1 The Problem

Decision-analytic models have been applied to different areas in artificial intelligence, including diagnosis (Heckerman, Horvitz, & Nathwani, 1989), learning (Star, 1987; Buntine, 1987), vision (Levitt et al., 1988), and control of inference (Horvitz, 1989; Breese & Fehling, 1988). An activity common to these models is the agent’s updating his belief in relevant propositions on the basis of evidence. The models usually leave implicit the decision maker’s belief in the method by which the data were obtained. To be done properly, updating must include this belief in each of many possible models of observation of the data. We shall show that, in certain contexts, the space of all possible observational contexts can be parameterized to be both assessable and computable. Scientific research is one such context; specific biases can be used to provide the necessary parameterization.

Parameterization of the observational contexts is domain-dependent at different levels of the meaning of domain. We use the following hierarchy. The topmost level is the general field of scientific or systematic observation. The second level is the field of research aimed at discerning causal relations, as opposed, say, to exploratory descriptions. A third level is that of medical research, which eliminates from consideration a number of destructive experimental designs. A fourth level is the class of study, including, for instance, balanced-design, case-control, cohort, or randomized, studies. A fifth level is the object (domain of interest), such as cardiology. Our goal is to offer a structure that allows parameterization of all studies within the fourth domain. A successful parameterization at this level should enable us to handle a wide variety of medical (object) domains, while the structure will probably be effective at higher levels as well.

We may visualize the problem using the influence diagrams (Howard & Matheson, 1981) of Figure 1. In Figure 1a shows that the decision maker makes his decision, D, knowing the data, x, at the time of the decision, and thinking about the effect of the parameter, $\theta$, on relevant outcomes, $\Omega$, which affect the value, $V$, of the decision maker. The calculation of expected utility for the decision requires the prior probability distribution for the parameter $\theta$, in addition to the preposterior distribution $P(x \mid \theta)$. This formulation, however, leaves out the possibility that the data were obtained in different ways, which is equivalent to its preventing the decision maker from modeling his uncertainty in the preposterior distribution. In Figure 1b, we include the observational context explicitly, operationalized (or parameterized) in terms of a bias parameter, $\phi$, and make explicit the types of data, $y$, that bear on $\phi$, separately from those that bear on $\theta$. To use this structure, we need the prior over $\phi$ and the preposterior distribution, $P(x \mid \theta, \phi)$. The latter distribution contains our knowledge about the mechanism by which the data are obtained in a particular experimental context.

As an example of the importance of the observational context, consider the following problem. I have two coins, one of which I may bring to a gambling event. I would, of course, prefer the coin that gives me the greatest odds of winning me the most
greater number of heads as the coin to take (unless that
could be determined). The coins are apparently identical, but they
may have different chances of landing heads. I flip each
coin 100 times, asking an assistant to give me the
coins alternatingly. This process gives me two lists of
tosses and outcomes, one for each coin. Most utility
functions would have me choose the coin with the
higher number of heads as the coin to take (unless that
proportion is too high, in which case I risk being found
too easy or too hard to cheat).

To find the posterior distribution of $\theta_i$ after
observing $y_i$, we must integrate out the observational parameters.

$\mathbf{2. A Model for the Use of Reported Scientific Data}$

We narrow our attention to study designs for
medical research, at the fourth level of our domain
hierarchy, for a number of reasons. First, providing
data for high-stakes decisions relating to individual
situations is a major purpose of medical research, as
evidenced by the large number of clinical studies.
Second, while our discussion will remain general, it
will be focused by our considering a narrower domain
than all scientific research, thereby clarifying the model.
Third, the concept of bias in medical research is well
established, giving us a baseline against which to judge
the validity of our model.

$\mathbf{2.1 Details of the General Model}$

Our general model, depicted in Figure 2, is an
expansion of Figure 1, based on Shachter, et al. (1989).
It consists of a central framework with peripheral
adjustments. The framework allows the representation
of a number of modeling decisions, separate from the
domain issue of which therapy to implement. We will
point out these modeling decisions as they come up.
One general approach for making modeling decisions is
for the physician to explore each potential model
resulting from one modeling decision, and integrate
expected value across these models, weighted by a prior
probability on each model. A second approach is for
the physician to perform a sensitivity analysis across
some or all models, and either continue with a single
best model, or integrate across models, depending on the
outcome of the analysis.

We now circumnavigate our general model, Figure 2.
We have made explicit that the physician is
concerned about a particular Outcome of Interest, such as
mortality, morbidity, or cost. The fact that he uses
certain parameters to help him assess the likelihood of
that outcome occurring is a result of a separate decision
as to the probabilistic model he chooses to use.

We have split the general Parameter of Interest, $\theta$, from
Figure 1 into four separate parameters: the Patient
Parameter, $\theta_{pt}$, the Population Parameter, $\theta_{pop}$, the
Sample Parameter, $\theta_{sample}$, and the Effective Sample
Parameter, $\theta_{sample}^\prime$. By separating $\theta_{pt}$ from $\theta_{pop}$, we
allow the physician to take two types of modeling
actions. One is for the physician to use the same data
for many different clinical situations, if he knows how
to derive the distribution for $\theta_{pt}$ from Hyperparameters
updated by $\theta_{pop}$ in a hierarchical Bayes framework
(Berger, 1985), which may require traditional statistical
models. A second type of modeling action is for him
to effect a metaanalysis (L'Abbé, 1987), using multiple
sources of data (several different papers) to update his

$\mathbf{Figure 1. General influence-diagram models for belief}

updating. (a) Using primary data to update belief in
the parameter of interest. (b) Parameterizing the
observational context and using additional data to
update belief in the observational model.
Figure 2. Influence-diagram model for using research data in the general medical decision-making problem.

The Data node of Figure 1 has been split into an Experimental Outcome node, representing the actual results from the study as performed; an Observed Data node, representing the data recorded by the experimenters; and a Reported Data node, representing the data as reported in the written article and the only data available to the reader. The likelihood of the experimental outcome given the Effective Sample Parameter is the probability distribution that depends on the Probabilistic Model the physician chooses for modeling the outcome of the experiment. For mortality studies, as an example, this model is usually binomial.

If the physician knew the Measurement Reliability of the recording instruments, say the true sensitivity and specificity, and the true model relating the reliability to the actual and the observed data, he could calculate
exactly the **Observed Data** from the Experimental Outcome. Similarly, if he knew exactly the Credibility of the reporters, he could calculate the **Reported Data** from the **Observed Data**.

Researchers often report in their papers only their estimate of the parameter, rather than all the observed data. This estimate is a **Statistical Function** of the observed data, such as a mean or a regression coefficient. Statistical decision theory (Berger, 1985) concerns itself with the choice of that function. We note that, without at least the observed data, we lose information that could potentially alter our decision. The sufficient statistics proposed by statistical decision theory, then, appear to be context dependent, and our model makes explicit just this context.

### 2.2 An Example of Navigating the Model

To illustrate how all this might work in a specific instance, we consider a 55 year old white woman who has just had a heart attack and who has been brought into the hospital almost immediately after symptoms of chest pain, nausea, and sweating set in. Her physician, besides needing to stabilize her acute cardiovascular status, wants to prevent worsening of her general cardiac condition. The doctor knows that a drug, metoprolol, is considered possibly to do so. He is primarily concerned with minimizing the patient’s chance of death, and thereby maximizing the heart attack victim’s life expectancy. There are some known side effects of the medication. Should he use the drug?

Let us go through an abbreviated analysis using a study (Hjalmarson, et al., 1980) that bears on this question. As discussed before, we leave the choice of the value model to be implicit. The **Outcome of Interest** is mortality. We make the modeling decision to use the patient’s probability of death as the Patient Parameter, which we will assume to be constant over time (constant hazard model). For the modeling decision of the choice of referent Population, we have at least two choices on the basis of cardiology-domain knowledge: middle-aged women and middle-aged adults. If we choose the population of both sexes, there will be a larger number of studies, each with a large sample size, that we can bring to bear on this problem, which, in concert, may affect the Hyperparameters as much as if we used only the subgroup of women only. Clearly, there is a modeling decision trade-off between specificity of the data versus its the amount of data available. For the purposes of this paper, we shall take the modeling action of using only the combined population of middle-aged adults.

The **Sample** in the study consists of all heart-attacks victims from south Sweden in the late 1970s. This characterization represents Selection from our population on ethnic grounds, but not on the basis of referral, diagnostic purity, or diagnostic access biases (Sackett, 1979). The **Protocol Design** is reported to have been that of a double-blinded and randomized clinical trial, in which the assignment of a patient to a given treatment is independent of the patient’s baseline status. There is evidence to support the claim that the Protocol Implementation was identical to the design. For instance, the compositions of the metoprolol and placebo groups are similar with respect to relevant characteristics, based on reported baseline data, corroborating the implementation of randomization. The number of withdrawals from the study on the basis of side-effects is also similar between the two groups, suggesting that if there were some unblinding of the care providers such that the treating physicians became aware of the true treatment assignments, its degree was the same in both groups.

Estimating the actual degree of withdrawal explicitly is important for calculating a posterior distribution on $\theta_{\text{sample}}$. Withdrawal refers to a patient’s not receiving the treatment to which he was assigned. This estimation adds a bias parameter to be inferred, which, in turn, results in our considering a space of observational models larger than we would be considering without including the withdrawal bias. The withdrawal bias parameter in this study models the fact that the effective sample parameter for metoprolol was a result of mixing the treatment group with a third group of patients receiving no treatment, that is, a group with the baseline mortality risk (the group of patients withdrawn). The new parameter to be inferred is the degree of mixing, $\phi$. Shachter and colleagues (1989) offer a mathematical form for the effective sample parameter,

$$
\theta'_{\text{sample}, \text{metoprolol}} = (1 - \phi) \cdot \theta_{\text{sample}, \text{metoprolol}} + \phi \cdot \theta_{\text{sample}, \text{baseline}},
$$

showing that $\theta'_{\text{sample}}$ is a function of $\theta_{\text{sample}}$ and of $\phi$, as represented by the deterministic node in Figure 2. We note the similarity to our coin problem, in Section 1, where now, $\theta_1=\theta_2=\phi$. In the study, the reported overall withdrawal rate is 19.1 per cent in both groups, and we could use this to update our belief in $\phi$.

Continuing around Figure 2, we find that the investigators use the binomial Probabilistic Model, in keeping with our definition of the parameter of interest. Measurement Reliability depends on the sensitivity and the specificity of the sensing mechanisms. For mortality studies, the sensitivity, $P(\text{labeling patient as "dead" | patient deceased})$, and specificity, $P(\text{labeling the patient as "alive" | patient is alive})$, depend on patients who have dropped out of the study. The authors assure us that the mortality status of each patient entered into the study was assessed, regardless of subsequent treatment status, and their credentials are such that we consider them to have high Credibility. Finally, the authors report both mortality rates and life tables as their Statistical Functions of the data.
Clinical Studies

We now have the basic architecture for parameterizing the space of observational models through expanding the peripheral nodes of Figure 2. We gave the details of one instance in the mixture model resulting from patients withdrawn from the study. Our present concern is simply to locate all potential biases in a single model. We wish, therefore, for as comprehensive as possible a set of biases that spans the space of all studies. To show this set, we need to examine more closely the top line of Figure 2: the relationships among \( \theta_{\text{pop}}, \theta_{\text{sample}} \), and \( \theta_{\text{sample}} \). In causal studies, each of these parameters is a probability (e.g., mortality risk), or a parameter of a probability distribution, and hence represents an abstraction of a local node group of an influence diagram. The most general form of such a local node group is given in Figure 3: the node Patient's Event is dependent on the nodes Patient's Baseline State and Patient's Exposure to an Agent of Interest. For instance, \( \theta_{\text{sample}} \) is defined by the probability distribution of the events observed in the sample patients, given the baseline states of the sample patients and the agents to which those patients were exposed. Similarly for the population and for the effective sample. The language comes from Feinstein (1985), who uses this local node group to account for the widest possible range of initial states (e.g., healthy, diseased), agents (e.g., environmental exposure, medical therapy, process intervention), and events (e.g., mortality, pain, contraction of disease), thereby allowing for the same structure to be used in analyzing the entire class of comparative studies. Thus, to explore the relationship between specific biases and the parameter in which we are interested, we need to examine the primary belief network of which the parameter is an abstraction, and to locate the dependencies of the parameter on those biases. Then, the relationship between two parameters can be worked out at the level of these primary local node groups.

In Figure 4, we present a fragment of such an expanded belief network, showing the interplay between different classes of bias and the relationship between the Sample Parameter and the Effective Sample Parameter. The citation sources for the biases are indicated. As an example, we note that Classification Error is a class of bias upon which the assessment of Effective Sample Initial State is dependent. There is a large list of specific biases which fall into this category, such as Previous Opinion Bias and Diagnostic Suspicion Bias. These biases lead to an difference between the Sample Initial State and the Effective Sample Initial State; this difference leads, in turn, to a difference between the Sample Parameter and the Effective Sample Parameter. This fragment, then, is the mechanistic interpretation (or, expansion) of the arc in Figure 2 between the Sample Parameter and the Effective Sample Parameter.

We note that the model incorporates a wide variety of methodological elements, such as misclassification, misassignment, and conduction of the study (blindfolding) all into a single model. This analysis of mechanism allows us to preserve (or define) the semantics of the biases, while providing a numerical environment in which to use them.

4 Previous Attempts to Model the Use of Scientific Data

Rennels (1986) uses AI heuristics in constructing a system, ROUNDSMAN, that offers therapeutic suggestions for a particular patient, on the basis of articles in its knowledge base. The primary heuristic is the calculation of the “distance” of a paper to a particular domain decision. For the program to function, a domain expert must pre-process each article; the user enters the defining characteristics for the patient. Problematic in Rennels' approach is that all types of biases and adjustments are combined into a single score, without an underlying structure like the one we have developed. Furthermore, by not considering the probabilistic model for the data, ROUNDSMAN is unable to give an integrated numerical solution to the question of what the physician should do on the basis of the data.

Our model is in the same spirit as Eddy's confidence profile method (Eddy, 1989). His approach is motivated more by the desire to perform metaanalyses than the need to analyze in depth a single article. His "chains" are concerned with the causal connections between parameters and outcomes of interest. He deals with biases as correction factors, similar to our peripheral nodes in Figures 2.
The goal of the REFEREE research endeavor (Lehmann, 1988) is to create a system that aids a user in evaluating the methodological quality of a paper. The REFEREE team first implemented that goal in a rule-based program. Because of semantic and representational deficiencies, they redefined the goal to be the replicability of the conclusion of the study, and implemented the new goal in a probabilistic program and in a multiattribute-value-based program. However, even with these normative bases, it is not clear what should be done with the output of these systems. The approach we have taken in this paper is an answer to that question.

Finally, the field of clinical epidemiology is "concerned with studying groups of people to achieve the background evidence needed for clinical decisions in patient care" (Feinstein 1985, p. 1). Besides bringing epidemiological and statistical techniques to the medical bedside, clinical epidemiologists are concerned with physicians' coherent reading of the clinical research literature. Sackett, Haynes, and Tugwell (1985) have published a sequential algorithm for using the literature: If the article fails any step along the path, it is eliminated from consideration. L'Abbé, Detsky, and O'Rourke (1987) describe sequential steps to be taken for using an article in a metaanalysis. Their measure of quality is based on the rating-sheet approach of Chalmers and colleagues (1981). Our approach, in contrast, is global in that an article is implicitly discarded only after the probability distribution, P(x|θ), is determined; a distribution close to the prior distribution over θ suggests that the biases and adjustments have washed out any meaningfulness from the reported data. The primary advantage of the global approach is that it does not explicitly throw out data, unlike the sequential algorithm. Although a study may be designed and executed poorly or may be somewhat irrelevant, its data may still have an important bearing

Figure 4. Primary influence diagram, defining the Effective Sample Parameter, and its relationship to the Sample Parameter. Thickly drawn nodes and arcs indicate the local node groups of Figure 3. The horizontally hatched arcs indicate that the destination node is an abstraction of the probability distribution of the destination node. Footnote symbols indicate citation source for biases: * Sackett (1979); † Feinstein (1985); ‡ Lehmann (1988).
on the calculation of expected value. The disadvantage of the global approach is its computational complexity.

5 Uses of the Model

The model may be used in several ways. At the least, it may help a reader to organize the study of research results. This use leads to a qualitative analysis that, alone, may result in all the insights the user may want. We focus our comments on computer applications, however. A quantitative approach helps a user to organize the clinical epidemiological concerns and provides the basis for a decision support system and statistical workstation, where the resulting probability distributions may be displayed and studied, and where distributions over probability models may be considered as well.

In using the model to construct decision-support systems, we must construct models of how evidence in the study report updates our belief in a model. Extending the model results in our building a large knowledge base of research designs. With our general layout of the space of studies, it becomes easier to accrue new biases and research designs. The model we have given serves as the core, the methodological and statistical knowledge base (Figure 5). Domain knowledge is incorporated as new conditions on the biases (new predecessors), or new sources of evidence for the different biases (new descendents). In using the model, we begin with the knowledge base of biases, and use either methodologic or object-domain knowledge heuristically to prune that KB on the basis of which biases are irrelevant for the context of interest. With this reduced model, we then expand the possible evidential nodes for the bias parameters and search for evidence in the study report that bears on the bias parameters. Once we have updated our belief in those parameters, we examine the primary data themselves, which update both the bias parameters and the domain parameter. Finally, we remove the bias parameters as nuisance parameters. Shachter (1988) gives the general approach for this, and Barlow, Irony, and Shor (1988) give an example pertaining to experimental designs. This removal leaves us with a posterior probability distribution on the Population Parameter. We then derive the distribution for the Patient Parameter and calculate the expected utility for each action. We may do the reverse as well, and ask: what prior probability distribution would have us take different action?

We have presented an architecture for a large knowledge base of science methodology. The details of this knowledge base have implications for designing scientifically (rationally) functioning computer agents which collect data about the real world. The model we have presented eliminates most theoretical problems with previous approaches and provides a framework for future work. Extensions of our ideas include generalizing to other evidential domains in the hierarchy of domains presented at the beginning of this paper.

![General architecture for a decision support system.](image)

We also need to make more explicit the various modeling decisions the reader undertakes in performing the type of analysis we have been discussing. The work we present here can be followed now by a practical instantiation.

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References

Barlow, Richard E., Irony, Telba Z., and Shor, S. W. W. Informative sampling methods: The influence of experimental design on decision. Conference on Influence Diagrams for Decision Analysis, Inference, and Prediction. May 9–11, 1988. Engineering Systems Research Center, Bechtel Engineering Center, University of California at Berkeley (1988).

Berger, James O. Statistical Decision Theory and Bayesian Analysis (New York: Springer-Verlag, 1985).

Buntine, Wray. Decision tree induction systems: A Bayesian analysis. Proceedings of the Third Workshop in Uncertainty in Artificial Intelligence, University of
Washington, Seattle, July 10–12, 1987, pp. 190–107 (1987).
Breese, John S., and Fehling, Michael R. Decision-theoretic control of problem solving: Principles and architecture. *Proceedings of the Fourth Workshop in Uncertainty in Artificial Intelligence*, University of Minnesota, Minneapolis, August 19–21, 1988, pp. 30–37 (1988).
Chalmers, Thomas C., Smith, Harry, Jr, Blackburn, Bradley, et al. A method for assessing the quality of a randomized control trial. *Controlled Clinical Trials*, 2:31–49 (1981).
Eddy, David M. The confidence profile method: A Bayesian method for assessing health technologies. *Operations Research* (1989).
Feinstein, Alvan R. *Clinical Epidemiology: The Architecture of Clinical Research* (Philadelphia: W. B. Saunders Company, 1985).
Heckerman, David E., Horvitz, Eric J., and Nathwani, Bharat N. Toward effective normative decision systems: Update on the Pathfinder project. *Knowledge Systems Laboratory, Medical Computer Science*, Stanford University, Stanford, California. KSL-89-25. Submitted to the Thirteenth Annual Symposium on Computer Applications in Medical Care. (1989).
Hjalmarson, A., Herlitz, J., Malek, I., et al. Effect on mortality of metoprolol in acute myocardial infarction. *Lancet* 2(8251):823–827 (1980).
Horvitz, E. J. Reasoning about beliefs and actions under computational resource constraints. In L. N. Kanal, J. F. Lemmer, (Eds.) (1989). *Uncertainty in Artificial Intelligence 3*. Amsterdam: North-Holland, pp. 301–324.
Howard, Ronald A., and Matheson, James E. *Readings on the Principles and Applications of Decision Analysis*. (Menlo Park, CA: Strategic Decision Group, 1981).
L’Abbe, Kristan A., Detsky, Allan S., O'Rourke, Keith. *Meta-Analysis in clinical Research*. *Annals of Internal Medicine*. 107:224–233 (1987).
Lehmann, Harold P. Knowledge acquisition for probabilistic expert systems. *Proceedings of the Twelfth Annual Symposium on Computer Applications in Medical Care*, Washington, D.C., November 6–9, 1988, pp. 73–77.
Levitt, Tod S., Binford, Thomas O., Ettinger Gil J., and Gelband, Patrice. Utility-based control for computer vision. *Proceedings of the Fourth Workshop in Uncertainty in Artificial Intelligence*, University of Minnesota, Minneapolis, August 19–21, 1988, pp. 245–256 (1988).
Rennels, Glenn D. *A Computational Model of Reasoning from the Clinical Literature*. Ph.D. Thesis, Division of Medical Informatics, Stanford University, Stanford, CA. (1986).
Sackett, David L. Bias in analytic research. *Journal of Chronic Diseases*. 32:51–63 (1979).
Sackett, David L., Haynes, R. Brian, and Tugwell, Peter. *Clinical Epidemiology* (Boston: Little, Brown and Company, 1985).
Shachter, Ross D. Probabilistic inference and influence diagrams. *Operations Research* 36(4):589–604 (1988).
Shachter, Ross D., Eddy, David M., and Hasseblad, Victor. An influence diagram approach to medical technology assessment. To appear in R. M. Oliver and J. Q. Smith (eds), *Influence Diagrams, Belief Networks, and Decision Analysis* (New York: John Wiley & Sons, in press).
Self, Matthew, and Cheeseman, Peter. Bayesian prediction for artificial intelligence. *Proceedings of the Third Workshop in Uncertainty in Artificial Intelligence*, University of Washington, Seattle, July 10–12, 1987, pp. 61–69.
Star, Spencer. Theory-based inducting learning: An integration of symbolic and quantitative methods. *Proceedings of the Third Workshop in Uncertainty in Artificial Intelligence*, University of Washington, Seattle, July 10–12, 1987, pp. 237–248 (1987).