

# **Covariate Plots**

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# 1 Purpose

This script picks up after model. Rnw to process bootstrap results and make covariate plots.

# 1.1 Summarize bootstrap models.

## Listing 1:

```
> #wait for bootstraps to finish
> getwd()
```

[1] "/data/metrumrg/inst/example/project/script"

# Listing 2:

```
> require(metrumrg)
> boot <- read.csv('../nonmem/1005bootlog.csv',as.is=TRUE)
> head(boot)
```

	Χ	tool	run	parameter	moment	value
1	1	nm7	1	ofv	minimum	2459.17577212358
2	2	nm7	1	THETA1	estimate	9.90624
3	3	nm7	1	THETA1	prse	<na></na>
4	4	nm7	1	THETA1	se	<na></na>
5	5	nm7	1	THETA2	estimate	21.8851
6	6	nm7	1	THETA2	prse	<na></na>

# Listing 3:

## > unique(boot\$parameter)

```
[1] "ofv" "THETA1" "THETA2" "THETA3" "THETA4" "THETA5"
[7] "THETA6" "THETA7" "OMEGA1.1" "OMEGA2.1" "OMEGA2.2" "OMEGA3.1"
[13] "OMEGA3.2" "OMEGA3.3" "SIGMA1.1" "SIGMA2.1" "SIGMA2.2" "cov"
[19] "prob" "min" "data"
```

# Listing 4:

# > text2decimal(unique(boot\$parameter))

```
[1] NA 1.0 2.0 3.0 4.0 5.0 6.0 7.0 1.1 2.1 2.2 3.1 3.2 3.3 1.1 2.1 2.2 NA NA [20] NA NA
```

## Listing 5:

```
> boot$X <- NULL
```

It looks like we have 14 estimated parameters. We will map them to the original control stream.



# Listing 6:

```
> boot <- boot[!is.na(text2decimal(boot$parameter)),]
> head(boot)

tool run parameter moment value
2 nm7 1 THETA1 estimate 9.90624
3 nm7 1 THETA1 prse <NA>
4 nm7 1 THETA1 se <NA>
5 nm7 1 THETA1 se <NA>
6 nm7 1 THETA2 estimate 21.8851
6 nm7 1 THETA2 prse <NA>
```

## Listing 7:

<NA>

```
> unique(boot$moment)
```

1

nm7

```
[1] "estimate" "prse" "se"
```

THETA2

#### Listing 8:

```
> unique(boot$value[boot$moment=='prse'])
```

#### [1] NA

prse, and therefore moment, is noninformative for these bootstraps.

se

# Listing 9:

```
> boot <- boot[boot$moment=='estimate',]
> boot$moment <- NULL
> unique(boot$tool)
```

[1] "nm7"

# Listing 10:

```
> boot$tool <- NULL
> head(boot)
```

> nead (boot)

```
run parameter
                 value
               9.90624
   1 THETA1
               21.8851
    1
        THETA2
8
        THETA3 0.0708172
  1
11
        THETA4
               3.36908
  1
       THETA5
               94.6441
14
17
   1
        THETA6 0.972458
```

## Listing 11:

```
> unique(boot$value[boot$parameter %in% c('OMEGA2.1','OMEGA3.1','OMEGA3.2')])
```



[11] "0.118664" "0.00243396" "0.0290797" "0.126793" "0.00496537" "0.00397874" "1] "0.00340756" "0.0793852" "0.0166321" "0.02546231" "0.003398784" "0.03308387" "0.00239167" "0.0332063" "0.00239167" "0.032480" "0.0293795" "0.066518" "0.0329284" "0.0239167" "0.0332063" "0.0239167" "0.0239167" "0.0338091" "0.026952" "0.0338701" "0.12233" "0.0239167" "0.03380984" "0.01619745" "0.026952" "0.00833897" "0.01619745" "0.026952" "0.00833897" "0.01619745" "0.0266518" "0.00330984" "0.01619745" "0.0266121" "0.0876049" "0.026657" "0.082661" "0.0047025" "0.0246687" "0.085661" "0.0047025" "0.0285775" "0.012475" "0.085661" "0.0266121" "0.0876049" "0.0266575" "0.023942" "0.0239338" "0.1910199" "0.0263532" "0.023316" "0.0263532" "0.0980333" "0.0663306" "0.023942" "0.023942" "0.0234159" "0.0341351" "0.0246527" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0234159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0334159" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344316" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344316" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344315" "0.0344316" "0.034431	F 1 1	"0.118664"	"0.00243896"	"-0.0290797"	"0.126793"	"0.00496537"
[11]   "-0.00800534"   "-0.0604644"   "-0.0376862"   "-0.032265"   "-0.0431811"   [12]   "0.0029284"   "0.0929795"   "0.0060518"   "0.0124331"   "0.0029337"   "0.0107017"   "0.0244607"   "0.0124313"   "0.0269052"   "-0.00833871"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.0389781"   "0.03849571"   "0.0385641"   "0.0086704951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.0867064951"   "0.09478857"   "0.01693787"   "0.0224571"   "0.0396722"   "0.0468236"   "0.005901131"   "0.09478857"   "0.08570647"   "0.0224571"   "0.106584"   "0.00468236"   "0.005901131"   "0.09478857"   "0.0867074"   "0.0237443"   "0.00484551"   "0.09870751"   "0.0118657"   "0.0118757"   "0.026927"   "0.0997955"   "0.04627827"   "0.0118757"   "0.0237443"   "0.00484551"   "0.09870751"   "0.0127766"   "0.02374428"   "0.00957745"   "0.04278272"   "0.0118757"   "0.0246251"   "0.00446751"   "0.00644955"   "0.00644955"   "0.00649566"   "0.002495657"   "0.004279272"   "0.0162017"   "0.0162017"   "0.00388678"   "0.00429366"   "0.00389271"   "0.00388271"   "0.01660047"   "0.002457827"   "0.0163088"   "0.00396725"   "0.00398727"   "0.00398271"   "0.01660047"   "0.00386557"   "0.00649587"   "0.00664966"   "0.00386578"   "0.00398271"   "0.00386578"   "0.00398271"   "0.00398271"   "0.00398271"   "0.00398271"   "0.00398271"   "0.00398271"   "0.00398271"   "0.003982871"						
1						
C21						
[26]   "0.0107017"   "-0.0244607"   "0.112813"   "0.0269052"   "-0.00838987"   "0.0129468"   "0.0100472"   "-0.0266121"   "0.0876049"   "0.123498"   "0.0100472"   "-0.0206121"   "-0.0376049"   "0.0129994"   "0.0285775"   "0.0852641"   "-0.010661618"   "-0.0344951"   "0.0129994"   "0.0285775"   "-0.0412473"   "-0.0114133"   "-0.06633522"   "0.0851618"   "-0.0477025"   "0.128111"   "-0.0431012"   "-0.0414133"   "-0.0643106"   "-0.025822"   "-0.0369338"   "0.190189"   "-0.0250822"   "-0.0254325"   "-0.025822"   "-0.0369338"   "0.190189"   "-0.0250822"   "-0.0254359"   "-0.0254325"   "-0.0254325"   "-0.02648537"   "-0.02648538"   "-0.04648548"   "-0.04648548"   "-0.04648548"   "-0.04648548"   "-0.04648548"   "-0.04648548"   "-0.04648548"   "-0.04648548"   "-0.044848138"   "-0.04446818"   "						
33						
136						
(41)						
146						
Total   Tota						
1.56						
[66]   "-0.0508149"   "0.128197"   "0.0232717"   "-0.026485"   "0.167175"   "171   "-0.0211708"   "-0.0381045"   "0.165601"   "0.00264623"   "-0.00201151"   "0.0947895"   "-0.0169357"   "-0.0396992"   "0.0463236"   "-0.00201151"   "0.0947895"   "0.0169357"   "0.106584"   "-0.0245055"   "0.104538"   "0.108904"   "-0.018904"   "-0.0224571"   "0.106584"   "-0.0245055"   "0.104538"   "0.108904"   "-0.0118657"   "0.105584"   "-0.0399795"   "-0.0395158"   "0.1085047"   "-0.0237443"   "-0.0408458"   "0.118172"   "0.10617929"   "0.11275"   "-0.0256919"   "-0.0452782"   "0.042172"   "-0.0113253"   "0.14246"   "-0.0102746"   "1111   "-0.0246251"   "0.17737"   "0.0528248"   "0.00957745"   "0.106911"   "1161   "0.0246751"   "0.07737"   "0.0528248"   "0.00957745"   "0.106911"   "1161   "0.0246734"   "-0.00448131"   "-0.00448131"   "-0.0328265"   "-0.0328265"   "-0.0478436"   "0.01610825"   "-0.0328265"   "-0.0478436"   "0.01610825"   "-0.00248251"   "0.17037"   "0.056426"   "-0.00247972"   "-0.00428521"   "0.10326"   "0.00847916"   "-0.00428521"   "-0.00248551"   "-0.00248551"   "-0.00248551"   "-0.00348565"   "-0.00248551"   "-0.00348565"   "-0.00248551"   "-0.00348565"   "-0.00248551"   "-0.00348565"   "-0.002485251"   "-0.00348565"   "-0.002485251"   "-0.002485251"   "-0.002485251"   "-0.00348565"   "-0.002485251"   "-0.00348565"   "-0.002485251"   "-0.00348565"   "-0.002485251"   "-0.00348565"   "-0.00487866"   "-0.0025719"   "-0.0038571"   "-0.00348565"   "-0.00348565"   "-0.00348565"   "-0.00348566"   "-0.00293871"   "-0.00348565"   "-0.0048386"   "-0.00348566"   "-0.00349877"   "-0.00348567"   "-0.00348568"						
Til						
Total   10.0947895"   10.0169357"   10.0396992"   10.0463236"   10.00590113"   1811   10.00567564"   10.194381"   10.016843"   10.0245055"   10.104538"   10.104538"   10.104538"   10.108904"   10.108904"   10.108904"   10.00859947"   10.002692"   10.099795"   10.0395158"   196						
[81]       "-0.0567564"       "0.194381"       "-0.016843"       "-0.0245055"       "0.104538"         [86]       "0.00451804"       "-0.0224571"       "0.105884"       "-0.0108647"       "-0.0395158"         [96]       "-0.0396872"       "0.0850947"       "0.0237443"       "0.0256919"       "-0.0395158"         [101]       "-0.035141"       "-0.0617929"       "0.01275"       "-0.0256919"       "-0.0452782"         [106]       "0.238867"       "0.0421172"       "-0.0513253"       "0.104246"       "-0.012746"         [111]       "-0.246251"       "0.17737"       "0.0528248"       "0.00957745"       "0.106911"         [116]       "0.03847151"       "-0.0370734"       "0.0610825"       "-0.0328265"       "-0.0478436"         [121]       "0.144272"       "0.0044813"       "-0.00319021"       "-0.017437"       "0.0549816"         [126]       "-0.0287111"       "0.0982603"       "-0.00319021"       "-0.017437"       "0.0743285"         [136]       "0.104497"       "-0.00684955"       "0.0086426"       "-0.0427972"       "0.0428527"         [136]       "0.104597       "-0.00885034"       "0.00867696"       "-0.0427972"       "0.0161017"         [141]       "-0.0432612"       "0.1063088"       "0						
[86]       "0.00451804"       "-0.0224571"       "0.106584"       "-0.0108647"       "-0.0250814"         [91]       "0.108904"       "-0.0111865"       "-0.02692"       "0.099795"       "-0.0395158"         [96]       "-0.035141"       "-0.0617929"       "0.11275"       "-0.0266919"       "-0.0452782"         [106]       "0.238867"       "0.0421172"       "-0.0113253"       "0.14246"       "-0.0102746"         [111]       "-0.0246251"       "0.17737"       "0.0528248"       "0.00957745"       "0.106911"         [116]       "0.04467151"       "-0.0370734"       "0.0610825"       "-0.0328265"       "-0.0478436"         [121]       "0.144272"       "0.00444813"       "-0.04304711"       "0.0328265"       "-0.0074346"         [126]       "-0.0287111"       "0.0982603"       "-0.003319021"       "-0.0017437"       "0.071037"         [136]       "0.104497"       "-0.00644951"       "-0.0432612"       "-0.04478436"       "-0.0427972"       "-0.0428521"         [146]       "-0.0432612"       "0.10326"       "0.0087696"       "-0.04259631"       "-0.0161017"         [146]       "-0.0432612"       "0.10326"       "0.017339"       "0.0567219"       "0.0384519"         [156]       "0.0275455"						
[91]         "0.108904"         "-0.0111865"         "-0.02692"         "0.099795"         "0.118172"           [96]         "-0.035647"         "0.0850947"         "0.0237443"         "-0.0408458"         "0.118172"           [106]         "0.238867"         "0.0617929"         "0.11275"         "-0.0256919"         "-0.0452782"           [106]         "0.238867"         "0.0421172"         "0.0113253"         "0.14246"         "-0.0102746"           [111]         "-0.0246251"         "0.17737"         "0.0528248"         "0.00957745"         "0.106911"           [121]         "0.144272"         "0.00370734"         "0.04304711"         "0.1322424"         "-0.00549816"           [122]         "0.144272"         "0.00444813"         "-0.04304711"         "0.1322424"         "-0.00549816"           [123]         "0.0245734"         "-0.0006495"         "0.0966426"         "-0.0427972"         "-0.04228521"           [136]         "0.104497"         "-0.0085034"         "-0.0241402"         "0.0487264"         "-0.0161017"           [141]         "-0.0432612"         "0.10326"         "0.0087696"         "-0.0427972"         "-0.0384519"           [151]         "0.179545"         "0.0253152"         "0.017339"         "0.0567219"         "0.038271"<						
196						
[101]         "-0.035141"         "-0.0617929"         "0.11275"         "-0.0256919"         "-0.0452782"           [106]         "0.238867"         "0.0421172"         "-0.0113253"         "0.14246"         "-0.0102746"           [111]         "-0.00246251"         "0.17737"         "0.05128248"         "0.00957745"         "0.106911"           [121]         "0.144272"         "0.00370734"         "0.0610825"         "-0.0328265"         "-0.0479436"           [126]         "-0.0287111"         "0.00982603"         "-0.000319021"         "-0.0017437"         "0.171037"           [131]         "0.0245734"         "-0.00686034"         "-0.0087966"         "-0.0427972"         "-0.0422852"           [136]         "0.104497"         "-0.0085034"         "-0.0241402"         "0.0483264"         "-0.0161017"           [141]         "-0.0432612"         "0.0087696"         "-0.0425963"         "0.0835945"           [146]         "-0.00345655"         "-0.0447935"         "0.112744"         "0.00295219"         "-0.0384519"           [151]         "0.179545"         "0.128876"         "-0.017339"         "0.0567219"         "0.0384519"           [156]         "0.146557"         "0.0264507"         "0.0185966"         "-0.0249431"         "0.117255" <td></td> <td></td> <td></td> <td></td> <td></td> <td></td>						
[106]         "0.238867"         "0.0421172"         "-0.0113253"         "0.14246"         "-0.0102746"           [111]         "-0.0246251"         "0.17737"         "0.0528248"         "0.00957745"         "0.106911"           [121]         "0.144272"         "0.00444813"         "-0.0430471"         "0.132424"         "-0.0078436"           [126]         "-0.0287111"         "0.0982603"         "-0.000319021"         "-0.0017437"         "0.171037"           [131]         "0.0245734"         "-0.00685034"         "0.0966426"         "-0.0427972"         "-0.0422852"           [136]         "0.104497"         "-0.00858034"         "0.0241402"         "0.0482564"         "-0.0161017"           [141]         "-0.0432612"         "0.10326"         "0.0087696"         "-0.0425963"         "0.0835945"           [146]         "-0.00345655"         "-0.0447935"         "0.112744"         "0.00295219"         "-0.0161017"           [156]         "-0.179545"         "0.0253152"         "-0.017339"         "0.0567219"         "0.0384519"           [156]         "0.1661076"         "0.0264507"         "0.0867032"         "-0.0249431"         "0.117255"           [166]         "0.161076"         "0.0163088"         "0.00365636"         "0.110393"         "-						
[111] "-0.0246251" "0.17737" "0.0528248" "0.00957745" "0.106911" [116] "0.00847151" "-0.0370734" "0.0610825" "-0.0328265" "-0.0478436" [121] "0.144272" "0.00444813" "-0.0430471" "0.132424" "-0.00549816" [126] "-0.0287111" "0.0982603" "-0.000319021" "-0.0017437" "0.171037" [131] "0.0245734" "-0.0064495" "0.0966426" "-0.04279722" "-0.0422852" [136] "0.104497" "-0.00685034" "-0.0241402" "0.0483264" "-0.0161017" [141] "-0.0432612" "0.10326" "0.0087696" "-0.0425963" "0.0835945" [146] "-0.000345655" "-0.0447935" "0.112744" "0.00925219" "-0.0384519" [151] "0.179545" "0.0253152" "-0.0185966" "-0.02494311" "0.117255" [166] "0.0161076" "0.0163088" "0.0867032" "-0.0341645" "-0.0468786" [166] "0.161076" "0.0163088" "0.00365636" "0.110393" "-0.0199049" [171] "-0.0610041" "0.0933731" "0.00429236" "-0.0384517" "0.13266" "-0.02273357" "-0.044518" "0.0740837" "-0.0385571" "0.13606" [176] "-0.0273357" "-0.044518" "0.0740837" "-0.0385527" "-0.032824" [181] "0.114814" "0.000488372" "-0.0327205" "0.166113" "0.0260557" [186] "-0.0151667" "-0.0408356" "0.0177434" "-0.0210069" "0.0320893" "-0.0349383" [201] "-0.0312059" "0.069709" "-0.0238348" "-0.03220893" "-0.00249383" "-0.00249383" "-0.00249383" "-0.00366835" "-0.00249383" "-0.00298848" "-0.0269827" "0.1666721 "-0.00276325" "-0.0163874" "-0.00269827" "0.163874" "-0.00269827" "0.163874" "-0.00269827" "0.163874" "-0.00385522" "0.157213" "-0.00249383" "-0.00366835" "-0.00366835" "-0.00366835" "-0.003698835" "-0.003689835" "-0.003689835" "-0.003689835" "-0.003689835" "-0.003689835" "-0.003646688" "-0.00362551" "-0.00362551" "-0.0044916" "0.166451" "0.00968355" "-0.006646968" "-0.00362551" "-0.000407164"						
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[146]       "-0.000345655"       "-0.0447935"       "0.112744"       "0.00295219"       "-0.0384519"         [151]       "0.179545"       "0.0253152"       "-0.017339"       "0.0567219"       "0.00398271"         [156]       "-0.0299789"       "0.180876"       "-0.00185966"       "-0.0249431"       "0.117255"         [161]       "0.0146557"       "-0.0264507"       "0.0867032"       "-0.0341645"       "-0.0468786"         [166]       "0.161076"       "0.0163088"       "0.00365636"       "0.110393"       "-0.0199049"         [171]       "-0.0610041"       "0.0933731"       "0.00429236"       "-0.0585371"       "0.131606"         [176]       "-0.0273357"       "-0.0414518"       "0.0740837"       "-0.0393725"       "-0.0532824"         [181]       "0.114814"       "0.000498372"       "-0.0327205"       "0.166113"       "0.0260557"         [186]       "-0.013542"       "0.202145"       "0.0177434"       "-0.0210069"       "0.0910233"         [191]       "0.0151667"       "-0.0408356"       "0.0869729"       "0.0132574"       "-0.0349298"         [196]       "0.121655"       "-0.0173966"       "-0.0312672"       "0.117305"       "-0.00249383"         [201]       "-0.0312059"       "0.069709"						
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[156]       "-0.0299789"       "0.180876"       "-0.00185966"       "-0.0249431"       "0.117255"         [161]       "0.0146557"       "-0.0264507"       "0.0867032"       "-0.0341645"       "-0.0468786"         [166]       "0.161076"       "0.0163088"       "0.00365636"       "0.110393"       "-0.0199049"         [171]       "-0.0610041"       "0.0933731"       "0.00429236"       "-0.0585371"       "0.131606"         [176]       "-0.0273357"       "-0.0414518"       "0.0740837"       "-0.0393725"       "-0.0532824"         [181]       "0.114814"       "0.000498372"       "-0.0327205"       "0.166113"       "0.0260557"         [186]       "-0.013542"       "0.202145"       "0.0177434"       "-0.0210069"       "0.0910233"         [191]       "0.0121655"       "-0.0173966"       "-0.0312672"       "0.117305"       "-0.00249383"         [201]       "-0.0312059"       "0.069709"       "-0.0238348"       "-0.0435522"       "0.157213"         [206]       "0.0276325"       "-0.0167408"       "0.103765"       "-0.0320893"       "-0.0491547"         [21]       "0.127115"       "0.0693332"       "-0.0315349"       "0.109701"       "-0.00298643"         [221]       "-0.0606384"       "-0.0582304"						
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[186]       "-0.013542"       "0.202145"       "0.0177434"       "-0.0210069"       "0.0910233"         [191]       "0.0151667"       "-0.0408356"       "0.0869729"       "0.0132574"       "-0.0369298"         [196]       "0.121655"       "-0.0173966"       "-0.0312672"       "0.117305"       "-0.00249383"         [201]       "-0.0312059"       "0.069709"       "-0.0238348"       "-0.0435522"       "0.157213"         [206]       "0.0276325"       "-0.0167408"       "0.103765"       "-0.0320893"       "-0.0491547"         [211]       "0.127115"       "0.00963332"       "-0.0315349"       "0.109701"       "-0.00298643"         [216]       "-0.0269827"       "0.163874"       "-0.0222174"       "-0.0279429"       "0.149759"         [221]       "-0.0606384"       "-0.0582304"       "0.156683"       "-0.00684463"       "-0.0128832"         [226]       "0.132937"       "0.0117909"       "-0.0325853"       "0.0667211"       "-0.0396385"         [231]       "-0.0444916"       "0.16451"       "0.00956835"       "-0.0156386"       "0.0973435"         [236]       "-0.00795893"       "-0.0376994"       "0.1143"       "-0.00646968"       "-0.0362551"         [241]       "0.130343"       "-0.0293751"	-					
[191]       "0.0151667"       "-0.0408356"       "0.0869729"       "0.0132574"       "-0.0369298"         [196]       "0.121655"       "-0.0173966"       "-0.0312672"       "0.117305"       "-0.00249383"         [201]       "-0.0312059"       "0.069709"       "-0.0238348"       "-0.0435522"       "0.157213"         [206]       "0.0276325"       "-0.0167408"       "0.103765"       "-0.0320893"       "-0.0491547"         [211]       "0.127115"       "0.00963332"       "-0.0315349"       "0.109701"       "-0.00298643"         [216]       "-0.0269827"       "0.163874"       "-0.0222174"       "-0.0279429"       "0.149759"         [221]       "-0.0606384"       "-0.0582304"       "0.156683"       "-0.00684463"       "-0.0128832"         [226]       "0.132937"       "0.0117909"       "-0.0325853"       "0.0667211"       "-0.0396385"         [231]       "-0.0444916"       "0.16451"       "0.00956835"       "-0.0156386"       "0.0973435"         [236]       "-0.00795893"       "-0.0376994"       "0.1143"       "-0.00646968"       "-0.0362551"         [241]       "0.130343"       "-0.0293751"       "-0.0610221"       "0.146619"       "-0.000407164"	-					
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	[236]		"-0.0376994"			
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	[246]	"-0.0189185"	"0.137894"	"0.000294066"	"-0.0289474"	"0.0894661"



[251]	"-0.0458925"	"-0.0433672"	"0.146665"	"0.0142544"	"-0.00460381"
[256]	"0.128807"	"0.00755358"	"-0.0270419"	"0.173962"	"0.0191587"
[261]	"-0.0230961"	"0.105145"	"-0.0287821"	"-0.0461986"	"0.174007"
[266]		"-0.0154687"	"0.157457"	"-0.024208"	"-0.043364"
[271]	"0.11283"	"-0.0196416"	"-0.035826"	"0.110426"	"-0.0343319"
[276]	"-0.0621871"	"0.119436"	"0.000846538"	"-0.0184177"	"0.0932987"
[281]	"-0.0145868"	"-0.0412257"	"0.116972"	"-0.0102762"	"-0.0421894"
[286]	"0.12102"	"-0.0340955"	"-0.0461667"	"0.20483"	"0.00482516"
[291]	"-0.0163381"	"0.102248"	"-0.0446729"	"-0.0417648"	"0.100401"
[296]	"-0.0187281"	"-0.0527303"	"0.105437"	"-0.0330351"	"-0.0412061"
[301]	"0.133189"	"-0.0168328"	"-0.0265733"	"0.0945628"	"-0.023821"
[306]	"-0.046713"	"0.115873"	"-0.0174054"	"-0.0383742"	"0.151988"
[311]	"-0.00223515"	"-0.0378195"	"0.111794"	"-0.0362"	"-0.0342003"
[316]	"0.115687"	"-0.0487321"	"-0.0605172"	"0.0491989"	"-0.0400207"
[321]	"-0.0576997"	"0.0924036"	"-0.00301072"	"-0.0217227"	"0.120697"
[326]		"-0.0419027"	"0.0841434"	"-0.0272731"	"-0.0373285"
[331]	"0.139445"	"-0.0562158"	"-0.0628585"	"0.133842"	"-0.0058623"
[336]	"-0.0465414"	"0.117257"	"0.00585463"	"-0.0212939"	"0.141695"
[341]	"-0.0128165"	"-0.0454878"	"0.0762859"	"-0.0419356"	"-0.0446045"
[346]	"0.115748"	"-0.0270666"	"-0.0334317"	"0.13824"	"0.0159619"
[351]	"-0.0182228"	"0.153652"	"-0.0133617"	"-0.0312735"	"0.129189"
[356]		<b>"</b> -0.0375778 <b>"</b>	"0.0784215"	"-0.0189919"	"-0.0278138"
[361]	"0.0859133"	"-0.0112831"	"-0.0467855"	"0.152543"	"-0.0117078"
[366]	"-0.0259284"	"0.146406"	"-0.00833782"	"-0.0340645"	"0.117956"
[371]	"-0.0228683"	"-0.0302881"	"0.0998222"	"-0.0056598"	"-0.0270215"
[376]	"0.148125"	"-0.035818"	"-0.0466027"	"0.154802"	"-0.00387403"
[381]	"-0.0344275"	"0.0821857"	"0.0179231"	"-0.0208862"	"0.159922"
[386]	"-0.00843247"	"-0.0361851"	"0.154316"	"-0.0204364"	"-0.0313654"
[391]	"0.0876008"	"0.0186172"	"-0.0384452"	"0.145706"	"-0.0513642"
[396]	"-0.0353288"	"0.0960684"	"-0.0153065"	"-0.0325897"	"0.113952"
[401]	<b>"</b> -0.034477 <b>"</b>	"-0.0391484"	"0.120386"	<b>"</b> -0.0235295 <b>"</b>	"-0.040302"
[406]	"0.146426"	<b>"</b> -0.00909298 <b>"</b>	<b>"</b> -0.0229452 <b>"</b>	"0.097815"	<b>"</b> -0.0228671 <b>"</b>
[411]	"-0.0477668"	"0.0527434"	<b>"</b> -0.0401562 <b>"</b>	"-0.0404198"	"0.191286"
[416]	"0.0233172"	"0.00230177"	"0.0966339"	"-0.010117"	"-0.0304394"
[421]	"0.102042"	"-0.0675102"	<b>"</b> -0.0323489 <b>"</b>	"0.0669474"	"-0.00414405"
[426]	"-0.0350421"	"0.117324"	"0.019366"	<b>"</b> -0.0293495 <b>"</b>	"0.043366"
[431]	<b>"</b> -0.037891 <b>"</b>	"-0.0554599"	"0.116669"	"-0.0318554"	"-0.0605897"
[436]	"0.0694246"	"-0.0246743"	"-0.0545532"	"0.0898996"	"-0.0190038"
[441]	"-0.0526655"	"0.115315"	"-0.0448101"	"-0.0434573"	"0.121016"
[446]	"-0.00117652"	"-0.040854"	"0.0741172"	"-0.0189367"	"-0.0253948"
[451]	"0.104378"	"-0.00161245"	<b>"</b> -0.02001 <b>"</b>	"0.157005"	"-0.00523799"
[456]	"-0.0247991"	"0.351464"	"0.0448184"	"0.0023031"	"0.118066"
[461]	"-0.0221416"	<b>"</b> -0.0276645 <b>"</b>	"0.114711"	"-0.00405511"	<b>"</b> -0.0277706 <b>"</b>
[466]	"0.125923"	<b>"</b> -0.0129499 <b>"</b>	<b>"</b> -0.0347455 <b>"</b>	"0.0982356"	"0.0112521"
[471]	<b>"</b> -0.0208778 <b>"</b>	"0.069048"	<b>"</b> -0.0578171 <b>"</b>	"-0.0478397"	"0.116005"
[476]	<b>"</b> -0.0531913 <b>"</b>	<b>"</b> -0.0461022 <b>"</b>	"0.189958"	"0.023422"	<b>"</b> -0.00411683 <b>"</b>
[481]	"0.0874007"	<b>"</b> -0.0666566 <b>"</b>	"-0.0453463"	"0.250447"	"0.00770081"
[486]	<b>"</b> -0.0208701 <b>"</b>	"0.167599"	"0.0451788"	<b>"</b> -0.00065829 <b>"</b>	"0.102168"
[491]	"-0.0143335"	<b>"</b> -0.0314068 <b>"</b>	"0.089994"	"-0.0436014"	<b>"</b> -0.0577496 <b>"</b>
[496]	"0.0724951"	<b>"</b> -0.0250448 <b>"</b>	"-0.0245528"	"0.105756"	"-0.0395233 <b>"</b>



[501]	"-0.031799"	"0.113582"	"0.0199422"	"-0.0149443"	"0.0744757"
[506]	"-0.0676757"	"-0.045086"	"0.0890981"	"-0.0412376"	"-0.0493254"
[511]	"0.114201"	"-0.0385651 <b>"</b>	"-0.0429911"	"0.0888071"	"-0.0233529"
[516]	<b>"</b> -0.0528072 <b>"</b>	"0.043756"	<b>"</b> -0.0220733 <b>"</b>	"-0.0363111"	"0.108755"
[521]	"-0.00844895"	"-0.0437119"	"0.0888473"	"-0.0272006"	"-0.0455575"
[526]	"0.109073"	"0.0282737"	"-0.0144904"	"0.129467"	<b>"</b> -0.00760703 <b>"</b>
[531]	"-0.0198483"	"0.124011"	"0.0141876"	<b>"</b> -0.0382787 <b>"</b>	"0.0587984"
[536]	"-0.0244563"	<b>"</b> -0.0366547 <b>"</b>	"0.151269"	"-0.00472419"	<b>"</b> -0.029383 <b>"</b>
[541]	"0.174937"	<b>"</b> -0.00865366 <b>"</b>	"-0.0339614"	"0.156336"	"-0.0134474"
[546]	<b>"</b> -0.0319209 <b>"</b>	"0.146132"	"-0.0145849"	<b>"</b> -0.0205749 <b>"</b>	"0.146571"
[551]	"-0.014698"	<b>"</b> -0.0412586 <b>"</b>	"0.164571"	"-0.0107431"	"-0.0206866 <b>"</b>
[556]	"0.0803535"	<b>"</b> -0.0214819 <b>"</b>	<b>"</b> -0.0432427 <b>"</b>	"0.112315"	"-0.0225172 <b>"</b>
[561]	"-0.0452995"	"0.182547"	"-0.0240036"	<b>"</b> -0.0307118 <b>"</b>	"0.148057"
[566]	"-0.00531293"	<b>"</b> -0.0421697 <b>"</b>	"0.10471"	"0.00909561"	"-0.0103992"
[571]	"0.141531"	"-0.0117441"	<b>"</b> -0.0268305 <b>"</b>	"0.055915"	"-0.0145141"
[576]	"-0.0399355"	"0.2861"	"0.0647719"	"0.00905442"	"0.226185"
[581]	"0.0465552"	"-0.0167005"	"0.0863951"	"-0.0242882"	"-0.0445673"
[586]	"0.106754"	"0.00710941"	"-0.0384524"	"0.128791"	"0.00935985"
[591]	"-0.0255152"	"0.151828"	"0.0441336"	"0.00135239"	"0.112871"
[596]	"-0.00344835"	"-0.022351"	"0.0481443"	"-0.0179547"	"-0.055449"
[601]	"0.0818499"	"-0.0253572"	"-0.0342841"	"0.0963881"	"-0.00883748"
[606]	"-0.0304162"	"0.139391"	"-0.0187507"	"-0.0402836"	"0.155407"
[611]	"-0.0104272"	"-0.0216455"	"0.0635618"	"-0.00394322"	"-0.0362427"
[616]	"0.134227"	"0.00362554"	"-0.00676369"	"0.0945227"	"-0.0698679"
[621]	"-0.0602625"	"0.0923166"	"-0.0150987"	"-0.0350389"	"0.081674"
[626]	"-0.00441006"	"-0.0490822"	"0.128433"	"-0.0261758"	"-0.0399649"
[631]	"0.109765"	"-0.0263731"	"-0.0386598"	"0.0884195"	"0.0352562"
[636]	"-0.0224681"	"0.12504"	"-0.016216"	"-0.0186849"	"0.0836959"
[641]	"0.00447469"	"-0.0381655"	"0.113755"	"0.0275129"	"-0.00949459"
[646]	"0.0651385"	"-0.0287313"	"-0.0593346"	"0.12926"	"-0.0386841"
[651]	"-0.0235969"	"0.141795"	"0.00184889"	"-0.0213231"	"0.113659"
[656]	"-0.0188672"	"-0.0347941"	"0.0657835"	"-0.0261609"	"-0.051177"
[661]	"0.119641"	"-0.010961"	"-0.0345783"	"0.107459"	"-0.0279097"
[666]	"-0.0412287"	"0.128838"	"-0.00840944"	"-0.0275247"	"0.0641978"
[671]	"-0.0448826"	"-0.0548623"	"0.105479"	"-0.00756974"	"-0.0405811"
[676]	"0.171146"	"0.00200264"	"-0.01219"	"0.0862845"	"-0.0229536"
[681]	"-0.0273753"	"0.183248"	"0.00835915"	"-0.0156605"	"0.0791216"
[686]	"-0.0363752"	"-0.0454898"	"0.233876"	"0.00372023"	"-0.0186535"
[691]	"0.142954"	"-0.00156208"	"-0.0336852"	"0.0595711"	"-0.023845"
[696]	"-0.0408747"	"0.0778225"	"-0.0396712"	"-0.0301178"	"0.0918891"
[701]		"-0.0291887"	"0.11211"	"0.0144046"	"-0.0306082"
[701]	"0.138055"	"-0.0309795"	"-0.043204"	"0.138132"	"0.00912754"
[711]	"-0.0332121"	"0.138756"	"-0.0134344"	"-0.0507371"	"0.124444"
-	"-0.0479321"	"-0.0479316"	"0.171498"	"-0.0121693"	"-0.024209"
[716] [721]	"0.0540019"	"-0.04/9316" "-0.0110472"	"-0.0497729"	"0.0957406"	"-0.024209" "-0.0272068"
[721]	"-0.0377253"	"0.105232"	"-0.0497729" "-0.0423657"	"-0.0309091"	"0.0272068"
		"-0.0425191"	"0.14017"	"-0.0588466"	"-0.0585397"
[731]	"-0.0061838" "0.117701"	"-0.0425191" "-0.0279007"	"-0.0488742"	"0.141549"	"0.0282864"
[736]		"0.150651"			
[741]	"-0.00360357"		"0.00336836"	"-0.0222498"	"0.141123"
[/46]	"-0.0345781"	"-0.0358519"	"0.126264"	"0.00663694"	"-0.0317072"



```
[751] "0.127508"
                     "-0.0124047"
                                    "-0.0283794"
                                                   "0.131374"
                                                                  "-0.0134399"
[756] "-0.0361739"
                    "0.148282"
                                   "-0.0190484"
                                                   "-0.0179618"
                                                                  "0.121144"
[761] "-0.0326408"
                     "-0.051974"
                                   "0.115299"
                                                   "-0.0400513"
                                                                  "-0.0586101"
[766] "0.153749"
                     "-0.0078094"
                                    "-0.0310534"
                                                   "0.072155"
                                                                  "-0.0137717"
[771] "-0.0349942"
                     "0.106628"
                                    "0.0016075"
                                                   "-0.0459419"
                                                                  "0.13816"
[776] "-0.0181902"
                                                                  "-0.0385028"
                     "-0.0264274"
                                    "0.0938884"
                                                   "-0.0191998"
[781] "0.146527"
                     "-0.00176885"
                                   "-0.0262183"
                                                   "0.0941705"
                                                                  "0.00247482"
[786] "-0.0389402"
                     "0.153674"
                                    "0.0248971"
                                                   "0.0031693"
                                                                  "0.135016"
[791] "-0.0159752"
                     "-0.0366186"
                                    "0.150774"
                                                   "-0.0121317"
                                                                  "-0.0210343"
                     "-0.0100324"
                                    "-0.0380679"
                                                   "0.0781693"
[796] "0.100948"
                                                                  "-0.0131155"
[801] "-0.0260249"
                     "0.183734"
                                    "0.0471517"
                                                   "-0.00331566"
                                                                  "0.122793"
[806] "0.0128808"
                     "-0.022205"
                                    "0.0961979"
                                                   "0.00881516"
                                                                  "-0.0339731"
                                    "-0.0250672"
                                                   "0.106903"
[811] "0.0988059"
                     "0.0129752"
                                                                  "-0.0307499"
[816] "-0.0488798"
                     "0.199367"
                                                   "-0.034998"
                                                                  "0.103325"
                                    "-0.00270252"
[821] "0.0245558"
                     "-0.00192005"
                                   "0.10619"
                                                   "0.00493672"
                                                                  "-0.0361216"
[826] "0.0844764"
                    "0.00496451"
                                    "-0.0254248"
                                                   "0.0585779"
                                                                  "-0.00589244"
[831] "-0.0442521"
                     "0.0701998"
                                    "-0.00732916"
                                                   "-0.0466255"
                                                                  "0.0715442"
[836] "-0.0347355"
                     "-0.0415529"
                                    "0.0926787"
                                                   "-0.0344976"
                                                                  "-0.0327243"
[841] "0.121283"
                     "-0.0321919"
                                    "-0.0385139"
                                                   "0.099353"
                                                                  "0.00059543"
[846] "-0.0240711"
                     "0.149382"
                                    "-0.0155042"
                                                   "-0.0419845"
                                                                  "0.158858"
[851] "0.0105719"
                     "-0.00492554"
                                   "0.067364"
                                                   "-0.0108857"
                                                                  "-0.0470531"
[856] "0.127813"
                     "0.00668929"
                                    "-0.0184073"
                                                   "0.148973"
                                                                  "0.0134121"
[861] "-0.0248297"
                     "0.135644"
                                    "0.0179563"
                                                   "-0.00793724"
                                                                  "0.0606008"
[866] "0.00193866"
                     "-0.0211141"
                                    "0.0592926"
                                                   "-0.0327239"
                                                                  "-0.0356362"
[871] "0.136618"
                     "-0.0223643"
                                    "-0.0262967"
                                                   "0.106394"
                                                                  "-0.0196676"
[876] "-0.0533358"
                     "0.0742905"
                                    "-0.00833212"
                                                   "-0.0373445"
                                                                  "0.0998243"
[881] "-0.00384154" "-0.0251419"
                                    "0.170587"
                                                   "-0.0143729"
                                                                  "-0.0394336"
[886] "0.0868"
                     "-0.0287053"
                                    "-0.0297056"
                                                   "0.100429"
                                                                  "0.00791036"
[891] "-0.0297891"
                    "0.0597762"
                                    "-0.0391322"
                                                   "-0.03771"
                                                                  "0.112944"
[896] "0.00219604"
                    "-0.017267"
                                    "0.174094"
                                                   "0.0131618"
                                                                  "-0.0141539"
```

# Listing 12:

#### > unique(boot\$parameter[boot\$value=='0'])

#### [1] "SIGMA2.1"

Off-diagonals (and only off-diagonals) are noninformative.

#### Listing 13:

```
> boot <- boot[!boot$value=='0',]
> any(is.na(as.numeric(boot$value)))
```

#### [1] FALSE

#### Listing 14:

```
> boot$value <- as.numeric(boot$value)
> head(boot)
```



```
run parameter value
2 1 THETA1 9.9062400
5 1 THETA2 21.8851000
8 1 THETA3 0.0708172
11 1 THETA4 3.3690800
14 1 THETA5 94.6441000
17 1 THETA6 0.9724580
```

# 1.2 Restrict data to 95 percentiles.

We did 300 runs. Min and max are strongly dependent on number of runs, since with an unbounded distribution, (almost) any value is possible with enough sampling. We clip to the 95 percentiles, to give distributions that are somewhat more scale independent.

# Listing 15:

```
> boot <- inner(</pre>
      boot,
       preserve='run',
       id.var='parameter',
       measure.var='value'
+ )
> head(boot)
                  value
 run parameter
  1 THETA1 9.9062400
2 1
       THETA2 21.8851000
       THETA3 0.0708172
4 1
       THETA4 3.3690800
5 1 THETA5 94.6441000
       THETA6 0.9724580
                                    Listing 16:
> any(is.na(boot$value))
[1] TRUE
                                    Listing 17:
> boot <- boot[!is.na(boot$value),]</pre>
```

# 1.3 Recover parameter metadata from a specially-marked control stream.

We want meaningful names for our parameters. Harvest these from a reviewed control stream.

# Listing 18:

```
> wiki <- wikitab(1005,'../nonmem')
> wiki
```



```
description
  parameter
1
     THETA1
                                  apparent oral clearance
2
     THETA2
                            central volume of distribution
3
     THETA3
                                  absorption rate constant
4
     THETA4
                              intercompartmental clearance
5
     THETA5
                        peripheral volume of distribution
6
     THETA6
                                 male effect on clearance
7
                                weight effect on clearance
     THETA7
8
  OMEGA1.1
                interindividual variability of clearance
             interindividual clearance-volume covariance
9
   OMEGA2.1
10 OMEGA2.2 interindividual variability of central volume
11 OMEGA3.1
                 interindividual clearance-Ka covariance
12 OMEGA3.2
                   interindividual volume-Ka covariance
13 OMEGA3.3
                        interindividual variability of Ka
14 SIGMA1.1
                                       proportional error
15 SIGMA2.2
                                            additive error
                                                               model tool run
1 CL/F (L/h) ~ theta_1 * theta_6 ^MALE * (WT/70) ^theta_7 * e^eta_1 nm7 1005
                          V_c /F (L) \sim theta_2 * (WT/70)^1 * e^eta_2
                                                                      nm7 1005
3
                                      K_a (h^-1) \sim theta_3 * e^eta_3
                                                                      nm7 1005
4
                                                 Q/F (L/h) ~ theta_4
                                                                      nm7 1005
5
                                                 V_p /F (L) ~ theta_5
                                                                      nm7 1005
6
                                                 MALE_CL/F ~ theta_6 nm7 1005
7
                                                   WT_CL/F \sim theta_7 nm7 1005
8
                                                 IIV_CL/F \sim Omega_1.1 \quad nm7 \quad 1005
9
                                                 cov_CL, V ~ Omega_2.1 nm7 1005
10
                                               IIV_V_c /F ~ Omega_2.2 nm7 1005
11
                                               cov_CL, Ka ~ Omega_3.1 nm7 1005
12
                                                cov_V, Ka ~ Omega_3.2 nm7 1005
13
                                                IIV_K_a \sim Omega_3.3
                                                                      nm7 1005
                                                err_prop ~ Sigma_1.1
                                                                      nm7 1005
14
15
                                                 err_add ~ Sigma_2.2 nm7 1005
     estimate prse
    9.50789 9.75
                    0.92708
1
      22.791 9.55
                    2.17764
2
    0.0714337 7.35 0.00525283
     3.47451 15.4 0.535797
5
     113.277 21
                     23.7452
6
     1.02435 11.1
                    0.114056
7
     1.19212 28.3
                    0.33679
    0.213879 22.8 0.0488369
8
9
    0.12077 26.4 0.0319144
10 0.0945105 33.2 0.0313616
11 -0.0116278 173 0.0200776
12 -0.0372064 36.1 0.0134244
13 0.0465631 34.8 0.0161816
14 0.0491707 10.9 0.00538135
15
   0.201769 33.5 0.0676087
```



## Listing 19:

```
> wiki$name <- wiki2label(wiki$model)</pre>
> wiki$estimate <- as.numeric(wiki$estimate)</pre>
> unique(wiki$parameter)
 [1] "THETA1"
                "THETA2"
                           "THETA3"
                                       "THETA4"
                                                  "THETA5"
 [7] "THETA7"
               "OMEGA1.1" "OMEGA2.1" "OMEGA2.2" "OMEGA3.1" "OMEGA3.2"
[13] "OMEGA3.3" "SIGMA1.1" "SIGMA2.2"
                                      Listing 20:
> unique(boot$parameter)
 [1] "THETA1"
                "THETA2"
                            "THETA3"
                                       "THETA4"
                                                   "THETA5"
                                                              "THETA6"
 [7] "THETA7"
                "OMEGA1.1" "OMEGA2.1" "OMEGA2.2" "OMEGA3.1" "OMEGA3.2"
[13] "OMEGA3.3" "SIGMA1.1" "SIGMA2.2"
                                      Listing 21:
> boot <- stableMerge(boot, wiki[,c('parameter','name')])</pre>
> head(boot)
  run parameter
                     value
                                name
        THETA1 9.9062400
                                CL/F
   1
        THETA2 21.8851000
                               V_c/F
2.
   1
3
  1
        THETA3 0.0708172
                                K_a
  1
        THETA4 3.3690800
                                 Q/F
5
  1
        THETA5 94.6441000
                              V_p/F
        THETA6 0.9724580 MALE_CL/F
```

# 1.4 Create covariate plot.

Now we make a covariate plot for clearance. We will normalize clearance by its median (we also could have used the model estimate). We need to take cuts of weight, since we can only really show categorically-constrained distributions. Male effect is already categorical. I.e, the reference individual has median clearance, is female, and has median weight.

# 1.4.1 Recover original covariates for guidance.

## Listing 22:

```
> covariates <- read.csv('../data/derived/phase1.csv',na.strings='.')
> head(covariates)
```



```
C ID TIME SEQ EVID AMT DV SUBJ HOUR HEIGHT WEIGHT SEX AGE DOSE FED
   C 1 0.00 0 0 NA 0.000 1 0.00 174 74.2 0 29.1 1000 1
2 <NA> 1 0.00 1 1 1000 NA 1 0.00 174 74.2 0 29.1 1000
3 <NA> 1 0.25 0 0 NA 0.363 1 0.25
                                     174 74.2 0 29.1 1000
4 <NA> 1 0.50 0 NA 0.914
                            1 0.50
                                      174
                                           74.2 0 29.1 1000
                                                             1
5 <NA> 1 1.00 0 NA 1.120
                                            74.2 0 29.1 1000
                                      174
                              1 1.00
                                                            - 1
6 <NA> 1 2.00 0 NA 2.280
                             1 2.00
                                            74.2 0 29.1 1000
                                       174
                                                             1
 SMK DS CRCN TAFD TAD LDOS MDV predose zerodv
  0 0 83.5 0.00 NA NA
                       0
                             1
     0 83.5 0.00 0.00 1000
                        1
                               0
                        0
   0
     0 83.5 0.25 0.25 1000
                               0
   0 0 83.5 0.50 0.50 1000
                        0
                               0
                       0
                               Ω
                                     0
  0 0 83.5 1.00 1.00 1000
  0 0 83.5 2.00 2.00 1000
                        0
                               0
```

## Listing 23:

```
> with(covariates,constant(WEIGHT,within=ID))
```

[1] TRUE

#### Listing 24:

```
> covariates <- unique(covariates[,c('ID','WEIGHT')])
> head(covariates)
```

```
1 1 74.2
16 2 80.3
31 3 94.2
46 4 85.2
61 5 82.8
76 6 63.9
```

ID WEIGHT

## Listing 25:

```
> covariates$WT <- as.numeric(covariates$WEIGHT)
> wt <- median(covariates$WT)
> wt
```

[1] 81

## Listing 26:

```
> range(covariates$WT)
```

[1] 61 117

#### 1.4.2 Reproduce the control stream submodel for selective cuts of a continuous covariate.

In the model we normalized by 70 kg, so that cut will have null effect. Let's try 65, 75, and 85 kg. We have to make a separate column for each cut, which is a bit of work. Basically, we make two more copies



of our weight effect columns, and raise our normalized cuts to those powers, effectively reproducing the submodel from the control stream.

# Listing 27:

```
> head(boot)
  run parameter
                     value
                                name
        THETA1 9.9062400
                                CL/F
         THETA2 21.8851000
                                V_c/F
         THETA3 0.0708172
                                 K_a
         THETA4 3.3690800
                                 Q/F
         THETA5 94.6441000
                                V_p/F
         THETA6 0.9724580 MALE_CL/F
                                      Listing 28:
> unique(boot$name)
 [1] "CL/F"
                 "V c/F"
                                          "O/F"
                                                       "V_p/F"
                                                                   "MALE CL/F"
 [7] "WT_CL/F"
                 "IIV_CL/F"
                              "cov_CL,V" "IIV_V_c/F" "cov_CL,Ka" "cov_V,Ka"
[13] "IIV_K_a"
                 "err_prop"
                              "err_add"
                                      Listing 29:
> clearance <- boot[boot$name %in% c('CL/F','WT_CL/F','MALE_CL/F'),]</pre>
```

# > head(clearance)

```
run parameter
               value
                          name
   1 THETA1 9.906240
1
                          CL/F
6
   1
       THETA6 0.972458 MALE_CL/F
7
   1
       THETA7 1.469340 WT_CL/F
16 2 THETA1 9.030570
                       CL/F
21 2 THETA6 1.038960 MALE_CL/F
22 2 THETA7 0.999512
                       WT_CL/F
```

## Listing 30:

```
> frozen <- data.frame(cast(clearance,run ~ name),check.names=FALSE)</pre>
> head(frozen)
```

```
CL/F MALE_CL/F WT_CL/F
1 9.90624 0.972458 1.469340
2 9.03057 1.038960 0.999512
 3 9.33170 0.846669 1.909640
 4 9.25626 0.940994 1.697690
 5 10.27090 1.252490 1.159250
 6 9.42002 0.967179 1.484550
```

## Listing 31:

```
> frozen$`WT_CL/F:65` <- (65/70)**frozen$`WT_CL/F`</pre>
> frozen$`WT_CL/F:75` <- (75/70)**frozen$`WT_CL/F`
> frozen$`WT_CL/F:85` <- (85/70)**frozen$`WT_CL/F`
```



## 1.4.3 Normalize key parameter

## Listing 32:

```
> #cl <- median(boot$value[boot$name=='CL/F'])
> cl <- with(wiki, estimate[name=='CL/F'])
> cl
```

[1] 9.50789

# Listing 33:

#### > head(frozen)

```
CL/F MALE_CL/F WT_CL/F:65 WT_CL/F:75 WT_CL/F:85
      9.90624 0.972458 1.469340 0.8968292 1.106690 1.330136
     9.03057 1.038960 0.999512
                               0.9286050
                                         1.071392
                                                    1.214171
   3 9.33170 0.846669 1.909640 0.8680382
                                         1.140825
3
                                                    1.448847
                                                    1.390435
  4 9.25626 0.940994 1.697690 0.8817803 1.124264
  5 10.27090 1.252490 1.159250 0.9176771
                                         1.083265
                                                   1.252417
   6 9.42002 0.967179 1.484550 0.8958189
                                          1.107852
                                                   1.334070
```

## Listing 34:

```
> frozen[['CL/F']] <- frozen[['CL/F']]/cl
> head(frozen)
```

```
CL/F MALE_CL/F WT_CL/F:65 WT_CL/F:75 WT_CL/F:85
 run
  1 1.0418968 0.972458 1.469340 0.8968292
                                          1.106690 1.330136
   2 0.9497975
              1.038960 0.999512 0.9286050
                                           1.071392
                                                     1.214171
                                          1.140825
                                                    1.448847
   3 0.9814691 0.846669 1.909640 0.8680382
4
  4 0.9735346 0.940994 1.697690 0.8817803
                                          1.124264 1.390435
5
  5 1.0802502 1.252490 1.159250 0.9176771
                                          1.083265 1.252417
  6 0.9907582 0.967179 1.484550 0.8958189
                                           1.107852 1.334070
```

## Listing 35:

```
> frozen$`WT_CL/F` <- NULL
> molten <- melt(frozen,id.var='run',na.rm=TRUE)
> head(molten)
```

```
run variable
                  value
         CL/F 1.0418968
2
   2
         CL/F 0.9497975
3
         CL/F 0.9814691
   3
4
         CL/F 0.9735346
  4
5
  5
        CL/F 1.0802502
         CL/F 0.9907582
```

#### 1.4.4 Plot.

Now we plot. We reverse the variable factor to give us top-down layout of strips.



# Listing 36:

## > levels(molten\$variable)

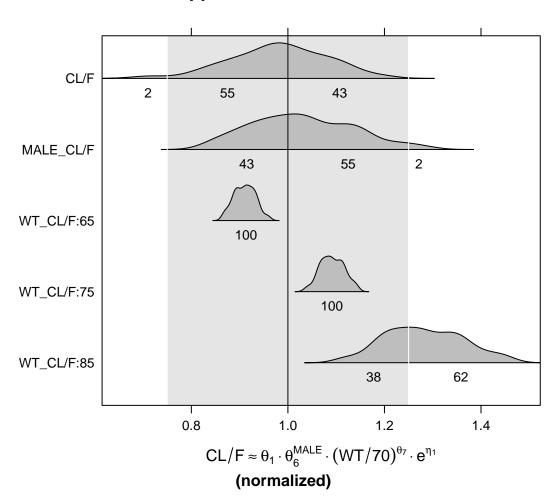
```
[1] "CL/F" "MALE_CL/F" "WT_CL/F:65" "WT_CL/F:75" "WT_CL/F:85"
```

## Listing 37:

```
> molten$variable <- factor(molten$variable,levels=rev(levels(molten$variable)))
> print(
+    stripplot(
+    variable ~ value,
+    data=molten,
+    panel=panel.covplot,
+    xlab=parse(text=with(wiki,wiki2plotmath(noUnits(model[name=='CL/F'])))),
+    main=with(wiki,description[name=='CL/F']),
+    sub=('(normalized)\n\n\n')
+    )
+ )
```



# apparent oral clearance



## 1.4.5 Summarize

We see that clearance is estimated with good precision. Ignoring outliers, there is not much effect on clearance of being male, relative to female. Increasing weight is associated with increasing clearance. There is some probability that an 85 kg person will have at least 25 percent greater clearance than a 70 kg person.