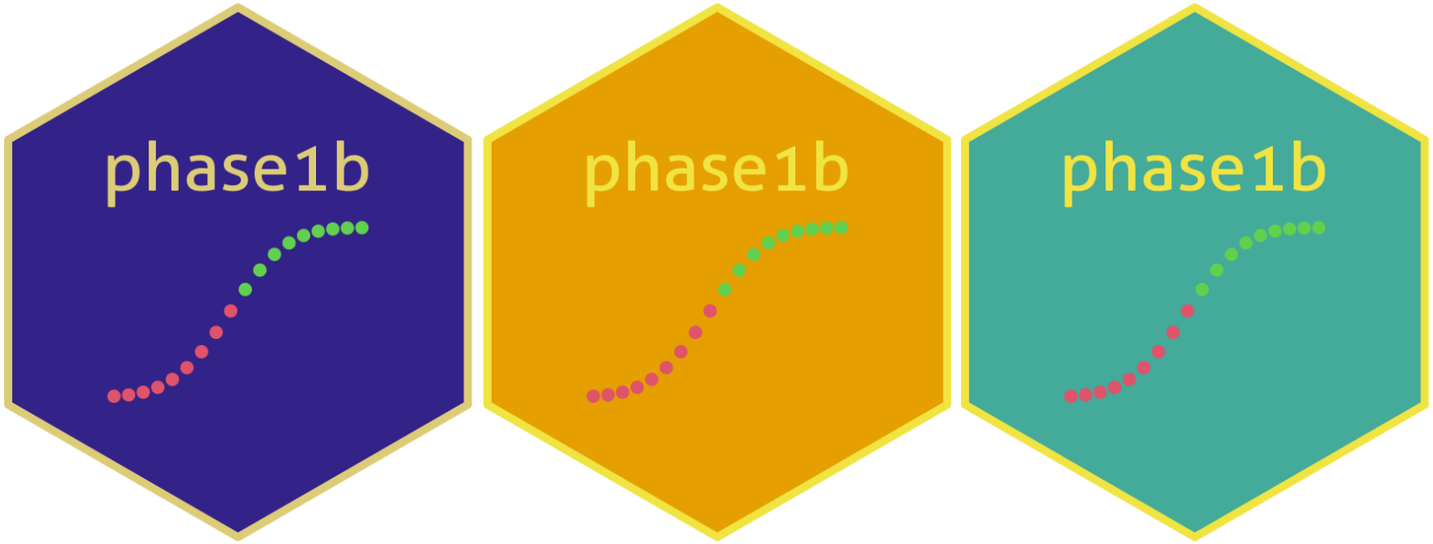
# A Bayesian approach to decision making in early development clinical trials: An R solution

**Audrey Yeo**

user!2024, Salzburg, AT 𝄞

*This presentation has ALT text and as much as possible, uses colour-blind*

# Early oncology trials and why `phase1b`?



# History and how to install :

- 2015 : Started as a need in Roche's early development group, package development led by Daniel Sabanés Bové in 2015.
- 2023 : Refactoring, Renaming, adding Unit and Integration tests as current State-of-Art Software Engineering practice.
- 100% written in R and Open Source.
- website : genentech.github.io/phase1b/

```
library(devtools)
devtools::install_github("https://github.com/Genentech/phase1b")
library(phase1b)
```

# Use case:

A single arm novel therapeutic with an assumed control response rate is at most 60%

| Example | Interim | Final |
|---|---|---|
| Responders | 16 | 23 |
| n | 23 | 40 |
| Response rate | 69.57 % | 57.5 % |
| Posterior probability* | ask phase1b | ask phase1b |
| Predictive posterior probability* | ask phase1b | - |
| Decision to develop molecule further : Go/Stop/Grey Zone | ask phase1b | ask phase1b |

* Posterior Probability : $P(\pi > 60\% | \alpha + n, \beta + n - x)$
* Predictive Posterior Probability : $P(\text{success or failure at final})$

# Updating the Posterior and making a decision

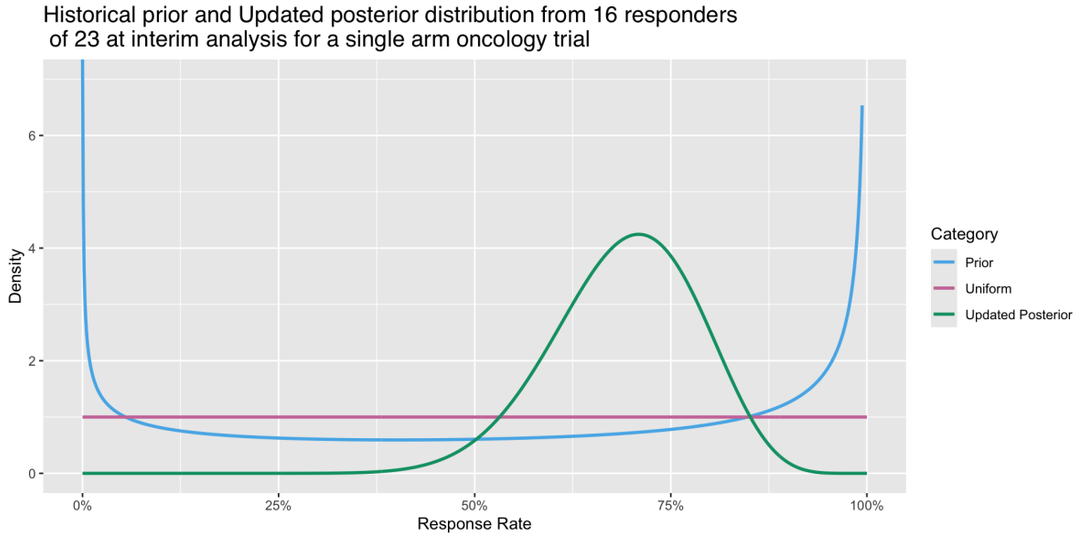
- Conjugate Prior is $f(\pi)$, where $\pi \sim Beta(\alpha, \beta)$, same family of distribution of Posterior (see below)
- We know the mean response rate (RR) is :

$$\pi = \frac{\alpha}{\alpha + \beta}$$

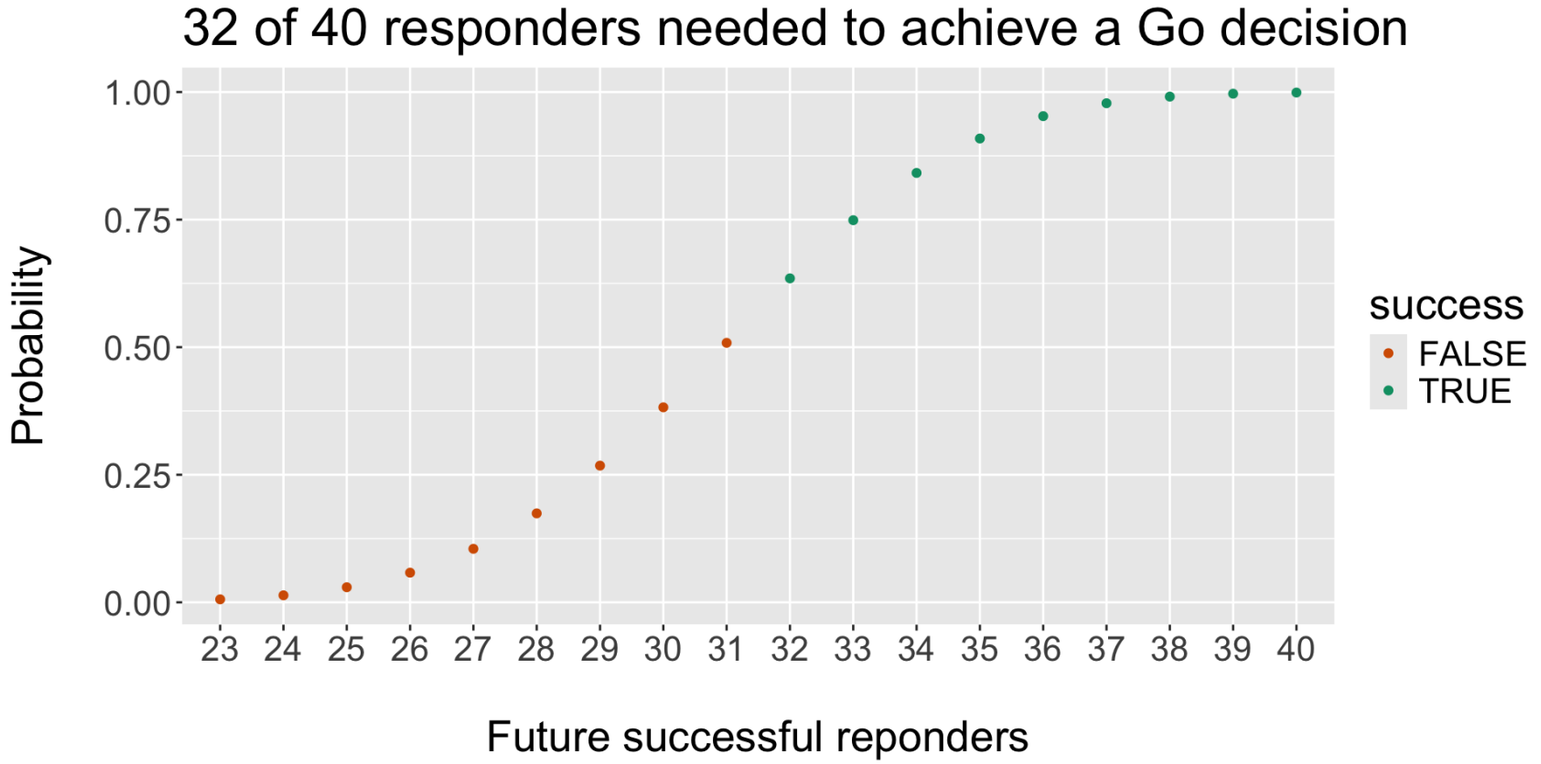
- Likelihood is $f(x|\pi)$, where $x \sim Binomial(x, n)$
- The updated Posterior will have the parameters $\alpha + x$ and $\beta + n - x$.

–> –> –> –> –>

- With the prior of $Beta(0.6, 0.4)$ and the result of our interim results our Posterior has these parameters: $Beta(16.6, 7.4)$



# Predictive Posterior Probability




1. Go if $P(\pi > 0.6 |$ interim data$) > 60\%$

```
control = 0.6
result <- predprob(
  x = 16, n = 23, Nmax = 40, p = control, thetaT = 0.6,
  parE = c(0.6, 0.4)
)
result$result
```

```
[1] 0.9004913
```

# Rules and Operating characteristics. A use case for `ocPostprob()`:

- Look for Efficacy: Go if $\mathrm{P}(\pi > 60\% | \text{ data}) > 90\%$
- Look for Futility: Stop if $\mathrm{P}(\pi < 60\% | \text{ data}) > 60\%$
- Prior of treatment arm $\mathrm{Beta}(0.6, 0.4)$.

```r
set.seed(2025)
res <- ocPostprob(
  nnE = c(23, 40), truep = 0.60, p0 = 0.60, p1 = 0.60, tL = 0.60, tU = 0.90, parE = c(0.6, 0.4),
  sim = 500, wiggle = TRUE, nnF = c(23, 40)
)
res$oc
```

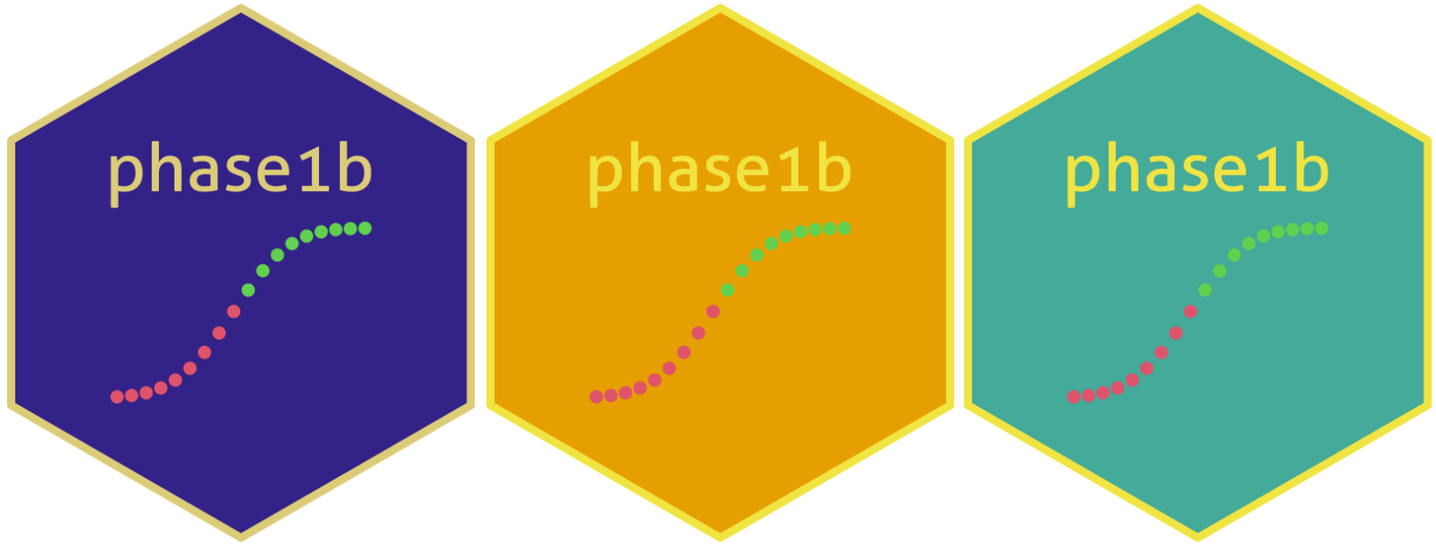
```
  ExpectedN PrStopEarly PrEarlyEff PrEarlyFut PrEfficacy PrFutility PrGrayZone
1    31.878       0.486      0.088      0.398       0.11       0.51       0.38
```

# Expanded features

…. and wiggle room!

| | SOC uncertainty | single-arm | two-arm | simulation | plotting | boundaries |
|---|---|---|---|---|---|---|
| postprob | | ✓ | | | | |
| postprobDist | ✓ | ✓ | | | | |
| predprob | | ✓ | | | | |
| predprobDist | ✓ | ✓ | | | | |
| ocPostprob | | ✓ | | ✓ | | |
| ocPostprobDist | ✓ | ✓ | | ✓ | | |
| ocPredprob | | ✓ | | ✓ | | |
| ocPredprobDist | ✓ | ✓ | | ✓ | | |
| ocRctPostprobDist | ✓ | ✓ | ✓ | ✓ | | |
| ocRctPredprobDist | ✓ | ✓ | ✓ | ✓ | | |
| plotBeta | | | | ✓ | ✓ | |
| plotDecision | | | | | ✓ | |
| plotOc | | | | | ✓ | |
| plotBounds | | | | | ✓ | |
| boundsPostprob | | | | | | ✓ |
| boundsPredprob | | | | | | ✓ |

# Concluding remarks




- Big thank you to Daniel Sabanés Bové for mentorship. Data Science Acceleration colleagues who collaborated and supported.
- Extension to other disease areas that use response rate as endpoint if beta priors are appropriate
- Contact me to collaborate. Open issues here

# References


- Thall P F, Simon R (1994), Practical Guidelines for Phase IIB Clinical Trials, Biometrics, 50, 337-349
- Lee J J, Liu D D (2008), A Predictive probability design for phase II cancer clinical trials, 5(2), 93-106, Clinical Trials
- Yeo, A T, Sabanés Bové D, Elze M, Pourmohamad T, Zhu J, Lymp J, Teterina A (2024). Phase1b : Calculations for decisions on Phase 1b clinical trials. R package version 1.0.0, https://genentech.github.io/phase1b
- Code for this presentation