

# Economic effects of clinical pharmacy interventions: A literature review

THOMAS DE RIJDT, LUDO WILLEMS, AND STEVEN SIMOENS

During the past few decades, clinical pharmacy services have developed around the world.<sup>1</sup> While there is no consensus on the definition of “clinical pharmacy,” all proposed definitions refer to the contribution that pharmacists can make to the realization of high-quality and rational drug therapy.<sup>2,3</sup> In a hospital setting, clinical pharmacy can be defined as the contribution of hospital pharmacists and their assistants to drug therapy as a part of the total care given to patients, in cooperation with physicians and nursing staff, with the goal to optimize the efficiency, effectiveness, and safety of drug therapy.

A recent literature review found that clinical pharmacy interventions in inpatient medical care contribute to improved patient outcomes.<sup>4</sup> Pharmacist participation on physician rounds, drug reconciliation at admission or discharge, and drug-class-specific pharmacist services reduced the frequency of adverse drug events (ADEs) and medication errors and improved medication adherence, patients’ knowledge about their medications, and medication appropriateness. Clinical pharmacy

**Purpose.** Economic evaluations of clinical pharmacy interventions are reviewed.

**Summary.** A variety of clinical pharmacy interventions have been assessed, but the body of evidence relating to any particular type of intervention is small. Cost-saving interventions comprise a small percentage of clinical pharmacy interventions, but they generated substantial savings. Clinical pharmacists provided added value by participating in multidisciplinary teams attending rounds. Clinical pharmacy interventions reduced preventable adverse drug events and prescribing errors, thereby yielding savings related to cost avoidance. Interventions relating to antibiotic therapy lowered costs of care without adversely affecting clinical outcomes. The results of cost-benefit analyses suggested that general clinical pharmacy interventions are associated with cost savings. Most economic evaluations of clinical pharmacy interventions suffered from a number of methodological limitations relating to the absence of a control group without clinical pharmacy interventions, limited scope of costs and outcomes, focus on direct health care costs only, exclusion of pharmacist

employment cost, use of intermediate outcome measures, exclusion of health benefits, and absence of incremental cost analysis. Some avenues for designing future economic evaluations include the use of a control group, detailed descriptions of the interventions provided, evaluations conducted from a societal perspective, consideration of patients’ health benefits when assessing economic effect of interventions and hospital costs, and the inclusion of sensitivity and incremental analyses.

**Conclusion.** Most pharmacoeconomic evaluations of clinical pharmacy interventions demonstrated limitations in their methodological quality and applicability to current practice. Future evaluations should use a comparative study design that includes the incremental cost-effectiveness or cost:benefit ratio of clinical pharmacy interventions from a societal perspective.

**Index terms:** Clinical pharmacists; Clinical pharmacy; Interventions; Methodology; Pharmaceutical services; Pharmacoeconomics; Research

**Am J Health-Syst Pharm.** 2008;65:1161-72

interventions are also associated with cost savings.<sup>5,6</sup> A number of studies have demonstrated the clinical and

economic benefits of clinical pharmacy interventions in hospital and primary care settings.<sup>7-10</sup>

THOMAS DE RIJDT, PHARM.D., is Assistant Head Pharmacist, Department of Pharmacy, University Hospitals, Leuven, Belgium. LUDO WILLEMS, PHARM.D., PH.D., is Professor of Pharmaceutical Sciences, University of Leuven, and Head Clinical Pharmacist, University Hospitals, Leuven. STEVEN SIMOENS, M.SC., PH.D., is Professor of Pharmaco-economics, Research Centre for Pharmaceutical Care and Pharmaco-economics, University of Leuven.

Address correspondence to Dr. De Rijdt at the Department of Pharmacy, University Hospitals Leuven, Herestraat 49, B-3000, Leuven, Belgium (thomas.derijdt@uz.kuleuven.ac.be).

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DOI 10.2146/ajhp070506

Faced with skyrocketing health care costs and limited resources, public policymakers and health care payers have grown increasingly concerned about the costs of health care. Studies of the economic effect of clinical pharmacy can aid decision-makers in determining whether the costs of clinical pharmacy interventions are justified. Three techniques can be used to conduct an economic evaluation of clinical pharmacy interventions: cost-effectiveness analysis, cost-utility analysis, and cost-benefit analysis.<sup>11</sup> Cost-effectiveness analyses quantify a single outcome in a natural unit (e.g., number of ADEs). The incremental cost-effectiveness ratio is calculated as the difference in costs between alternatives divided by the difference in outcomes measurement. This type of analysis is only possible if the same outcomes are being measured. In a cost-minimization analysis—a specific type of cost-effectiveness analysis—only costs are analyzed, and the least costly alternative is chosen, provided that outcomes are known to be equal among alternatives. Cost-utility analyses measure outcomes by specific health-related quality-of-life measures, such as quality-adjusted life years (QALYs). The QALY describes both the quantity and quality of life. Quality of life associated with health is measured on a scale of 0 (reflecting death) to 1 (reflecting perfect health). Quality-of-life data are then combined with estimates of the time period for which the health benefits were used to generate QALYs. Cost-benefit analysis refers to an economic evaluation where outcomes are valued in monetary terms. A monetary value can be assigned to health benefits by means of, for instance, the willingness-to-pay technique. This allows direct comparison with the costs of the clinical pharmacy intervention and the estimation of net worth (benefits minus costs) of the treatment alternatives. The results of a cost-benefit analysis may be stated

in the form of a net benefit, a net loss, or a cost:benefit ratio.

This article reviews the most recent data related to the efficiency of clinical pharmacy interventions, identifies gaps in the evidence base, and proposes avenues for designing future economic evaluations of clinical pharmacy interventions.

### Methods

**Study design.** A literature review focused on clinical pharmacy interventions in the hospital setting was conducted. Studies concerning outpatient clinics, veterans clinics, and nursing homes were excluded, as the specific populations and diseases treated and their financing make them incomparable with inpatient hospitals. To be included in the review, studies had to exhibit the two defining characteristics of an economic evaluation: a comparison of at least two treatment options (i.e., to provide clinical pharmacy services or not) in terms of both costs and outcomes.<sup>11</sup> Costs refer to direct health care costs, including costs of drugs, laboratory tests, contacts with health care professionals, and hospitalization, and indirect costs of productivity loss incurred by patients. Some economic evaluations of clinical pharmacy interventions use the terms “cost savings” to denote savings resulting from a change in drug therapy and “cost avoidance” to refer to the financial effect of avoiding an ADE or additional hospital days. Outcomes (e.g., length of hospital stay, days to readmission, death rate, number of ADEs, quality of life, need to restart therapy) refer to the benefits of the therapy received by the patient.

Studies were identified by searching the following electronic databases through August 2007: PubMed, National Health Service Economic Evaluation Database, Cochrane Library, EconLit, and Social Sciences Citation Index. Search terms included “clinical pharmacy,” “pharmaceutical

care,” “inpatient,” “hospitalization,” “hospital pharmacy,” “pharmacy,” “pharmacist,” “economic evaluation,” “cost-utility analysis,” “cost-benefit analysis,” “cost-effectiveness analysis,” “outcome,” “morbidity,” “mortality,” “drug errors,” and “adverse drug reactions” alone and in combination with each other. The bibliography of each study was checked for other relevant studies.

The studies included for review were limited to those published between 1996 and 2007. Earlier publications were considered of limited relevance due to developments in clinical pharmacy interventions over time. Studies were eligible for inclusion regardless of the language in which they were written.

**Data collection and analysis.** For each study, a data collection form was completed which collected information about authors, type of economic evaluation, sample size, setting, intervention, length of study period, cost year, costs, and outcomes. Details about the number of patients or clinical pharmacy interventions studied were also included. If reported, data regarding the type of hospital and type of ward in which clinical pharmacy interventions occurred were also included.

Data collection forms were independently completed by two reviewers (a hospital pharmacist and a pharmacoeconomist). Any disagreements between the two reviewers were resolved by a third reviewer (a hospital pharmacist). If there was still no consensus, a decision was made by the team of seven clinical pharmacists and one pharmacoeconomist working at University Hospitals Leuven.

A qualitative appraisal of the methodological quality of included studies was conducted by using a checklist to assess the perspective of the study, study design, scope of costs and outcomes, measurement and valuation of costs and outcomes, allowance for uncertainty, and appli-

cation of an incremental analysis of costs and outcomes.<sup>11</sup> An economic evaluation can be carried out from different perspectives such as that of the society, health care payer, hospital, or patient. The perspective determines which and how costs and outcomes are identified, measured, and valued in the economic evaluation. In terms of study design, an economic evaluation can accompany a clinical study (a piggyback study). Piggyback studies can track clinical pharmacy interventions or compare a group of patients who received clinical pharmacy interventions with a group who did not. In addition to piggyback studies, economic evaluations can model treatments, costs, and outcomes associated with clinical pharmacy interventions.

The scope of costs and outcomes refers to whether the economic evaluation has considered all costs and outcomes that are relevant to the perspective of the evaluation, as all relevant costs and outcomes must be appropriately measured and valued. The robustness of results can be tested by conducting a sensitivity analysis to account for uncertainty of key estimates and assumptions made during the identification, measurement, and valuation of costs and outcomes. Finally, insight into the pharmacoeconomic value of clinical pharmacy interventions requires that the additional costs and effectiveness of clinical pharmacy interventions be calculated and compared with current treatment practices in the absence of clinical pharmacy interventions. This necessitates the calculation of incremental costs rather than average cost-effectiveness ratios.

## Results

The literature search yielded 314 articles. Based on the abstract, articles were excluded from the review because of consideration of costs only ( $n = 24$ ), consideration of clinical aspects only ( $n = 53$ ), no pharmacist intervention documented ( $n$

$= 174$ ), and other reasons ( $n = 16$ ). Of the remaining 47 articles, 26 were excluded because they related to an outpatient clinic, nursing home, or veterans clinic ( $n = 6$ ), consideration of costs only ( $n = 2$ ), absence of pharmacoeconomic aspect ( $n = 3$ ), no pharmacist intervention documented ( $n = 3$ ), and other reasons ( $n = 12$ ). A total of 21 studies met the inclusion criteria. The characteristics of the studies reviewed are shown in Table 1.

**Clinical pharmacy interventions.** The various interventions that clinical pharmacists conducted in the studies reviewed are listed in Table 2. In general, these interventions were undertaken by hospital pharmacists and did not involve dispensing drugs. A variety of clinical pharmacy interventions were assessed, but the body of evidence relating to any particular type of intervention was small. The types of clinical pharmacy interventions in the studies reviewed included cost-saving interventions, multidisciplinary teams attending rounds, prevention of ADEs, prevention of prescribing errors, management of antibiotic therapy, and general clinical pharmacy interventions.

*Cost-saving interventions.* Even though cost-saving interventions may comprise a small percentage of clinical pharmacy interventions, one cost-minimization analysis showed that such interventions can generate substantial savings without compromising patient outcomes.<sup>12</sup> Cost-saving interventions used included discontinuing unnecessary drugs, recommending an oral drug formulation, switching to a less expensive agent, and decreasing a drug's dosage.

*Multidisciplinary teams attending rounds.* One cost-benefit analysis of interventions that occurred in an intensive care unit pointed to cost savings arising from a clinical pharmacist who participated in rounds with a health care team, gathered patient information, evaluated patients' drug therapy, and made therapeutic

recommendations.<sup>13</sup> Another cost-benefit analysis of interventions conducted in a coronary care unit also detected savings in drug costs resulting from recommendations made by a clinical pharmacist.<sup>14</sup> In a cost-effectiveness analysis of interventions that occurred in internal medicine wards at a teaching hospital, pharmacist-recommended modifications to drug therapy resulted in hospital cost savings (excluding the salary of the clinical pharmacist) and a decrease in length of stay.<sup>15</sup>

*Prevention of ADEs and prescribing errors.* Three studies demonstrated a reduction in preventable ADEs with the interventions made by clinical pharmacists.<sup>16-18</sup> One study found a 66% decrease in the number of preventable ADEs per 1000 hospital days,<sup>17</sup> while the number of preventable ADEs per 1000 hospital days documented in another study decreased from 26.5 in the control group to 5.7 in the intervention group.<sup>18</sup> Estimates of the reduction in preventable ADEs differed among studies because the interventions analyzed were conducted in different hospital wards and the definition of ADEs varied among these institutions. One cost-benefit analysis indicated that the prospective review of prescriptions by a clinical pharmacist prevented prescribing errors and generated savings related to cost avoidance.<sup>19</sup>

*Management of antibiotic therapy.* Two cost-effectiveness analyses found savings as a result of a clinical pharmacist reviewing medical records and optimizing antibiotic therapy<sup>20</sup> and as a result of antibiotic therapy interventions made by a multidisciplinary consultation team.<sup>21</sup> As both trials did not find statistically significant differences in clinical outcomes, the authors conducted cost-minimization analyses.

Four cost-effectiveness analyses focused on specific clinical pharmacy interventions related to antibiotic therapy.<sup>22-25</sup> One study demonstrated

Table 1.  
**Characteristics of Studies Included in Literature Review<sup>a</sup>**

Ref.	Type of Evaluation	No. Interventions or Patients	Study Setting (Country)	Study Period (Cost Year)
12	Cost-minimization analysis	259 interventions	University hospital (United States)	30 days (1997)
13	Cost-benefit analysis	193 interventions	MICU in community-based academic center (United States)	8 wk (1996)
14	Cost-benefit analysis	2,879 patients	CCU in acute care teaching hospital (United States)	3 periods of 9 mo <sup>b</sup> (1999)
15	Cost-effectiveness analysis	867 patients	Tertiary care teaching hospital (United States)	9 mo (1994–95)
16	Cost-benefit analysis	37 interventions	University teaching hospital (Canada)	3 mo (2001)
17	Cost-effectiveness analysis, cost-benefit analysis	362 interventions, 125 patients	MICU (intervention) and CCU (control) in teaching hospital (United States)	26 and 40 wk (1995)
18	Cost-effectiveness analysis	147 interventions, 165 patients	GMU in general hospital (United States)	3 mo (2000)
19	Cost-benefit analysis	351 interventions <sup>c</sup>	1 teaching hospital, 1 general hospital (Netherlands)	5 consecutive days per site (2002)
20	Cost-minimization analysis	225 patients	Tertiary care teaching hospital (United States)	3 mo (1997)
21	Cost-minimization analysis	238 interventions	Community hospital (United States)	18 mo (1999)
22	Cost-benefit analysis	199,082 patients	961 hospitals (United States)	1 yr (1996)
23	Cost-benefit analysis	16,860 interventions	Community hospital (United States)	18 mo (1998)
24	Cost-effectiveness analysis, cost-benefit analysis	102 patients	2 tertiary care teaching hospitals (United States)	172 days (1994)
25	Cost-effectiveness analysis	7,219 patients	Teaching hospital (United States)	2 periods of 2 yr (1996)
26	Cost-benefit analysis	57 interventions	ICU in general hospital (Malaysia)	1 mo (2001)
27	Cost-benefit analysis	172 interventions	PICU in university-affiliated children's hospital (United States)	24 wk (1997)
28	Cost-benefit analysis	4,959 interventions	Tertiary care academic hospital (United States)	1 yr (1999)
29	Cost-benefit analysis	4,050 interventions	Acute care hospital (United States)	10 mo (1994–95)
30	Cost-benefit analysis	3,030 interventions	Community hospital (United States)	27 mo (2001)

Pharmacist's Intervention(s)	Outcome(s)
Reviewed drug profiles only regarding cost-saving recommendations	\$5,700 saved on cost-limiting interventions, extrapolated to savings of \$86,000/yr for studied wards and of \$301,000/yr for hospital; no effect on LOS, mortality, or readmission rate
Attended rounds and advised changes in therapy	\$3,218 saved, extrapolated to savings of \$25,140/yr
Attended rounds	\$192,681 saved during both intervention periods, extrapolated to savings of \$372,384/yr
Attended rounds; provided DI, pharmacotherapeutic consultation, and suggestions for alternative therapies	Mean savings of \$301 on pharmacy costs and \$1,654 on hospital costs per intervention; cost of labor for clinical pharmacist not considered; decreased LOS by 1.3 days
Focused on preventing ADEs (e.g., order clarification and correction, altering dosage, DI)	\$13,798 saved, extrapolated to savings of \$16,557/yr
Attended rounds and consulted with focus on preventing prescribing errors	58 ADEs prevented (equivalent to savings of \$270,000/yr)
Attended rounds with focus on preventing ADEs, mostly related to dosage changes and addition of medication	78% reduction in preventable ADEs; no change in total drug charges, LOS, time to resolution of condition, or readmission rate
Reviewed prescriptions with focus on avoiding prescribing errors	Savings of 9,582 € (\$8,657), extrapolated to savings of 479,100 € (\$432,830)/yr, <sup>a</sup> and prevention of 18,252 prescribing errors
Reviewed medical records to optimize antibiotic therapy	Savings of \$386.80 per patient based on charges, extrapolated to savings of \$390,000/yr; lesser use of antibiotics expressed as diminution of 3.43 defined daily doses of i.v. antibiotics and 1.41 days of antibiotic therapy
Optimized antibiotic therapy	Differences of \$4,404/intervention in median patient charges and \$2,642/intervention in median patient costs; cost of personnel estimated at \$21,000/yr
Managed vancomycin and aminoglycoside therapy	Savings of 6% on total charges, 8% on drug charges, and 8% on laboratory charges; decreases of 7% in death rate and 12% in LOS
Substituted antibiotics in the treatment of CAP	Savings of \$22,316/yr; decrease of 1.2 days in LOS; lower readmission rate (2.4% vs. 3.4%)
Reviewed antibiotic therapy for switching i.v. drugs to oral drugs	Estimated savings of \$5,800/yr; costs of operating such a program estimated at \$22,200/yr
Reviewed prescriptions for restricted or nonformulary i.v. antimicrobials	Savings of \$291,885. Decline of 31% in i.v. antimicrobial costs, extrapolated to savings of \$145,942/yr; mean decreases of 2.4 days in LOS and 1.67% in mortality
Reviewed prescriptions and suggested changes in therapy	Savings of \$4,014, extrapolated to savings of \$26,315/yr, accounted for pharmacist salary
Attended rounds, provided DI, suggested dosage changes, initiated or discontinued therapy, provided TDM	Savings of \$1,977, extrapolated to savings of \$9,135/yr; more-expensive drugs used in a superior therapy not added into the calculation
Suggested dosage adjustments, route switch, pharmacokinetics, TDM, and DI	Savings of \$187,852
Optimized therapy (e.g., DI; provided pharmacokinetic consultation; adjusted dosage, frequency, and route of administration; provided TDM)	Estimated savings of \$464,833, extrapolated to savings of \$557,800/yr; decrease of 372 days in LOS
Reviewed clinical pharmacy intervention records	Savings of \$894,150, extrapolated to savings of \$397,400/yr

Continued on next page

Table 1 (continued)

Ref.	Type of Evaluation	No. Interventions or Patients	Study Setting (Country)	Study Period (Cost Year)
31	Cost-benefit analysis	511 interventions	8 acute care, government-funded, tertiary teaching hospitals (Australia)	22 days <sup>e</sup> (2001)
32	Cost-benefit analysis	2,150 interventions	ED in university-affiliated urban trauma center (United States)	4 mo (2003)

<sup>a</sup>LOS = length of stay, MICU = medical intensive care unit, CCU = coronary care unit, DI = drug information, ADE = adverse drug event, GMU = general medicine unit, CAP = community-acquired pneumonia, ICU = intensive care unit, PICU = pediatric intensive care unit, TDM = therapeutic drug monitoring, ED = emergency department.

<sup>b</sup>Data analysis based on a one-year period.

<sup>c</sup>Number of prescriptions.

<sup>d</sup>Costs were expressed in U.S. dollars using a conversion rate of \$1 = € 1.1069 in 2002.

<sup>e</sup>Average period of data collection per site (range, 14–39 days).

Table 2. Interventions Conducted by Clinical Pharmacists in Studies Reviewed

- Adjusted dosages for renal and hepatic clearance<sup>16,27-30,33</sup>
- Advised the initiation, discontinuation, or alteration of therapies<sup>18,27,29,33</sup>
- Advised therapeutic drug monitoring<sup>18,33</sup>
- Detected and prevented pharmacologic and physicochemical interactions<sup>16,18,28,29,33</sup>
- Detected and prevented prescribing and transcription errors<sup>19</sup>
- Detected, followed up on, and prevented adverse drug events<sup>16,18,27</sup>
- Provided drug information to physicians, nurses, and patients<sup>16,27-30</sup>
- Conducted drug-use evaluation<sup>34,35</sup>
- Evaluated drug history<sup>34,35</sup>
- Followed up on microbial laboratory test results and antibiogram<sup>18,27,28</sup>
- Implemented and tracked use of guidelines for correct use of drugs<sup>33</sup>
- Implemented formulary<sup>16,29</sup>
- Inquired about and counseled patients on admission and discharge drugs<sup>30</sup>
- Optimized dosing and posology<sup>16,18,28,29,33</sup>
- Participated in physician rounds<sup>13-15,17,27</sup>
- Substituted drugs according to formulary, allergies, contraindications, or costs<sup>16,28,29,33</sup>
- Switched administration route<sup>18,27,28,30,33</sup>

that clinical pharmacy interventions related to vancomycin and aminoglycoside therapy reduced drug charges, laboratory charges, total charges, death rate, and length of hospital stay.<sup>22</sup> In another study, clinical pharmacists participated in a clinical pathway for community-acquired pneumonia.<sup>23</sup> The pathway included pharmacist monitoring for optimum antibiotic selection, dosing, effectiveness, and conversion from intravenous to oral therapy. The authors detected savings (excluding the cost of providing clinical pharmacy interventions), a decrease

in length of hospital stay, and a lower readmission rate.

In a study evaluating the financial effect of the intervention of switching from i.v. to oral antibiotics, labor costs (defined as the costs of employment of the personnel involved in operating the studied clinical pharmacy program) exceeded savings, implying that this clinical pharmacy service was not profitable.<sup>24</sup> No differences were observed in length of hospital stay, inpatient mortality, or need to restart i.v. antibiotics between patients in the intervention and control groups.

Another study examined an antibiotic control program consisting of a clinical pharmacist who assisted the primary health care team in the event of changes in the disease course of patients, with interpretation of culture and susceptibility reports, with decisions about the duration of therapy, and with converting from i.v. to oral therapy.<sup>25</sup> The authors found a decrease in the cost of i.v. antibiotic therapy, a decrease in pharmacy costs other than i.v. antibiotics, a decrease in length of hospital stay, and decreased mortality rates.

*General interventions.* Cost-benefit analyses suggested that general clinical pharmacy interventions were associated with cost savings.<sup>26-32</sup> Net savings were demonstrated when a pharmacist reviewed patients' progress charts and drug profiles in an intensive care unit.<sup>26</sup> The recommendations to discontinue certain drugs and switch from i.v. to oral therapy had the greatest effect on cost savings.

One study focused on the effect of a clinical pharmacist attending rounds with the pediatric intensive care unit team and reviewing drug lists.<sup>27</sup> The authors found drug cost savings but did not account for costs relating to switching from a less expensive to a more expensive drug as recommended by the pharmacist and did not include cost savings arising from avoidance of an ADE.

One study evaluated the economic effect of a clinical pharmacist in a university hospital who monitored

Pharmacist's Intervention(s)	Outcome(s)
Recommended changes to patient management or therapy	Savings of \$251,764, extrapolated to savings of \$4,254,345/yr
Provided TDM, adjusted dosages, answered nursing questions	Estimated savings of \$1,029,776, extrapolated to savings of \$3,089,328/yr

drug therapy; conducted pharmacokinetic evaluations; assessed for ADEs, drug interactions, and drug information; adjusted dosages; and recommended switching from i.v. to oral drugs.<sup>28</sup> The authors found that the drug-related cost savings and cost avoidance associated with pharmacist-provided clinical interventions exceeded the expenses of providing clinical pharmacy services, yielding a net economic benefit of almost \$400,000.

In an acute care hospital, clinical pharmacy interventions consisted of correction of an inappropriate dose or dosage schedule, pharmacokinetic consultation, discontinuation of therapeutic duplication, or avoidance of allergic reaction to drugs.<sup>29</sup> These interventions generated drug-related cost savings and prevented additional hospital stays.

One cost-benefit analysis focused on clinical pharmacy interventions concerning dosage or frequency change, switch in route of administration, and pharmacokinetic consultation in general medicine, intensive care, and hematology-oncology units.<sup>30</sup> Drug-related cost savings and cost avoidance (excluding the salary of clinical pharmacists) were realized as a result of these interventions.

Clinical pharmacy interventions related to initiation and discontinuation of therapy, change of dosage, change of drug, and patient monitoring were conducted in eight teaching hospitals.<sup>31</sup> Savings as a result of a reduction in length of hospital stay

were more important than savings as a consequence of a reduction in readmissions. Improvements in treatment efficacy or reductions in symptoms were observed but were not considered in the cost-benefit analysis.

A final cost-benefit analysis pointed to drug-related cost savings associated with pharmacist interventions in an emergency department of a university-affiliated trauma center.<sup>32,36</sup>

**Analysis of methodologies.** Economic evaluations of clinical pharmacy interventions suffered from a number of methodological limitations (Table 3).

**Study design.** All economic evaluations were conducted from a hospital perspective. A number of economic evaluations were conducted for case series.<sup>16,28-31</sup> Those studies tracked clinical pharmacy interventions but did not observe costs and outcomes in the absence of clinical pharmacy interventions. Instead, estimates of drug-related cost savings and cost avoidance arising from the prevention of ADEs or additional hospital days were based on the literature and the opinion of a panel of experts. Studies did not discuss the degree to which estimates derived from the literature could be applied to the specific hospital ward and the specific hospital in which the economic evaluation was set. Finally, these studies did not assess the quality of the decisions made by the expert panels, and no guidelines

exist as to how such panels should make decisions.

**Scope of costs and outcomes.** Most economic evaluations were limited in the scope of costs considered. Studies generally measured direct health care costs associated with clinical pharmacy interventions, although some analyses were restricted to drug costs only.<sup>26,27,32</sup> A number of studies overestimated cost savings from clinical pharmacy interventions because they did not account for pharmacist labor costs.<sup>14,15,17,18,20,21,32</sup> In those studies that accounted for personnel costs, the net time spent by the clinical pharmacist was multiplied by the mean hourly wage.<sup>12-14,16,19,28-31</sup>

A variety of outcome measures were used in cost-effectiveness analyses, many of which were related to intermediate outcomes (e.g., need to restart i.v. therapy, number of preventable ADEs) rather than final outcomes (e.g., mortality).

**Measurement and valuation of costs and outcomes.** Multiple studies were conducted in teaching hospitals and mainly on intensive care units.<sup>12,14-17,19,20,24,25,28,31</sup> ADEs were more common in teaching hospitals than in community hospitals, possibly because medical interns and residents were involved in prescribing drugs.<sup>37,38</sup> Also, intensive care patients received more varied and expensive drugs than nonintensive care patients.

When measuring the benefits of clinical pharmacy interventions in cost-benefit analyses, financial ben-

Table 3. Evaluation of Methodologies Used in Studies of Clinical Pharmacy Interventions<sup>a</sup>

Ref.	Study Type <sup>b</sup>	Outcomes Evaluated <sup>c</sup>	
		Cost	Other
12	Prospective, randomized trial	Drugs, net time spent by clinical pharmacist	LOS, hospital mortality, 30-day readmission, need to restart i.v. therapy
13	Prospective case series	Drugs, laboratory use, salary of clinical pharmacist	None
14	Before–after study	Drugs	LOS, death rate
15	Prospective, blinded cohort study	Pharmacy and hospital cost per admission	LOS
16	Case series, including sensitivity analysis	Drugs, estimated cost avoidance per intervention, net time spent by clinical pharmacist	Prevention of ADEs
17	Before–after study	Valuation of prevented ADEs	Prevention of ADEs
18	Nonconcurrent cohort study	Drugs	No. preventable ADEs, LOS, time to respond to therapy
19	Prospective case series, including sensitivity analysis	Drugs, diagnostic procedures, medical interventions, time investment of nurses, physicians, pharmacists, and pharmacy assistants	Prevention of ADEs
20	Prospective, randomized controlled trial	Antibiotics	Clinical and microbial outcome
21	Prospective, randomized clinical trial	Antibiotics, laboratory, medications, room and board	LOS
22	Multicenter, retrospective cohort study	Drugs, laboratory monitoring	Death rate, LOS, no. complications
23	Prospective cohort study	Direct cost of use of antibiotics and overall hospital cost	LOS, readmission probability
24	Prospective, randomized clinical trial	Antibiotics	LOS, hospital mortality, 30-day readmission, need to restart i.v. therapy
25	Retrospective before–after study	Antibiotics	LOS, mortality, readmission
26	Prospective case series	Drugs	None
27	Prospective case series	Drugs	None
28	Prospective case series, including sensitivity analysis	Drugs, estimated cost avoidance per intervention, net time spent by clinical pharmacist, cost of equipment used to record interventions	None
29	Prospective case series	Drugs, laboratory use, net time spent by clinical pharmacist	LOS
30	Retrospective case series	Drugs, estimated cost avoidance per intervention, net time spent by clinical pharmacist	None
31	Multicenter, prospective case series	Drugs, medical procedures, laboratory monitoring, salary for clinical pharmacist, readmission rate, LOS	LOS, readmission probability, medical procedures and laboratory monitoring
32	Prospective case series	Drugs	None

<sup>a</sup>LOS = length of stay, ADE = adverse drug event, DRG = diagnosis-related group.

<sup>b</sup>No study included an incremental analysis.

<sup>c</sup>All evaluations were conducted from a hospital's perspective.

<b>Measurement and Valuation of Outcomes</b>	
Hospital's acquisition cost for drugs per group; hours spent by clinical pharmacist x \$30/hr	
Cost savings = hospital's acquisition cost for each medication + no. administered units; cost avoidance = difference in cost for drugs and laboratory use between both therapies x no. treatments; cost of clinical pharmacist = no. hours x \$25/hr	
Mean drug cost per admission from the pharmacy computer database, defined as the total drug cost divided by the number of admissions per study period; cost reduction calculated using CliniTrend (ASHP) for 1-yr period	
Based on patient records after discharge; origin of cost not specified	
Cost avoidance per intervention = estimated probability of ADE x \$5642; cost of time spent by personnel = no. months x mean salary (including benefits) of a beginning clinical pharmacist	
Cost savings = no. prevented ADEs x \$4685	
Use of charges; calculation and details not specified	
Drug costs based on the official national market price and the correct doses by <i>Physicians' Desk Reference</i> ; diagnostic tests valued using national health care tariffs; cost of personnel = average cost per intervention based on literature x assumption of needed time	
Charges for antibiotic therapy	
Charges derived from patient billing; conversion to hospital cost by multiplying patient charges by estimated factor of 0.60	
Costs calculated using charges for drugs and laboratories	
Costs of antibiotic therapy calculated using drug acquisition cost	
Difference in cost between antibiotic therapy before and after intervention; origin of cost not specified	
Acquisition cost per period	
Acquisition cost per dose x no. administered doses; addition of \$0.263 administration charges for all drugs involving i.v. infusion	
Acquisition cost x estimated average LOS	
Drug costs = acquisition cost x no. administered units (for i.v.-to-oral switch for 1.5 days; cost avoidance per intervention = estimated probability of ADE x \$5006; cost of time spent by personnel x salaries (including benefits)	
Acquisition cost of drugs; prediction of cost avoidance based on probability and change in mean LOS for each DRG	
Drug costs = unit cost x no. doses given in an (estimated) period of 2.5 days; time spent by personnel = no. interventions x mean duration of 8.3 min/intervention	
Drug costs = acquisition cost x no. administered doses; change in medical procedure and laboratory monitoring = probability x local hospital cost; readmission = average cost of the assigned DRG for the hospital x probability; LOS = no. days x average bed-day cost; cost of clinical pharmacist is site specific and based on time spent, salary, and related overhead costs	
Acquisition cost derived from Veterans Affairs center	

efits were generally included. These referred to drug-related cost savings and cost avoidance arising from the prevention of ADEs or additional hospital days. Health benefits were not assessed in any cost–benefit analysis, which can understate the true value of clinical pharmacy interventions.<sup>11</sup>

*Allowance for uncertainty and incremental cost analysis.* Few economic evaluations allowed for uncertainty, with three studies conducting a sensitivity analysis to account for uncertainty of key estimates and assumptions made during the identification, measurement, and valuation of costs and outcomes.<sup>16,19,28</sup> No study presented results in terms of an incremental cost-effectiveness ratio or incremental cost–benefit ratio of patients receiving clinical pharmacy interventions as compared with patients who do not receive such interventions. None of the economic evaluations discussed the transferability of results to other settings or countries.

### Discussion

Overall, the reviewed literature on economic evaluation of clinical pharmacy intervention was mostly from North America; therefore, the findings of these studies should be interpreted with caution when assessing their relevance to other countries, considering the variability of the funding, organization, and regulation governing hospital services among different countries. For instance, the length of hospital stay in the United States is mainly driven by financial motives, and patients are discharged as soon as possible. Such pressures are present to a lesser degree in countries where hospital stay is fully reimbursed by the government. Such differences are likely to influence the extent to which clinical pharmacy interventions can contribute to improving economic and clinical outcomes. Nearly all studies pointed to a financial benefit based on direct cost savings and estimated

cost avoidance arising from the prevention of ADEs and the reduction in length of stay. These savings were greater for specific interventions (e.g., preventing ADEs, switching from i.v. to oral therapy) and disciplines (e.g., intensive care unit versus geriatrics).

The size of cost avoidance observed in studies is likely to depend on the setting in which the economic evaluation was conducted. This may explain the larger size of cost avoidance arising from the prevention of ADEs in large, tertiary care teaching hospitals. In addition, it is unclear and difficult to predict the extent to which the cost savings and cost avoidance estimated for prevention of ADEs or additional hospital stays by using calculations from other literature and the opinion of an expert panel would be actually observed in real practice. Furthermore, the cost avoidance resulting from the prevention of ADEs or additional hospital days is likely to depend on the health care discipline, intensity of care, patient profile, and hospital. When setting up a new clinical pharmacy program, attention needs to be paid to the choice of ward and type of intervention as they are likely to influence the pharmacoeconomic value of the program.

Economic evaluations of clinical pharmacy interventions suffered from a number of methodological limitations relating to the absence of a control group without clinical pharmacy interventions, limited scope of costs and outcomes, focus on direct health care costs only, exclusion of pharmacist labor cost, use of intermediate outcome measures, exclusion of health benefits, and absence of incremental cost analysis. As studies used multiple outcome measures and did not combine them into a single index, it was not possible to get an idea of the overall cost-effectiveness of clinical pharmacy interventions. Therefore, it is impossible to compare the cost-

effectiveness of clinical pharmacy interventions with the cost-effectiveness of treatments for other diseases that are expressed in terms of generic measures such as the cost per life year gained or the cost per QALY gained.

It is interesting to note that, in one study,<sup>24</sup> there was no difference in length of hospital stay, inpatient mortality, or need to restart i.v. antibiotics between intervention and control groups. However, the absence of a significant benefit from the clinical pharmacy intervention may be explained by the fact that a strong program of antibiotic controls was already in place at the two hospitals; thus, there was little room to improve antibiotic therapy.

No economic evaluation addressed the issue of learning effects. Some studies examined the contribution of a single clinical pharmacist.<sup>15,27</sup> This may bias costs and outcomes in that outcomes may be influenced by the skills and competence of the clinical pharmacist in addition to reflecting the effect of clinical pharmacy interventions. Learning effects may also apply to physicians. A physician can learn from recommendations made by clinical pharmacists and apply these recommendations to other patients who are not reviewed by clinical pharmacists. When intervention and control groups are part of the same ward population, this may have an effect on the outcomes of the control group. Therefore, intervention and control groups should be selected from different wards, the populations of which should have similar demographic characteristics and comparable severity of disease.

As these limitations are not inherent to the techniques of economic evaluation, but arise from the suboptimal design of existing studies, more attention needs to be paid by researchers to the design of their studies. Therefore, a number of avenues are proposed for designing fu-

ture economic evaluations of clinical pharmacy interventions.

Studies need to employ a control group of patients who do not receive clinical pharmacy interventions. Having a clinical pharmacist in the control group of a randomized controlled trial who provides no advice or faulty advice raises ethical questions. Moreover, physician blinding is difficult to achieve as the physician is likely to notice that the pharmacist in the control group provides no advice or faulty advice. An alternative option is a preintervention and postintervention study comparing the period before the introduction of clinical pharmacy with the period after the introduction. Such a study can be nested in a cohort study to account for a possible trend.

Studies need to provide sufficient details of the clinical pharmacy intervention studied. They also need to consider the effect of program factors (e.g., type of hospital ward, type of hospital, level of expertise of clinical pharmacist) on the cost-effectiveness of clinical pharmacy interventions. Studies also need to discuss the applicability of their findings to other settings and to other countries.

Studies must consider costs of clinical pharmacy interventions from a societal perspective. Economic evaluations from a hospital's perspective are more common, as interest in clinical pharmacy interventions tends to focus on the type of interventions and their effect on the intensity and length of treatment in a hospital setting. This is important in developing the content and quality of clinical pharmacy interventions. However, the hospital perspective is too restrictive as clinical pharmacy interventions have wider implications on, for instance, patient absence from work. This implies that studies need to measure direct health care costs and indirect costs of productivity loss. Also, the cost of employing a clinical pharmacist needs to be subtracted from any cost savings with a

view to assessing the net cost effect of clinical pharmacy interventions.

Cost-benefit analyses must consider health benefits of clinical pharmacy interventions in addition to costs. The exclusion of patients' health benefits when determining the economic effect of an intervention is not necessarily a problem within a cost-benefit framework if the health benefits add to already positive net costs. Nevertheless, the exclusion of health benefits understates the true value of clinical pharmacy interventions. Various techniques such as willingness to pay exist to value health benefits. However, assigning monetary values to health benefits is controversial, and further work on methods to value health benefits is needed.

It is imperative that studies account for uncertainty surrounding key estimates and assumptions relating to costs and outcomes. Economic evaluations drawing on patient data can account for uncertainty by carrying out a sensitivity analysis. Alternatively, the nonparametric approach of bootstrapping can be considered to incorporate uncertainty around the point estimate of the incremental cost-effectiveness ratio. Bootstrapping is used to obtain the empirical sampling distribution of the incremental cost-effectiveness ratio and construct a confidence interval around this ratio.<sup>39</sup>

## Conclusion

Most pharmacoeconomic evaluations of clinical pharmacy interventions demonstrated limitations in their methodological quality and applicability to current practice. Future evaluations should use a comparative study design that includes the incremental cost-effectiveness or cost:benefit ratio of clinical pharmacy interventions from a societal perspective.

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