
Gerd Clabaugh, MPA, Marcia M. Ward, PhD
Department of Health Management and Policy, University of Iowa, Iowa City, IA, USA

ABSTRACT

Objectives: We undertake a systematic review to examine the methods used by researchers in developing cost-of-illness (COI) studies. This review aims to categorize the approaches that the published literature uses in terms of perspective, scope, components of care analyzed in the literature, data sets, and valuation approaches used for direct cost. It draws conclusions regarding the adequacy of current COI research methods and makes recommendations on improving them.

Methods: The online bibliographic information service HealthSTAR (which incorporates MEDLINE) was used to search for COI studies in the research literature published during the period from 2000 to 2004. The search strategy used the term “cost of illness” as a MeSH (medical subject heading) term.

Results: The HealthSTAR literature search identified references to 650 articles. Review of abstracts resulted in the identification of 170 of these for a more detailed review. This process identified 52 articles that met all criteria of COI studies. We identified 218 components of care analyzed across the 52 articles. Private-insurance or employer-claims data sets comprised the largest source of utilization and cost information among the studies.

Conclusion: Analyzing cost of illness presents useful opportunities for communicating with the public and policymakers on the relative importance of specific diseases and injuries. Our research, however, indicates that COI studies employ varied approaches and many articles have methodological limitations. Without well-accepted standards to guide researchers in their execution of these studies, policymakers and the general public must be wary of the methods used in their calculation and subsequent results.

Keywords: cost-of-illness, direct cost, standards, systematic review.

Introduction

Increasingly, researchers and policymakers have turned to cost-of-illness (COI) research to better describe health-care spending and populate cost-effectiveness models. This research promises to equip policymakers and health-care practitioners with information on the relative importance of specific illnesses and injuries in terms of utilization of all relevant components of health care and the cost involved.

The popular press is provided with information on the costs of a variety of illnesses often as a way for researchers to communicate with the public and policymakers on the relative impact of diseases at a population level. These cost figures often make their way into the public policy discussion as state and federal agencies attempt to fashion intervention programs aimed at reducing costs, improving health, or both. For example, the National Center for Chronic Disease Prevention and Health Promotion issues press releases on its Web site (http://www.cdc.gov/nccdphp/press) [1] which directly or indirectly reference cost of illness, such as:

- Estimates of the costs of obesity to the population in the year 2000 were more than $117 billion.
- The direct care expenditures for osteoporosis fractures range from $12.2 billion to $17.9 billion each year.
- Cigarette smoking and exposure to tobacco smoke resulted in $92 billion in productivity losses annually.
- During 1996, direct medical costs for persons with disability were $260 billion.

These examples support the point that COI studies have become increasingly important in both the substance and the rhetoric of developing interventions in battling illness and injury in the United States.

Hodgson and Meiners’s [2] seminal review in 1982 provided an analysis of the more than 200 COI studies that had been published up to that time. They gave credit to Malzberg (1950) [3] for publishing the first COI study. They also recognized Dorothy Rice, former head of the National Center for Health Statistics, for formalizing the methodology distinguishing direct
costs from indirect costs as used in COI studies. Figure 1 recaps the growing appearance of these studies in the research literature since 1990. With the growing popularity of COI studies, we found it surprising that there is little published guidance to support the choice of methodological approaches. Thus, we undertook a systematic review to examine the methods used by researchers in developing COI studies. More specifically, this review aims to categorize the approaches that the published literature uses in terms of perspective, scope, components of care analyzed in the literature, data sets, and valuation approaches used.

Methods
The online bibliographic information service HealthSTAR (which incorporates MEDLINE) was used to search for COI studies in the research literature published during the period from 2000 to 2004. Because the term “cost of illness” was a medical subject heading (MeSH) term during the period from 2002 to 2004, it was used as the sole search strategy. Other search terms were investigated, including “health expenditures,” “costs,” “cost analysis,” and “economic value of life,” but they yielded an overwhelming number of articles that were unrelated to cost of illness. Also, the purpose of this systematic review was to identify the most commonly used methodological approaches for COI studies, and the articles identified using “cost of illness” as a MeSH term provided a large and representative sample of such articles which was adequate for this purpose. Because the purpose of the study was to categorize methodologies and data-bases used in COI studies in the United States, review articles were excluded, as were studies using data sets from outside the United States and non-English-language articles.

The list of full references, and abstracts when available, were stored electronically. Two reviewers read the abstracts to determine whether each article appeared, in fact, to include a COI analysis. In studying COI research, our focus was to identify and analyze studies that met certain criteria. Hodgson and Meiners’s [2] earlier work on COI studies was biased in favor of analyses that attempted to be more inclusive of all direct and indirect medical costs associated with an illness. We adopted this bias with a pragmatic definition. We defined a COI study as one that includes cost estimates for at least two components of direct medical costs. Direct medical costs are defined as payments made for medical care provided [2]. Studies including just one component of direct medical cost were deemed too narrow to meet the intent of COI studies. Because of the complexity of the methodological approaches, this systematic review was limited to studies of direct cost. A similar review of methodologies for indirect costs could be the subject of a separate analysis. In addition, a number of articles were primarily cost-effectiveness analyses, which on examination relied on cost estimates from the literature rather than on original COI analyses, and thus were excluded. When both reviewers agreed from reading the abstract that the article appeared to include a COI analysis of direct cost in the United States, the full article was obtained for further examination. Where abstracts were unclear, we were liberal in including these articles in the more detailed review. Articles missing abstracts

Figure 1 Published cost-of-illness studies 1990–2004.
in the HealthSTAR search were eliminated from further consideration.

Once the full articles were available, the two reviewers examined the methodology, using a data collection tool to code specific information. Each reviewer coded the articles on two levels. The first level of data collected was at the article level. At this level, the primary screening questions confirmed the prior inclusion criteria: that the article reported original analyses, that the data sets were US-based, that the article included direct medical costs, that the article used an adequate population base, and that the article included data from more than one component of care with a breakdown of costs for more than one component. If the article met these criteria, then additional article-level information was collected including the perspective for the analysis (e.g., society, employer, and insurer) and whether the analyses calculated cost of illness using an incidence- or prevalence-based approach.

For articles that met the criteria of the first level of review, a second level of review collected information on the specific components of care analyzed in each article. Thirteen components of care were identified and coded, including inpatient hospitalization, emergency department, ambulatory surgery or procedure, outpatient visit, laboratory or test procedure, other therapies, nursing home, hospice, home care, medical devices, prescription medication, over-the-counter medication, and other. For each component of care, the sources of the utilization and cost data used in the calculations of cost of illness were identified.

Both reviewers coded independently. Disagreements between reviewers were resolved by consensus after the article was examined further and discussed by both.

Results

The HealthSTAR literature search identified references to 650 articles. The abstract review, described previously, resulted in the identification of 170 of these for the more detailed review. Although the abstracts for the 170 identified COI articles were examined by two reviewers and abstracts that did not meet criteria were excluded, there were a substantial number of articles excluded in the subsequent in-depth review step. The reasons for eliminating articles from further consideration were clustered into 10 categories. The most frequent reason for elimination was that articles focused on a single component of care in their analyses (55 articles). Other reasons for exclusion were that the article only reported estimates from the literature and did not include original analysis (26 articles), that the article reported total costs but did not report any details on how the costs were identified (16 articles), that it included a cost-effectiveness analysis without a COI component (9 articles), that it only included indirect costs (9 articles), or that the article was a review only (6 articles). An additional reason for excluding articles was that the results did not reflect the cost of usual care, for example, the article included a nonrepresentative sample (9 articles), analyzed an intervention (7 articles), or was a study that compared two drugs (7 articles). Some articles were excluded for multiple reasons. This process identified 52 articles (contained in Table 1) that met all criteria of COI studies and were subjected to additional analyses.

Perspective

We identified the perspectives of the 52 articles on direct cost. Among the perspectives identified were societal, health-care system, provider, Medicare/Medicaid, insurance, employer, and caregiver/patient. Because many articles did not specifically identify the perspective of costs represented, we deduced perspective from the types of utilization and direct cost data used in the analysis. Occasionally, researchers would use more limited data sources, but identify an attempt to use limited cost calculations in an effort to estimate a broader set of costs. Nearly half of the 52 articles (24) represent the capturing of direct costs from the perspective of society. A third (19 articles) represents the perspective of either employer or insurance-based health care. The perspective was Medicare or Medicaid for four articles, the caregiver/patient for three articles, and multiple perspectives for two articles. No articles reflected costs from the perspective of the health-care system or providers.

Incidence or Prevalence

Of the 52 articles reviewed, 44 (85%) used a prevalence approach, 6 (12%) used an incidence approach, and 2 (3%) used both. COI studies using an incidence approach employ methodologies that differ considerably from studies using a prevalence approach. Prevalence-based articles used a variety of cross-sectional data, while incidence-based articles most commonly used employer or insurer claims data that are linkable, permitting new cases of a disease or an injury to be identified and followed over the course of illness or multiple years.

Cost Component

Although our primary emphasis for this systematic review is on methods used to analyze direct medical costs, we found that 27 of the 52 articles meeting our study criteria for direct cost also contained indirect cost. It is clear that many studies that report direct cost also include indirect cost and thus examine a broader spectrum of disease burden. Recommendations regarding methods for indirect costs in COI analyses are beyond the scope of this article but should be addressed elsewhere.
Table I  References for studies in 2000–2004 that met criteria for cost-of-illness studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Citation</th>
<th>Cost component</th>
<th>Perspective</th>
<th>Incidence/prevalence</th>
<th>N</th>
<th>Count of components of care</th>
</tr>
</thead>
<tbody>
<tr>
<td>Centers for Disease Control and Prevention (2003)</td>
<td>MMWR 52(46):1124–7</td>
<td>2</td>
<td>1</td>
<td>p</td>
<td>22435</td>
<td>4</td>
</tr>
</tbody>
</table>
By definition, this systematic review identified articles that analyzed more than one component of care. We identified 218 components of care analyzed across the 52 articles, for an average of 4 components per article.

Eight articles contained just 2 components of care, 11 articles contained 3 components of care, and 15 articles contained 4 components of care. The frequency of components covered dropped quickly from that point, with eight articles covering five components, four articles covering six components, and six...
articles covering seven or more components of care. The frequency of each component was also determined. The most frequently analyzed components of care were outpatient care, including office visits (47 articles), hospitalization (44 articles), prescription medication (41 articles), emergency department (24 articles), other noncategorized components (21 articles), nursing home (9 articles), home care (12 articles), and laboratory or test procedure (9 articles).

**Utilization Data Sources**

The current review uncovered a considerable range of data sets used to identify utilization. These data sets included both public-use and proprietary data. Private insurance or employer-claims data sets comprised the largest source of utilization information among the studies (21 articles). Single utilization data sets from the National Center for Health Statistics (e.g., National Hospital Discharge Survey [NHDS], National Ambulatory Medical Care Survey [NAMCS]) were used in 11 articles. Medicaid and Medicare utilization data were used in six articles. Medical Expenditure Panel Survey/National Medical Expenditure Survey (MEPS)/NMES, which is a national survey with verification from other data sets for multiple components of care, was used in six articles. Other national data sets were used in five articles. Special surveys were cited in 10 articles.

**Cost Data Sources**

Perhaps not surprisingly, cost data sources used were similar to the utilization data sources. Employer-based health insurance and claims data were significant sources of cost information for these studies (23 articles). Medicare and Medicaid data also figured significantly as a source of cost-related information (16 articles). MEPS/NMES was used frequently as a single source of cost data for multiple components of care (nine articles). Average wholesale price was used in 10 articles to report cost of medication. Other noncategorized cost data sources were cited in nine articles.

**Illnesses Analyzed**

A wide variety of illnesses are studied in the COI literature. The most frequent illness studied in the COI articles that met our inclusion criteria was arthritis (six articles). Respiratory diseases, urinary diseases, and Alzheimer’s disease were the subject of three articles each. Chronic obstructive pulmonary disease, asthma, and allergic rhinitis were each the subject of two articles in the 5-year period (2000–2004).

**Discussion**

COI studies are being relied on increasingly to inform both public and private decision-makers with regard to the expenditures made on behalf of individuals for illnesses and injuries occurring in our population. These studies help drive decisions about future insurance benefits, research efforts in curbing and controlling disease and injury, and development of programs to improve the health of the population. Unfortunately, one of the findings of the current review of COI articles was the limitation in this body of research.

One of the most significant limitations reflects on the very definition of a COI study. Although one goal of this systematic review was to find research articles that broadly attempted to account for all components of care in the assessment of the costs for particular illness, we found that many COI articles only included one component of care. When these were eliminated, surprisingly, the remaining articles only averaged four components of care. This lack of breadth indicates that most studies are more limited in scope than the COI methodologies discussed in Hodgson and Meiners [2], Rice et al. [4], and Rice [5]. Readers of this literature must be aware that COI analyses of a limited number of components of care underestimate the full cost of treating the disease or injury under study. Such analyses will not be replicated by other studies examining other components of care, leading to disparate estimates of the magnitude of the cost for specific diseases.

Another troubling finding is that many studies in this review lacked clarity with regard to the methods used in calculating cost of illness. One of the most frequent omissions was specification of what constituted “cost.” For example, studies relying on insurance or claims-based data often did not clarify whether “cost” information represented charges from providers or actual reimbursed amounts. Charges have been shown to average more than twice the actual cost of delivering care [6], making COI calculations susceptible to considerable influence depending on which metric of “cost” is used. When the metric remains unclear or unspecified, the value of the COI findings is seriously diminished.

Despite these limitations, one purpose of this study was to identify the most commonly used approaches for conducting COI analyses, as a guide for future researchers. The current analyses identified three popular approaches. The most frequently used data sources were from insurance or employer claims data. The second most popular approach used publicly available data sets from the NCHS or from the Agency for Healthcare Research and Quality. Two data sources tied for third place in terms of popularity in COI studies. These were MEPS/NMES and Medicare/Medicaid data. Each of these approaches has advantages and disadvantages.

A number of studies relied on MarketScan data provided by MEDSTAT as a source of utilization information. The MarketScan database (The MEDSTAT Group, Ann Arbor, MI) contains claims information...
from approximately 65 large American corporations that provide coverage to their employees, dependents, retirees, and Consolidated Omnibus Reconciliation Act of 1986 (COBRA) continues. MarketScan data are available for sale to researchers. Its large population size permits COI analyses of most prevalent diseases. The fact that its database originates largely from employed individuals and their dependents permits COI analyses in the population less than 65 years of age including children. The large number of corporations contributing data assures geographic and demographic representation.

Another frequently cited source of utilization information was private insurance-based claims data, often from Fortune 100 companies. Articles that used insurance claims data to identify utilization also used those data to capture cost. Private insurance-based claims data are not publicly available, in that the data must be accessed from the insurer, if it is available to outside users at all. Some of the articles using these data were by researchers who were employed by a particular employer or insurance company. Additionally, many of the data sources used were proprietary and, in the cases of specific employer-based studies, the original source of the data was not precisely identified (the employer was not identified). Although these research efforts are meaningful for private employers, these studies may not be readily replicable and may not be generalizable for purposes of public policymaking.

Employer or insurance-based information will carry with it the biases inherent in the benefits structure of these programs. Because copays, deductibles, and breadth of insurance coverage are not uniform from employer to employer or from plan to plan, generalizing these findings over time and to broader populations may be inappropriate. Furthermore, because these cost calculations come from the experience of insured individuals, they cannot directly relate the cost of illness for the uninsured. Claims-based information provides the advantage, however, of more precisely matching value and utilization within a plan. This is a strength when analyzing cost of illness at the plan level, where benefits are similar, or within geographic areas that might have similar cost and benefit structures for a population of insured persons.

Medicare and Medicaid data also served as significant sources of utilization data for these studies. In addition, Medicare utilization data were often cited as a secondary source of data, effectively supplementing other sources of information in analyzing societal-level impact of particular illnesses. Use of Medicare or Medicaid utilization data can be appropriate in cases where the illness under study occurs predominantly in the publicly covered population. This could be true for certain types of health-care conditions that are particularly prevalent in the elderly, for example using Medicare data to examine the cost of illness of stroke or osteoarthritis. Where utilization is different between populations, however, these public data may be less reliable in providing complete information about all types of patients.

More often, Medicaid and Medicare data were used to inform the cost side of calculations for cost of illness. Because Medicaid cost data differ from state to state and within states, researchers and policymakers must be mindful as to how these cost data are applied to relevant utilization data and utilization from particular areas of the country. Additionally, in rural and underserved areas, critics often charge that Medicare programs provide low reimbursement to providers, and so this criticism must be factored into an analysis of costs that use these data. Certainly, if the perspective of the analysis reflects these public programs, then using this data would be appropriate. These issues can be resolved when national Medicare data are used to assign value to utilization.

A variety of other federal data sources were also utilized, with advantages and disadvantages to these data sets related to time frame, scope of utilization, and inclusion of cost data. A number of these, such as the Nationwide Inpatient Sample of the Healthcare Cost and Utilization Project (NIS/HCUP) and several data sets collected by the NCHS, focus on a single component of utilization. NCHS data sets include the NHDS, the NAMCS, the National Hospital Ambulatory Medical Care Survey, the National Nursing Home Survey, and the National Home and Hospice Care Survey. These data sets are publicly available at a low cost. Most are available annually. The samples for these data sets are carefully constructed and can be weighted to the US population. They cannot, however, be linked across data sets or across a year, prohibiting identification of episodes of care. Another shortcoming is that they do not include cost or charge information. Many researchers overcome this deficit by assigning national Medicare reimbursement rates to units of utilization. The NIS/HCUP data do include cost information, but it is limited to total hospital charges.

Several of these data sources span multiple components of care, a decided advantage for use in COI studies. The National Health and Nutrition Examination Survey III (NHANES III) contains survey data across components of care and has been used in several articles. Earlier NHANES data were collected on a continuous basis but released in 6-year increments, complicating 1-year analyses of cost of illness. More recent data are released in 2-year increments. The current review found that the MEPS was a popular source for utilization and cost information. MEPS is a nationally representative sample of households and their health services usage and costs—both insurance-based and out-of-pocket expenses. Efforts are made to verify utilization and cost data. In earlier years, it was
only available periodically, but now MEPS data are collected annually.

A concern with many data sets is the limited number of cases identified for the disease or for the injury under study. As shown in Table 1, the number of cases was not identified in some articles or was quite small in others, raising concerns about the stability of estimates and generalizability. For relatively rare illnesses or injuries, combining data sets across years may help alleviate this problem.

**Conclusion**

Analyzing cost of illness presents useful opportunities for communicating with the public and policymakers on the relative importance of specific diseases and injuries. Over time, these studies have become vitally important to the development of research and policy initiatives aimed at more cost-effectively treating and preventing illness. Our research indicates that, unfortunately, many COI studies have focused exclusively on a subset of total health-care expenditures, not all expenditures resulting from a particular disease or injury. Often, cost data used are proprietary, which presents difficulties in future replication and validation of this research. Without well-accepted standards to guide researchers in their execution of these studies, policymakers and the general public must be wary of the data sources and methods used in their calculation. This is particularly important in light of the natural tendency to compare costs of illness across diseases in prioritizing the allocation of scarce resources for research and intervention.

Because these studies will continue to be important contributions to understanding our investment in health care, public and private grant-makers and researchers should work to standardize terminology and methods of executing these studies. Among standards that should be established for these studies are:

- Disclosure of perspectives used in guiding the study. Understanding the perspective from which costs are captured is critical to a clear understanding of cost of illness.
- Inclusion, whenever possible, of all affected components of care. Analyses limited to only a few components of care will underestimate the cost of illness for the conditions under study and limit generalizability of the findings.
- Identification of the components of care analyzed. Researchers must clearly articulate those particular health-care cost segments included in their analysis. A standard language for components of care should be created and data elements should be matched against these to ensure clarity in the identification of cost categories.
- Description of data sources. This will enable future researchers to replicate and improve on the analysis of COI studies by understanding what the data used represent.
- Use, whenever possible, of publicly available data sets. This will permit other researchers to replicate the findings, will enhance generalizability across all payers, and will facilitate understanding of the data elements used in the analyses.
- Data sets should be used that permit a reasonable number of cases to be identified so that estimates are stable. Extracting data from multiple years may be helpful for relatively rare conditions.
- COI studies often project individual costs to the US population. Weights assigned to cases in public-use data sets can be used for such projections. Another approach multiplies prevalence estimates by average costs to project to national costs, in which case considerable care must be given to accurately identifying the prevalence for the condition.
- Identification of costs captured. Costs of care come in a wide variety of forms, including out-of-pocket, insurance-based reimbursement, charges, indirect costs, etc. Studies should clearly articulate whether the cost data used represent the actual cost of delivering care, dollars exchanged for the provision of care, or simply provider charges, which may be subject to inflating (such as for cardiac surgery) or discounting (such as in preferred provider arrangements).
-Disclosure of the year reflected in the utilization data and in its valuation. This is important for interpreting findings when patterns of treatment change over time. Also, the year that costs were valued is important when comparing findings across studies using different years, so that inflation factors can be appropriately applied and discounting can be employed.
- Description of the strategy for using primary and secondary diagnosis data. Where diagnostic data are used, studies should declare how they have dealt with the use of primary and secondary diagnoses in capturing cost information [7]. In particular, were cases limited to utilization where the specific International Classification of Diseases, Ninth Revision codes were listed first or was a broader inclusion rule used? In addition, were all costs for persons with the disease included, or only those costs for treating the specific disease?

As called for by Bloom [8], standards to guide the methodology of COI studies will aid interpretation of findings and comparison of results across studies and diseases. At the very least, as listed above, researchers should be mindful of their responsibility to disclose
pertinent details of their methods to permit others to understand and replicate their results. With the increasing popularity of COI studies, the standardization of methods becomes more critical to permit policymakers and the general public to better understand our investment in health care, and to drive decisions about future insurance benefits, efforts in curbing and controlling disease and injury, and development of programs to improve the health of the population.

Source of financial support: This work was funded by the Agency for Healthcare Research and Quality through grant number HS015009.

References


6 Tompkins CP, Altman SH, Eilat E. The precarious pricing system for hospital services. Health Aff 2006;25:45–56.