



# **Bayesian Statistics for Genetics**

## **Lecture 2: Binomial Sampling, part 1**

*June, 2025*

# Outline

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Important ideas we will recap:

- Bayes' Theorem – a statement of conditional probability
- Bayesian inference – using probability to describe **belief**

In this session:

- More formal analysis of the ACE study's binomial model
- What to do with a posterior distribution?

# Bayes theorem: conditional probability

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For a *partition*  $\{H_1, \dots, H_K\}$ , the axioms of probability imply the following:

- Rule of total probability:

$$\sum_{k=1}^K \mathbb{P}[H_k] = 1$$

- Rule of marginal probability:

$$\mathbb{P}[A] = \sum_{k=1}^K \mathbb{P}[A \text{ and } H_k] = \sum_{k=1}^K \mathbb{P}[A|H_k]\mathbb{P}[H_k]$$

Simple case:  $K = 2$  with  $H_1 = B$  and  $H_2 = B^c$  (the complement of  $B$ ):

$$\begin{aligned}\mathbb{P}[A] &= \mathbb{P}[A \text{ and } B] + \mathbb{P}[A \text{ and } B^c] \\ &= \mathbb{P}[A|B]\mathbb{P}[B] + \mathbb{P}[A|B^c]\mathbb{P}[B^c].\end{aligned}$$

# Bayes' Theorem: conditional probability

Some genetics! Jo\* — a randomly-chosen father of two with at least one boy — has two kids. **Given that** at least one is a boy; what's the probability he has two boys?

Unconditional

		Older Child	
		Boy	Girl
Younger Child	Boy		
	Girl		

$$\mathbb{P}[2 \text{ Boys}] = 1/4 = 0.25$$

Conditional

		Older Child	
		Boy	Girl
Younger Child	Boy		
	Girl		

$$\mathbb{P}[2 \text{ Boys} | 1 \text{ Boy}] = 1/3 \approx 0.33$$

# Bayes' Theorem: conditional probability

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Now a problem – not a trick! – to show that conditional probability can be non-intuitive, and careful reasoning is needed;

**Q.** Jo has two children. **Given that** at least one is a *boy who was born on a Tuesday*; what's the probability he has two boys?

- The 'obvious' (but wrong!) answer is to stick with  $1/3$ . What can Tuesday possibly have to do with it?
- It may help your intuition, to note that a boy being born on a Tuesday is a (fairly) rare event;
  - Having two sons would give Jo two chances of experiencing this rare event
  - Having only one would give him one chance
  - 'Conditioning' means we **know** this event occurred, i.e. Jo was 'lucky' enough to have the event
- **Easier Q.** Is  $\mathbb{P}[2 \text{ Boys} | 1 \text{ Tues Boy}] > 1/3?$  or  $< 1/3?$

# Bayes' Theorem: conditional probability

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All the possible births and sexes;

			Younger Child													
			Boy							Girl						
			M	T	W	Th	F	Sa	Su	M	T	W	Th	F	Sa	Su
Younger Child	Boy	M														
		T														
		W														
		Th														
		F														
		Sa														
		Su														
	Girl	M														
		T														
		W														
		Th														
		F														
		Sa														
		Su														

Q. When we condition, which row and column are we considering?

# Bayes' Theorem: conditional probability

Conditioning on at least one Tuesday-born boy;

			Younger Child													
			Boy							Girl						
			M	T	W	Th	F	Sa	Su	M	T	W	Th	F	Sa	Su
Younger Child	Boy	M														
		T														
		W														
		Th														
		F														
		Sa														
		Su														
	Girl	M														
		T														
		W														
		Th														
		F														
		Sa														
		Su														

... giving  $\mathbb{P}[2 \text{ Boys} | 1 \text{ Tues Boy}] = 13/27 \approx 0.48$ , **quite different** from  $1/3 \approx 0.33$ .

# Bayes' Theorem: conditional probability

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**Formal example:** Let  $B = \text{Female}$  and  $B^c = \text{Male}$ . Suppose in a given population over the age of 18:

$$\mathbb{P}[B] = 0.55, \quad \mathbb{P}[B^c] = 0.45.$$

Event of interest:  $A = \text{being diagnosed with diabetes}$ .

In the US in 2018, for over 18 year olds,  $\mathbb{P}[A|B] = 0.095$  and  $\mathbb{P}[A|B^c] = 0.11$ , so

$$\begin{aligned} \mathbb{P}[A] &= \mathbb{P}[A|B]\mathbb{P}[B] + \mathbb{P}[A|B^c]\mathbb{P}[B^c] \\ &= 0.095 \times 0.55 + 0.11 \times 0.45 \\ &= 0.05225 + 0.0495 \\ &= 0.10175 \end{aligned}$$

So 10.2% of the population have diabetes.



# Bayes theorem: Flipping around the conditioning

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$$\text{Bayes theorem : } \mathbb{P}(H_j|E) = \frac{\overbrace{\mathbb{P}(E|H_j)}^{\text{"Likelihood"}} \overbrace{\mathbb{P}(H_j)}^{\text{"Prior"}}}{\underbrace{\mathbb{P}(E)}_{\text{Normalizing Constant}}} = \frac{\mathbb{P}(E|H_j)\mathbb{P}(H_j)}{\sum_{k=1}^K \mathbb{P}(E|H_k)\mathbb{P}(H_k)}$$

for  $j = 1, \dots, K$ .

Anticipating Bayesian inference:

- One begins with (**prior**) belief about events  $H_j$ ,  $\mathbb{P}(H_j)$ , and...
- ...updates it to (**posterior**) belief  $\mathbb{P}(H_j|E)$ , given that event  $E$  occurs.

Note that the likelihood, on its own, doesn't generally describe beliefs.

# Bayes theorem: Flipping around the conditioning

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What's the probability that a person with diabetes is female?

In probability speak:

$$\begin{aligned}\mathbb{P}(B|A) &= \frac{\mathbb{P}(A|B)\mathbb{P}(B)}{\mathbb{P}(A)} \\ &= \frac{0.095 \times 0.55}{0.10175} \\ &= 0.514\end{aligned}$$

So there is a 0.514 chance that a randomly sampled person with diabetes is female.

This is *updated* from our prior probability of being female  $\mathbb{P}(B) = 0.55$  – it's a slight reduction since males are more likely to have diabetes.

# Conditional independence

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Conditional independence is a key concept when constructing statistical models – we start by describing *independence*.

For events  $A$  and  $B$ , it is always true that,

$$\mathbb{P}(A \text{ and } B) = \mathbb{P}(A|B) \times \mathbb{P}(B).$$

Bayes theorem:

$$\mathbb{P}(B|A) = \frac{\mathbb{P}(A|B)\mathbb{P}(B)}{\mathbb{P}(A)}.$$

Viewed in a Bayesian way, knowledge that  $A$  occurs has *updated our beliefs* about  $B$ .

How about when we **don't** learn anything from  $B$ 's occurrence?

# Conditional independence

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Then

$$\mathbb{P}(B | A) = \mathbb{P}(B)$$

or equivalently

$$\mathbb{P}(A \text{ and } B) = \mathbb{P}(A) \times \mathbb{P}(B).$$

- The events  $A$  and  $B$  are said to be *independent*.
- Knowledge that  $A$  occurs does not affect our beliefs about  $B$ .
- Knowledge that  $B$  occurs does not affect our beliefs about  $A$ , i.e., this implies  $\mathbb{P}(A|B) = \mathbb{P}(A)$ .

If diabetes risk was the same in females and males, then knowing diabetes status,  $A$ , would not tell us anything about the sex of the person,  $B$ , i.e.,  $\mathbb{P}(B|A) = \mathbb{P}(B)$ .

# Conditional independence

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In statistical modeling, independence is rarely relevant, but conditional independence is ubiquitous.

Extending this idea, events  $F$  and  $G$  are *conditionally independent given  $H$* , if

$$\mathbb{P}(F \text{ and } G | H) = \mathbb{P}(F | H) \times \mathbb{P}(G | H),$$

Or written another way:

$$\mathbb{P}(F | G, H) = \mathbb{P}(F | H).$$

Given  $H$ , knowledge that  $G$  occurred does not alter our beliefs in  $F$  occurring.

# Conditional Independence: Example

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## Data:

Suppose we know events:

$F = \{ \text{a patient develops cancer} \}$

$G = \{ \text{patient's parent's genotype} \}$

$H = \{ \text{patient's genotype} \}$

## Informal statement:

If we know the patient's genotype  $H$ , does knowledge of the parents' genotype  $G$  give any additional information?

Formal statement:

Does

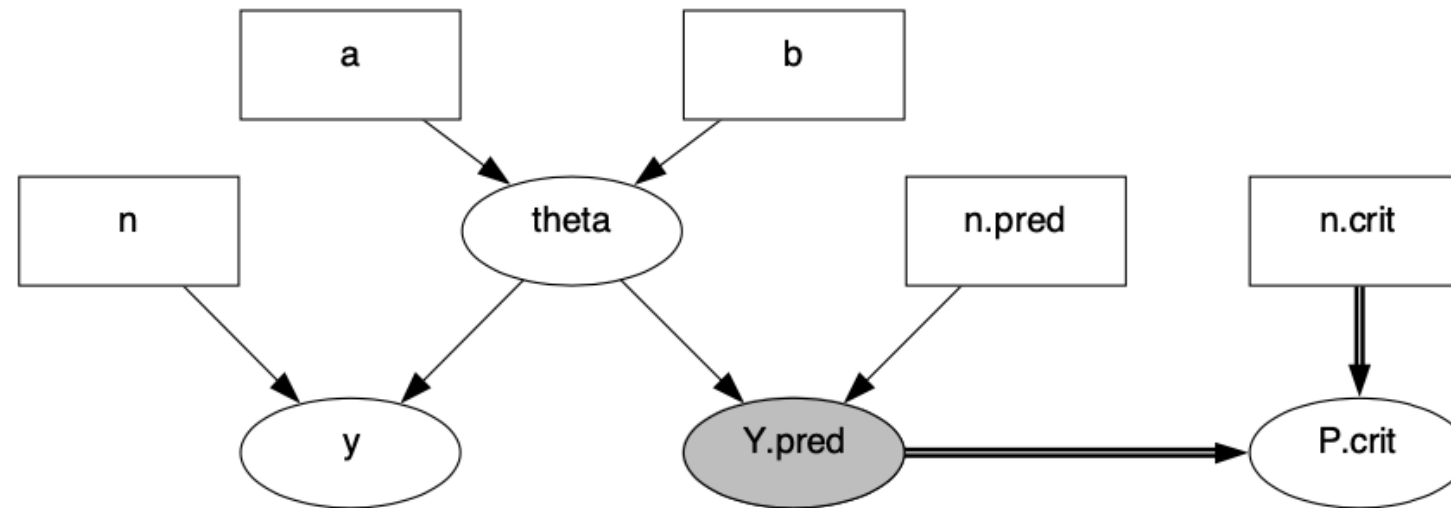
$$\mathbb{P}(F | H) = \mathbb{P}(F | G, H)?$$

**Answer:** In general, conditional independence will hold, but not on all occasions; in genomic imprinting genes are expressed in a parent-of-origin-specific manner, i.e., the expression of the gene depends upon the parent who passed on the gene.

# Conditional Independence: Example

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Conditional independencies can be neatly expressed through graphs, as in this example from the BUGS book (Lunn *et al* 2013)



Conditioning on a connecting node 'blocks' the path between other variables. (This format may also be familiar from causal analysis)

# Conditional Independence: Example

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In likelihood-based inference, conditional independence is *very* widely-used.

For example, the sampling model for data  $\mathbf{y} = [y_1, \dots, y_n]^T$  is often taken to be:

$$\begin{aligned} p(\mathbf{y}|\boldsymbol{\theta}) &= p(y_1, \dots, y_n|\boldsymbol{\theta}) \\ &= p(y_1|\boldsymbol{\theta}) \times p(y_2|y_1, \boldsymbol{\theta}) \times \dots \times p(y_n|y_{n-1}, \dots, y_1, \boldsymbol{\theta}) \\ &= p(y_1|\boldsymbol{\theta}) \times p(y_2|\boldsymbol{\theta}) \times \dots \times p(y_n|\boldsymbol{\theta}) \\ &= \prod_{i=1}^n p(y_i|\boldsymbol{\theta}) \end{aligned}$$

where we have assumed conditional independence, i.e., given  $\boldsymbol{\theta}$ , the observations are independent.

**Example:** For coin tosses, the outcomes are conditionally independent, given the probability of a head  $\theta$ . (But what happens if we have  $> 1$  coin?)



# Overview of Bayesian Inference

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At a high level, with a model specified and data available, Bayes is automatic. (Examples follow!) But it's worth noting that **integration**, i.e. averaging, in some form, is usually the biggest hurdle. Bayesian approaches to:

- **Estimation**: **marginal posterior distributions** on parameters of interest – similar approaches permit testing. Need to integrate over the other parameters
- **Prediction**: via the **predictive distribution**, integrating over parameter uncertainty
- **Hypothesis Testing**: **Bayes factors** give the relative support for different ranges of  $\theta$  – and a different form of testing. Need to average over different submodels

We'll describe all three in the context of a *binomial model* – in general we focus on **estimation** and **prediction**.

# Elements of Bayes Theorem for a Binomial Model

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Suppose the data consist of  $N$  Bernoulli (i.e. 0/1) responses  $y_i$ ,  $i = 1, \dots, N$ .

We assume these responses are conditionally independent, given a common “success” probability  $\theta$ .

Under this conditional independence assumption, the distribution of the total  $y = \sum_{i=1}^N y_i$  has to be a *binomial* distribution, in which

$$\mathbb{P}[Y = y | \theta] = \binom{N}{y} \theta^y (1 - \theta)^{N-y}$$

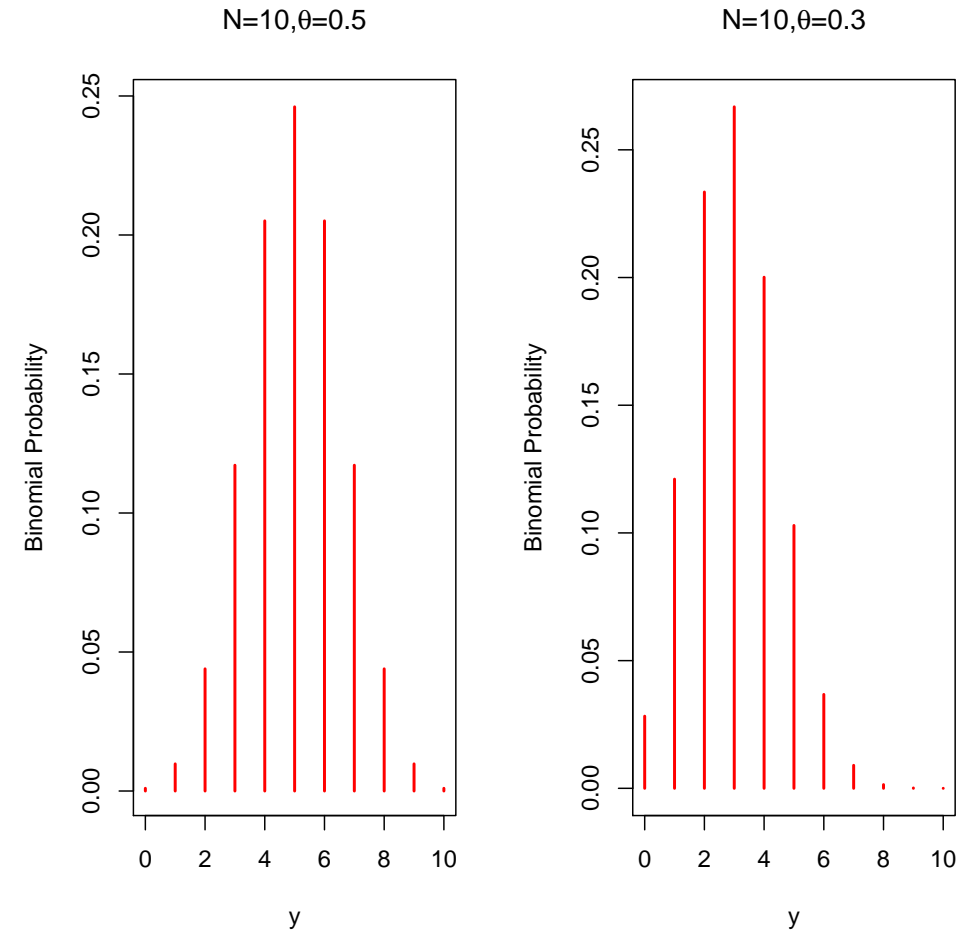
is the probability of seeing  $Y = y$ , for the permissible values  $y = 0, 1, \dots, N$  **given** the probability  $\theta$ .

# Elements of Bayes Theorem for a Binomial Model

Binomial **distributions** (right) for two values of  $\theta$  with  $N = 10$ .

Fixing  $y$ , we may view the probability of the data as a function of  $\theta$  – when it is known as the **likelihood function**:

$$L(\theta) = \theta^y (1 - \theta)^{N-y}.$$



# Elements of Bayes Theorem for a Binomial Model

The **maximum likelihood estimate** (MLE) is the proportion of successes:

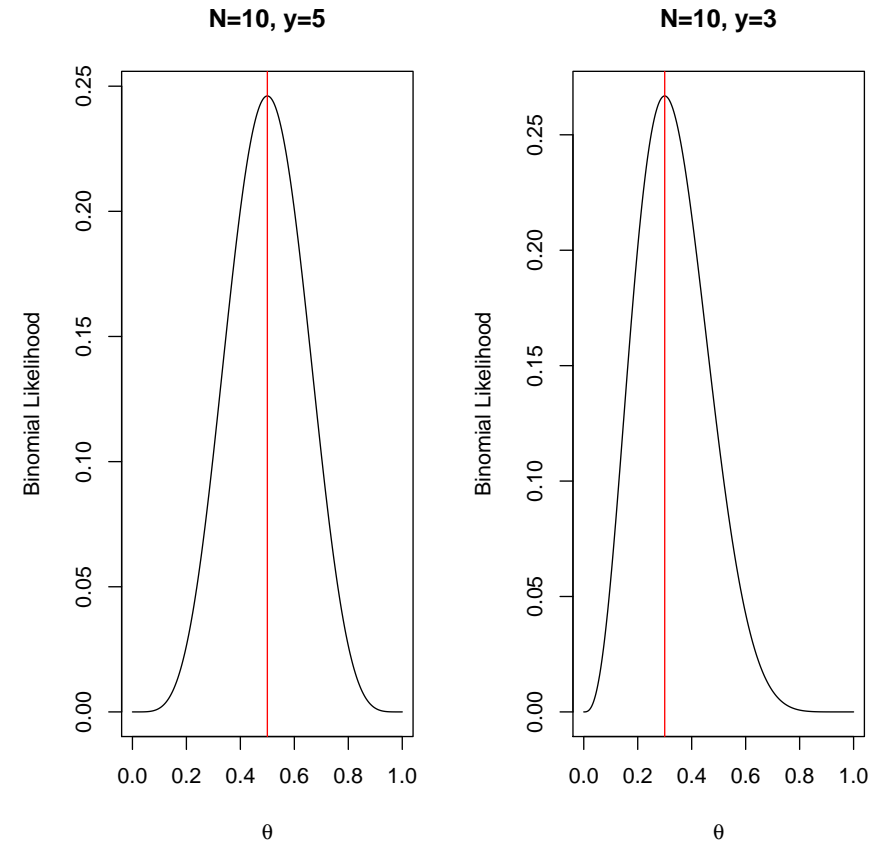
$$\hat{\theta} = \frac{y}{N} = \bar{y},$$

and gives the highest probability to the observed data, i.e., maximizes the likelihood function. The standard error of this estimate is

$$\sqrt{\theta(1 - \theta)/N}.$$

which we approximate by

$$\sqrt{\hat{\theta}(1 - \hat{\theta})/N}.$$



Binomial **likelihoods** for  $y = 5$  (left) and  $y = 10$  (right), with  $N = 10$ . The MLEs are indicated in **red**.

# Bayes and frequentist estimates for binomial

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If  $y = 0$  ( $y = N$ ), we get estimate  $\hat{\theta} = 0$  ( $=1$ ) and a standard error of 0, which is clearly problematic.

Agresti & Coull (1998) give a famous workaround, the “Adjusted Wald interval”: with estimate

$$\tilde{\theta} = \frac{4}{N+4} \frac{1}{2} + \frac{N}{N+4} \bar{y},$$

to give the interval:

$$\tilde{\theta} \pm 1.96 \sqrt{\tilde{\theta}(1 - \tilde{\theta})/N}.$$

It works well in practice, but what might be a more convincing justification for it?

# Beta priors for Binomial $\theta$

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Recall Bayes Theorem:  $p(\theta|y) \propto p(y|\theta) \times p(\theta)$ .

- Bayes theorem requires the *likelihood*, which we have already specified as binomial, and a *prior*.
- For a probability  $0 < \theta < 1$  an obvious candidate prior is the uniform (i.e. flat) distribution on  $(0,1)$ : but this is too restrictive for general use.
- The **beta distribution**,  $\text{Beta}(a,b)$ , is more flexible. (The uniform distribution is a special case with  $a = b = 1$ .) We specify  $a$  and  $b$  **in advance**, i.e., *a priori*.
- The form of the beta distribution is

$$p(\theta) = \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \theta^{a-1} (1-\theta)^{b-1}$$

for  $0 < \theta < 1$ , where  $\Gamma(\cdot)$  is the gamma function\*.

$$*\Gamma(z) = \int_0^\infty t^{z-1} e^{-t} dt$$

# Beta priors for Binomial $\theta$

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- The Beta( $a, b$ ) distribution is valid<sup>†</sup> for  $a > 0, b > 0$ .
- How can we think about specifying  $a$  and  $b$ ?
- As you may know, the Normal distribution is specified by its mean ( $\mu$ ) and variance ( $\sigma^2$ ), but the beta distribution's  $a$  and  $b$  are less simple.
- The mean and variance are:

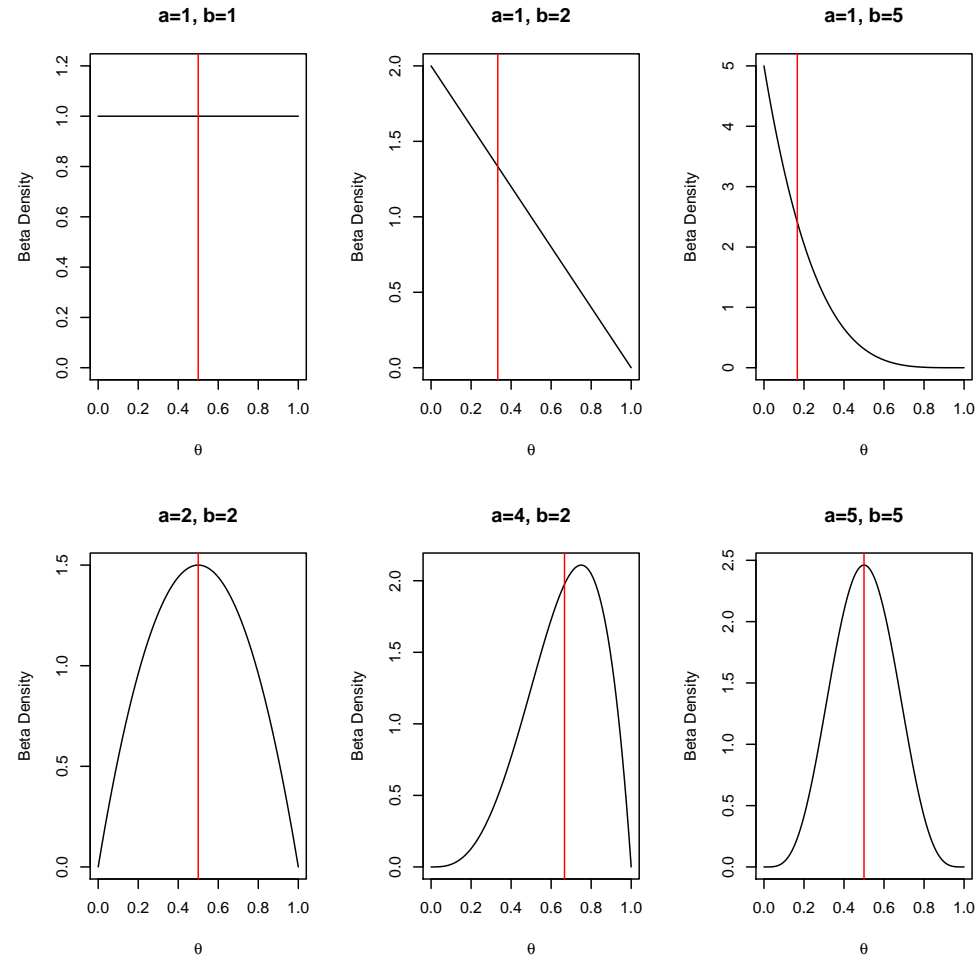
$$\begin{aligned}\mathbb{E}[\theta] &= \frac{a}{a+b} \\ \text{Var}[\theta] &= \frac{\mathbb{E}[\theta](1 - \mathbb{E}[\theta])}{a+b+1}.\end{aligned}$$

Hence, increasing  $a$  and  $b$  **concentrates** the distribution about the mean.

<sup>†</sup>A distribution is valid if it is non-negative and integrates to 1

# Beta priors for Binomial $\theta$

The quantiles, e.g. the median or the 10% and 90% points, are not available as a simple formula, but are easily obtained within software – in R we use the function `qbeta(p,a,b)`.



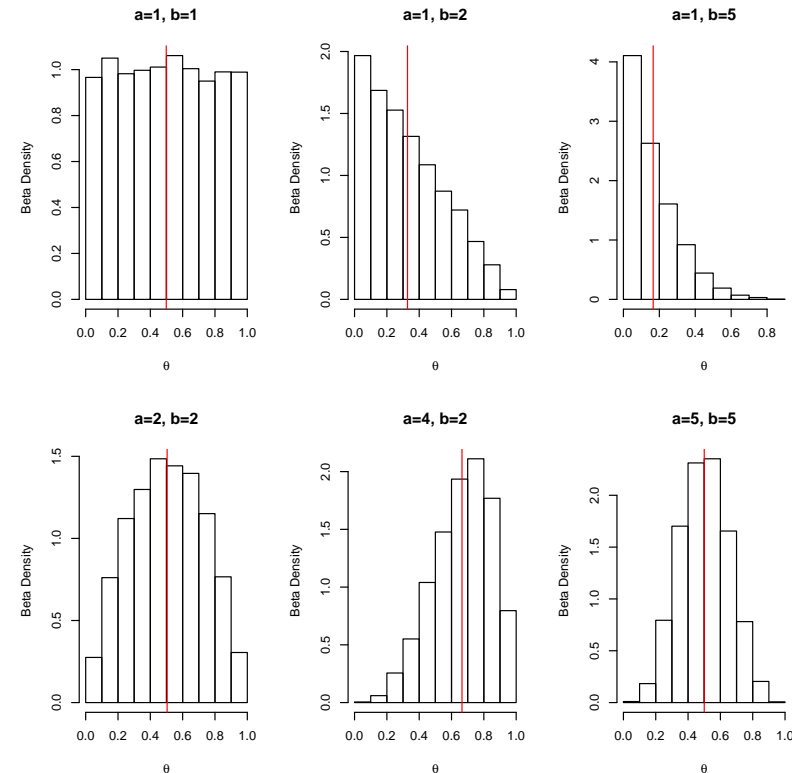
Beta distributions,  $\text{Beta}(a, b)$  (right).  
The **red** lines indicate the means.



# Samples to Summarize Beta Distributions

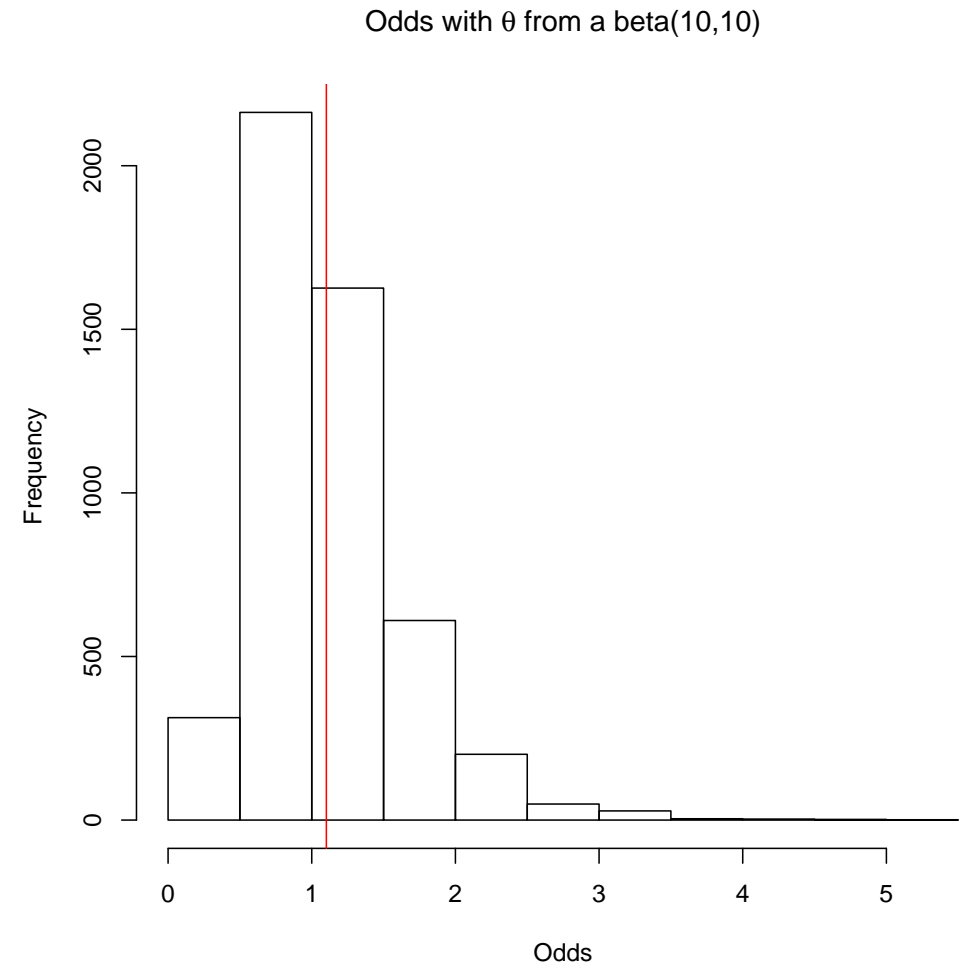
Probability distributions and samples from distributions are equivalent, in a sense: given a probability distribution we can generate samples, and given a big-enough sample we can reconstruct their probability distribution. (More on this later!)

- Probability distributions can be investigated by generating samples from them, and then examining histograms, moments and quantiles
- Right, some histograms of samples from beta distributions for different choices of  $a$  and  $b$ , with sample means in red
- Compare with previous slide to see the duality



# Samples for Describing Weird Parameters

- Generating samples for e.g. a Beta's mean seems overkill – recall 2.22
- But for **functions** of the probability  $\theta$ , such as the odds  $\theta/(1 - \theta)$ , sampling is the easiest method
- Once we have samples for  $\theta$  we can simply **transform** the samples to the functions of interest.
- We may have clearer prior opinions about the odds, than the probability.
- Right: samples from the prior on the odds  $\theta/(1 - \theta)$  with  $\theta \sim \text{Beta}(10, 10)$ . The **red** line indicates the sample mean.



# Issues with Uniform Priors

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If we have little prior information about a parameter, we might think that a **uniform prior**, i.e. a prior  $p(\theta) \propto \text{const}$  reflects this ignorance. But there are two problems:

1. We can't be uniform on all scales since, if  $\phi = g(\theta)$ :

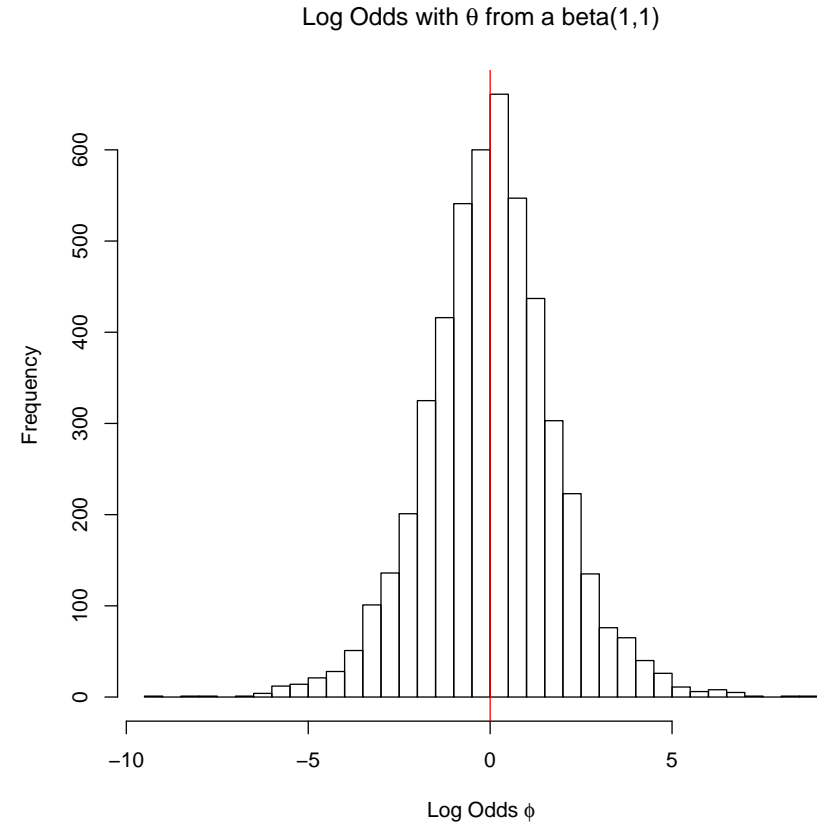
$$\underbrace{p_\phi(\phi)}_{\text{Prior for } \phi} = \underbrace{p_\theta(g^{-1}(\phi))}_{\text{Prior for } \theta} \times \underbrace{\left| \frac{d\theta}{d\phi} \right|}_{\text{Jacobian}}$$

and so if  $g(\cdot)$  is a nonlinear function, the Jacobian will be a function of  $\phi$  and hence not uniform.

2. If the parameter is not on a finite range, an **improper** distribution will result (that is, the form will not integrate to 1). This can lead to an improper posterior distribution, and without a proper posterior we can't do inference.

# Issues with Uniform Priors

- For example, what does a flat prior on Binomial  $\theta$  imply about log odds  $\phi = \log\left(\frac{\theta}{1-\theta}\right)$ ? (Both are arguable ‘natural’ choices)
- The answer (right) is a very **non**-uniform distribution



Not being uniform on all scales need not be a problem, but do be aware of it, and cautious with ‘flat’ priors. They don’t describe ignorance – often the opposite.

# Posterior Derivation: The Quick Way

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When we want to identify a particular probability distribution we *only* need to concentrate on terms that involve the random variable.

For example: as seen in 2.21, the form of the beta distribution is

$$p(\theta) = \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \theta^{a-1} (1-\theta)^{b-1}$$

**But** if we just knew the density was proportional to  $\theta^{a-1}(1-\theta)^{b-1}$ , we could work out the other terms – all they do is ensure  $p(\theta)$  integrates to 1.

(We haven't yet looked at Normal distributions, but for random variable  $X$  with density of the form  $p(x) \propto \exp(c_1x^2 + c_2x)$  for constants  $c_1$  and  $c_2$ , then we *know* that the random variable  $X$  *must* have a Normal distribution.)

# Posterior Derivation: The Quick Way

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For the binomial model with a beta prior, the **posterior** is

$$\begin{aligned} p(\theta|y) &= \mathbb{P}(y|\theta) \times p(\theta) \\ &= \binom{N}{y} \theta^y (1-\theta)^{N-y} \times \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \theta^{a-1} (1-\theta)^{b-1} \end{aligned}$$

but all we need to focus on is the terms in  $\theta$ :

$$\begin{aligned} p(\theta|y) &\propto \theta^y (1-\theta)^{N-y} \times \theta^{a-1} (1-\theta)^{b-1} \\ &= \theta^{y+a-1} (1-\theta)^{N-y+b-1}. \end{aligned}$$

From this form, we know the posterior **must** be a  $\text{Beta}(y+a, N-y+b)$  distribution – and so can work out its mean, quantiles etc, just like we did for Beta priors.

This is an example of a **conjugate** Bayesian analysis, in which the prior is in the same family as the posterior.

# Agresti and Coull's adjusted interval

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Recall, from earlier, the *adjusted Wald interval*:

$$\begin{aligned}\tilde{\theta} &\pm 1.96\sqrt{\tilde{\theta}(1 - \tilde{\theta})/N}, \text{ where} \\ \tilde{\theta} &= \frac{1}{2} \frac{4}{N + 4} + \bar{y} \frac{N}{N + 4}.\end{aligned}$$

Notice the link with the adjusted Wald interval for the 0 successes case, the estimate is equal to the posterior mean with a Beta( $a, b$ ) prior with  $a = b = 2$ .

# Posterior Summaries

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- Reporting a point estimate (e.g. posterior mean, or median) alone is rare
- **Credible intervals** – regions that capture a fixed proportion of the posterior support (usually 95%) are the standard way to describe uncertainty.
- These also permit a form of testing, by reporting whether a 95% interval contain the value  $\theta_0 = 0.5$
- A typical way to construct a 90% posterior credible interval  $(\theta_L, \theta_U)$  is to solve

$$\begin{aligned} 0.05 &= \int_0^{\theta_L} p(\theta|y) \, d\theta \\ 0.95 &= \int_0^{\theta_U} p(\theta|y) \, d\theta \end{aligned}$$



# Posterior Summaries

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- The quantiles of a beta are not available in closed form, but are easy to evaluate in R:

```
y <- 7; N <- 10; a <- b <- 1  
qbeta(c(0.05,0.5,0.95),y+a,N-y+b)  
[1] 0.4356258 0.6761955 0.8649245
```

- ...so the posterior median is 0.68 and a 90% credible interval is [0.44,0.86].
- Compare this to the MLE of 0.70 and asymptotic 90% confidence interval of  $0.70 \pm 1.645 \times \sqrt{0.7 \times 0.3/10} = [0.46, 0.94]$ .

# Bayes and Frequentist Estimates for Binomial

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**Example:**  $N = 10, y = 0$  gives

$$\tilde{\theta} = \frac{4}{10+4} \frac{1}{2} + \frac{10}{10+4} \bar{y} = \frac{4}{28} = 0.14$$

with adjusted standard error

$$\sqrt{\tilde{\theta}(1 - \tilde{\theta})/10} = \sqrt{\frac{4}{28} \left(1 - \frac{24}{28}\right) / 10} = 0.11$$

... but  $0.14 \pm 1.96 \times 0.11$  goes negative! Using Bayes instead with a Beta(2,2) prior for  $\theta$ :

```
y <- 0; N <- 10; a <- b <- 2; apost <- a+y; bpost <- b+(N-y)
qbeta(p=c(0.025,0.975), apost, bpost)
[1] 0.01920667 0.36029744
```

So a Bayesian 95% credible interval is (0.019,0.36).

# A more challenging example, from COVID

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Suppose a seroprevalence test is carried out with

- Sensitivity,  $\mathbb{P}[ \text{+ve test} \mid \text{disease} ]$  denoted  $\delta$  and assumed known
- Specificity,  $\mathbb{P}[ \text{-ve test} \mid \text{no disease} ]$  denoted  $\gamma$  and assumed known
- True prevalence denoted  $\pi$  – this is what's of interest

We test  $n$  people and  $y$  are recorded as having the disease. Our initial model is

$$y|p \sim \text{Binomial}(N, p)$$

where  $p$  is the probability of a +ve test result, with

$$\begin{aligned} p &= \mathbb{P}( \text{+ve test} ) \\ &= \mathbb{P}( \text{+ve test} \mid \text{disease} )\mathbb{P}( \text{disease} ) \\ &\quad + \mathbb{P}( \text{+ve test} \mid \text{no disease} )\mathbb{P}( \text{no disease} ) \\ &= \delta\pi + (1 - \gamma)(1 - \pi) = \pi(\delta + \gamma - 1) + (1 - \gamma) \end{aligned}$$

# A more challenging example, from COVID

---

With this binomial model the MLE is (exercise!):

$$\hat{\pi} = \frac{y - N(1 - \gamma)}{N(\delta + \gamma - 1)}.$$

This estimate, and approximate confidence intervals, don't do a good job of avoiding negative prevalences.

A Bayesian model is

$$\begin{aligned} y|\pi &\sim \text{Binomial}(N, \pi(\delta + \gamma - 1) + (1 - \gamma)) \\ \pi &\sim \text{Beta}(a, b) \end{aligned}$$

Not conjugate!

However, a simple rejection algorithm ([Gelfand & Smith 1992](#)) can be implemented that simulates samples from the posterior  $p(\pi|y)$ .

# A more challenging example, from COVID

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We'll use a *rejection algorithm* to generate samples from the posterior. For unknown parameter  $\boldsymbol{\theta}$  with likelihood  $p(\mathbf{y} \mid \hat{\boldsymbol{\theta}})$  with maximum value  $M = p(\mathbf{y} \mid \hat{\boldsymbol{\theta}})$  for MLE  $\hat{\boldsymbol{\theta}}$ , the algorithm has two steps:

1. Generate  $\boldsymbol{\theta} \sim \pi(\boldsymbol{\theta})$  from the prior
2. Generate  $U \sim U(0, 1)$  and if

$$U < \frac{p(\mathbf{y} \mid \boldsymbol{\theta})}{M},$$

accept that  $\boldsymbol{\theta}$  – otherwise return to 1.

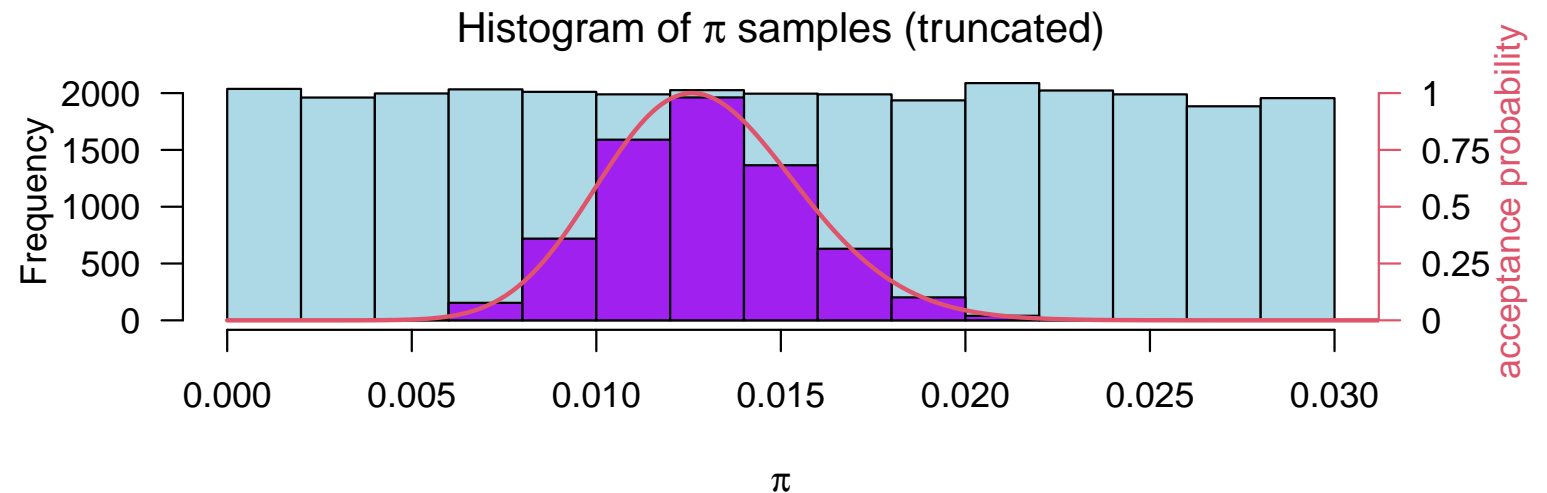
The probability that a point is accepted is given by

$$p_a = \frac{\int p(\mathbf{y} \mid \boldsymbol{\theta}) \pi(\boldsymbol{\theta}) d\boldsymbol{\theta}}{M} = \frac{p(\mathbf{y})}{M}.$$

# A more challenging example, from COVID

In early April, 2020, [Bendavid et al](#) recruited  $n=3330$  residents of Santa Clara County, California and tested them for COVID-19 antibodies. With  $y=50$  positive tests, the naïve estimate is 1.50%. We'll assume sensitivity is  $\delta = 0.8$  and specificity is  $\gamma = 0.995$ , and use a flat prior parameters with  $a = b = 1$ ;

Prior and posterior samples for prevalence  $\pi$ . The posterior median is 1.28% and a 90% interval is (0.87%, 1.77%).



See [Gelman & Carpenter 2020](#) for a more comprehensive Bayesian analysis

# A more challenging example, from COVID

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R code to do the analysis:

```
lik <- function(pi){ dbinom(y, n, pi*(delta+gamma-1) + (1-gamma) ) } # likelihood
M    <- dbinom(y, n, y/n)          # likelihood at MLE

set.seed(4) # random number seed
bigB      <- 1E6 # number of step 1 samples to take
many.pi   <- rbeta(bigB, 1,1) # samples from prior
many.u    <- runif(bigB)      # samples from uniform

post.pi <- subset( many.pi, many.u < lik(many.pi)/M ) # evaluation step

# summarize the posterior
length(post.pi)
[1] 6677
quantile(post.pi, c(0.5, 0.05, 0.95))
      50%      5%      95%
0.012841460 0.008695393 0.017657390
```

This method works (eventually!) for any bounded likelihood.

# Summary

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Conjugate analyses are computationally convenient but rarely available in practice.

Historically, the philosophical standpoint of Bayesian statistics was emphasized, now pragmatism is taking over.

Benefits of a Bayesian approach:

- Inference is based on probability and output is very intuitive
- Framework is flexible, and so complex models can be built
- Can incorporate prior knowledge
- If the sample size is large, prior choice is less crucial (generally!)



# Summary

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## Challenges of a Bayesian analysis:

- Requires a **likelihood** and a **prior**, and inference is only as good as the appropriateness of these choices.
- **Computation** can be daunting, though software is becoming more user-friendly and flexible; later we will describe and illustrate a number of approaches including INLA and Stan.
- One should be wary of models becoming **too elaborate** – we have the technology to contemplate complicated models, but do the data support complexity?

# Posterior Derivation: The Long Way

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- The posterior can also be calculated by keeping in all the normalizing constants:

$$\begin{aligned} p(\theta|y) &= \frac{\mathbb{P}(y|\theta) \times p(\theta)}{\mathbb{P}(y)} \\ &= \frac{1}{\mathbb{P}(y)} \binom{N}{y} \theta^y (1-\theta)^{N-y} \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \theta^{a-1} (1-\theta)^{b-1}. \end{aligned}$$

- The normalizing constant is

$$\begin{aligned} \mathbb{P}(y) &= \int_0^1 \mathbb{P}(y|\theta) \times p(\theta) d\theta \\ &= \binom{N}{y} \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \int_0^1 \theta^{y+a-1} (1-\theta)^{N-y+b-1} d\theta \\ &= \binom{N}{y} \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \frac{\Gamma(y+a)\Gamma(N-y+b)}{\Gamma(N+a+b)} \end{aligned}$$

- The integrand on line 2 is a  $\text{Beta}(y+a, N-y+b)$  distribution, up to a normalizing constant, and so we know what this constant has to be.

# Posterior Derivation: The Long Way

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- The normalizing constant is therefore:

$$\mathbb{P}(y) = \binom{N}{y} \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} \frac{\Gamma(y+a)\Gamma(N-y+b)}{\Gamma(N+a+b)}$$

- This is a probability distribution, i.e.  $\sum_{y=0}^N \mathbb{P}(y) = 1$  with  $\mathbb{P}(y) > 0$ , for  $y = 0, 1, \dots, N$ .
- For a particular  $y$  value, this expression tells us the probability of that value **given** the model, i.e. the likelihood and prior we have selected: this will reappear later in the context of **hypothesis testing**.
- Substitution of  $\mathbb{P}(y)$  into (1) and canceling the terms that appear in the numerator and denominator gives the posterior:

$$p(\theta|y) = \frac{\Gamma(N+a+b)}{\Gamma(y+a)\Gamma(N-y+b)} \theta^{y+a-1} (1-\theta)^{N-y+b-1}$$

which is a **Beta( $y+a, N-y+b$ )**.

# The Posterior Mean: A Summary of the Posterior

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- Recall the mean of a  $\text{Beta}(a, b)$  is  $a/(a + b)$ .
- The posterior mean of a  $\text{Beta}(y + a, N - y + b)$  is therefore

$$\begin{aligned}\mathbb{E}[\theta|y] &= \frac{y + a}{N + a + b} \\ &= \frac{y}{N + a + b} + \frac{a}{N + a + b} \\ &= \frac{y}{N} \times \frac{N}{N + a + b} + \frac{a}{a + b} \times \frac{a + b}{N + a + b} \\ &= \text{MLE} \times W + \text{Prior Mean} \times (1 - W).\end{aligned}$$

- The **weight**  $W$  is

$$W = \frac{N}{N + a + b}.$$

- As  $N$  increases, the weight tends to 1, so that the posterior mean gets closer and closer to the MLE.

# The Posterior Mean: A Summary of the Posterior

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- Notice that the **uniform** prior  $a = b = 1$  gives a posterior mean of

$$\mathbb{E}[\theta|y] = \frac{y + 1}{N + 2}.$$