

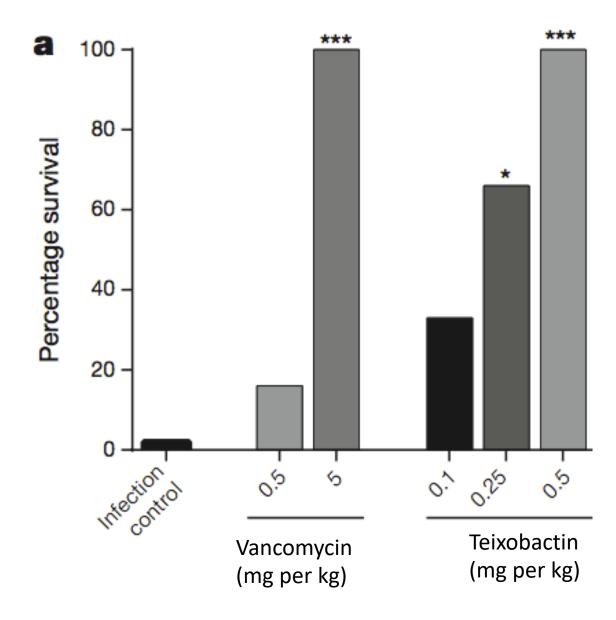


A new antibiotic

The paper announced the discovery of a new polypeptide antibiotic (tiexobactin).

Mice were given a lethal infection, and then treated with two antibiotics at different doses.

Something about the graph is funny.

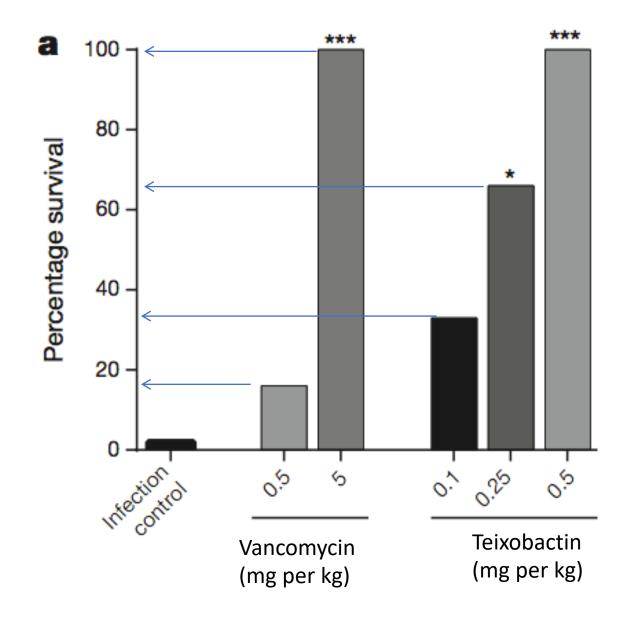


A new antibiotic

The paper announced the discovery of a new polypeptide antibiotic (tiexobactin).

Mice were given a lethal infection, and then treated with two antibiotics at different doses.

Something about the graph is funny.



A new antibiotic

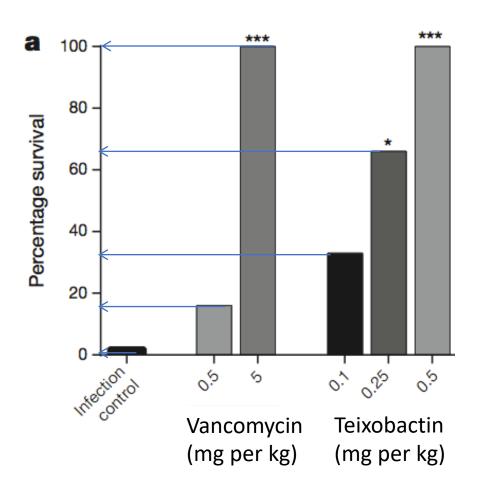
The paper announced the discovery of a new polypeptide antibiotic (tiexobactin).

Mice were given a lethal infection, and then treated with two antibiotics at different doses.

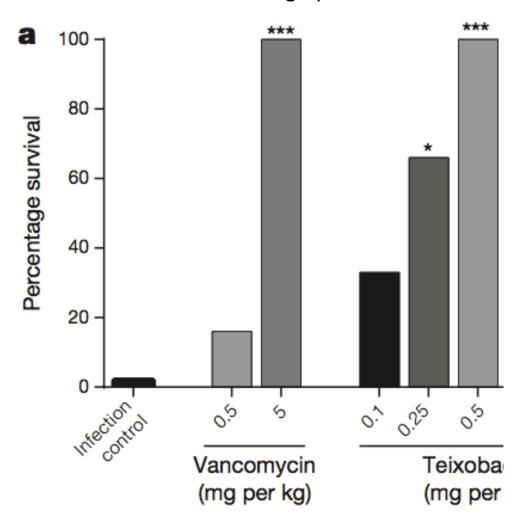
Something about the graph is funny.

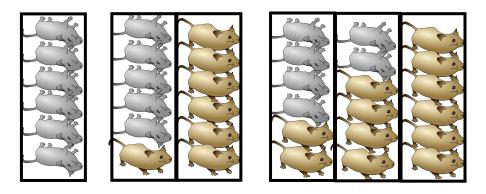
All of the bars are multiples of 1/6. Read the fine print..

Ling et al. Nature 517:455 (2015)



This graph summarizes the fates of thirty-six mice, six cages of six mice each.





$$P_{\text{Binomial}}(k; n, p) = {}_{n}C_{r} p^{k} (1-p)^{n-k}$$

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = \binom{n}{k} p^{k} (1-p)^{n-k}$$

$$P_{\text{Binomial}}(k; n, p) = \frac{n!}{k!(n-k!)} p^{k} (1-p)^{n-k}$$

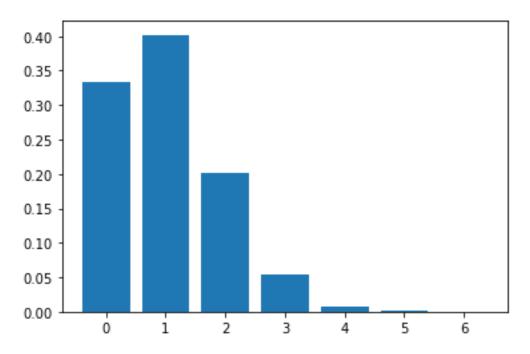
This is the number of outcomes (these are rows from Pascal's triangle)

This is the probability of each outcome

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = {}_{n}C_{r} p^{\mathbf{k}} (1-p)^{n-\mathbf{k}}$$

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = \binom{n}{k} p^{\mathbf{k}} (1-p)^{n-\mathbf{k}}$$

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = \frac{n!}{k!(n-k!)} p^{\mathbf{k}} (1-p)^{n-\mathbf{k}}$$



We normally think about this as a function over k, which defines all the (n+1) outcomes in the sample space $k = \{0,1,2,3,4...n\}$.

The sum of $P_{binomial}(k; n, p)$ over k at constant n and p is always 1.

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = {}_{n}C_{r} p^{k} (1-p)^{n-k}$$

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = \binom{n}{k} p^{k} (1-p)^{n-k}$$

$$P_{\text{Binomial}}(k; n, p) = \frac{n!}{k!(n-k!)} p^{k} (1-p)^{n-k}$$

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = {}_{n}C_{\mathbf{r}} p^{\mathbf{k}} (1-p)^{n-\mathbf{k}}$$

$$P_{\text{Binomial}}(\mathbf{k}; \mathbf{n}, \mathbf{p}) = \binom{n}{k} p^{k} (1-p)^{n-k}$$

$$P_{\text{Binomial}}(k; n, p) = \frac{n!}{k!(n-k!)} p^{k} (1-p)^{n-k}$$

This is the number of outcomes

This is the probability of each outcome

$$P_{\text{Binomial}}(\mathbf{p}; \mathbf{n}, \mathbf{k}) = f(n, \mathbf{k}) p^{\mathbf{k}} (1-p)^{n-\mathbf{k}}$$

This is the number of outcomes

This is the probability of each outcome

Binomial log - likelihood

$$\log P_{\text{Binomial}}(p; n, k) = \log(f(n, k)) + k \log(p) + (n-k) \log (1-p)$$

Term that depends on n, k but independent of p

Terms that depend on p

Binomial log - likelihood

$$\log P_{\text{Binomial}}(p; n, k) = \log(f(n, k)) + k \log(p) + (n-k) \log (1-p)$$

Term that depends on n, k but independent of p

Terms that depend on p

Sometimes we use log-likelihood because it turns multiplication into addition and this makes some inferences easier.

Other times we use log-likelihood for numerical reasons; we may want to take the ratio of two likelihoods that are smaller than 10^{-16}

$$f(x; a, b) = \frac{1}{B(a, b)} x^{a-1} (1 - x)^{b-1}$$

a and b are number of successes and number of failures (almost) k, (n-k)

This is a number

Two terms with powers of x and 1-x x is probability of success

$$f(x; a, b) = \frac{1}{B(a, b)} x^{a-1} (1 - x)^{b-1}$$

The late David MacKay pointed out that probability distributions are often named for their normalization constants.

"Normalization constant" – jargon for "the number you have to multiply the math by to make the probability sum to 1"

$$f(x; a, b) = \frac{1}{B(a, b)} x^{a-1} (1 - x)^{b-1}$$

You can think of this as the binomial probability reorganized to add up to 1 when integrated over x instead of summed over k.

$$f(x; a, b) = \frac{1}{B(a, b)} x^{a-1} (1 - x)^{b-1}$$

Expectation value

$$\mu = \frac{a}{a+b}$$

Standard deviation

$$\sigma = \frac{ab}{(a+b)^2(a+b+1)}$$

Mode
$$\frac{a-1}{a+b-2} \text{ for a, b > 1}$$
 any value in [0,1] for α , β = 1 {0, 1} (bimodal) for α , β < 1 0 for α ≤ 1, β > 1 1 for α > 1, β ≤ 1

Bayesian inference

Event A: unknown state of nature

Event C: experiment

$$P(A \mid C) = P(C \mid A) P(A) / P(C)$$

$$\uparrow \qquad \uparrow \qquad \uparrow$$

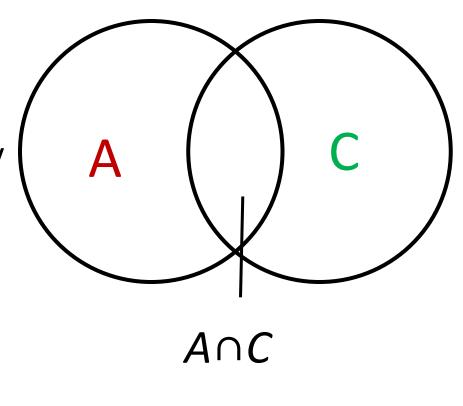
Life's persistent question "What is death rate?"

Term that depends on experiment in this case binomial

Term with knowledge for event and bias about A

prior

Probability that is no longer uncertain evidence



posterior

likelihood

posterior density = prior density * likelihood (function of the data)

Beta is a conjugate prior for the binomial distribution: Beta priors * binomial likelihoods = Beta posteriors

Beta (α, α) prior x Binomial likelihood with m successes and n failures = Beta $(\alpha + m, \alpha + n)$

As long as we write a paragraph justifying our choice of prior, we can easily get exact confidence intervals for parameters known by binomial sampling.

$$f(x; a, b) = \frac{1}{B(a, b)} x^{a-1} (1 - x)^{b-1}$$

$$p(x; 0/3) = 4(1 - x)^{3}$$

$$p(x; 1/3) = 12x(1 - x)^{2}$$

$$p(x; 2/3) = 12x^{2}(1 - x)$$

$$p(x; 3/3) = 4x^{3}$$

The posterior distributions for 0, 1, 2, and 3 successes out of 3 are "polynomial functions" known as middle- and highschool torture instruments.

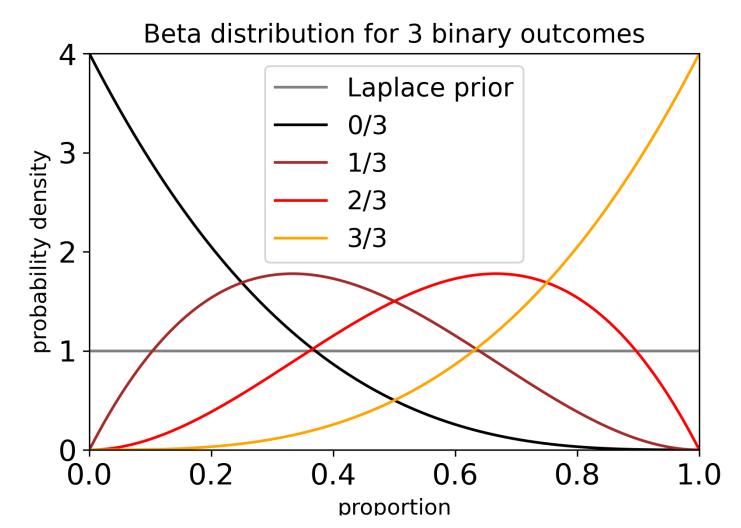
Beta distributions for all possible outcomes of an n=3 binomial experiment

$$p(x; 0/3) = 4(1 - x)^{3}$$

$$p(x; 1/3) = 12x(1 - x)^{2}$$

$$p(x; 2/3) = 12x^{2}(1 - x)$$

$$p(x; 3/3) = 4x^{3}$$

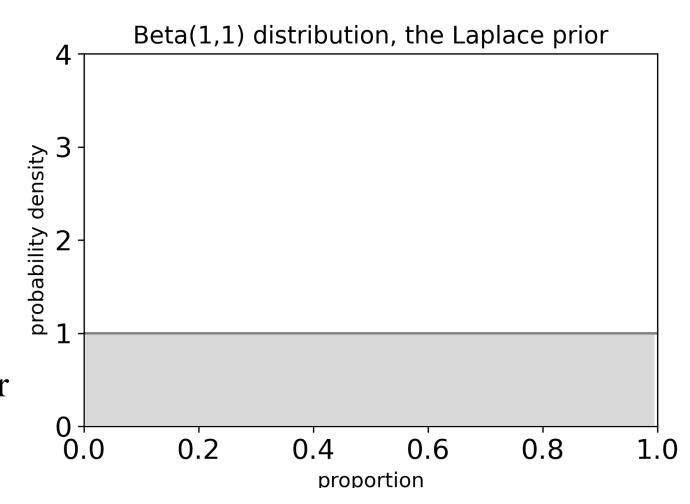


What does ignorance look like?

Before I do the experiment, I don't know much about the proportion.
But we're grownups, so I have to put numbers on my ignorance.

The oldest choice is the "flat" prior

Beta(a=1, b=1) =
$$x^0 (1-x)^0 = 1$$



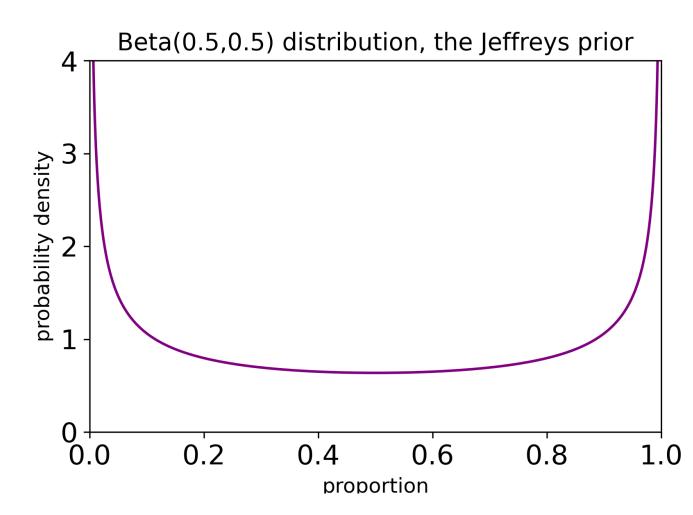
This prior introduces "bias" — it has an expectation value of 0.5!!!

What does ignorance look like?

Perhaps there is reason to prefer the extremes?

Jeffreys prior does that.

Note the symmetry: if a = b, your prior does not prefer successes or failures.

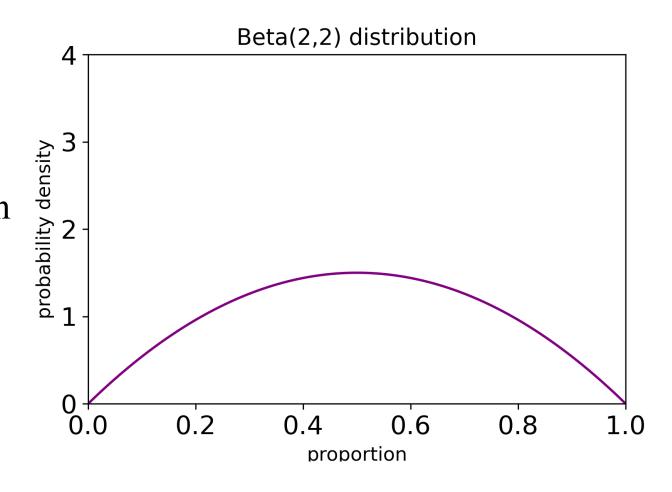


Beta(a=0.5, b=0.5) =
$$c x^{-0.5} (1-x)^{-0.5} = \frac{c}{\sqrt{p(1-p)}}$$

What does ignorance look like?

Note the symmetry: if a = b, the prior does not prefer successes or failures.

a = b = 2 is reasonable if we are certain that both successes and failures are possible (p cannot be exactly 0 or exactly 1)



Beta(a=2, b=2) =
$$c \times (1-x)$$

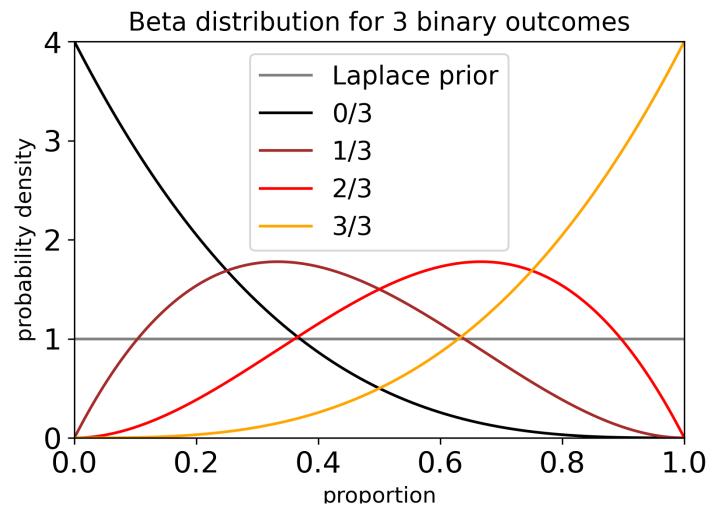
Beta for n=3 binomial trial

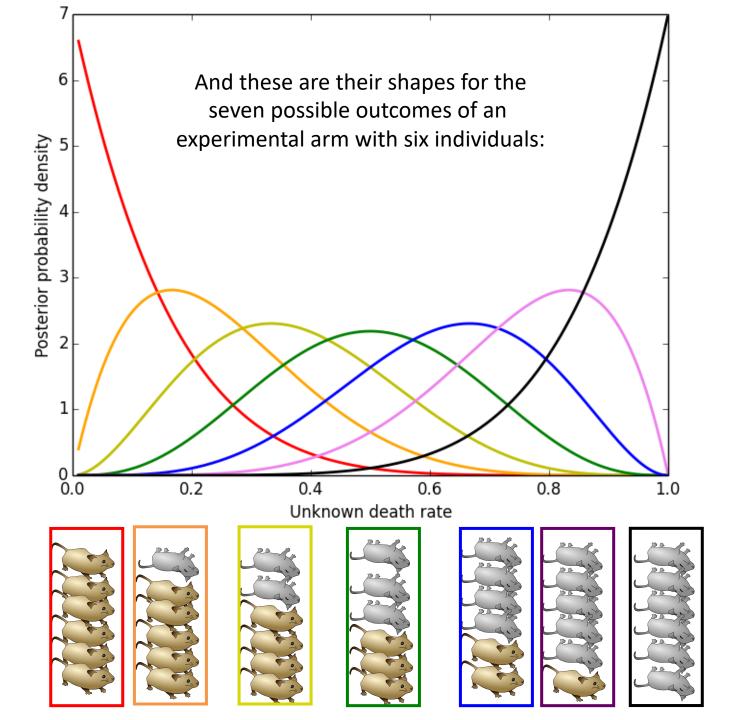
$$p(x; 0/3) = 4(1-x)^3$$

$$p(x; 1/3) = 12x(1-x)^2$$

$$p(x; 2/3) = 12x^2(1-x)$$

$$p(x; 3/3) = 4x^3$$





The biased top

200 spins of a four-sided top.

Outcome A: 1

Outcome B: 34

Outcome C: 87

Outcome D: 78



The biased top



200 spins of a four-sided top.

Outcome A: 1 Here be dragons

Outcome B: $34 0.17 \pm 1.96 * S.E.M.$

Outcome C: $87 0.435 \pm 1.96 * S.E.M.$

Outcome D: $78 0.39 \pm 1.96 \text{*S.E.M.}$

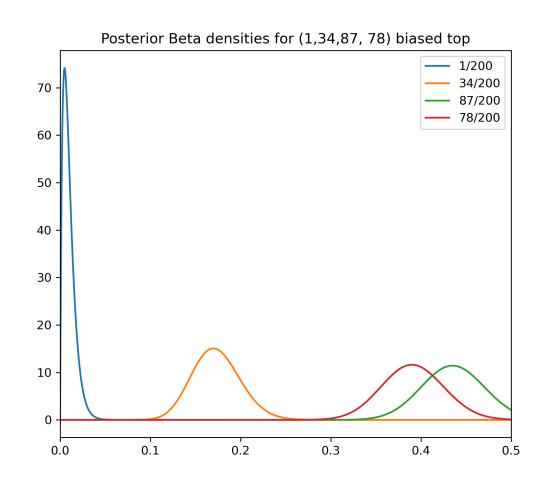
Outcome NOT A: 199/200 (can't use Standard Error on the Mean!)

SEM only useful when min (Np, N(1-p)) > 30

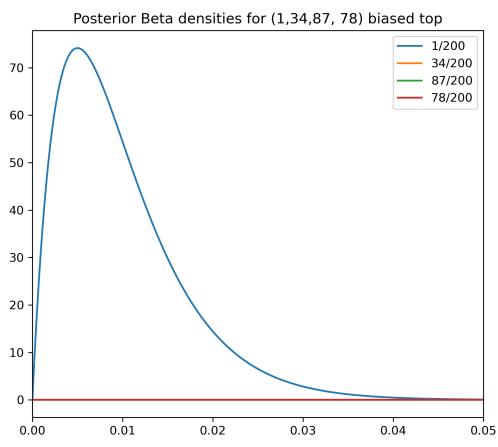
The biased top

200 spins of a four-sided top.









Where does probability come from?

Symmetry

- "All of the cards I haven't seen face up are equally likely"
- "The six faces of the die are equally likely"

Observations

- Sampling: Interpret (a small number of) observations as a sample from an infinite process.
- Historical weather data, testing data, demographic data...
- Scrambled versions of sampled data to explore contrary-to-fact symmetries

Modeling – when you can draw samples from the distribution of interest

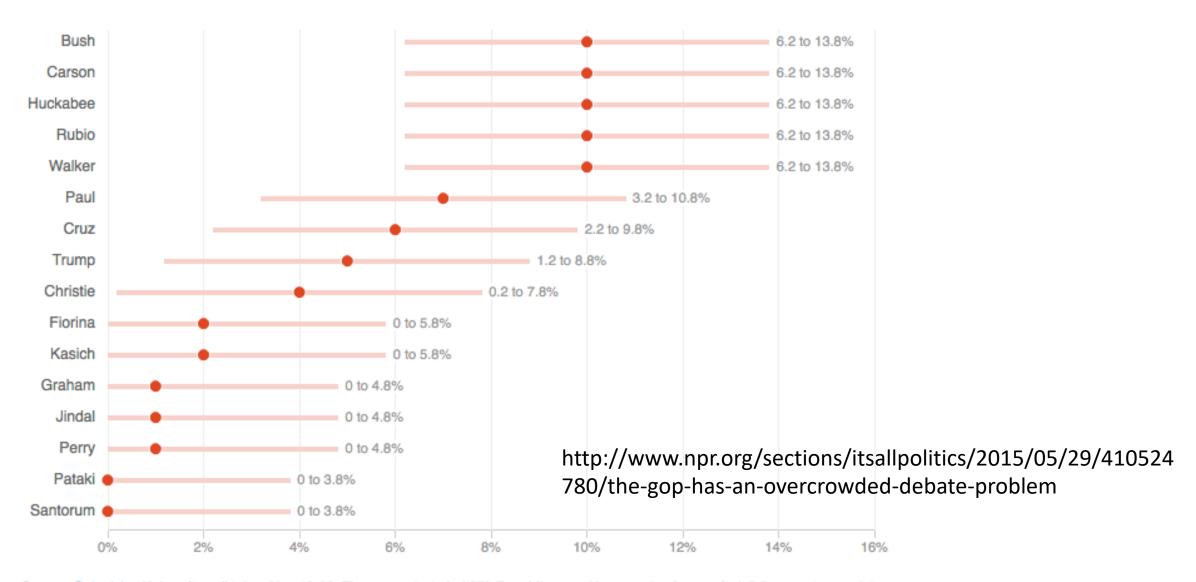
- "Monte Carlo" methods generate random samples
- Weather, asteroids, pandemics

Expert opinion

- All you get for events like "North Korea will test another supersonic missile in Q1 2022"
- Needs to map from "very likely" "highly unlikely" to real numbers
- Numerical decisionmaking can extend into the wild and improbable (aliens, singularity..)

Republican Candidate Support, Factoring In The Margin Of Error

Among respondents who said they were Republican or leaning Republican

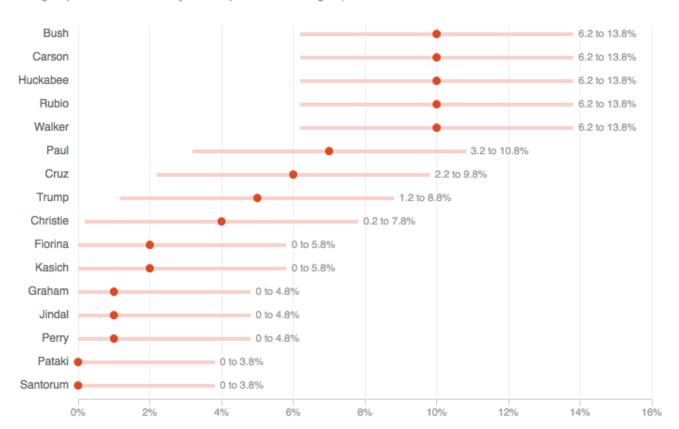


Source: Quinnipiac University poll taken May 19-26. The survey included 679 Republicans, with a margin of error of +/- 3.8 percentage points.

Credit: Alyson Hurt and Danielle Kurtzleben/NPR

Republican Candidate Support, Factoring In The Margin Of Error

Among respondents who said they were Republican or leaning Republican



- Proportions have been rounded.
 - Error bars are symmetrical, clipped at zero
 - Error bars are independent of point estimates!

Source: Quinnipiac University poll taken May 19-26. The survey included 679 Republicans, with a margin of error of +/- 3.8 percentage points.

Credit: Alyson Hurt and Danielle Kurtzleben/NPR

In essence, the error bars are inappropriate.