

# Characterising effect of anaemia on mortality in severe malaria

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## Background

This looks at the severe malaria legacy dataset from MORU

```
library(lme4)

## Loading required package: Matrix
# For the GAM modelling
library(mgcv)

## Loading required package: nlme
##
## Attaching package: 'nlme'
## The following object is masked from 'package:lme4':
##
##      lmList
## This is mgcv 1.8-22. For overview type 'help("mgcv-package")'.
# For the CART modelling
library(rpart)
library(rpart.plot)
```

## Exploratory analysis

Let's look at the key predictive variables. We use a random effects term to model differences between studies.

```
par(las=1, mfrow=c(2,2))
## Base Excess and HCT
plot(jitter(Leg_data$HCT,amount=1), jitter(Leg_data$BD),
     col=Leg_data$studyID, pch='*', xlab='Haematocrit', ylab='Base Deficit')
legend('topright', col=unique(Leg_data$studyID), legend = unique(Leg_data$studyID), pch='*')
mod = lmer(formula = BD ~ HCT + (1 | studyID), data = Leg_data)
ys = predict(object = mod, newdata = data.frame(HCT=8:50, studyID=NA), re.form=NA)
lines(8:50, ys, lwd=3, col='black')

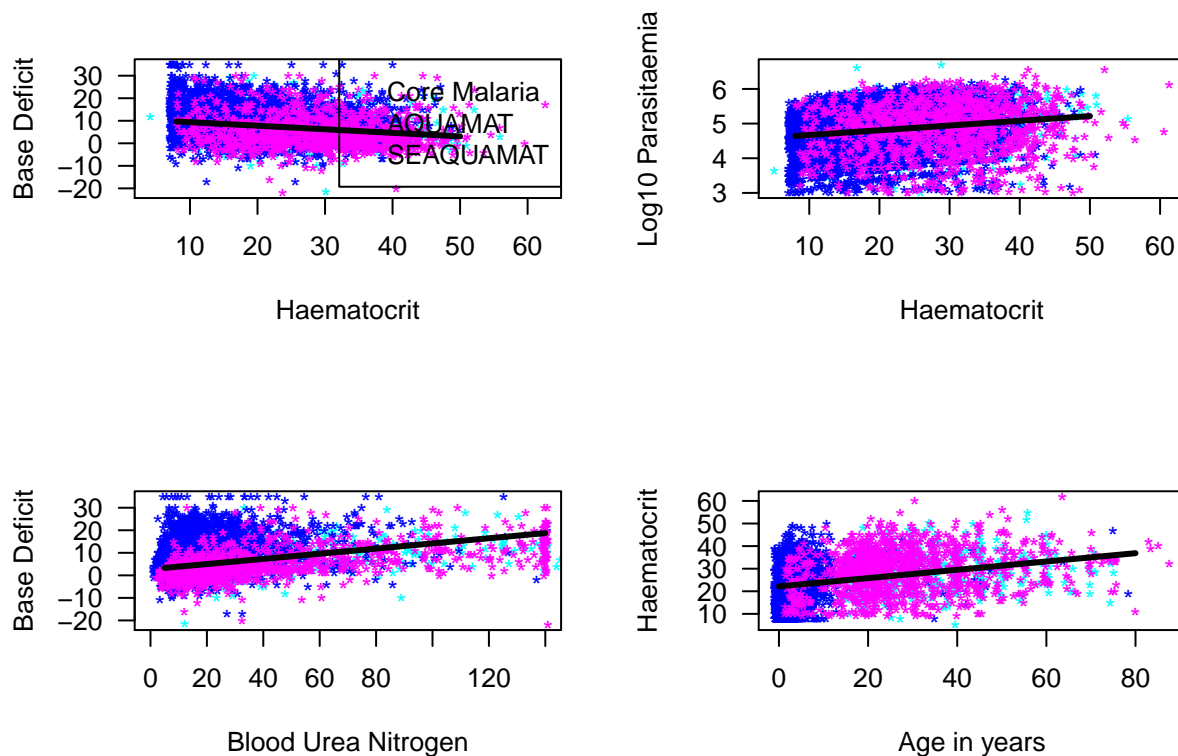
## Parasitaemia and Anaemia
plot(jitter(Leg_data$HCT,amount=1), Leg_data$LPAR,
```

```

col=Leg_data$studyID, pch='*', xlab='Haematocrit', ylab='Log10 Parasitaemia')
#legend('topright', col=unique(Leg_data$studyID), legend = unique(Leg_data$studyID), pch='*')
mod = lmer(formula = LPAR ~ HCT + (1 | studyID), data = Leg_data)
ys = predict(object = mod, newdata = data.frame(HCT=8:50, studyID=NA), re.form=NA)
lines(8:50, ys, lwd=3, col='black')
## BUN and BD
plot(jitter(Leg_data$BUN,amount=1), jitter(Leg_data$BD), xlim=c(0,140),
     col=Leg_data$studyID, pch='*', xlab='Blood Urea Nitrogen', ylab='Base Deficit')
#legend('topright', col=unique(Leg_data$studyID), legend = unique(Leg_data$studyID), pch='*')
mod = lmer(formula = BD ~ BUN + (1 | studyID), data = Leg_data)
ys = predict(object = mod, newdata = data.frame(BUN=5:140, studyID=NA), re.form=NA)
lines(5:140, ys, lwd=3, col='black')

## Parasitaemia and Anaemia
plot(jitter(Leg_data$AgeInYear,amount=1), Leg_data$HCT,
     col=Leg_data$studyID, pch='*', xlab='Age in years', ylab='Haematocrit')
#legend('topright', col=unique(Leg_data$studyID), legend = unique(Leg_data$studyID), pch='*')
mod = lmer(formula = HCT ~ AgeInYear + (1 | studyID), data = Leg_data)
ys = predict(object = mod, newdata = data.frame(AgeInYear=0:80, studyID=NA), re.form=NA)
lines(0:80, ys, lwd=3, col='black')

```



## Predictive value of anaemia on death adjusting for confounders

Before fitting the more complex GAM models we explore the standard glm (logistic regression) models.

```

mod_full = glmmer(outcome ~ HCT + LPAR + AgeInYear + BUN + BD + (1 | studyID),
                  data=Leg_data, family=binomial)

```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl = control$checkConv, : Model is nearly unidentifiable:
## - Rescale variables?
```

```
summary(mod_full)
```

```
## Generalized linear mixed model fit by maximum likelihood (Laplace
## Approximation) [glmerMod]
## Family: binomial ( logit )
## Formula: outcome ~ HCT + LPAR + AgeInYear + BUN + BD + (1 | studyID)
## Data: Leg_data
##
##          AIC          BIC    logLik deviance df.resid
##    3214.5    3260.4   -1600.2   3200.5     5221
##
## Scaled residuals:
##      Min       1Q   Median       3Q      Max
## -3.0755 -0.3426 -0.2344 -0.1681  9.1819
##
## Random effects:
## Groups Name             Variance Std.Dev.
## studyID (Intercept) 0.05531  0.2352
## Number of obs: 5228, groups: studyID, 3
##
## Fixed effects:
##              Estimate Std. Error z value Pr(>|z|)
## (Intercept) -4.216794   0.392658 -10.739 < 2e-16 ***
## HCT          0.019182   0.005440   3.526 0.000422 ***
## LPAR         0.002291   0.066768   0.034 0.972622
## AgeInYear    0.021372   0.004786   4.465 8.00e-06 ***
## BUN          0.011738   0.001711   6.860 6.87e-12 ***
## BD           0.135063   0.006930  19.491 < 2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Correlation of Fixed Effects:
##              (Intr) HCT    LPAR   AgInYr BUN
## HCT          -0.241
## LPAR         -0.759 -0.171
## AgeInYear    -0.269 -0.136  0.030
## BUN          -0.115  0.074 -0.047 -0.099
## BD           -0.120  0.254 -0.140  0.070 -0.271
## convergence code: 0
## Model is nearly unidentifiable: very large eigenvalue
## - Rescale variables?
```

Now let's make counterfactual predictions of anaemia on death for the patients in the database:

```
par(las=1)
plot(NA,NA, xlim=c(4,45), ylim=c(0,40),ylab='% predicted mortality', xlab='Haematocrit')
title('Counterfactual predictions: Overall mortality')
for(HCT in 4:45){
  mydata = Leg_data
  mydata$HCT=HCT
  ys = 100*predict(mod_full, newdata = mydata, re.form=NA, type='response')
  points(HCT,mean(ys), pch=18)
```

```
points(rep(HCT,2), quantile(ys, probs=c(0.1,0.9)), pch='-', col='red')
}
abline(h=10, lwd=3, col='blue')
```

### Counterfactual predictions: Overall mortality

