Prices, Quantities, and Costs: Using Data on Health Care Prices and Resource Use to Inform Decisions about Health Care Interventions

by

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Abstract

Given the importance of managing costs in today's health care delivery system, decision makers must consider the total costs of interventions in addition to evidence of better outcomes. Formal tools for evaluating health care interventions like cost-effectiveness analysis, cost-utility analysis and cost-benefit analysis, have been developed. These tools depend on a variety of estimates of costs and benefits associated with the health care interventions. Such analyses are generally based on expected costs and expected benefits.

The statistical literature regarding specifically the estimation of expected costs (μ_c) has typically treated individuals' health costs as observable quantities. Estimates of μ_c may be based either on directly observed cost or indirectly on observed resource use data; while the former is preferable, in practice the assumption that individuals' health costs are observable is questionable. When only resource use is observed, cost estimation requires the assignment of a monetary value to individuals' resource use, or "resource costing."

This dissertation examines the effect that resource costing has on the estimation of parameters of the cost distribution. In particular, the impact of assigning fixed-price estimates to observed resource use quantities, and second, the effect that data aggregation has on estimates are explored.

To address these issues, the theoretical aspects of various resource costing methodologies are examined, and it is shown that the use of fixed-price estimates can result in biased estimates of the mean and variance (μ_c, σ_c^2). This is due to the use of

fixed-price estimates while implicitly assuming zero covariation between prices and resource use quantity, and zero variation in price. For the estimation of μ_c, it is demonstrated that the bias increases in magnitude as the actual magnitude of the covariance between price and quantity increases.

Next, it is shown that the level of detail at which resources are measured, and at which fixed prices are assigned, can affect the estimates of average cost. This is due primarily to differences between the case-mix of the study sample and sample used to estimate the fixed price. Using data from a randomized clinical study, we demonstrate that the level of aggregation at which data are collected and assigned a fixed-price estimate can result in significantly different average cost estimates.

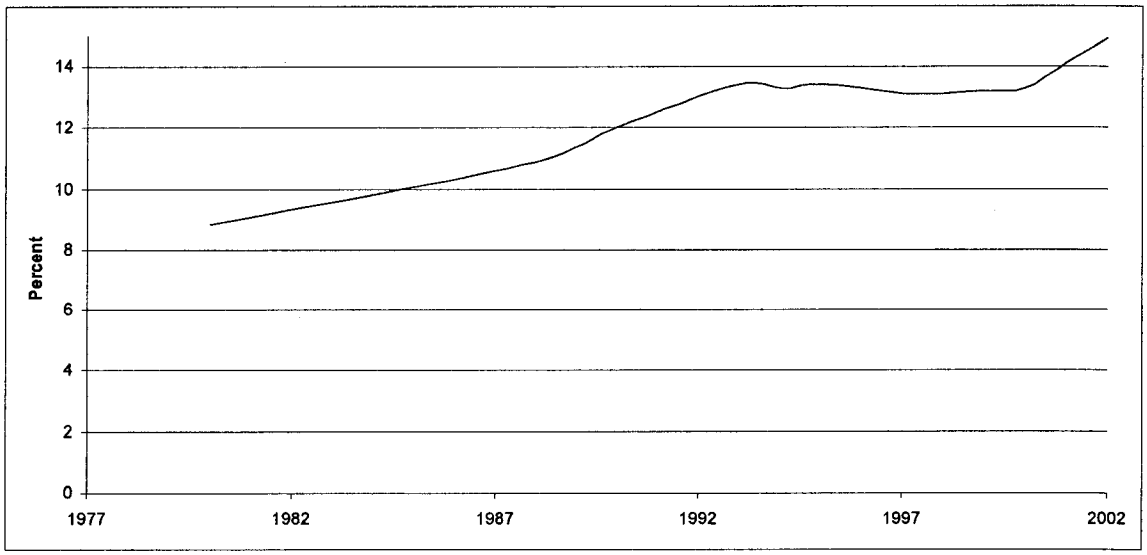
Give the imperfect nature of resource costing, additional information may be needed in order to obtain unbiased parameter estimates. In lieu of obtaining unbiased estimates, traditional sensitivity analyses, informed by information regarding covariation and case-mix, can be used in economic evaluation where uncertainty remains concerning prices.

1 Introduction

Between 1994 and 2003, the medical care component of the consumer price index (CPI) rose an average of 4.1 % per year, while the overall CPI increased 2.4% per year during this period (U.S. Department of Labor: Bureau of Labor Statistics 2004). In 2000 dollars, national health expenditures totaled $1,498 billion or 14.9 percent of the Gross Domestic Product (GDP) in 2002, up from $1,389 billion in 2001, and $1,309 billion in 2000 (Centers for Medicare & Medicaid Services 2004). Historically, as a percentage of the GDP, national health expenditures have trended upwards, except during the mid-1990s (Figure 1). The era between 1992 and 2000 was dominated by managed care, which slowed the growth in the quantity and intensity of services at the same time there was a reduction in medical prices (Levit, Smith et al. 2003). Health care spending accelerated beginning in 2001, partially due to managed care's waning influence, and thus contributed to an acceleration of overall spending (Levit, Smith et al. 2003).

National health expenditures are projected to total $3.4 trillion and reach 18.4% of the GDP by 2013(Centers for Medicare & Medicaid Services 2004). There are a number of potential explanations for the rise in health care expenditures in the United States: the aging population, costly technology, physician incomes, administrative costs, and prescription drugs to name only a few (Mehrotra, Dudley et al. 2003). While there is no single reason for the rise in health care expenditures, there is undeniably a tension between health care costs and actually providing health care, and this tension creates pressure on health care delivery systems to manage those costs.

Figure 1: National Health Expenditures as a Percentage of the Gross Domestic Product, 1980-2002



Source: Centers for Medicare and Medicaid Services, Office of the Actuary: National Health Statistics Group.

Given the importance of managing costs in today's health care delivery systems, insurers, and payers in general, as well as hospitals, physician groups, and other health care providers, must consider the total health care costs of interventions[1] in addition to evidence of better outcomes. The growth of managed care as well as budget constraints for public payers such as Medicare/Medicaid and the Veterans' Administration have precipitated the need for new and more rigorous economic evaluations of health care interventions.

Formal tools for evaluating health care interventions, which account for health care costs and health outcomes, have been developed (e.g., cost-effectiveness analysis, cost-

[1] The use of the term "intervention" is a general one representing a source of change in the health care delivery system (e.g., treatment, policy, payment rates).

utility analysis and cost-benefit analysis (Drummond, O'Brien et al. 1997)). While not a new science, these tools offer a new approach to economic evaluation of health care interventions base on traditional economic cost-benefit analysis. These tools depend on a variety of estimates of costs and benefits associated with health care intervention. Such analyses are generally based on expected costs (μ_c) and on the expected benefits or effectiveness (μ_e) – consistent with mainstream welfare economics (Garber and Phelps 1997). Current principles of cost-effectiveness analysis emphasize the rank ordering of interventions by expected economic return defined as a ratio of $\frac{\Delta\mu_c}{\Delta\mu_e}$ (e.g., additional dollar expended per additional quality-adjusted life-years gained). Typically, evaluation of health care interventions considers the benefit (i.e., effectiveness) in tandem with the costs, although pure cost analyses are also conducted (Drummond, O'Brien et al. 1997). In either case, analyses are most often incremental, estimating the extra benefit and/or extra cost associated with an intervention compared to the benefit or cost of the current practice or treatment (e.g., $\mu_1 - \mu_0$).

In recent years a substantial body of literature has been developed regarding the statistical analyses of cost data (see, e.g., Rutten-van Molken, van Doorslaer et al. 1994; Mullahy and Manning 1995; Manning, Fryback et al. 1996; Stinnett and Mullahy 1998). This literature has generally treated individuals' health costs as observable quantities, and focused on methods of analysis. However, in practice, the assumption that individuals' health costs are observable is questionable. Cost estimates may depend on either

observed cost or observed resource use data; while the former is preferable, when only resource use is observed, cost estimation requires that a monetary value be assigned to individuals' resource use (generically referred to as "resource costing"). For instance, in a recent, highly-publicized cost-effectiveness study of lung-volume-reduction surgery for patients with severe emphysema, cost estimates were based on both types of data: dollar-valued Medicare claims data for inpatient and outpatient service costs, and interview data for counts of prescription medication use and caregiver time (National Emphysema Treatment Trial Research Group, Ramsey et al. 2003). Resource costing methods were required to convert the measures of medication use and caregiver time into monetary units.

Although the number of studies employing resource costing methods is not documented, it is certainly common. For example, a search of the *New England Journal of Medicine's* website from August 2002 to August 2004 revealed five articles reporting the results of studies evaluating the cost-effectiveness of an intervention. All five of these studies use resource costing in their estimation of expected costs (Hulscher, van Sandick et al. 2002; Khan, Muennig et al. 2002; Manns, Lee et al. 2002; Nathoe, van Dijk et al. 2003; National Emphysema Treatment Trial Research Group, Ramsey et al. 2003). Consideration of the properties of resource costing methods is the major focus of this dissertation.

In this dissertation, the main analytical objective or problem is estimating parameters of cost distributions from price and resource use data observed from different samples. However, in general, prices and quantities follow a joint population distribution

whose covariance structure is in part governed by market interactions. Given the imperfect nature of the data used in current resource costing methods, additional information may be needed in order to obtain unbiased estimates of parameters such as μ_c and the variance in costs, σ_c^2.

1.1 Resource Costing in Practice

Resource costing processes consist of three primary steps: (a) identify and measure resource use, (b) measure unit price, and (c) assign prices to resource utilization. These steps are interdependent. A choice made in (a) inevitably constrains the set of choices for (b) and (c). For example, choosing to measure hospitalizations by number of days, regardless of medical condition, rules out the use of unit price information by type of admission (e.g., surgical or medical). Typically, converting resource utilization to cost by assigning prices to observed resource use, mechanically amounts to little more than multiplying prices and quantities, and then adding up these products (Lee, Bott et al. 2003). In this dissertation we define "price" as a proxy for opportunity cost per unit of resource utilization[2]. The question of "opportunity cost to whom" is addressed in a later section on perspective (see section 1.2), but for now we treat price generally as representing whatever measure is selected to convert resource utilization into monetary units.

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[2] This definition of price is consistent with that of the Canadian Coordinating Office for Health Technology Assessment (1996). However, other guidelines prefer use of the term unit cost, e.g., see Oostenbrink, J. B., M. A. Koopmanschap, et al. (2000). Manual for costing: methods and standard costs for economic evaluations in health care [in Dutch]. Amstelveen, College voor zorgverzekeringen.

A more precise, yet also more general, definition of resource costing, and one that will be used here, is the use of resource use and unit price information to estimate the parameters of a cost distribution (e.g., mean, variance). In short, resource costing is often used to estimate average cost based on price and quantity data, which follow an unobserved joint population distribution. We are left to make our estimates on the basis of observed data from marginal distributions of price and resource use quantity.

1.1.1 Identifying and Measuring Resource Use

The identification of resource units raises two questions. First, what types of resource use are relevant to the intervention being studied? Second, to what degree of detail must they be measured? This step considers the resource utilization resulting from the application of a health care intervention and from any comparator interventions aimed at effecting health outcomes (i.e., this is tantamount to specifying the production functions). Often, in practice, a decision tree for all interventions being considered and for the resulting resource use that occurs downstream (e.g., hospitalizations, pharmacy use) is developed. The service or resource categories that are affected by the intervention along the pathway should be identified.

Ideally, all resource categories are identified, but practically speaking, some are ignored if the interventions are deemed to have little or no effect on the resource utilization category. Even if they were included, resources not affected by an intervention would have no effect on estimates of incremental costs. More important, depending on the perspective one takes, some services or resources may or may not be

included in the analysis. For example, patients' time costs are unlikely to be considered by third-party payers and are thus not collected and/or evaluated as part of a cost-effectiveness analysis.

In most cases in which data collection is required, a decision is made regarding the level of detail and precision that the analysis demands. In essence, a separate cost-benefit analysis is undertaken to determine the benefits and costs of alternative data collection strategies. For hospital in-patient care, for example, this may involve deciding whether to use a crude figure, such as standard per diem prices, or more detailed figures, such as ordinary ward and ICU per diem prices. In essence, this step informs or guides us by identifying which resources to enumerate.

The measurement of resource use consists of determining the quantities of resources required for each intervention. A number of approaches have been recommended that can be grouped under two broad categories: synthetic methods consisting of using secondary data such as administrative databases, an expert panel, and retrospective chart reviews; and primary data gathering or the prospective collection of data specifically for the study at hand, either as part of a trial or as a study on its own. The main differences in these collection methods are in measurement cost and researcher control. Typically, synthetic methods have lower costs than primary data collection; while primary data collection allows the researcher more control over details, such as the how resources are measured (e.g., units of measure, the level of detail).

In general, measurements of resource utilization are enumerated in "natural units" such as number of physician visits, number of days of hospitalization, or number of each laboratory test. While researchers typically enumerate in natural units, resource utilization can be enumerated at varying levels of detail (Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996; Luce, Manning et al. 1996; Oostenbrink, Koopmanschap et al. 2002). To illustrate, we consider two cost-effectiveness studies—one in the area of depression treatment and one in the area of alcohol and substance abuse.

Simon et al. (Simon, Manning et al. 2001), in their multi-site cost-effectiveness study of a depression management program, estimate costs for inpatient services, outpatient services, and time in treatment. The authors base hospitalization estimates on the number of hospitalizations by Diagnosis Related Group (DRG), collected from administrative databases. Similarly, a study evaluating the cost-benefit of brief physician advice for the treatment of problem drinking based the estimated cost for inpatient service on the patient-reported number of hospital days (regardless of diagnosis or other information) (Fleming, Mundt et al. 2000).

The choice in the level of detail selected, or available, when one is identifying and measuring resource use determines the level of detail at which the evaluation step can be conducted.

1.1.2 Measuring and Assigning Unit Prices

In order to convert measured resource use to monetary amounts, a source of the unit price must be chosen for each resource unit previously identified. Regardless of perspective, the unit price of the resource should approximate (be a proxy for) the perspective-relevant opportunity cost (the value foregone by not putting this resource into the best alternative use). Unfortunately, opportunity costs are not easily calculated. However, under certain assumptions regarding market conditions, the market price of a resource can be considered a reflection of its opportunity cost (Luce, Manning et al. 1996). It should be acknowledged that the market price of each resource could vary with any number of factors including: geographical location, type of institution, time period, and by categories of patients and care provided (Lynk 2001; Hay 2003). In general this step should measure the unit prices for resources consumed from the point of view of the stated audience (discussed in detail below, in section 1.2).

Assigning unit prices to measured resource use is often referred to as cost valuation (Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996; Oostenbrink, Koopmanschap et al. 2002). One typically does this by first multiplying each unit of resource use by its unit price, and then summing it up to arrive at a calculated total health care cost. For example, for the economic evaluation component of an asthma treatment study, researchers may observe individuals' asthma-related ER visits. In order to estimate the average cost per individual, analysts would first have to convert each ER visit to a monetary value by multiplying the number of ER visits by a

unit price. Ideally, the unit price assigned to the observed resource use approximates its perspective-relevant unit opportunity cost. From a societal perspective, the prices selected would proxy the most comprehensive set of opportunity costs, while studies taking a third party-payer perspective would select paid amounts.

In practice, the unit price represents whatever measure is selected to convert measures of resource utilization into monetary units. The source of such unit price information can come from an internal or external source. Internal price information is obtained from the same source as the measure of resource utilization. For example, to inform a decision to implement an asthma management program, an HMO may collect information on inhaled steroid use among enrolled asthmatics via survey; then apply the price it pays for inhaled steroids. The literature may not accurately reflect the frequency of internal price data use because the results are likely proprietary and not published (e.g., they exist in the form of business assessments of interventions). In addition, some health resources such as patient time have no internal source of price information.

It is more often the case that external price sources are used. Similar to researchers in the example above, researchers wishing to evaluate an asthma management program may collect information on inhaled steroid use among asthmatics via survey; then apply the published average wholesale price (AWP) for inhaled steroids. External price sources may be used because the results can ostensibly be generalized (how well do our unit prices represent the unit prices in the "real" world?) or because an internal price source for price information does not exist. This dissertation will focus largely on the

issue of external sources of price information, but most results are applicable also when the price source in internal.

1.1.3 Resource Costing Methods

The previous two sections described the process of identifying and measuring resource use and assigning prices. Both of these processes, rather than a single one, are necessary to yield cost estimates.

Two approaches are available to researchers when it comes to resource costing: micro-cost methods and gross-costing (Luce, Manning et al. 1996). Micro-costing includes such methods as direct measurement to determine the cost of new interventions and programs. Inputs such as staff time and supplies are directly measured to develop a precise cost estimate. The time of each type of staff is estimated, and its unit price determined. The analyst may directly observe staff time, have staff keep diaries of their activities, or survey managers. The cost of supplies and equipment, as well as other expenses, must also be determined. In essence, micro-costing calls for the direct enumeration and costing out of every resource consumed in the treatment of a patient (Luce, Manning et al. 1996).

Gross-costing[3] methods assume that every encounter with the same characteristics has the same price. Gross-cost estimates are needed because detailed micro-costing is

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[3] The Health Economics Resource Center, a national center that assists VA researchers in assessing the cost-effectiveness of medical care, calls this "average-costing" (http://www.herc.research.med.va.gov). We choose to refer to this as "gross-costing"

often too time-consuming and laborious a method to apply to all possible healthcare utilization. In many studies, and for some of the healthcare utilization in nearly every study, a "gross-costing method" can be used. This dissertation will focus on gross-cost methods.

A common source of price information used with gross-costing is Medicare reimbursement rates (e.g., Medicare fee schedules, DRG prospective payments), which can be found throughout the economic evaluation literature (Lave, Frank et al. 1998; Simon, Manning et al. 2001; Mahoney, Jurkovitz et al. 2002). In theory, Medicare reimbursement rates represent the average cost to the provider of providing a medical service (Edwards, Honemann et al. 1994). Internationally, Australia and the Netherlands have composed lists of standard prices that are average unit costs of standard resource items (Oostenbrink, Koopmanschap et al. 2002).

Other sources of price information are billing or administrative records and samples or surveys. For example, the Nationwide Inpatient Sample (NIS) collects discharge data from over 1,000 U.S. hospitals. Charge and diagnostic information from NIS data can be used to estimate the average charge per hospitalization (or per hospital day). One may wish to adjust charge data (using cost-to-charge ratios) to better estimate opportunity costs (Finkler 1982). However, cost-to-charge is not necessarily a panacea, since estimates of average cost has been shown to vary by cost-to-charge methodology (Taira, Seto et al. 2003).

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because the term "average-costing" may imply that average prices were used exclusively.

1.2 Perspective Issues

There is one issue all resource costing steps share—perspective. That is to say, the point of view from which the analysis is undertaken determines: (1) which resources we identify as being pertinent, and (2) the price of those resources. The choice of perspective has a direct effect on the valuation or costing of the intervention(s). The issue of perspective, as it relates to resource costing, is addressed by several published guidelines (Commonwealth Department of Health Housing and Community Services (CDHHCS) 1992; Luce, Manning et al. 1996; Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1997). While these guidelines emphasize the estimation of cost from a societal perspective, other perspectives have been described (Luce, Manning et al. 1996). To illustrate how identification and pricing of resource use vary by perspective, consider Table 1, which describes the medical costs that must be counted in the case of each perspective.

From the patient's perspective, only out-of-pocket payments for medical care are considered. To capture out-of-pocket payments, only resources paid for out-of-pocket by the patient need be enumerated, and price estimates should represent the amounts paid out-of-pocket by the patient. In contrast, a third-party payer, such as an insurer or Medicare, need only enumerate covered services and use price estimates based on paid amounts and administrative costs, but not amounts borne by others (e.g., the patient's out-of-pocket expenses). All medical care resource utilization is included from society's perspective, and the price should proxy the "opportunity cost"—the value of all the other

goods and services that we must give up in order to produce it. More thorough discussions of perspectives are found in the literature (Gold, Siegel et al. 1996; Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1997). However, the intent of the present discussion is to highlight the role that perspective plays in resource costing. While the focus, in this dissertation, is on the assigning prices to resource use, we acknowledge the important role that perspectives play through identifying and enumerating resource use and measuring unit prices.

Table 1: Costs Under Alternative Perspectives

Cost Element	*Societal*	*Patient and Patient Family*	*Third-Party Insurer*
Medical Care	All medical care costs	Out-of-pocket expenses	Covered Payments
"Resource Units"	All Units	Those paid out-of-pocket	Those Covered
"Price"	Opportunity Cost (incl. Admin. Cost)	Amount paid out-of-pocket	Amount paid + Admin. Cost

Source: Adapted from Luce et al. (1996), Table 6.1.

1.3 Issues Addressed by this Dissertation

In this dissertation, the main analytical objective or problem is estimating parameters of cost distributions from price and resource use data observed from different samples. However, in general, prices and quantities follow a joint population distribution whose covariance structure is in part governed by market interactions. In notational form:

$$\phi(C;\theta) \text{ or } \phi(p,x;\theta)$$

where ϕ is the cost distribution, $\theta = (\mu_c, \sigma_c^2, ...)$ is a vector of population parameters, and in general terms $C = \sum_i p_i x_i$ (where i indexes the resource used). Given the imperfect nature of the data used in current resource costing methods, additional information may be needed in order to obtain unbiased estimates of parameters such as μ_c and the variance in costs, σ_c^2.

Optimally, information (or data) on costs would be used to obtain these parameter estimates. When cost information is not available, one could acquire separate data on resource use and unit prices, i.e., sample in some manner (not necessarily randomly) from the marginal distributions of $\phi(x)$ and $\phi(p)$. The question is, "What method should be used to combine these two pieces of information, such that they provide the same parameter estimates of interest that using cost information provides?"

Applied resource costing methods typically result in unbiased and consistent estimates of relevant cost parameters (i.e., μ_c). Many of the issues related to resource costing are addressed in the economic evaluation literature and resource costing

guidelines (Commonwealth Department of Health Housing and Community Services (CDHHCS) 1992; Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996; Drummond and Jefferson 1996; Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1997; Oostenbrink, Koopmanschap et al. 2002). However, the effect of how unit prices are assigned to measured resource use has not been explored fully. This dissertation will focus on the effect of (1) price/resource use relationships, and (2) data aggregation on the estimation of μ_c. More specifically, it will explore the implied assumptions of using fixed-price estimates and the level-of-detail at which resources are enumerated.

The relationship between price and resource use is seldom mentioned or examined in the costing literature, although there are exceptions. In *Cost-Effectiveness in Health and Medicine*, Luce, Manning et al. (1996) briefly discuss the circumstances under which unit prices may change due to the implementation of an intervention, noting that: "market prices may not give an adequate representation of the marginal costs ... when the decision to implement an intervention would result in real changes in cost" (page 199). For example, the authors note that the availability of resources could be affected by the large-scale implementation of an intervention. If the resulting increase in demand were large enough, it would cause a shortage of those resources and an increase in the price of those resources. However, little has been done empirically to examine this issue. To address this gap in the literature, I examine the theoretical consequences of covariance of price and resource use. I analyze various alternative price and resource use

data and resource costing methods from theoretical and applied viewpoints, specifically focusing on their implications for the estimation of mean cost.

While covariance is a stochastic concept, one potential source of covariation is economic relationships, often represented as elasticity (e.g., elasticity of demand/supply, price elasticity). For example, price elasticity is define as the ratio of the response in quantity demanded or supplied to a change in price, $\frac{\Delta X}{\Delta P}$, or using calculus notation $\frac{\delta X}{\delta P}$. Intuitively, we would expect the sign of the covariance term to be the same as that of the price elasticity. Consider the following example where quantity, X, is a nonlinear function of price, P, and α represents the price elasticity parameter,

$$X = P^{\alpha}.$$

Apply the natural log to each side of the equation results in the linear equation:

$$\ln X = \alpha \ln P.$$

The covariance between price and the quantity is:

$$\begin{aligned} &C(\ln X, \ln P) = C(\alpha \ln P, \ln P) \\ &= \alpha E(\ln P * \ln P) - \alpha \ln(P) \ln(p) \\ &= \alpha V(\ln P) \end{aligned}$$

Here the sign of the covariance between ln(P) and ln(X) depends only on the price elasticity parameter.

While the literature discusses heterogeneity of price and resource use information, the solution offered seems to be more detailed (i.e., less aggregated) information on both resource use and unit prices (Canadian Coordinating Office for Health Technology

Assessment (CCOHTA) 1996). For example, when assigning unit prices to hospitalizations, the application of an overall per diem amount is considered less precise than the application of the amount per DRG (Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996). Since resource costing involves multiplying a fixed price by observed resource use, the level of detail of each factor must be the same. For example, inpatient hospitalization enumerated by number of days is multiplied by the estimated per diem price of a hospitalization—not the per-stay price of a hospitalization. At one extreme, gross-costing resource use is enumerated at a very aggregate level, and at the other end of the spectrum, enumeration can be conducted at a very high level of detail. One of the two major themes of this dissertation is the effect data aggregation has on the estimation of μ_c. In particular, we address the question of how the level of detail of price and resource use information affects estimation bias and precision.

The cost parameter of greatest interest in the economic evaluation of medical interventions is the mean or expected cost, μ_c. Expected cost has an intuitive appeal because of its relationship to total cost and its usefulness in cost-effectiveness analysis, cost analysis, and cost-benefit analysis. One advantage of the mean is that it extrapolates well to totals. Suppose, for example, that each month of medication costs an insurer an average of $5,000. If we took the average number of months of treatment per enrollee times 5,000, we would get an estimate of the average per enrollee total cost to the insurer. You could not do that with a median. In medicine, the cost-benefit analyses almost always use a mean rather than a median (or a log transformation), even when the data are

highly skewed, because doing so helps the hospital, insurance company, etc. better understand the impact on their bottom line.

It should be noted, however, that while the value of estimating μ_c is apparent in the literature, the estimation of $\sigma_c^2 = \text{var}(c)$ is less so. Yet, σ_c^2 potentially plays at least two roles in the economic evaluation of health care interventions. First, σ_c^2 may be of direct interest to risk-averse decision-makers (O'Brien and Sculpher 2000; Palmer and Smith 2000; Zivin 2001). For example, in addition to μ_c, smaller third-party payers, who have less risk pooling, may find σ_c^2 of value as it reflects *ex ante* uncertainty of costs. Second, the precision of $\bar{C}$, an estimator of μ_c, is a function of σ_c^2 and N (sample size). Although large N may mitigate any differences in key inferences about μ_c, due to alternative resource costing methods' estimates of σ_c^2, sufficiently large N's are rare in many studies. They are especially scarce in those powered for efficacy or effectiveness (e.g., clinical trials).

This dissertation will examine the effect resource costing methodology has on estimates of both μ_c and σ_c^2, although the primary focus will be on μ_c. While the effects of resource costing methodology on properties of estimators of μ_c (e.g., precision) and on other parameters/moments of $\phi(C;\theta)$ (e.g., skewness) may also be of interest, such considerations are left to future research.

1.4 Research Objectives

This study has five objectives:

1. To define a generic cost function that is capable of encompassing most health care intervention costs.
2. To examine conceptually the effect that economic relationships between resource use and prices can have on estimation bias through resource costing methods
3. To demonstrate empirically the effects that economic relationships between resource use and prices have on properties of estimators of μ_c by:
    a. utilizing the properties of lognormal distributions; and
    b. using data from a randomized clinical study of a depression intervention.
4. To examine conceptually the effect data aggregation can have on estimation bias through resource costing methods.
5. To demonstrate empirically the effect of data aggregation on estimators of μ_c using data from a randomized clinical study of a depression intervention.

2 Related Literature

This dissertation builds upon the literature on economic evaluation in health care, specifically on resource costing methodology. This body of literature has two major components: the published guidelines for economic evaluation and reporting, and the applied economic evaluation literature. The applied literature illustrates current practice, while the guidelines represent "best" practice as it pertains to resource costing.

This literature review is divided into three main sections. The first section summarizes the published health care cost assessment guidelines, and focuses on several steps in the economic evaluation of health interventions related to resource costing. The second section describes the current application of resource costing in economic evaluation of medical interventions. The final section identifies and summarizes the gaps in the literature, and specifies this dissertation's contribution in addressing those gaps.

2.1 Health Care Cost Assessment Guidelines

Several guidelines have been published regarding cost assessment in economic evaluations (Commonwealth Department of Health Housing and Community Services (CDHHCS) 1992; Canadian Coordinating Office for Health Technology Assessment (CCOTHA) 1994; Drummond and Jefferson 1996; Luce, Manning et al. 1996; Russell, Gold et al. 1996; Oostenbrink, Koopmanschap et al. 2002). These guidelines cover several issues relevant to resource costing including: perspective, identification and measurement of resource use, prices, and the valuation of resources.

The Australian and Canadian governments have adopted legislation, requiring formal economic studies prior to reimbursement by the governments to provider for pharmaceuticals (Commonwealth Department of Health Housing and Community Services (CDHHCS) 1992; Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1994). These Australian and Canadian guidelines recommend a societal perspective, the use of final outcome measures, incremental analysis of costs, and probabilistic sensitivity analysis. While the Australian guidelines "provide a means to identify and format the necessary information" (Walker 2001), the Canadian guidelines "suggest a reporting format to ensure that studies are reported adequately and in a consistent manner to facilitate their review and comparison" (Walker 2001). The Canadian guidelines are prescriptive and more sophisticated than the Australian guidelines—they form a "how-to" guide of sorts. In addition, the Canadian guidelines have been updated (Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1997) and also reference an additional document on the costing process itself (Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996).

More recently the *Dutch Manual for Costing: Methods and Standard Costs for Economic Evaluations in Health Care* was published (Oostenbrink, Koopmanschap et al. 2000). This manual provides guidelines and recommendations for costing in economic evaluations in the Netherlands. Related publications include a section in English regarding the standardization of cost (Oostenbrink, Koopmanschap et al. 2002). This section of the *Dutch Manual* introduces a six-step procedure for costing. These steps

closely mirror other published guidelines by addressing perspective, identification and measuring of resource units, unit prices, and the valuation of resources.

In addition to government guidelines, several peer-review journals have published guidelines for economic evaluations submitted for publication (Kassirer and Angell 1994; Mason and Drummond 1995; Russell, Gold et al. 1996; Weinstein, Siegel et al. 1996). Arguably, the most prominent among these are the recommendations of the *British Medical Journal* (BMJ) and the *Journal of the American Medical Association* (JAMA). In a 2001 publication, Walker (2001) compared the Australian, Canadian, BMJ, and JAMA guidelines, concluding that "the available guidelines for cost and cost-effectiveness analyses differ in terms of the target audience, objectives and, to a lesser extent, methods recommended."

Although the guidelines provide insight into choosing the perspective and identifying and measuring resource use, it is notable that they provide less or no guidance on methodological issues such as assigning unit prices to those resources. In particular, they provide only very general rules regarding the level of detail, and virtually no assistance on how to handle the potentially significant effects of economic relationships between resource use and prices on properties of parameter estimates (e.g., μ_c). The guidelines typically include statements such as the following, regarding level of detail:

> *For most resource categories (goods or services), different costing options exist. Each costing option entails a certain amount of complexity, time and effort and*

> *yields a certain precision. Detailed (micro) costing is often an option. However, in some instances the use of cruder estimates may be sufficient. The challenge is to strike the appropriate balance between the need for precision and the avoidance of bias and the effort needed to provide the increased precision. Clearly, precise unbiased cost estimates are the ideal; similarly, imprecise biased estimates are the least valuable. The relative desirability of biased/precise estimates versus unbiased/imprecise estimates will, however, depend on the context. In some cases a precise but biased estimate might suffice.*
>
> *— A guidance document for the costing process (Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996).*

Similar statements can be found in many of the published guidelines (Commonwealth Department of Health Housing and Community Services (CDHHCS) 1992; Luce, Manning et al. 1996; Oostenbrink, Koopmanschap et al. 2002). While these guidelines direct our attention to the fact that problems can arise when one implements resource costing techniques, they do little to emphasize the significance of specific choices on resource costing methodology.

To that end, Rittenhouse and his colleagues appear to be the only authors who analytically examined the effect that choices of price estimates have on comparisons of expected costs (Rittenhouse, Dulisse et al. 1999). In particular, they focused on how the

choice of price estimates affects statistical inference regarding between-group differences in mean costs. The authors touch briefly on the theoretical consequences of using fixed-price estimates as they relate to the assumption their use makes regarding covariance between price and resource use, but this is not the central point of their paper. Rittenhouse and his colleagues conclude that "regardless of the appropriateness of the constant price assumptions, the central point of the paper—that the analyst's choice of price estimate can have an important effect on the conclusions drawn from hypothesis tests—holds."

2.2 Applied Resource Costing

The two main concerns raised when assigning unit price to measured resource utilization, as it is currently applied, are that: (1) data for utilization and price are often from two different sources, and (2) the level of detail at which this assignment occurs may not be sufficient. As previously noted, resource costing uses separate resource use and unit price information to estimate parameters of cost distributions. While the source of resource use information is expected to vary based on study design (e.g., randomized clinical trial, observational study) and intervention of interest (e.g., policy change, clinical intervention), there also appears to be no standard set of unit prices. Studies have used internal unit price information based on cost-accounting systems and external unit price information such as Medicare reimbursement rates (Johannesson, Jonsson et al. 1997; Medical Research Council Laparoscopic Groin Hernia Trial Group 2001; Simon, Manning et al. 2001).

Regarding the actual assignment itself, the level of detail at which unit prices are assigned varies by study. A single unit price estimate is often applied to all resource use within a given resource service area. For example, Project TrEAT, a randomized controlled clinical trial of alcohol treatment designed to test the efficacy of brief physician advice for the treatment of problem drinkers, used a fixed Medicare average per diem cost for all inpatient stays and emergency room visits (Fleming, Mundt et al. 2000). Another study examining the cost-effectiveness of two chronic bronchitis treatments used observed hospitalization day from the GLOBE study and mean cost per day estimates obtained from the Health Care Finance Administration's MEDPAR inpatient bills (Halpern, Palmer et al. 2002). The use of a simple unit price estimate has been found to be inaccurate because of wide variations in service use, both between and within service categories (Coyle, Godfrey et al. 1997).

Many studies use more detailed price information. Examples are: average wholesale prices for pharmaceuticals, applied by specific drug, Medicare's Physician Fee Schedules for specific physician services, and Medicare's inpatient prospective payment system for inpatients stays, based on DRGs (Medical Research Council Laparoscopic Groin Hernia Trial Group 2001; Simon, Manning et al. 2001). Using Medicare's price data, further adjustments can be made (e.g., accounting for differences in reimbursement rates between geographic locations).

Although the use of this more detailed price information appears to be an improvement over the single unit price estimates, the precision of these estimates is still

of concern. In a study examining the costs of hospital care for cardiac and HIV patients, Heerey and his colleagues found up to a 66% difference between DRG-calculated costs and costs derived from micro-costing methods (Heerey, McGowan et al. 2002).

Because micro-costing is expensive and time-consuming, sensitivity analyses using different price sources are sometimes used. Mark et al. (1995) investigated the cost-effectiveness of thrombolytic therapy with tissue plasminogen activator as compared with streptokinase for acute myocardial infarction. When estimating the costs of hospitalization, they used two sources of price data, the total cost estimates from the Duke Transition One cost-accounting system, and Medicare's DRG reimbursement rates. Similarly, cost for thrombolytic agents were estimated in two ways, from the *Drug Topics Red Book* average wholesale price and from the drug costs observed in 16 study hospitals, and a sensitivity analysis based on these different price estimates was published (the use of the latter price estimate resulting in slightly lower cost per life year saved, $32,678 versus $27,115). Although these approaches illustrate the effects different price sources can have on parameter estimates (e.g., μ_c), they do not address the effects of data level of detail.

2.3 Filling in the Gaps

Typically, resource costing methods employed that are involve assigning unit prices to measured resource use by combining the two pieces of information. Neither the published guidelines nor the applied literature provides an adequate examination of the effect that (1) covariance structures and (2) the level of detail, at which prices are

assigned, have on estimates of μ_c and σ_c^2. There exists a body of literature quantifying relationships between prices, in general, and resource use. For example, copayments have been shown to affect medical utilization (Manning, Newhouse et al. 1987; Newhouse, Manning et al. 1987; Selby, Fireman et al. 1996). There are also examples in the health care policy literature where Medicare reimbursement rates are shown to affect physician visits (Christensen 1992). In any case, while economic theory and literature do suggest that relationships between prices and quantities exist, the resource costing literature provides no guidance on addressing these relationships. That the relationships between prices and quantities be specifically addressed within the resource costing literature is particularly important because of the potential for biased parameter estimates. Commonly used resource costing methods seem intuitively correct. However, further study of these methods can highlight sources of bias, providing valuable insight to researchers, analysts, and decision-makers.

To date, some of the resource costing literature has addressed the effect that level of detail has on the estimation of μ_c. However, this literature is limited to illustrative examples and does not examine, analytically or conceptually, the effect that data aggregation has on the estimators of μ_c. Although the level-of-detail of resource use data is discussed in some of the costing literature (see the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996), to the best of my knowledge, its effect on parameter estimates has not been studied. The general consensus is that more detail is better, although to obtain it increases the expense of conducting research. Some

studies have examined the use of micro-costing a opposed to more aggregate price data (Heerey, McGowan et al. 2002). However, no study has parsed the effect of data aggregation from that of the source of price data.

In light of these gaps and other considerations, this dissertation addresses two important issues. First, the effect covariation between prices and resource use quantity has on estimates of μ_c and σ_c^2, and second, effect data aggregation has on estimates of μ_c. This will be demonstrated theoretically as well as empirically with data from the CARE study—a randomized study designed to examine the cost-effectiveness of a depression management program. The purpose is to illustrate clearly the magnitude of the potential biases involved, and to serve as a resource for researchers and analysts estimating μ_c from measured resource use and unit price estimates. While closing the described gaps in the resource costing literature, this work will also help put to rest the misguided assumption that estimating μ_c based on separate price and resource use information is identical to estimating μ_c based on cost data itself.

3 Conceptual Framework

As I noted earlier, I use the term "health care interventions" generically to include any purposeful action intended to modify a health care process or situation. Examples of an intervention might include the adoption of depression treatment guidelines calling for an increase in primary care physician visits and better access to pharmacological treatments (see Katzelnick, Simon et al. 2000), or cuts in Medicare reimbursements to oncologists for the medications they administer in their offices (see Lueck 2004). Other examples are the FDA approval of fluoxetine (Prozac) for the treatment of clinical depression (see Millenson 1987), the UW Hospital making four parking spaces designated for capers or motor homes available to out-of-town patients or relatives at no charge (see Ingersoll 2004), or a third-party payer approving the use of MRI scans, instead of mammograms, for the detection of breast cancer among high-risk women (see Associated Press 2004).

In this chapter we link intervention examples to a common conceptual framework grounded in economic theory, for the purpose of empirically analyzing health care costs. The chapter has three main objectives: (1) defining health care production functions and establishing that their structure has an impact on the structure of cost functions; (2) defining a corresponding cost function that is capable of encompassing most health care intervention costs; and (3) describing how a variety of health care interventions have cost implications that can be conceptualized using this cost function.

3.1 Health Production Function

This dissertation builds on the concepts of health production, cost minimization, and interventions that target either input prices or input quantities. Some very specific examples of these interventions are listed above. A great deal of the economic literature has been devoted to studying the behavior of profit-maximizing firms in both competitive and non-competitive environments (Varian 1999). Valuable insight is often gained through breaking up the profit maximization problem into two pieces: how to minimize the cost of producing a given level of output, and how to choose the most profitable level of output production. Next, we consider the first part—minimizing the cost of producing a given level of output.

Consider a general production frontier function for which we have n inputs of production:

$$q = \Phi(\mathbf{x};\boldsymbol{\alpha}). \tag{1}$$

This function can be generically thought of as producing "health." For example, an HMO considering the implementation of a depression management program has the goal of improving the mental health of its enrollees. From the perspective of the decision-maker implementing an intervention, $\mathbf{x} = (x_1,...,x_n)$ is a vector of inputs that produce, maximally, some level of output q through a production function having a vector of

parameters α. It is the price of the inputs (resources) consumed (used), along with the function's parameters, which determines the cost of production.

3.2 Cost Function

Consider the impact of interventions on the behavior of decision-makers who are interested in containing costs, but not necessarily minimizing them. This is of interest because of the insight it provides concerning both profit-maximizing firms, such as private payers (e.g., managed care), and non-profit-maximizing decision-makers, such as Medicare, Medicaid, and the Veterans Health Administration. While the level of output a particular firm wishes to produce may differ between (and within) each of these decision-makers, this study is essentially interested in producing a given level of output while controlling cost—regardless of how or why the level of output was determined.

To this end, it is important to recognize that the structure of the health production function implies the structure of the cost function. A traditional example looks at cost-minimization from the point-of-view of a price-taking firm. Suppose we have two inputs of production that have prices p_1 and p_2, and that we want to determine the way to product a given level of output, q, at the lowest cost. If we let x_1 and x_2 measure the amounts used of the two inputs, and specify a production function, we can identify the cost function that will identify the minimum cost necessary to achieve the desired level of output. A common production function for 2-inputs is a Cobb-Douglas production function, where the level of output is a function of x_1 and x_2, and parameters α and β,

which represent rate at which x_1 and x_2 can be substituted for one another to produce a given level of output. In this case we can use calculus to solve

$$\begin{aligned} C(\mathbf{p},q) &= \min_{x_1,x_2} p_1x_1 + p_2x_2 \\ &\text{such that } q = x_1^{\alpha}x_2^{\beta} \end{aligned} \tag{2}$$

and show that the cost function will have the form

$$C(p_1,p_2,q;\alpha,\beta) = p_1x_1^* + p_2x_2^*, \tag{3}$$

where x_1^* and x_2^* are the amount of the two inputs uses to produced the desired level of output at the lowest cost. Specifically, a this cost function will have the form

$$C(p_1,p_2,q;\alpha,\beta) = Kp_1^{\frac{\alpha}{\alpha+\beta}}p_2^{\frac{\beta}{\alpha+\beta}}q^{\frac{1}{\alpha+\beta}}, \tag{4}$$

where K is a constant that depends on both α and β.

3.3 Generic Cost Function

Our goal is to study the role of resource costing in the economic evaluation of health care interventions. Incremental costs are used to evaluate health care interventions, and the estimation of average cost is a necessary component to estimating incremental costs.

To that end, I have developed this simple framework, grounded in economic theory, to illustrate the complexity of calculating the cost to a payer associated with an intervention. The framework for realized costs to the payers, not necessarily minimum costs, is presented in this chapter and has four main components:

$$C(\mathbf{p},\bar{\mathbf{x}},\bar{q},\delta;\boldsymbol{\alpha}) = C^{(a)}(\mathbf{p},\bar{q};\boldsymbol{\alpha}) + C^{(b)}(\mathbf{p},\bar{\mathbf{x}},\bar{q};\boldsymbol{\alpha}) + C^{(c)}(\mathbf{p},\bar{q};\boldsymbol{\alpha}) + C^{(d)}(\mathbf{p},\bar{q},\delta;\boldsymbol{\alpha}), \quad (5)$$

where $\mathbf{p}$ is vector of prices, $\bar{x}$ is the quantity of fixed inputs, $\bar{q}$ is the desired level of output, δ is a parameter representing market effects, and $\boldsymbol{\alpha}$ is a vector or parameters from the production function.

As few as one or as many as all four features may be represented when determining a payer's cost of an intervention at any one time. The traditional textbook case, $C^{(a)}$, treats decision-makers as cost minimizers, and in which interventions target either prices or parameters of the cost function. The case in which interventions target fixed resources (e.g., setting minimum postpartum hospital stays) is represented by $C^{(b)}$, the case in which resource use is taken to be exogenously determined, and payers must pay for whatever quantity is transacted is represented by $C^{(c)}$, and $C^{(d)}$ is the case in which interventions target a parameter representing market structure effects on how x affects p.

3.3.1 Traditional Case

Consider the cost function, $C(\mathbf{p},\bar{q};\boldsymbol{\alpha})$, where $\mathbf{p} = [p_1,...,p_m]$ is a vector of prices, $\bar{q}$ is a target output (e.g., depression-free days), and $\boldsymbol{\alpha}$ is a vector representing the parameters of the production function (e.g., $\boldsymbol{\alpha} = [\alpha,\beta]$ in the case of the Cobb-Douglas production function above). This representation of the cost function comes from the structure of the production function and implies cost-minimizing behavior. In such a framework, the only apparent

intervention involves modification of one or more of the prices, $\mathbf{p}$, or of the parameters of the production function, $\boldsymbol{\alpha}$.

The traditional textbook case assumes that inputs (x_i's) are chosen to minimize cost, given $q = \Phi(\mathbf{x};\boldsymbol{\alpha})$ and $\mathbf{p} = [p_1,...,p_m]$:

$$C(\mathbf{p},\bar{q};\boldsymbol{\alpha}) = \sum_{i=1}^{m} p_i * x_i^*(\mathbf{p},\bar{q};\alpha). \quad (6)$$

Given a target output ($\bar{q}$), a level of input is selected based on prices of inputs and parameters of the production function. This framework can be used to describe interventions that change one or more price or somehow alter the production function's parameters.

Consider the simple example that an HMO has contracted with a physician group to provide depression treatment for its enrollees. Furthermore, assume that providers have the option of treating their patients with an antidepressant drug or psychotherapy, or with both. The realized cost to the third-party payer can be written as:

$$C = p_1 * x_1^*(p_1,p_2,\bar{q};\alpha) + p_2 * x_2^*(p_1,p_2,\bar{q};\alpha), \quad (7)$$

where $i = 1$ represents antidepressant therapy, and $i = 2$ represents psychotherapy. Here, interventions can be of two types: (1) those that change input prices or (2) those that change the parameters of the production function. Either type of intervention alters the realized cost to the payer by shifting the input levels and, perhaps, the unit prices paid to use them. For example, a drop in the antidepressant's price would result in cost-minimizing physicians using more

antidepressant and less psychotherapy [note: this depends on α]. The incremental cost of this change in price, from the perspective of the HMO, is the change in the payer's cost:

$$\Delta C = C(\mathbf{p}_1, \bar{q}; \boldsymbol{\alpha}) - C(\mathbf{p}_0, \bar{q}; \boldsymbol{\alpha}). \quad (8)$$

Likewise, the FDA approval of a "new" antidepressant (e.g., Prozac), and subsequent use of it as first-line depression therapy instead "older" antidepressants (e.g., amitriptyline—a tricyclic antidepressant), have the effect of altering parameters of the cost function as they represent the production technology confronting the decision-maker at a given point in time. To put it more explicitly, assume the output of interest (e.g., depression-free days) is represented by a Cobb-Douglas production function as specified in equation (2). For example, replacing amitriptyline with Prozac may change α because, presumably, Prozac results in better outcomes than amitriptyline. In reality, a change from amitriptyline to Prozac may have better outcomes but also a higher unit price.

Many health care interventions have particular features that require expansion of this simple framework. Consider the addition of two features to the cost function: (1) a vector of inputs that are fixed ($\bar{\mathbf{x}}$), in the sense that their use cannot be varied in the short run by the decision-maker due to regulation, contracts, etc., and (2) a parameter (δ) representing market structure effects of x on p, e.g. drug volume discount rates, (Genuardi, Stiller et al. 1996) or monopsony effects in the market for nurses (Sullivan 1989).

3.3.2 Changing Fixed Resources

Consider an intervention that directly changes the level of use of inputs that are typically considered fixed to the payer, at least in the short run. The cost can be written as:

$$C(\mathbf{p}, \bar{\mathbf{x}}, \bar{q}; \boldsymbol{\alpha}) = \sum_{j=m+1}^{n} p_j * \bar{x}_j, \tag{9}$$

where $\bar{\mathbf{x}} = [x_{m+1}, ..., x_n]$ is a vector of fixed inputs—those not chosen by the decision-maker.

For example, consider the postpartum discharge laws enacted between 1995 and 1998 that empower the mother to decide on length of stay up to the minimum 48 or 96 hours. The laws have been shown to increase the number of two- and three-night stays while decreasing the number of one-night stays, and thus to increase the cost per early discharge averted (Liu, Dow et al. 2004). Part of the realized cost to a third-party payer, such as an HMO, depends on the number of bed days and the price of those bed days. Unlike the traditional case in section 3.3.1, the payer is not free to choose the length of stay, let alone choose the length of stay based on cost-minimizing behavior.

Another example is the Accreditation Council for Graduate Medical Education's (ACGME's) new requirements for resident duty hours (Accreditation Council for Graduate Medical Education 2003). Although resident duty hours will most directly affect surgical trainees, they will undoubtedly also affect surgical faculty. In fact, the new mandates explicitly state that "faculty schedules must be structured to provide residents with continuous supervision and consultation" (Accreditation Council for Graduate

Medical Education 2003). Although these guidelines acknowledge the need for restructuring of faculty schedules in order to improve resident oversight, there is a concern that they may have a more dramatic and direct impact on faculty work hours (Winslow, Bowman et al. 2004). The requirements for a reduction in resident hours, it is argued, will mean the transfer of responsibility for tasks traditionally performed by trainees to others, such as nurse practitioners, physician assistants, and surgical faculty (Winslow, Bowman et al. 2004). This mandated change in input (resident time) implicitly requires substitution with more expensive inputs.

3.3.3 Resource Use Exogenously Determined

When the level of input use is taken to be exogenously determined, and where payers must pay for whatever quantity if transacted, the realized cost to the payer can be written as:

$$C(\mathbf{p}, \bar{q}; \boldsymbol{\alpha}) = \sum_{k=n+1}^{r} p_k * x_k(p_k). \tag{10}$$

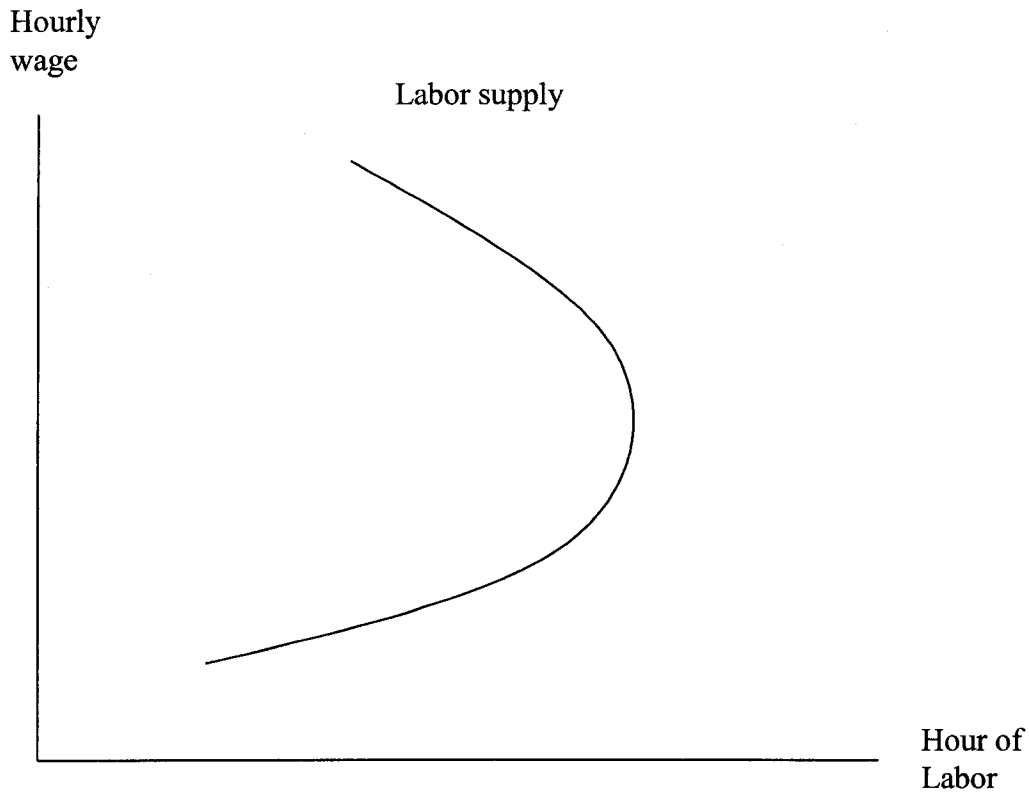
Here, interventions targeting the prices would cause a shift in input use, not because of cost - minimizing behavior on the part of the payer, but because the behavior of other parties (e.g., patients, providers) is influenced by price.

As an example, consider the case of physician payment reform under Medicare through Medicare's fee schedule (Congressional Budget Office 1990). Textbooks have suggested that some labor supplies may be "backward bending," and that a decrease in reimbursement may cause an increase in the number of physician visits if physicians attempt to maintain some "target" income level (Phelps 1992) (see Figure 2). This physician response to changes in

Medicare reimbursement policy was demonstrated by Christensen (1992). The realized cost function in this section differs from the traditional case as described in section 3.3.1, in that the physicians' behavior (not Medicare's) is determining the level of input for which Medicare pays.

This feature could also be applied to the estimation of patient time costs from the patient or societal perspective. Consider the case in which wages are used as a proxy for the patients' opportunity cost, and higher wages, p_k, were associated with an increased (or decreased) probability of office visits, x_k.

Figure 2: Labor Supply as a Function of Wage



Source: Adapted from Phelps (1992) Figure 6.2

3.3.4 Discounts and Discount Rates

The final set of interventions depicted by this framework is through a parameter representing the market structure effects of x on p (δ). Here, δ would be directly altered by an intervention.

$$C(\mathbf{p},\bar{q},\delta;\boldsymbol{\alpha}) = \sum_{l=r+1}^{s} p_l\left(x_l(\mathbf{p},\bar{q},\delta)\right) * x_l(\mathbf{p},\bar{q},\delta) \qquad (11)$$

As an applied example in health care, consider manufacture-direct rebates for antidepressant medication from pharmaceutical companies to large prescription payers (e.g., HMOs). Prior to the entry of generic fluoxetine (Prozac), there were several selective serotonin reuptake inhibitors (SSRIs), a newer class of antidepressant, but no generic SSRIs available. Since SSRIs are associated with fewer medically significant side-effects than tricyclic antidepressants (TCAs), they are recommended as the first-line of therapy (Brigham and Women's Hospital 2001). Given that more than one SSRI is available, large third-party payers often make contractual agreements with one SSRI manufacture for a discount in return for market share—causing a significant increase in the number of prescriptions for that manufacturer's drug (Department of Health and Human Services (DHHS) 2000). These rebates have been reported to be in the range of 24 percent of prescription sales price (Genuardi, Stiller et al. 1996). To increase the market share of one SSRI, the third-party payer would provide incentives to physicians to prescribe the SSRI as first-line therapy, which would increase the use of the SSRI. The result of such an intervention would be the third-party payer's decrease in the price paid per antidepressant prescription.

3.4 Summary

This general framework has been developed to illustrate the complexity of how costs are incurred by payers. To clarify this process, realized costs are broken into four main components and described above:

$$C(p,\bar{x},\bar{q},\delta;\alpha) =$$

$$\underbrace{\sum_{i=1}^{m} p_i * x_i(\mathbf{p},\bar{q};\alpha)}_{C^{(a)}} + \underbrace{\sum_{j=m+1}^{n} p_j * \bar{x}_j}_{C^{(b)}} + \underbrace{\sum_{k=n+1}^{r} p_k * x_k(p_k)}_{C^{(c)}} + \underbrace{\sum_{l=r+1}^{s} p_l\left(x_l(\mathbf{p},\bar{q},\delta)\right) * x_l(\mathbf{p},\bar{q},\delta)}_{C^{(d)}} \quad (12)$$

As few as one or as many as all four features may be represented when we determine a payer's cost of an intervention. This framework illustrates that there are scenarios in which cost is not simply the product of price and quantity of resource use.

4 Issue 1: Resource Costing and Economic Relationships Between Price and Resource Use Quantity

In both the applied economic evaluation literature and the published guidelines for resource costing, prices are often treated as fixed values rather than random variables. Here "random" means there exists *ex ante* uncertainty (i.e., stochastic and/or heterogeneous), whereas "fixed" means non-stochastic but does allow for *ex post* heterogeneity (e.g., the geographic variation in physician reimbursement). Project TrEAT, a randomized, controlled clinical trial of alcohol treatment designed to test the efficacy of brief physician advice for the treatment of problem drinkers, multiplied a fixed price equal to Medicare's average per stay and per visit amount by the number of inpatient stays and emergency room visits when it estimated the average cost of hospitalizations and ER visits (Fleming, Mundt et al. 2000).

When estimating mean costs from price and resource utilization information, treating prices as fixed has statistical implications and can lead to bias. For example, a large enough reduction in Medicare/Medicaid reimbursement to physicians may change physician behavior (e.g., they might cutback, or refuse to offer, services to Medicaid patients). Likewise, Project TrEAT's use of a fixed per diem price for inpatient stays makes the assumption that the length of stay does not covary with the per diem price. Failure to account for price/quantity relationships such as these could result in biased cost estimates when the cost of the interventions are determined.

We study the effect that assumptions about fundamental economic behavior that are implicit in traditional resource costing methodology have on the estimation of μ_c and σ_c^2. The major goal of this chapter is to examine the effect ignoring that relationship between resource use and unit prices can have on estimators of μ_c and σ_c^2. We examine this issue both analytically and through the use of concrete examples. The upshot of this analysis is that resource costing methods must accommodate the covariance between price and resource utilization if estimates of μ_c and σ_c^2 are to be unbiased.

In this chapter, the effects of common resource costing methods will be explored: (1) as we analytically examine the expected cost derived as expected value of a product of two variables, and (2) through the use of examples illustrating the effects of omitting covariance in the estimation of patient time costs using data from the CARE study. While the general results are not new, their application to health care costs, as a product of price and resource use, has not been addressed before—although the population variation in, and covariation between, quality and longevity has been investigated in the estimation of expectations of various health, quality, utility, and disability adjusted life years or life expectancy (Mullahy 2001). In section 4.1, we develop notation that identifies cost as a product of unit price and resource use, then examine, in theory, the expected value of the product of two random variables. In section 4.2, we extend this discussion to include multiple inputs. In section 4.2.2, we examine conditional mean costs, which allow us to address issues related to incremental costs (i.e., mean cost

differences between interventions) as well as effects in subpopulations, a concern raised in the cost-effectiveness literature (Phelps 1997). In section 4.3, informed by data from the Nationwide Inpatient Sample, we use lognormal distributional assumptions to illustrate analytically the bias caused by the use of fixed-price estimates in the estimation of expected costs. Section 4.4 uses data from CARE, a randomized study of a depression management program, to illustrate how differences in expected cost estimates exist as a result of using fixed-price estimates. An appendix addressing the estimation of variance of cost is provided in section 4.6.

4.1 Estimation of Mean Costs

Consider an example, in which one wishes to estimate the cost of a treatment, T_A. Data are gathered from a trial in which a sample of n_A patients is drawn from a larger population of size N, and assigned[4] to treatment group A. For the sake of simplicity, assume for now that costs are incurred due to the utilization of one input resource, R_X (this assumption will be relaxed later). As an example, R_X could represent nursing time or a prescription fill. While obviously unrealistic for most cases, such single-input analyses are often the focus in applied studies, particularly clinical trials (Johannesson, Jonsson et al. 1997; Halpern, Palmer et al. 2002). The amount of R_X consumed by the i^{th} patient receiving treatment T_A is denoted X_{Ai}, and the sample mean of X_{Ai}

[4] The use of the word "assignment" is a general one, and is not intended to imply a particular mode (e.g., self-selection, randomization).

$(i = 1 \rightarrow n_A)$ is denoted $\bar{X}_A$. The point estimate for the unit price of resource R_X is denoted $\hat{P}_X$, and the mean cost for patients receiving treatment T_A is estimated as:

$$\hat{C}_A = \hat{P}_X * \bar{X}_A . \tag{13}$$

4.1.1 Treatment of Prices as Fixed Values

In both the applied economic evaluation literature and the published guidelines, it is common to find fixed prices multiplied by measured resource utilization. In essence, resource costing treats cost as a product of a fixed and random variable representing price and quantity, respectively. However, it can be argued that prices are seldom fixed—at least at the level at which prices are applied to resource utilization measures. For example, in a sample of N =19,540 hospitalizations captured by the Nationwide Inpatient Sample for the year 2000 (NIS 2000), the cost[5] per hospital day for a discharge with DRG 1(Craniotomy, Age Greater than 17 Except for Trauma) has a sample mean of $3,112, with a sample standard deviation of $2,296. The variation in price may be due to, among other things, variation of demand, input markets, traditional discriminatory pricing practices (Philips 1983), and the differential negotiating power of large purchasers.

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[5] Cost-to-charge ratios were applied to charges reported in the Nationwide Inpatient Sample (NIS 2000) for year 2000 hospital admissions.

Because the estimator $\bar{P}_X = \frac{\sum_{i=1}^{n} P_{X_i}}{n}$ is an unbiased and consistent estimator of $E(P_X)$ — under the assumption that a true mean actually exists — it is often used as the monetary amount assigned to measured resource use. The implicit assumption seems to be that an unbiased estimator of the mean price, multiplied by an unbiased estimator of the mean resource utilization, yields an unbiased estimator of the mean cost. However, as the following proof shows, $\bar{P}_X * \bar{X}_A$ is not generally an unbiased estimator of $E(P_{Xi} * X_{Ai})$, even if $\bar{P}_X$ is an unbiased estimator of the average price of R_X:

$$\begin{aligned} Cov(P_{Xi}, X_{Ai}) &= E(P_{Xi} * X_{Ai}) - E(P_{Xi}) * E(X_{Ai}) \\ \Rightarrow E(P_{Xi} * X_{Ai}) &= Cov(P_{Xi}, X_{Ai}) + E(P_{Xi}) * E(X_{Ai}) \end{aligned} \qquad (14)$$

The quantity $\bar{P}_X * \bar{X}_A$ is a consistent estimator of $E(P_{Xi}) * E(X_{Ai})$ by Slutsky's theorem, but is a biased and inconsistent estimator of the expected cost $E(P_{Xi} * X_{Ai})$, unless the covariance between price and resource utilization is zero. Zero covariance would be implied by a constant price inelastic demand and/or supply function[6], which may not reflect the true relationship between prices and resource use. This highlights an important source of bias in economic analysis, since typical resource costing methodology often treats resources as having fixed prices.

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[6] Of course, determine whether it is a demand or supply function is generally not possible without additional assumptions to—this is a standard econometric identification problem.

Many prices (or unit opportunity costs) are not fixed. For example, consider the use of the Nationwide Inpatient Sample for 2000 (NIS 2000) as a source to estimate the price of an inpatient hospital day. The NIS is an all-payer inpatient care database that is publicly available in the United States, and it contains data on 5 to 8 million hospital stays from about 1000 hospitals sampled to approximate a 20-percent stratified sample of U.S. community hospitals. Table 2 contains summary statistics for NIS 2000 hospitalizations assigned a DRG of 1. Notice that the mean length of stay (LOS) multiplied by the mean per diem price (a proxy for the unit opportunity cost) does not equal the mean cost estimated directly from the cost data ($26,452 vs. $20,023).

$$E(LOS) * E(price) = 8.50 * \$3112 = \$26452 \quad (15)$$

This suggests that the covariance between LOS and price is less than zero—that hospitalizations with longer stays have a lower per diem price. In fact, after estimating the covariance based on the sample to be -$6,418 and accounting for it in our estimation of expected costs, we find that the mean cost estimated from LOS and per diem price information approximately equals the estimated mean cost from the actual cost data (and any difference is due to rounding):

$$E(LOS) * E(price) + Cov(LOS, price) = 8.50 * \$3112 - \$6418 = \$20034. \quad (16)$$

Table 2: Nationwide Inpatient Sample for 2000 (Wisconsin, DRG 1)

Statistic	LOS	Per Diem Price	Cost
Mean	8.50	$3,111.73	$20,023.86
Std. Dev.	9.18	$2,295.66	$19,242.79
Skewness	4.23	$3.37	$4.04
Kurtosis	40.56	$23.14	$33.94

4.1.2 Fixed Price Other Than the Mean

A second source of bias is the choice of fixed price. Using a fixed price other than the mean, even when the covariance between price and resource utilization is zero, results in biased estimates of $E(P_{Xi} * X_{Ai})$, as would be expected. Our general notation does not specify the value of $\hat{P}_X$. This estimate can be based on, among other things, data or expert opinion. Consider the case in which the unit prices of prescription drugs are based on the Red Book average wholesale prices (First Data Bank, San Bruno, CA). As recently reports have indicated, average wholesale price may not accurately reflect the average price paid for drugs (See *The Wall Street Journal* 2004). Therefore, we can write $\hat{P}_X = \bar{P}_X + \tau$, where $\bar{P}_X$ is the unbiased estimate of $E(X_{Ai})$, and τ is the bias correction factor. Assuming the covariance between price and resource utilization is zero,

$$E(\hat{P}_{Xi} * X_{Ai}) = \hat{P}_{Ai} * E(X_{Ai}) = (\bar{P}_X + \tau) * E(X_{Ai}) = \bar{P}_X * E(X_{Ai}) + \tau * E(X_{Ai}). \quad (17)$$

The bias depends on the direction and magnitude of τ. This highlights the fact that, even under the assumption of zero covariance between price and resource use, the estimate of cost is no longer unbiased or consistent. While in some sense this is obvious, many existing studies ignore the issue, making no attempt to correct, even approximately, what is a widely recognized bias (Lave, Frank et al. 1998; Simon, Manning et al. 2001; Salomon, Weinstein et al. 2003).

In a 1999 article, Rittenhouse et al. addressed the implications of selecting different fixed-price estimates on statistical inference (Rittenhouse, Dulisse et al. 1999). The authors found that varying price estimates can have a non-negligible effect on statistical inference regarding between-group cost differences. The between-group differences in average cost per patient could be statistically significant or insignificant, regardless of whether differences in resource utilization were statistically significant. Rittenhouse and his colleagues' results highlighted the importance of recognizing that cost evaluation based on resource costing may be sensitive to the relative prices of resources. Later in their article, the authors raise the matter of bias when using fixed-price estimates—omitting the covariance term. This chapter will focus entirely on the effect omitted covariance has on the estimation of μ_c and σ_c^2. Omitted covariance is a consequence of using a fixed-price estimate when resource costing. In order to focus exclusively on the issue of omitted covariance, we assume, wherever possible, that the fixed-price estimate is an unbiased estimator of $E(P_i)$.

4.1.3 Effect of Using Fixed Prices on Estimates of the Variance

While the interest in unbiased estimates of μ_c may be of primary concern, the use of fixed-price estimates in resource costing also has implications for other parameters. Of particular interest here is the estimation of $\sigma_c^2 = \text{var}(c)$. As previously argued, σ_c^2 potentially plays at least two roles in the economic evaluation of health care interventions. First, σ_c^2 may be of direct interest to risk-averse decision-makers (O'Brien and Sculpher 2000; Palmer and Smith 2000; Zivin 2001). Second, the precision of $\bar{x}$, the unbiased estimator of μ_c, is a function of σ_c^2 and N (sample size). Rittenhouse et al., primarily focus on the choice of fixed-price estimate.

The effect of using fixed-price estimates on the estimation of σ_c^2 is examined in detail in this chapter's appendix. The effect that resource costing methods have on the estimation of σ_c^2 is much more complicated analytically. In addition, beside the omission of the covariance term, resource costing methods using fixed-price estimates also imply $\text{var}(P_i) = 0$. This chapter's appendix examines the effect of using fixed-price estimates on estimates of σ_c^2.

Note that bias in the estimation of mean cost is due to three parameters of the joint distribution $\phi(p, x; \theta)$: the mean price (μ_p), mean resource use (μ_x), and covariation between price and resource use (σ_{px}), but not on the variance in price (σ_p^2) or resource

use (σ_x^2). In contrast, bias in the estimation of variance in cost is due to all five parameters.

4.2 Extension to 2-inputs

Consider an extension of the example in Section 4.1 to the case in which costs are composed of two types of inputs, R_X and R_Y. As an example, R_X could represent nursing time, and R_Y could represent pharmaceuticals. Recall that the amount of R_X consumed by the i^{th} patient receiving treatment T_A is denoted as X_{Ai}, and the sample mean of X_{Ai} $(i=1 \rightarrow n_A)$ is denoted as $\bar{X}_A$. Unit price for input R_X is denoted as $\hat{P}_X$. Measures and utilization for R_Y are denoted analogously. The mean cost for patients receiving treatment T_A is estimated as:

$$\hat{C}_A = \hat{P}_X * \bar{X}_A + \hat{P}_Y * \bar{Y}_A. \tag{18}$$

4.2.1 Treatment of Prices as Fixed Values

Similar to the proof in section 4.1.1, the following proof shows that $\bar{P}_X * \bar{X}_A + \bar{P}_Y * \bar{Y}_A$ is not generally an unbiased estimator of $E(P_{Xi} * X_{Ai} + P_{Xi} * X_{Ai})$, even if $\bar{P}_X$ and $\bar{P}_Y$ are unbiased estimators of the average price of R_X and R_Y:

$$
\begin{aligned}
&E\left(P_{Xi} * X_{Ai} + P_{Yi} * Y_{Ai}\right) = \\
&E\left(P_{Xi} * X_{Ai}\right) + E\left(P_{Yi} * Y_{Ai}\right) = \\
&E\left(P_{Xi}\right)E\left(X_{Ai}\right) + Cov\left(P_{Xi}, X_{Ai}\right) + E\left(P_{Yi}\right)E\left(Y_{Ai}\right) + Cov\left(P_{Yi}, Y_{Ai}\right)
\end{aligned}
\qquad (19)
$$

The quantities $\bar{P}_X * \bar{X}_A$ and $\bar{P}_Y * \bar{Y}_A$ are consistent estimators of $E\left(P_{Xi}\right) * E\left(X_{Ai}\right)$ and $E\left(P_{Yi}\right) * E\left(Y_{Ai}\right)$, but these are biased and inconsistent estimators of the expected cost $E(P_{Xi} * X_{Ai} + P_{Xi} * X_{Ai})$, unless every covariance is zero, or the sum of all the covariance terms is zero (i.e., $\left[Cov\left(P_{Xi}, X_{Ai}\right) + Cov\left(P_{Yi}, Y_{Ai}\right)\right] = 0$)—which would only be a coincidence.

4.2.2 Estimation of Incremental Costs of Interventions

The two-input case can be extended to include more inputs, or, more than one treatment. Consider the estimation of incremental cost where we estimate the difference in the costs between interventions T_A and T_B. The mean incremental cost for patients receiving treatment T_A versus T_B is estimated as:

$$
\hat{C}_A - \hat{C}_B = \left[\hat{P}_X * \bar{X}_A + \hat{P}_Y * \bar{Y}_A\right] - \left[\hat{P}_X * \bar{X}_B + \hat{P}_Y * \bar{Y}_B\right]. \qquad (20)
$$

This is similar to the finding of Section 4.2.1, in that our statistic of interest, $\Delta\hat{C} = \hat{C}_A - \hat{C}_B$, is a linear combination of products. If both the prices and resource use

are not fixed then the equation above yields a biased estimate of $E(\Delta C)$, even if the $\hat{P}^{'s}$ are unbiased estimates of expected prices, and the $\bar{X}^{'s}$ and $\bar{Y}^{'s}$ are unbiased estimates of expected resource utilization—unless every covariance is zero, or the sum of all covariance terms is zero.

$$
\begin{aligned}
&E(\Delta C) = \\
&E(C_A - C_B) = \\
&E(C_A) - E(C_B) = \\
&E(P_{Xi} * X_{Ai} + P_{Yi} * Y_{Ai}) - E(P_{Xi} * X_{Bi} + P_{Yi} * Y_{Bi}) = \\
&E(P_{Xi})E(X_{Ai}) + Cov(P_{Xi}, X_{Ai}) + E(P_{Yi})E(Y_{Ai}) + Cov(P_{Yi}, Y_{Ai}) \\
&\qquad - E(P_{Xi})E(X_{Bi}) - Cov(P_{Xi}, X_{Bi}) - E(P_{Yi})E(Y_{Bi}) - Cov(P_{Yi}, Y_{Bi})
\end{aligned}
\tag{21}
$$

4.3 Analytical Example using Lognormally Distributed Prices and Resource Use

The statistical theory of random variables presented above provides confirmation that using fixed-price estimates in resource costing can lead to biased estimates of μ_c—through the omission of covariance terms. To illustrate the effect of sign and magnitudes of covariance between price and resource use, we make distributional assumptions about price and resource use.

Random lognormal variates have three desirable properties for this illustration: (1) lognormal distributions are very flexible—they are often used to depict the distribution of health care costs, (2) the product of lognormal variates is also a lognormal variate, and (3) the simple relationship between covariance and elasticity for exponential demand and supply functions.

4.3.1 Overview of Lognormal Distribution

The following is an overview of the lognormal distribution (Aitchison and Brown 1957).

Let Z be a positive variate $(0 < z < \infty)$ such that $Y = \log Z$ is normally distributed with mean μ and variance σ^2. We say that Z is lognormally distributed or that Z is a Λ – variate and write: $Z \sim \Lambda(\mu, \sigma^2)$, and correspondingly, $Y \sim N(\mu, \sigma^2)$. It should be noted that Z cannot be zero, since $Y = \log Z$ is not defined for $Z = 0$. From the moment-generating function of the normal distribution, the mean of Z is given by

$$E(Z) = e^{\mu + \frac{1}{2}\sigma^2}. \tag{22}$$

The use of the lognormal distributional assumption may be plausible for resource utilization and prices, because both can be represented as positive values, and their distributional shapes are often "roughly" lognormal. However, while the data used here may not in fact be jointly lognormal, we are using this lognormal assumption, mainly because of its analytical tractability.

In particular, the product of lognormal variates is also lognormally distributed. Furthermore, these variables need not be independent—only have a multivariate lognormal distribution.

From Theorem 2.4 (Aitchison and Brown 1957):

If $\mathbf{Z}$ *is a multivariate lognormal and* $\mathbf{b}$ *is a vector of constants, then the product*

$c\prod_{j}^{n}\mathbf{Z}_j^{b_j} \sim \Lambda\left(a+\mathbf{b}'\boldsymbol{\mu},\mathbf{b}'\mathbf{V}\mathbf{b}\right)$ *where* $c=e^a$ *is a positive constant.*

Simplification of Theorem 2.4 for the product of two lognormal variates:

If Z_1 *and* Z_2 *are lognormal, the product*

$Z_1 * Z_2 \sim \Lambda\left(\mu_1+\mu_2,(\sigma_1^2+2\sigma_{12}+\sigma_2^2)\right)$ *where* σ_{12} *is the covariance between* Z_1 *and* Z_2.

This property is useful in examining resource costing, because we are estimating the expectation of resource use multiplied by price.

4.3.2 Analytical Illustration—Lognormal Distributional Assumption

Consider the estimation of the cost of an intervention where the realized cost of the intervention centers around one input—hospitalizations. Suppose price is exogenous and lognormally distributed. Further consider that resource use (in a demand relationship) is a function of price such that:

$$X = P^{\alpha}\varepsilon, \tag{23}$$

where $\varepsilon \sim \Lambda\left(1,\sigma_1\right)$ and $P \sim \Lambda\left(\mu_P,\sigma_p^2\right)$. This structure implies that for $\alpha \neq 0$, the level of resource use will depend, in part on the unit price of that resource (α is considered the price elasticity in economics).

For this analytical example, we use data for hospitalization with a DRG=1 from NIS 2000, which was first introduced in Table 2. Per diem costs were calculated by applying a cost-to-charge ratio to reported hospital charges, and then dividing this per stay cost by the reported length of stay (LOS). The per diem cost data can be interpreted as a proxy for opportunity cost (which is being referred to as price). While the logged per diem price and hospital costs appear normally distributed with all nonzero values (Figure 4 and Figure 5, respectively), logged LOS appears more skewed to the left. However, as stated earlier, we are using lognormal assumptions mainly because of its analytical tractability.

Figure 3: NIS 2000 Logged Length of Stay (DRG 1, WI)

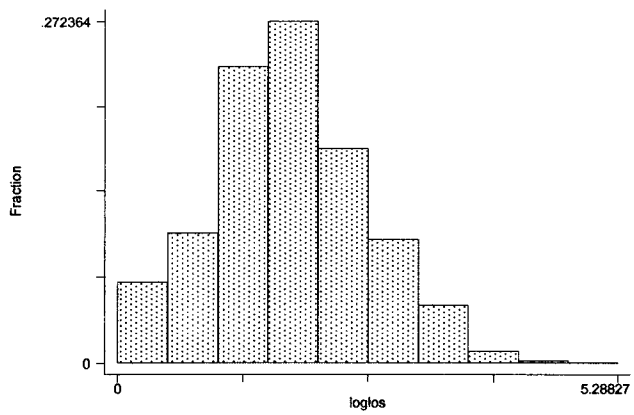


Figure 4: NIS 2000 Logged Price (WI, DRG 1)

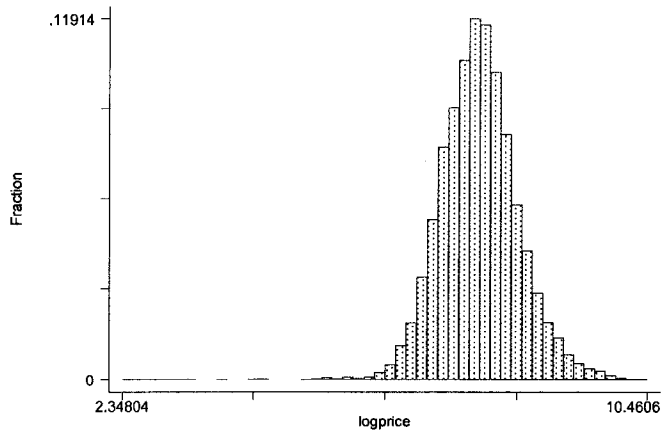
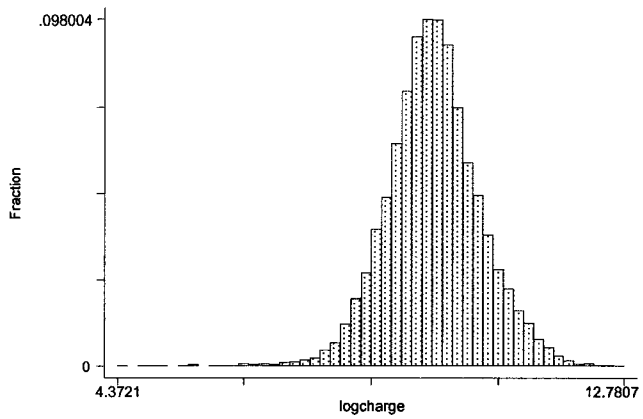


Figure 5: NIS 2000 Logged Cost (DRG 1, WI)



From this point forward we assume that per diem price and resource utilization are random lognormal variates. Let P_X represent unit price, and X_A represent LOS for hospitalization with DRG=1. Based on estimates from NIS 2000,

$$\begin{aligned} P_X &\sim \Lambda(7.86, 0.36) \\ X_A &\sim \Lambda(1.75, 0.77) \end{aligned}. \tag{24}$$

Based on Theorem 2.4 from Aitchison and Brown (1957):

$$P_X * X_A \sim \Lambda\left(7.86+1.75,(0.36+2\sigma_{P_X X_A}+0.77)\right), \tag{25}$$

where $\sigma_{P_X X_A}$ is the covariance between unit price and LOS. Similarly, the distribution of $P_Y * Y_A$ is also lognormal with five parameters with expectation:

$$E\left(P_X X_A\right) = e^{(9.61)+\frac{1}{2}\left(1.13+2\sigma_{P_X X_A}\right)}. \tag{26}$$

Using a fixed-price estimate simplifies the expectation of this product:

$$E\left(P_X\right)E\left(X_A\right) = e^{(9.61)+\frac{1}{2}(1.13)} = \$26{,}239. \tag{27}$$

The covariance term, estimated from the sample, is $Cov(P,X) = -0.27$. This indicates that as LOS increases, the per diem price decreases (at least for DRG 1). In contrast, typical resource costing methods may use a fixed-price estimate equal to the average per diem price. In our example, setting $Cov(P,X) = 0$ resulted in an estimated average cost of $26,239 per hospitalization. This is an overestimate of the actual expected cost by $6,209, which would result from the use of fixed-price estimates.

Table 3 shows the average cost for a range of value for $Cov(P,X)$ (including $Cov(P,X) = -0.27$ and $Cov(P,X) = 0$). The table also contains the bias under the assumption that the true covariance is –0.27. In reality, interventions likely affect more than one input, but for simplicity, a one-input example is used here. It adequately illustrates the effect of resource costing methods using fixed-price estimates.

Table 1: Bias Associated with Resource Costing Using Fixed Price Estimates

Mean		Var				
Price (log $)	LOS (log days)	Price (log $)	LOS (log days)	Cov(P,X)	Avg. Cost ($)	Bias ($)
7.86	1.75	0.36	0.77	-0.5	$15,915	$4,116
7.86	1.75	0.36	0.77	-0.4	$17,588	$2,442
7.86	1.75	0.36	0.77	-0.3	$19,438	$592
7.86	1.75	0.36	0.77	-0.27	$20,030	$0
7.86	1.75	0.36	0.77	-0.2	$21,483	-$1,452
7.86	1.75	0.36	0.77	-0.1	$23,742	-$3,712
7.86	1.75	0.36	0.77	0	$26,239	-$6,209
7.86	1.75	0.36	0.77	0.1	$28,999	-$8,968
7.86	1.75	0.36	0.77	0.2	$32,048	-$12,018
7.86	1.75	0.36	0.77	0.3	$35,419	-$15,389
7.86	1.75	0.36	0.77	0.4	$39,144	-$19,114

4.4 Case Study: Estimation of Patient Time Costs in Project CARE

The CARE study was a multi-site randomized study designed to examine the incremental cost and cost-effectiveness of a population-based program to identify and treat depression (Simon, Manning et al. 2001). The CARE study used a double screening method to identify depression among patients with histories of high medical utilization. Of the 410 eligible patients, 407 consented to enroll in the study, where 218 were randomized to the depression management group (DMP), and 189 were randomized to usual care (UC). Utilization and estimated cost results were based on 374 subjects (92% of those randomized) enrolled in the participating health plans throughout the 12-month follow-up period. Previously published results further describe the study design and indicate that this program produces an increase in the probability of patients and physicians initiating depression treatment, an increased intensity of depression treatment, and led to significant improvements in both clinical and functional outcomes (Pearson, Katzelnick et al. 1999; Katzelnick, Simon et al. 2000).

As part of the follow-up assessments, the CARE study collected detailed questions regarding time required for outpatient visits (including travel and waiting time). In addition, time "lost" for each day of inpatient treatment was estimated at 16 hours. These time estimates were multiplied by the actual number of outpatient visits and hospitalization days (based on claims data). Information on wage rate was calculated

based on reported number of hours of work and earning in the past year. Although the practice of using wage rates to estimate society's value of time has some drawbacks, it is often used and recommended (Luce, Manning et al. 1996). Because some individuals did not report any earnings, time costs were estimated using predicted wage rates based on age, sex, education, and site, treatment group, baseline physical and mental health status. A Heckman selection model[7] was used in the prediction of wage rates (Heckman 1979).

Using CARE data, we estimated time costs in two ways: (1) by multiplying observed time by predicted wage rate at the individual level, and (2) by multiplying observed time by the average wage rate in the CARE sample.

(1) $E(T_i * w_i)$

(2) $E(T_i * \bar{w})$, where $\bar{w} = \frac{1}{374}\sum_{i=1}^{374} w_i$

In this example, methods (1) and (2) will give the same answer only if $\mathrm{cov}(T_i, w_i) = 0$. A $\mathrm{cov}(T_i, w_i) < 0$ would indicate that patients with higher wage rates would incur less lost time due to medical appointments and hospitalizations, and $\mathrm{cov}(T_i, w_i) > 0$ would indicate the opposite. The popular impression is that office visits and hospital care are time-intensive relative to other goods and services. Earlier research has provided evidence that elasticity of demand for office visits and hospital care are negative with

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[7] Although we used predicted wage rates for individual patients, in this example we treat the predicted wage rates as observed data in order to illustrate the covariance issue.

respect to earned income (Acton 1975). Therefore, we anticipate the covariation between wage and patient time to be negative as well.

Table 6 shows that the average time cost based on observed time and predicted wage information was estimated as $1,369 per patient in the depression management program (DMP) group, and as $1,195 in the usual care (UC) group. The average time costs using observed time but a fixed wage rate, equal to the expected wage rate in the CARE sample ($12.14), were $1,436 and $1,206 for the DMP group and the UC group, respectively. The difference in the estimated time cost is due to the omission of the covariance term in the second method. In the CARE sample, the covariance was estimated to be -$41.83, indicating that patients with higher wage rates incur less "lost" time, whether it is due to hospitalizations or medical appointments.

Figure 6: Patient Time Cost Estimates—CARE Study

	DMP	UC
N	205	169
Average Time in Treatment (hours)	118.28	99.31
Average Wage ($/hour)	$11.92	$12.41
(1)	$1,368.97	$1,195.18
(2)	$1,436.21	$1,205.94

4.5 Conclusions

In this chapter, we have demonstrated analytically that the use of fixed-price estimates implies a certain relationship between prices and resource use—namely zero covariance.

The impact of this assumption can significantly bias estimates of mean cost, even when all other relevant parameter estimates are themselves unbiased. However, without an estimate of covariance, correcting for this omission is not possible.

In lieu of this information, researchers could and should conduct sensitivity analyses based on a reasonable *ex ante* range of possible covariance. At the very least, researchers, given an *ex ante* sign for covariance, can give readers and decision-makers a sense of the direction of the potential bias. For example, in the CARE example above, we had some indication before running the analyses, based on prior research, that the covariance between patient time and wage rate was negative (Acton 1975). If we had not had access to the individual level wages, we could have used this information to suggest that our average patient time cost estimates based on method (2) were overestimates.

Correcting cost estimates based on typical resource costing methods is not always feasible—and is rarely an exact science. However, there is value in proving a problem exists. In this chapter, we demonstrated that estimates of the average cost based on cost data are not generally equivalent to those based on separate price and resource use data.

4.6 Appendix: Variance Estimation

While the interest in unbiased estimates of μ_c may be of primary concern, the use of fixed-price estimates in resource costing has implications for other parameters. Here, we examine the effect that fixed-price estimates have on the estimation of $\sigma_c^2 = \text{var}(c)$. As previously argued, σ_c^2 potentially plays at least two roles in the economic evaluation of

health care interventions. First, σ_c^2 may be of direct interest to risk-averse decision-makers (O'Brien and Sculpher 2000; Palmer and Smith 2000; Zivin 2001). Second, the precision of $\bar{x}$, the unbiased estimator of μ_c, is a function of σ_c^2 and N (sample size), and statistical inference is a function of parameters. For example, if μ is normally distributed $N(\mu, \sigma^2)$, then a standard t-statistic for testing $H_0 : \bar{x} = 0$ is:

$$t = \frac{\bar{x}}{\sqrt{\hat{\sigma}^2 / N}}. \tag{28}$$

The issue of inference and hypothesis testing is addressed in the context of resource costing, but, the primary focus in the literature has been on the choice of fixed-price estimates, not on an examination of using fixed-price estimates (Rittenhouse, Dulisse et al. 1999).

Now that the estimation of μ_c has been addressed, we examine the role of resource costing method in the estimation of σ_c^2. Our focus is on the effect that resource costing methods, which basically multiply fixed-price estimates by observed resource use, have on the estimation of σ_c^2. In general statistical notation, the variance of the product of observed resource use and a fixed-price estimate is written as:

$$VAR(\hat{P}_i * X_i) = \hat{P}_i^2 * VAR(X_i). \tag{29}$$

The issue is how, and under what conditions, is this estimation different from $Var(C_i)$. This is best examined in two cases: (1) by assuming that price and quantity do not covary, and (2) by making no assumptions regarding covariance.

Case 1: independently distributed prices and quantities

Assume price and quantity are independently distributed. The variance of the product can be written as:

$$VAR(P_i * X_i) = E(P_i)^2 V(X_i) + E(X_i)^2 V(P_i) + V(P_i)V(X_i). \quad (30)$$

One can see that equation (29) would yield smaller variance estimates than equation (30)—assuming $\hat{P}_i$ is a consistent estimator of $E(P_i)$. This is the case because the variance of a product of random variables is a function of $V(P_i)$ not just $V(X_i)$.

Case 2: prices and quantities covary

Note that while the mean of a product of random variables can be expressed in terms of means and covariances, the variance of the product requires higher-order moments—unless the assumption of zero covariance is made. Because of the complexity of the solution, approximations for the product have been made (Mood, Graybill et al. 1974). A second-order Taylor Series expansion can be used to derive:

$$\begin{aligned} &VAR(XY) \\ &= E(X)^2 V(Y) + E(Y)^2 V(X) + 2E(X)E(Y)Cov(X,Y) - [Cov(X,Y)]^2 \\ &+ E[(X - E(X))^2 (Y - E(Y))^2] + 2E(Y)E[(X - E(X))^2 (Y - E(Y))] \\ &+ 2E(X)E[(X - E(X))(Y - E(Y))^2] \end{aligned} \quad (31)$$

Making no assumptions regarding the independence of prices and resource use, one can see that equation is vastly more complex. In fact, since the higher order terms can be + or -, we can reach no conclusion as to the direction of the bias, as we could when we assumed prices and resource use were independent.

4.6.1 Example: Lognormally Distributed Prices and Resource Use

The statistical theory of random variables presented above provides confirmation that using fixed-price estimates in resource costing can lead to biased estimate of σ_c^2, through the omission of covariance terms. To illustrate the effect of sign and magnitudes of covariance between price and resource use, we make a lognormal distributional assumption, as in Section 4.3.2.

As in Section 4.3.1, let Z be lognormally distributed $Z \sim \Lambda\left(\mu, \sigma^2\right)$. From the moment-generating function of the normal distribution, the variance of Z is given by:

$$\begin{aligned} V(Z) &= e^{2\left(\mu+\frac{1}{2}\sigma^2\right)}\left(e^{\sigma^2}-1\right) \\ &= \left[E(Z)\right]^2\left(e^{\sigma^2}-1\right) \end{aligned} \quad . \tag{32}$$

Assume that per diem price and resource utilization are random lognormal variates, and P_X represents unit price, while X_A represents LOS for hospitalization with DRG=1. Based on our sample from NIS 2000 (described in Section 4.1.1),

$$\begin{aligned} P_X &\sim \Lambda(7.86, 0.36) \\ X_A &\sim \Lambda(1.75, 0.77) \end{aligned} \quad . \tag{33}$$

Based on Theorem 2.4 from Aitchison and Brown (1957):

$$P_X * X_A \sim \Lambda\left(7.86+1.75,(0.36+2\sigma_{P_X X_A}+0.77)\right), \tag{34}$$

where $\sigma_{P_X X_A}$ is the covariance between unit price and LOS. Similarly, the distribution of $P_Y * Y_A$ is also lognormal with five parameters with variance:

$$\begin{aligned} V\left(P_Y * Y_A\right) &= e^{2\left(9.61+\frac{1}{2}\left(1.13+2\sigma_{P_X X_A}\right)\right)}\left(e^{1.13+2\sigma_{P_X X_A}}-1\right) \\ &= \left[E\left(P_Y * Y_A\right)\right]^2\left(e^{1.13+2\sigma_{P_X X_A}}-1\right) \end{aligned}. \tag{35}$$

Using a fixed-price estimate equal to the expected price simplifies the variance of expectation of this product:

$$\begin{aligned} E\left(P_X\right)^2 V\left(X_A\right) &= \left[e^{7.86+\frac{1}{2}(0.36)}\right]^2\left[\left(e^{1.75+\frac{1}{2}(0.77)}\right)^2\left(e^{0.77}-1\right)\right] \\ &= \$798{,}478{,}404 \end{aligned} \tag{36}$$

Table 4 provides the variance using varying covariance values. Note that under the assumption of zero covariance, the variance is much larger ($1,442,822,165). Further note that using the sample covariance of –0.27 results in a smaller variance ($322,569,631). In this example, the variance in inpatient costs for DRG=1 was noticeably reduced when costs were based on fixed-price estimates *if* the true covariance between price and LOS was zero. However, if the covariance between price and LOS

was not zero, the bias associated with using a fixed-price estimate could be larger or smaller, depending on the direction and magnitude of the covariance.

Table 4: Covariance and Bias

Mean		Var				
Price (log $)	LOS (log days)	Price (log $)	LOS (log days)	Cov(P,X)	Actual Cost ($)	Actual Var
7.86	1.75	0.36	0.77	-0.5	$15,915	$35,162,237
7.86	1.75	0.36	0.77	-0.4	$17,588	$120,947,940
7.86	1.75	0.36	0.77	-0.3	$19,438	$264,089,500
7.86	1.75	0.36	0.77	-0.27	$20,030	$322,569,631
7.86	1.75	0.36	0.77	-0.2	$21,483	$496,153,366
7.86	1.75	0.36	0.77	-0.1	$23,742	$864,974,492
7.86	1.75	0.36	0.77	0	$26,239	$1,442,822,165
7.86	1.75	0.36	0.77	0.1	$28,999	$2,338,618,428
7.86	1.75	0.36	0.77	0.2	$32,048	$3,716,210,335
7.86	1.75	0.36	0.77	0.3	$35,419	$5,821,683,307
7.86	1.75	0.36	0.77	0.4	$39,144	$9,024,174,270

4.6.2 Case Study: Estimation of Patient Time Costs in CARE

By comparison the variance estimates for the CARE example above (see Section 4.4), we find that using a fixed-price estimate resulted in slightly larger estimates of the standard deviation of cost in the DMP group, but a small decrease in variance of cost in the UC group. The associated bias, (2)-(1), is positive for DMP and negative for UC.

Table 5: Standard Deviations for CARE Time Costs

	DMP	UC
N	205	169
Time in Treatment (hours)	117.83	84.51
Wage ($/hour)	$3.43	$4.12
(1)	$1,325.87	$1,089.85
(2)	$1,430.80	$1,026.21

5 Issue 2: Resource Costing and Data Aggregation

Cost-effectiveness, cost-utility and cost-outcome analyses are major components of health economics research. What they have in common is the necessity of measuring the cost of health care interventions. In most cases, as with this dissertation, the cost parameter of interest is the expected or average cost.

Resource costing has not been applied in a consistent fashion because there is a spectrum of specificity as to the level of detail used to identify the health care resources that make up the cost of medical care. On one extreme is the micro-costing method, and on the other extreme is the gross-costing method (Luce, Manning et al. 1996). As described in Chapter 1, the micro-costing method involves the identification and costing out of every health care service item consumed during a patient's medical care. The gross-costing method involves the identification and costing out of health care encounters or other health care units that represent an aggregate of a bundle of service items. While the unit prices for the micro-costing method are typically based on observed prices of service items, the unit prices for the gross-costing method are typically based on average prices of all encounters that share the same characteristics. Often, gross-costing methods using average prices are referred to as average-costing methods.

While the micro-costing method may be more precise and accurate, it is more expensive and time-consuming than the gross-costing method. Because there could be hundreds or even thousands of service items bundled into a single health care encounter, identifying and tracking these items require considerable investigative effort.

The total number of hospitals days or the number of hospital stays is a typical example of a gross resource unit used for the gross-costing method in some clinical trials (Fleming, Mundt et al. 2000; Halpern, Palmer et al. 2002). Other examples can be found for physician visit or an emergency room visit (Fleming, Mundt et al. 2000; Halpern, Palmer et al. 2002). While in reality, the health care resources used will differ among hospitalizations, these studies use a fixed-price applied to encounters, presumably representing the expected price in some population. This method, while easier to implement than micro-costing, may be problematic. For example, in a study examining the cost of hospital care for cardiac and HIV patients, Heerey and colleagues found up to a 66% difference between DRG calculated costs and costs derived from micro-costing methods (Heerey, McGowan et al. 2002).

Because the evaluation of cost related to an intervention will likely involve more than one resource or input, resource costing may require many sources of unit prices. What is typically used in research is a hybrid of various forms of price information such as average wholesale prices (AWP) for drugs, Medicare's Physician Fee Schedules for specific physician services, and Medicare's inpatient prospective payment system for inpatient stays based on diagnostic-related groups (DRGs) (Medical Research Council Laparoscopic Groin Hernia Trial Group 2001; Simon, Manning et al. 2001). While sources for the AWP of drugs may provide price information for each drug listed in the National Drug Codes (NDC), a product identifier for drugs, this is less detailed price information for inpatient hospitalization categorized by DRG. Medicare's DRG

payments are based on an averaging process, as each DRG contains a range of patient costs and lengths of stay (Edwards, Honemann et al. 1994). Although there are currently 540 DRGs (Federal Register 2003), the number of NDC codes in the Red Book (First Data Bank, San Bruno, CA), a popular source for drug information, range into the tens of thousands and are identified by, among other things, manufacturer, package size, branded-versus-generic version, and administration type.

During the design phase of a clinical trial, one must define the level of detail for identifying the health care resources that make up the cost of medical care. There is typically a trade-off between the precision of the cost estimate in terms of the level of detail of the information, and the time, energy, and resources devoted to collect that information (Luce, Manning et al. 1996). Yet the conditions under which it may be possible to bundle resources while maintaining precision have never been described. The goal here is to assess the effects of using various levels of detailed data in the estimation of costs. We will often refer to methods using "less" detailed data as aggregative methods, or to aggregated data as less detailed. In the example above, inpatient data by DRG are more aggregated than drug data by NDC number.

Where Chapter 4 primarily focused on the economic relationships between prices and resource use, Chapter 5 examines a mechanical issue related to the assignment of prices to resource use. Specifically, we consider the level of detail at which these fixed-price estimates are defined, and we examine the effect that choice of the level of detail (or data aggregation) has on estimators of μ_c. In this chapter, we make the implicit

assumption that prices are non-stochastic, but we do allow heterogeneity among the levels of detail. For example, the average cost for DRG 1 and DRG 2 based on NIS 2000 data are $20,024 and $21,907, respectively. Using these average costs as fixed-price estimates allows for heterogeneity between these DRGs but suppresses stochastic properties within each DRG (e.g., variance, covariance).

Note that it is entirely possible that, within a resource category, the issues addressed in Chapter 4 are still relevant. The example in Section 4.1.1 illustrates such a case. In that example, the NIS data are categorized by DRG, and within one of those groups (DRG 1), the covariance is $6,418. Ideally, we would examine the issues in Chapter 4 and Chapter 5 simultaneously; however, in order thoroughly to examine the effect of data aggregation, we make the broad assumption that the covariance between price and resource use is zero. In reality, estimates of average health care costs may be more or less biased than we demonstrate here, depending on the direction and magnitude of bias related to the omission of covariation between prices and quantity of resource use and data aggregation.

In this chapter, we explore the effect of the level of detail at which resources are identified by: (1) examining, conceptually, the effect data that aggregation can have on estimation bias through resource costing methods, and (2) demonstrating the effect of data aggregation on estimators of μ_c using data from a randomized clinical study of a depression intervention. In Section 5.1, we describe data aggregation and develop a notation for the 2-input case that will be used and extended in subsequent sections. This

section serves to define a notation that can be used to examine the relationships between the estimation of average cost and the level of detail at which resources are defined. Section 5.2 defines the conditions of equivalence between estimators of μ_c resulting from resource costing methods that vary in the level of detail at which prices are assigned to resource use. In Section 5.3, taking data on inpatient resource use from a clinical trial of a depression management program, we will demonstrate how both cost estimates and estimates of incremental costs of an intervention vary across three bundling levels of inpatient resources. Section 5.4 concludes with a discussion, and suggestions, regarding the implications of data aggregation for both the study design and resource costing phases of a study.

5.1 Data Aggregation

Consider the situation in which one wishes to compare the average medical costs of two interventions, T_A and T_B (previously defined in Chapter 4). One conducts a trial by drawing a sample of size n from the population N, and randomly assigning n_A patients to treatment group A, and assigning n_B patients to treatment group B, with the total sample size being $n=n_A+n_B$. For simplicity, assume that medical costs are composed of two types of resources, X and Y. As an example, let X represent days in the ICU, and let Y represent regular care days. The amount of X consumed by the i^{th} patient receiving treatment j is denoted as X_{ij} and the amount of Y consumed by the i^{th} patient receiving treatment j is denoted as Y_{ij}.

Fixed-price estimates for resources X and Y are denoted by $\hat{P}_X$ and $\hat{P}_Y$, and defined in Chapter 4. These fixed-price estimates do not vary across patients, *i*, or treatments, *j*. For our purposes, we assume that these fixed prices are estimated from prices observed in a sample. We can apply these unit price estimates to X_{ij} and Y_{ij} to get a per subject cost estimate

$$C_{ij} = \hat{P}_X X_{ij} + \hat{P}_Y Y_{ij}. \tag{37}$$

Mean costs for treatment group *j* is:

$$\bar{C}_j = \frac{1}{n_j}\sum_{i=1}^{n_j} C_{ij} = \frac{1}{n_j}\left(\hat{P}_X \sum_{i=1}^{n_j} X_{ij} + \hat{P}_Y \sum_{i=1}^{n_j} Y_{ij}\right). \tag{38}$$

As discussed in Chapter 4, $\bar{C}_j$ is only an unbiased estimator of $E(C_j)$ if $\hat{P}_X$ and $\hat{P}_Y$ are unbiased estimators of $E(P_X)$ and $E(P_Y)$ and the sum of all covariance terms is zero. In order to focus on the role the level of detail plays in estimates of $E(C_j)$, we make these assumptions in this section and denote the fixed-price estimates under this assumption as $\bar{P}_X$ and $\bar{P}_Y$.

Next, we define the combining of X and Y into a more aggregated resource unit, Z, as bundling. Resource unit Z is a gross resource unit because it does not make a distinction between the number of units of X and the number of micro units of Y. It bundles them together to create a gross resource unit Z. While bundling still more detailed resources may have created X and Y, they are defined with more detail than Z. Relative to Z, X and Y can be referred to here as "micro" resource units. For example, if

X is number of ICU days, and Y is number of regular care days, then Z is number of hospital days. In another example, if X is number of are physician visits in a clinic, and Y is number of visits to a physician in an outpatient hospital, or other non- clinic facility setting, then Z would be number of ambulatory visits—thus bundling several places of service. The amount of Z consumed by the i^{th} patient receiving treatment j is denoted by Z_{ij} and is defined as $Z_{ij} = X_{ij} + Y_{ij}$.

The average unit price for this bundled resource is $\bar{P}_Z$, where $\bar{P}_Z$ is a weighted average of $\bar{P}_X$ and $\bar{P}_Y$:

$$\bar{P}_Z = \gamma_X \bar{P}_X + (1-\gamma_X)\bar{P}_Y, \tag{39}$$

$$\text{where } \gamma_x = \frac{\sum_{i=1}^{m} X_i}{\left(\sum_{i=1}^{m} X_i + \sum_{i=1}^{m} Y_i\right)} = \frac{\mu_X}{(\mu_X + \mu_Y)}. \tag{40}$$

Essentially, γ_x is the proportion of resource unit X in the price data sample, or the probability weight of X. While the price data sample could be the same sample as the resource utilization, it is assumed here that the samples are different. Therefore, the price data sample is denoted with a sample size of m.

This unit price can be applied to Z_{ij} to get a per patient bundled cost estimate:

$$C_{ij}^{G} = \bar{P}_z Z_{ij}. \tag{41}$$

The mean costs using bundling for treatment group j is

$$\bar{C}_j^G = 1/n_j \sum_{i=1}^{n_j} C_{ij}^G = \frac{\bar{P}_Z}{n_j} \sum_{i=1}^{n_j} Z_{ij} \,. \tag{42}$$

5.2 Conditions for Equivalence

This section examines, theoretically, the conditions under which estimates of the expected cost will be equivalent among resource costing methods using varying levels of detailed data. First, we identify the condition for equivalence for an individual subject using the notation developed above for the 2-input case. Second, we identify the conditions for equivalence between the average cost using aggregated data, $\bar{C}_j^G$, and for those using a greater level of detail, $\bar{C}_j$. Third, we extend the notation developed above to the multiple-input case and define the conditions for the equivalence in estimates of average cost.

While, here, the motivation for defining equivalence for the 2-input case is a desire for simplicity, there are real-world examples of aggregated measures being a bundle of two resources. For instance, similar to the ICU example above, the DRG system defines inpatient hospitalizations as one of two types: surgical or medical. Measuring hospitalizations as total days can be viewed as bundling number of days for two types of hospitalizations. Once defined, the 2-input case can be expanded to address the multiple-input case where we are bundling the number of DRG days.

5.2.1 Subject Level Costs: 2-Input Case

In order better to understand the impact of bundling or data aggregation on estimates of the average cost, we begin by exploring equivalence of subject level cost data.

Equivalence at the subject level, $C_{ij} = C_{ij}^{G}$, occurs when $\frac{X_i}{(X_i + Y_i)} = \gamma_x$ for the i^{th} individual (see Proof 1 the chapter appendix). Costs calculated using varying levels of detail are equivalent at the subject level when the proportion of the resources used by the subject is equivalent to the proportion of the resources in the price sample.

Another interpretation is that the intensity of services provided to the individual is equivalent to the average intensity of service in the sample used to estimate the fixed price. This assumes that the price denotes the intensity of a service (e.g., higher prices reflect greater intensity of service). The ideal condition is when there is no variation among subjects that make up the bundle in the intensity of service (i.e., all subjects have 25% of their hospitalizations in ICU), and this intensity is equivalent to the intensity of service in the sample from which the price estimates were obtained. In reality, these simultaneous equivalences seem unlikely and are less interesting to analyze, given that we are primarily concerned with the estimation of average costs for a group of individuals.

5.2.2 Estimation of Average Cost: 2-Input Case

Researchers and decision-makers are typically not interested in the cost associated with an individual. Rather, the focus is often on estimates of the average cost for a group of individuals. For example, economic evaluation alongside RCTs estimate the average cost for the group receiving an intervention—as well as the control group.

Equivalence at the group mean level, $\bar{C}_j = \bar{C}_j^G$, occurs when $\frac{\bar{X}_j}{(\bar{X}_j + \bar{Y}_j)} = \gamma_x$ (see Proof 2 the chapter appendix). Mean costs for a treatment group based on varying levels of detail will be equivalent when the proportion of each resource used by the treatment group is equivalent to the proportion of the resources appearing in the price data. This condition is less restrictive than the condition for equivalence at the subject level. There can be variation within subjects, as long as the average service intensity for the treatment group is equivalent to the average service intensity in the price sample.

An inequality exists when the service intensity in the price sample is not equal to the service intensity of the treatment group. When the sample used to estimate the average price has a lower proportion of high-priced (or more intensive) services compared to the sample of services for the group, $\frac{\bar{X}_j}{(\bar{X}_j + \bar{Y}_j)} > \gamma_x$, the average cost estimates will be lower using the aggregated method, $\bar{C}_j > \bar{C}_j^G$ (see Proof 3 the chapter appendix). The contrary is true in cases where the price sample represents more intensive services.

In many instances we would anticipate the average service intensity being differential between the sample of resource data and the sample from which price estimates were obtained. For example, Medicare's Prospective Payment System for inpatient hospitalizations reimburses providers with what is claimed to be the hospitals average cost of providing a hospitalization (Edwards, Honemann et al. 1994). Project TrEAT researchers used the average per diem paid amount as the fixed-price estimate when estimating the cost of inpatient hospitalizations, because the data collection methods they used limited their measurement of hospital utilization to the total number of days (Fleming, Mundt et al. 2000). When assessing whether a more detailed collection method would have resulted in larger or smaller cost estimates, we may consider that Medicare's reimbursement amounts are primarily intended to represent service costs for individuals over 65 years of age. In contrast, Project TrEAT's study population consists of problem drinkers between the ages of 18 and 65 years old.

5.2.3 Conditions for Equivalence: Multiple-Input Case

Now consider expanding the previous notation to the general case where the bundling involves more than two resources. For example, the CARE study, introduced earlier, collected patient-level inpatient hospital days by DRG. At the time of the study, there were 511 DRGs, and we could bundle all DRG-defined hospital days into one aggregate measure (e.g., total hospital days) or two aggregated measures (e.g., surgical and medical hospital days). In either case, we can compare estimates of the average cost by noting the aggregation levels of the data.

To do this, we expand the previous notation, letting X_{ijk} represent k^{th} resource consumed by the i^{th} subject in treatment j. We will continue to make the assumptions regarding fixed prices, $\bar{P}_{X_k}$. The aggregated or bundled resource use Z_{ijk} is calculated as:

$$Z_{ij} = \sum_{k=1}^{r} X_{ijk}, \tag{43}$$

where r is the number of resources or services being bundled.

Similar to the 2-input case, the average unit price for this bundled resource is $\bar{P}_Z$, where $\bar{P}_Z$ is a weighted average of the $\bar{P}_{X_k}^{'s}$:

$$\bar{P}_Z = \sum_{k=1}^{r} w_{X_k} \bar{P}_{X_k}, \tag{44}$$

$$\text{where } w_{X_k} = \frac{X_k}{\sum_{k=1}^{m} X_k}.$$

Essentially, w_{X_k} is the proportion of resource unit X_k in the price data sample (the probability weight of X_k).

The average cost for each treatment group can therefore be calculated using the most detailed resource and price information or the aggregate information:

$$\bar{C}_j = \sum_{k=1}^{r} \left[\frac{1}{n_i} \sum_{i=1}^{n} \bar{P}_{X_k} X_{ijk} \right]$$

or

$$\bar{C}_j^G = \frac{1}{n_i} \sum_{i=1}^{n} \bar{P}_Z Z_{ij}.$$

As with the 2-input case, selecting the level of detail that is to be collected for the resource use data implicitly specifies the number of price estimates. For example, collecting the total number of hospital days predetermines that converting this measure of hospital use to dollars requires an overall per diem prices estimate and not a per diem price estimate for each DRG or type of admission.

5.2.4 Estimation of Average Cost: Multiple-Input Case

The effect that data aggregation has on estimates of the average cost in the multiple-input case is more complicated, as one may expect. In general $\bar{C}_j = \bar{C}_j^G$ if

$$\sum_{k=1}^{r}\left[\bar{P}_{X_k}\left(\frac{\bar{X}_{jk}}{\sum_{k=1}^{r}\bar{X}_{jk}}\right)\right] = \sum_{k=1}^{r} w_{X_k}\bar{P}_{X_k} \tag{45}$$

(see Proof 4 the chapter appendix). However, other than the condition in which $\left(\frac{\bar{X}_k}{\sum_{k=1}^{r}\bar{X}_k}\right) = w_k$ for all $k = 1 \rightarrow r$ resources, it is not readily apparent under which circumstances $\bar{C}_j = \bar{C}_j^G$.

What is apparent is that aggregated data can provide less of an adjustment for the intensity of service—this is often referred to as case-mix adjustment (Pope, Ellis et al. 2000). Predicting the direction and magnitude of the difference in the multiple-input case

depends on the direction and magnitude of $\left(\frac{\bar{X}_k}{\sum_{k=1}^{r}\bar{X}_k}\right) - w_k$ for all $k = 1 \rightarrow r$ and their associated prices, $\bar{P}_{X_k}$.

To demonstrate the complexity of the multiple-input case, consider the estimation of average cost based on three inputs. The 3-input case has two unique conditions for equivalence.

For simplicity, let $v_{X_k} = \frac{\bar{X}_{jk}}{\sum_{k=1}^{3}\bar{X}_{jk}}$ and assume $\bar{P}_{X_1} \neq \bar{P}_{X_2} \neq \bar{P}_{X_2}$.

It can be shown that $\bar{C}_j = \bar{C}_j^G$ if

(1) $v_{X_2} = w_{X_2}$ and $w_{X_3} = v_{X_3}$

or

(2) $\frac{\left(\bar{P}_{X_2} - \bar{P}_{X_1}\right)}{\left(\bar{P}_{X_3} - \bar{P}_{X_1}\right)} = \frac{\left(w_{X_3} - v_{X_3}\right)}{\left(v_{X_2} - w_{X_2}\right)}$ when $v_{X_2} \neq w_{X_2}$

(see Proof 5 the chapter appendix).

The condition for equivalence in the 2-input case relied upon the case-mix in the resource use sample and price sample. However, equivalence is also possible in the 3-input case, even when the case-mix is not equal. This second condition not only depends on the case-mix of the resource use and price samples but on the difference between the prices of each resource unit. While striking these delicate balances is unlikely in the 3-

input case, one can imagine the complexity that would be required for equivalence as the number of inputs increases.

5.3 Case Study: Estimation of Inpatient Costs in Project CARE

While it is simple enough to demonstrate conditions for equality in the 2-input case, we rely on the following example to demonstrate the effect that aggregation of multiple-inputs has on estimates of average cost.

For this example, inpatient hospitalization data were obtained for the CARE study, which examined the incremental cost-effectiveness of an organizational depression management program for high utilizers of medical care (Pearson, Katzelnick et al. 1999; Katzelnick, Simon et al. 2000; Simon, Manning et al. 2001). Computerized records at three health maintenance organizations were obtained for adult patients randomly assigned to continued usual care (UC) or to an organized depression management program (DMP). Due to disenrollment during the twelve months following randomization, reliable inpatient data were available on 169 of 189 patients randomized to UC, and 205 of 218 patients randomized to DMP. The DMP group recorded more hospitalizations (57 vs. 38) with similar average lengths of stay. However, the DMP patients were more likely to have a surgical admission.

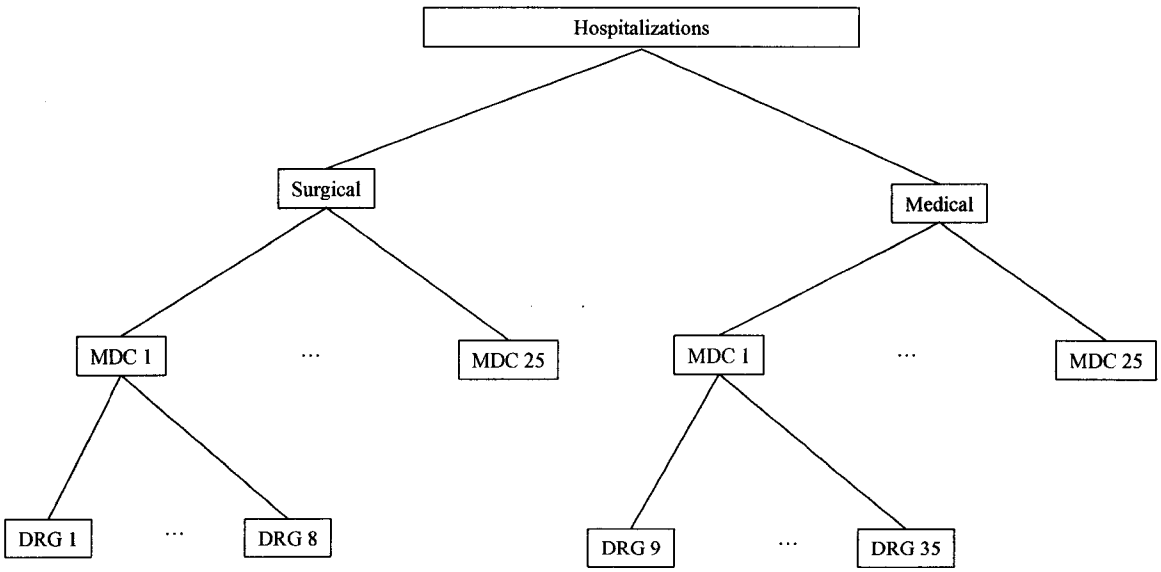

Figure 7: DRG flowchart

A discharge record defined by DRG number represents each hospitalization. The DRG number is commonly used to assigned payment amounts for a hospitalization but, can also be used to define each hospitalization by type (surgical or medical) or by major disease classification (MDC). While each DRG is **either** surgical or medical, all MDCs contain both types of admissions. For example, MDC 1 ("Diseases and Disorders of the Nervous System") contains DRG 1 though 35. DRGs 1 ("Craniotomy, Age > 17 Except for Trauma") is surgical, while DRG 9 ("Spinal Disorders and Injuries") is medical. Figure 7 provides a flowchart illustrating the relationships between DRGs, MDCs, and types of admission.

Inpatient hospitalizations for project CARE are broken down by type and length of stay in Table 6. MDC and DRG breakdowns by UC and DMP are provided in Table 8 and Table 9 in this chapter's appendix.

Table 6: Types of hospitalization in CARE

	UC (n=169)	DMP (205)
Hospitalizations	38 (22.5%)	57(27.8%)
LOS	3.29	3.30
Type		
Medical	22 (57.89%)	30 (52.63%)
Surgical	16 (42.11%)	27 (47.37%)

To illustrate the effect that level of detail has on the estimation of average costs, we use the CARE inpatient data for the measured resource utilization and data from the Nationwide Inpatient Sample (NIS 2000) to estimate the average cost per hospital day. NIS data rather than existing price estimates such as the average Medicare per diem paid amounts are used, because this allows us to examine the case-mix of the price sample. The average price estimate is then multiplied ("assigned") by individuals' measured hospital days to calculate the cost of each hospitalization. This "assignment" is done with four levels of detail: by total hospital days, by admission type (surgical or medical), by MDC, and by DRG. A simple average is then calculated based on the set of calculated costs. (This method of calculating the average cost is equivalent to assigning a fixed-price estimate to the average length of stay of each detail level).

Let X_{ij} and Y_{ij} be two types of hospitalization (e.g., medical and surgical admissions) such that they represent all hospitalizations (i.e., $prob[X \cup Y] = 1$). The average cost under intervention j is:

$$\bar{C}_j = \left(\frac{\sum_{i=1}^{n_j} \bar{p}_x X_{ij}}{n_j} \right) + \left(\frac{\sum_{i=1}^{n_j} \bar{p}_y Y_{ij}}{n_j} \right) = \bar{p}_x \left(\frac{\sum_{i=1}^{n_j} X_{ij}}{n_j} \right) + \bar{p}_y \left(\frac{\sum_{i=1}^{n_j} Y_{ij}}{n_j} \right) = \bar{p}_x \bar{X}_j + \bar{p}_y \bar{Y}_j . \quad (46)$$

This formula can be extended to include more detailed hospitalizations (e.g., DRG level data).

Table 7 shows the averages by randomization group for the two most aggregated methods, and the results for the two most detailed methods. (More detail for resource costing at the MDC and DRG level can be found in Table 10 and Table 11 in this chapter's appendix.) We see that the incremental average cost varies with the level of detail. The most detailed method (using DRG) resulted in incremental costs that were $611 smaller than they were for the most aggregated method. Why the difference across methods? Greater level of detail allows for a greater level of case-mix adjustment provided the studies sample size is sufficient enough to provide precise estimates. Consider that the CARE hospitalization data are made up of 57.83% medical admissions and 42.17% surgical admissions in the post-randomization year (this differs slightly by randomization group). In contrast, NIS 2000 hospitalizations are 73.8% medical and 26.2% surgical. Therefore, the most aggregate method assigned a price that is weighted

toward the price of a medical admission at a greater weight than the CARE population indicates. In other words, the patients in CARE have more severe hospitalizations than hospitalized patients in the general population.

The CARE study also allowed us to identify hospital days at the DRG. However, over 500 DRGs existed at the time the study was conducted but only 407 patients participated in the study. This low sample size, relative to the number of DRGs, may results in imprecise estimates of DRG specific length of stays.

Table 7: Estimates of Average Cost for the CARE study by Level of Aggregation

		UC (N=169)		DMP (N=205)	
Level of Aggregation	Price ($/day)	Total LOS (days)	Mean Cost ($/patient)	Total LOS (days)	Mean Cost ($/patient)
All Hospitalizations	$1,598	125	$3,755 (624)	188	$4,000 (684)
Hospitalizations by Type			$4,984 (970)		$4,818 (988)
Medical	$1,194	77		104	
Surgical	$2,748	48		84	
Hospitalizations by Major Disease Classifications (MDC)			$4,438 (713)		$4,587 (875)
Hospitalizations by DRG			$5,480 (962)		$5,113 (1036)

Bootstrapped standard errors in ( ).

5.4 Conclusions

A substantial body of literature exists regarding methods for statistical analysis in economic evaluations of health interventions. However, the amount of detail of resource use data collected can also affect the results of economic evaluation. As we have shown, in theory, it is possible to obtain equivalent estimates of average costs among methods varying in aggregation level. However, even under the most favorable conditions, this possibility seems unlikely and is difficult to predict.

In our example using clinical trial data collected at the DRG level, aggregation resulted in noticeably smaller estimates of average inpatient costs than methods utilizing the DRG level data. These differences likely occurred because the case-mix or severity in the general population based sample, NIS 2000, used to estimate fixed prices was less severe than our research sample of depressed patients that were high utilizers of medical services.

Investigators should consider the level of detail captured when documenting resource consumption in study design phases if economic evaluation is to be undertaken. While bundling of services is a useful shortcut when one is collecting resource use data, its implications for cost estimates based on resource costing should be considered. When data collection methods are determined at the beginning of a study, researchers should consider the population being studied and either collect detailed resource use information or find aggregate price estimates that more accurately reflect the unit prices of the study

population. Using more detailed resource use data allows for at better case-mix adjustment. Because resource costing often uses separate data sources for resource use and prices, the underlying populations may vary in the severity. For example, randomized clinical trials may yield datasets with a higher proportion of "more severe" hospitalization than common source of the price information.

Detailed information allows for an adjustment of case-mix difference between the resource use sample and price sample only when the detail necessary for assigning prices to observed resource use is available. Often researchers must be conducted their own cost-benefit analysis to determine if the cost of collect more detailed information justifies the benefit. In general, the greater the effect the cost estimate will have on the result of the analysis, the more precise this cost estimate should be. While our examination make explicit the role data aggregation can play but it is the responsibility of the researcher to make this determination.

5.5 Appendices

Proof 1

$$C_{ij} = C_{ij}^{G} \text{ if } \frac{X_{ij}}{\left(X_{ij} + Y_{ij}\right)} = \gamma_x$$

Proof:

$$C_{ij} = C_{ij}^{G}$$
$$\bar{P}_X X_{ij} + \bar{P}_Y Y_{ij} = \bar{P}_Z Z_{ij}$$
$$\bar{P}_X X_{ij} + \bar{P}_Y Y_{ij} = \left(\gamma_x \bar{P}_X + (1-\gamma_x)\bar{P}_Y\right)\left(X_{ij} + Y_{ij}\right)$$
$$\bar{P}_X X_{ij} + \bar{P}_Y Y_{ij} = \left(\gamma_x \bar{P}_X + \bar{P}_Y - \gamma_x \bar{P}_Y\right)\left(X_{ij} + Y_{ij}\right)$$
$$\bar{P}_X X_{ij} + \bar{P}_Y Y_{ij} = \gamma_x \left(\bar{P}_X - \bar{P}_Y\right)\left(X_{ij} + Y_{ij}\right) + \bar{P}_Y \left(X_{ij} + Y_{ij}\right)$$
$$\bar{P}_X X_{ij} + \bar{P}_Y Y_{ij} - \bar{P}_Y \left(X_{ij} + Y_{ij}\right) = \gamma_x \left(\bar{P}_X - \bar{P}_Y\right)\left(X_{ij} + Y_{ij}\right)$$
$$\frac{\bar{P}_X X_{ij} + \bar{P}_Y Y_{ij} - \bar{P}_Y \left(X_{ij} + Y_{ij}\right)}{\left(\bar{P}_X - \bar{P}_Y\right)\left(X_{ij} + Y_{ij}\right)} = \gamma_x$$
$$\frac{\bar{P}_X X_{ij} - \bar{P}_Y X_{ij}}{\left(\bar{P}_X - \bar{P}_Y\right)\left(X_{ij} + Y_{ij}\right)} = \gamma_x$$
$$\frac{X_{ij}}{\left(X_{ij} + Y_{ij}\right)} = \gamma_x$$

Proof 2

$$\bar{C}_j = \bar{C}_j^G \text{ if } \frac{\bar{X}_j}{\bar{X}_j + \bar{Y}_j} = \gamma_x$$

Proof:

$$\bar{C}_j = \bar{C}_j^G$$

$$1/n_j\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right) = \frac{\bar{P}_Z}{n_j}\sum_{i=1}^{n_j}Z_{ij}$$

$$1/n_j\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right) = 1/n_j\left(\left(\gamma_x\bar{P}_X + (1-\gamma_x)\bar{P}_Y\right)\sum_{i=1}^{n_j}\left(X_{ij}+Y_{ij}\right)\right)$$

$$\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right) = \left(\left(\gamma_x\bar{P}_X + (1-\gamma_x)\bar{P}_Y\right)\left(\sum_{i=1}^{n_j}X_{ij} + \sum_{i=1}^{n_j}Y_{ij}\right)\right)$$

$$\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} = \gamma_x\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \gamma_x\bar{P}_X\sum_{i=1}^{n_j}Y_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} - \gamma_x\bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \gamma_x\bar{P}_X\sum_{i=1}^{n_j}Y_{ij}$$

$$\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} = \gamma_x\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_X\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right)$$

$$\bar{P}_X\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} = \gamma_x\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_X\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right)$$

$$\frac{\bar{P}_X\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij}}{\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_X\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}} = \gamma_x$$

$$\frac{\left(\bar{P}_X - \bar{P}_Y\right)\sum_{i=1}^{n_j}X_{ij}}{\bar{P}_X\sum_{i=1}^{n_j}\left(X_{ij}+Y_{ij}\right) - \bar{P}_Y\sum_{i=1}^{n_j}\left(X_{ij}+Y_{ij}\right)} = \gamma_x$$

$$\frac{\sum_{i=1}^{n_j}X_{ij}}{\sum_{i=1}^{n_j}\left(X_{ij}+Y_{ij}\right)} = \gamma_x$$

$$\frac{\bar{X}_j}{\bar{X}_j + \bar{Y}_j} = \gamma_x$$

Proof 3

$$\bar{C}_j > \bar{C}_j^G \text{ if } \frac{\bar{X}_j}{\bar{X}_j + \bar{Y}_j} > \gamma_x$$

Let $\bar{P}_X > \bar{P}_Y$.

$$\bar{C}_j > \bar{C}_j^G$$

$$1/n_j\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right) > \frac{\bar{P}_Z}{n_j}\sum_{i=1}^{n_j}Z_{ij}$$

$$1/n_j\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right) > 1/n_j\left(\left(\gamma_x\bar{P}_X + (1-\gamma_x)\bar{P}_Y\right)\sum_{i=1}^{n_j}\left(X_{ij}+Y_{ij}\right)\right)$$

$$\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right) > \left(\left(\gamma_x\bar{P}_X + (1-\gamma_x)\bar{P}_Y\right)\left(\sum_{i=1}^{n_j}X_{ij} + \sum_{i=1}^{n_j}Y_{ij}\right)\right)$$

$$\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} > \gamma_x\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \gamma_x\bar{P}_X\sum_{i=1}^{n_j}Y_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} - \gamma_x\bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \gamma_x\bar{P}_X\sum_{i=1}^{n_j}Y_{ij}$$

$$\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij} > \gamma_x\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_X\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right)$$

$$\bar{P}_X\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} > \gamma_x\left(\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_X\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}\right)$$

$$\frac{\bar{P}_X\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij}}{\bar{P}_X\sum_{i=1}^{n_j}X_{ij} + \bar{P}_X\sum_{i=1}^{n_j}Y_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}X_{ij} - \bar{P}_Y\sum_{i=1}^{n_j}Y_{ij}} > \gamma_x$$

$$\frac{\left(\bar{P}_X - \bar{P}_Y\right)\sum_{i=1}^{n_j}X_{ij}}{\bar{P}_X\sum_{i=1}^{n_j}\left(X_{ij}+Y_{ij}\right) - \bar{P}_Y\sum_{i=1}^{n_j}\left(X_{ij}+Y_{ij}\right)} > \gamma_x$$

$$\frac{\bar{X}_j}{\bar{X}_j + \bar{Y}_j} > \gamma_x$$

Proof 4

$$\bar{C}_j = \bar{C}_j^G \text{ if } \sum_{k=1}^{r}\left[\bar{P}_{X_k}\left(\frac{\bar{X}_{jk}}{\sum_{k=1}^{r}\bar{X}_{jk}}\right)\right] = \sum_{k=1}^{r} w_{X_k}\bar{P}_{X_k}$$

Proof:

$$\bar{C}_j = \bar{C}_j^G$$

$$1/n_i \sum_{i=1}^{n}\sum_{k=1}^{r}\bar{P}_{X_k}X_{ijk} = 1/n_i \sum_{i=1}^{n}\bar{P}_Z Z_{ij}$$

$$\sum_{k=1}^{r}\bar{P}_{X_k}\bar{X}_{jk} = \bar{P}_Z\bar{Z}_{ij}$$

$$\sum_{k=1}^{r}\bar{P}_{X_k}\bar{X}_{jk} = \left[\sum_{k=1}^{r} w_{X_k}\bar{P}_{X_k}\right]\left[\sum_{k=1}^{r}\bar{X}_{jk}\right]$$

$$\frac{\sum_{k=1}^{r}\bar{P}_{X_k}\bar{X}_{jk}}{\sum_{k=1}^{r}\bar{X}_{jk}} = \sum_{k=1}^{r} w_{X_k}\bar{P}_{X_k}$$

$$\sum_{k=1}^{r}\left[\bar{P}_{X_k}\left(\frac{\bar{X}_{jk}}{\sum_{k=1}^{r}\bar{X}_{jk}}\right)\right] = \sum_{k=1}^{r} w_{X_k}\bar{P}_{X_k}$$

Proof 5

Proof: Expanding on proof 4

let $v_{X_k} = \dfrac{\bar{X}_{jk}}{\sum_{k=1}^{3} \bar{X}_{jk}}$ and $\bar{P}_{X_1} \neq \bar{P}_{X_2} \neq \bar{P}_{X_3}$ then

$$v_{X_1}\bar{P}_{X_1} + v_{X_2}\bar{P}_{X_2} + v_{X_3}\bar{P}_{X_3} = w_{X_1}\bar{P}_{X_1} + w_{X_2}\bar{P}_{X_2} + w_{X_3}\bar{P}_{X_3}$$

substitute $v_{X_1} = 1 - v_{X_3} - v_{X_3}$ and $w_{X_1} = 1 - w_{X_3} - w_{X_3}$

$$\Rightarrow v_{X_2}\left(\bar{P}_{X_2} - \bar{P}_{X_1}\right) + v_{X_3}\left(\bar{P}_{X_3} - \bar{P}_{X_1}\right) = w_{X_2}\left(\bar{P}_{X_2} - \bar{P}_{X_1}\right) + w_{X_3}\left(\bar{P}_{X_3} - \bar{P}_{X_1}\right)$$

$$\Rightarrow \left(v_{X_2} - w_{X_2}\right)\left(\bar{P}_{X_2} - \bar{P}_{X_1}\right) = \left(w_{X_3} - v_{X_3}\right)\left(\bar{P}_{X_3} - \bar{P}_{X_1}\right)$$

Only if $v_{X_2} = w_{X_2}$ and $w_{X_3} = v_{X_3}$

or

$$\frac{\left(\bar{P}_{X_2} - \bar{P}_{X_1}\right)}{\left(\bar{P}_{X_3} - \bar{P}_{X_1}\right)} = \frac{\left(w_{X_3} - v_{X_3}\right)}{\left(v_{X_2} - w_{X_2}\right)} \text{ when } v_{X_2} \neq w_{X_2}$$

Table 1: Frequency of Major Disease Classification (MDC) in CARE

	DMP		UC		TOTAL	
MDC	COUNT	PERCENT	COUNT	PERCENT	COUNT	PERCENT
1	6	10.53%	0	0.00%	6	6.32%
2	1	1.75%	0	0.00%	1	1.05%
3	1	1.75%	0	0.00%	1	1.05%
4	4	7.02%	4	10.53%	8	8.42%
5	4	7.02%	9	23.68%	13	13.68%
6	4	7.02%	3	7.89%	7	7.37%
7	4	7.02%	1	2.63%	5	5.26%
8	11	19.30%	6	15.79%	17	17.89%
10	1	1.75%	0	0.00%	1	1.05%
11	6	10.53%	1	2.63%	7	7.37%
12	1	1.75%	0	0.00%	1	1.05%
13	6	10.53%	3	7.89%	9	9.47%
14	1	1.75%	2	5.26%	3	3.16%
17	0	0.00%	5	13.16%	5	5.26%
18	0	0.00%	1	2.63%	1	1.05%
19	4	7.02%	0	0.00%	4	4.21%
21	0	0.00%	2	5.26%	2	2.11%
23	2	3.51%	1	2.63%	3	3.16%
99	1	1.75%	0	0.00%	1	1.05%

Table 2: Frequency of DRGs in CARE

DRG	DMP COUNT	DMP PERCENT	UC COUNT	UC PERCENT	TOTAL COUNT	TOTAL PERCENT
1	1	1.75%	0	0.00%	1	1.05%
13	1	1.75%	0	0.00%	1	1.05%
14	1	1.75%	0	0.00%	1	1.05%
25	2	3.51%	0	0.00%	2	2.11%
29	1	1.75%	0	0.00%	1	1.05%
39	1	1.75%	0	0.00%	1	1.05%
56	1	1.75%	0	0.00%	1	1.05%
76	0	0.00%	1	2.63%	1	1.05%
78	1	1.75%	0	0.00%	1	1.05%
79	0	0.00%	1	2.63%	1	1.05%
88	1	1.75%	2	5.26%	3	3.16%
100	2	3.51%	0	0.00%	2	2.11%
106	2	3.51%	0	0.00%	2	2.11%
112	0	0.00%	1	2.63%	1	1.05%
120	1	1.75%	0	0.00%	1	1.05%
125	0	0.00%	1	2.63%	1	1.05%
132	1	1.75%	0	0.00%	1	1.05%
139	0	0.00%	3	7.89%	3	3.16%
140	0	0.00%	1	2.63%	1	1.05%
143	0	0.00%	2	5.26%	2	2.11%
144	0	0.00%	1	2.63%	1	1.05%
151	0	0.00%	1	2.63%	1	1.05%
160	1	1.75%	1	2.63%	2	2.11%
182	1	1.75%	0	0.00%	1	1.05%
183	0	0.00%	1	2.63%	1	1.05%
188	2	3.51%	0	0.00%	2	2.11%
204	1	1.75%	0	0.00%	1	1.05%
208	0	0.00%	1	2.63%	1	1.05%
209	2	3.51%	1	2.63%	3	3.16%
216	0	0.00%	1	2.63%	1	1.05%
223	1	1.75%	0	0.00%	1	1.05%
227	0	0.00%	1	2.63%	1	1.05%
243	2	3.51%	1	2.63%	3	3.16%
249	1	1.75%	0	0.00%	1	1.05%
286	1	1.75%	0	0.00%	1	1.05%
316	2	3.51%	0	0.00%	2	2.11%
320	1	1.75%	0	0.00%	1	1.05%
321	0	0.00%	1	2.63%	1	1.05%
324	3	5.26%	0	0.00%	3	3.16%
336	1	1.75%	0	0.00%	1	1.05%
356	1	1.75%	0	0.00%	1	1.05%
358	1	1.75%	1	2.63%	2	2.11%
359	3	5.26%	0	0.00%	3	3.16%
361	0	0.00%	1	2.63%	1	1.05%
362	0	0.00%	1	2.63%	1	1.05%
369	1	1.75%	0	0.00%	1	1.05%
373	1	1.75%	1	2.63%	2	2.11%
381	0	0.00%	1	2.63%	1	1.05%
403	0	0.00%	3	7.89%	3	3.16%
410	0	0.00%	2	5.26%	2	2.11%
419	0	0.00%	1	2.63%	1	1.05%
426	1	1.75%	0	0.00%	1	1.05%
430	3	5.26%	0	0.00%	3	3.16%
443	0	0.00%	2	5.26%	2	2.11%
461	1	1.75%	1	2.63%	2	2.11%
462	1	1.75%	0	0.00%	1	1.05%
468	1	1.75%	0	0.00%	1	1.05%
491	1	1.75%	0	0.00%	1	1.05%
493	3	5.26%	0	0.00%	3	3.16%
497	2	3.51%	0	0.00%	2	2.11%
498	1	1.75%	1	2.63%	2	2.11%
502	1	1.75%	1	2.63%	2	2.11%

Table 3: Estimates of Average Cost for the CARE study by MDC

		UC (N=169)		DMP (N=205)	
Level of Aggregation	Price ($/day)	Total LOS (days)	Mean Cost ($/patient)	Total LOS (days)	Mean Cost ($/patient)
Hospitalizations by Major Disease Classifications (MDC)			$4,438		$4,587
1	$1,769	0		22	
2	$2,318	0		1	
3	$1,802	0		1	
4	$1,248	17		11	
5	$2,498	23		19	
6	$1,537	10		12	
7	$1,908	1		20	
8	$2,416	14		39	
9		0		0	
10	$1,341	0		3	
11	$1,585	3		18	
12	$2,177	0		1	
13	$2,131	11		10	
14	$1,318	5		2	
15		0		0	
16		0		0	
17	$1,833	33		0	
18	$1,207	5		0	
19	$634	0		23	
20		0		0	
21	$1,753	2		0	
22		0		0	
23	$1,601	1		5	
24		0		0	
25		0		0	

Table 4: Estimates of Average Cost for the CARE study by DRG

		UC (N=169)		DMP (N=205)	
Level of Aggregation	Price ($/day)	Total LOS (days)	Mean Cost ($/patient)	Total LOS (days)	Mean Cost ($/patient)
Hospitalizations by DRG			$5,480		$5,113
1	$2,993	0		11	
13	$1,138	0		3	
14	$1,326	0		1	
25	$1,501	0		5	
29	$1,554	0		2	
39	$11,670	0		1	
56	$3,379	0		1	
76	$1,587	9		0	
78	$1,236	0		7	
79	$1,125	1		0	
88	$1,121	7		2	
100	$1,886	0		2	
106	$4,131	0		16	
112	$4,988	2		0	
120	$2,073	0		1	
125	$2,962	3		0	
132	$1,572	0		2	
139	$1,501	7		0	
140	$1,677	1		0	
143	$1,936	4		0	
144	$1,501	6		0	
151	$1,836	6		0	
160	$2,376	3		1	
182	$1,267	0		2	
183	$1,486	1		0	
188	$1,247	0		9	
204	$1,270	0		7	
208	$1,748	1		0	
209	$2,734	4		7	
216	$1,838	1		0	
223	$2,933	0		1	
227	$2,664	1		0	
243	$1,209	1		13	
249	$1,199	0		1	
286	$3,020	0		3	
316	$1,298	0		6	
320	$1,078	0		3	
321	$1,180	3		0	
324	$1,566	0		9	
336	$1,873	0		1	
356	$2,578	0		1	
358	$2,028	9		2	
359	$2,188	0		6	
361	$3,251	1		0	
362	$23,234	1		0	
369	$1,728	0		1	
373	$1,251	4		2	
381	$2,257	1		0	
403	$1,423	23		0	
410	$1,967	10		0	
419	$1,234	5		0	
426	$669	0		3	
430	$589	0		20	
443	$2,508	2		0	
461	$1,978	1		1	
462	$697	0		4	
468	$1,981	0		1	
491	$3,711	0		2	
493	$2,349	0		13	
497	$3,781	0		13	
498	$4,760	6		1	
502	$1,642	1		1	

6 Summary and Future Research

6.1 Summary of Results

This dissertation has addressed the role of resource costing in the estimation of expected costs and the variation in costs. It has focused on two issues that arise when estimates are made using separate price and resource utilization information: (1) the use of fixed-price estimates, which implicitly fail to account for covariation between prices and resource use quantities; and (2) the level at which resource use is aggregated and therefore assigned fixed-price estimates.

While these are only two of several central issues in the literature surrounding the economic evaluation of health care interventions, they are relatively unexplored. Other issues include perspective, which is covered in nearly every published economic evaluation guideline[8] and the choice of fixed-price estimate, which was examined by Rittenhouse (1999). However, neither the published guidelines nor the applied literature provides adequate examination of the effects that covariation and data aggregation have on estimates of μ_c and σ_c^2.

First, we provided a general framework for a cost function that separated a payer's realized cost by the type of intervention. This framework allowed us to view the

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[8] See Commonwealth Department of Health Housing and Community Services (CDHHCS) (1992); Drummond, M. F. and T. O. Jefferson (1996); Luce, B. R., W. G. Manning, et al. (1996); Canadian Coordinating Office for Health Technology Assessment (CCOHTA) (1997); and Oostenbrink, J. B., M. A. Koopmanschap, et al. (2002).

estimation of costs as a process that may vary depending on the type of intervention being evaluated—and on the structure of the relevant market place.

Second, we showed cost estimations are biased when fixed-price estimates are used. The direction and magnitude of this bias was demonstrated analytically using lognormally distributed price and resource use quantities. In addition, using data from a randomized trial (the CARE study), it is shown that the use of a fixed wage rate would result in an overestimate of the patient time cost in all treatment arms.

Third, we found that estimates of average cost varied by level of data aggregation. Using inpatient resource use data from the CARE study, we found that the level of data aggregation and subsequently assigned resource use price, vary the estimate of average inpatient cost by as much as 31%.

6.2 Implications

In general, we have shown that estimates of average costs based on separate price and resource utilization information are unlikely to be equivalent to estimates based on data drawn from the joint cost distribution, $\phi(p,x;\theta)$. Our examination of the issues of covariation and data aggregation, in addition to those regarding the choice of fixed-price estimates addressed by Rittenhouse (1999), are important for several reasons.

First, identifying a problem is the first step to correcting it. Although the calculation of a variable representing cost as a function of observed resource use and a price estimate may be intuitively appealing, the estimates based on these data are unlikely to yield the same results as those based on actual cost data.

Second, cost estimation, ideally, should utilize observed cost data. However, given the viability and feasibility of collecting this type of data, resource costing is still likely to play a prominent role. The traditional methods of sensitivity analysis should continue to play an important role in resource costing practices when informed by economic theory, prior research and basic epidemiology. Sensitivity analysis is widely recommended for assessing problems of data uncertainty in the economic evaluation of health care interventions (Luce and Elixhauser 1990; Commonwealth Department of Health Housing and Community Services (CDHHCS) 1992). According to Drummond and colleagues (Drummond, O'Brien et al. 1997), one of the main limitations of sensitivity analysis is that the analyst has discretion over the variables and alternative values that are included in the sensitivity analysis. This dissertation provides insight into potential values that should be included based on economic theory, prior research, and basic epidemiology.

Chapter 4 provides insight into the effect ignoring basic economic behavior can have on cost estimation results. We suggest that economic theory and prior research be used to provide insight into the direction and magnitude of covariation between prices and resource use quantities to improve traditional sensitivity analysis. For instance, traditional sensitivity analysis typically varies the values symmetrically. In contrast, economic theory or prior evidence of covariation between prices and quantity may suggest using larger (or smaller) values in the cost estimation. The result would be an

asymmetric set of values (e.g., prices) within which resides the value used for the primary cost estimate.

Insight obtained from Chapter 5 can also be used to address the concern over the selection of values when conducting sensitivity analyses. We showed, both empirically and illustratively, that case-mix difference between the source of price data and the source of resource use data can lead to biased estimates of mean costs. Basic epidemiology provides insight into the severity or case-mix of a population being studied. This insight can guide researchers who must use highly aggregated data for their selection of price estimates. Price estimates, or samples from which to estimate prices, need to reflect the service intensity of the population being studied. In lieu of a perfect case-mix balance, knowledge of case-mix differences can be used, much in the same was as information regarding covariation, to provide asymmetric values for sensitivity analysis.

Third, researchers designing a study should take heed of the implicit assumptions they make when making choices regarding data collection. Often, it is difficult to obtain more detailed information on resource use once a study has concluded. Realizing that data aggregation can influence results, researchers should be vigilant when designing surveys or requesting data.

6.3 Future Research

The issues of covariation and aggregation are largely unexplored in the evaluation of health care intervention literature. Future research should examine their impact on the estimation of incremental cost.

Incremental costs are the basis for economic evaluation in health care. The effect of resource costing methodology on estimated costs is an enlightening but initial step in examining its effect on incremental costs. Under what conditions do the effects of covariation and aggregation in each group cancel out or mitigate each other? When are these conditions likely? Both theoretical and applied research can be used to address these issues by first defining when and how bias occurs and then estimating its realized impact on estimation.

While this dissertation has examined the issues of covariation and aggregation as separate issues, they likely have a simultaneous effect on cost estimation results. Consider the estimation of hospitalization costs in the CARE example from Chapter 5 where we assumed the prices were fixed for each utilization category (e.g., surgical and medical hospital days). Given the arguments presented in Chapter 4, one can imagine a context in which this assumption results in biased estimates of mean costs for a utilization category even if the price data source and resource use data source have equivalent case-mix.

Even using the finest level of detail available does not alleviate this problem. Consider again the inpatient hospital aggregation example in chapter 5. Here, we

collected and assigned costs to inpatient days at the DRG level, assuming prices for each DRG-defined day was fixed (zero covariation between prices and LOS). Given the resource, we could collect data at a more micro-level (e.g., physician visits, nursing time). However, this detail cannot evade the relationships that may exists between price and resource use.

6.4 Augmenting the Guidelines

Typically, resource costing methods involve assigning unit prices to measured resource use by combining these two pieces of information. Current versions of economic evaluation guidelines do not provide an adequate discussion on the effects that (1) covariance structures and (2) the level of detail, at which prices are assigned, have on estimates of μ_c and σ_c^2. While economic theory and literature suggest that relationships between prices and quantities exist, the guidelines created to address resource costing provide no guidance on addressing these relationships.

To date, some of the resource costing literature has addressed the effect that level of detail has on the estimation of μ_c. However, this literature is limited to illustrative examples and does not examine, analytically or conceptually, the effect that data aggregation has on the estimation of μ_c. Although the level-of-detail of resource use data is discussed in some of the costing literature (see the Canadian Coordinating Office for Health Technology Assessment (CCOHTA) 1996), to the best of my knowledge, its effect on parameter estimates has not been specifically addressed. The general consensus

is that more detail is better, although to obtain it increases the expense of conducting research.

Given the issues raised in this dissertation, it would seem natural that the next generation of guidelines addressing resource costing methodology would include a discussion of (1) covariance structures and (2) the level of detail, at which prices are assigned, and the effect they have on estimates of μ_c and σ_c^2. Specifically, discussions related to covariance structure should include their link to functional relationships such as demand and supply functions. While covariation between prices and quantity of resources used is a stochastic concept, by relating covariation to these economic relationships the guidelines could assist researchers in determining its direction and magnitude.

To addressing data aggregation, already partially addressed in some of the guidelines, the focus should be on 1) when to cost at a more detailed level; and 2) how to correct estimates based on resource costing methods using highly aggregated data. The guidelines already contain adequate guidance on obtaining more detailed price estimates. However, guidance for studies which do not have access to more detailed resource use data is omitted—other than a recommendation to collect more detailed data next time. In particular, revising current guidelines to introduce methods for correcting cost estimates based on available information on patient case-mix from which the price estimates were obtained.

Although the next generation of guidelines may not provide concrete answers to which is the best resource costing method, its purpose could also be to illustrate clearly the magnitude of the potential biases involved, and to serve as a resource for researchers and analysts estimating μ_c from measured resource use and unit price estimates. Closing the described gaps in the resource costing guidelines would also help put to rest the misguided assumption that estimating μ_c based on separate price and resource use information is identical to estimating μ_c based on actual cost data.

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