CBA	Historical group	Personnel time, stethoscope, reference books	Cost avoided due to reduced health care resource utilization	Over the 1-yr study period, costs avoided due to the intervention totaled $54,731 of which $16,786 were prescription costs avoided and $37,945 were other health care costs avoided; the B:C ratio was 5.8:1.	Clinical outcomes also measured.
To determine if a clinical pharmacist could affect resource use, and economic and humanistic outcomes in an ambulatory high-risk population[59]	CA	Control group	Hospital and clinic visits and cost, laboratory and drug costs	None	No significant difference was noted between the intervention and control groups in health care costs either at baseline or after the follow-up or when adjusted for age, sex, or site.	Humanistic outcomes also measured, all economic variables were considered costs and combined, multiple site study.
To describe the experience and outcomes of a clinical pharmacy service in a primary care clinic setting[60]	OD	None	None	Drug costs avoided	In the most recent full yr of the service (1999), 24,873 interventions were made from which the estimated cost avoidance was $1,085,560.	Clinical outcomes also measured, no consideration of costs to provide service, no control group, cost evaluation a minor part of this study, and costing methods not well described.
Target drug program						
To identify the clinical and economic impact of a pharmacist-based program encouraging the use of less costly therapeutic alternatives[61]	OD	None	None	Drug cost savings	Over the 12-mo evaluation period, interventions reduced drug costs by $349,925 ($155/patient).	Clinical outcomes also measured, no consideration of cost to provide service, no control group.

Appendix 1. Fifty-nine Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service (continued)

Objective	Analytic Method	Comparison Group	Input Costs Included in the Study	Resource Use or Economic Outcomes Included in the Study	Economic Results[a]	Comments by Reviewers
Patient education program						
To describe outcomes of a multidisciplinary self-care program and health promotion pharmacy service[62]	COD	None	Work hrs, resources, drugs, supplies	Change in emergency department and clinic visits and associated costs, use of nonprescription drugs	Estimated 6-mo potential cost avoidance was $42,300 for the clinics and $27,150 for the emergency department, the program cost was $12,109, and the B:C ratio was determined by the authors as 11:1 but calculated by reviewers as 5.7:1[b].	No control group, apparent discrepancy in the calculation of B:C ratio.
Other						
To document outcomes of a pharmacist and nurse telephone-based care program that provides clinical consultation and interventions[63]	COD	None	Personnel time and benefits, program start-up costs	Cost avoidance due to unnecessary visits	The service prevented an estimated 16 office visits/day; estimated annual net cost avoidance was $677,671 (costs avoided less program costs).	Humanistic outcomes also measured, no information on proportion of savings due to pharmacist services vs nurse services, only total savings of program provided, no comparison group.
Free-standing clinic or physician's office						
Disease management						
To compare the quality of care and financial impact of a drug service compared with a joint drug and pharmacotherapy service for patients with diabetes [64]	CBA	Control group	Personnel time, laboratory tests	Reduction in medical care charges due to reduced A1C	Over the 3-mo study period, there was a projected reduction of $6860 in medical charges due to improved A1C and a reduction of $1326 due to decreased physician visits; the cost to provide the service was $1542, and net savings was $6,644; the B:C ratio was 5.31:1[b].	Clinical outcomes also measured, small sample, methods not well described.
Other						
To determine whether pharmacists in general practitioner offices result in reduced drug costs in excess of personnel costs[65]	CBA	Control group	Personnel time, training, set-up costs	Change in drug costs	Cost of service was 163,000 pounds for 1 yr, the rise in cost/prescription was 0.85 pound in the intervention group and 2.25 pounds for the control, a difference of 347,000 pounds resulting from the program; the net savings of the program was 184,000 pounds and the B:C ratio was 2.13:1[b].	Conducted in the United Kingdom, monetary unit expressed in British pounds, conducted at multiple sites (physicians' offices).
Intermediate or long-term care facility						
General pharmacotherapy monitoring						
To describe outcomes of clinical pharmacy services in a capitated geriatric care program[66]	CA	Before and after intervention	Personnel costs and cost of drugs dispensed	None	The total cost to provide pharmaceutical services (salary plus drugs) decreased from $120/patient/mo to $77 after 1 yr; gross cost savings were $102,768 in 1995.	All economic variables were considered costs.
To measure the impact of clinical pharmacy services on drug utilization costs and drug errors in an intermediate care facility for the developmentally disabled[67]	OA	Historical group	None	Pharmacy drug cost/resident day	Despite a reduction in the number of drug doses/day after the intervention, there was an overall increase in pharmacy drug cost/resident day (65%).	Clinical outcomes also measured, methodology not well described, components of "pharmacy cost" not defined.
Community pharmacy						
Disease management						
To evaluate the impact of clinical pharmacy services in a community pharmacy on blood pressure control, quality of life, patient satisfaction, quality of care, and cost of care[68]	OA	Control group	None	Change in physician office visits and prescriptions and associated charges	Charges associated with office visits and drugs were higher in the intervention than in the control group (mean total charges $1106 vs $526), though the intervention group had more comorbid conditions.	Clinical and humanistic outcomes also measured, no consideration of costs to provide service, conducted at multiple sites.
To evaluate the economic impact of pharmacist interventions using a disease management model in a retail pharmacy for patients with diabetes, hypertension, asthma, or hyperlipidemia[69]	OA	Control group	None	Medical and prescription utilization and costs	After controlling for age, comorbid conditions, and disease severity, total costs (medical and prescription claims) were lower in the intervention group ($723 vs $1017/patient/mo), while prescription costs did not differ during the 17-mo study.	Did not include cost to provide service in the analysis but stated it in the Discussion, did not discount dollar values over study period, conducted at multiple sites.

Appendix 1. Fifty-nine Articles Included in This Review by Setting of Evaluation and Type of Clinical Pharmacy Service (continued)

Objective	Analytic Method	Comparison Group	Input Costs Included in the Study	Resource Use or Economic Outcomes Included in the Study	Economic Results[a]	Comments by Reviewers
General pharmacotherapeutic monitoring						
To determine the economic impact of an intervention program in community pharmacies and effect of advanced education and payment for services of pharmacists[70]	CA	Control group and before and after intervention	Program costs, drug costs, health care costs	Economic outcomes combined with input costs	The proactive intervention group reduced prescription costs by $85 (Australian dollars)/1000 prescriptions (a 6-fold savings compared with control); potential savings to the Australian health care system is $15 million (Australian dollars)/yr.	Conducted in Australia, monetary units expressed in Australian dollars, intervention not well described, program costs included telephone calls and pharmacist time.
To document pharmaceutical care activities and associated outcomes in rural community pharmacies[71]	OD	None	None	Potential health care cost savings due to reduced hospitalization and office visits	Over a 2-mo period, 878 interventions were made; the estimated cost savings was $752,391.	No consideration of costs to provide services, no control group, costing methodology not well described and was based on costs obtained from external sources, multiple site study.
Patient education or cognitive service						
To assess a resource-based system of payment to pharmacies for cognitive services provided to Medicaid enrollees, and to assess factors associated with the provision of cognitive service[72]	CA	Control group	Payment to pharmacies, change in drug costs	None	Costs appear to have exceed benefits for those pharmacies who received payment (cognitive service fee) for providing the service.	Costs to provide program were included as cognitive service fee paid to one of the three groups but in analysis lumped together with drug costs (savings), conducted at 300 community pharmacies, a second article using the same data was excluded from this review but may provide additional information.[10]
Other						
To increase accessibility of flu vaccinations in a rural community by establishing a community pharmacy-based vaccine administration program[73]	COD	None	Vaccine and supplies, advertising, (not personnel time)	Reimbursement from patients or Medicare	During first year, 343 doses of vaccine were administered from which reimbursement of $3276 was received (170 patients paid cash at $11 each, 173 patients covered by Medicare at $8 each); costs incurred were for vaccines ($652), supplies ($257), advertising and other ($500); net profit was $1868.	Clinical outcomes also measured, pharmacist time not considered as a program cost.
Health maintenance organization						
Patient education or cognitive service						
To investigate the effects of three pharmacist-consultation models on clinical and resource outcomes in health maintenance organization–owned community pharmacies[74]	OA	Control group	None	Utilization and costs of office visits, drugs, hospital stays, and total health care costs	The group that received consultation based on the intervention model had a reduction in hospital admissions and overall health care costs; there was no change in drug costs or office visits.	Clinical and humanistic outcomes also measured, no consideration of costs to provide service, conducted at multiple sites.
To assess the impact on health care utilization and costs of pharmacist consultation provided to patients with diabetes in health maintenance organization–owned community pharmacies[75]	OA	Control group, before and after intervention, randomized	None	Change in hospital and office visit costs, change in drug costs	Pharmacy services in the Kaiser and state groups, respectively, resulted in a 21.9% and 9.9% decrease in total costs for each new prescription filled over a 2-yr period.	No consideration of cost to provide service, multiple site study, separate analyses of a subgroup of patients from a previous study.[74]

A1C = hemoglobin A_1; B:C = benefit:cost ratio; CA = cost analysis; CBA = cost-benefit analysis; CEA = cost-effectiveness analysis; CMA = cost-minimization analysis; COD = cost and outcome description; G-CSF = granulocyte colony-stimulating factor; HIV = human immunodeficiency virus; LOS = length of stay; OA = outcome analysis; OD = outcome description.

[a]Monetary values (except those calculated in B:C ratios) have been rounded to the nearest single whole unit (i.e., the nearest $1).

[b]Calculated by the reviewers.