### Idea of Statistical Modeling

ISTA 410 / INFO 510 - Bayesian Modeling and Inference

University of Arizona School of Information August 25, 2021

#### **Outline**

#### Outline for today:

- Goals of Bayesian analysis
- Example: kidney cancer death rates
- Types of uncertainty
- More involved example: vaccine effectiveness

### Motivation: Bayesian analysis

#### Goal: analyze and quantify uncertainty

- uncertain quantities get a probability distribution
- probability distribution is updated based on new observations

#### Bayesian approach:

- Named for Thomas Bayes English minister in the 18th century
- Considered the problem of inverse probability
- Didn't invent the whole theory, but was one of the earliest to solve a problem with it (along with Laplace)

### Generative probabilistic models

### Core component: generative models

- given values of model parameters, can generate outcomes
  - given a value for the probability a coin comes up heads, we can simulate a sequence of flips
  - given a mean and standard deviation, we can simulate normally distributed values

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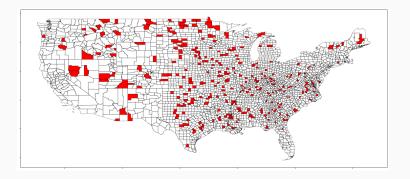
The inverse problem is: given the outcomes, infer a probability distribution for the parameters

 Both Bayes's and Laplace's early work deal with a binomial model (like the coin flip)

## Case study: kidney cancers

### Where is kidney cancer highest?

The following map shows the counties with the highest 10% death rates due to kidney cancer (1980-89).



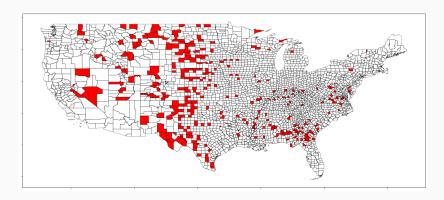
#### What do we notice?

What we can notice: most counties in the middle of the country, not coasts.

Why?

### Where is kidney cancer lowest?

The following map shows the counties with the *lowest* 10% death rates due to kidney cancer (1980-89).



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Possible explanation: sample size

- Rates in small samples are more variable than larger samples
- Kidney cancer is a rare cause of death, and USA has a lot of very low population counties
- A county with 1000 people is likely to record zero deaths
- A county with 1000 people that records 1 death jumps to a rate of 100 deaths per 100,000 people, easily enough to jump to the top 10%

### A simple model

To see if the sample size effect is enough to explain this, we can try a generative model.

- Model is a procedure for generate simulated versions of our observed outcomes
- What are our outcomes? Deaths due to kidney cancer.
- Idea: establish a minimal model, see if it replicates the qualitative behavior of the real data
- We need to pick a probability distribution for our outcomes

Common choice for this sort of count: Poisson distribution

#### Poisson distribution

- Defined on natural numbers  $\{0, 1, 2, \ldots\}$
- Models a count of events occurring independently at a fixed rate
- ullet Depends on a rate parameter most often written  $\lambda$

Probability mass function:

$$P(X=k) = \frac{\lambda^k e^{-\lambda}}{k!}$$

#### Our model

We'll make the simplest possible assumption: there is no effect of geography on kidney cancer, and the only relevant feature of a county is population.

So, our model has one parameter,  $\theta$  (the underlying death rate).

Then, the death count in each county,  $y_j$ , follows a Poisson distribution:

$$y_j \sim \text{Poisson}(\theta n_j)$$

where  $n_j$  is the population of the county. (In Poisson models this scaling factor is sometimes called an *exposure*.)

Let's try simulating...

# Case study for inference

### Inference with a generative model

#### Previous example:

- Generative procedure allowed us to explain one of the qualitative features of the data set
- However, we didn't set the model up to do any *inference*, e.g. estimating the actual death rate
  - $\bullet$  we used a fixed value of  $\theta$
  - ullet we used the same heta for every county
- In practice, we often want to estimate un-observed parameters

### Using a Bayesian model

#### Steps:

- Set up a probabilistic model for the observed data, dependent on un-observed parameters
- Apply a prior distribution to the parameters, representing our knowledge before observing data
- Apply Bayes' theorem to update the distribution of the parameters, resulting in a posterior distribution
- Summarize relevant results

### Bayes' theorem

Recall Bayes' theorem:

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

Terminology:

- P(H|E) posterior probability
- P(H) prior probability
- P(E|H) likelihood
- P(E) normalizing constant

Variant on example from last time: cookie problem. Bowl 1 has 1/2 chocolate, 1/2 vanilla cookies; Bowl 2 is the same; Bowl 3 has 3/4 vanilla, 1/4 chocolate. We draw a chocolate cookie; what's the probability we are drawing from bowl 3?

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More commonly, our parameters are not discrete (bowl 1 vs. 2 vs. 3) but continuous.

#### Differences:

- instead of finitely many "hypotheses", any allowed value of
- we have to work with probability density functions

### Bayes' theorem with densities

Most commonly we have probability density functions that depend on unknown parameters:

- y − data
- $\theta$  parameters

$$p(\theta|y) = \frac{p(y|\theta)p(\theta)}{p(y)}$$
$$p(\theta|y) \propto p(y|\theta)p(\theta)$$

The normalizing constant p(y) is gotten by marginalizing over  $\theta$  by computing  $\int p(y|\theta)p(\theta)d\theta$ ; this integral may be intractable, so we work with the proportionality statement.

#### **Binomial model**

If we are observing binary categorical outcomes, a binomial likelihood makes sense. Binomial( $n, \theta$ ) is the distribution of the count of "successes" in n independent trials with a fixed probability  $\theta$  of success.

$$p(y \text{ successes}|\theta) = \binom{n}{y} \theta^y (1-\theta)^{n-y}$$

### A continuous prior

A common choice of prior for a binomial likelihood is a beta distribution:

$$\theta \sim \text{Beta}(\alpha, \beta)$$

where  $\alpha, \beta > 0$  are chosen ahead of time.

Beta distribution: defined on [0,1] by the PDF

$$p(\theta) = \frac{1}{B(\alpha, \beta)} \theta^{\alpha - 1} (1 - \theta)^{\beta - 1}$$

 $B(\alpha, \beta)$  is the normalizing constant, called a *Beta function*. There are formulas for it but not important for us right now.

### What is the data-generating process?

The generative procedure now:

- 1. Draw a value of  $\theta$  from Beta $(\alpha, \beta)$
- 2. Draw a value of y from Binomial $(n, \theta)$

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#### The generative procedure now:

- 1. Draw a value of  $\theta$  from Beta $(\alpha, \beta)$
- 2. Draw a value of y from Binomial $(n, \theta)$ 
  - The cookie problem: y's distribution is a finite mixture of binomials, with equal weight
  - $\bullet$  Now: y's distribution is an infinite mixture of binomials, weighted by the PDF of  $\theta$

### Conjugate prior

One reason for the choice of beta prior: conjugacy

A distribution  $p(\theta)$  is conjugate to a likelihood  $p(y|\theta)$  if the posterior distribution  $p(\theta|y)$  is a member of the same family as  $p(\theta)$ :

In the beta-binomial model,

$$p(\theta|y) = \frac{1}{p(y)} \frac{1}{B(\alpha, \beta)} p(k|\theta) \begin{pmatrix} n \\ k \end{pmatrix} \theta^{y} (1-\theta)^{n-y} \theta^{\alpha-1} (1-\theta)^{\beta-1}$$

The leading three factors don't depend on  $\theta$ , so we absorb them into a single constant.

### Conjugate prior

Now:

$$\rho(\theta|y) = \frac{1}{Z}\theta^{y}(1-\theta)^{n-y}\theta^{\alpha-1}(1-\theta)^{\beta-1}$$
$$= \frac{1}{Z}\theta^{\alpha+y-1}(1-\theta)^{\beta+(n-y)-1}$$

Since the dependence of the density on  $\theta$  is that of a beta distribution with parameters  $(\alpha + y, \beta + (n - y))$ , the constant Z must be the corresponding beta function, and

$$\theta|y \sim \text{Beta}(\alpha + y, \beta + (n - y))$$

Computationally very convenient! Convenience less important these days than it used to be, though.

#### Posterior distribution

So, in a beta-binomial model:

$$y \sim \text{Binomial}(n, \theta)$$
  
 $\theta \sim \text{Beta}(\alpha, \beta)$ 

if we observe y successes and n-y failures, the posterior distribution of  $\theta$  is

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Interpretation: we may think of the prior parameters  $\alpha-1,\beta-1$  as pseudocounts

Summarizing inferences; example

### Inferences from the posterior

The posterior distribution is the primary product of inference; it contains all that we know about the parameter after incorporating prior and data.

In practice, often want to distill out some summary statistics:

- posterior mean expected value of  $\theta$  under the posterior distribution
- posterior intervals 95% common, but arbitrary. Note difference between highest density and central intervals
- maximum a posteriori estimate often not a good choice, especially if the model has many parameters

### Example: Pfizer's vaccine trial

Prominent recent example: beta-binomial model in analysis of Pfizer's COVID-19 vaccine

#### Trial procedure:

- Study participants divided randomly into two "arms": control/placebo and vaccine
- Control arm given placebo, vaccine arm given vaccine
- Watch both groups and count cases, running the analysis when a predetermined number of cases is observed

#### Beta-binomial model

#### Defining parameters:

- $\pi_c$ : probability that a control subject becomes ill
- $\pi_{v}$ : probability that a vaccinated subject becomes ill
- Derived quantity: Vaccine efficacy:

$$VE = 1 - \frac{\pi_v}{\pi_c}$$

Parameter for the model:

$$\theta = \frac{1 - VE}{2 - VE} = \frac{\pi_v}{\pi_v + \pi_c}$$

Measures the probability that a case came from the vaccine arm

### Pfizer's prior

Let y be the number of cases that come from the vaccinated group.

The model:

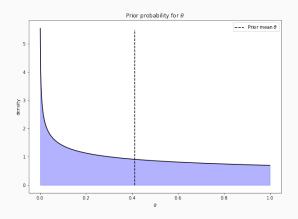
$$y \sim \text{Binomial}(\theta, n)$$
  
 $\theta \sim \text{Beta}(0.700102, 1)$ 

Prior was stated in Pfizer's press release. No specific reason given for these parameters, but:

- VE at prior mean  $\theta$  is 30%
- fairly uninformative: 95% interval is about (-26.2, 0.995).

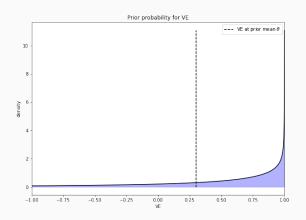
### Pfizer's prior

#### On the $\theta$ scale:



### Pfizer's prior

#### On the VE scale



#### What's the data?

The result of the study submitted to the FDA to obtain an emergency use authorization had a total of 170 observed cases, 8 of which were in the vaccine arm. So:

$$\theta | y \sim \text{Beta}(0.700102 + 8, 1 + 162)$$

Let's examine this graphically...

#### Next week

#### Next week:

- More models
- Going beyond conjugate priors with various approximations