

# The prior is a key ingredient to the assurance calculation

Discuss with your neighbour(s) what the prior for the confirmatory study could look like.

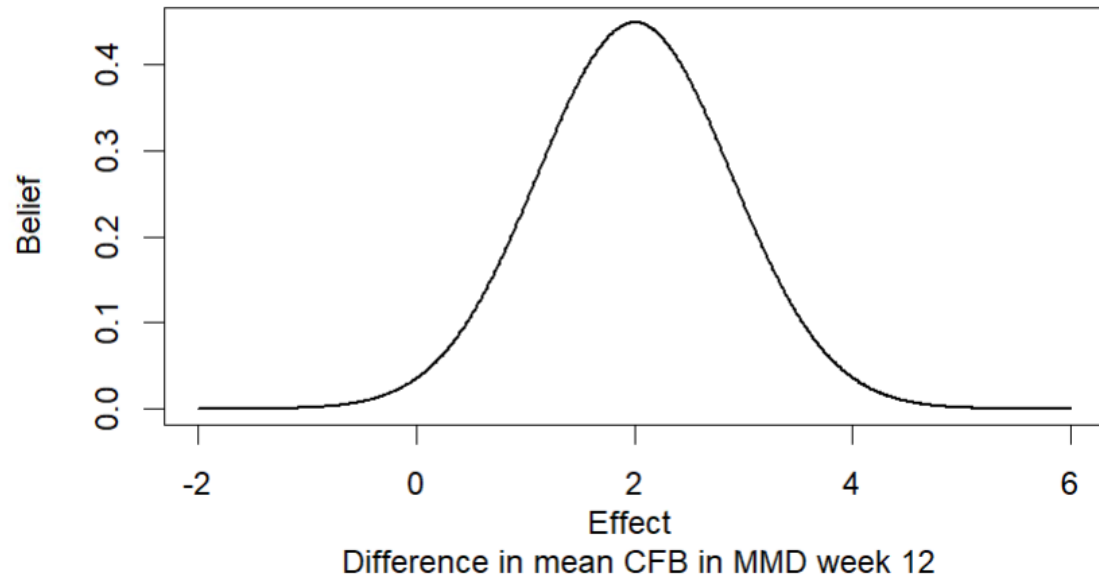
How confident are you about your prior? Are there any aspects you would like to understand better before deciding on a final prior?

# A prior based on data alone

If data is available, this is very valuable in defining a prior

The effect estimate and its standard error could be used to define a prior using a normal distribution

For the proof of concept study the effect estimate was 2 MMD, with a SE of 0.89

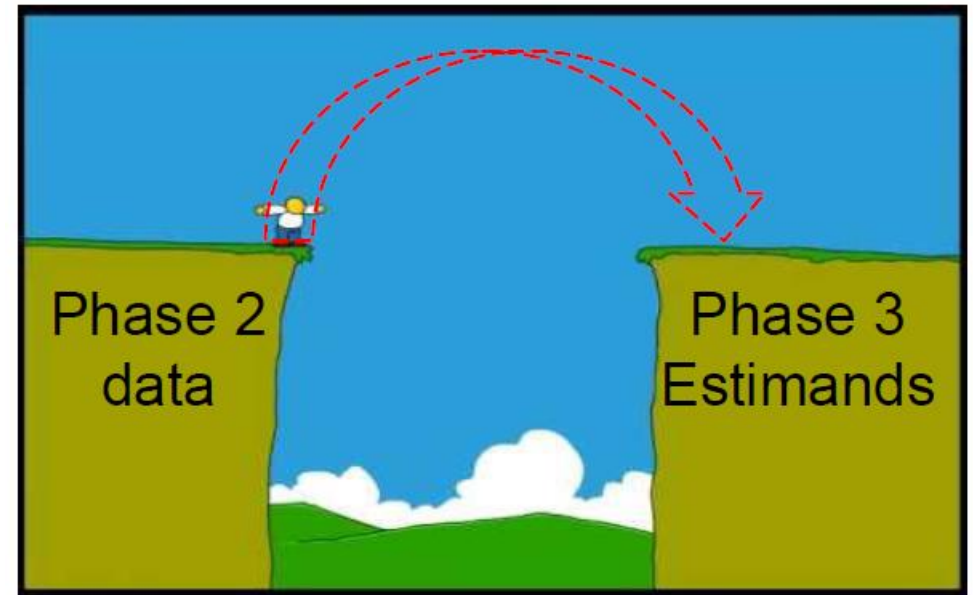


Note that a normal prior assumes that it is equally likely that the effect is smaller or larger than the observed effect from the proof of concept study (symmetric prior)

# Unfortunately, available data does not always reflect what we need

There are many differences between the proof of concept study and the confirmatory study that makes it difficult to translate the results directly to expectations for the confirmatory study

- Endpoint collected at different timepoints (Week 4 versus Week 12)
- Larger sample size (possibly including more countries/different sites)
- Different mode of administration
- More frequent dosing



Source: Joe Cartoon

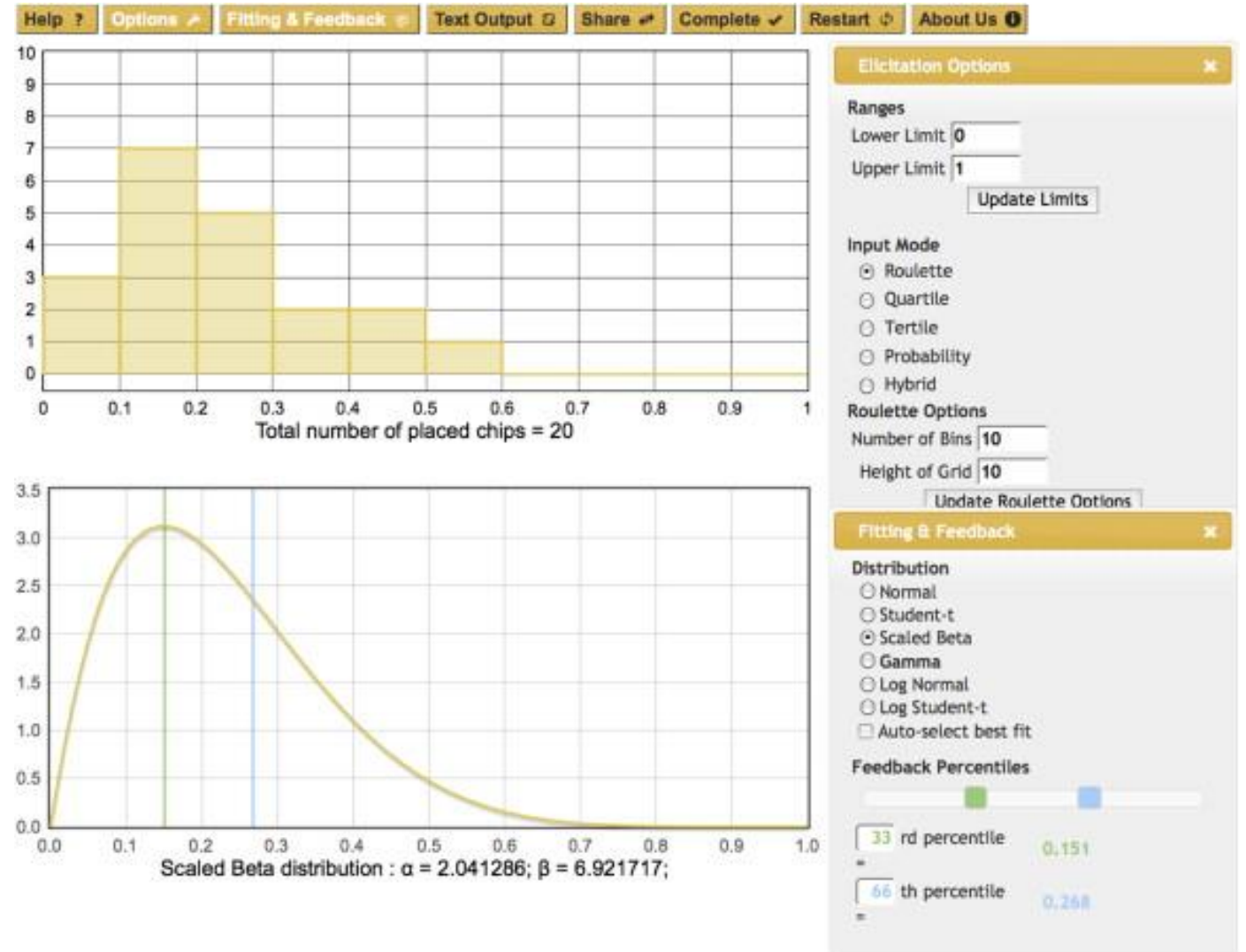
# Prior elicitation from clinical experts can be used to take into account uncertainties that are not captured by data

- Priors are based on a mixture of internal and external data which typically requires modelling to link the different sources.
  - E.g. internal data from proof of concept study, data from other (internal or external) studies on likely placebo effect, effect at 12 weeks etc.
- In some cases, little or no relevant data are available
- In both situations it can be helpful to draw on expert knowledge to translate available information into a prior distribution, either for the target parameter (effect), or for nonidentifiable parameters in a complex quantitative model
- Formal prior elicitation methods have been developed to derive priors based on input from clinical experts

# Prior elicitation – Roulette Method

- The expert defines a range of plausible values
- This range is divided into a number of bins
- A fixed number of ‘chips’ is provided to the expert who is to distribute them over the bins (typically 20 works well)
- The proportion of chips in a bin gives the probability that the value of interest lies in this range

Method is often considered intuitive, but risk of too much focus on making distribution look ‘nice’ – training needed



# Prior elicitation – modified PERT distribution

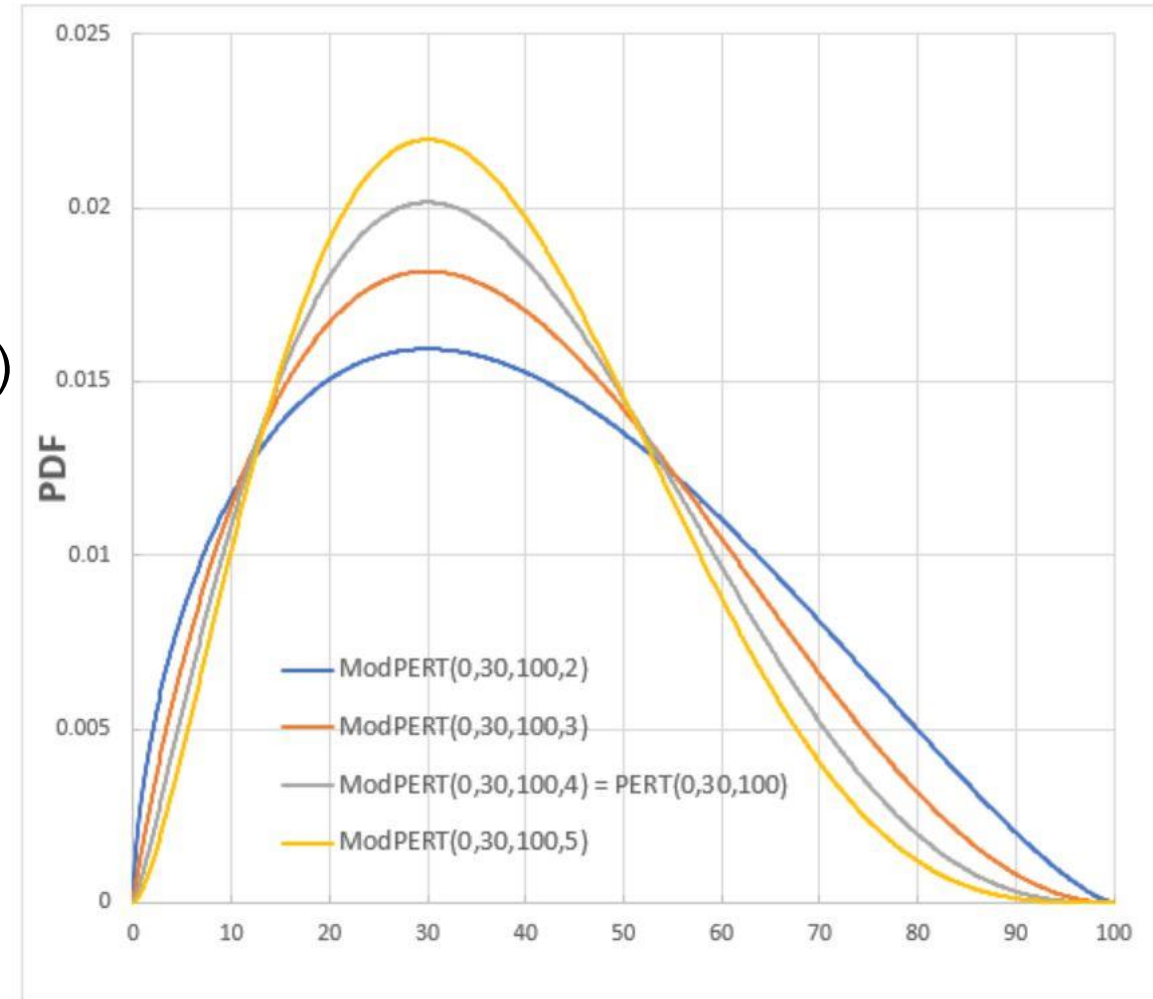
Defined by four parameters that are easy to interpret:

- Minimum possible value (a)
- Maximum possible value (c)
- Most likely value (b)
- Shape parameter ( $\gamma$ , make curve flatter or narrower)

Related to a beta distribution with additional assumption that the mean is:

$$\mu = \frac{a + \gamma b + c}{\gamma + 2}$$

Used for prior elicitation due its easy interpretation of the parameters



# The SHELF elicitation framework discussed in the previous session can be used to obtain a prior from multiple experts

**TABLE 1** Main steps in SHELF elicitation process

1. Select experts (and a good moderator)	These can be both internal and external to the company and should involve only those that have a good understanding of the details that need to be elicited.
2. Train experts	Provide experts with an overview of the elicitation process and the use of subjective probabilities and probability distributions
3. Evidence dossier	Prepare and review an evidence dossier that captures all pertinent information that the experts would rely upon to formulate their opinion.
4. Elicit individual priors	Elicit, in a masked fashion, individual priors from each expert (ie, experts are unaware of what other experts believe at this point)
5. Discuss individual priors	Share and review results from individual elicitations including each expert's rationale for their beliefs; discuss differences between experts.
6. Agree consensus prior	Where possible, elicit a "consensus" prior from the experts through discussion of what they collectively agree a "rational independent observer" would determine after having observed the previous conversations.
7. Documentation	Provide a written record of the elicitation session



# Combining priors from different experts

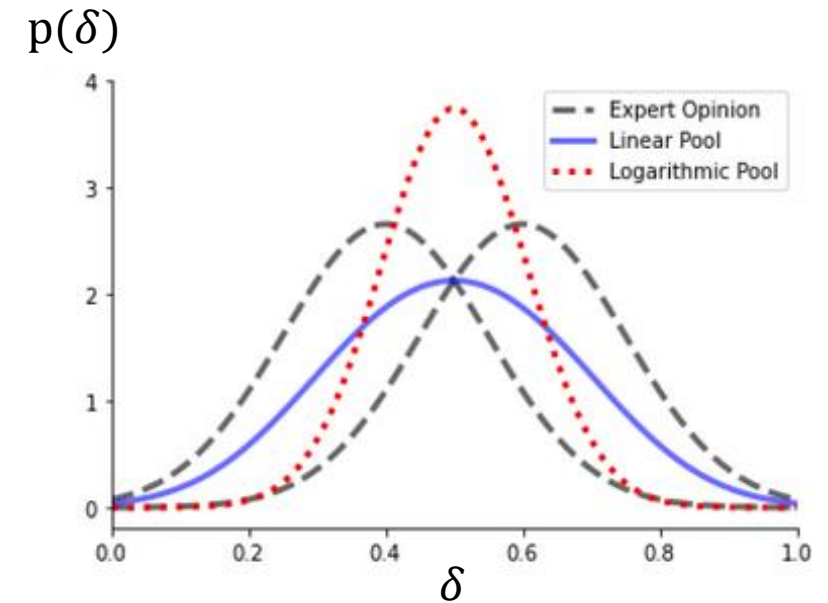
Once priors  $p_1(\delta), \dots, p_k(\delta)$  have been obtained from different experts, they need to be combined into a consensus prior  $p(\delta)$ .

1. Consensus through discussion – experts reveal their priors and agree on a common prior through discussion
2. Linear pooling

$$p(\delta) = \sum_{i=1}^k w_i p_i(\delta)$$

3. Logarithmic pooling

$$p(\delta) = c \prod_{i=1}^k p_i(\delta)^{w_i}$$



Where  $w_i$  ( $i = 1, \dots, k$ ) are weights summing to one that can be used to give more weight to specific experts.



# Be aware of cognitive bias when designing/eliciting a prior

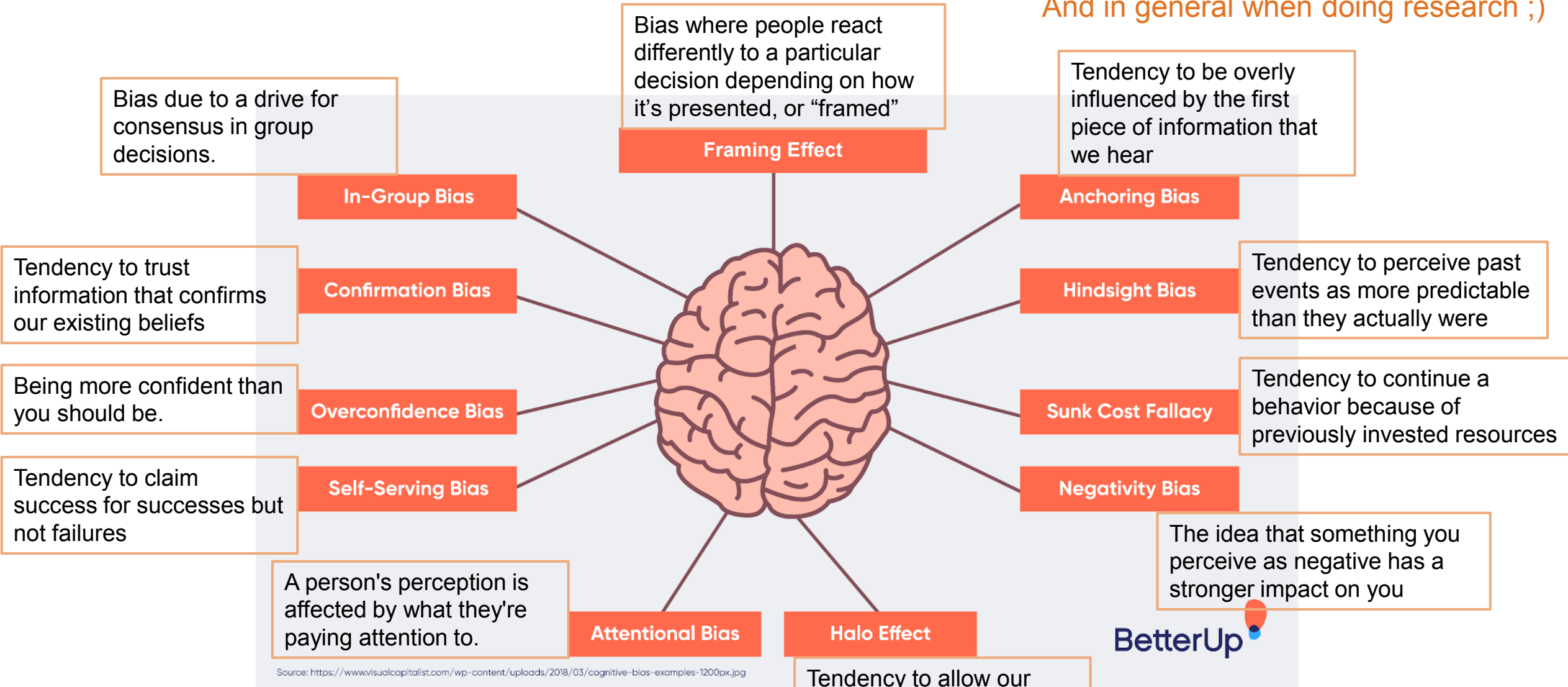
How biased are you? 😊

Anders is from Denmark and loves playing the trumpet. Which occupation is Anders more likely to have:

- A. Anders is a musician in the national orchestra
- B. Anders is a farmer

# Cognitive bias - to be aware of when designing a prior

And in general when doing research ;)



This is a non-exhaustive list.

Image from: [Cognitive and Unconscious Bias: What It Is and How to Overcome It \(betterup.com\)](https://www.betterup.com/blog/cognitive-and-unconscious-bias-what-it-is-and-how-to-overcome-it)

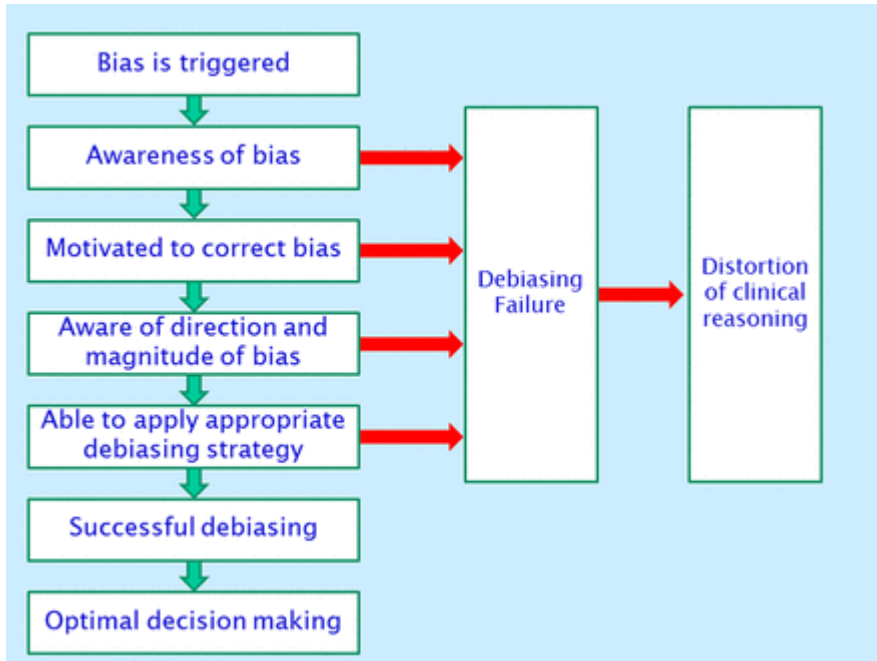
For Internal Use - Internal



# Discuss with your neighbour(s)

Discuss which types of bias can be reduced using the SHELF framework.

Do you have any other suggestions to avoid cognitive bias?



# Probability of success evaluation based on expert opinions

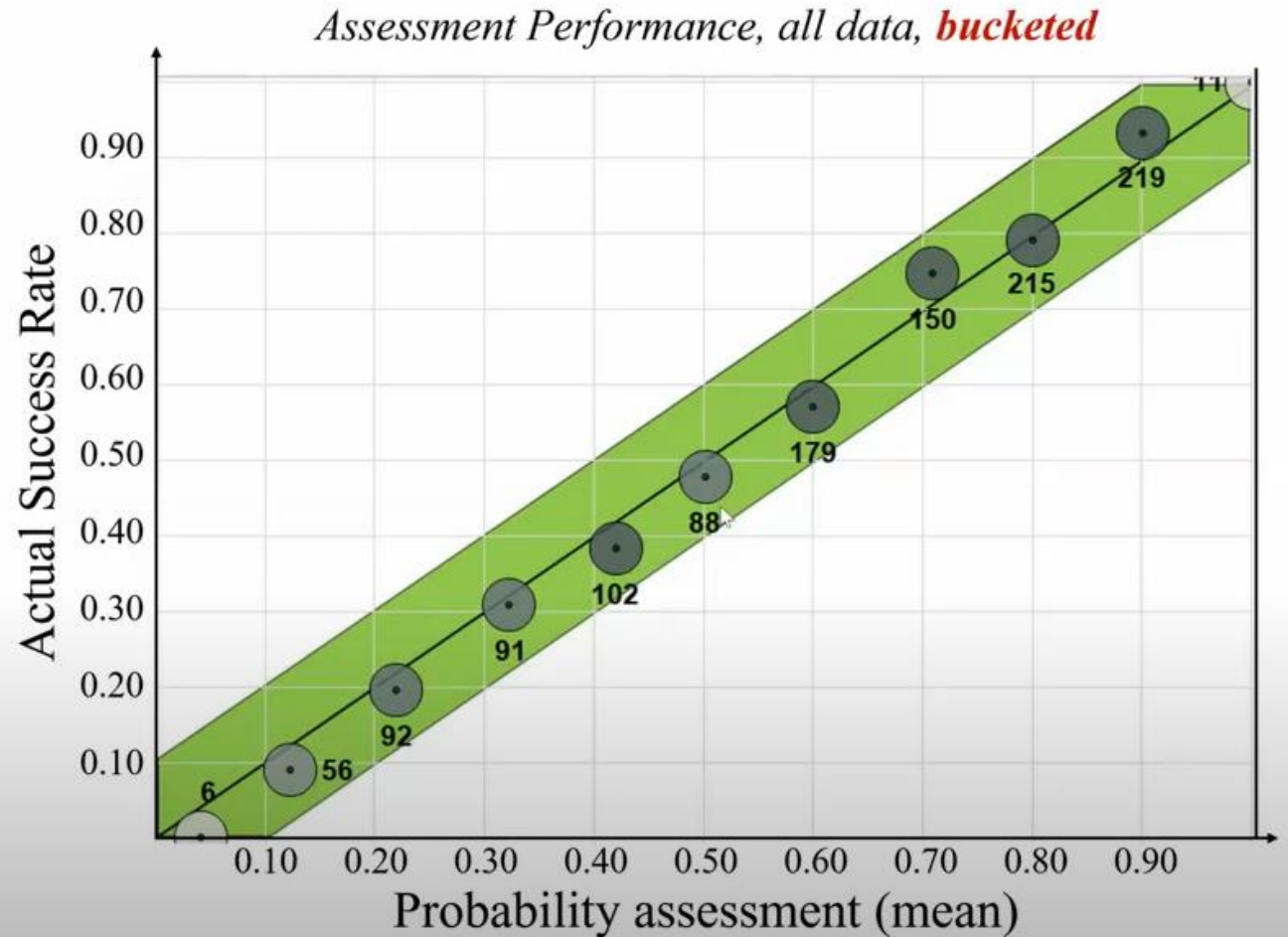
It can be done!

At Eli Lilly, probabilities of success (PoS) of drug development projects were elicited from a trained assessment group in collaboration with project teams

20 years of data shows that they were quite accurate

Evaluation of Performance  
1997-2017 (1,209 datapoints)

1/30/2019



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[Toward Superforecasting®: Lessons from the Eli Lilly Probability Assessment Panel | SDG – YouTube](#)

Further reading on avoiding bias: Superforecasting: The Art and Science of Prediction by P.E. Tetlock and Dan Gardner