Practice of Epidemiology

Revealing the Complexity of Health Determinants in Resource-poor Settings

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An epidemiologic systems analysis of diarrhea in children in Pakistan is presented. Application of additive Bayesian network modeling to 2005–2006 data from the Pakistan Social and Living Standards Measurement Survey reveals the complexity of child diarrhea as a disease system. The key distinction between standard analytical approaches, such as multivariable regression, and Bayesian network analyses is that the latter attempt to not only identify statistically associated variables but also, additionally and empirically, separate these into those directly and indirectly dependent upon the outcome variable. Such discrimination is vastly more ambitious but has the potential to reveal far more about key features of complex disease systems. Additive Bayesian network analyses across 41 variables from the Pakistan Social and Living Standards Measurement Survey identified 182 direct dependencies but with only 3 variables: 1) access to a dry pit latrine (protective; odds ratio = 0.67); 2) access to an atypical water source (protective; odds ratio = 0.49); and 3) no formal garbage collection (unprotective; odds ratio = 1.32), supported as directly dependent with the presence of diarrhea. All but 2 of the remaining variables were also, in turn, directly or indirectly dependent upon these 3 key variables. These results are contrasted with the use of a standard approach (multivariable regression).

Bayesian network; diarrhea; epidemiologic determinants; graphical model; socioeconomic factors

Presented here is an epidemiologic systems approach for identifying potential determinants of diarrhea in children under 5 years using data from the Pakistan Social and Living Standards Measurement (PSLSM) Survey. Childhood diarrhea is the second biggest cause of worldwide mortality in children under 5 years of age (1, 2), and health surveys targeting this disease are common (3–6). Although such study designs are not without issue, potentially suffering from data quality and reliability concerns (7), they are widely used as low cost methods of data collection in developing countries.

A major challenge when analyzing data from surveys is that they are typically exploratory in nature, where the precise etiology of health outcomes is not known, and information on a large number of variables is often collected, not all of which are necessarily complete or relevant. It is also typical that many variables of potential interest are interrelated, both to each other and also to health outcomes. Such data may be conceptualized as describing an epidemiologic system (8–11), that is, a collection of mutually interdependent variables some or all of which can predict or affect the health outcomes of interest.

Additive Bayesian networks are introduced as a methodology for identifying statistical dependencies in complex disease systems by using observational data. Ultimately, what is desired in many epidemiologic analyses is the identification of causal pathways (12–14), which can be extremely challenging in systems such as diarrheal disease where many high level casual factors have been postulated (15), and the identification of statistical dependencies can be invaluable for informing such analyses.

The key distinction between standard multivariable regression analyses and Bayesian network-type analyses is that multivariable regressions seek to identify covariates
associated with some outcome variable, for example, the presence of diarrhea. Bayesian network analyses go much further and attempt to not only identify associated variables but also, additionally and crucially, empirically, separate these into those directly and indirectly dependent upon the outcome variable. The latter is vastly more ambitious but has the potential to reveal far more about key features of complex disease systems than existing commonly used approaches. This is the central message of the work presented: Additive Bayesian network analyses are superior to standard approaches for inferring statistical dependencies from complex observational data.

IDENTIFYING STATISTICAL DEPENDENCIES BY USING MULTIVARIABLE REGRESSION

When exploratory analyses of data comprising many variables are performed, it is common to utilize some form of multivariable regression in which a variable selection process is then used, the goal being to search for variables that are statistically significantly associated with, for example, an outcome variable such as disease presence. Stepwise regression searches are widely used (16–19) despite being viewed rather negatively in the epidemiologic and biostatistical literature (20–22). Such automated searches are arguably oversused or, rather, the results from such analyses are too often presented without sufficient additional checks to ensure the robustness of associations against overfitting (23).

In rapidly developing and increasingly data-rich fields such as genetic epidemiology, computational biology, and bioinformatics, automation in statistical modeling is standard and, indeed, arguably essential when faced with exploring observations from large numbers of potentially interdependent variables. That automated searches tend to overfit is well known. There are, however, well-established techniques for addressing this; of the most commonly utilized are model averaging (24, 25) and parametric bootstrapping (26), both of which are explored in the later case study analyses.

IDENTIFYING STATISTICAL DEPENDENCIES BY USING BAYESIAN NETWORKS

Bayesian network analysis is a form of statistical modeling that derives, from empirical data, a graphical network describing the dependency structure between variables, where this is formally depicted as a directed acyclic graph (DAG). Bayesian networks are widely used in areas such as systems biology (27–29), human immunodeficiency virus (HIV) and influenza research (30–33), and also analyses of complex disease systems (34–37). The origins of Bayesian network modeling lie within the machine-learning and data-mining literature (27, 38) with an accessible non-technical introduction (28).

In multivariable regression analyses, the goal is to identify statistically significant associations between an outcome variable and one or more covariates. Here, “association” denotes that the variables are statistically dependent; it says nothing on whether the variables are directly or indirectly dependent. To borrow an example from Hernán et al. (14), in multivariable regression analyses with “lung cancer” as the outcome variable and “smoking” and “yellow fingers” as covariates, it may then be expected that one or both of these covariates would be identified as statistically significantly associated with lung cancer. In contrast, in a Bayesian network analysis, it would be expected that smoking and lung cancer be identified as directly dependent, yellow fingers and smoking as directly dependent, but that yellow fingers and lung cancer not be identified as directly dependent. In terms of a DAG, this would describe a model with 2 arcs (one between lung cancer and smoking and a second between yellow fingers and smoking) but with no arc between yellow fingers and lung cancer. Note, we have not specified the direction of these arcs. In a Bayesian network analysis, each DAG is formally a factorization of the joint probability distribution of the observed data and, because of likelihood equivalence, it is the presence of arcs between variables and not their direction that is the notable feature.

Consider the joint probability of variables $X$ and $Y$, $P(X, Y)$. Theory gives $P(X, Y) = P(Y|X)P(Y)$ and $P(X, Y) = P(X|Y)P(Y)$, where the former can be depicted as a DAG with one arc, from $X$ to $Y$, and the latter with one arc, from $Y$ to $X$. The practical implication of this is that, by using observed data alone, it is not possible to statistically discriminate between different DAGs from within the same likelihood equivalence class, as these are probabilistically identical. However, determining likelihood equivalence between DAGs is extremely difficult in all but the simplest cases; refer to Web Appendix 1, the first of 13 Web appendices available on the Journal’s website (http://aje.oxfordjournals.org/), for more details. Because of these complications, it is typical to ignore arc direction in Bayesian network analyses (30–33, 39), although notable exceptions are analyses of longitudinal data where dynamic Bayesian networks may be utilized (40). Using prior belief to impose explicit arc direction may be of some value in analyses that attempt to combine statistical dependency with causality, and this is returned to later.
Bayesian network modeling formulation

Standard multivariable statistical models—linear or generalized linear models or their variants—are additive, that is, they describe the mean value of some response variable conditional on a given covariate pattern, as an additive contribution from each covariate. In contrast, Bayesian network models for categorical data, the most commonly utilized form of Bayesian network, use a parameterization where each and every covariate pattern is modeled by using independent sets of parameters; that is, the parameters cannot be interpreted as main effects or interaction effects (Web Appendix 4). This formulation may also be far from parsimonious (41) and does not provide any ready interpretation of the model parameters. The standard formulation of Bayesian networks (27) does facilitate conjugacy; that is, all parameter estimates in a Bayesian network can be computed analytically for the 3 usual types of Bayesian network (categorical, Gaussian, and a special variant of mixed categorical and Gaussian variables (42)).

At the cost of a loss of conjugacy, it is possible to formulate Bayesian network models that are direct analogs of standard multivariable linear and generalized linear models, where each variable in the data is modeled by an additive multivariable regression model, with an appropriate link function (e.g., a logit) if required (Figure 1). As in classical Bayesian network models, additive Bayesian networks are described by a DAG. The price for this considerably greater model flexibility is that the goodness of fit and model parameters now must be estimated numerically rather than analytically. Laplace approximations (43) are used here.

Bayesian inference requires prior distributions, and in a Bayesian network there are 2 possible types of priors: priors on the model parameters and priors on the DAG. In terms of parameter priors, the approach utilized here assumes uninformative Gaussian priors with zero mean and large variance for each of the regression parameters across all parts of the model, as well as diffuse gamma priors for the precision parameter in Gaussian nodes of the model. In terms of structural priors, it is currently assumed that each DAG structure is equally plausible in the absence of any data. Imposing prior causal knowledge onto network structures, for example, by imposing conditions on arc direction, is returned to later.

Model selection in statistical analyses

Statistical model selection comprises 3 parts, denoted “A” (choosing a general form of model); “B” (deciding the scope of the model search space and how to cross it); and “C” (deciding how to summarize the results from “B”).

For the PLSM case study, the first analysis presented comprises a conventional stepwise regression search. Therefore, “A” is standard multivariable logistic regression. “B,” a stepwise search, forwards from a null model and backwards from a full model, with comparisons performed within a maximum likelihood framework, as that is what is provided in common statistical software and is most usual in practice, and with the Akaike Information Criterion (AIC) as the goodness-of-fit metric. For “C,” the single best model found in “B” was then subjected to parametric bootstrapping to identify any issues of overfitting (Web Appendix 5).

In the Bayesian network analyses, for “A” an additive form of Bayesian network is used. For “B,” the 2 most widely utilized “structure discovery” approaches are used. First, the local search heuristic given by Heckerman et al. (27) is analogous to the usual stepwise search in multivariable regression. Second, there is a search over node orderings rather than DAG structures. Order-based approaches were introduced by Friedman and Koller (44) and then substantially extended by Koivisto and Sood (45). The motivation behind local heuristics (including stepwise searches in multivariable regression) is that they will identify high-scoring, well-fitting models when it is not computationally feasible to identify the very best model with any certainty. The second approach for searching for optimal Bayesian network models is to collapse DAGs over node orderings: a node ordering is simply a list of the nodes, for example, as indices 1 through n, where a given DAG structure is consistent with an ordering if, and only if, the parents of each node precede their child node in this list. Orderings can be thought of as groups of DAG structures (those structures which are consistent with that particular ordering), and note that each DAG may be consistent with more than one ordering; for example, the empty DAG (no arcs) is consistent with every possible ordering. The basic idea is that, by searching across orders, the dimension of the
search space is vastly reduced from \( n^2 \) unique DAGs down to \( n! \) unique orders (45), although the latter may still be computationally impractical. The price for this reduction in size of search space is that searching across orders is biased relative to searching across DAGs.

Finally, consider step “C,” how to summarize the results of Bayesian network model searches. Two options are either to construct some form of summary or “average” model by pooling across heuristic search results or else to select a single “best” model. A popular approach for the former is to construct a majority consensus network that builds a DAG comprising all those arcs present in at least a majority (>50%) of the DAGs identified by using heuristic searches (30, 35). Because of likelihood equivalence, it is common to collapse over arc direction to avoid missing important structural features. For example, if an arc \( X \rightarrow Y \) appears in 50% of heuristic results, and \( Y \rightarrow X \) appears in the other 50%, then even although this direct dependency between \( X \) and \( Y \) is not necessarily the same in every search result it will never appear in a (directed) majority consensus network. For this reason, collapsing over arc direction when presenting results of Bayesian network analyses is common (30, 39). The purpose of summarizing over many DAGs is to address concerns of overfitting, and it is directly analogous to the ubiquitous use of majority consensus trees in phylogenetics (46). The second option in “C” is to choose a single best model, with the most obvious concern being overfitting, and parametric bootstrapping is not generally computationally feasible here. An accepted approach for choosing a single best model is to use the exact order-based method (45) that finds the globally most probable posterior DAG.

All modeling results were carried out in R (47) by using an R library called “abn” developed by the authors for the purpose of analyzing epidemiologic data. This software is freely available for download from CRAN (http://cran.r-project.org/).

RESULTS

Multivariable regression

Table 1 shows the variables in the optimal model from the stepwise multivariable regression analysis (Web Appendix 6). There are 12 covariates, many of which have low \( P \) values. To identify spurious covariates arising from overfitting, we used parametric bootstrapping to generate 10,000 data sets from the optimal model. The parametric bootstrapping results provide convincing evidence that each of the 12 identified covariates is robust in terms of being statistically associated with the presence of diarrhea (Web Appendix 6). This regression model can be represented as a DAG where each of the explanatory variables is a node with an arc directed toward the node for the response variable (Figure 2).

Additive Bayesian network

Three different, although related, sets of results are presented, all with the same goal of identifying those variables directly dependent upon the presence of diarrhea.

<table>
<thead>
<tr>
<th>Indicator</th>
<th>Odds Ratio</th>
<th>( P ) Value</th>
<th>Bayesian Odds Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Child’s age</td>
<td>1.05</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>No. of rooms</td>
<td>0.95</td>
<td>0.007</td>
<td></td>
</tr>
<tr>
<td>Sex, male</td>
<td>1.14</td>
<td>0.012</td>
<td></td>
</tr>
<tr>
<td>Dwelling type, part of compound</td>
<td>0.70</td>
<td>0.020</td>
<td></td>
</tr>
<tr>
<td>Drinking water source</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Piped</td>
<td>0.85</td>
<td>0.011</td>
<td></td>
</tr>
<tr>
<td>Canal/river/stream</td>
<td>0.65</td>
<td>0.0087</td>
<td></td>
</tr>
<tr>
<td>Spring</td>
<td>0.76</td>
<td>0.13</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>0.46</td>
<td>0.0016</td>
<td>0.49</td>
</tr>
<tr>
<td>Type of toilet</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flush, connected to open drain</td>
<td>0.84</td>
<td>0.046</td>
<td></td>
</tr>
<tr>
<td>Dry pit latrine</td>
<td>0.66</td>
<td>&lt;0.0001</td>
<td>0.67</td>
</tr>
<tr>
<td>Connection to sewerage, yes, covered drains</td>
<td>0.72</td>
<td>0.064</td>
<td></td>
</tr>
<tr>
<td>Organizer of garbage collection from house, no formal system</td>
<td>1.23</td>
<td>0.0048</td>
<td>1.32</td>
</tr>
</tbody>
</table>

Heuristic search across 13 variables. The standard local heuristic search (27) was applied to the subset of 12 covariates identified in the optimal multiple regression model. A (directed) majority consensus additive Bayesian network model was constructed by pooling results across 20,000 heuristic searches; it was sufficient for robust results (Web Appendix 7). This summary network (Web Appendix 7) identifies “dry pit latrine” and access to an atypical “other water source” as directly dependent upon diarrhea. Figure 3 shows an undirected majority consensus additive Bayesian network constructed from the same 20,000 heuristic searches. This now additionally has “no formal garbage collection” as directly dependent upon diarrhea, although its structural support is relatively weaker in terms of how often it was chosen for inclusion in each locally optimal DAG (Web Appendix 7), compared with the other 2 variables. Posterior density estimates for the 3 variables directly dependent upon diarrhea can be found in Web Appendix 8. Note that the odds ratio estimates in Table 1 and posterior densities will be identical in any additive Bayesian network that has only these 3 variables with arcs to diarrhea.

Exact search for most probable DAG across 13 variables. The most probable posterior DAG was identified by using the exact method (45), again on the reduced set of 13
variables (specific details are given in Web Appendix 9). This exact search identifies a maximal additive Bayesian network that has “dry pit latrine” and access to an atypical “other water source” as directly dependent upon diarrhea but not “no formal garbage collection.” The goodness of fit of this model is −105,028.4 (log marginal likelihood), and it has 32 arcs in total. During the previous 20,000 search heuristics across DAGs, a number of models with improved goodness of fit were identified (e.g., −105,025.9 with 34 arcs), which demonstrates the bias toward parsimony in order-based searches, as the fewer arcs a DAG has, the more orders it will be consistent with.

**Heuristic search across all 41 variables.** The standard heuristic search (27) over 41 variables was not computationally feasible, nor was the exact order-based method. By necessity, an ad-hoc approach was instead utilized by adding several constraints to the standard heuristic search (Web Appendix 10). A majority consensus additive Bayesian network model was constructed by pooling results across ≈500,000 separate searches. This model identifies the same 3 variables as directly dependent upon diarrhea as in the undirected majority consensus network with 13 variables. The additive Bayesian network model supports 182 interdependencies among the 41 variables, where 179 are dependencies indirectly related to the presence of diarrhea, that is, between variables which can potentially affect disease presence, but only through their associations with other variables (refer to Web Appendix 11 for a detailed description of the model).

**DISCUSSION**

The objective of the analyses presented was to identify potential determinants of the presence of diarrhea and, in particular, to contrast results by using standard multivariable regression with those of an epidemiologic systems approach utilizing additive Bayesian networks.

**Comparison of methods**

Table 1, along with Figures 2 and 3, shows clearly that the 2 approaches provide very different, though overlapping, results. The additive Bayesian network results suggest that most—9 out of 12—of the covariates identified in the
Only 3 variables (no formal garbage collection, access to a dry pit latrine, and access to an atypical other water source) are supported as directly dependent upon the presence of diarrhea.
multivariable regression analyses, while associated with the presence of diarrhea, are only indirectly rather than directly related to this outcome.

Additive Bayesian network models are simply multivariate extensions of standard multivariable regression and nothing more. The single key conceptual difference is that additive Bayesian network models are multidimensional and consider all associations among all variables simultaneously. It is therefore intuitively reasonable to expect both approaches—additive Bayesian network and multivariable regression—to both identify in common those variables with the strongest degree of statistical support (and irrespective of whether different goodness-of-fit metrics or inferential framework is used, e.g., AIC or marginal likelihood, Bayesian or non-Bayesian). This is exactly what was found in the analyses presented (Table 1): The 3 variables with lowest $P$ values in the multivariable regression are also those supported as directly dependent upon diarrhea in the additive Bayesian network results.

In the multivariable regression analyses, “number of rooms” was identified as associated with diarrhea and, with $P = 0.007$ sufficiently low to be typically considered strong statistical evidence, this was further supported through the bootstrapping results. This variable has many direct dependencies in the additive Bayesian network (Figure 3; Web Appendix 11) but only with variables other than diarrhea. Biologically, “number of rooms” cannot be directly dependent upon diarrhea as, although it is likely to be related to the living and environmental conditions in a household and the additive Bayesian network model provides empirical evidence of this, intuitively, it cannot contribute directly to diarrheal infection. This suggests that “number of rooms” has been identified in the multivariable regression model as a result of association induced with diarrhea through a network of interdependencies across the disease system. This highlights the difficulty of interpretation in the traditional multivariable regression model where it is possible for variables with low $P$ values to be identified as associated with disease but that are likely to be only indirectly related to the outcome variable.

**Biologic interpretation of results**

The decreased risk of diarrhea from dry pit latrines suggests that infectious enteric pathogens are efficiently removed from fecal-oral transmission cycles. Using a univariate regression model, we found that the absence of a toilet in a household was a substantially greater risk factor for diarrhea (odds ratio = 5.7, 95% confidence interval: 5.07, 6.50) than the presence of any type of toilet. The absence of arcs connecting “no toilet in the household” to childhood diarrhea suggests, however, that those houses lacking toilets have a network of confounding factors that modify the risk of enteric infection. For example, a fuller description of the disease system (Web Appendix 11) shows that the absence of a toilet is dependent upon other descriptions of the household, such as the absence of an electrical connection (as an indicator of socioeconomic status), with certain water sources, especially those that do not require infrastructure, such as ponds, streams, and springs, and also no formal garbage collection. What might be deduced from this is that the lack of a toilet is an index of lower socioeconomic status and therefore living conditions. Socioeconomic status is itself associated with educational levels and certain behaviors, for example, unhygienic practices that increase the risk of diarrhea.

Using “other” sources of water is comparatively unusual in the data (2.1% of households). Given the breadth of options covered across the other 5 categories of water sources (Web Appendix 2), “other water source” is somewhat vague but includes buying water from a local seller and collecting water from a tanker-supplied public standpipe. Water that is further removed from either natural water courses or pipe/well systems may be less susceptible to leakage between sewerage systems and the water table and thereby at risk of contamination with water-borne pathogens. Examination of the 41-variable additive Bayesian network model shows connections from each of the water sources to at least the alternative sewerage connections or to the type of toilet, demonstrating the tight linkage among these 3 risk categories in determining the exposure of children to enteric pathogens. The relatively large uncertainty in the log odds estimate between “other” water sources and diarrhea (Web Appendix 8) is likely due to both the rarity of this water source in the data and also the ambiguous definition of this variable. Web Appendix 3 contains a list of additional references and a summary of previous variables associated with diarrhea, including age, which is also briefly discussed.

In the language of Hernán et al. (14), the components of a disease system are the disease outcome, an exposure (that directly results in disease), and a series of confounding variables that act on either the exposure or both exposure and disease outcome. Survey data, as in the PSLSM Survey, do not necessarily contain the sort of proximal exposure that results in infection (contact with enteric pathogens), so much as a collection of variables that might be considered common to both exposure (infection) and disease (pathogenesis). It is, therefore, arguably less useful to discuss causality with respect to such an exploratory model; however, what is both possible and useful is the partitioning of factors into those that are directly or indirectly dependent upon disease outcome. To illustrate this point, consider the type of toilet that is present in a house: There are several types of toilet in the PSLSM data, but these are all variants of the same underlying theme of how the household disposes of human excreta. It is not practical to question whether a flushing toilet is causal of diarrheal disease so much as the relative risk of disease given the different types of toilet present; the actual exposure is still the contact with enteric pathogens, which can then be stratified (assuming such data exist) by type of toilet. In this context, “toilet” is a confounder (according to Hernán et al.) that can be used to stratify the more proximal exposure.

Following through a series of DAGs as subsets of the more complete system may offer a closer parallel to causal models that are based on expert opinion (Web Appendix 12). Assuming that the absence of formal garbage collection is the exposure leading to diarrheal disease, 4 alternative routes involving 4 additional confounding factors were compared. The reason
for selecting “no formal garbage collection” was because this variable was identified as dependent upon diarrhea in all but the most probable DAG. There was little change in the odds of diarrhea when no formal garbage collection was combined with different combinations of other confounders in the alternative DAGs. The interesting exception is the combination of “other” sources of water and no formal garbage collection. With the more defined water sources, the odds of diarrhea in houses lacking formal garbage collection are approximately 1.2; however, the odds rise to 1.3 when water sources are “other.” The explanation for this may be the results of lack of running water to remove the buildup of refuse (and potentially excreta) when garbage is not regularly removed. The accumulation of refuse that has no formal disposal and its removal that is presumably irregular provide a permissive breeding ground for enteric pathogens. This hypothesis requires more targeted studies; however, neither garbage nor water is of itself the “cause” of diarrheal disease despite both being likely sources of enteric pathogens.

Introducing prior causal knowledge

Bayesian network modeling is typically concerned with automated structure discovery (searching for a DAG which best describes the statistical relations in observational data), in this case, the PSLSM. In causal inference, on the other hand, the focus is typically on testing whether a given set of assumptions is sufficient for quantifying causal effects from observational data, conditional on a causal diagram that encodes all the relevant domain-specific assumptions (12, 14). The former is objective (empirically derived DAGs) but lacks a causal component, while the latter provides causal insight but whose weakness is the potentially subjective justification of the causal diagram. An obvious question is, therefore, how can prior causal knowledge be integrated into automated structure discovery?

A very rudimentary approach that repeats the previous heuristic additive Bayesian network analyses (across 13 variables) by introducing some simple commonsense prior causal constraints is given in Web Appendix 13. This modeling prohibits arcs emanating from the diarrheal node and prevents “number of rooms” being directly dependent upon diarrhea. This simple informative structural prior now gives an undirected majority consensus DAG with the same 3 variables as previously identified as directly dependent upon diarrhea, but where support for an arc connecting “no formal garbage collection” to diarrhea is now 100% (appears in all 20,000 searches), whereas using the previous uninformative structural prior, this was only 58% and it also didn’t appear in the previous directed majority consensus network (Web Appendix 7). The use of directional constraints alters the model search space (as the data can discriminate between DAGs where the arcs in these constraints are reversed provided these are in different equivalence classes) (Web Appendix 1) and so may provide different results. The key question is whether imposing such directional constraints/informative prior—motivated by causal considerations—is conceptually reasonable. This is an open question.

An alternative approach—and one that seems preferable given the complications of likelihood equivalence—is suggested by Heckerman et al. (27, p. 224). Rather than use an informative structural prior, it is proposed to append onto the observed data additional and likely highly incomplete synthetic observations that reflect causal beliefs. The structure learning process is then applied to all of the data as usual, except with the additional functionality necessary to marginalize over missing data (48). This is an elegant approach, but its feasibility and practicality with respect to additive Bayesian network modeling are an open question and an exciting area of future work.

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