The focus of the practical problem being addressed is the elimination, via fumigation with Methyl Bromide (MeBr), of insect pests (various species of pine beetle) from logs intended for export from New Zealand. The statistical problem is to determine interval estimates (explicitly 95% confidence intervals) for lethal dose values LD_p which are the values of dose of MeBr (in $\mathrm{gm/m}^3$) such that

$$\Pr(\text{Dead} \mid \text{Dose} = \mathrm{LD}_p) = p$$

where p is a (large) probability value. Explicity 0.999968, the so-called "probit-9" value is what we are interested in.

We have a number of data sets from which to attempt to estimate LD_p values, and to these data sets we have been fitting binomial models of the form

$$p = g^{-1}(\alpha_i + Z_1 + (\beta_i + Z_2)x)$$

where $g()$ is the link function (logit, probit, or cloglog), the index i indicates treatment group, Z_1 and Z_2 are (Gaussian) random effects associated with replicates which are nested within treatment groups, and x is "`Dose`". From the fitted models we calculate 95% confidence intervals for LD_p using Fieller's formula. The treatment groups are determined by combinations of temperature and exposure time (e.g. 10° C. and 8 hours).

Up to now we have been fitting the models using the function `glmer()` from the `lme4` package. The syntax of a call to `glmer()` is of the form:

```
fit <- glmer(cbind(Dead,Alive) ~ (Trt + 0)/Dose + (Dose | Rep),
             family=binomial(link="cloglog"),data = Dat)
```

In the foregoing `Dead`, `Alive`, `Trt`, `Dose` and `Rep` are columns of the data frame `Dat`. Columns `Dead` and `Alive` are counts of dead and alive insects in a given log, column `Trt` is a factor indicating treatment group, column `Dose` is numeric and indicates the dose applied to the given log, and column `Rep` is a factor indicating replicate and is nested within `Trt`.

It was recently suggested that we might try re-parameterising the model in terms of the quantity in which we are actually interested, namely LD_p. So as to simplify notation, let us consider a single treatment group (and suppress the treatment group subscript i). In terms of the usual parameterisation, LD_p is given by

$$\mathrm{LD}_p = \frac{g(p) - \alpha}{\beta} \, .$$

To determine α and β uniquely we need another equation. We (arbitrarily) take

$$\mathrm{LD}_{0.5} = \frac{g(0.5) - \alpha}{\beta} \, .$$

Setting $\gamma_0 = \mathrm{LD}_{0.5}$, $\gamma_1 = \mathrm{LD}_p$, $g_0 = g(0.5)$ and $g_1 = g(p)$, and solving for α and β we get

$$\begin{aligned} \beta &= \frac{g_1 - g_0}{\gamma_1 - \gamma_0} \\ \alpha &= g_0 - \left(\frac{g_1 - g_0}{\gamma_1 - \gamma_0} \right) \gamma_0 \, . \end{aligned}$$

Thus in terms of the new parameters γ_0 and γ_1 the model that we wish to fit becomes

$$p = g^{-1}\left(g_0 - \left(\frac{g_1 - g_0}{\gamma_1 - \gamma_0}\right)\gamma_0 + Z_1 + \left(\frac{g_1 - g_0}{\gamma_1 - \gamma_0} + Z_2\right)x\right) \ .$$

This model is non-linear in γ_0 and γ_1 whence it cannot be fitted using `glmer()`.

Given that the "repeated" package handles only a single random effect, I decided to try removing the Z_2 term and fitting

$$p = g^{-1}\left(g_0 + \left(\frac{g_1 - g_0}{\gamma_1 - \gamma_0}\right)\gamma_0 + Z_1 + \left(\frac{g_1 - g_0}{\gamma_1 - \gamma_0}\right)x\right) \ .$$

Bruce Swihart, the maintainer of the "repeated" package managed to get this to fly for me. However the use of a single random effect seems suspect in the practical context.

If one does

```
fit0 <- glmer(cbind(Dead,Alive) ~ (Trt + 0)/Dose + (1 | Rep),
              family=binomial(link="cloglog"),data = Dat)
fit1 <- glmer(cbind(Dead,Alive) ~ (Trt + 0)/Dose + (Dose | Rep),
              family=binomial(link="cloglog"),data = Dat)
anova(fit0,fit1)
```

(where `Dat` is one of a number of our "real" data sets) one gets p-values `< 2e-16`. (The same applies with the logit and probit links.)