Population health thinking with Bayesian networks

Tomás J. Aragón, MD, DrPH[1–4,*]

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Contents

[1] Health Officer, City and County of San Francisco
[2] Director, Population Health Division, San Francisco Department of Public Health
[3] Affiliate faculty, UC San Francisco, Department of Epidemiology and Biostatistics
[4] Adjunct faculty, University of California, Berkeley School of Public Health
* Contact: tomas.aragon@sfdph.org PDF: bit.ly/ph-thinking

> *Our comforting conviction that the world makes sense rests on a secure foundation: our almost unlimited ability to ignore our ignorance.*
>
> — Daniel Kahneman [1]

1 Introduction: data science and decision quality

Population health is a systems framework for studying and improving the health of populations through collective action and learning [2]. *Population health data science* (PHDS) is the art and science of transforming data into actionable knowledge to improve health [2]. *Actionable knowledge* is information that informs, influences or optimizes decisions. A *decision* is a choice between two or more alternatives that involves an irrevocable allocation of resources [3,4]. Every decision has an *opportunity cost*—the lost net benefit of the better option not chosen. Hence: "The roads we take are more important than the goals we announce. Decisions determine destiny."[1]

Decisions drive strategic, tactical and operational execution. Decisions are based on causal *and* probabilistic assumptions ("choosing and doing action A (over say, B) will acheive net effect Y with probability p."). This "prior probability" is a *prediction*. Based on our evaluation, we adjust our causal and/or prediction assumptions—this is *learning*. Learning leads to new decisions and new actions (adaptation). *Improvements* are adaptations that make processes and/or results better. Continuous improvement is one of the foundational pillars of a *learning organization*.[2] Population health improvement requires continuous decision improvement.

The human brain specializes in prediction (also called concepts, memory, schema, etc.) [6]. In 2002, psychologist Daniel Kahneman won the Nobel Prize in Economics for the pioneering studies that cataloged human cognitive biases and pitfalls that formed the foundation of the new field of behavioral economics [1]. It turns out that humans are not good at estimating probabilities (probabilistic reasoning), especially for novel circumstances. We also have nonconscious cognitive biases that affect our ability to draw valid causal inferences and to change course when we are wrong. We are prone to defensiveness to protect our ego and to avoid our fears [7]. This journey will require *intellectual humility* to acknowledge our innate cognitive limitations and *curiosity* to experiment with a new way of computational and inferential thinking [8].

In epidemiology, analyses are generally classified as descriptive or analytic. In PHDS we extend this to five analytic domains (Table 1), all of which should produce actionable knowledge in service of a strategic, tactical or operational goal or objective.

Table 1. Population health data science analytic domain level

Level	Analysis	Population health action
1	Description	measuring risk or protective factors, and outcomes
2	Prediction	early detecting and targeting of prevention interventions
3	Explanation	discovering and estimating causal or intervention effects
4	Simulation	modeling for epidemiologic or decision insights
5	Optimization	informing, influencing or optimizing decisions, etc.

[1] — Frederick Speakman

[2] A *learning organization* requires other components. For details, see Aragón, et al. [5]

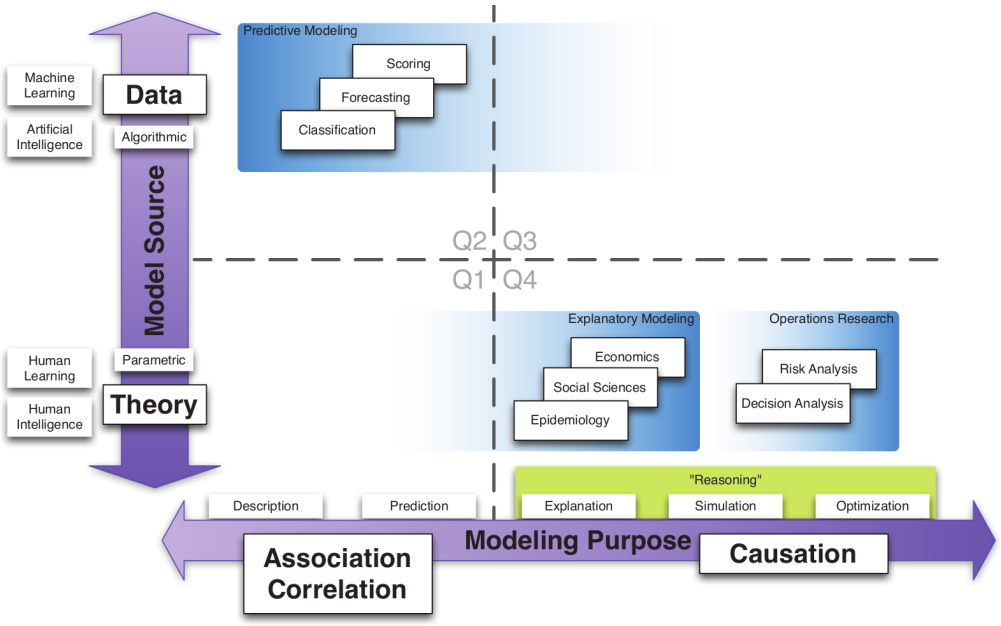


Figure 1. Population health data science landscape (source: http://www.bayesia.com/)

The purpose of this paper is to introduce a "Reasoning" framework (see Figure 1) which I call **population health thinking** (PHT); that is, the conceptual or computational use of Bayesian networks (BNs) for

1. **probabilistic reasoning** (PR) with *BNs*,
2. **causal inference** (CI) with *causal BNs* (i.e., directed acyclic graphs), and
3. **decision quality** (DQ) with *decision BNs* (Table 2).

BNs are probabilistic graphical models that can be drawn using one's expert knowledge and wisdom. First, to get the most out of PHT, master the BN concepts with pencil and paper. Second, explore deploying computational tools to work your intuition and build your confidence. In this article I illustrate the concepts using R—an open source language and environment for statistical computing and graphics [9]. Advanced PHT usually requires turning to computers or to colleagues for computational support.

For those who only want the *minimum core PHT*, (a) commit to intellectural humility and curiosity, (b) use DQ as a checklist, and (c) study program theory on p. 4. Every public health intervention has a program theory ("theory of change").

Table 2. Decision quality requirements: A decision is only as strong as its weakest link

Name	Quality requirements	Key DQ questions
Frame	Appropriate frame	What are we deciding and why?
Reasoning	Sound reasoning	Are we thinking straight?
Information	Actionable knowledge	What do we need to know?
Prospects	Values, results & trade-offs	What consequences do we care about?
Choices	Creative alternatives	What choices do we have?
Commitment	Commitment to action	Is there commitment to action?

2 Program theory is for the DAGs (motivation)

Basded on causal and prediction assumptions (often implicit), we make decisions and takes actions towards our goals. Our programmatic activities are built upon these causal assumptions which collectively we call **program theory**. Every public health intervention has a program theory; however, many practitioners cannot describe the program theory supporting their primary programmatic activity or research. I too could not describe the program theories supporting my own work until I read Funnell Rogers' book *Purposeful Program Theory* [10].

It turns out that program evaluators not only live and breathe program theory, but they call it by different names: logic model, program logic, theory of change, causal model, results chain, intervention logic, etc. Hence the confusion! From BetterEvaluation.org:[3] "A program theory explains how an intervention (a project, a program, a policy, a strategy) is understood to contribute to a chain of results that produce the intended or actual impacts."[4]

In public health, the logic model is very popular. For me, a logic model is a good high-level summary for non-technical purposes (summary, communication, etc.); however, I do not like them (or variants) as a place to start. For me, *program theory is for the DAGs—directed acyclic graphs—and must include the theories of causation, change, and action.*

Program theory has three components and answers why? what? and how?:

- theory of *causation* (*Why?* primary *roots causes* before an intervention),
- theory of *change* (*What?* key *strategies* to affect the root causes), and
- theory of *action* (*How?* key specific *interventions* to activate theory of change).

In public health we have two common *DAG archetypes* [11]: a *risk (adverse) event* and a *benefit (opportunity) event* (Figure 2). For both, a trigger is an exposure, condition, activity, or incident that increases the probability of a risk or benefit event. A trigger can be a cumulative process. *Before an intervention*, these DAGs represent the **theory of causation** component of program theory.

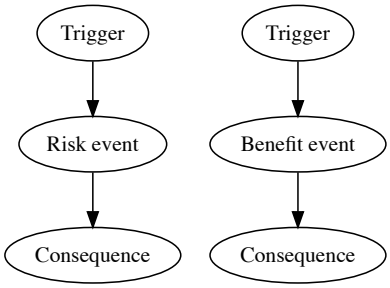


Figure 2. Causal taxonomy for risk event (left) vs. benefit event (right)

Figure 3 depicts the program theory for a public health intervention to reduce automobile crash injuries (a risk event). The **theory of change** has three *strategies* (prevention, control, and mitigation), and the **theory of action** has three *interventions* (speed bumps, automatic breaking, and seat belts).

[3] See http://www.betterevaluation.org/en/plan/define/develop_logic_model.>
[4] See PDF: http://www.betterevaluation.org/sites/default/files/Define%20-%20Compact.pdf.

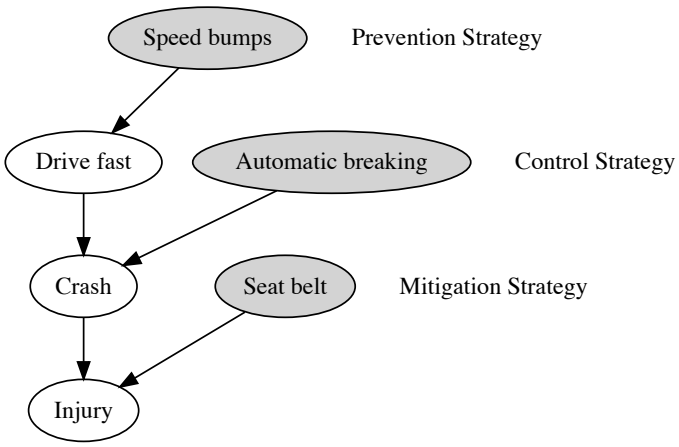


Figure 3. Risk-reduction program theory: theory of causation, theory of change (strategy), and theory of action (intervention)

In a risk-event outcome (consequence), the **5 whys** of root-cause analysis move backwards: Why was there an injury? Because of a crash. Why was there a crash? Because of fast driving? Why was there fast driving? We cannot answer this question (yet).

The program theory is not complete. We must also understand why people drive fast. We have not included the theory of causation from drivers' perspectives. Suppose, for instructional purposes, Figure 4 represents the most common DAG that explains why drivers speed. Therefore, why was he or she driving fast? To make a meeting. Why was this meeting important? To win a contract? Why was this contract important? (unemployment?)

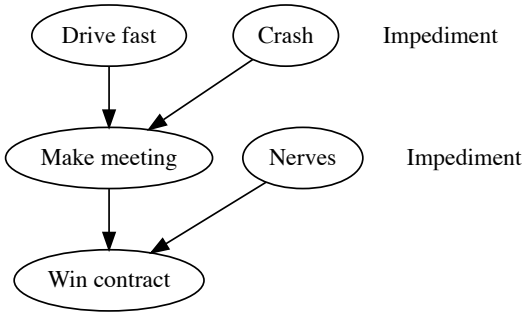


Figure 4. Benefit-event model from the driver's perspective

We can now really appreciate the importance of evaluating multiple perspectives (other causal drivers—not to be confused with vehicle driver in the example). For example, the motivation to drive fast might cancel out the effect of any traditional public health intervention (Figure 3). We must be able to integrate multiple causal pathways reflecting multiple perspectives.

Figure 5 depicts the unified DAG that integrates driver motivation into a holistic, improved public health program theory. We cannot emphasize enough the importance of building causal graphs from multiple perspectives that include risks and benefits,

and different strategy levels. This DAG is a big improvement.

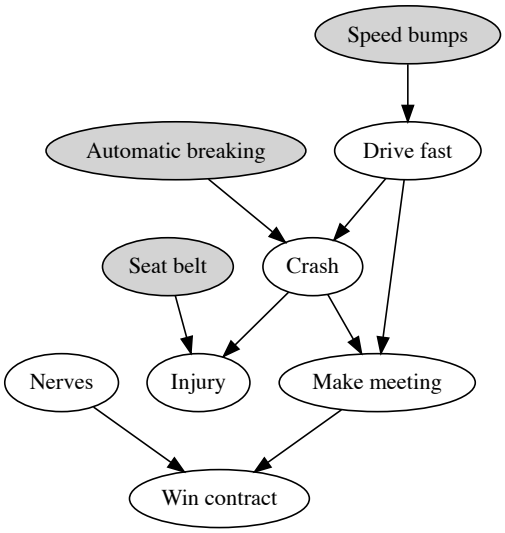


Figure 5. Unified causal model that includes driver's perspective (benefit-seeking) and program theory (risk-reduction)

However, when you review it with subject matter experts they suggest adding "gender" and "age" nodes because both are causally associated with driving fast and wearing seat belts (Figure 6). This will enable you to evaluate the effectiveness of the public health intervention while controlling for the confounding effects of gender and age. For example, if drivers are predominately young males (who drive fast and do not wear seat belts) then the seat belt intervention may appear falsely ineffective. These DAGs encode expert and community knowledge and wisdom, and are used for causal, evidential, and decision reasoning.

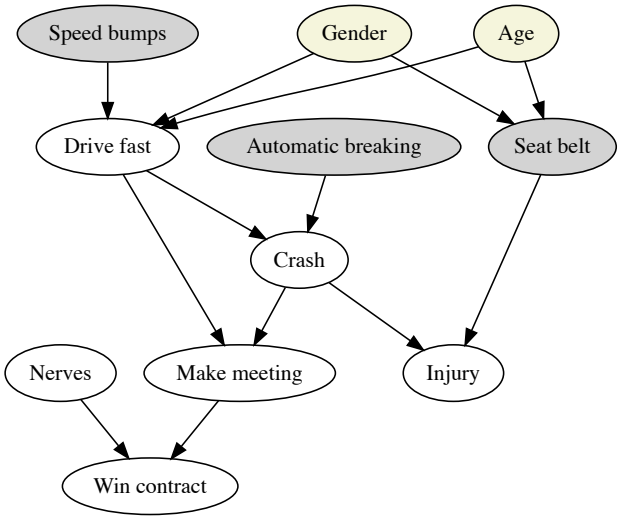


Figure 6. Expanded unified causal model with age and gender

If we would like to know if one of our interventions (e.g., seat belt use) is working

we need to design a study or analysis to test our hypothesis. Unfortunately, without a causal model (Figure 6) to guide us, we cannot know what variables are required to test our intervention, and what variables to control for ("confounders") that threaten the validity of our conclusions.

Here is a summary of program theory:

1. *Every* intervention has a *program theory* (whether expressed or not).
2. Program theory includes *theories of causation, change, and action.*
3. DAGs have *archetypes*: *risk (adverse) event* and *benefit (opportunity) event.*
4. Always include *multiple causal perspectives* (other causal drivers).
5. Use DAGs for *root cause analyses* and *program theory design.*
6. Don't forget to consider *confounders* (that threaten validity).
7. Use DAGs to *test interventions* and to *control confounding.*

Getting this right is important because future decisions and resource allocations depends on these causal inferences. Understanding the basics of program theory is foundational. The sections ahead cover population health thinking concepts and computational tools that support program theory and population health data science.

3 Probabilistic reasoning (with Bayesian networks)

A Bayesian network (BN) is a graphical model for representing probabilistic, but not necessarily causal, relationships between variables called *nodes* [12,13]. The nodes are connected by lines called *edges* which, for our purposes, are always *directed* with an arrow. Consider this *noncausal* BN:

Smell smoke ⟶ Fire nearby

Smelling smoke increases the probability of a fire burning nearby, but obviously smoke alone does not cause a fire. In other words, does knowing X (smell smoke) change the *credibility* of Y (fire nearby)? In contrast, now consider this *causal* BN:[5]

Fire ⟶ Smoke

This causal BN depicts fire causing smoke. Notice that both noncausal and causal BNs have probabilistic dependence which we will use for probabilistic reasoning. Noncausal BNs are commonly used in *influence diagrams*[6] for decision analysis which we cover later.

A two-node causal BN which has two types of proabilistic reasoning (Table 3).

Cause ⟶ Effect

Table 3. Types of probabilistic reasoning for two-node causal Bayesian network

Probabilistic reasoning	Conditional probabilities
Causal (predictive) reasoning	$P(\text{Effect} \mid \text{Cause})$
Evidential (diagnostic) reasoning	$P(\text{Cause} \mid \text{Effect})$

When a causal effect is not firmly established, the BN asserts this concept:

[5] also called a *causal graph* or a *directed acyclic graph* (DAG)
[6] also called *decision networks* or *relevance diagrams*

$$\text{Hypothesis} \longrightarrow \text{Evidence}$$

Table 4. Bayesian network involving a hypothesis and evidence

Conditional probabilities	Probabilistic reasoning
$P(\text{Evidence} \mid \text{Hypothesis})$	Causal reasoning
$P(\text{Hypothesis} \mid \text{Evidence})$	Evidential reasoning

Evidential reasoning require Bayes Theorem.

$$P(H \mid E) = \frac{P(E \mid H)P(H)}{P(E)}$$

$P(H)$ is the *prior (old) belief*, $P(H \mid E)$ is the *posterior (new) belief*, and $P(E \mid H)$ is called the *likelihood*. The likelihood is critical because it is usually measurable. The challenge is that we need Bayes Theorem for two reasons:

1. to use evidence and theory to update our belief from $P(H)$ to $P(H \mid E)$, and
2. to avoid the *fallacy of the transposed conditional*; i.e., confusing $P(E \mid H)$ with $P(H \mid E)$.[7]

3.1 Example 1: HIV testing

For example, from Neapolitan (p. 491, [14]), suppose Sam takes a test (evidence) to determine whether he has HIV infection (hypothesis). Here is the BN:

$$\text{HIV} \longrightarrow \text{Test}$$

In diagnostic testing we use Bayes Theorem to calculate the post-test probability from the test results, pre-test probability (prevalence of infection), and test characteristics (sensitivity, specificity). Table 5 displays the data we need for applying Bayes Theorem.

Table 5. Probabilities for using Bayes Theorem in diagnostic testing

Name	Probabilities	Value
Pre-test (prior) probability of HIV+	$P(\text{HIV}+)$	0.00001
Sensitivity	$P(\text{Test}+ \mid \text{HIV}+)$	0.999
Specificity	$P(\text{Test}- \mid \text{HIV}-)$	0.998
Post-test (posterior) probability	$P(\text{HIV} \mid \text{Test})$	TBD

For illustrative purposes, we calculate the "positive predictive value" (PPV).

$$P(H+ \mid T+) = \frac{P(T+ \mid H+)P(H+)}{P(T+ \mid H+)P(H+) + P(T+ \mid H-)P(H-)}$$

This is easy to calculate in R.

[7] For example, because African Americans make up a high proportion in our criminal justice system, some people believe, mistakenly, that a high proportion African Americans are involved in crime. To understand this phenomenon we would need a full causal model.

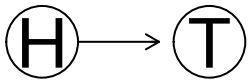
```
prior <- 0.00001
sens <- 0.999
spec <- 0.998
(sens*prior)/(sens*prior+(1-spec)*(1-prior)) # PPV
```

```
## [1] 0.004970223
```

Calculating the PPV (or NPV) is evidential reasoning and it requires applying Bayes Theorem. Our brains are not capable of this calculation; we need computational tools. In other words, our brains are not able to "flip the arrow" from $P(\text{Evidence} \mid Hypothesis)$ to $P(\text{Hypothesis} \mid \text{Evidence})$ and make valid Bayesian calculations.

Since we need computational tools, why not just use BN tools that can scale to the complexity of any problem and always provide us with valid Bayesian calculations. Here is the same calculation using the `bnlearn` package in R [12].

```
library(bnlearn)
dag <- empty.graph(nodes = c("H", "T"))   ## create nodes
dag <- set.arc(dag, from = "H", to = "T") ## link nodes
graphviz.plot(dag, layout = "circo")
```




```
H.lv <- c("Pos", "Neg") ## create levels
T.lv <- c("Pos", "Neg")
#### create conditional probability tables
H.prob <- array(c(prior, 1-prior), dim = 2, dimnames = list(H = H.lv))
T.prob <- array(c(sens, 1-sens, 1-spec, spec), dim = c(2, 2),
  dimnames = list(T.lv, H.lv))
cpt <- list(H = H.prob, T = T.prob)
bn <- custom.fit(dag, cpt)
```

We have captured this BN as an "expert knowledge system" in the R object `bn` which we can now query.

```
names(bn)
```

```
## [1] "H" "T"
```

```
bn$T
```

```
##
##   Parameters of node T (multinomial distribution)
##
## Conditional probability table:
##
##      H
## T       Pos   Neg
##   Pos 0.999 0.002
##   Neg 0.001 0.998
```

With BNs we can can ask "What if?" questions. For example, we can ask what is the probability of HIV infection given a positive test? Again, $P(H+ \mid T+)$ is the positive predictive value. We have the choice between two R packages:

1. `gRain` for exact inference, or
2. `bnlearn` for approximate inference

3.1.1 Exact inference

```
library(gRain) # for exact inference
junction <- compile(as.grain(bn))
jtest <- setEvidence(junction, nodes = "T", states = "Pos")
querygrain(jtest, nodes = "H")$H # Positive Predictive Value (PPV)
```

```
## H
##         Pos         Neg
## 0.004970223 0.995029777
```

3.1.2 Approximate inference (Monte Carlo simulation)

Approximate inference approach is necessary for very large BNs.

```
cpquery(bn, event = (H == "Pos"), evidence = (T == "Pos"), n = 10^6)
```

```
## [1] 0.007688611
```

3.2 Example 2: Evaluating respiratory diseases

For example, Figure 7 is from Neapolitan (p. 491, [14]) and depicts a BN representing relationships among respiratory disease variables.

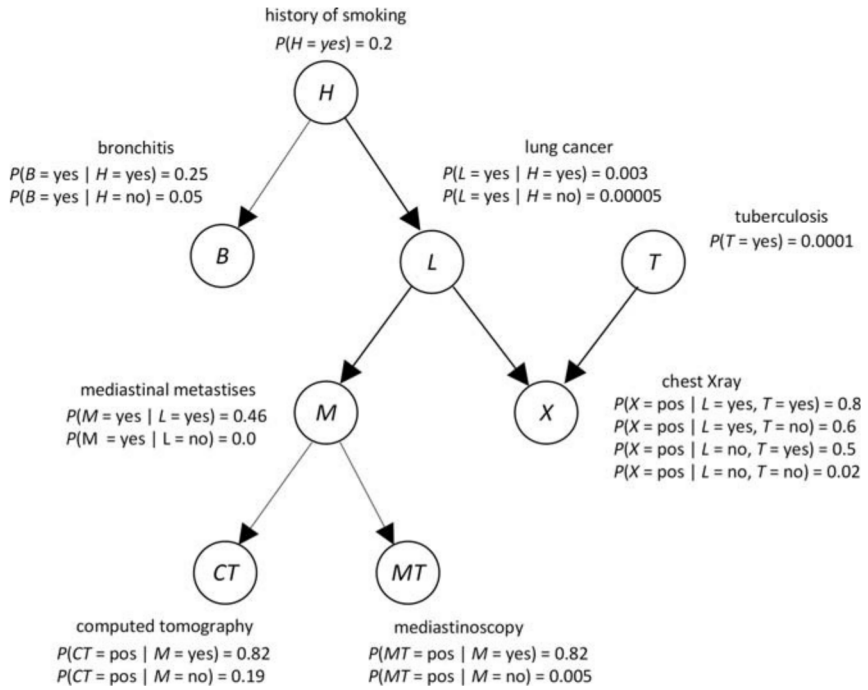
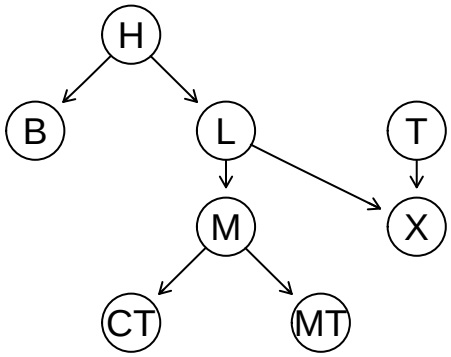


Figure 7. A Bayesian network of relationships among respiratory disease variables

```
dag2 <- empty.graph(nodes=c("H", "B", "L", "T", "M", "X", "CT", "MT"))
dag2 <- set.arc(dag2, from = "H", to = "B")
dag2 <- set.arc(dag2, from = "H", to = "L")
dag2 <- set.arc(dag2, from = "L", to = "M")
dag2 <- set.arc(dag2, from = "L", to = "X")
dag2 <- set.arc(dag2, from = "T", to = "X")
dag2 <- set.arc(dag2, from = "M", to = "CT")
dag2 <- set.arc(dag2, from = "M", to = "MT")
graphviz.plot(dag2)
```




```
#### create levels
yn <- c("Yes", "No"); pn <- c("Pos", "Neg")
H.lv <- yn; B.lv <- yn; L.lv <- yn; T.lv <- yn; M.lv <- yn
X.lv <- pn; CT.lv <- pn; MT.lv <- pn
#### create conditional probability tables
H.prob <- array(c(0.2,1-0.2), dim = 2, dimnames = list(H = H.lv))
B.prob <- array(c(0.25,1-0.25,0.05,1-0.05), dim=c(2,2),
  dimnames = list(B=B.lv, H=H.lv))
L.prob <- array(c(0.003,1-0.003,0.00005,1-0.00005), dim=c(2,2),
  dimnames = list(L=L.lv, H=H.lv))
T.prob <- array(c(0.0001,1-0.0001), dim=2, dimnames=list(T = T.lv))
M.prob <- array(c(0.46,1-0.46,0,1 - 0), dim=c(2,2),
  dimnames = list(M=M.lv, L=L.lv))
X.prob <- array(c(0.8,1-0.8,0.6,1-0.6,0.5,1-0.5,0.02,1-0.02),
  dim=c(2,2,2), dimnames = list(X=X.lv, T=T.lv, L=L.lv))
CT.prob <- array(c(0.82,1-0.82,0.19,1-0.19), dim=c(2,2),
  dimnames = list(CT=CT.lv, M=M.lv))
MT.prob <- array(c(0.82,1-0.82,0.005,1-0.005), dim=c(2,2),
  dimnames = list(MT=MT.lv, M=M.lv))
cpt <- list(H=H.prob, B=B.prob, L=L.prob, T=T.prob,
            M=M.prob, X=X.prob, CT=CT.prob, MT=MT.prob)
bn2 <- custom.fit(dag2, cpt)
```

Creating the conditional probability tables was straight forward. In the Neapolitan paper the authors ask: "if a patient has a smoking history (H = yes), a positive chest X-ray (X = pos), and a positive computer tomogram (CT = pos), we can determine the probability of the patient having lung cancer (L = yes)." That is,

what is $P(L = \text{Yes} \mid H = \text{Yes}, X = \text{Pos}, CT = \text{Pos})$?

3.2.1 Exact inference

```
junction2 <- compile(as.grain(bn2))
# test P(M|L)
querygrain(junction2, nodes = c("M", "L"), type = "conditional")
```

```
##      M
## L      Yes   No
##   Yes 0.46 0.54
##   No  0.00 1.00
```

```
# Neapolitan, p. 492
jriskfactors <- setEvidence(junction2, nodes = c("H","X","CT"),
  states = c("Yes","Pos","Pos"))
p <- querygrain(jriskfactors, nodes = "L")$L # Pos. Predictive Value
p
```

```
## L
##       Yes        No
## 0.1852825 0.8147175
```

The $P(L = \text{Yes} \mid H = \text{Yes}, X = \text{Pos}, CT = \text{Pos}) = 0.1852825$. The prior probability of lung cancer in this model is 0.0064. So, the evidence has increased the probability of lung cancer substantially.

For practice, how did we determine the prior probability of lung cancer? For this query I do not need to set evidence, only query the marginal probability of L (lung cancer) from the fitted BN.

```
querygrain(junction2, nodes = c("L"), type = "marginal")$L
```

```
## L
##     Yes      No
## 0.00064 0.99936
```

3.2.2 Approximate inference (Monte Carlo simulation)

```
cpquery(bn2, event = (L == "Yes"), evidence = (H == "Yes") & (X=="Pos")
  & (CT=="Pos"), n = 10^6)
```

```
## [1] 0.1738661
```

3.3 Example 3: Fitting Bayesian network to data

TBD

4 Causal inference (with causal Bayesian networks)

4.1 Directed acyclic graph (DAG)

Causal BNs are directed acyclic graphs (DAGs) (also called causal graphs) [15–17]. All of the probabalistic reasoning concepts we learned with BNs continue to apply. With BNs the causal links are

1. *assumptions* based on expert knowledge,
2. *evidenced-based* from scientific research, or
3. *conjecture* to gain insights of new assumptions.

Causal inference is drawing valid, unbiased conclusions about cause-effect relationships. In causal inference we set out to

1. *discover* new causal pathways *or* models,
2. *test* causal hypotheses,
3. *estimate* causal effects.

Consider two variables (nodes), X and Y. What can explain an association (correlation) between X and Y?

1. direct cause: $X \to Y$
2. reverse cause: $X \leftarrow Y$
3. pure coincidence: chance only
4. cyclic cause (causal loop): $X \leftrightarrows Y$
5. common cause: $X \leftarrow Z \to Y$
6. collider bias: $X \to \boxed{Z} \leftarrow Y$ (when conditioning on Z or a descedent of Z)

By design DAGs are not causal loops. Causal loops have an important role in systems thinking and modeling but will not be discussed further. Statistical inference supports causal inference with quantitative methods for estimation, chance, and bias. A common cause involves three or more nodes and is discussed next.

Figure 8 displays the core DAG patterns of three nodes with two causal links. In a *chain* ($X \to Y \to Z$), also called a *sequential cause*, X and Z are *unconditionally dependent*. This means that X and Z are dependent without conditioning on any variable. Likewise, in a *fork* ($Y \leftarrow X \to Z$), also called a *common cause*, X and Z are *unconditionally dependent*. In epidemiology, forks are the principle cause of **confounding**.

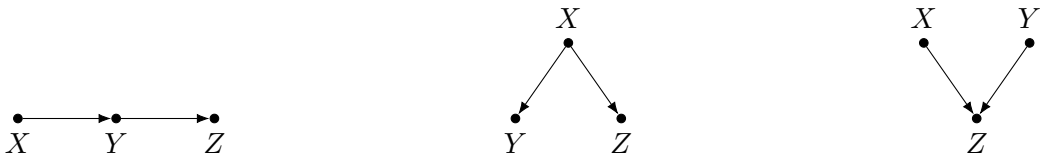


Figure 8. Core DAG patterns for three nodes and two edges: (a) chain (sequential cause), (b) fork (common cause), and (c) collider (common effect).

Chains and forks make intuitive sense, colliders do not. In a *collider* ($X \to Z \leftarrow Y$), also called a *common effect*, X and Y are *unconditionally independent*. However, when we condition on Z (or any descendent of Z), X and Y become *conditionally*

dependent. Epidemiologists specialize in "adjusting for potential confounders." When we condition ("adjust") on a collider we introduce a spurious association—and worse—might conclude that the association is causal—which is impossible because X and Y are unconditionally independent! In other words, we *introduce confounding* where none existed! This is considered *epidemiologic malpractice!*[8]

Here is the classic example of *collider bias*. We flip a fair coin twice $\{0 = \text{tail}, 1 = \text{head}\}$. T_1 is the outcome of the first coin flip $\{0, 1\}$; T_2 is the outcome of the second coin flip $\{0, 1\}$; and S is sum of T_1 and T_2 $\{0, 1, 2\}$. Knowing the value of T_1 tells us absolutely nothing about the value of T_2, and vice versa. They are completely independent (represented by no solid edge in the DAG).

However, if we are told the value of S (say, 1) (this is "conditioning"), then T_1 and T_2 are now dependent (Figure 9). If $T_1 = 0$, then we know the value of T_2 must be 1. If $T_1 = 1$, then we know the value of T_2 must be 0. The reverse is true: knowing T_2 informs us of the value of T_1. For an epidemiologic example see Cole [18].

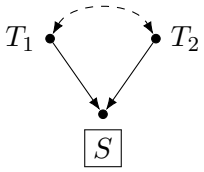


Figure 9. Collider bias when flipping two fair coins. Conditioning on collider S introduces a dependency (dashed edge) between T_1 and T_2.

Our motivation for introducing DAGs is to emphasize that our causal and probabilistic reasoning is very vulnerable—even when we have 'lots of data! Do your analysts understand colliders and their perils? If not, why not?

4.2 Deconfounding (controlling for confounding)

Remember, while causal arrows are unidirectional, probabilistic dependence propagates in both directions. By conditioning on a variable we block this propagation unless it is a collider. In an observation study A is either a treatment or exposure, and Y is the outcome or effect. If we are interested in measuring the causal effect of A on Y we want to block all pathways that have arrows pointing into A (backdoor) and that have arrows pointing into Y, but that are not descendents of A (frontdoor).

Figure 10 depicts four DAGs and the possible combinations of nodes that can be chosen to block the backdoor pathway. The backdoor pathways are pathways that point into X *and* connect to Y *and* do not have a collider. Colliders block propagation unless we condition on them. If you condition on a collider you must also condition on another variable to block the new pathway the conditioned collider just opened.

In Figure 10(b), conditioning on M (a collider) opens the path from A to Y by creating a dependency between V and W. Figure 11 illustrates this new path which is called M-bias. To the untrained analyst M behaves like a confounder because V and W are common causes (forks) that create an association between M and A, and

[8] Or *statistical malpractice* if you are a statistician.

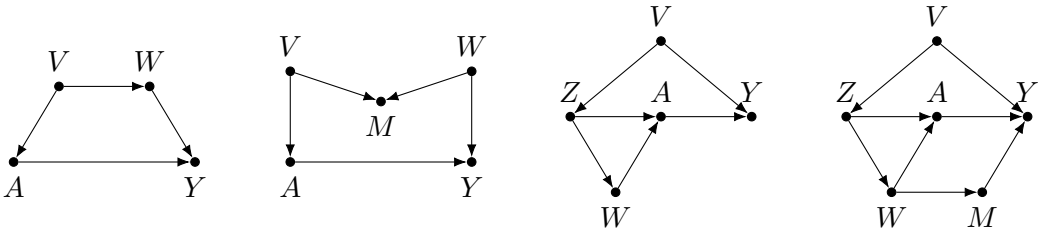


Figure 10. In an observational study, A is either a treatment or exposure, and Y is the outcome or effect. To measure the causal effect of A on Y we must block backdoor pathways from A to Y by conditioning on a set of correct variables. We do not want to condition on descedents of A, including intermediate nodes between A and Y. We do not want to condition on colliders alone otherwize we introduce spurious associations. For (a) we can condition on $\{V\}$, $\{W\}$, or $\{V, W\}$. For (b) we can condition on $\{\}$, $\{V\}$, $\{W\}$, $\{M, W\}$, $\{M, V\}$, $\{M, V, W\}$, but not on $\{M\}$ (collider bias). For (c) we can condition on $\{V\}$, $\{V, Z\}$, $\{Z, W\}$, $\{V, Z, W\}$, but not on $\{Z\}$ alone (collider bias), and not on $\{W\}$ (leaves other path open). Finally for (d) we can condition on $\{W, Z\}$, $\{W, V\}$, $\{M, Z\}$, $\{M, V\}$, $\{W, Z, V\}$, $\{M, Z, V\}$, $\{W, M, Z\}$, $\{W, M, V\}$, or $\{W, M, Z, V\}$.

between M and Y. Without DAGs to guide us, controlling for confounders is like flying blind: you are bound to get into trouble (i.e., introduce bias).

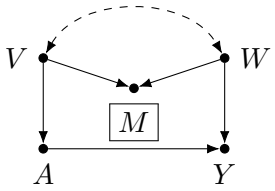


Figure 11. Conditioning on M, a collider, introduces M-bias.

By deconfounding we mean estimating a specific causal effect while controlling for confounding, and without introducing bias (e.g., collifer bias). In general, we have three methodologic approaches:

1. Backdoor criterion
2. Frontdoor criterion
3. Instrumental variable (commonly used in economics)

For all of these we need to have a full DAG for the process we are studying. This requires reviewing the scientific literature and collaborating with subject matter experts (SMEs). Having a complete DAG does not mean we have data on every variable. We may not need it depending on which variables we select for adjustment. Hence, DAGs are also important for study and analysis design.

4.3 Backdoor criterion

DAGs are great because they are valid for whatever functional forms that connect the variables (e.g., linear vs. nonlinear). So far, we have selected a set of variables that will block the backdoor path. This approach is called the **backdoor criterion**:

1. block all spurious paths between A and Y,
2. leave all directed paths from A to Y unperturbed, and
3. create no new spurious paths.

Now we need a calculation formula. Pearl developed *do*-calculus as a method to derive this formula. The thinking goes like this: if I disconnect all backdoor arrows into A ("graph surgery") and set $X = x$ for *everyone* in the population, then I get the modified DAG in Figure 12(b). This $do(A = a)$ is a hypothetical intervention. The magic of *do*-calculus is to derive a formula that only has variable terms representing the observation data from Figure 12(a).

Figure 12. Backdoor criterion: (a) unmodified causal graph where A affects Y, and X represents the covariate set of variables selected for adjustment; (b) modified causal graph where for everyone in the population X is set to x. This is *do*-calculus, and is used to derive an adjustment formula.

Using *do*-calculus Pearl derived this **backdoor adjustment formula** [16]:

$$\begin{aligned} P(y \mid do(x)) &= \sum_x P(Y = y \mid A = a, X = x) P(X = x) \\ &= \sum_x \frac{P(Y = y, A = a, X = x)}{P(A = a \mid X = x)} \end{aligned}$$

In this formula, the joint probability, $P(y, a, x)$ is weighted by the term $1/P(a \mid x)$, also called *inverse probability weighting* When the denominator term is used to calculate the probability of treatment $(A = 1)$ given covariate set X it is called the *propensity score* or $P(A = 1 \mid X)$

Now we can calculate the **average causal effect** (ACE) or causal effect difference:

$$P(Y = 1 \mid do(A = 1)) - P(Y = 1 \mid do(A = 0))$$

Our goal is to measure the causal effect of A on Y. Our DAG guided the selection of a set of variables (X) that will block the backdoor path. From the bookdoor adjustment formula we have some options.

1. Match on covariates set X of selected confounders
2. Match on propensity score $P(A = 1 \mid X)$
3. Inverse probability weighting (IPW) and Marginal Structural Model (MSM)

Until this section is completed, I highly recommend viewing or taking the Coursera course by Dr. Jason Roy, Professor of Biostatistics, University of Pennsylvania [19].

4.3.1 Matching on covariate set of confounders

In this section I briefly review some of the analyses from Professor Jason Roy's Coursera course [19]. This is an outstanding course and I highly recommend that everyone view or take it. My review is no substitute for his course. Here are the general steps:

1. Prepare data
2. Match on covariate set X (using Mahalanobis distance)
3. Check for balanced covariate means (using standardized mean differencee)
4. Estimate average causal effect (as if randomized controlled trial)
5. Sensitivity analysis for hidden bias (not shown; instead see [19])

We will be pairwise matching control subjects ($A = 0$) to treated subjects ($A = 1$). Remember that "treated" is a general term for being exposed and "control" for not being exposed.[9] By matching on an appropriate set of confounders we are actually

- simulating a randomized controlled study, and
- measuring the **average causal effect of treatment on the treated** (ATT).

There are several R packages for matching: Matching, optmatch, MatchIt

Table 6. R packages for matching

Method or task	`tableone`	`Matching`	`rcbalance`
Mahalanobis distance		✓	✓
Robust M-distance			✓
Greedy matching		✓	
Optimal matching			✓
Assessing balance	✓		

The Mahalanobis distance is a multi-dimensional measure of mean distance between two vectors of covariates comparing treated to control. The smaller the M-distance the better the match. Because mean values can be influencd by outliers, an alternative is the robust M-distance that uses a rank statistic.

Greedy (nearest neighbor) matching is computationally fast but not globally optimized. Optimal matching finds the best global match but is computationally demanding. We will use greedy matching.

We will analyze data from a health care observational study on right health catheterization (treatment) and death (outcome). We will match on a set of confounders, including age, sex, and mean blood pressure.

```
#load packages
library(tableone)
library(Matching)
```

[9] In a case-control study this would be matching controls (non-disease) to cases (disease).

```
#read in data
load(url("http://biostat.mc.vanderbilt.edu/wiki/pub/Main/DataSets/rhc.sav"))

#### create smaller data set and binary (0, 1) X variables
ARF <- as.numeric(rhc$cat1=='ARF')
CHF <- as.numeric(rhc$cat1=='CHF')
Cirr <- as.numeric(rhc$cat1=='Cirrhosis')
colcan <- as.numeric(rhc$cat1=='Colon Cancer')
Coma <- as.numeric(rhc$cat1=='Coma')
COPD <- as.numeric(rhc$cat1=='COPD')
lungcan <- as.numeric(rhc$cat1=='Lung Cancer')
MOSF <- as.numeric(rhc$cat1=='MOSF w/Malignancy')
sepsis <- as.numeric(rhc$cat1=='MOSF w/Sepsis')
female <- as.numeric(rhc$sex=='Female')
died <- as.numeric(rhc$death=='Yes')
age <- rhc$age
treatment <- as.numeric(rhc$swang1=='RHC')
meanbp1 <- rhc$meanbp1

#### new dataset
mydata <- cbind(ARF,CHF,Cirr,colcan,Coma,lungcan,MOSF,sepsis,
                age,female,meanbp1,treatment,died)
mydata <- data.frame(mydata)

#### covariate set
xvars <- c("ARF","CHF","Cirr","colcan","Coma","lungcan","MOSF","sepsis",
           "age","female","meanbp1")

#### look at a table 1
table1 <- CreateTableOne(vars=xvars,strata="treatment", data=mydata,
                         test=FALSE)
#### include standardized mean difference (SMD)
print(table1, smd = TRUE)
```

```
##                       Stratified by treatment
##                        0              1              SMD
##   n                     3551           2184
##   ARF (mean (SD))       0.45 (0.50)    0.42 (0.49)    0.059
##   CHF (mean (SD))       0.07 (0.25)    0.10 (0.29)    0.095
##   Cirr (mean (SD))      0.05 (0.22)    0.02 (0.15)    0.145
##   colcan (mean (SD))    0.00 (0.04)    0.00 (0.02)    0.038
##   Coma (mean (SD))      0.10 (0.29)    0.04 (0.20)    0.207
##   lungcan (mean (SD))   0.01 (0.10)    0.00 (0.05)    0.095
##   MOSF (mean (SD))      0.07 (0.25)    0.07 (0.26)    0.018
##   sepsis (mean (SD))    0.15 (0.36)    0.32 (0.47)    0.415
##   age (mean (SD))      61.76 (17.29)  60.75 (15.63)   0.061
##   female (mean (SD))    0.46 (0.50)    0.41 (0.49)    0.093
```

```
##   meanbp1 (mean (SD)) 84.87 (38.87) 68.20 (34.24)  0.455
```

In the table we want the standardized mean difference (SMD) to be less than 0.1. We see that several variables are not balanced (cirrhosis, coma, sepsis, and mean BP). Now let's perform the greedy match.

```
greedymatch <- Match(Tr=treatment,M=1,X=mydata[xvars],replace=FALSE)
matched <- mydata[unlist(greedymatch[c("index.treated","index.control")]), ]

#### get table 1 for matched data with standardized differences
matchedtab1 <- CreateTableOne(vars=xvars, strata ="treatment",
                              data=matched, test = FALSE)
print(matchedtab1, smd = TRUE)
```

```
##                       Stratified by treatment
##                        0              1              SMD
##   n                     2184           2184
##   ARF (mean (SD))       0.42 (0.49)    0.42 (0.49)    0.006
##   CHF (mean (SD))       0.10 (0.29)    0.10 (0.29)   <0.001
##   Cirr (mean (SD))      0.02 (0.15)    0.02 (0.15)   <0.001
##   colcan (mean (SD))    0.00 (0.02)    0.00 (0.02)   <0.001
##   Coma (mean (SD))      0.04 (0.20)    0.04 (0.20)   <0.001
##   lungcan (mean (SD))   0.00 (0.05)    0.00 (0.05)   <0.001
##   MOSF (mean (SD))      0.07 (0.26)    0.07 (0.26)   <0.001
##   sepsis (mean (SD))    0.24 (0.43)    0.32 (0.47)    0.177
##   age (mean (SD))      61.53 (16.15)  60.75 (15.63)   0.049
##   female (mean (SD))    0.44 (0.50)    0.41 (0.49)    0.042
##   meanbp1 (mean (SD)) 73.12 (34.28)  68.20 (34.24)   0.144
```

Once we have matched we can precede with the analysis as if we had data from a randomized controlled trial.

```
#### outcome analysis
y_trt <- matched$died[matched$treatment == 1]
y_con <- matched$died[matched$treatment == 0]

#### pairwise difference
diffy <- y_trt - y_con

#### paired t-test
t.test(diffy)
```

```
##
##  One Sample t-test
##
## data:  diffy
## t = 3.9289, df = 2183, p-value = 8.799e-05
## alternative hypothesis: true mean is not equal to 0
## 95 percent confidence interval:
##  0.02706131 0.08099730
## sample estimates:
```

```
## mean of x
## 0.0540293
```

```
#### McNemar test is an alternative
(mctab <- table(y_trt, y_con))
```

```
##      y_con
## y_trt   0   1
##     0 303 395
##     1 513 973
```

```
mcnemar.test(mctab)
```

```
##
##  McNemar's Chi-squared test with continuity correction
##
## data:  mctab
## McNemar's chi-squared = 15.076, df = 1, p-value = 0.0001033
```

4.3.2 Matching on propensity score

A propensity score (PS), $P(A = 1 \mid X)$ is the probability of treatment given the selected covariate set X. The PS is a *balancing score*, meaning that if we match controls to treated using PS, we also balance the distribution of covariates between treated and controls. *That's really cool!*[10] We will use logistic regression to calculate the PS. Once we have successfully matched the analysis proceeds as before.

```
psmodel <- glm(treatment~ARF+CHF+Cirr+colcan+Coma+lungcan+MOSF+
               sepsis+age+female+meanbp1+aps, family=binomial(),
               data=mydata)
summary(psmodel)
#### create propensity score
pscore < -psmodel$fitted.values

#### do greedy matching on logit(PS) using Match with a caliper
logit <- function(p) {log(p)-log(1-p)}
psmatch <- Match(Tr = mydata$treatment, M = 1, X = logit(pscore),
                 replace = FALSE, caliper = .2)
matched <- mydata[unlist(psmatch[c("index.treated","index.control")]),]
xvars<-c("ARF","CHF","Cirr","colcan","Coma","lungcan","MOSF","sepsis",
         "age","female","meanbp1")

#### get standardized differences
matchedtab1<-CreateTableOne(vars = xvars, strata ="treatment",
                            data = matched, test = FALSE)
print(matchedtab1, smd = TRUE)

#### outcome analysis
y_trt <- matched$died[matched$treatment == 1]
```

[10] To understand the theory see [19].

```
y_con <- matched$died[matched$treatment == 0]
#### pairwise difference
diffy <- y_trt-y_con
#### paired t-test
t.test(diffy)
```

4.3.3 Inverse probability weighting (IPW)

In the previous examples with matching we estimated the **average causal effect of treatment on the treated** (ATT). The ATT is not the average causal effect (ACE) on p. 16 that was based on Pearl's *do*-calculus and the backdoor adjustment formula; however, we consider the ATT a valid alternative to the ACE, so we use it.

In contrast to matching and the ATT, we can also estimate the ACE by creating a synthetic study population where everyone is treated (exposed) ($A = 1$) and compared to where everyone is a control (non-exposed) ($A = 0$). We use inverse probability weighting (IPW) to create this synthetic study population called a **marginal structural model** (MSM). By "marginal" we measure the average causal effect in the population without conditioning on any variables (e.g., confounders). By "structural" we mean modeling potential outcomes, not observed outcomes. The general MSM is represented by

$$g\{E(Y^a \mid V)\} = h(a, V; \psi),$$

where h is some parametric function, usually linear and additive; and g is a link function (log, logit, identity) in a generalized linear model for estimating

- causal risk ratio,
- causal odds ratio, or
- causal risk difference.

V represents additional variables that might be used, for example, for evaluating effect modification. For our purposes, we will ignore V.

Recall that the IPW is related to the propensity score. The IPW for treated subjects is

$$W_i = \frac{1}{P(A = 1 \mid X_i)} = \frac{1}{\text{propensity score}},$$

and the IPW for control subjects is

$$W_i = \frac{1}{P(A = 0 \mid X_i)} = \frac{1}{1 - \text{propensity score}}.$$

We have everything we need to estimate ACEs with IPW/MSM. Here are the general steps:

1. Estimate propensity scores
2. Create inverse probability weights
3. Specify the MSM of interest (causal RR, OR, or RD)
4. Fit IPW generalized linear model
5. Use asymptotic (sandwich) variance estimator (or bootstrapping) to account for artificial "sample size" of synthetic population.

The R code that follow shows step-by-step approach, or all together using the `ipw` package.

```
#### load packages
library(tableone)
library(ipw)
library(sandwich) #for robust variance estimation
library(survey)

expit <- function(x) {1/(1+exp(-x)) }
logit <- function(p) {log(p)-log(1-p)}

#### use RHC 'mydata' data frame that was created before
#### use 'xvars' from before

#### look at a table 1
table1 <- CreateTableOne(vars = xvars, strata = "treatment",
                         data = mydata, test = FALSE)

#### include standardized mean difference (SMD)
print(table1,smd=TRUE)

#### propensity score model
psmodel <- glm(treatment ~ age + female + meanbp1+ARF+CHF+Cirr+colcan+
         Coma+lungcan+MOSF+sepsis, family  = binomial(link ="logit"))

#### value of propensity score for each subject
ps <- predict(psmodel, type = "response")

#### create IP weights
weight <- ifelse(treatment==1,1/(ps),1/(1-ps))

#### apply weights to data
weighteddata<-svydesign(ids = ~ 1, data =mydata, weights = ~ weight)

#### weighted table 1
weightedtable <-svyCreateTableOne(vars = xvars, strata = "treatment",
                                  data = weighteddata, test = FALSE)
#### Show table with SMD
print(weightedtable, smd = TRUE)

### #to get a weighted mean for a single covariate directly:
mean(weight[treatment==1]*age[treatment==1])/(mean(weight[treatment==1]))

#### Causal Risk Difference with weigthed GLM
glm.obj <- glm(died ~ treatment, weights = weight, family =
               quasibinomial(link="identity"))
```

```
#summary(glm.obj)
betaiptw <- coef(glm.obj)
SE <- sqrt(diag(vcovHC(glm.obj, type="HC0")))

causalrd <- (betaiptw[2])
lcl <- (betaiptw[2]-1.96*SE[2])
ucl <- (betaiptw[2]+1.96*SE[2])
c(lcl, causalrd, ucl)

#### Causal Risk Ratio with weighted GLM
glm.obj <- glm(died ~ treatment, weights = weight, family =
               quasibinomial(link=log))
#summary(glm.obj)
betaiptw <- coef(glm.obj)

#### To account for weighting, use asymptotic (sandwich) variance
SE <- sqrt(diag(vcovHC(glm.obj, type="HC0")))

#### get point estimate and CI for risk ratio
causalrr <- exp(betaiptw[2])
lcl <- exp(betaiptw[2]-1.96*SE[2])
ucl <- exp(betaiptw[2]+1.96*SE[2])
c(lcl, causalrr, ucl)

#### truncate weights at 10

truncweight<-replace(weight,weight>10,10)

#### Causal Risk difference with truncate weights
glm.obj<-glm(died ~ treatment, weights = truncweight, family =
             quasibinomial(link="identity"))
#summary(glm.obj)
betaiptw <- coef(glm.obj)
SE <- sqrt(diag(vcovHC(glm.obj, type="HC0")))

causalrd <- (betaiptw[2])
lcl <- (betaiptw[2]-1.96*SE[2])
ucl <- (betaiptw[2]+1.96*SE[2])
c(lcl, causalrd, ucl)

##################################
#### alternative: use ipw package
##################################

#### first fit propensity score model to get weights
weightmodel <- ipwpoint(exposure = treatment, family = "binomial",
```

```
          link ="logit", denominator = ~ age + female + meanbp1 +
          ARF + CHF + Cirr + colcan + Coma + lungcan + MOSF + sepsis,
          data = mydata)

#### numeric summary of weights
summary(weightmodel$ipw.weights)

#### plot of weights
ipwplot(weights = weightmodel$ipw.weights, logscale = FALSE,
         main = "weights", xlim = c(0, 22))
mydata$wt<-weightmodel$ipw.weights

#### fit a marginal structural model (risk difference)
msm <- (svyglm(died ~ treatment, design = svydesign(~ 1, weights = ~wt,
                  data =mydata)))
coef(msm)
confint(msm)


#### fit propensity score model to get weights, but truncated
weightmodel <- ipwpoint(exposure = treatment, family = "binomial",
          link ="logit", denominator = ~ age + female + meanbp1 +
          ARF + CHF + Cirr + colcan + Coma + lungcan + MOSF + sepsis,
          data = mydata, trunc =.01)

#### numeric summary of weights
summary(weightmodel$weights.trun)

#### plot of weights
ipwplot(weights = weightmodel$weights.trun, logscale = FALSE,
        main = "weights", xlim = c(0, 22))
mydata$wt<-weightmodel$weights.trun

#### fit a marginal structural model (risk difference)
msm <- (svyglm(died ~ treatment, design = svydesign(~ 1, weights = ~wt,
                                                    data =mydata)))
coef(msm)
confint(msm)
```

4.4 Front-door criterion

For public health epidemiologists, the backdoor criterion is our go-to approach. However, we have occasions where unmeasured or unknown potential confounders complicate our health promotion strategy. For example, because studies linking smoking to lung cancer were observational (i.e., not randomized controlled trials) the tobacco industry argued that investigators were unable to control for unknown

confounders such as a "carcinogenic genotype that also induces an inborn craving for nicotine" [16].

Figure 13(a) depicts this challenge faced by investigators: The DAG does not satisfy the backdoor criterion because the variable U (carcinogenic genetype) is unobserved and cannot be used to block the backdoor path from A (smoking) to Y (lung cancer) ($A \leftarrow U \rightarrow Y$). The causal effect of smoking on lung cancer is not identifiable in this DAG.

Figure 13. Frontdoor criterion: (a) backdoor criterion will not work; we cannot block backdoor path ($A \leftarrow U \rightarrow Y$); (b) in the presence of a mediator (M) we can apply the backdoor criterion twice and measure the causal effect of A on Y. This is called the frontdoor criterion.

However, if a measurable mediator exist between A (smoking) and Y (lung cancer), for example, M (tar deposits), then we can measure the causal effect $P(Y = y \mid do(X = x))$ through two consecutive application of the backdoor criterion (see Figure 13(b)). The effect of A on M is identifiable because there is no backdoor path from A to M. Also, the effect of M on Y is identifiable because there is no backdoor path from M to Y.

For the frontdoor criterion, the backdoor criterion is applied twice: A to M, then M to Y. Here is the full expression:

$$P(Y = y \mid do(A = a)) = \sum_m P(Y = y \mid do(M = m))P(M = m \mid do(A = a))$$

Solving for each expression on the right side yields:

$$P(M = m \mid do(A = a)) = P(M = m \mid A = a)$$

$$P(Y = y \mid do(M = m)) = \sum_a P(Y = y \mid M = m, A = a)P(A = a)$$

And by substituting back into to full expression we get the **front-door adjustment formula**, where $P(Y = y \mid do(A = a)) =$

$$\sum_m \sum_{a'} P(Y = y \mid M = m, A = a')P(A = a')P(M = m \mid A = a)$$

And the front-door adjustment formula can be written in shorter form:

$$P(y \mid do(a)) = \sum_m P(m \mid a) \sum_{a'} P(y \mid m, a')P(a')$$

4.4.1 Example: lung cancer, smoking, tar and carcinogenic genotype

Pearl presents a hypothetical population of 800,000 subjects at high risk for lung cancer due to smoking and other exposures [16]. Data was available on smoking history (A), lung cancer (Y), and lung tar deposits (M). Figure 13(b) represents the DAG for this data. The data numbers are in the thousands.

```
A.lv <- c("Smokers", "Non.smokers")
M.lv <- c("Tar", "No.tar")
Y.lv <- c("Cancer", "No.cancer")
tab.yma <- array(c(323, 57, 18, 2, 1, 19, 38, 342), dim = c(2, 2, 2),
                 dimnames = list(Y = Y.lv, M = M.lv, A = A.lv))
tab.may <- aperm(tab.yma, perm=c(2,3,1))
tab.amy <- aperm(tab.yma, perm=c(3,2,1))
ftable(tab.may)
```

```
##                     Y Cancer No.cancer
## M      A
## Tar    Smokers           323        57
##        Non.smokers         1        19
## No.tar Smokers            18         2
##        Non.smokers        38       342
```

```
ftable(tab.amy)
```

```
##                     Y Cancer No.cancer
## A           M
## Smokers     Tar           323        57
##             No.tar         18         2
## Non.smokers Tar             1        19
##             No.tar         38       342
```

This hypothetical data set could be analyzed in such a way to make smoking appear healthy (smokers have less lung cancer), or that tar deposits are unhealthy (tar deposits associated with lung cancer).[11] However, we recognize this as an opportunity to use the front-door criterion to assess the causal effect of smoking on lung cancer while controlling for unknown confounders.

Here is the front-door adjustment formula again where $P(y \mid do(a)) =$

$$\sum_m P(m \mid a) \sum_{a'} P(y \mid m, a') P(a')$$

We need the sum of these products over all combinations of m and a'. Because there are two summations we will use nested `for` loops twice: once for nonsmokers ($A = 0$) and once for smokers ($A = 1$).

```
(P.m_a <- prop.table(apply(tab.yma, c(2,3), sum),2))
```

```
##          A
## M         Smokers Non.smokers
##   Tar        0.95        0.05
```

[11] See Pearl [16], p. 67, for these arguments.

```
##   No.tar    0.05        0.95
```

```
(P.y_m.a <- prop.table(tab.yma,c(2,3)))
```

```
## , , A = Smokers
##
##            M
## Y            Tar No.tar
##   Cancer    0.85    0.9
##   No.cancer 0.15    0.1
##
## , , A = Non.smokers
##
##            M
## Y            Tar No.tar
##   Cancer    0.05    0.1
##   No.cancer 0.95    0.9
```

```
(P.a <- prop.table(apply(tab.yma, 3, sum)))
```

```
##     Smokers Non.smokers
##         0.5         0.5
```

```
####
#### Calculate front-door adjustment
#### Y = cancer among nonsmokers
pY1_do.A0.vec <- rep(NA, length(A.lv)*length(M.lv))
y1 <- Y.lv[1] # cancer
a0 <- A.lv[2] # nonsmokers
step <- 1
for(ap in A.lv){
  for(m in M.lv){
    pY1_do.A0.vec[step] <- P.y_m.a[y1, m, ap] * P.a[ap] * P.m_a[m, a0]
    step <- step + 1
} }
(pY1_do.A0 <- sum(pY1_do.A0.vec))
```

```
## [1] 0.4975
```

```
####
#### Y = cancer among smokers
pY1_do.A1.vec <- rep(NA, length(A.lv)*length(M.lv))
y1 <- Y.lv[1] # cancer
a1 <- A.lv[1] # smoker
step <- 1
for(ap in A.lv){
  for(m in M.lv){
    pY1_do.A1.vec[step] <- P.y_m.a[y1, m, ap] * P.a[ap] * P.m_a[m, a1]
    step <- step + 1
} }
(pY1_do.A1 <- sum(pY1_do.A1.vec))
```

```
## [1] 0.4525
```

This problem is fully worked out here: http://bayes.cs.ucla.edu/BOOK-2K/ch3-3.pdf. Because this is a hypothetical data set the final answer is contrary to known facts about smoking and lung cancer. This exercise was designed implement the front-door adjustment.

4.5 Instrumental variable

TBD

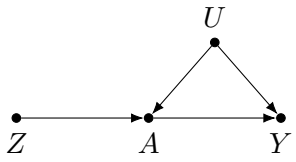


Figure 14. Instrumental variable

```
#### read dataset
data(card.data)

#IV is nearc4 (near 4 year college)
#outcome is lwage (log of wage)
#'treatment' is educ (number of years of education)

#summary stats
mean(card.data$nearc4)
par(mfrow=c(1,2))
hist(card.data$lwage)
hist(card.data$educ)

#is the IV associated with the treatment? strenght of IV
mean(card.data$educ[card.data$nearc4==1])
mean(card.data$educ[card.data$nearc4==0])


#make education binary
educ12<-card.data$educ>12
#estimate proportion of 'compliers'
propcomp<-mean(educ12[card.data$nearc4==1])-
  mean(educ12[card.data$nearc4==0])
propcomp

#intention to treat effect
itt<-mean(card.data$lwage[card.data$nearc4==1])-
  mean(card.data$lwage[card.data$nearc4==0])
itt
```

```
#complier average causal effect
itt/propcomp


#two stage least squares

#stage 1: regress A on Z
s1<-lm(educ12~card.data$nearc4)
## get predicted value of A given Z for each subject
predtx <-predict(s1, type = "response")
table(predtx)

#stage 2: regress Y on predicted value of A
lm(card.data$lwage~predtx)


#2SLS using ivpack
ivmodel=ivreg(lwage ~ educ12, ~ nearc4, x=TRUE, data=card.data)
robust.se(ivmodel)


ivmodel=ivreg(lwage ~ educ12 + exper + reg661 + reg662 +
                reg663 + reg664 + reg665+ reg666 + reg667 + reg668,
                ~ nearc4 + exper +
                  reg661+ reg662 + reg663 + reg664 + reg665 + reg666 +
                reg667 + reg668, x=TRUE, data=card.data)
```

5 Decision quality (with decision Bayesian networks)

Public health practice is replete with claims of "data-driven decision-making." This usually means reading scientific articles, looking at local data and information, and implementing evidence-based strategies. With few exceptions, there is generally no formal, deliberative, structured process for translating data into actionable knowledge, and for *knowledge integration*—the management, synthesis, and translation of knowledge into decision support systems to improve policy, practice, and—ultimately—population health.

Because we make intuitive decisions daily, most of us are not formerly trained in decision making. Decisions are oftens based on power, politics, advocacy, organizational history and culure, and personal interests. Yet, decisions determine how we spend our time and allocate scarce resources, so they should be driven by strategic goals, stakeholder needs, evidence, and decision quality (DQ).

DQ (Table 2, p. 3) is a checklist for continuous decision improvement (decision competence), and a road map for advanced methods such as decision analysis (DA). DA is a formal method for tackling decisions in the face of uncertainty and trade-offs. DA is usually conducted with decision trees (Figure 15) where squares represent decision nodes and ellipses represent uncertainty (chance) nodes. On the right side of the decision tree are the utilities (weighted outcomes [usually weighted by preference]). The general approach is to calculate the expected utility (value) for each decision option, and to choose the option that maximizes this utility.

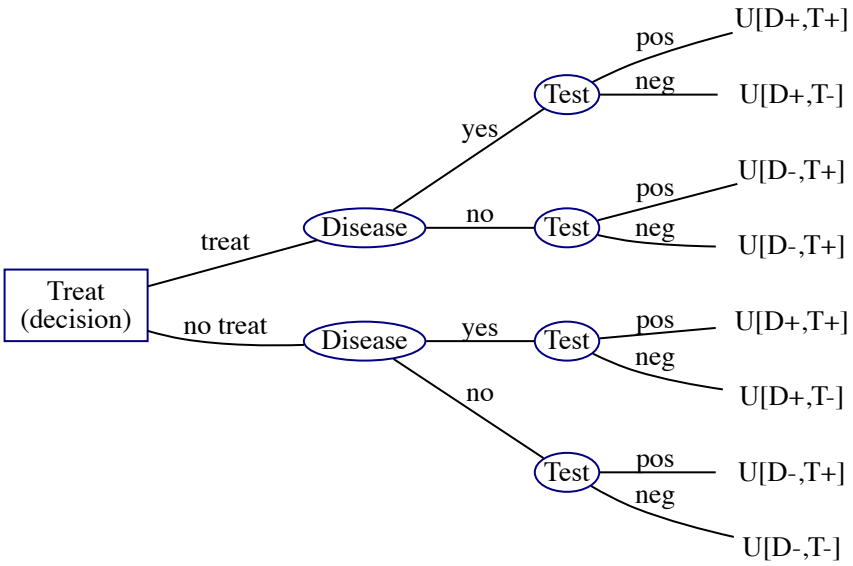


Figure 15. A decision tree for decision analysis

An alternative way to structure a decision is with a decision Bayesian network (BN) (also called an influence diagram). An **influence diagram** is a BN that includes *decision*, *uncertainty* (chance), *calculation* (deterministic), and *value* (utility) nodes (Figure 16).

Figure 17 (p. 31) is the influence diagram version of Figure 15 (p. 30). Compared to decision trees, influence diagrams can more efficiently represent complex decision

problems. Figure 17 has some key features:

1. Decision nodes alway connect to the final utility (value) node.
2. A node connecting into a decision node (e.g., "Test") represents information that is available to "influence" the decision node.
3. The disease node has a causal effect on the diagnostic test results.
4. The disease node has a causal effect on the final outcome (utility node).

Notice that this influence diagram is able to integrate disease prevalence (prior probability), diagnostic testing, test characteristics (sensitivity, specificity), and outcomes.

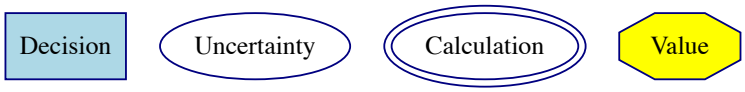


Figure 16. Node definitions for influence diagrams

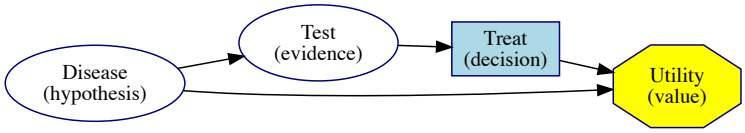


Figure 17. A Bayesian decision network (influence diagram) for decision analysis

5.1 Example 1: Decision to buy stock

A basic decision that involves uncertainty is to choose between (a) an option with an uncertain outcome and payout, or (b) continue with the status quo. Figure 18 from Neapolitan (p. 492, [14]) is the decision tree that represents the decision ("d1") to invest $1000 and buy stock X with a 0.6 chance to grow in value to $1100 and 0.4 chance to shrink in value to $900, or the decision ("d2") to do nothing and keep the $1000.

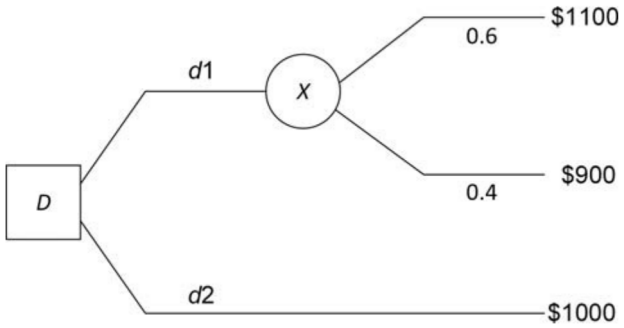


Figure 18. Simple decision tree for decision whether to buy stock X.

Figure 19 (p. 32) from Neapolitan (p. 492, [14]) is the influence diagram version of the Figure 18 decision tree. Now, here are the expected value calculations for each decision option:

$$E(\text{d1}) = 0.6 \times \$1100 + 0.4 \times \$900 = \$1020$$

$$E(\text{d2}) = \$1000$$

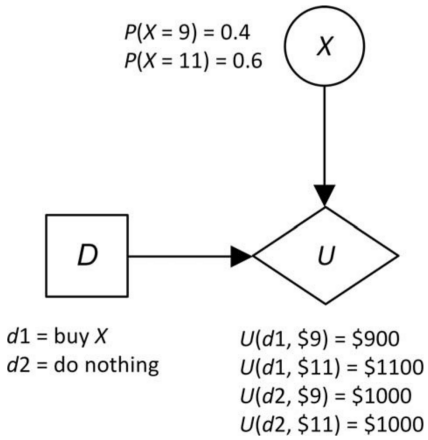


Figure 19. Simple influence diagram for decision whether to buy stock X.

Using R, we create the decision BN. Actually, it is a regular BN with minor tweaks. For the decision node, we set the probabilities for each decision option (d1, d2) to 0.5. To get the expected value (EV) we set the decision node evidence to "d1" and calculate EV, and then to "d2" and calculate EV again.

For the utility (value) node we set the possible dollar outcome levels as 900, 1100, and 1000. After setting decision node evidence to "d1", we derive the new distribution of dollar outcomes, and we calculate the EV. We repeat this for "d2". See the R code below with the details.

```
#### reload R packages if necessary
#### library(bnlearn)
#### library(gRain)
dag3 <- empty.graph(nodes=c("D", "U", "X"))
dag3 <- set.arc(dag3, from = "X", to = "U")
dag3 <- set.arc(dag3, from = "D", to = "U")
## graphviz.plot(dag3)
#### create levels
X.lv <- c("9", "11")
D.lv <- c("d1", "d2")
U.lv <- c("900", "1100", "1000") ## possible dollars outcomes
#### create conditional probability tables
X.prob <- array(c(0.4,1-0.4), dim = 2, dimnames = list(X = X.lv))
D.prob <- array(c(0.5,0.5), dim = 2, dimnames = list(D = D.lv))
U.prob <- array(c(1,0,0,0,1,0,0,0,1,0,0,1), dim = c(3,2,2),
 dimnames = list(U = U.lv, X=X.lv, D=D.lv))
cpt3 <- list(X=X.prob, D=D.prob, U=U.prob)
bn3 <- custom.fit(dag3, cpt3)
```

```
junction3 <- compile(as.grain(bn3))
querygrain(junction3) ## display BN
```

```
## $D
## D
##  d1  d2
## 0.5 0.5
##
## $U
## U
##  900 1100 1000
##  0.2  0.3  0.5
##
## $X
## X
##   9  11
## 0.4 0.6
```

```
#### Expected value for D = "d1" (buy stock X)
jbuy <- setEvidence(junction3, nodes = "D", states = "d1")
U.buy <- querygrain(jbuy, nodes = "U")$U
(EV.buy <- sum(U.buy*as.numeric(names(U.buy))))
```

```
## [1] 1020
```

```
#### Expected value for D = "d2" (do nothing)
jdont <- setEvidence(junction3, nodes = "D", states = "d2")
U.dont <- querygrain(jdont, nodes = "U")$U
(EV.dont <- sum(U.dont*as.numeric(names(U.dont))))
```

```
## [1] 1000
```

5.2 Example 2: Decision to buy Spiffycar

From Neapolitan (p. 492, [14]) we now tackle a decision problem that includes a diagnostic test (Figure 20, p. 34):

> "... Suppose Sam has the opportunity to buy a 1996 Spiffycar automobile for $10,000, and he had a prospect that would be willing to pay $11,000 for the auto if it were in excellent mechanical shape. Suppose further that if the transmission is bad, Sam will have to spend $3000 to repair it before he could sell the vehicle. So he would end up with only $8,000 if he bought the vehicle and its transmission was bad. Finally, suppose Sam has a friend who could run a test on the transmission, and we have the following:"

$$P(Test = \text{positive} \mid Tran = \text{good}) = 0.3$$

$$P(Test = \text{positive} \mid Tran = \text{bad}) = 0.9$$

$$P(Tran = \text{good}) = 0.8$$

The Bayesian network (Figure 20) "in this influence diagram contains 2 nodes, $Tran$ and $Test$. There is an edge from $Tran$ to $Test$ because the value of the test is probabilistically dependent on the state of the transmission. There is an edge from $Test$ to D because the outcome of the test will be known at the time the decision is made. That is, D follows $Test$ in sequence. Finally, the utility U depends only on the value of $Tran$ and the decision D. It does not depend on the outcome of the $Test$. So there are arrows from $Tran$ and D to U. If Sam makes decision `d1` and $Tran$ is good, the utility of the outcome will be \$11 000. On the other hand, if Sam makes decision `d1` and $Tran$ is bad, the utility of the outcome will be \$8,000. However, if Sam makes decision `d2`, the utility of the outcome is \$10,000 regardless of whether $Tran$ is good or bad because he has decided not to buy the car."

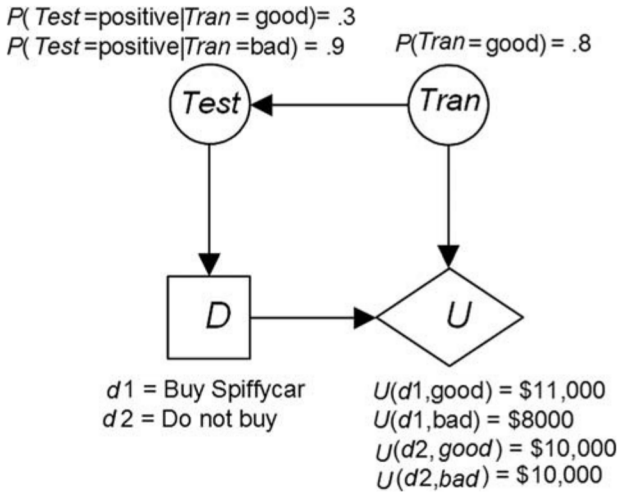


Figure 20. Influence diagram representing decision to buy Spiffycar.

Using R, we create the "decision BN." Actually, it is a regular BN with minor tweaks. For the decision node, we set the probabilities for each decision option (d1, d2) to 0.5. To get the expected utility (EU) we set the decision node evidence to "d1" and calculate EU, and then to "d2" and calculate EU again.

For the utility (value) node we set the possible dollar outcome levels as 8000, 10000, and 11000. After setting decision node evidence to "d1", we derive the new distribution of dollar outcomes, and we calculate the EU. We repeat this for "d2". See the R code below with the details.

```
dag4 <- empty.graph(nodes=c("Test", "Tran", "D", "U"))
dag4 <- set.arc(dag4, from = "Tran", to = "Test")
dag4 <- set.arc(dag4, from = "Tran", to = "U")
dag4 <- set.arc(dag4, from = "Test", to = "D")
dag4 <- set.arc(dag4, from = "D", to = "U")
#### create levels
Tran.lv <- c("Good", "Bad")
Test.lv <- c("Pos", "Neg")
```

```
D.lv <- c("d1", "d2") ## d1 = buy spiffycar; d2 = do not buy
U.lv <- c("11000", "8000", "10000")
#### create conditional probability tables
Tran.prob <- array(c(0.8,1-0.8), dim = 2, dimnames = list(Tran = Tran.lv))
Test.prob <- array(c(0.3,1-0.3,0.9,1-0.9), dim = c(2,2),
  dimnames = list(Test = Test.lv, Tran = Tran.lv))
D.prob <- array(c(.5, .5, .5, .5), dim = c(2,2),
  dimnames = list(D = D.lv, Test = Test.lv))
U.prob <- array(c(1,0,0,0,1,0,0,0,1,0,0,1), dim = c(3,2,2),
 dimnames = list(U = U.lv, Tran=Tran.lv, D=D.lv))
cpt4 <- list(Tran=Tran.prob, Test=Test.prob, D=D.prob, U=U.prob)
bn4 <- custom.fit(dag4, cpt4)
junction4 <- compile(as.grain(bn4))
querygrain(junction4) ## display BN
```

```
## $Test
## Test
##  Pos  Neg
## 0.42 0.58
##
## $Tran
## Tran
## Good  Bad
##  0.8  0.2
##
## $D
## D
##  d1  d2
## 0.5 0.5
##
## $U
## U
## 11000  8000 10000
##   0.4   0.1   0.5
```

What is the EU of choosing "d1" even if the transmision test is positive? That is, what is $EU(D = \text{d1}, Test = \text{positive})$?

```
#### What is EU(D = d1, Test = positive)?
jTest.pos_D.d1 <- setEvidence(junction4, nodes = c("Test", "D"),
                              states = c("Pos", "d1"))
U_T.p_D.d1 <- querygrain(jTest.pos_D.d1, nodes = "U")$U
(EU_T.p_D.d1 <- sum(U_T.p_D.d1 * as.numeric(names(U_T.p_D.d1))))
```

```
## [1] 9714.286
```

What is the EU of choosing "d1" even if the transmision test is negative? That is, what is $EU(D = \text{d1}, Test = \text{negative})$?

```
#### What is EU(D = d1, Test = negative)?
jTest.neg_D.d1 <- setEvidence(junction4, nodes = c("Test", "D"),
                              states = c("Neg", "d1"))
U_T.n_D.d1 <- querygrain(jTest.neg_D.d1, nodes = "U")$U
(EU_T.n_D.d1 <- sum(U_T.n_D.d1 * as.numeric(names(U_T.n_D.d1))))
```

```
## [1] 10896.55
```

What is the EU of choosing "d2" regardless of transmission test results? That is, what is $EU(D = \text{d2})$?

```
#### What is EU(D = d2)?
jD.d2 <- setEvidence(junction4, nodes = "D", states = "d2")
U_D.d2 <- querygrain(jD.d2, nodes = "U")$U
(EU_D.d2 <- sum(U_D.d2 * as.numeric(names(U_D.d2))))
```

```
## [1] 10000
```

5.3 Example 3: Comparing complex policy options

TBD

5.4 Example 4: Discrete time Markov chains

TBD

5.5 Example 5: Cost-effective analysis

TBD

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