

# **SAMPLING PROBABILITY DISTRIBUTIONS**

From conjugacy to Hamiltonian Monte Carlo

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## Last time:

- Bayesian inference *always* starts with a model for the **joint distribution** of  $\theta$  and  $y$ .

$$\pi(\theta, y) = f(y|\theta)\pi(\theta) = \pi(\theta|y)m(y).$$

- $\pi(\theta|y)$  is the **posterior distribution** of  $\theta$  given  $y$ ,
- $f(y|\theta)$  is the **sampling distribution** for  $y$  given  $\theta$ ,
- $\pi(\theta)$  is the **prior distribution** of  $\theta$ ,
- $m(y)$  is the **marginal distribution** of  $y$ .

- Bayes rule** yields the **posterior distribution**

$$\pi(\theta|y) = \frac{f(y, \theta)}{m(y)} = \frac{f(y|\theta)\pi(\theta)}{m(y)} \propto \text{Likelihood} \times \text{Prior}.$$

- All of the information used in the *update* to our prior is encoded in the **likelihood**,

$$L(\mathbf{y}|\theta) = \prod_{i=1}^N f(y_i|\theta).$$

- Likelihood principle*: implies proportional likelihoods encode equivalent updates for a single observer.
- Two people can have different epistemic uncertainty (different priors).
- The likelihood principle does not imply equivalent Bayesian inferences (corollary to Gelman, 2017).

# Lecture 10 of Statistical Rethinking

Key takeaways:

- Bayes is all about the posterior distribution, not how you compute it.
- Sometimes, we can't get the posterior analytically, but we can approximate it by sampling.
- Samples also give us a way to approximate the distributions of complicated functionals of the posterior.
- Markov Chain Monte Carlo is one way to sample.
  - Metropolis/Metropolis-Hastings.
  - Hamiltonian Monte Carlo.

## Iterations on Bayesian analysis of binomial data

- Motivating example — PREVAIL II Trial.
- Analysis with conjugate priors, beta-binomial model.
- Prior selection.
- Analysis with non-conjugate priors.
- First look at Stan if there's time.

# Motivating Example — PREVAIL II Trial

## Context:

- 2014–2016 Ebola virus disease (EVD) outbreak in Guinea, Liberia, and Sierra Leone.
- Over 28,000 suspected or confirmed cases and 11,000 fatalities.
- Urgent need to identify effective therapeutics to reduce mortality.

## Partnership for Research on Ebola Virus in Liberia (PREVAIL) II trial:

- Adaptive trial to determine the effectiveness of Zmapp, and possibly other agents, in reducing Ebola mortality.
- Primary endpoint: 28 day mortality on optimized standard of care (oSOC) vs. Zmapp + oSOC.
- 72 patients enrolled at sites in Liberia, Sierra Leone, Guinea, and the US.
  - Overall mortality: 21/71 died (30%),
  - SOC alone: 13/35 (37%),
  - Zmapp + SOC: 8/36 (22%).
- ~~Super-duper~~ Barely Bayesian design (Proschan, 2016).

## Motivating Example — PREVAIL II Trial

**Target of inference:**  $\pi(p_T, p_C | y_T, y_C)$ , the posterior distributions for probability of death on treatment (T) and control (C).

- $p_T, p_C$ : probabilities of 28 day mortality on T and C.
- $y_T, y_C$ : # of deaths on T and C.
- $N_T, N_C$ : # participants randomized to T and C.

### Some questions of interest:

- Evidence for Zmapp + oSOC more effective than oSOC alone:  $\Pr(p_T < p_C | y_T, y_C)$ .
- Effectiveness of Zmapp + oSOC, effectiveness of oSOC alone:  $\pi(p_T | y_T)$ ,  $\pi(p_C | y_C)$ .

# A Simple Model for Count Data

## Binomial count model:

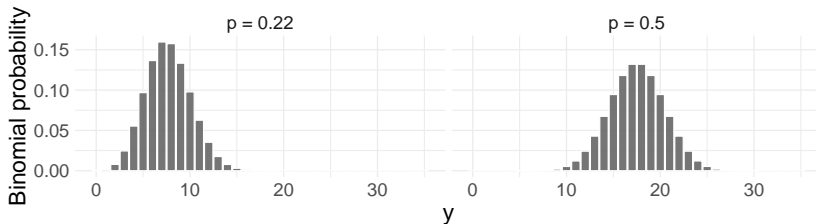
- Arises as a model for *independent* binary random variables (RVs),  $Z_i \in \{0, 1\}$ ,  $i = 1, \dots, N$ , with *common success probability*,  $p$ .
- Let  $Y = \sum_{i=1}^N Z_i$ . The probability of seeing  $Y = y$  successes in  $N$  trials is

$$\begin{aligned}\Pr(Y = y|p) &= \binom{N}{y} p^y (1 - p)^{N-y}. \\ &\propto p^y (1 - p)^{N-y}\end{aligned}\tag{1}$$

- For fixed  $y$ , we can view (1) as a function of  $p$  – this is the **likelihood function**.
- The maximum likelihood estimate (MLE),  $\hat{p} = y/N$ , is the value of  $p$  under which the observed data are most likely (i.e.,  $\hat{p}$  maximizes the likelihood).

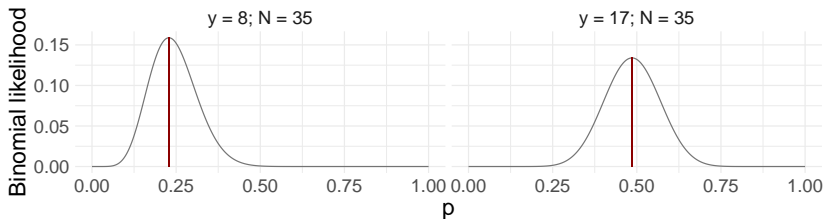
# A Simple Model for Count Data

## Binomial distributions for two values of $p$



## Binomial likelihoods for two datasets

Likelihoods in black, MLEs in red





# Beta Distribution as a Prior for a Binomial Probability

## Beta distribution

- If we thought all values of  $p$  were equally likely, could take  $p \sim \text{Unif}(0, 1)$ . In general, this is too restrictive.
- More flexible:  $\theta \sim \text{Beta}(a, b)$ , with  $a > 0, b > 0$ , where

$$\begin{aligned}\pi(\theta|a, b) &= \frac{\Gamma(a+b)}{\Gamma(a)\Gamma(b)} p^{(a-1)}(1-p)^{b-1}, \\ &\propto p^{(a-1)}(1-p)^{b-1},\end{aligned}\tag{2}$$

for  $0 < p < 1$  and where  $\Gamma(\cdot)$  is the gamma function<sup>1</sup>.

- $p \sim \text{Unif}(0, 1)$  is equivalent to  $p \sim \text{Beta}(1, 1)$ .
- Moments:

$$\begin{aligned}\mathbb{E}(p|a, b) &= \frac{a}{a+b}, \\ \text{Var}(p|a, b) &= \frac{ab}{(a+b)^2(a+b+1)}.\end{aligned}$$

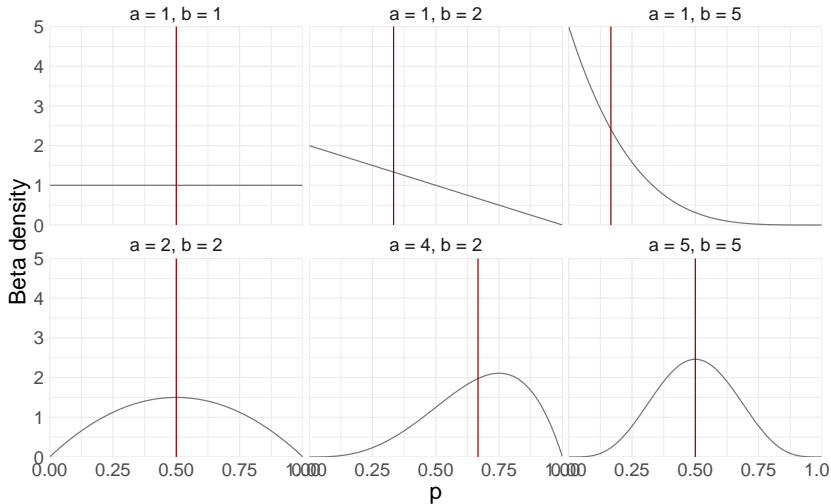
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<sup>1</sup> $\Gamma(z) = \int_0^\infty t^{z-1} e^{-t} dt$ , more on the Beta distribution [here](#).

# Beta Distribution as a Prior for a Binomial Probability

## Beta densities for various hyperparameters

Density in black, mean in red



# Posterior Derivation

In the Beta-Binomial hierarchy, concentrate only on terms that involve  $\theta$ .

$$\begin{aligned}\pi(p|y) &\propto L(y|p)\pi(p), \\ &= p^y(1-p)^{N-y} \times p^{a-1}(1-p)^{b-1}, \\ &= p^{y+a-1}(1-p)^{N-y+b-1}, \\ &= p^{\tilde{a}-1}(1-p)^{\tilde{b}-1},\end{aligned}$$

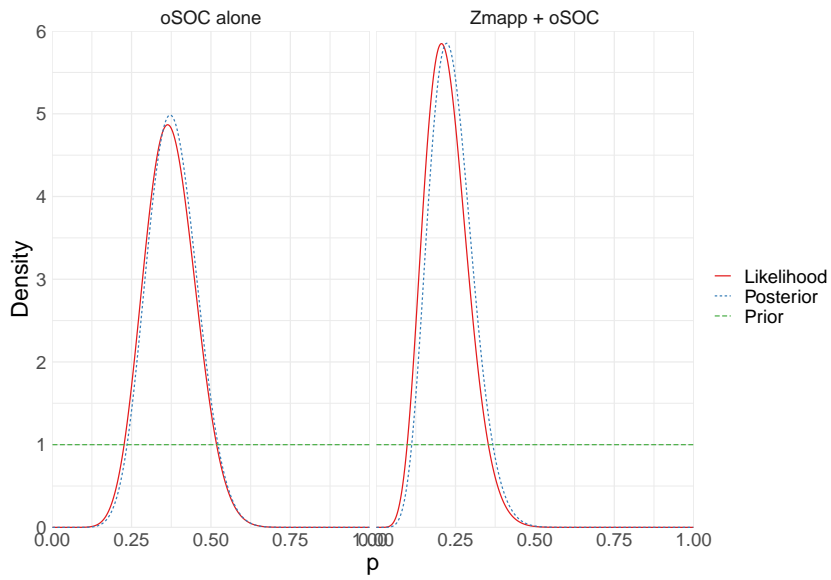
where  $\tilde{a} = y + a$  and  $\tilde{b} = N - y + b$ .

- The posterior takes the form of a  $\text{Beta}(\tilde{a}, \tilde{b})$ !
- We say the prior is *conjugate* when the posterior is of the same form as the prior.
- Fun fact: all exponential family distributions have conjugate priors!

## PREVAIL II Posterior Distributions

- Priors:  $p_T \sim \text{Beta}(1, 1)$  and  $p_C \sim \text{Beta}(1, 1)$ .
- Data:  $y_T = 8$  and  $y_C = 13$ , with  $N_T = 36$  and  $N_C = 35$ .
- Posteriors:  $p_T|y_T \sim \text{Beta}(9, 29)$  and  $p_C|y_C \sim \text{Beta}(14, 23)$ .
  - Posterior medians (95% Credible Intervals):
    - Zmapp + oSOC,  $p_T|y_T$  0.23 (0.12, 0.38),
    - oSOC alone,  $p_C|y_C$ : 0.38 (0.23, 0.54).
    - Risk difference,  $p_T - p_C \mid y_T, y_C$ : -0.14 (-0.34, 0.06).
    - Risk ratio,  $p_T/p_C \mid y_T, y_C$ : 0.62 (0.29, 1.24).
    - Odds ratio,  $[(p_T/(1 - p_T)) / (p_C/(1 - p_C))] \mid y_T, y_C$ : 0.50(0.18, 1.36)
    - $\Pr(p_T < p_C|y_T, y_C) \approx 0.91$ .

# PREVAIL II Posterior Distributions



# Posterior Mean and Likelihood-Prior Interaction

- 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

$$\begin{aligned} E(p|y) &= \frac{y + a}{N + a + b} \\ &= \frac{y}{N + a + b} + \frac{a}{N + a + b} \\ &= \frac{y}{N} \times \frac{N}{N + a + b} + \frac{a}{a + b} \times \frac{a + b}{N + a + b} \\ &= \text{MLE} \times W + \text{PriorMean} \times (1 - W), \end{aligned}$$

where 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 to the MLE.
- Notice that the uniform prior  $a = b = 1$  gives a posterior mean of  $E(p|y) = \frac{y+1}{N+2}$ .

# Choosing Prior Hyperparameters

## How to specify hyperparameters $a$ and $b$ ?

- *Suggestion #1:* Use information about prior mean prior “sample size.”
  - Prior mean:  $m_{\{prior\}} = a/(a+b)$ .
  - Recall,  $E(p|y) = \frac{y+a}{N+a+b}$ , so the denominator is like the posterior sample size,  
 $\implies N_{prior} = a + b$ .
  - Solve for  $a$  and  $b$  via

$$a = N_{prior} \times m_{prior},$$
$$b = N_{prior} \times (1 - m_{prior}).$$

- *Intuition:* view  $a$  and  $b$  as pseudo-observations of successes and failures.
- *Suggestion #2:* Choose  $a$  and  $b$  by specifying two quantiles for  $p$  associated with prior probabilities.
  - e.g.,  $\Pr(p < 0.2) = 0.1$  and  $\Pr(p > 0.6) = 0.1$ .
  - Can find values of  $a$  and  $b$  numerically.
  - In more complicated models, simulate.

# How to Specify Priors in General?

**Theme:** What aspects of my model do I know something about? How do I encode that knowledge?

- **Containment:** Does my prior predictive distribution produce realistic datasets?
- **Caveat:** People who don't interrogate and justify their priors deserve what's coming to them.
  - Table of priors with references.
  - Prior predictive checks.
  - Sensitivity analyses.



# Issues with Uniformity

We might think that if we have little prior opinion about a parameter then we can simply assign a **uniform prior**, i.e. a prior  $p(\theta) \propto \text{constant}$ .

There are two problems with this strategy:

- 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 (more on this in a bit).

- 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 all kinds of paradoxes (see e.g., Dawid, 1973).
- And importantly, improper priors are non-generative  $\implies$  cannot interrogate their predictive distribution.

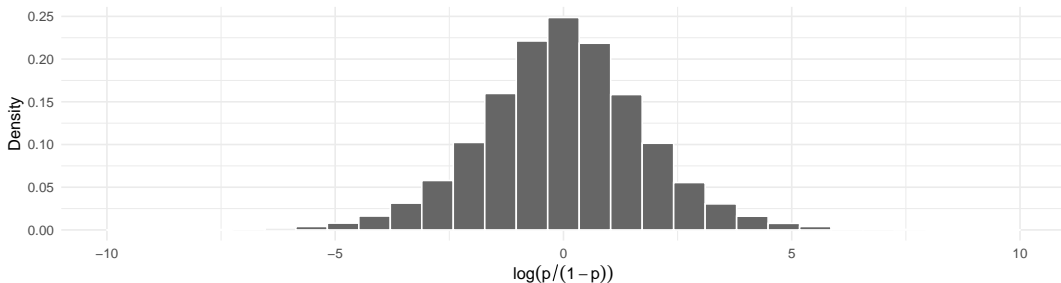
# Are Priors Really Uniform?

- In the binomial example,  $p \sim \text{Unif}(0, 1)$  seems a natural choice.
- But suppose we are going to model on the logistic scale so that

$$\phi = \log \left( \frac{\theta}{1 - \theta} \right)$$

is a quantity of interest. -A uniform prior on  $\theta$  produces the very non-uniform distribution on  $\phi$ .  
-Not being uniform on all scales is not a problem, and is correct probabilistically, but one should be aware of this characteristic.

Uniform(0,1) samples on the log-odds scale

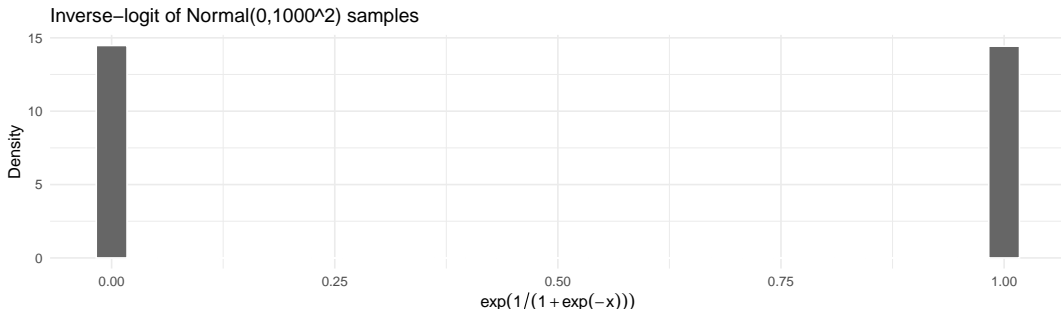


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# Non-Conjugate Priors

Suppose we want to model mortality on the log-odds scale,  $\theta = \log(p/(1 - p))$ .

Bayesian inference *always* starts with a model for the **joint distribution** of  $\theta$  and  $y$ .

- The parameter in our model is  $\theta$ .
- Lose conjugacy, no closed form for the posterior, now we rely on MCMC.
- Our MCMC targets the posterior  $\pi(\theta|y) \propto \pi(\theta, y) = L(y|\theta)\pi(\theta)$ .
- If our prior is on the log-odds of death, we have no problems. It does not matter that  $L(y|\theta) = \text{Binomial}(N, 1/(1 + \exp(-\theta)))$ .
- If our prior is on the probability of death but our model is defined in terms of the log-odds, we must include a Jacobian adjustment.

**Critical:** We must never lose sight of how our model is defined.

For more on this, see this [case study](#) by Bob Carpenter.

# Why Non-Conjugate Priors?

- Information encoded naturally on other scales.
- More flexible/natural representation using other types of distributions.
- Hierarchical information.
- Computational considerations.
- Induce particular features in the posterior, e.g., sparsity.

# Next week

Linear regression. Watch lecture 3 (SmaRt).

We'll talk about:

- Bayesian linear regression.
- Weekly informative priors.

# References

P.A. Dawid, M. Stone, and J.V. Zidek. "Marginalization paradoxes in Bayesian and structural inference." *Journal of the Royal Statistical Society: Series B (Methodological)* 35.2 (1973): 189-213.

A. Gelman, D.A. Simpson, and M. Betancourt. "The prior can often only be understood in the context of the likelihood." *Entropy* 19.10 (2017): 555.

The PREVAIL II Writing Group and Multi-National PREVAIL II Study Team. "A randomized, controlled trial of ZMapp for Ebola virus infection." *The New England Journal of Medicine* 375.15 (2016): 1448.

M.A. Proschan, L.E. Dodd, and D. Price. "Statistical considerations for a trial of Ebola virus disease therapeutics." *Clinical Trials* 13.1 (2016): 39-48.

