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# Incorporating clinicians elicited informative prior distributions into planned Bayesian analysis

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## Introduction

Bayesian analyses with informative prior distributions are valuable for trials that have restricted populations (e.g., rare diseases, highly specialised subgroups etc.).

There are two main approaches to developing informative prior distributions for model parameters: a mathematical data-driven approach or a behavioural approach.

Based on the recommendation by Dallow et al. (1) we used a behavioural approach for the **TREAT** trial.

TREAT is a non-inferiority trial aiming to determine whether Mepolizumab is as efficacious as Omalizumab at reducing asthma attacks in children and adolescents with severe therapy-resistant asthma.

**We show how to incorporate the elicited transformed prior distributions in the planned Bayesian analysis model.**

## Methods

A **Poisson regression model** is planned to compare the 52-week exacerbation rate between the treatment arms adjusting for randomisation (1:1) stratification variables including centre, blood eosinophils (<300/≥300 per mcl), IgE (<30, 30-1500, >1500IU/ml) and type of asthma (RDA/STRA):

$$y_{ij} \sim \mathbf{Poisson}(\mu_{ij})$$

$$log\ (\mu_{ij}) = \alpha + \beta_1 Treat_i + \beta_2 Ige_{1i} + \beta_3 Ige_{2i} + \beta_4 Type_i + \beta_5 Blood_i + log(Time_{ij}) + Centre_{ij}$$

Informative priors are used for two model parameters:

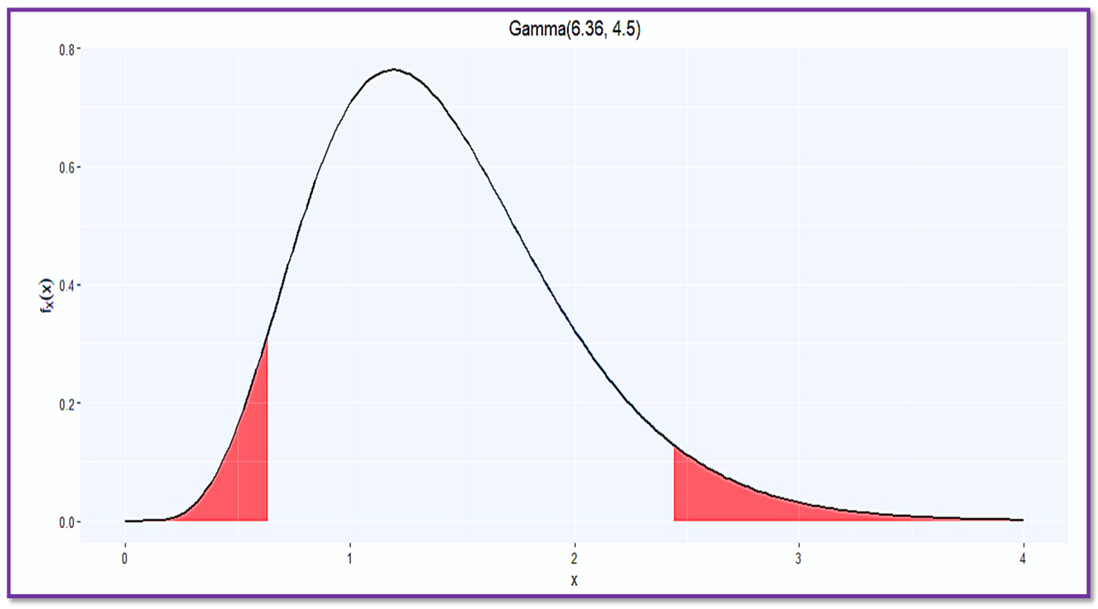
- log mean of exacerbation rate in the control arm **(α)**
- between-arm change in log exacerbation rate **(β1)**

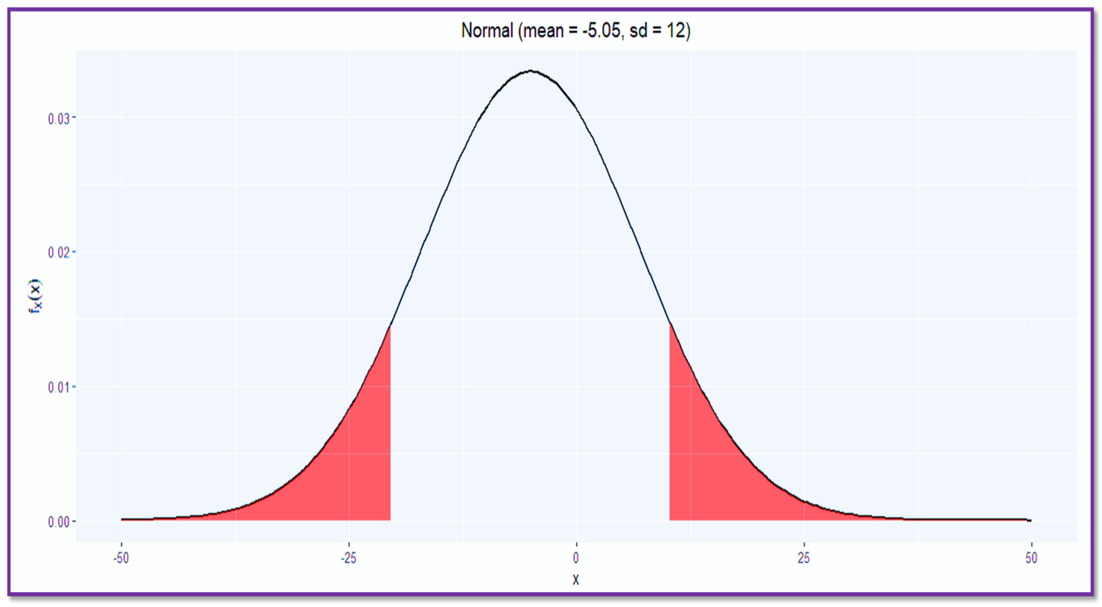
To facilitate clinical interpretation, we elicited clinicians' opinions for transformations of these: the mean exacerbation rate in the control arm (**parameter 1**) and the relative treatment change as a percentage (**parameter 2**).

We conducted a prior elicitation workshop using the Sheffield Elicitation Framework (**SHELF**)(2) and the roulette method.

The 2-day workshop was held in **March 2021** and **eight** experts participated.

We sought solutions to fitting the elicited distributions based on the clinicians' opinions to the planned analysis model which was achieved using the flexible ***rjags*** package.




***Left: Fig 1 –*** *Final elicited prior distribution for parameter one, the mean 52-week exacerbation rate for the study population on Omalizumab.* ***Right: Fig 2 –*** *Final elicited prior distribution for parameter two, the relative effect of Mepolizumab compared to Omalizumab expressed as a percentage.* ***Below: Fig 3 –*** *rjags command, rjags version 4-12 to include the elicited priors in our model.*

## Results

A **Gamma distribution (6.36,4.5)** was selected as a final prior for parameter 1: mean of exacerbation rate in Omalizumab arm **exp(α)** (**Figure 1**).

$$\exp(\alpha) \sim Gamma\ (6.36, 4.5)$$

A **Normal distribution (mean=-5.05, sd=12)** was confirmed as a prior distribution for parameter 2: percentage change in exacerbation rate between Mepolizumab & Omalizumab **(exp(β1)-1)*100** (**Figure 2**).

$$(\exp(\beta 1) - 1) * 100 \sim N\ (-5.05, 12)$$

A solution to incorporating the elicited transformed distributions was found using ***rjags*** (3) into our final model to obtain posterior distributions for parameters of interest (**Figure 3**).

```
M = model {
        #Likelihood
        for (i in 1: N){
        y[i] ~ dpois(lambda[i])
        log(lambda[i]) <- mu[i]
        mu[i]<-alpha+b1*trt[i]+b2*Ige_1[i]+b3*Ige_2[i]+b4*type[i]+b5*blood[i]+ log(time[i])+u[center[i]]
        }

        # m centers
        for (j in 1:m) {
                u[j] ~ dnorm(0, tau)
                }

        #Priors
        alpha <- log(R0)
        b1 <- log (IRR)
        IRR <- (Rc/100) +1
        R0 ~ dgamma(6.36,4.5)
        Rc ~ dmnorm(-5.05,0.007) #tau=1/sigma^2 and sigma=12#
        b2 ~ dnorm(0, 0.001)
        b3 ~ dnorm(0, 0.001)
        b4 ~ dnorm(0, 0.001)
        b5 ~ dnorm(0, 0.001)
        tau ~ dgamma(0.001,0.001)
        }
```

## Discussion

Elicitation is a reliable way to develop prior distributions for model parameters, but it is sometimes challenging to directly obtain clinical opinions about the parameters in the model.

We have shown how to use a clinically relevant transformation of parameters for elicitation and then use flexible Bayesian modelling packages to incorporate the resulting prior distributions into the final model.

The ***rjags*** package is available to use in **RStudio**, and was found to be a flexible tool for this approach.

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3) Martyn Plummer (2021). rjags: Bayesian Graphical Models using MCMC. R package version 4-12. https://CRAN.R-project.org/package=rjags

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