Homework 3

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1. Piece-wise linear mixed-effects models

First, without covariates, we consider some simple piece-wise linear mixed-effects models of post-infection CD4 as a function of time since HIV-infection. Suppose that we pick two interior knots at t = 2, 4 years after HIV infection. Give your final chosen model, and estimates and 95% CI's for the fixed effects under the following three scenarios.

$$Y_{ij} = \beta X_{ij} + b_i Z_{ij} + \epsilon_{ij}$$

Y_{ij}: Post-infection CD4 β: The fixed effect b_i: The random effect for subject i. X_{ij}, Z_{ij}: Covariate matrices for subject i. $\epsilon_{ij} \sim N(0,σ2)$ is the measurement error.

1.1 local constant fit

Using the basis functions B1(t) = 1[t<2], B2(t) = 1[2≤t<4] and B3(t) = 1[4≤t], with random-effects for each of the basis functions;

Model:

$$Y_{ij} = (\beta_1 + b_{1i})B_1(t_{ij}) + (\beta_2 + b_{2i})B_2(t_{ij}) + (\beta_3 + b_{3i})B_3(t_{ij}) + \epsilon_{ij}$$

```
time=BMACS$Time
B1<-function(t) I(t<2)
B1=as.numeric(B1(time))
B2<-function(t) I((t<4)& (t>=2))
B2=as.numeric(B2(time))
B3<-function(t) I(t>=4)
B3=as.numeric(B3(time))
B4<-function(t) t*I(t<2)
B4=as.numeric(B4(time))
B5<-function(t) t*I((t<4)& (t>=2))
B5=as.numeric(B5(time))
B6<-function(t) t*I(t>=4)
B6=as.numeric(B6(time))
b1=1
b2=function(t) return(t)
b2=as.numeric(b2(time))
b3=function(t) return(ifelse(t>2, t-2, 0))
b3=as.numeric(b3(time))
b4=function(t) return(ifelse(t>4, t-4, 0))
b4=as.numeric(b4(time))

data1<-cbind(BMACS, B1,B2,B3, B4,B5,B6,b1,b2,b3,b4)
model.1.1<-lmer(CD4~ B1+B2+B3 -1 +(B1+B2+B3 -1 |ID), data= data1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00642437
## (tol = 0.002, component 1)
```

```
summary(model.1.1)
```

```
## Linear mixed model fit by REML ['lmerMod']
## Formula: CD4 ~ B1 + B2 + B3 - 1 + (B1 + B2 + B3 - 1 | ID)
##    Data: data1
##
## REML criterion at convergence: 12415.2
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -4.0325 -0.5233 -0.0133  0.5175  3.9660
##
## Random effects:
##  Groups   Name Variance Std.Dev. Corr
##  ID       B1    69.19    8.318
##           B2    98.28    9.914    0.83
##           B3   145.41   12.059    0.66 0.92
##  Residual       31.08    5.575
## Number of obs: 1817, groups:  ID, 283
##
## Fixed effects:
##     Estimate Std. Error t value
## B1   33.0369     0.5395   61.24
## B2   27.0514     0.6765   39.99
## B3   23.5989     0.9351   25.24
##
## Correlation of Fixed Effects:
##    B1    B2
## B2 0.678
## B3 0.469 0.751
## convergence code: 0
## Model failed to converge with max|grad| = 0.00642437 (tol = 0.002, component 1)
```

Use Bootstrap to compute 95% confidence interval.

```
set.seed(1)
unique.ID=unique(BMACS$ID)
nID=length(unique.ID)
bootsample=function(){
  resample.ID=sample(unique.ID,nID,replace=T)
  do.call("rbind",lapply(1:nID,function(i) subset(BMACS,ID==resample.ID[i])))
  }
bootstrap.1.1=sapply(1:200,function(o){
  b=bootsample()
  t=b$Time
  B1<-function(t) I(t<2)
  B1=as.numeric(B1(t))
  B2<-function(t) I((t<4)& (t>=2))
  B2=as.numeric(B2(t))
  B3<-function(t) I(t>=4)
  B3=as.numeric(B3(t))
  b<-cbind(b, B1,B2,B3)
  boot.1.1<-lmer(CD4~ B1+B2+B3 -1 +(B1+B2+B3 -1 |ID), data= b)
  return(fixef(boot.1.1))
  })
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00220908
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00856673
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00321427
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00492095
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00222261
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00224653
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0068525
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0125243
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00267139
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0121323
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00635224
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00482803
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00259056
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00709216
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00411974
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00364958
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00954143
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00369521
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00543689
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0141801
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00231763
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00933153
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00256831
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00351866
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00542109
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00230842
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00305915
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0117816
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00294174
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00341783
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00290978
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00844393
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0037073
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00212161
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00535532
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00518227
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0129016
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00217855
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00244716
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00444202
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00445306
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00212565
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00317359
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.018399
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00358028
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00404998
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00204446
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0043261
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00307013
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00252409
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0103633
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0124394
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00690284
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00210715
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0209106
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00349202
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00970574
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.002652
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00753942
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00803499
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00655989
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00718806
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00218382
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0102949
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00523073
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00202332
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00463027
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0089004
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00407611
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00269219
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00690298
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00300092
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00291619
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0107292
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00233376
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00239657
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0125484
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0238787
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0218575
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00752482
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00567252
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0023703
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00481473
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.015146
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00547963
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00911799
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00685248
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0109838
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00417198
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00372753
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00304288
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00653601
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00438608
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0391239
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0024841
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00431015
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00304222
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00953235
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00382228
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00524973
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0109404
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00517511
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00289916
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00902339
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0113726
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0047439
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0032883
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00823675
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00321383
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00221544
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00232516
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00222819
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00452097
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00444975
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0058784
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00522834
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00474734
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0076148
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0044308
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00495009
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00331432
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00687575
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0186218
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00452971
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0035234
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00316736
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00617355
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00908558
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0033402
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0469821
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0152048
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00263844
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00628438
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00699319
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00570424
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0112661
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00329146
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00213523
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00288976
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00380877
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00308634
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0064739
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00365006
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00266101
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00905638
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.002629
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0112703
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0046077
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0216486
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00529482
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00239339
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00561932
## (tol = 0.002, component 1)
```

```
bootstrap.1.1=as.matrix(bootstrap.1.1)
upper95=apply(bootstrap.1.1,1,quantile,0.975)
lower95=apply(bootstrap.1.1,1,quantile,0.025)
estimate=fixef(model.1.1)
cbind(estimate,lower95,upper95)
```

```
##      estimate   lower95  upper95
## B1  33.03691  32.28070  33.90475
## B2  27.05142  25.98202  28.16932
## B3  23.59889  22.20210  25.05686
```

1.2 local linear fit without assuming continuity at the knots.

Three separate straight lines at t < 2, 2 ≤ t < 4 and 4 ≤ t, with random-effects for the intercepts only.

Model:

$$Y_{ij} = (\beta_1 + b_{1i})B_1(t_{ij}) + (\beta_2 + b_{2i})B_2(t_{ij}) + (\beta_3 + b_{3i})B_3(t_{ij}) + \beta_4 B_4(t_{ij}) + \beta_5 B_5(t_{ij}) + \beta_6 B_6(t_{ij}) + \epsilon_{ij}$$

The model fit 3 lines with own intercept and slop, and the knots are not forced to beconnected. Only the intercept terms have random effect.

```
model.1.2<-lmer(CD4~ B1+B2+B3 -1 +B4 + B5 + B6 +(B1+B2+B3 -1 |ID), data= data1)
summary(model.1.2)
```

```
## Linear mixed model fit by REML ['lmerMod']
## Formula: CD4 ~ B1 + B2 + B3 - 1 + B4 + B5 + B6 + (B1 + B2 + B3 - 1 | ID)
##    Data: data1
##
## REML criterion at convergence: 12211.2
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -4.2844 -0.5123 -0.0176  0.5173  4.1792
##
## Random effects:
##  Groups    Name Variance Std.Dev. Corr
##  ID        B1    69.25    8.322
##            B2   103.36   10.166   0.81
##            B3   151.36   12.303   0.65 0.92
##  Residual        26.37    5.135
## Number of obs: 1817, groups:  ID, 283
##
## Fixed effects:
##     Estimate Std. Error t value
## B1  36.9512     0.6196  59.642
## B2  35.1255     1.3002  27.015
## B3  30.6644     2.7162  11.289
## B4  -4.2504     0.3406 -12.478
## B5  -2.9737     0.3920  -7.585
## B6  -1.6081     0.5353  -3.004
##
## Correlation of Fixed Effects:
##     B1     B2     B3     B4     B5
## B2   0.299
## B3   0.137  0.130
## B4  -0.507  0.015  0.008
## B5  -0.001 -0.849  0.010  0.003
## B6   0.000 -0.004 -0.938  0.000  0.005
```

```
set.seed(1)
bootstrap.1.2=sapply(1:200,function(o){
  b=bootsample()
  t=b$Time
  B1<-function(t) I(t<2)
  B1=as.numeric(B1(t))
  B2<-function(t) I((t<4)& (t>=2))
  B2=as.numeric(B2(t))
  B3<-function(t) I(t>=4)
  B3=as.numeric(B3(t))
  B4<-function(t) t*I(t<2)
  B4=as.numeric(B4(t))
  B5<-function(t) t*I((t<4)& (t>=2))
  B5=as.numeric(B5(t))
  B6<-function(t) t*I(t>=4)
  B6=as.numeric(B6(t))
  b<-cbind(b, B1,B2,B3,B4,B5,B6)
  fit1.2<-lmer(CD4~ B1+B2+B3 -1 +B4 + B5 + B6 +(B1+B2+B3 -1 |ID), data= b)
  return(fixef(fit1.2))
})
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00867838
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0103108
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00851671
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00707882
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00712933
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00206851
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0183315
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00574627
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00858646
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00212266
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00263442
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00448007
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00235939
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00923734
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00294727
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00277455
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00296463
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0128852
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00465728
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00446697
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00288329
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00340342
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.008612
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00494531
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00367587
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00297096
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0207832
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0029065
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00349047
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00507791
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0036336
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0182394
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00358739
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0194179
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00795192
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00392241
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00368726
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00256654
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00200239
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00578315
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00620206
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00350389
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00963585
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00564232
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0346518
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00223758
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00392579
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00782933
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00299599
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00205341
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00310093
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00468199
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00229812
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0102623
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00233833
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0106423
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00370824
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.018832
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00324739
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0124661
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0102514
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00335906
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00255289
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00693007
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0115016
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0130126
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.017436
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0129157
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00417867
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00750816
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00995554
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0052707
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00834084
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00202379
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0187494
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00327826
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0117278
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00569745
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00384368
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00878796
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00533669
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.011782
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00206759
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00605387
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00200078
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0160727
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00736673
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00236131
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00517555
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00464121
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00267445
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00566353
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00359455
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00417946
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00734118
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00569488
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0144283
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00268356
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00328771
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0114044
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00319596
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00473522
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00450067
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0194618
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00448758
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00380231
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00302744
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00332929
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00621499
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0156127
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00942868
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0231709
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00540788
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00236486
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0255366
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00902882
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00879823
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00352829
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00650492
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00918165
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00638041
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.013129
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00368243
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00355605
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0226767
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00407058
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00773929
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00652961
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0326263
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00452295
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0144839
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00342052
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0127915
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00380593
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00302803
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00607805
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.011367
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0141681
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00944172
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0028368
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00504437
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00225272
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0104262
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00384959
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00801699
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0206883
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00377185
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00904954
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00625028
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00270745
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0107735
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0331009
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00649768
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0324134
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00563365
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00634607
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00423816
## (tol = 0.002, component 1)
```

```
bootstrap.1.2=as.matrix(bootstrap.1.2)
estimate=fixef(model.1.2)
upper95=apply(bootstrap.1.2,1,quantile,0.975)
lower95=apply(bootstrap.1.2,1,quantile,0.025)
cbind(estimate,lower95,upper95)
```

```
##     estimate    lower95    upper95
## B1 36.951184  35.762789 38.0564636
## B2 35.125475  33.252375 38.2445655
## B3 30.664368  25.290012 35.0678674
## B4 -4.250410  -5.023388 -3.1854724
## B5 -2.973743  -3.966518 -2.3608914
## B6 -1.608075  -2.423214 -0.4683855
```

1.3 local linear fit with continuity at the knots

Using B1(t) = 1, B2(t) = t, B3(t) = (t−2)+ and B4(t) = (t−4)+, with random-effects for each of the basis functions.

Model:

$$Y_{ij} = \beta_1 + b_{1i} + (\beta_2 + b_{2i})t_{ij} + (\beta_3 + b_{3i})(t_{ij} - 2)^+ + (\beta_4 + b_{4i})(t_{ij} - 4)^+ + \epsilon_{ij}$$

```
model.1.3<-lmer(CD4~b2+b3+b4+(b2+b3+b4|ID), data= data1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00562395
## (tol = 0.002, component 1)
```

```
summary(model.1.3)
```

```
## Linear mixed model fit by REML ['lmerMod']
## Formula: CD4 ~ b2 + b3 + b4 + (b2 + b3 + b4 | ID)
##    Data: data1
##
## REML criterion at convergence: 12075.3
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -4.4905 -0.5299 -0.0254  0.4937  4.5621
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  ID       (Intercept) 87.46    9.352
##           b2          21.81    4.670    -0.45
##           b3          27.03    5.199     0.29 -0.77
##           b4          15.10    3.886    -0.04  0.12 -0.53
##  Residual             21.58    4.645
## Number of obs: 1817, groups:  ID, 283
##
## Fixed effects:
##             Estimate Std. Error t value
## (Intercept)  36.8266     0.6531  56.385
## b2           -4.0310     0.3905 -10.324
## b3            1.4370     0.5666   2.536
## b4            1.3995     0.6735   2.078
##
## Correlation of Fixed Effects:
##    (Intr) b2     b3
## b2 -0.586
## b3  0.407 -0.782
## b4 -0.086  0.213 -0.556
## convergence code: 0
## Model failed to converge with max|grad| = 0.00562395 (tol = 0.002, component 1)
```

```
set.seed(1)
bootstrap.1.3=sapply(1:200, function(o) {
  b=bootsample()
  t=b$Time
  B2=function(t) return(t)
  B2=as.numeric(B2(t))
  B3=function(t) return(ifelse(t>2, t-2, 0))
  B3=as.numeric(B3(t))
  B4=function(t) return(ifelse(t>4, t-4, 0))
  B4=as.numeric(B4(t))
  cd41.3<-cbind(b, B2,B3,B4)
  fit1.3<-lmer(CD4~B2+B3+B4+(B2+B3+B4|ID), data= b)
  return(fixef(fit1.3))
})
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00384433
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00550403
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0208836
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00594188
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00200718
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.01029 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00463198
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0145629
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0682363
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00480124
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00623515
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.004451
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0127015
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00353983
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00677175
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00815437
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00372729
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0232877
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00949217
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00535032
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00472507
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00922235
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0085798
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00568694
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00539185
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0128462
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00325239
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.035569
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00283714
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0114285
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00485423
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00572065
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00263985
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00203326
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00413278
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00977152
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00314208
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.011041
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0187912
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0134982
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00580748
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00260219
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0056004
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0115839
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0106843
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00334063
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00471752
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0189258
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00454542
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00937425
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00285798
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00548997
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00503191
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00320263
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0102486
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00329819
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00412478
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00769657
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0127321
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00317027
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00300699
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0035155
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00838136
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0395938
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00652525
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0102937
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00507529
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0025557
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0188041
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00407003
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00297808
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00273143
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00505201
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00700015
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0028388
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00414937
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00408104
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00324462
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00995 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0132264
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00356912
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00417925
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0121701
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00259923
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00317965
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00599315
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00918851
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00405551
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00272526
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0415357
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00234929
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0123262
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0134227
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00365007
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00343651
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00579819
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00246241
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00689848
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.02032 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00325157
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00973215
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0277613
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00521767
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00716412
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00803469
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00285395
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00357831
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0106967
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00309141
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00340108
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00762624
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0060754
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00737225
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00607602
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0126621
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0111093
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00579075
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00490348
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00393578
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00415862
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00781805
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00425069
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0090783
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0083185
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0133835
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00552621
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0045915
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0184496
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0154533
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00231783
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00544614
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00666717
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00930759
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00446868
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.002994
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00333101
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00222528
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00788248
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00318781
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00356038
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00417526
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0068087
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00453019
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00754983
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00935535
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00689469
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0105421
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00478234
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00793688
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.025727
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00693634
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00567073
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0175097
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00574195
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00315322
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0107042
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00537261
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00500506
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00352351
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00812539
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00592465
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00289318
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00459441
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00213241
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0049812
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00581842
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0046414
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00341528
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00338308
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00265337
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00414553
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0163441
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00596458
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00880092
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00517144
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00236199
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00233471
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00773931
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0178807
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00224644
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00539758
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00319438
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00529979
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00649701
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00662583
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0119097
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0132367
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00527679
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00441374
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00549592
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00547383
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00216565
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00264734
## (tol = 0.002, component 1)
```

```
bootstrap.1.3=as.matrix(bootstrap.1.3)
estimate=fixef(model.1.3)
upper95=apply(bootstrap.1.3,1,quantile,0.975)
lower95=apply(bootstrap.1.3,1,quantile,0.025)
cbind(estimate,lower95,upper95)
```

```
##               estimate    lower95    upper95
## (Intercept) 36.826588 35.8096534 37.770249
## b2          -4.030985 -4.5829069 -3.355410
## b3           1.436992  0.1517599  2.058722
## b4           1.399518  0.6574406  2.857244
```

1.4 Interpretations and clinical conclusions

What are your interpretations and clinical conclusions from the results obtained in #1.1, #1.2 and #1.3?

```
anova(model.1.1,model.1.2,model.1.3,refit=F)
```

```
## Data: data1
## Models:
## model.1.1: CD4 ~ B1 + B2 + B3 - 1 + (B1 + B2 + B3 - 1 | ID)
## model.1.2: CD4 ~ B1 + B2 + B3 - 1 + B4 + B5 + B6 + (B1 + B2 + B3 - 1 | ID)
## model.1.3: CD4 ~ b2 + b3 + b4 + (b2 + b3 + b4 | ID)
##          Df   AIC   BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## model.1.1 10 12435 12490 -6207.6   12415
## model.1.2 13 12237 12309 -6105.6   12211 203.94      3  < 2.2e-16 ***
## model.1.3 15 12105 12188 -6037.7   12075 135.88      2  < 2.2e-16 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Model.1.3 is the best model because its AIC is the smallest.

In conclusion, patients' post CD4 level decreases as time passes by since infection. The decreasing speed is the fastest in the first two years after infection, becomes slower in the 2nd-4th year, and even slower after the 4th year.

2. Extend the analysis in #1 by including smoking status as the covariate.

In this case, you will consider the varying-coeffcient mixed-effects models of the form

$$Y_{ij} = \beta_0(t) + b_{0i}(t) + \beta_1(t)X_i(t) + b_{1i}(t)X_i(t) + \epsilon_t$$

where Xi(t) is the smoking status, b0i(t) and b1i(t) are subject-specific deviation curves and ϵ_t is the independent measurement error.

Give your final chosen model, and estimates and 95% CI's for the fixed effects under the following three scenarios:

2.1 Local constant fit

Local constant fit using the basis functions in #1.1 for β0(t), b0i(t), β1(t) and b1i(t);

Model:

$$Y_{ij} = (\beta_1 + b_{1i})B_1t_{ij} + (\beta_2 + b_{2i})B_2t_{ij} + (\beta_3 + b_{3i})B_3t_{ij} + \beta_4 B_1t_{ij}S_{ij} + \beta_5 B_2t_{ij}S_{ij} + \beta_6 B_3t_{ij}S_{ij} + \epsilon_{ij}$$

#yij =β1B1(tij)+β2B2(tij)+β3B3(tij)+ (β4 +b4i)B1(tij)Sij +(β5 +b5i)B2(tij)Sij +(β6 +b6i)B3(tij)Sij +□ij (2.1.2) #yij =(β1 +b1i)B1(tij)+(β2 +b2i)B2(tij)+(β3 +b3i)B3(tij)+ (β4 +b4i)B1(tij)Sij +(β5 +b5i)B2(tij)Sij +(β6 +b6i)B3(tij)Sij +□ij

```
smoke=BMACS$Smoke
S1=B1*smoke
S2=B2*smoke
S3=B3*smoke
S4=B4*smoke
S5=B5*smoke
S6=B6*smoke
s1=b1*smoke
s2=b2*smoke
s3=b3*smoke
s4=b4*smoke

data2=cbind(data1,S1,S2,S3,S4,S5,S6,s1,s2,s3,s4)
model.2.1<-lmer(CD4~-1+B1+B2+B3+S1+S2+S3+(-1+B1+B2+B3|ID), data= data2)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00343388
## (tol = 0.002, component 1)
```

```
summary(model.2.1)
```

```
## Linear mixed model fit by REML ['lmerMod']
## Formula: CD4 ~ -1 + B1 + B2 + B3 + S1 + S2 + S3 + (-1 + B1 + B2 + B3 |
##     ID)
##    Data: data2
##
## REML criterion at convergence: 12402.3
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -3.9959 -0.5247 -0.0138  0.5129  3.9590
##
## Random effects:
##  Groups   Name Variance Std.Dev. Corr
##  ID       B1    68.78    8.293
##           B2    96.42    9.819   0.83
##           B3   145.81   12.075   0.66 0.93
##  Residual       31.09    5.576
## Number of obs: 1817, groups:  ID, 283
##
## Fixed effects:
##    Estimate Std. Error t value
## B1  32.4066     0.6700  48.370
## B2  25.9628     0.8298  31.288
## B3  22.9001     1.1316  20.237
## S1   1.7244     1.1252   1.533
## S2   3.1522     1.4128   2.231
## S3   1.6618     2.0278   0.820
##
## Correlation of Fixed Effects:
##    B1     B2     B3     S1     S2
## B2  0.690
## B3  0.490  0.769
## S1 -0.595 -0.411 -0.292
## S2 -0.405 -0.587 -0.452  0.660
## S3 -0.273 -0.429 -0.558  0.445  0.730
## convergence code: 0
## Model failed to converge with max|grad| = 0.00343388 (tol = 0.002, component 1)
```

Bootstrap

```
set.seed(1)
bootstrap.2.1=sapply(1:200,function(o){
  b=bootsample()
  t=b$Time
  s=b$Smoke
  B1<-function(t) I(t<2)
  B1=as.numeric(B1(t))
  B2<-function(t) I((t<4)& (t>=2))
  B2=as.numeric(B2(t))
  B3<-function(t) I(t>=4)
  B3=as.numeric(B3(t))
  S1=B1*s
  S2=B2*s
  S3=B3*s
  cd42.1<-cbind(b, B1,B2,B3,S1,S2,S3)
  fit2.1<-lmer(CD4~-1+B1+B2+B3+S1+S2+S3+(-1+B1+B2+B3|ID), data= b)
  return(fixef(fit2.1))
})
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00626406
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0121879
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00799786
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00500773
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00367439
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00411408
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00923054
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0089244
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00229953
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00353559
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00591715
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00810924
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00809334
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0129773
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00413514
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00463014
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00366877
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00310144
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0128063
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00740285
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0256185
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0112257
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00787423
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00399586
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0196126
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00212264
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0038125
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.018624
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00207939
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0111905
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0131609
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0052103
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00567091
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00824391
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0077935
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00273776
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00229275
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00408391
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00294715
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00233833
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00429758
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00364677
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0250653
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00254417
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00669343
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00537635
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00901422
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00945702
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00289326
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00840554
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0029947
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00286477
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00369891
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00301397
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0123931
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00372099
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00231682
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00550318
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0189838
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0161483
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00556755
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0154762
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00266372
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00275529
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0160953
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.003029
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0024335
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00837139
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00236139
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00315542
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0759306
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00873746
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00578203
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00499378
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00243631
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00896204
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00624841
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00956391
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00528904
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00285088
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00831083
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00663622
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00244104
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00943303
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00743218
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00331409
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00379275
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00727321
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.004599
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00382286
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00363262
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00295143
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00832509
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0214752
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00568432
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00939935
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0101802
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0158872
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00322281
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0023264
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00308113
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00563334
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00654622
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00205609
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00652632
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00357281
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00628323
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00274259
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00267929
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00527013
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00401486
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.010283
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0507372
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00541955
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00946018
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00243091
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00225901
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0264062
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0030532
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0024319
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00585076
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00308048
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00482877
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00499936
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00551224
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.013557
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00588862
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00462182
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00558159
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0085357
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00208697
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00383603
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00236591
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00490955
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00493105
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0103069
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0206549
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00257886
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0027285
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00228569
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00794409
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00478159
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00246742
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00318504
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0193929
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00382909
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0112978
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00392507
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00259232
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00646648
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00384864
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00364685
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00360775
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00259649
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0035177
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0197822
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00649769
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0218206
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00238264
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00224831
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0109961
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00323744
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0135762
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00256307
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0062768
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00202179
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0113553
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00356426
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00504816
## (tol = 0.002, component 1)
```

```
bootstrap.2.1=as.matrix(bootstrap.2.1)
estimate=fixef(model.2.1)
upper95=apply(bootstrap.2.1,1,quantile,0.975)
lower95=apply(bootstrap.2.1,1,quantile,0.025)
cbind(estimate,lower95,upper95)
```

```
##      estimate     lower95    upper95
## B1 32.406614 31.4784741 33.532124
## B2 25.962782 24.4663774 27.300904
## B3 22.900084 20.9781115 24.665406
## S1  1.724428  0.1234384  3.682452
## S2  3.152200  1.1931642  5.213286
## S3  1.661812 -0.8567107  4.284879
```

2.2 Local linear fit without assuming continuity at the knots Local linear fit without assuming continuity at the knots for β0(t), b0i(t), β1(t) and b1i(t), i.e., using the basis functions as in #1.2;

Model:

$$Y_{ij} = \sum_{k=1}^{6}(\beta_k + b_{ki})B_k t_{kj} + \sum_{k=7}^{12}\beta_k B_{k-6}(t_{kj})S_{ij} + \epsilon_{ij}$$

```
model.2.2<-lmer(CD4~-1+B1+B2+B3+B4+B5+B6+S1+S2+S3+S4+S5+S6+ (-1+B1+B2+B3+B4+B5+B6|ID), data= data2)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0758756
## (tol = 0.002, component 1)
```

```
summary(model.2.2)
```

```
## Linear mixed model fit by REML ['lmerMod']
## Formula: CD4 ~ -1 + B1 + B2 + B3 + B4 + B5 + B6 + S1 + S2 + S3 + S4 +
##     S5 + S6 + (-1 + B1 + B2 + B3 + B4 + B5 + B6 | ID)
##    Data: data2
##
## REML criterion at convergence: 12025
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -4.7090 -0.5044 -0.0208  0.4806  4.7382
##
## Random effects:
##  Groups   Name Variance Std.Dev. Corr
##  ID       B1    92.472  9.616
##           B2   146.095  12.087    0.58
##           B3   128.970  11.356    0.62  0.45
##           B4    26.847   5.181   -0.51  0.21  0.01
##           B5    11.529   3.395   -0.23 -0.57  0.23  0.18
##           B6     5.854   2.420   -0.32 -0.07 -0.37  0.56  0.37
##  Residual        19.870  4.458
## Number of obs: 1817, groups:  ID, 283
##
## Fixed effects:
##     Estimate Std. Error t value
## B1 35.96129    0.84269  42.675
## B2 34.70729    1.57023  22.103
## B3 29.02047    2.96096   9.801
## B4 -3.80888    0.56111  -6.788
## B5 -3.19370    0.52346  -6.101
## B6 -1.36325    0.63609  -2.143
## S1  2.79647    1.41245   1.980
## S2  2.70984    2.81916   0.961
## S3  4.14107    5.53275   0.748
## S4 -1.25956    0.96835  -1.301
## S5 -0.01128    0.96052  -0.012
## S6 -0.65797    1.19457  -0.551
##
## Correlation of Fixed Effects:
##     B1     B2     B3     B4     B5     B6     S1     S2     S3     S4
## B2  0.277
## B3  0.155  0.064
## B4 -0.625  0.112  0.003
## B5 -0.098 -0.844  0.059  0.065
## B6 -0.089 -0.028 -0.923  0.132  0.084
## S1 -0.597 -0.165 -0.092  0.373  0.059  0.053
## S2 -0.154 -0.557 -0.035 -0.062  0.470  0.016  0.252
## S3 -0.083 -0.034 -0.535 -0.002 -0.031  0.494  0.137  0.049
## S4  0.362 -0.065 -0.002 -0.579 -0.038 -0.077 -0.623  0.106  0.005
## S5  0.054  0.460 -0.032 -0.035 -0.545 -0.046 -0.091 -0.861  0.056  0.058
## S6  0.047  0.015  0.492 -0.071 -0.045 -0.532 -0.082 -0.033 -0.930  0.117
##     S5
## B2
## B3
## B4
## B5
## B6
## S1
## S2
## S3
## S4
## S5
## S6  0.080
## convergence code: 0
## Model failed to converge with max|grad| = 0.0758756 (tol = 0.002, component 1)
```

Bootstrap

```
set.seed(1)
bootstrap.2.2=sapply(1:100,function(o){
  b=bootsample()
  t=b$Time
  s=b$Smoke
  B1<-function(t) I(t<2)
  B1=as.numeric(B1(t))
  B2<-function(t) I((t<4)&(t>=2))
  B2=as.numeric(B2(t))
  B3<-function(t) I(t>=4)
  B3=as.numeric(B3(t))
  B4<-function(t) t*I(t<2)
  B4=as.numeric(B4(t))
  B5<-function(t) t*I((t<4)&(t>=2))
  B5=as.numeric(B5(t))
  B6<-function(t) t*I(t>=4)
  B6=as.numeric(B6(t))
  S1=B1*s
  S2=B2*s
  S3=B3*s
  S4=B4*s
  S5=B5*s
  S6=B6*s
  cd42.2<-cbind(b, B1,B2,B3,B4,B5,B6,S1,S2,S3,S4,S5,S6)
  fit2.2<-lmer(CD4~-1+B1+B2+B3+B4+B5+B6+S1+S2+S3+S4+S5+S6+
                 (-1+B1+B2+B3+B4+B5+B6|ID), data= b)
  return(fixef(fit2.2))
})
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.149315
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.310827
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.19428 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0883187
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.133764
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.149218
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0825072
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.183222
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0465642
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.159379
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.167696
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0153243
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.047274
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0813189
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0491585
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.340067
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : unable to evaluate scaled gradient
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge: degenerate Hessian with 1
## negative eigenvalues
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0420642
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.172878
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.244185
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0364288
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.119513
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0511786
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0650507
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.104097
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.341237
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.34496 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0523937
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.378283
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.17931 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0365395
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.038773
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0747419
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.116405
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0887849
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0137429
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.248851
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.13235 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.149572
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0736307
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.048332
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.100069
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0419632
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.265644
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.226445
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.098647
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0841813
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0283251
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.124693
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0694976
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.180334
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0310201
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0721865
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.217586
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.157742
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0323453
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0954944
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0757462
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0508772
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.070939
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.222489
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0361571
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0513087
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0523796
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.071436
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0790841
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0354591
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0191824
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0387749
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0741306
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.176423
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0499896
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.126854
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0479434
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.104939
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.100005
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0443719
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0548004
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0416886
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.116761
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0786234
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0241125
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.058375
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0233708
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0741281
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.166033
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.108942
## (tol = 0.002, component 1)
```

```
## boundary (singular) fit: see ?isSingular
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0427485
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0124643
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0627717
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0594576
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.248336
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0752689
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0748648
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.15631 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0777068
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.11534 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.153169
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0244696
## (tol = 0.002, component 1)
```

```
bootstrap.2.2=as.matrix(bootstrap.2.2)
estimate=fixef(model.2.2)
upper95=apply(bootstrap.2.2,1,quantile,0.975)
lower95=apply(bootstrap.2.2,1,quantile,0.025)
cbind(estimate,lower95,upper95)
```

```
##       estimate    lower95    upper95
## B1 35.96129458 34.6872007 37.4010601
## B2 34.70729341 32.7614908 37.9929169
## B3 29.02047295 25.5580445 34.0008059
## B4 -3.80887700 -4.8884098 -2.9647985
## B5 -3.19369768 -4.0601390 -2.4545433
## B6 -1.36325395 -2.3540289 -0.6475405
## S1  2.79646819  0.7843236  4.9777257
## S2  2.70984085 -1.2807460  7.8351402
## S3  4.14107049 -5.0176445 12.3485412
## S4 -1.25956211 -2.5072596  0.4835669
## S5 -0.01127876 -1.7960817  1.2931933
## S6 -0.65796835 -2.5683122  1.4367535
```

###2.3 Local linear fit with continuity at the knots Local linear fit with continuity at the knots for β0(t), b0i(t), β1(t) and b1i(t), i.e., using the basis functions as in #1.3.

Model:

$$Y_{ij} = \sum_{k=1}^{4}(\beta_k + b_{ki})B_k(t_{kj}) + \sum_{k=5}^{8}\beta_k B_{k-4}(t_{kj})S_{ij} + \epsilon_{ij}$$

Where

$$B_1(t) = 1, B_2(t) = t, B_3(t) = (t-2)^+, B_4(t) = (t-4)^+$$

```
model.2.3<-lmer(CD4~b2+b3+b4+s1+s2+s3+s4+ (b2+b3+b4|ID), data= data2)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00531314
## (tol = 0.002, component 1)
```

```
summary(model.2.3)
```

```
## Linear mixed model fit by REML ['lmerMod']
## Formula: CD4 ~ b2 + b3 + b4 + s1 + s2 + s3 + s4 + (b2 + b3 + b4 | ID)
##    Data: data2
##
## REML criterion at convergence: 12063.5
##
## Scaled residuals:
##     Min      1Q  Median      3Q     Max
## -4.4651 -0.5208 -0.0256  0.4926  4.5480
##
## Random effects:
##  Groups   Name        Variance Std.Dev. Corr
##  ID       (Intercept) 87.13    9.334
##           b2          22.05    4.696    -0.46
##           b3          27.80    5.272     0.29 -0.77
##           b4          15.71    3.963    -0.02  0.16 -0.56
##  Residual             21.56    4.643
## Number of obs: 1817, groups:  ID, 283
##
## Fixed effects:
##             Estimate Std. Error t value
## (Intercept)  36.0511     0.8120  44.395
## b2           -3.9302     0.4822  -8.150
## b3            1.1842     0.6896   1.717
## b4            1.9510     0.7987   2.443
## s1            2.1685     1.3635   1.590
## s2           -0.2945     0.8270  -0.356
## s3            0.8097     1.2272   0.660
## s4           -2.0190     1.4980  -1.348
##
## Correlation of Fixed Effects:
##    (Intr) b2     b3     b4     s1     s2     s3
## b2 -0.587
## b3  0.412 -0.790
## b4 -0.084  0.227 -0.567
## s1 -0.596  0.349 -0.245  0.050
## s2  0.342 -0.583  0.461 -0.132 -0.590
## s3 -0.231  0.444 -0.562  0.318  0.402 -0.776
## s4  0.045 -0.121  0.302 -0.533 -0.079  0.220 -0.560
## convergence code: 0
## Model failed to converge with max|grad| = 0.00531314 (tol = 0.002, component 1)
```

Bootstrap

```
set.seed(1)
bootstrap.2.3=sapply(1:200,function(o){
  b=bootsample()
  t=b$Time
  s=b$Smoke
  B2=function(t) return(t)
  B2=as.numeric(B2(t))
  B3=function(t) return(ifelse(t>2, t-2, 0))
  B3=as.numeric(B3(t))
  B4=function(t) return(ifelse(t>4, t-4, 0))
  B4=as.numeric(B4(t))
  S1=s
  S2=B2*s
  S3=B3*s
  S4=B4*s
  cd42.3<-cbind(b, B2,B3,B4,S1,S2,S3,S4)
  fit2.3<-lmer(CD4~B2+B3+B4+S1+S2+S3+S4+
                (B2+B3+B4|ID), data= b)
  return(fixef(fit2.3))
})
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00840511
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00428156
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0119241
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0461594
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0113066
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00233015
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00407779
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0037686
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00552758
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0049891
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00325756
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00233252
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0119261
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0156451
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0132147
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00234365
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00738808
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0151702
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00246832
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00269151
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00302506
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00647235
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00513743
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00309147
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00480925
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00371943
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00248132
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0167164
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00828814
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0100643
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0028388
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00219429
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00514973
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00803471
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00671286
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00363518
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00778763
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00259619
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00954872
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0361168
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00300014
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00416237
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0085052
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00722409
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00563682
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00430431
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00512301
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00375469
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0065597
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00605818
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0109871
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0205501
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0203599
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00420855
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00441389
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.004241
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.014756
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00528676
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00505965
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00686355
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0233946
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00401119
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00370813
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00517117
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00654202
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0538421
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00956012
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.003816
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0104448
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00504334
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00585625
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00275715
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00788088
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00532663
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00220145
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00645739
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0339135
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00296469
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00396968
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00977214
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00596165
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00547271
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00209155
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.035429
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00537473
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0043288
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0098875
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00567367
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00654192
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00404267
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00334215
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00323466
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00604486
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00434449
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00311154
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00968102
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0175863
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00273888
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00584104
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00785083
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0141438
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00555958
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00416051
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00459319
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0026695
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00485377
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00258512
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00758383
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00308144
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00751397
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00584585
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00874817
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00623804
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00570856
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00747033
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00463285
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00349791
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00791251
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00290337
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00520842
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00443318
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00938686
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00854969
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0105745
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0121012
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00402856
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00228822
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00488592
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0186342
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00418579
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0126832
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.026256
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00203689
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0044171
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00854208
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00219139
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00565785
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00371826
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0036099
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00310209
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0250264
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00546777
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00364044
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00305367
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00379612
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0111652
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0162624
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.012603
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0139901
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00544736
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00554403
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0269909
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.02949 (tol
## = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00762653
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00861782
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00809114
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00946077
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00839422
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00274084
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0102433
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00660997
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00257927
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00507825
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00822009
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00679056
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00649742
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0185189
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00279631
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00307722
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0178104
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00331884
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0104224
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00521366
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0136652
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0109946
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0103638
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00938945
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00531351
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00508556
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00409838
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0074971
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00508742
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00276697
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00532242
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00773887
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00370049
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00577849
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00278924
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00232174
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.00630337
## (tol = 0.002, component 1)
```

```
## Warning in checkConv(attr(opt, "derivs"), opt$par, ctrl =
## control$checkConv, : Model failed to converge with max|grad| = 0.0235799
## (tol = 0.002, component 1)
```

```
bootstrap.2.3=as.matrix(bootstrap.2.3)
estimate=fixef(model.2.3)
upper95=apply(bootstrap.2.3,1,quantile,0.975)
lower95=apply(bootstrap.2.3,1,quantile,0.025)
cbind(estimate,lower95,upper95)
```
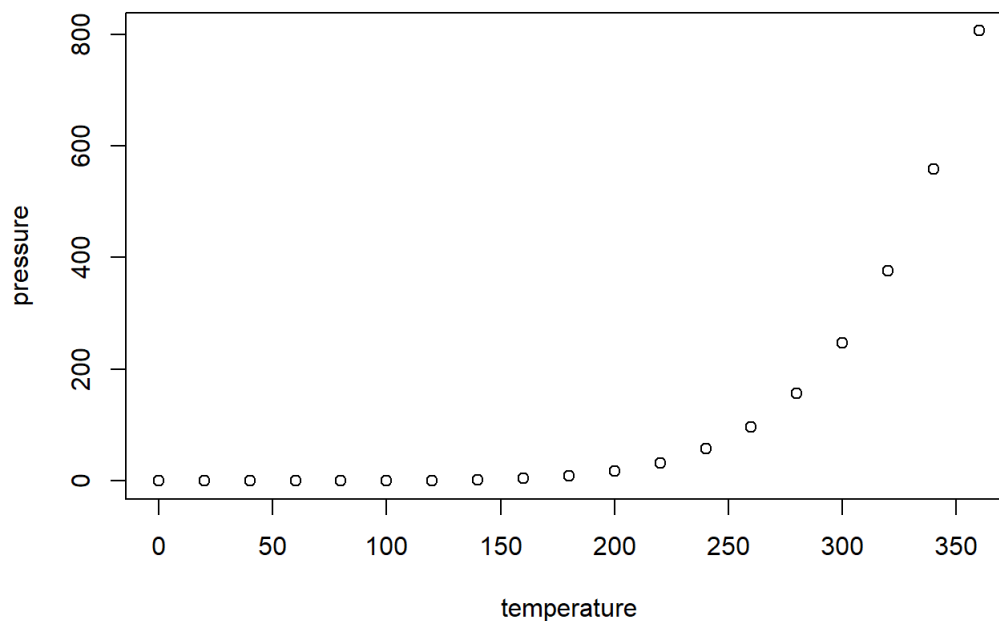
```
##                estimate    lower95    upper95
## (Intercept) 36.0511410 34.6159670 37.3196434
## b2          -3.9302049 -4.6689994 -3.0488934
## b3           1.1842017 -0.1162452  2.1833758
## b4           1.9510086  0.9120519  3.5340768
## s1           2.1685467  0.3467165  4.6542024
## s2          -0.2945300 -1.6647435  1.0449123
## s3           0.8097118 -1.4070638  2.9925775
## s4          -2.0190406 -4.6836495  0.4501607
```

2.4 Interpretations and clinical conclusions What are your interpretations and clinical conclusions about the effects of smoking status obtained in #2.1, #2.2 and #2.3?

```
anova(model.2.1,model.2.2,model.2.3,refit=F)
```

```
## Data: data2
## Models:
## model.2.1: CD4 ~ -1 + B1 + B2 + B3 + S1 + S2 + S3 + (-1 + B1 + B2 + B3 |
## model.2.1:     ID)
## model.2.3: CD4 ~ b2 + b3 + b4 + s1 + s2 + s3 + s4 + (b2 + b3 + b4 | ID)
## model.2.2: CD4 ~ -1 + B1 + B2 + B3 + B4 + B5 + B6 + S1 + S2 + S3 + S4 +
## model.2.2:     S5 + S6 + (-1 + B1 + B2 + B3 + B4 + B5 + B6 | ID)
##          Df   AIC   BIC  logLik deviance  Chisq Chi Df Pr(>Chisq)
## model.2.1 13 12428 12500 -6201.2    12402
## model.2.3 19 12102 12206 -6031.7    12064 338.851      6  < 2.2e-16 ***
## model.2.2 34 12093 12280 -6012.5    12025  38.492     15   0.000763 ***
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Model.2.2 is the best one because it has the smallest AIC. We can see from the model that smokers' post-CD4 level decreaseS faster then non-smokers in all time interval. The relationship between post-CD4 cell level and time is the same as the conclusion in 1.4.

Note that the `echo = FALSE` parameter was added to the code chunk to prevent printing of the R code that generated the plot.