

Summary of TMB runs

Lena Morrill

24/05/2021

```
## Warning in .recacheSubclasses(def@class$className, def, env): undefined subclass
## "numericVector" of class "Mnumeric"; definition not updated

## Loading required package: viridisLite

## Loading required package: ggplot2

## Loading required package: tikzDevice

## Loading required package: coda

## Loading required package: MASS

## Warning in .recacheSubclasses(def@class$className, def, env): undefined subclass
## "numericVector" of class "Mnumeric"; definition not updated

## ##
## ## Markov Chain Monte Carlo Package (MCMCpack)

## ## Copyright (C) 2003-2021 Andrew D. Martin, Kevin M. Quinn, and Jong Hee Park

## ##
## ## Support provided by the U.S. National Science Foundation

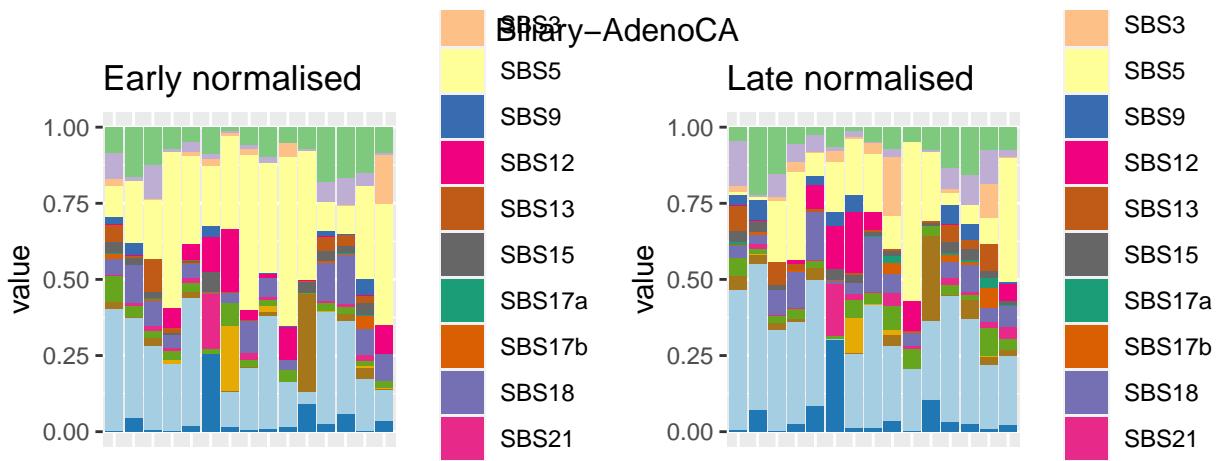
## ## (Grants SES-0350646 and SES-0350613)

## ##

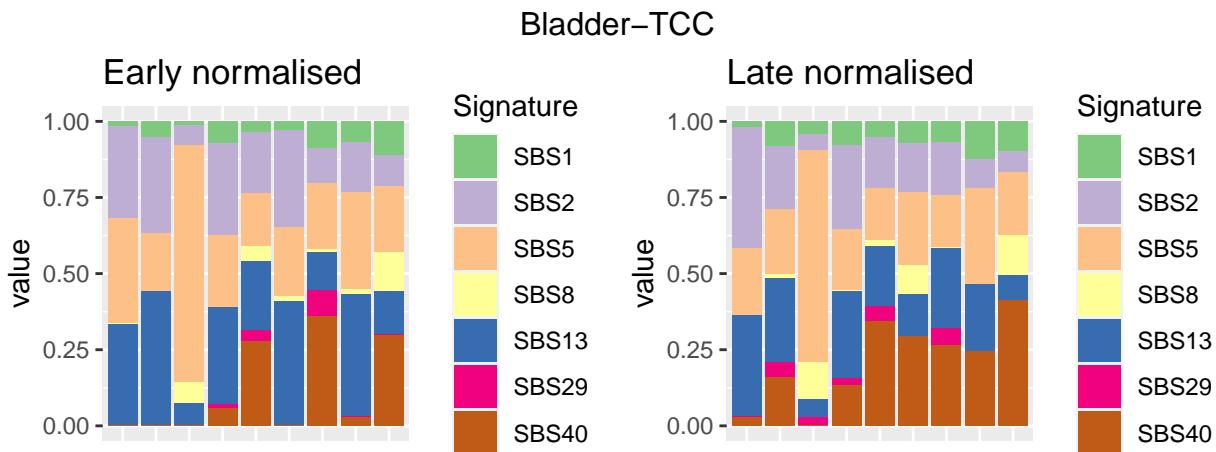
## 
## Attaching package: 'ggthemr'

## The following objects are masked from 'package:ggpubr':
## 
##     rotate_x_text, rotate_y_text

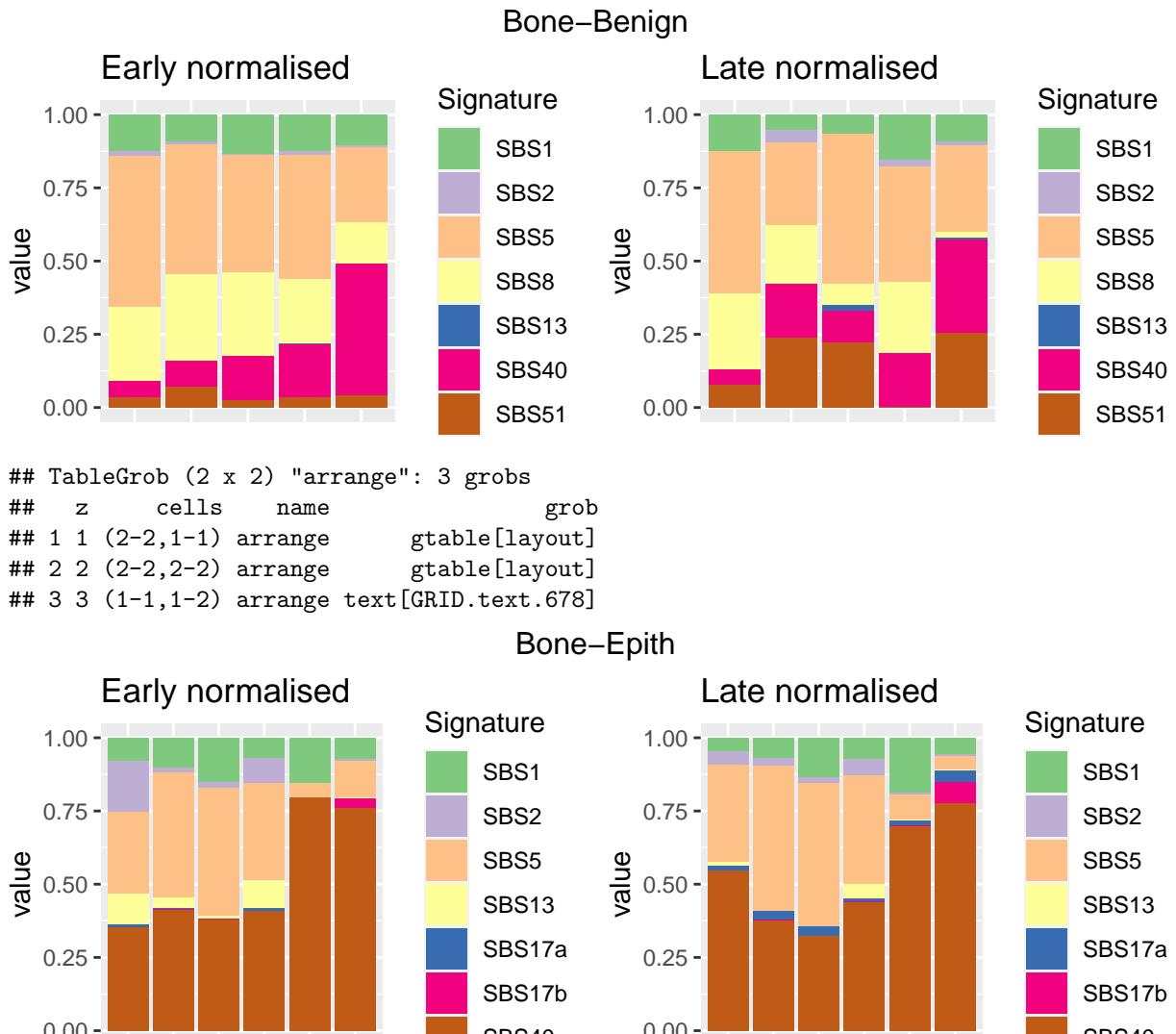
pcawg_palette <- pcawg.colour.palette(gsub("\\.*", "", enough_samples), scheme = "tumour.subtype")
names(pcawg_palette) <- enough_samples
```



```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.328]
```

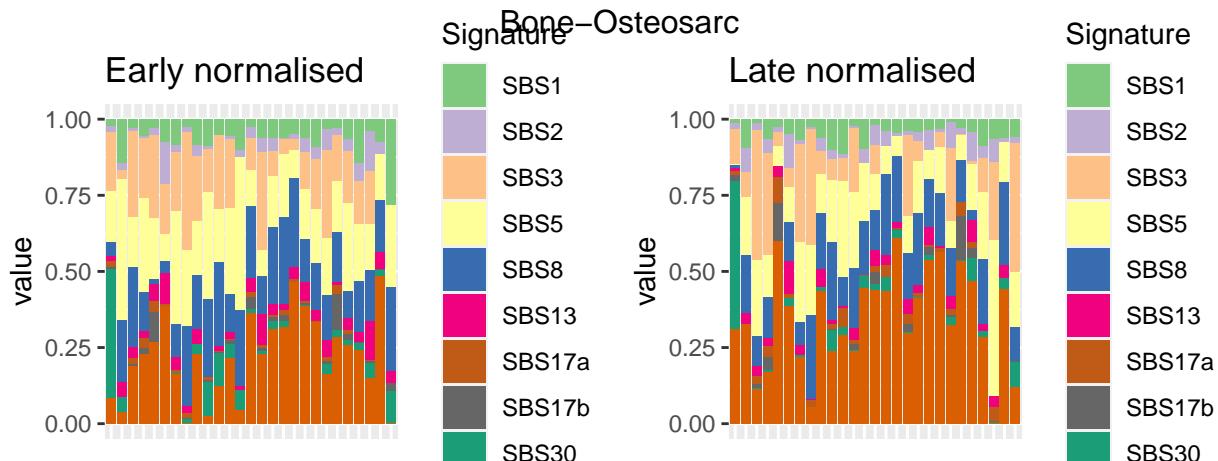


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.503]
```

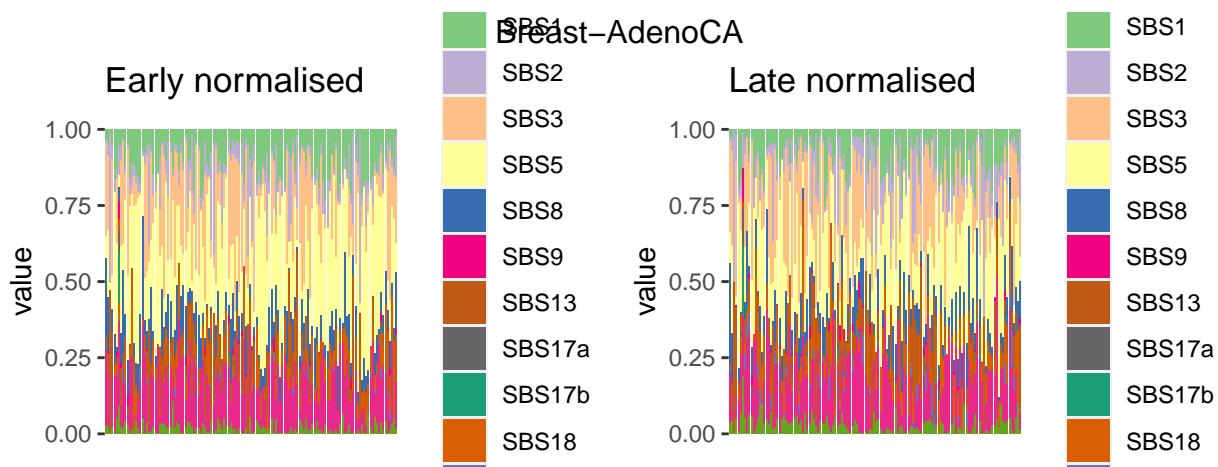


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.678]
```

```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.853]
```

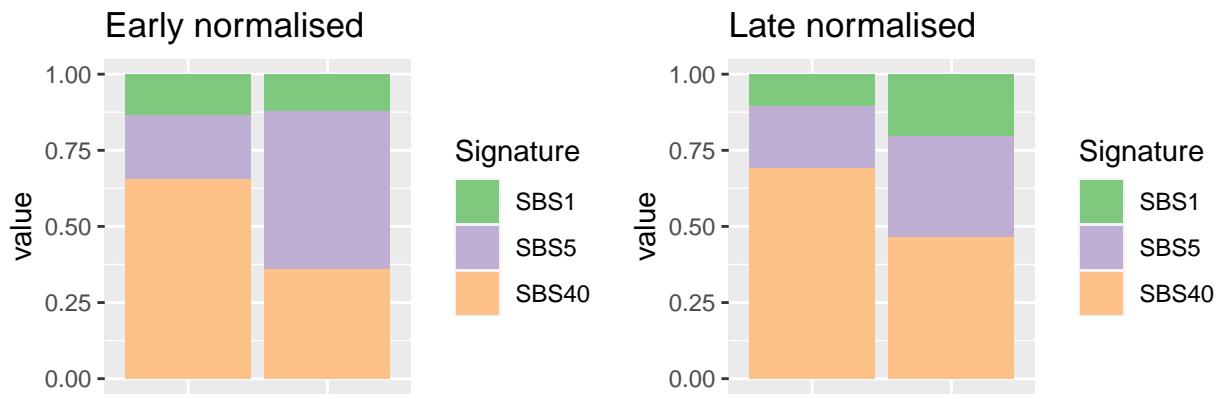


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1070]
```



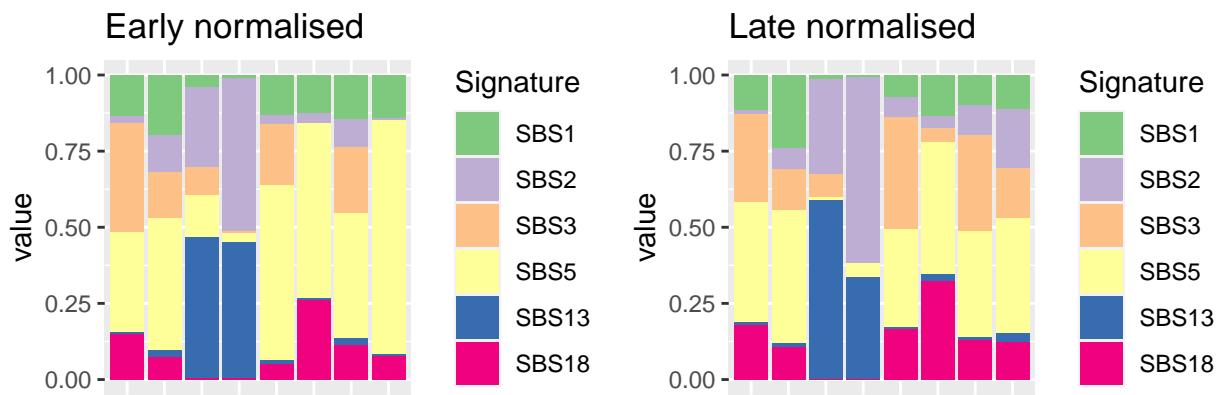
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1329]
```

Breast-DCIS



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1448]
```

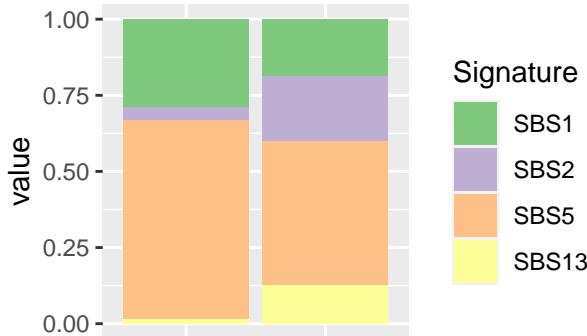
Breast-LobularCA



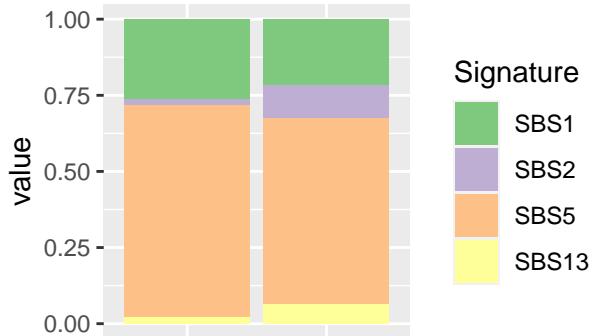
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1609]
```

Cervix–AdenoCA

Early normalised



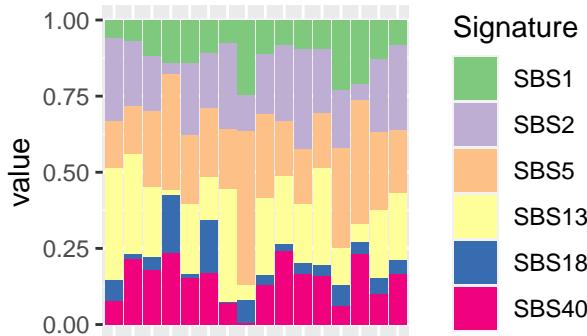
Late normalised



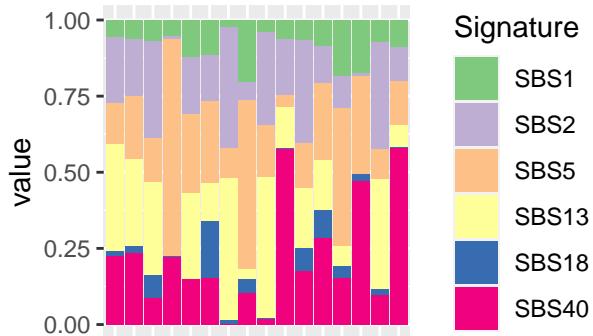
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1742]
```

Cervix–SCC

Early normalised

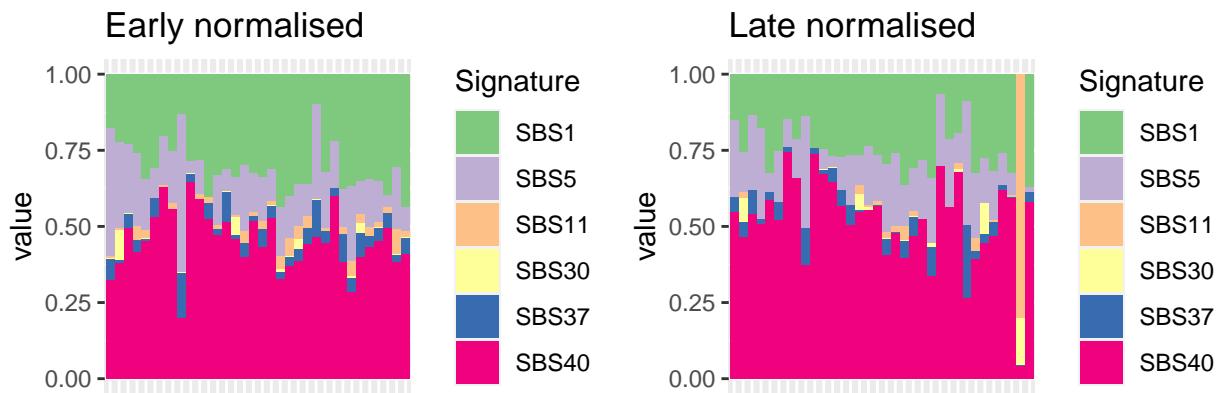


Late normalised



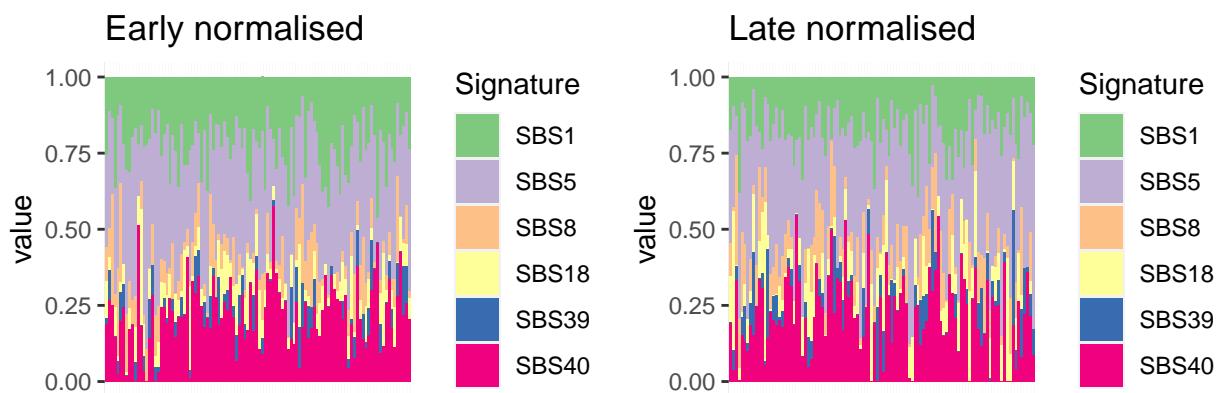
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1903]
```

CNS–GBM



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2064]
```

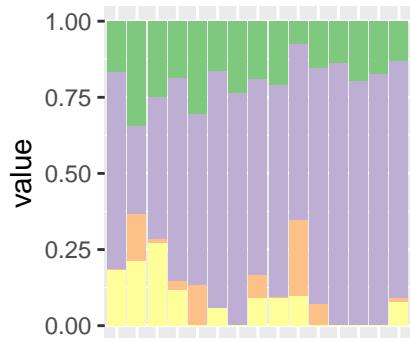
CNS–Medullo



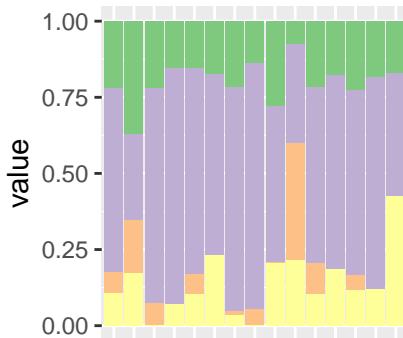
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2225]
```

CNS–Oligo

Early normalised



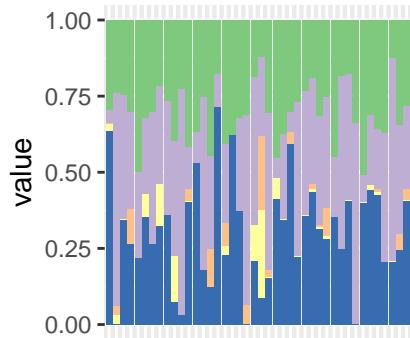
Late normalised



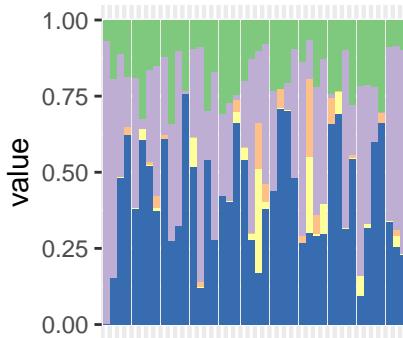
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2358]
```

CNS–PiloAstro

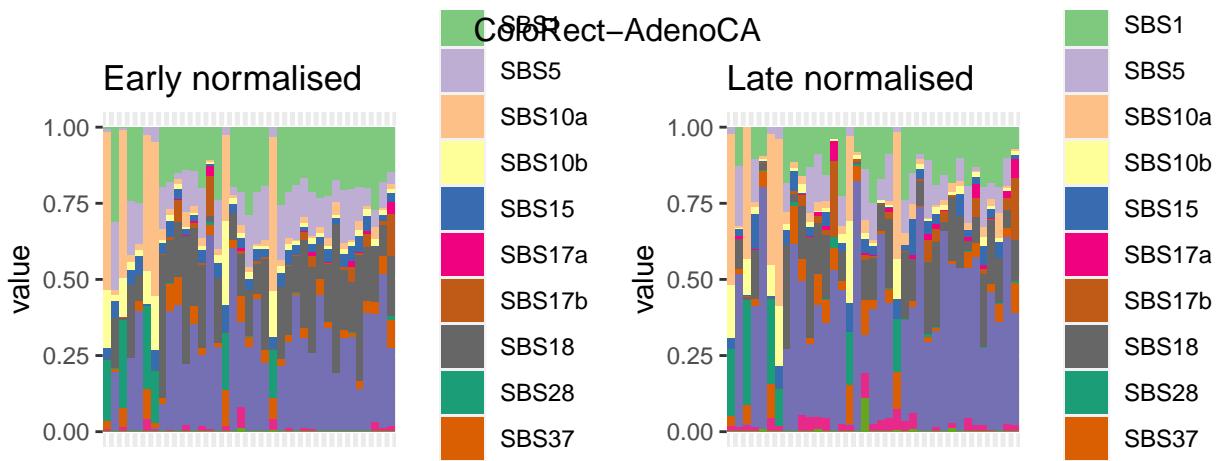
Early normalised



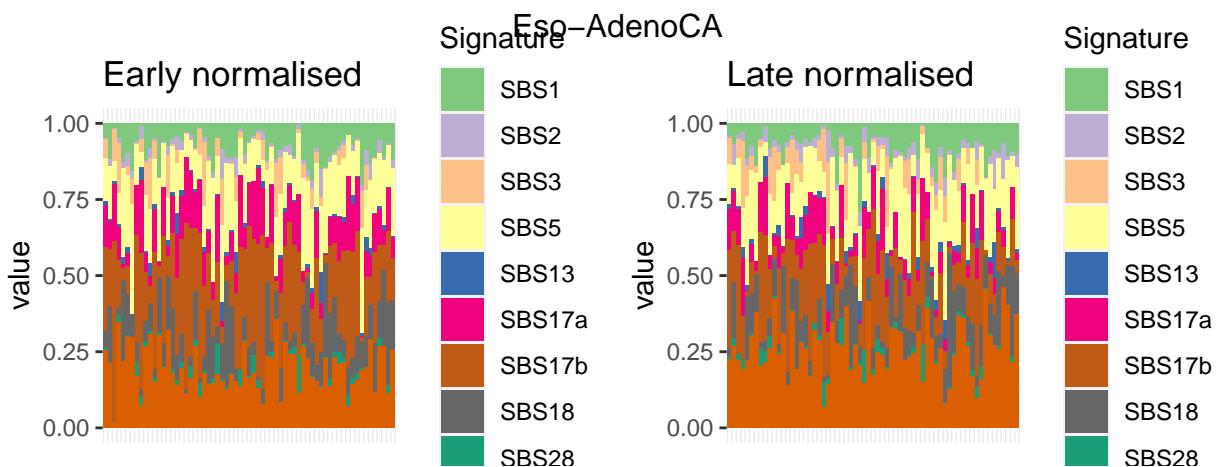
Late normalised



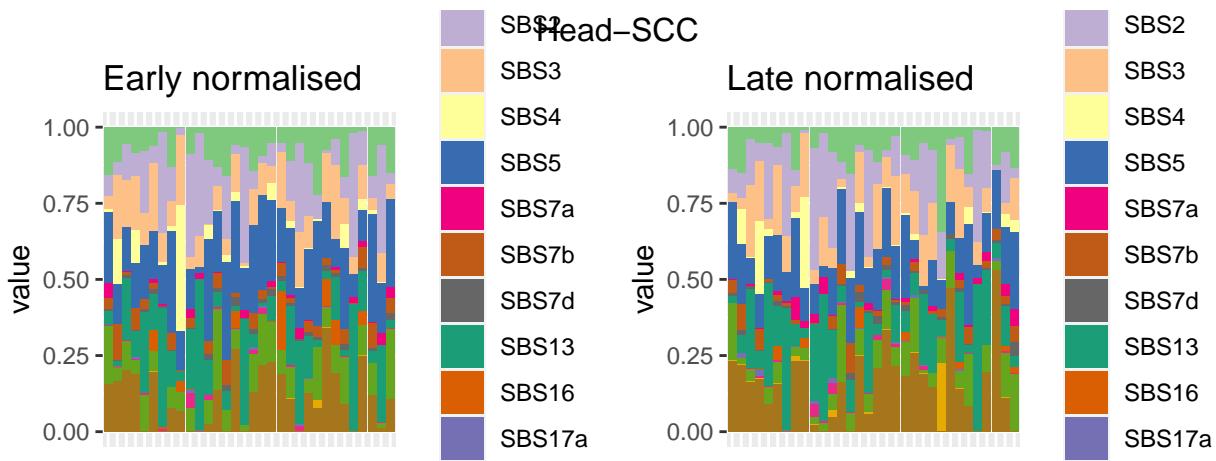
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2505]
```



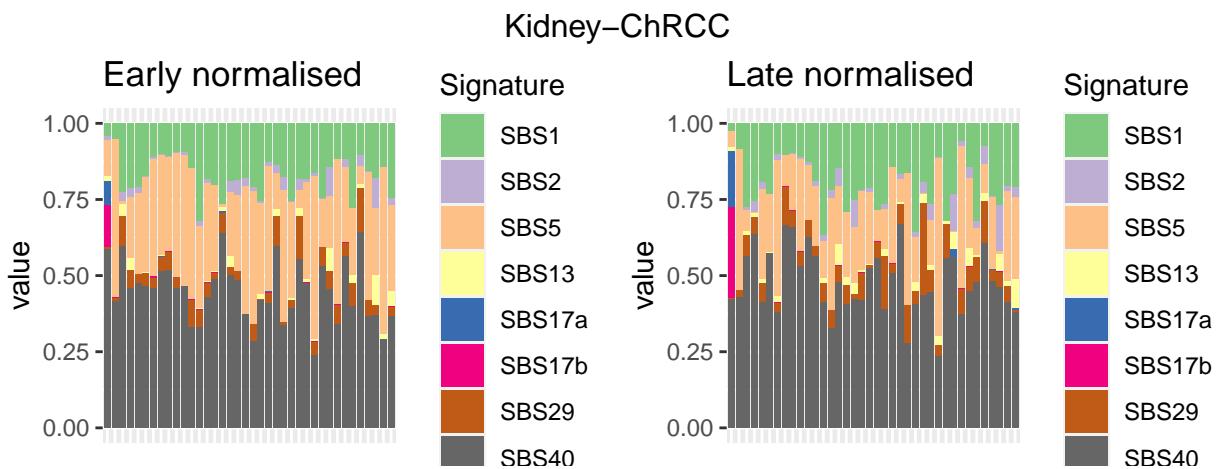
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2764]
```



```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2981]
```

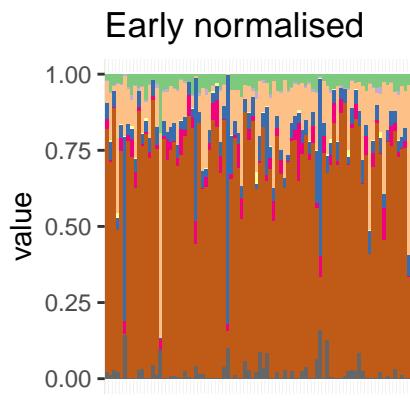


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3268]
```



```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3457]
```

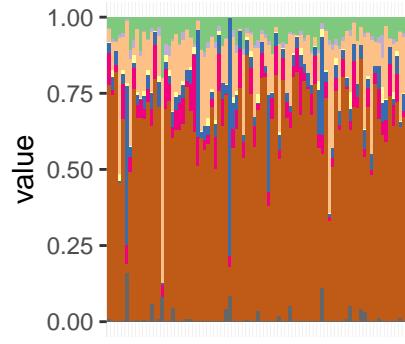
Kidney–RCC.clearcell



Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

Late normalised

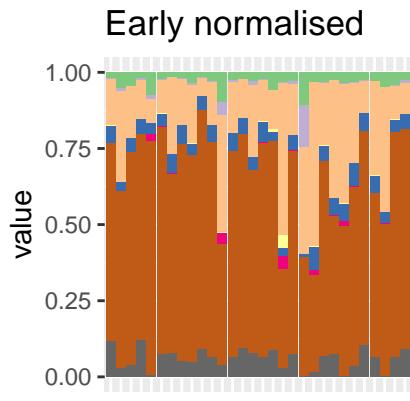


Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3646]
```

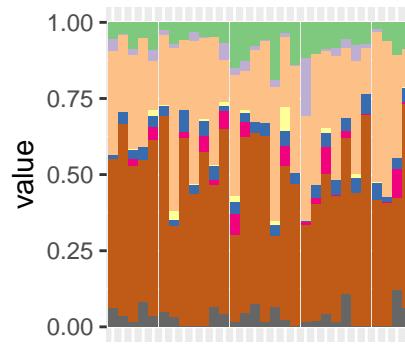
Kidney–RCC.papillary



Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

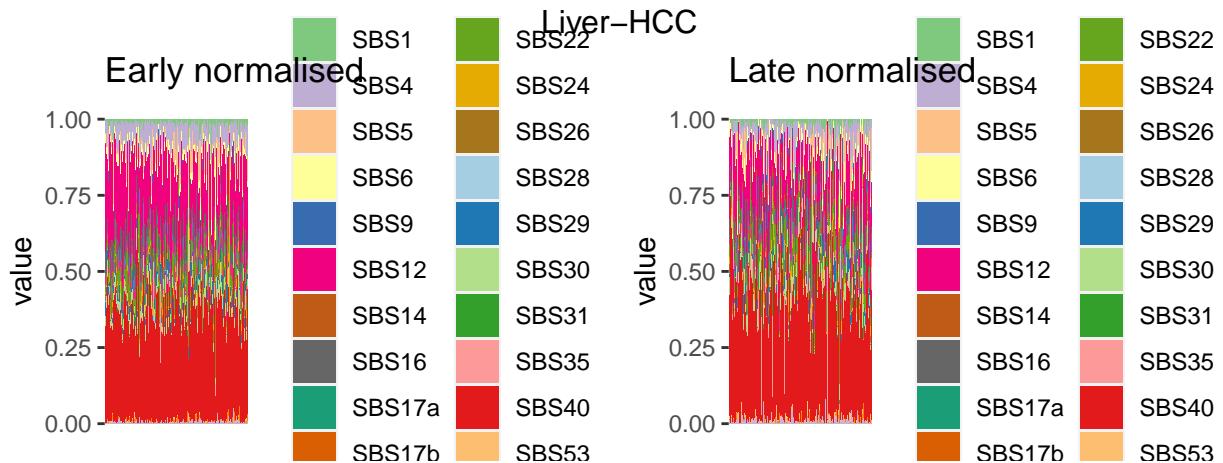
Late normalised



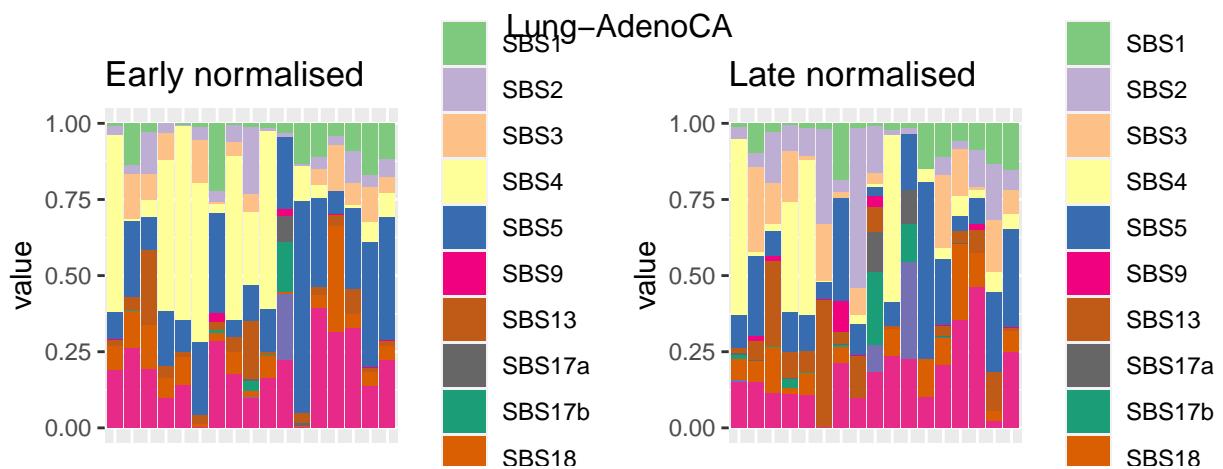
Signature

- SBS1
- SBS2
- SBS5
- SBS13
- SBS22
- SBS29
- SBS40
- SBS41

```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3835]
```



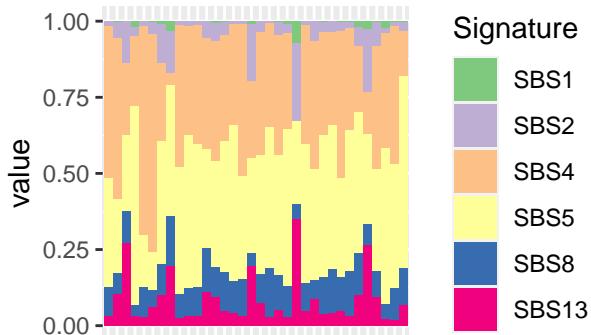
```
## TableGrob (2 x 2) "arrange": 3 grobs
## z cells name grob
## 1 1 (2-2,1-1) arrange gtable[layout]
## 2 2 (2-2,2-2) arrange gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4248]
```



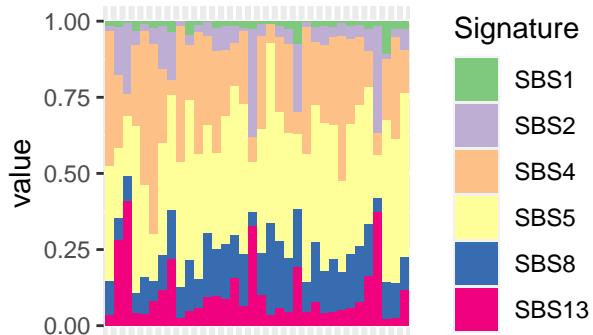
```
## TableGrob (2 x 2) "arrange": 3 grobs
## z cells name grob
## 1 1 (2-2,1-1) arrange gtable[layout]
## 2 2 (2-2,2-2) arrange gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4493]
```

Lung-SCC

Early normalised

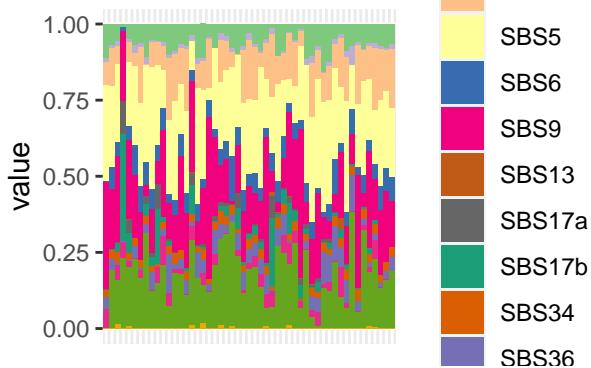


Late normalised

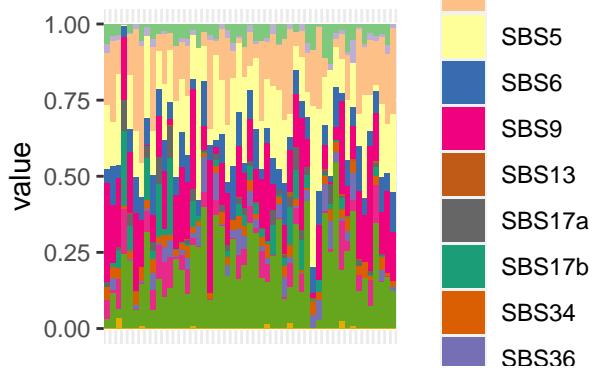


```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4654]
```

Early normalised



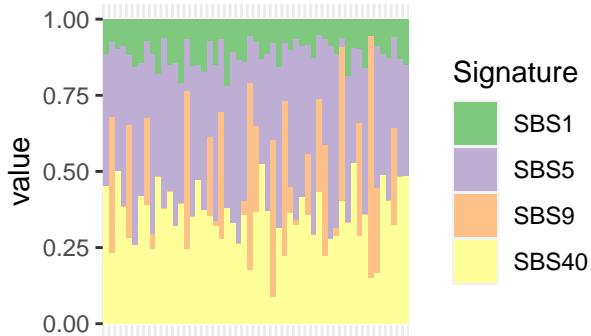
Late normalised



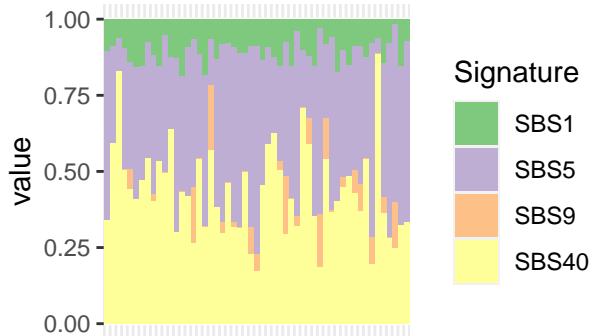
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4927]
```

Lymph-CLL

Early normalised



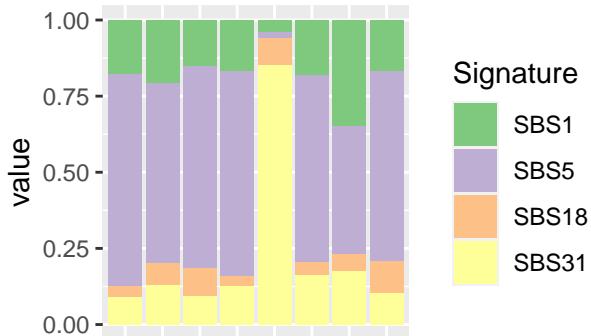
Late normalised



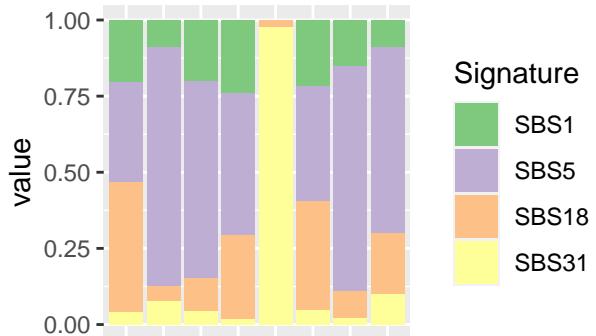
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5060]
```

Myeloid-AML

Early normalised

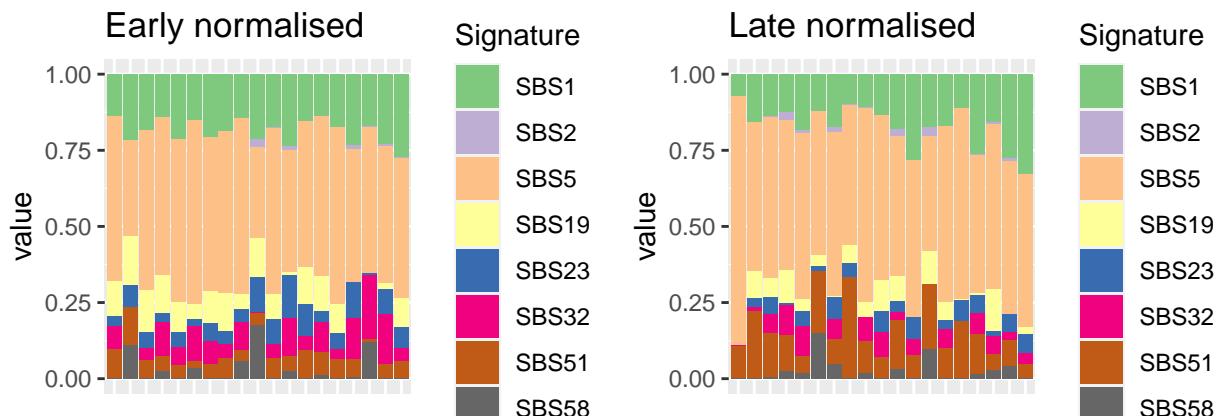


Late normalised

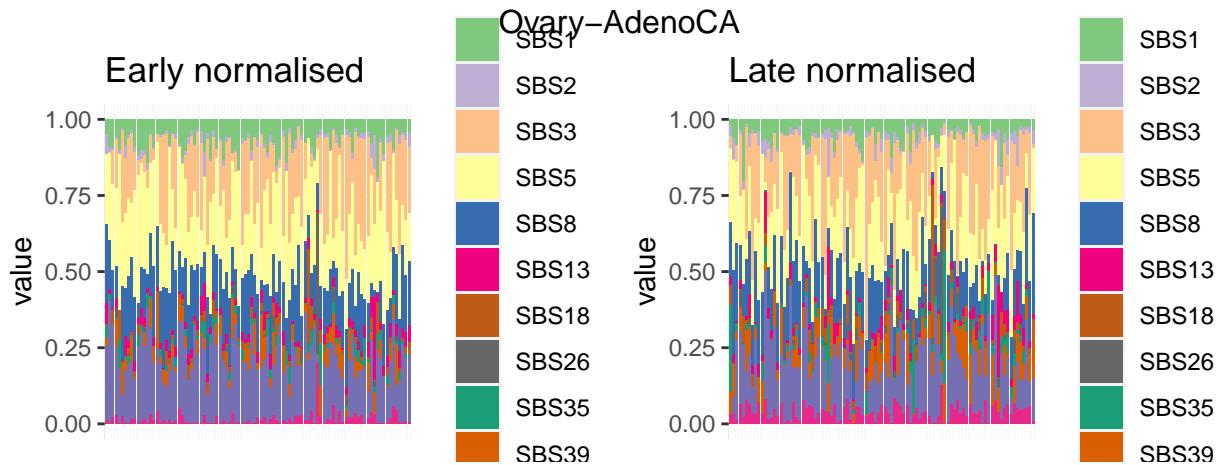


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5193]
```

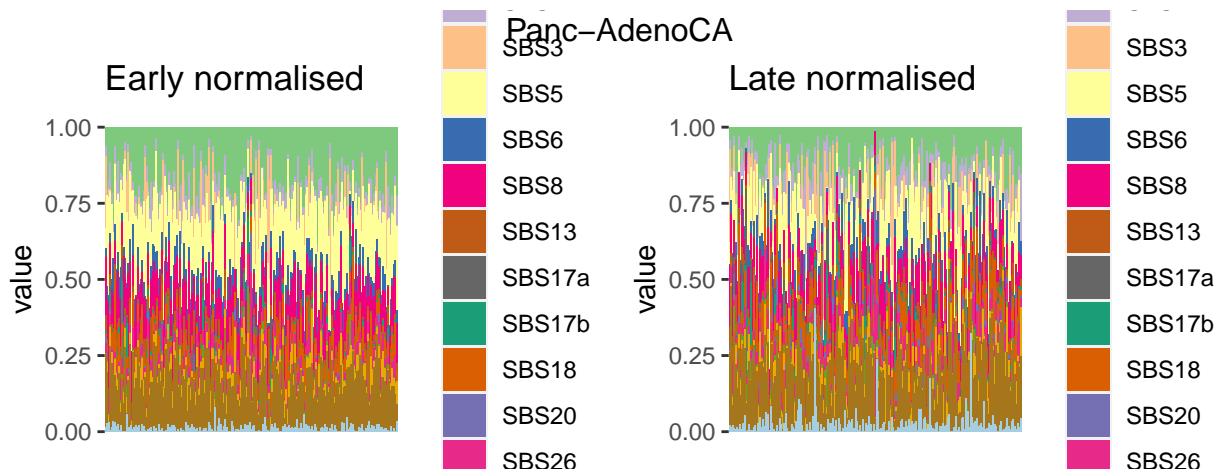
Myeloid–MPN



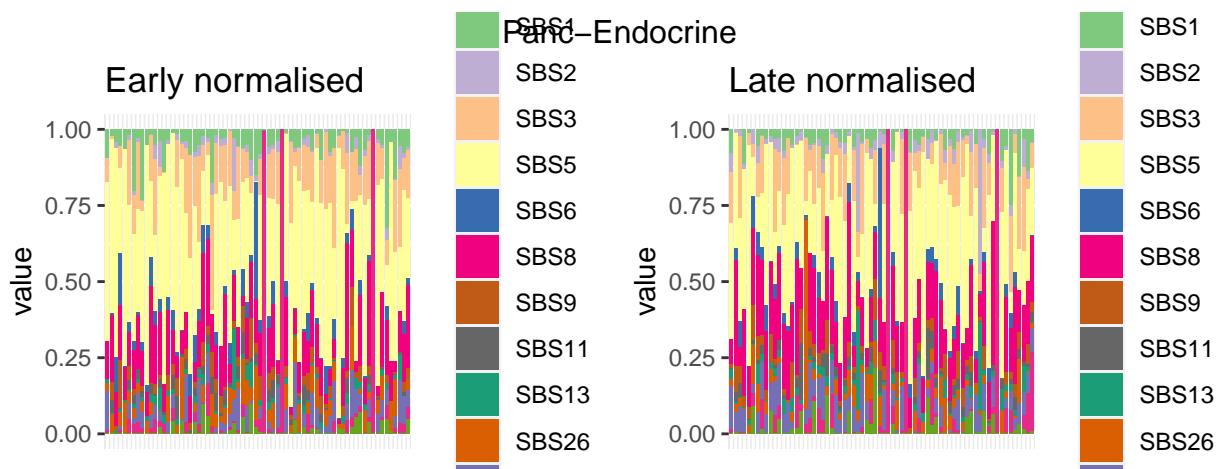
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5382]
```



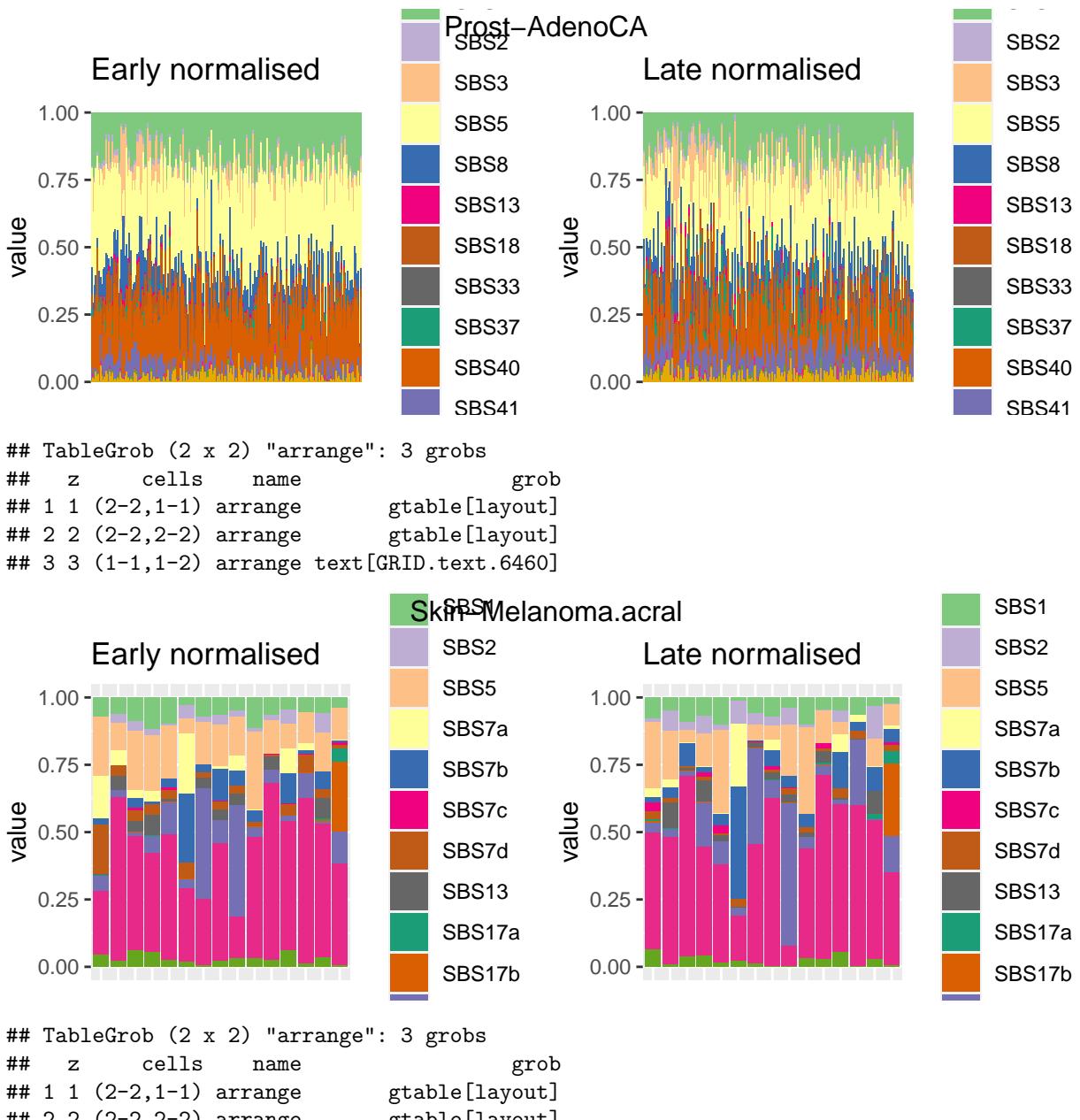
```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells  name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5627]
```

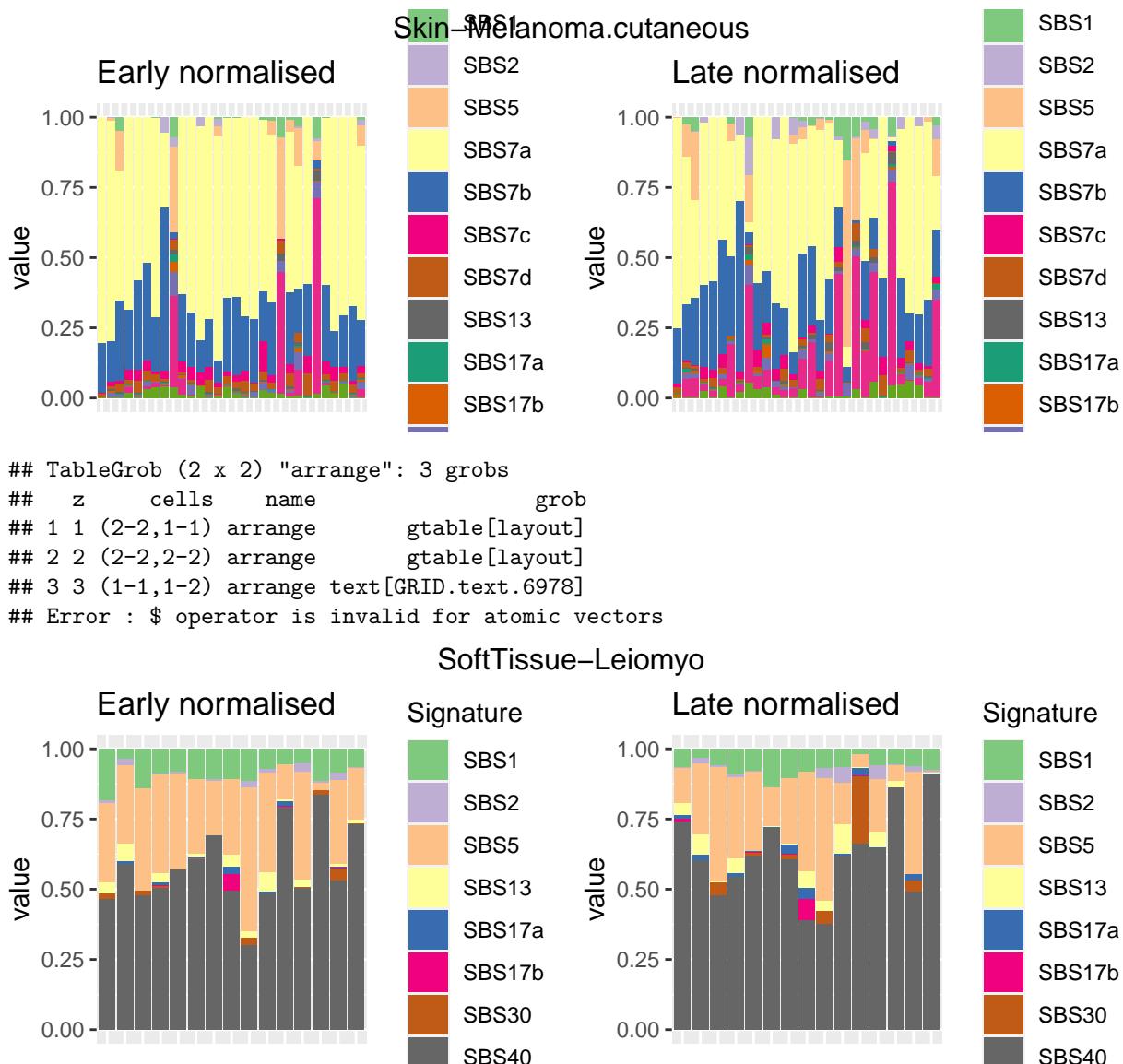


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5928]
```

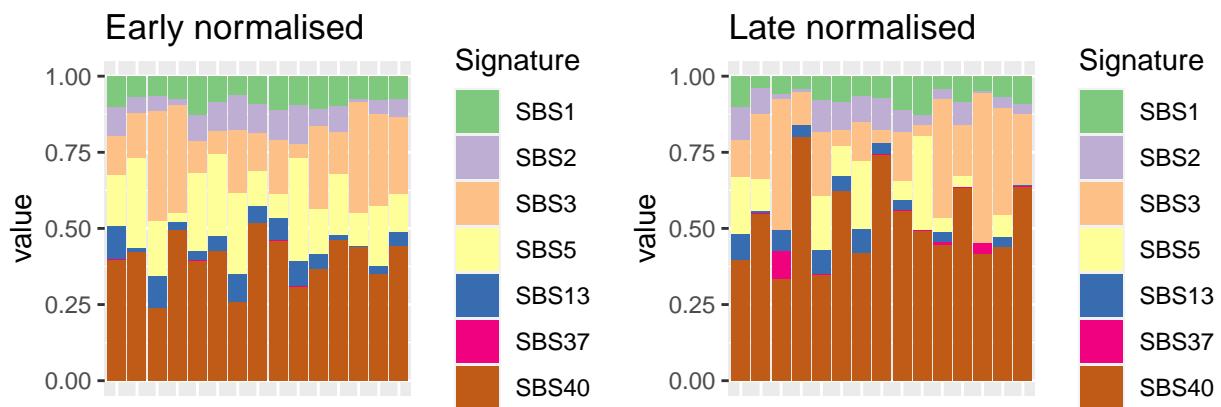


```
## # TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name      grob
## 1 1 (2-2,1-1) arrange    gtable[layout]
## 2 2 (2-2,2-2) arrange    gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6187]
```

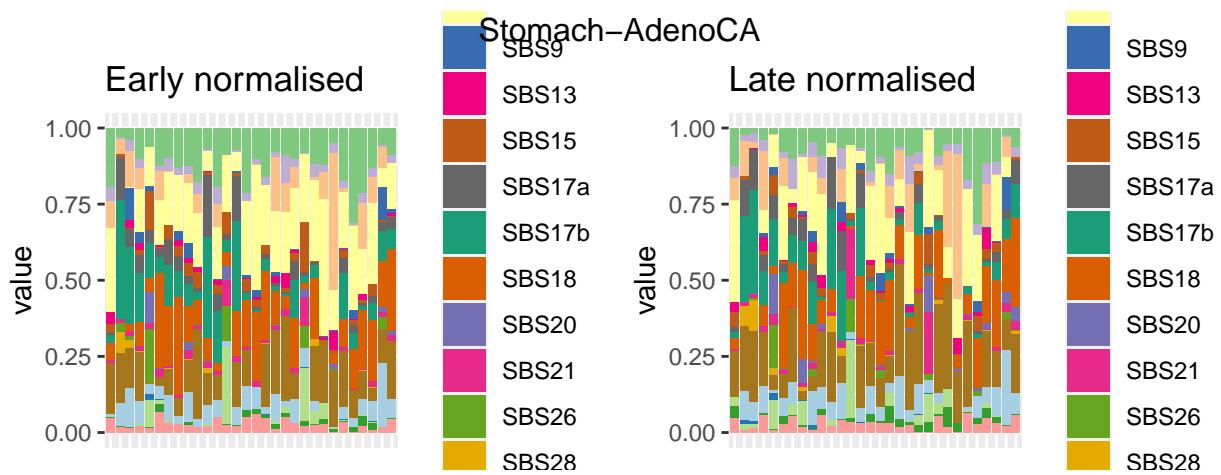




SoftTissue–Liposarc



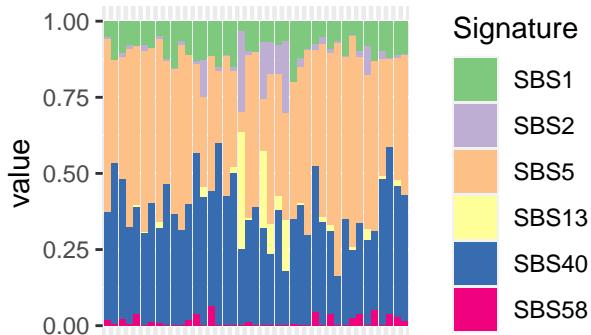
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7342]
```



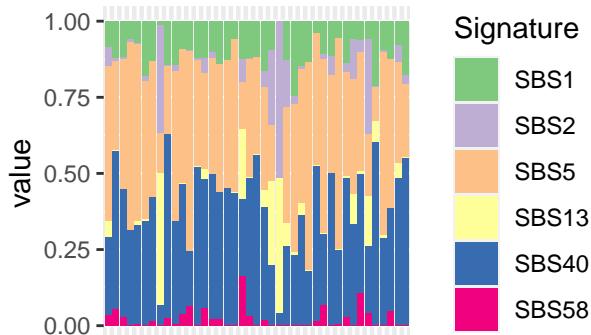
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7699]
```

Thy–AdenoCA

Early normalised



Late normalised



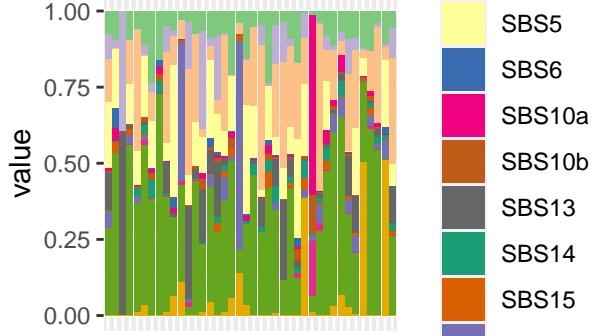
```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7860]
```

Early normalised

Uterus–AdenoCA

- SBS2
- SBS3
- SBS5
- SBS6
- SBS10a
- SBS10b
- SBS13
- SBS14
- SBS15
- SBS26

Late normalised



```
## TableGrob (2 x 2) "arrange": 3 grobs
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.8133]
```

```
## $`Biliary-AdenoCA`
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.328]
##
## $`Bladder-TCC`
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.503]
```

```

## 
## $`Bone-Benign` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.678]
##
## $`Bone-Epith` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.853]
##
## $`Bone-Osteosarc` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1070]
##
## $`Breast-AdenoCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1329]
##
## $`Breast-DCIS` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1448]
##
## $`Breast-LobularCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1609]
##
## $`Cervix-AdenoCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1742]
##
## $`Cervix-SCC` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.1903]
##
## $`CNS-GBM` 
##   z   cells   name           grob

```

```

## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2064]
##
## $`CNS-Medullo`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2225]
##
## $`CNS-Oligo`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2358]
##
## $`CNS-PiloAstro`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2505]
##
## $`ColoRect-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2764]
##
## $`Eso-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.2981]
##
## $`Head-SCC`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3268]
##
## $`Kidney-ChRCC`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3457]
##
## $`Kidney-RCC.clearcell`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3646]

```

```

## 
## $`Kidney-RCC.papillary` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.3835]
##
## $`Liver-HCC` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4248]
##
## $`Lung-AdenoCA` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4493]
##
## $`Lung-SCC` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4654]
##
## $`Lymph-BNHL` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.4927]
##
## $`Lymph-CLL` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5060]
##
## $`Myeloid-AML` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5193]
##
## $`Myeloid-MPN` 
##   z   cells   name           grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5382]
##
## $`Ovary-AdenoCA` 
##   z   cells   name           grob

```

```

## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5627]
##
## $`Panc-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.5928]
##
## $`Panc-Endocrine`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6187]
##
## $`Prost-AdenoCA`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6460]
##
## $`Skin-Melanoma.acral`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6719]
##
## $`Skin-Melanoma.cutaneous`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.6978]
##
## $`Skin-Melanoma.mucosal`
## [1] "Error : $ operator is invalid for atomic vectors\n"
## attr(,"class")
## [1] "try-error"
## attr(,"condition")
## <simpleError: $ operator is invalid for atomic vectors>
##
## $`SoftTissue-Leiomyo`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]
## 3 3 (1-1,1-2) arrange text[GRID.text.7167]
##
## $`SoftTissue-Liposarc`
##   z   cells   name          grob
## 1 1 (2-2,1-1) arrange      gtable[layout]
## 2 2 (2-2,2-2) arrange      gtable[layout]

```



```

pvals_fullRE_M_nonexo_SP <- sapply(fullRE_M_nonexo_SP, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullRE_DMSL_nonexo_SP <- sapply(fullRE_DMSL_nonexo_SP, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations <- sapply(fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullREDMonefixedlambdanonexo_SP <- sapply(fullREDMonefixedlambdanonexo_SP, function(i) try(wald_TMB_wrapper(i)))

## Check data - slope appears to be of length one (binomial)
pvals_fullREDMonefixedlambdanonexo_SPSaA <- sapply(fullREDMonefixedlambdanonexo_SPSaA, function(i) try(wald_TMB_wrapper(i)))

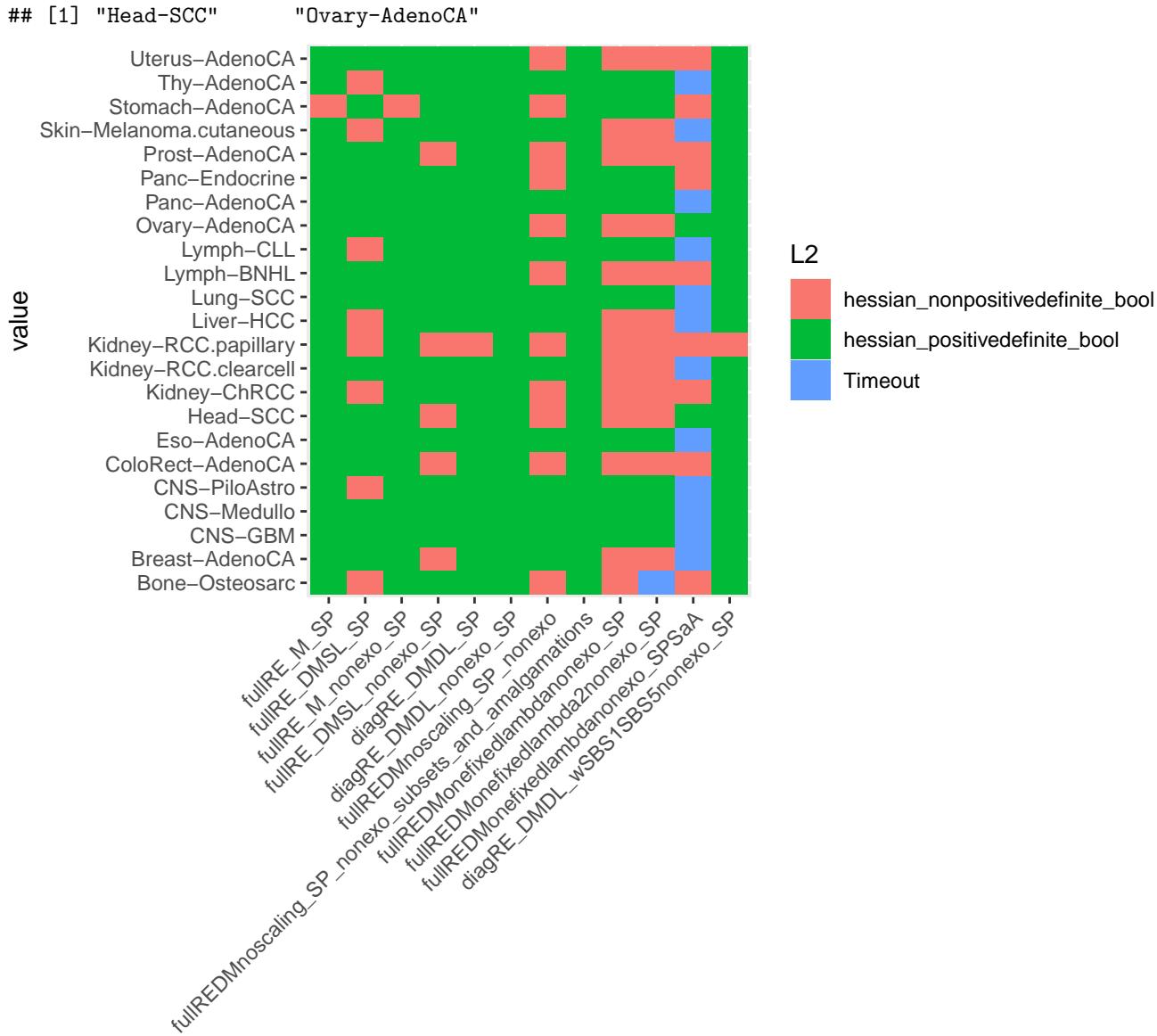
names(fullREDMonefixedlambdanonexo_SPSaA) <- names(pvals_fullREDMonefixedlambdanonexo_SP) <- names(pvals_fullRE_DMSL_nonexo_SP)
names(pvals_fullRE_DMSL_nonexo_SP) <- enough_samples

pvals_diagRE_DMDL_SP

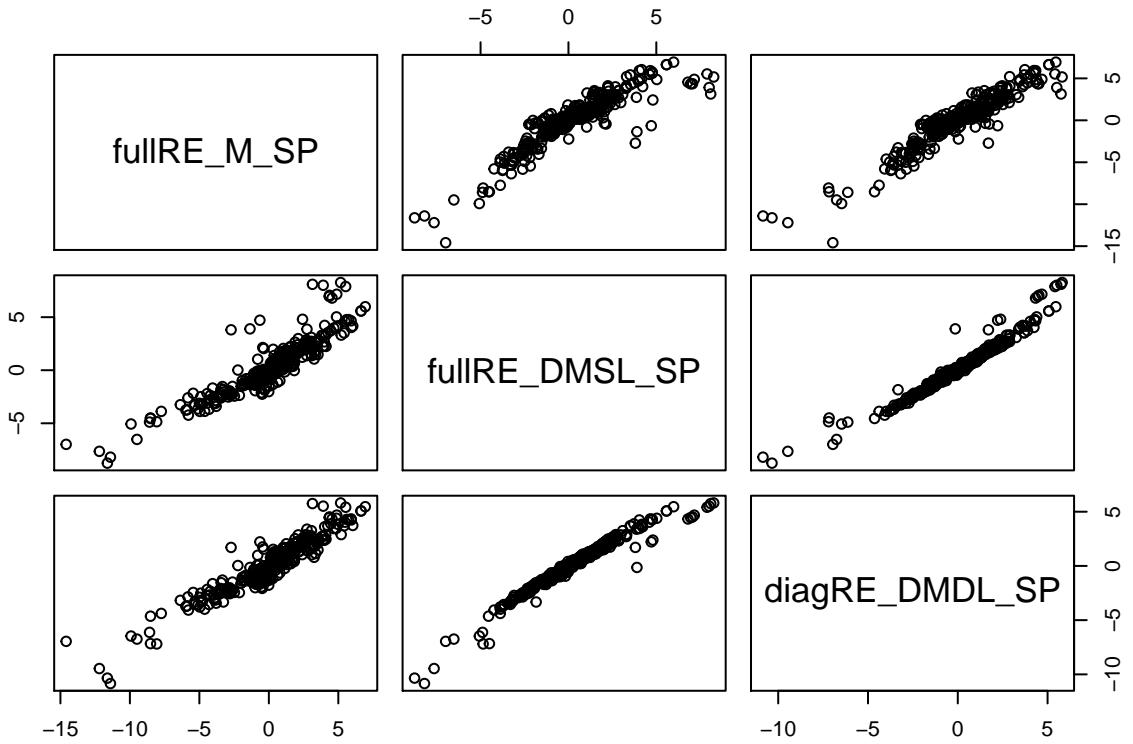
##          Bone-Osteosarc      Breast-AdenoCA        CNS-GBM
##          1.080828e-04      2.239756e-28      3.390137e-03
##          CNS-Medullo       CNS-PiloAstro       ColoRect-AdenoCA
##          8.431463e-03      5.615238e-04      6.356131e-26
##          Eso-AdenoCA        Head-SCC           Kidney-ChRCC
##          5.329093e-21      4.975610e-05      1.562125e-09
##          Kidney-RCC.clearcell Kidney-RCC.papillary Liver-HCC
##          4.027485e-18          NA                 4.747822e-107
##          Lung-SCC            Lymph-BNHL         Lymph-CLL
##          7.747310e-22      3.908637e-19      6.611927e-20
##          Ovary-AdenoCA       Panc-AdenoCA       Panc-Endocrine
##          8.965185e-38      4.096402e-119     3.987099e-10
##          Prost-AdenoCA      Skin-Melanoma.cutaneous Stomach-AdenoCA
##          6.474116e-99      9.272113e-25      1.715150e-06
##          Thy-AdenoCA         Uterus-AdenoCA
##          8.821583e-06      4.819867e-10

## $Timeout
## [1] "Breast-AdenoCA"      "CNS-GBM"
## [3] "CNS-Medullo"         "CNS-PiloAstro"
## [5] "Eso-AdenoCA"          "Kidney-RCC.clearcell"
## [7] "Liver-HCC"             "Lung-SCC"
## [9] "Lymph-CLL"             "Panc-AdenoCA"
## [11] "Skin-Melanoma.cutaneous" "Thy-AdenoCA"
##
## $hessian_nonpositivedefinite_bool
## [1] "Bone-Osteosarc"      "ColoRect-AdenoCA"      "Kidney-ChRCC"
## [4] "Kidney-RCC.papillary" "Lymph-BNHL"           "Panc-Endocrine"
## [7] "Prost-AdenoCA"        "Stomach-AdenoCA"       "Uterus-AdenoCA"
##
## $hessian_positivedefinite_bool

```



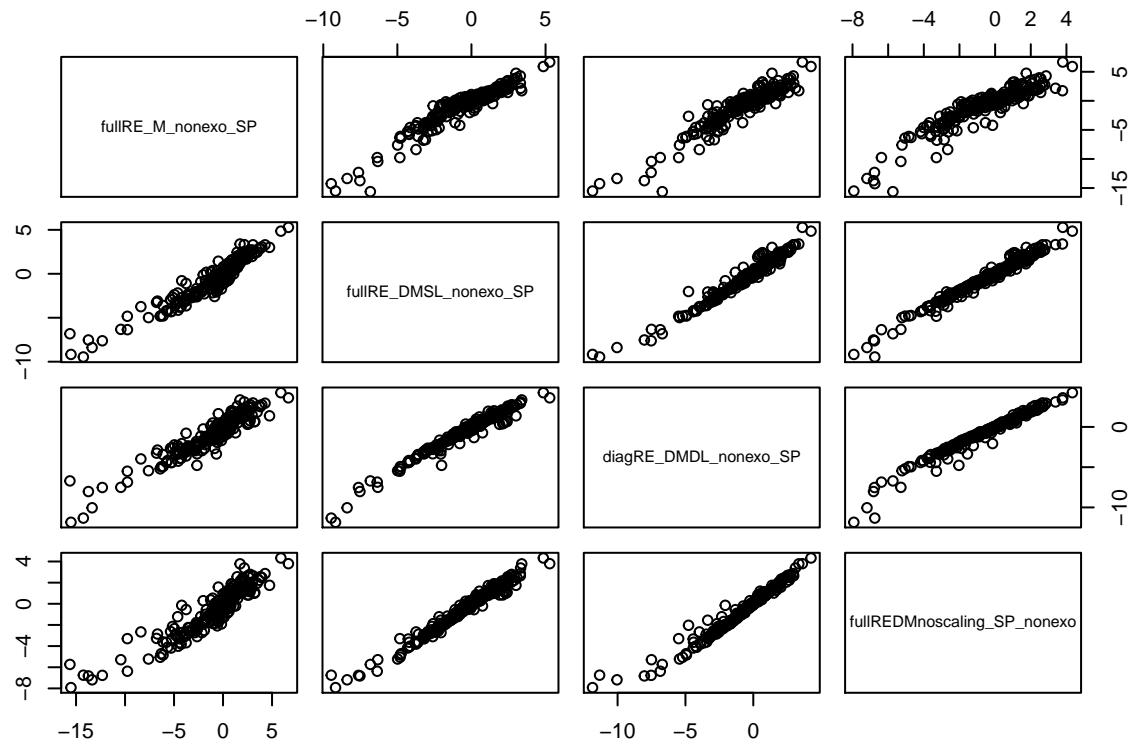
```
## comparison of betas
# give_betas(get(list_models_SP)[[1]][[1]])
all_betas_SP <- do.call('cbind', lapply(c( 'fullRE_M_SP', 'fullRE_DMSL_SP',
                                             'diagRE_DMDL_SP'), function(j) do.call('c', sapply(get(j), function(i) as.vector(give_b
colnames(all_betas_SP) <- c( 'fullRE_M_SP', 'fullRE_DMSL_SP',
                             'diagRE_DMDL_SP')
pairs(all_betas_SP)
```



```

all_betas_SP_nonexo <- do.call('cbind', lapply(c('fullRE_M_nonexo_SP','fullRE_DMSL_nonexo_SP',
                                                 'diagRE_DMDL_nonexo_SP', 'fullREDMnoscaling_SP_nonexo'), function(j) do.call('c', sapply
colnames(all_betas_SP_nonexo) <- c('fullRE_M_nonexo_SP','fullRE_DMSL_nonexo_SP',
                                         'diagRE_DMDL_nonexo_SP', 'fullREDMnoscaling_SP_nonexo')
pairs(all_betas_SP_nonexo)

```

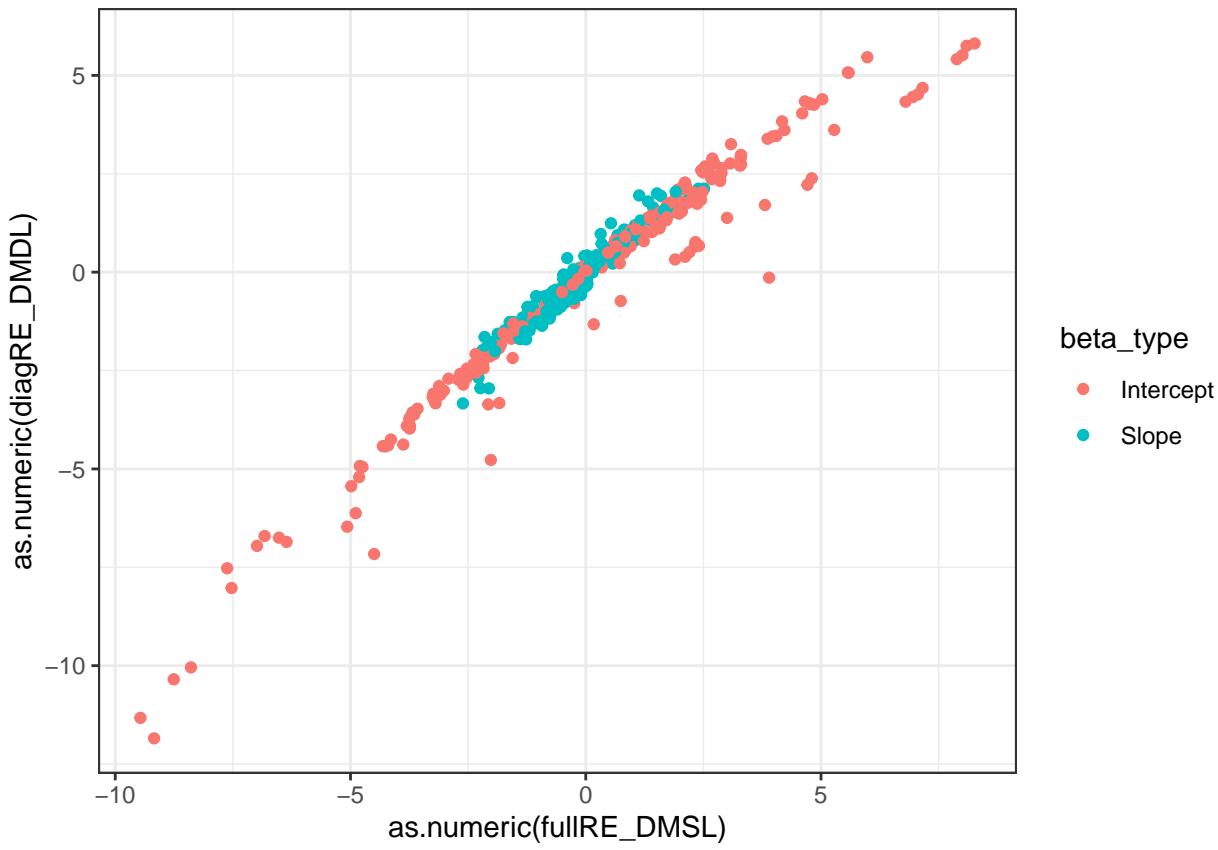


```

##   fullRE_DMSL diagRE_DMDL   fullRE_M beta_type      ct  ct2    sigs
## 1 -0.31531015 -0.1086854 -0.2237241 Slope Bone-Osteosarc B0 nonexo
## 2 -0.71770886 -0.6897242 -0.6712599 Slope Bone-Osteosarc B0 nonexo
## 3 -0.86019179 -0.7960993 -0.6637865 Slope Bone-Osteosarc B0 nonexo
## 4 -0.69897610 -0.4851852 -0.4948419 Slope Bone-Osteosarc B0 nonexo
## 5 -0.09619079  0.1160637  0.1756435 Slope Bone-Osteosarc B0 nonexo
## 6 -0.64276669 -0.4495100 -0.1553669 Slope Bone-Osteosarc B0 nonexo

## Warning: Removed 218 rows containing missing values (geom_point).

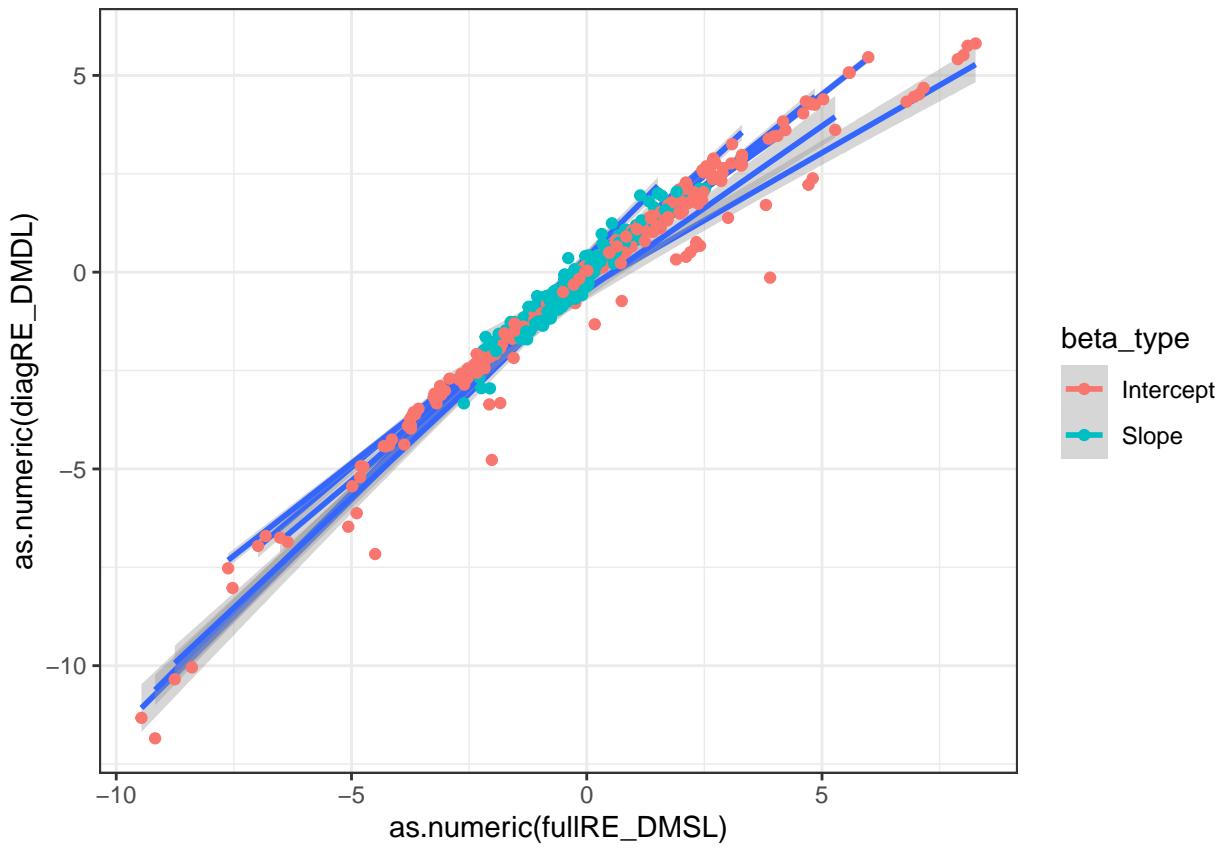
```



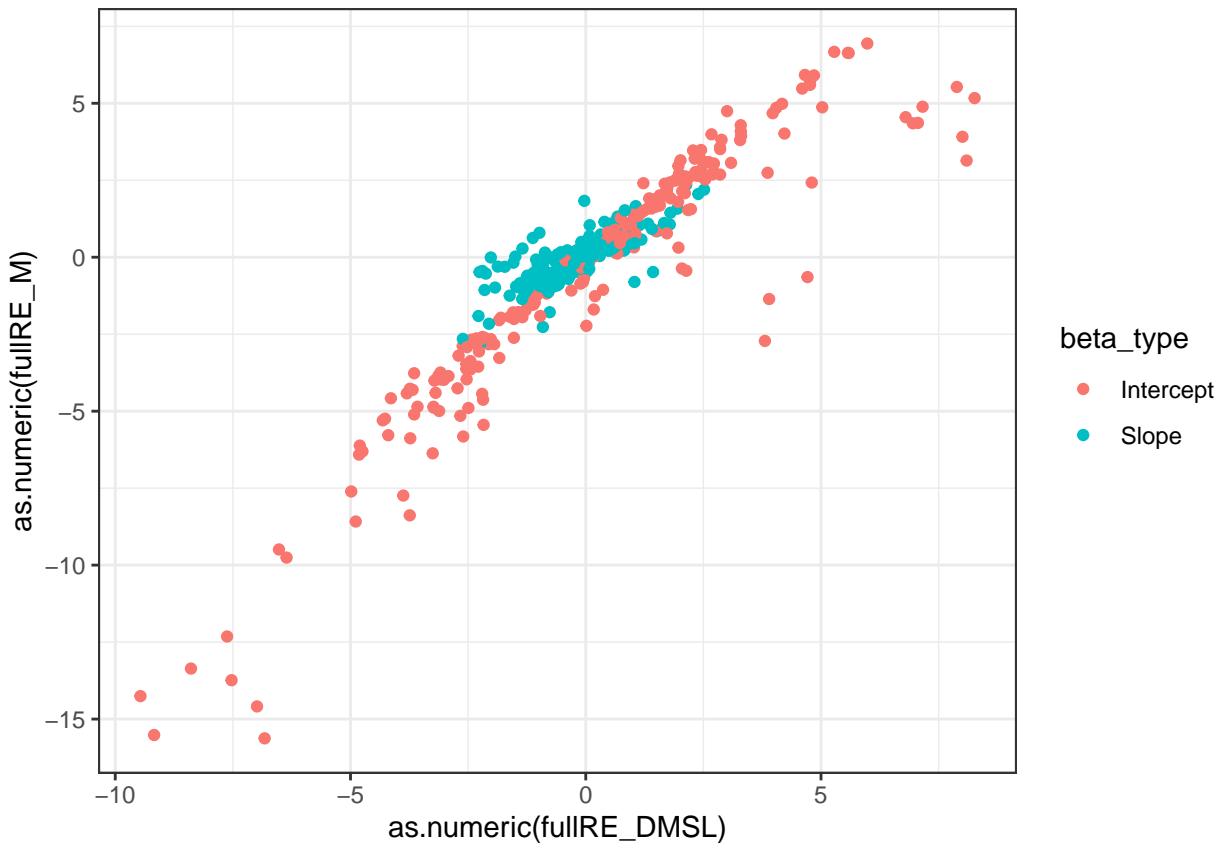
```

## `geom_smooth()` using formula 'y ~ x'
## Warning: Removed 218 rows containing non-finite values (stat_smooth).
## Warning in qt((1 - level)/2, df): NaNs produced
## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf
## Warning: Removed 218 rows containing missing values (geom_point).

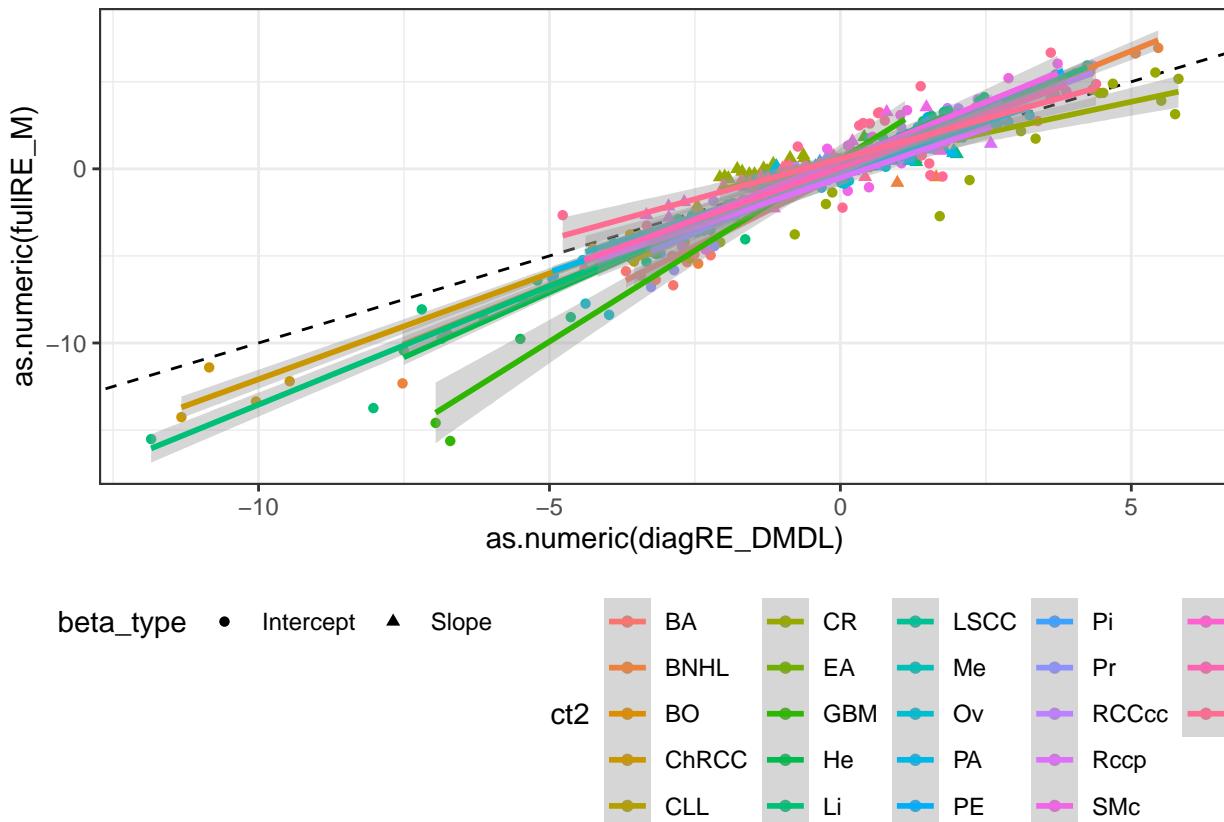
```



```
## Warning: Removed 284 rows containing missing values (geom_point).
```



```
## `geom_smooth()` using formula 'y ~ x'  
## Warning: Removed 80 rows containing non-finite values (stat_smooth).  
## Warning: Removed 80 rows containing missing values (geom_point).
```



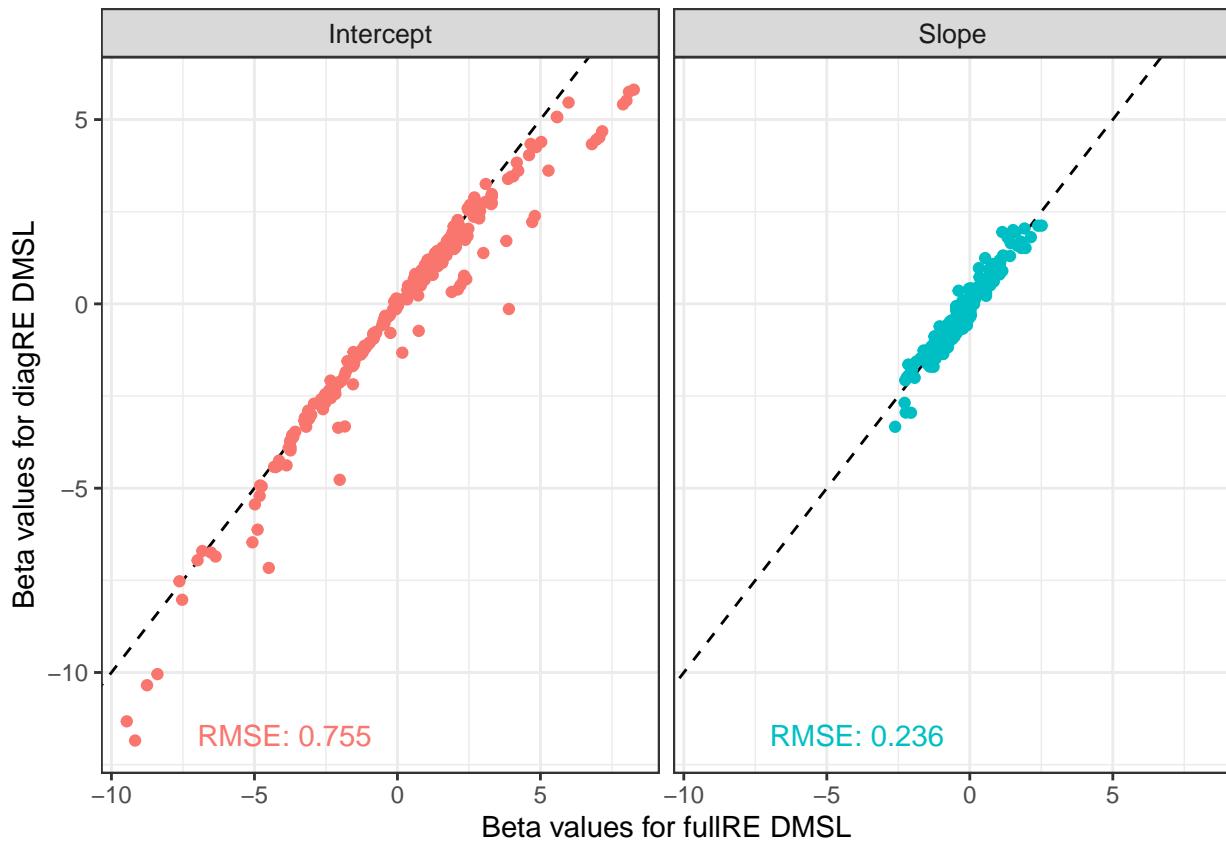
```

##   rmse_diag_full_DMSL rmse_fullDMSL_fullM beta_type
## 1      0.2362400          0.5467457     Slope
## 2      0.7551778          1.7127751 Intercept

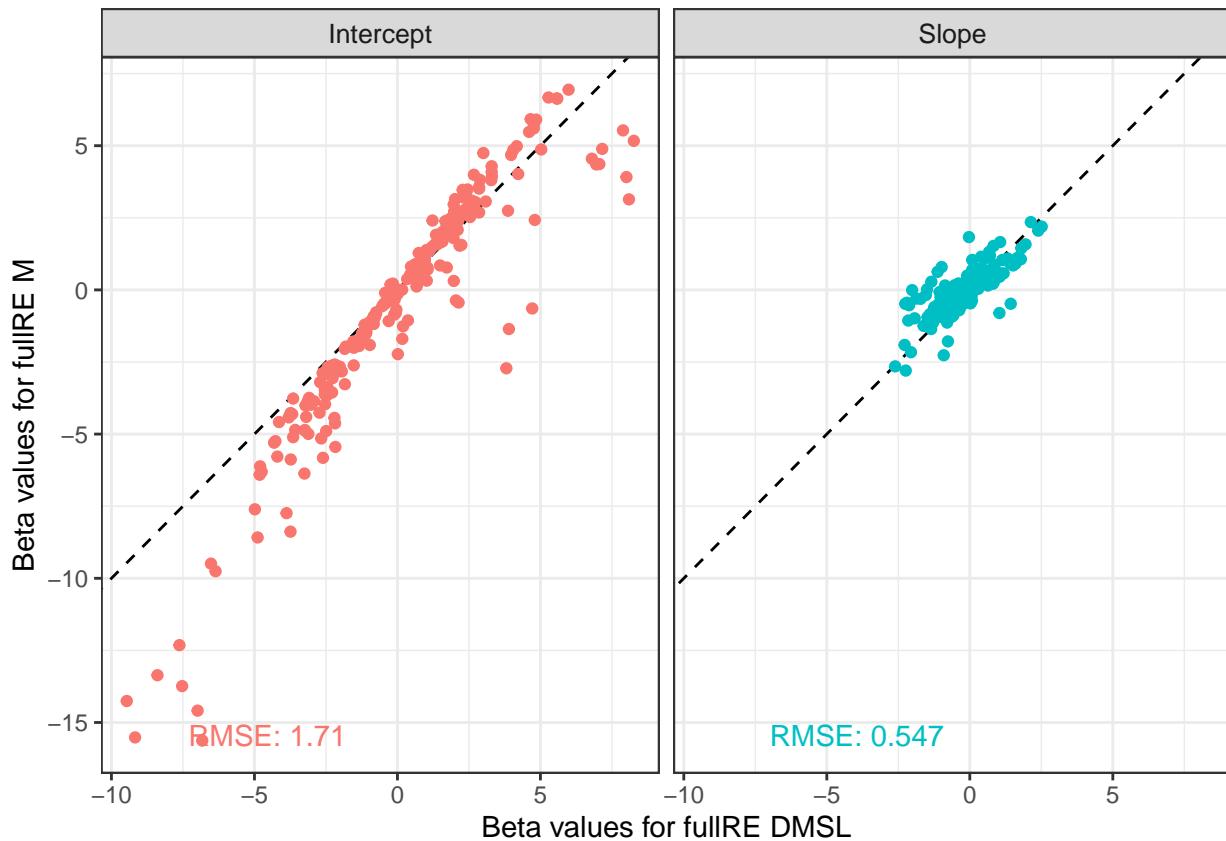
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 218 rows containing missing values (geom_point).

```



```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
## Warning: Removed 284 rows containing missing values (geom_point).
```



```

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 218 rows containing missing values (geom_point).

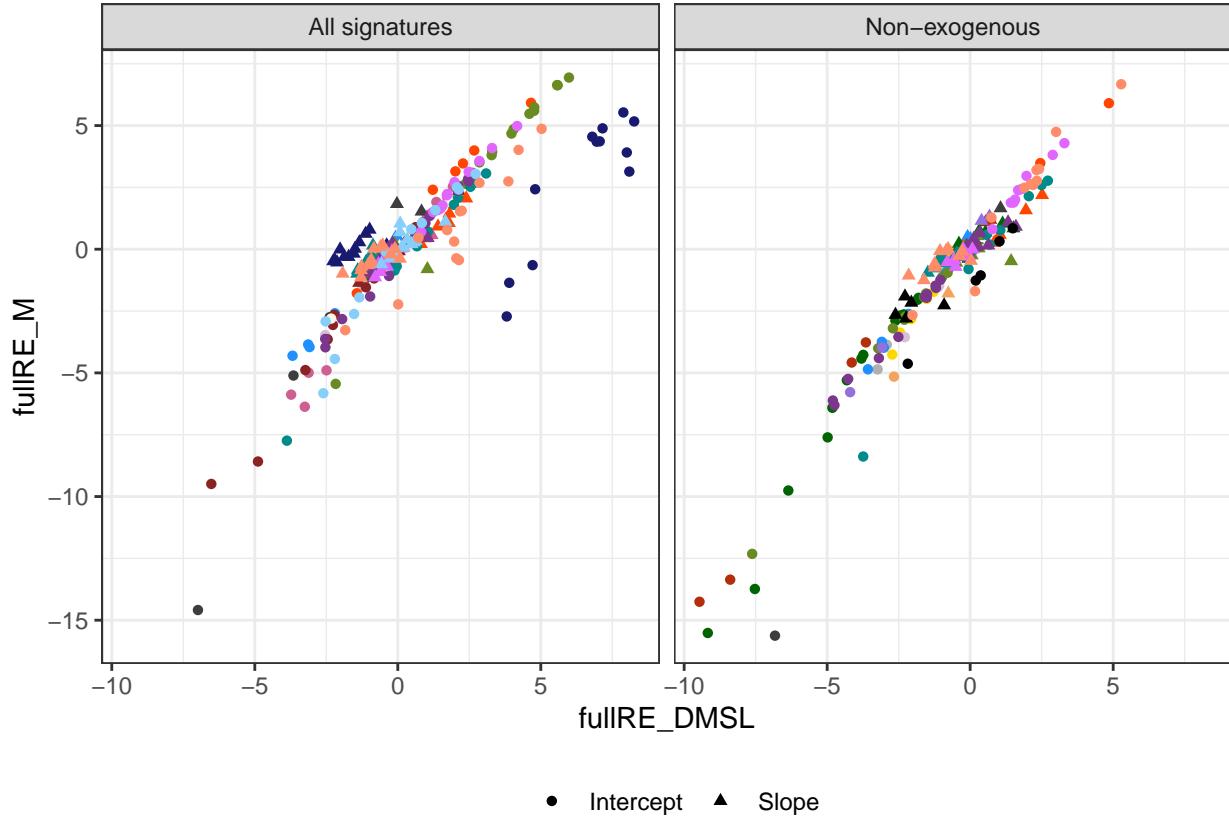
## Warning: Removed 284 rows containing missing values (geom_point).

## pdf
## 2

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 218 rows containing missing values (geom_point).

```



```
head(comparison_betas_models_rbind)
```

```
##   fullRE_DMSL diagRE_DMDL   fullRE_M beta_type      ct ct2      sigs
## 1 -0.31531015 -0.1086854 -0.2237241 Slope Bone-Osteosarc BO Non-exogenous
## 2 -0.71770886 -0.6897242 -0.6712599 Slope Bone-Osteosarc BO Non-exogenous
## 3 -0.86019179 -0.7960993 -0.6637865 Slope Bone-Osteosarc BO Non-exogenous
## 4 -0.69897610 -0.4851852 -0.4948419 Slope Bone-Osteosarc BO Non-exogenous
## 5 -0.09619079  0.1160637  0.1756435 Slope Bone-Osteosarc BO Non-exogenous
## 6 -0.64276669 -0.4495100 -0.1553669 Slope Bone-Osteosarc BO Non-exogenous

comparison_betas_models_rbind_stats_per_ct <- rbind.data.frame(
  cbind.data.frame(comparison_betas_models_rbind %>% filter(beta_type == 'Slope') %>%
    group_by(ct) %>%
    summarise(rmse_diag_full_DMDL=sqrt(mean( (diagRE_DMDL-fullRE_DMSL)^2, na.rm = T )),
              slope_diag_full_DMDL=as.numeric(try(coefficients(lm(y~x, data = cbind.data...
    rmse_fullDMSL_fullM=sqrt(mean( (fullRE_M-fullRE_DMSL)^2, na.rm = T )),
    slope_fullDMSL_fullM=as.numeric(try(coefficients(lm(y~x, data = cbind.data...
    beta_type='Slope')),
  cbind.data.frame(comparison_betas_models_rbind %>% filter(beta_type == 'Intercept') %>%
    group_by(ct) %>%
    summarise(rmse_diag_full_DMDL=sqrt(mean( (diagRE_DMDL-fullRE_DMSL)^2, na.rm = T )),
              slope_diag_full_DMDL=as.numeric(try(coefficients(lm(y~x, data = cbind.data...
    rmse_fullDMSL_fullM=sqrt(mean( (fullRE_M-fullRE_DMSL)^2, na.rm = T )),
    slope_fullDMSL_fullM=as.numeric(try(coefficients(lm(y~x, data = cbind.data...
    beta_type='Intercept')))
```

```

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

comparison_betas_models_rbind_stats_per_ct$ct2=renaming_pcawg[,2][match(comparison_betas_models_rbind_st

comparison_betas_models_rbind_stats_per_ct_pool_beta <- cbind.data.frame(comparison_betas_models_rbind%>%
  group_by(ct) %>%
  summarise(rmse_diag_full_DMDL=sqrt(mean( (diagRE_DMDL-fullRE_DMSL)^2, na.rm = T )),
            slope_diag_full_DMDL=as.numeric(try(coefficients(lm(y~x, data = cbind.data
  rmse_fullDMSL_fullM=sqrt(mean( (fullRE_M-fullRE_DMSL)^2, na.rm = T )),
  slope_fullDMSL_fullM=as.numeric(try(coefficients(lm(y~x, data = cbind.data

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

## Error in lm.fit(x, y, offset = offset, singular.ok = singular.ok, ...) :
##   0 (non-NA) cases

## Warning in mask$eval_all_summarise(quo): NAs introduced by coercion

comparison_betas_models_rbind_stats_per_ct_pool_beta$ct2=renaming_pcawg[,2][match(comparison_betas_models

pcawg_palette <- pcawg.colour.palette(gsub("\\\\..*", "", comparison_betas_models_rbind_stats_per_ct$ct),
                                         scheme = "tumour_subtype")
names(pcawg_palette) <- comparison_betas_models_rbind_stats_per_ct$ct

```

```

ggplot(comparison_betas_models_rbind, aes(x=as.numeric(fullRE_DMSL), y=as.numeric(fullRE_M), col=ct))+  

  geom_abline(slope = 1, intercept = 0, lty='dashed')+theme_bw()+
  geom_point()+theme_bw()+
  facet_wrap(~beta_type)+
  labs(x='Beta values for fullRE DMSL', y='Beta values for fullRE M')+
  geom_smooth(aes(group=ct2), method = "lm")+
  theme(legend.title=element_blank(),
        strip.text.x = element_text(size = 10),
        legend.text=element_text(size=10), legend.position = "bottom")+guides(col=FALSE)+  

  scale_color_manual(values = pcawg_palette)

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## `geom_smooth()` using formula 'y ~ x'

## Warning: Removed 284 rows containing non-finite values (stat_smooth).

## Warning in qt((1 - level)/2, df): NaNs produced

## Warning in qt((1 - level)/2, df): NaNs produced

## Warning in qt((1 - level)/2, df): NaNs produced

## Warning in qt((1 - level)/2, df): NaNs produced

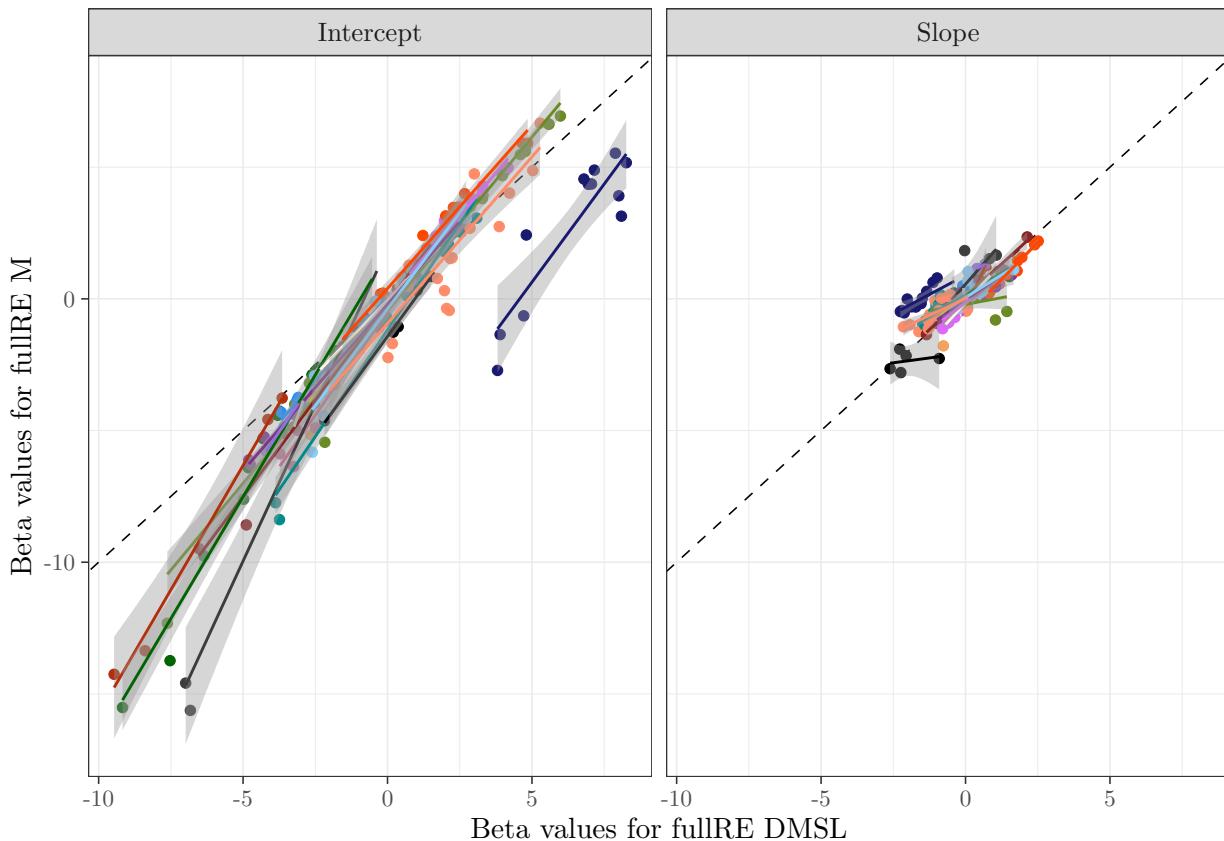
## Warning: Removed 284 rows containing missing values (geom_point).

## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf

## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf

## Warning in max(ids, na.rm = TRUE): no non-missing arguments to max; returning
## -Inf

```



```
# ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
#                                         y=slope_fullDMSL_fullM, col=ct, label=ct2))+ 
#   geom_point()+geom_label_repel()+theme_bw()+
#   labs(x='RMSE of betas between\nfullDMSL and fullM',
#        y = 'Slope of linear model of betas\n(fullDMSL ~ fullM)')

# ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
#                                         y=slope_fullDMSL_fullM, col=ct, label=ct))+ 
#   geom_point()+geom_label_repel()+theme_bw()+
#   facet_wrap(~beta_type)+theme(strip.text.x = element_text(size = 10))

# head(comparison_betas_models_rbind_stats_per_ct)

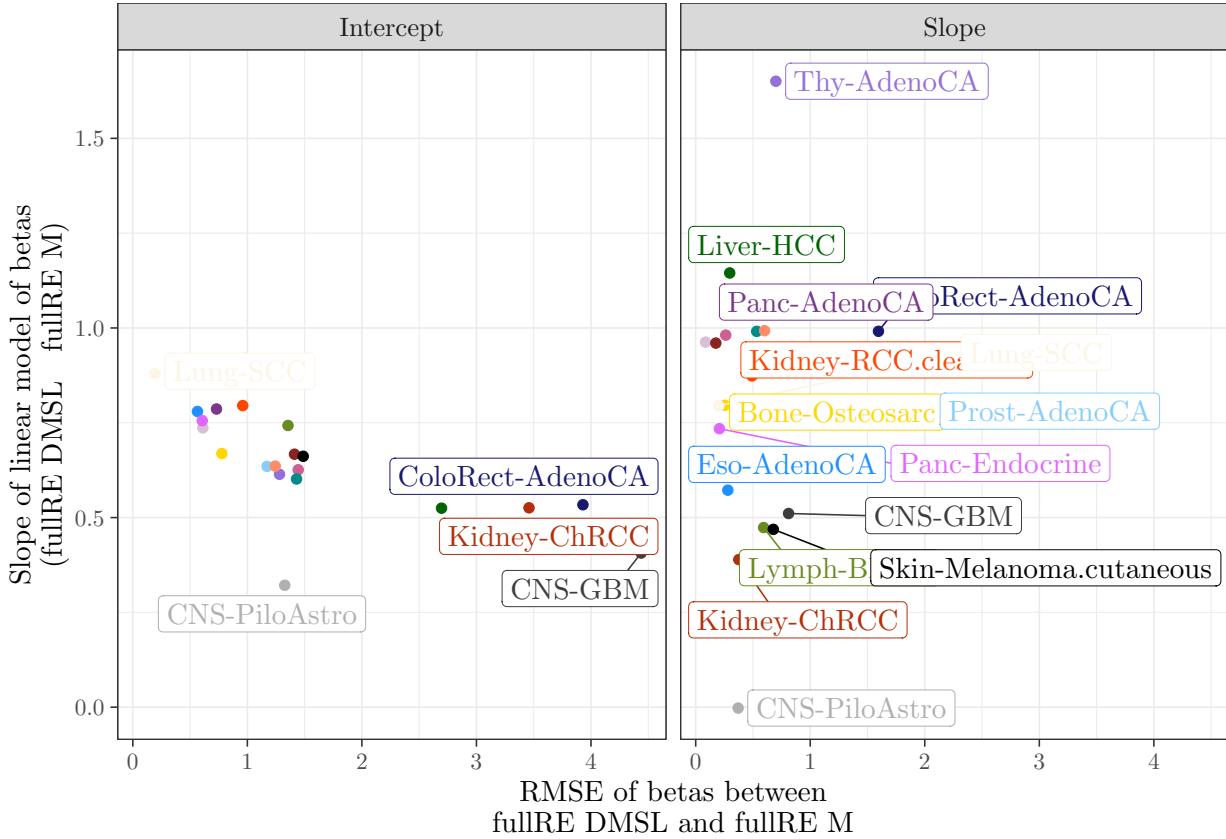
ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
#                                         y=slope_fullDMSL_fullM, col=ct, label=ct))+ 
  geom_point()+geom_label_repel()+theme_bw()+
  labs(x='RMSE of betas between\nfullRE DMSL and fullRE M',
       y = 'Slope of linear model of betas\n(fullRE DMSL ~ fullRE M)')+
  facet_wrap(~beta_type)+theme(strip.text.x = element_text(size = 10))+ 
  scale_color_manual(values = pcawg_palette)

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```

```

## Warning: Removed 6 rows containing missing values (geom_point).
## Warning: Removed 6 rows containing missing values (geom_label_repel).
## Warning: ggrepel: 15 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps
## Warning: ggrepel: 5 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



```

tikz( 'summary_TMB_PCAWG_SP_files/figure-latex/beta_coef_differences_in_models_plots_tikz2.tex',
      height = 2.5, width=5.5)
cowplot::plot_grid(ggplot(comparison_betas_models_rbind_cut, aes(x=fullRE_DMSL, y=fullRE_M, col=ct, shape=F)) +
  geom_abline(slope = 1, intercept = 0, lty='dashed')+
  geom_point() + theme_bw() + facet_wrap(~.sig)+ 
  scale_color_manual(values = pcawg_palette)+guides(col=F, shape=F)+ 
  labs(shape='', x='fullRE DMSL', y='fullRE M'),#+theme.legend.position = "bottom"),
ggplot(comparison_betas_models_rbind_cut, aes(x=fullRE_DMSL, y=diagRE_DMDL, col=ct, shape=beta_type))+ 
  geom_abline(slope = 1, intercept = 0, lty='dashed')+
  geom_point() + theme_bw() + facet_wrap(~.sig)+ 
  scale_color_manual(values = pcawg_palette)+guides(col=F, shape=F)+ 
  labs(shape='', x='fullRE DMSL', y='diagRE DMDL'), rel_widths = c(1, 1), ncol = 2)

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =

```

```

## "none")` instead.

## Warning: Removed 218 rows containing missing values (geom_point).

## Warning: Removed 218 rows containing missing values (geom_point).

dev.off()

## tikz output
##           2

tikz( 'summary_TMB_PCAWG_SP_files/figure-latex/beta_coef_differences_in_models_plots_tikz3.tex',
      height = 2.5, width=5.5)
  ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,
                                                          y=slope_fullDMSL_fullM, col=ct, label=ct))+
    geom_point() + geom_label_repel() + theme_bw() + labs(x='RMSE of betas between\nnfullRE DMSL and fullRE M',
                                                          y = 'Slope of linear model of betas\nn(fullRE DMSL ~ fullRE M)') +
    facet_wrap(.~beta_type) + theme(strip.text.x = element_text(size = 10)) +
    scale_color_manual(values = pcawg_palette) #+theme(legend.position = "bottom")

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 6 rows containing missing values (geom_point).

## Warning: Removed 6 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 18 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

## Warning: ggrepel: 17 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

dev.off()

## tikz output
##           2

head(comparison_betas_models_rbind_stats_per_ct)

##          ct rmse_diag_full_DMDL slope_diag_full_DMDL rmse_fullDMSL_fullM
## 1  Bone-Osteosarc      0.18479169      0.85364222      0.25351523
## 2  Breast-AdenoCA     0.10332852      0.91205139      0.26250850
## 3       CNS-GBM        0.28542654      1.01099718      0.81084551
## 4       CNS-Medullo    0.09067728      0.94821655      0.08629327
## 5  CNS-PiloAstro      0.32907695     -0.00807609      0.37025033
## 6 ColoRect-AdenoCA    0.24657998      0.95097590      1.59564225
##   slope_fullDMSL_fullM beta_type ct2
## 1          0.796157804 Slope BO
## 2          0.981125224 Slope BA
## 3          0.510734188 Slope GBM
## 4          0.962647186 Slope Me
## 5         -0.002269125 Slope Pi
## 6          0.991218105 Slope CR

tikz( 'summary_TMB_PCAWG_SP_files/figure-latex/beta_coef_differences_in_models_plots_tikz3b.tex',
      height = 2.5, width=5.5)
  ggplot(comparison_betas_models_rbind_stats_per_ct, aes(x=rmse_fullDMSL_fullM,

```

```

geom_point() + geom_label_repel(size=3) + theme_bw() +
  # labs(x='RMSE of betas between\nfullRE DMSL and fullRE M',
  #                               y = 'Slope of linear model of betas\n(fullRE DMSL ~ j'
  guides(col=F) +
  labs(x='rmse fullDMSL fullM', y='rmse diag full DMDL') +
  facet_wrap(~beta_type, scales="free") + theme(strip.text.x = element_text(size = 10)) +
  scale_color_manual(values = pcawg_palette) #+ theme(legend.position = "bottom")

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 4 rows containing missing values (geom_point).

## Warning: Removed 4 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 16 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

## Warning: ggrepel: 13 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

dev.off()

## tikz output
##      2

## `summarise()` has grouped output by 'ct'. You can override using the `groups` argument.
## `summarise()` has grouped output by 'ct'. You can override using the `groups` argument.

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## pdf
##      2

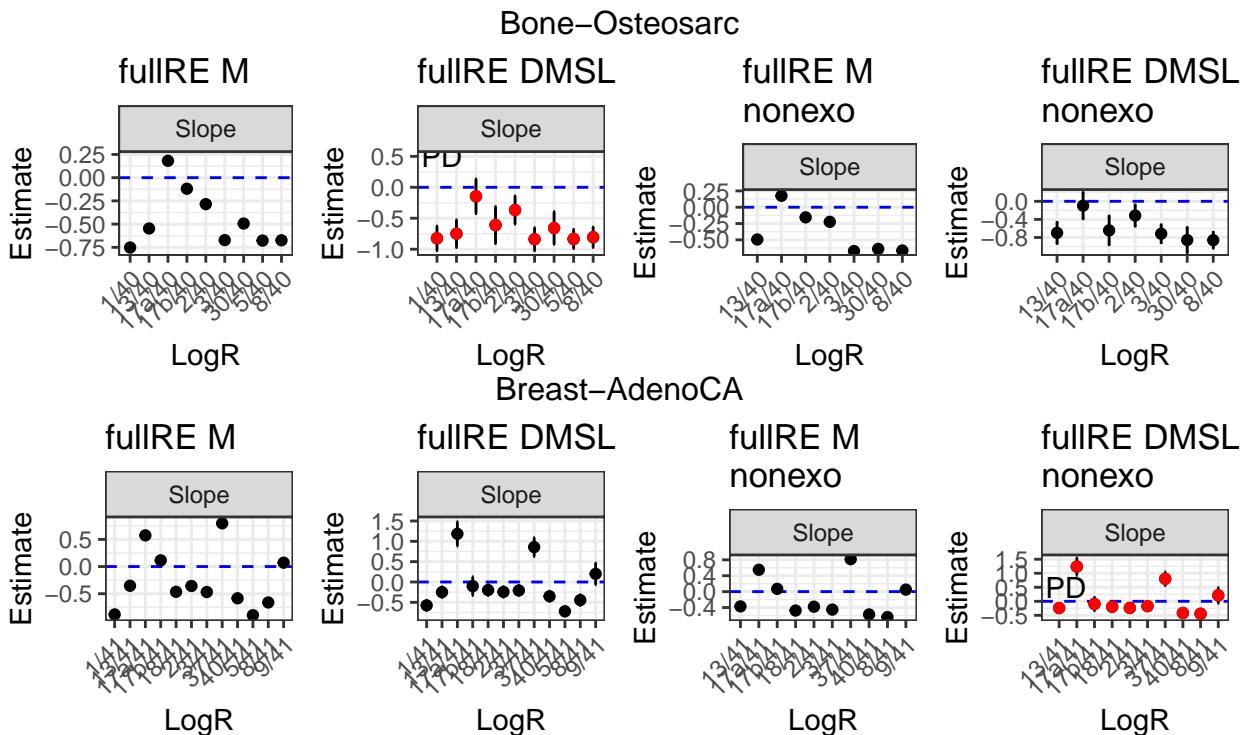
```

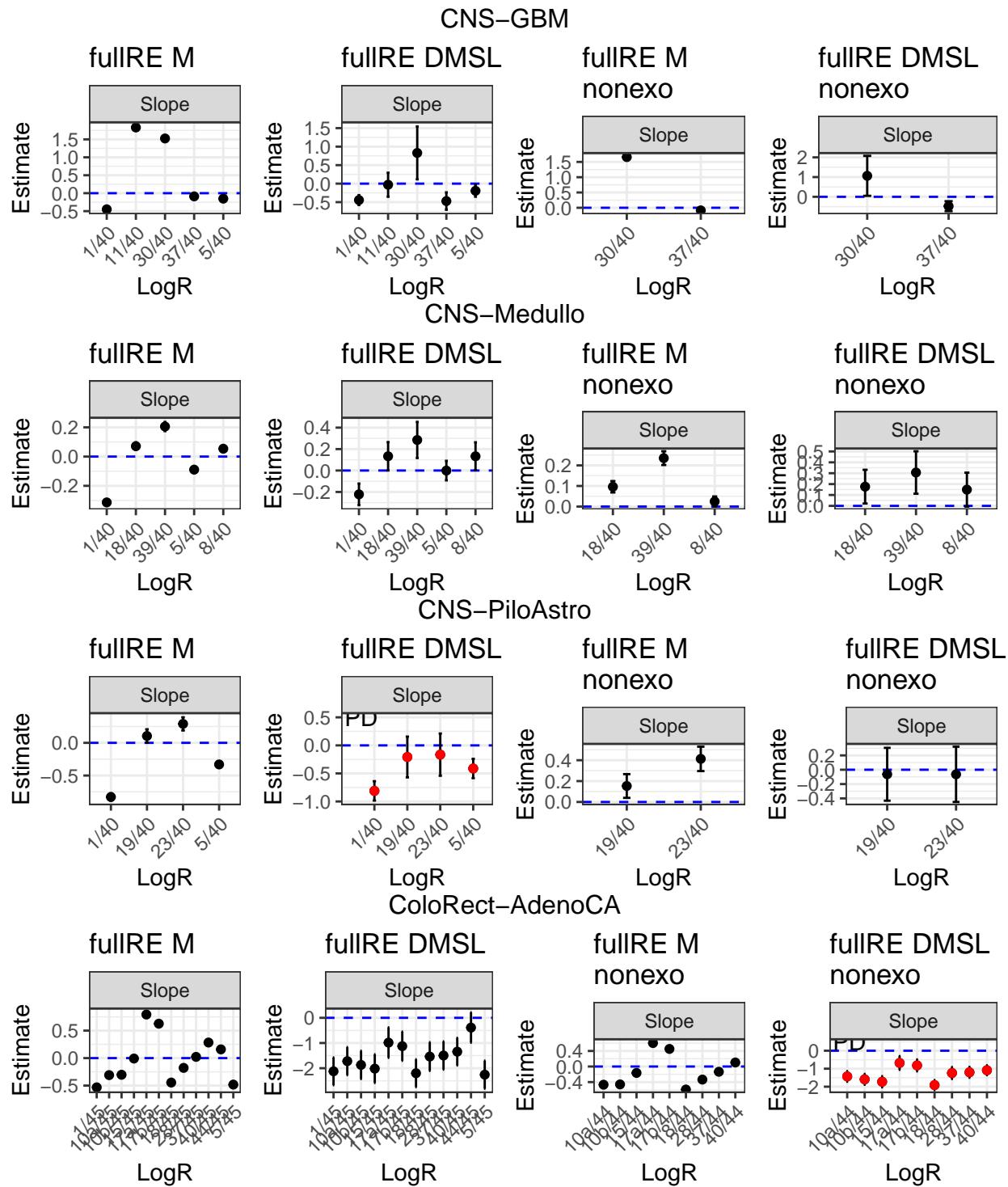
differences between signatures from sigprofiler from the paper, and the ones I get

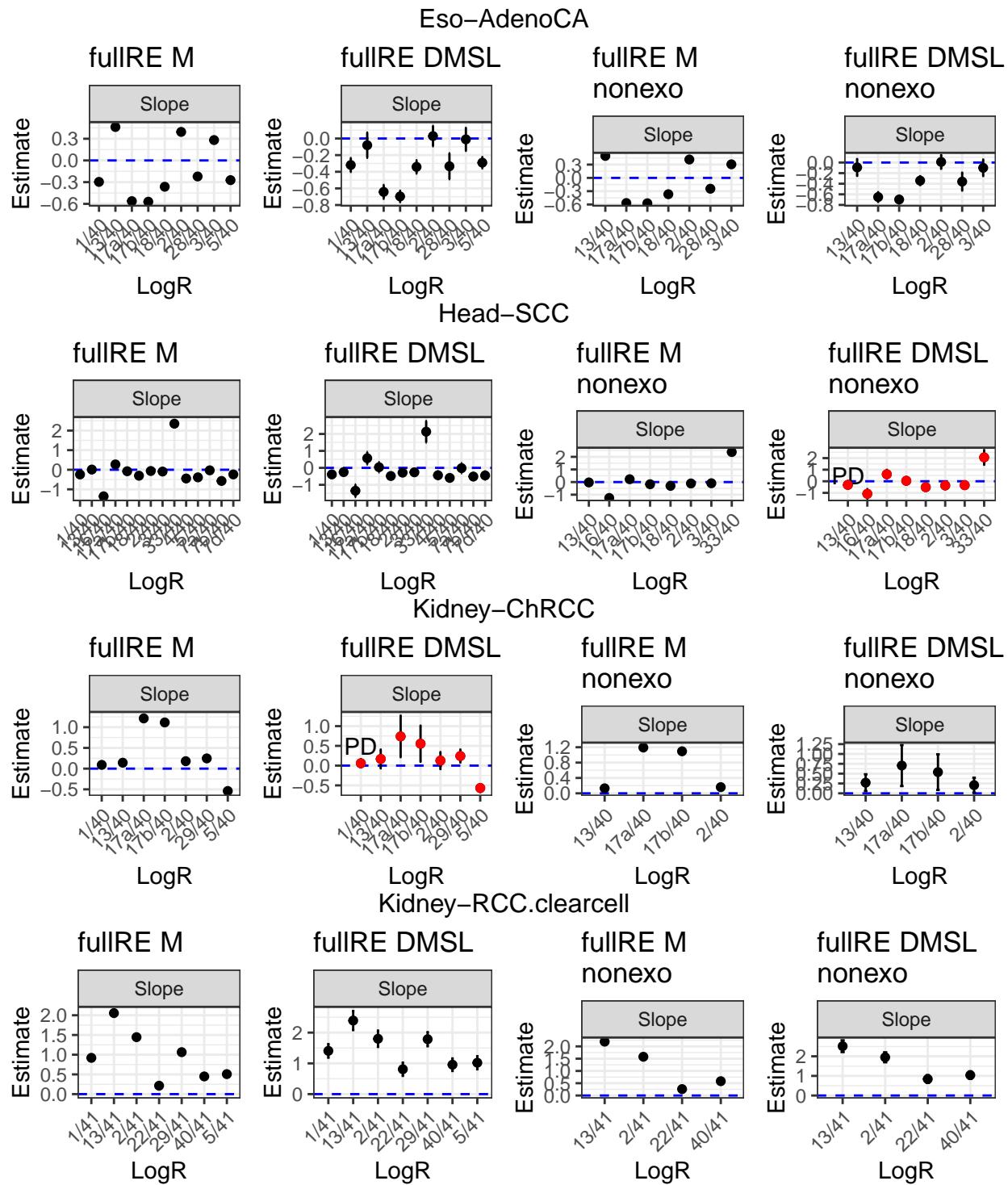
- biliary adenoca similar, though not exact
- bladder tcc: very similar
- bone benign: similar
- bone epith: extremely similar
- bone osteosarc: I have a lot of SBS8, which they don't. Other than that, similar
- breast adenicaL I have a lot of SBS9, which they don't. Other than that, similar
- breast DCIS: I have more SBS40 than they do
- breast lobularca: very similar
- cervix adenoca: very similar
- cervix SCC: very similar, although I have more SBS40
- CNS GBM: very similar, mine seem to be more homogeneous
- CNS medullo: very similar, mine seem to be more homogeneous
- CNS oligo: very similar, mine seem to be more homogeneous
- CNS piloastro: very similar, mine seem to be more homogeneous
- Colorect adenoca: quite similar
- eso adenoca: very similar
- head scc: very similar, mine seem to be more homogeneous
- kidney chrc: very similar

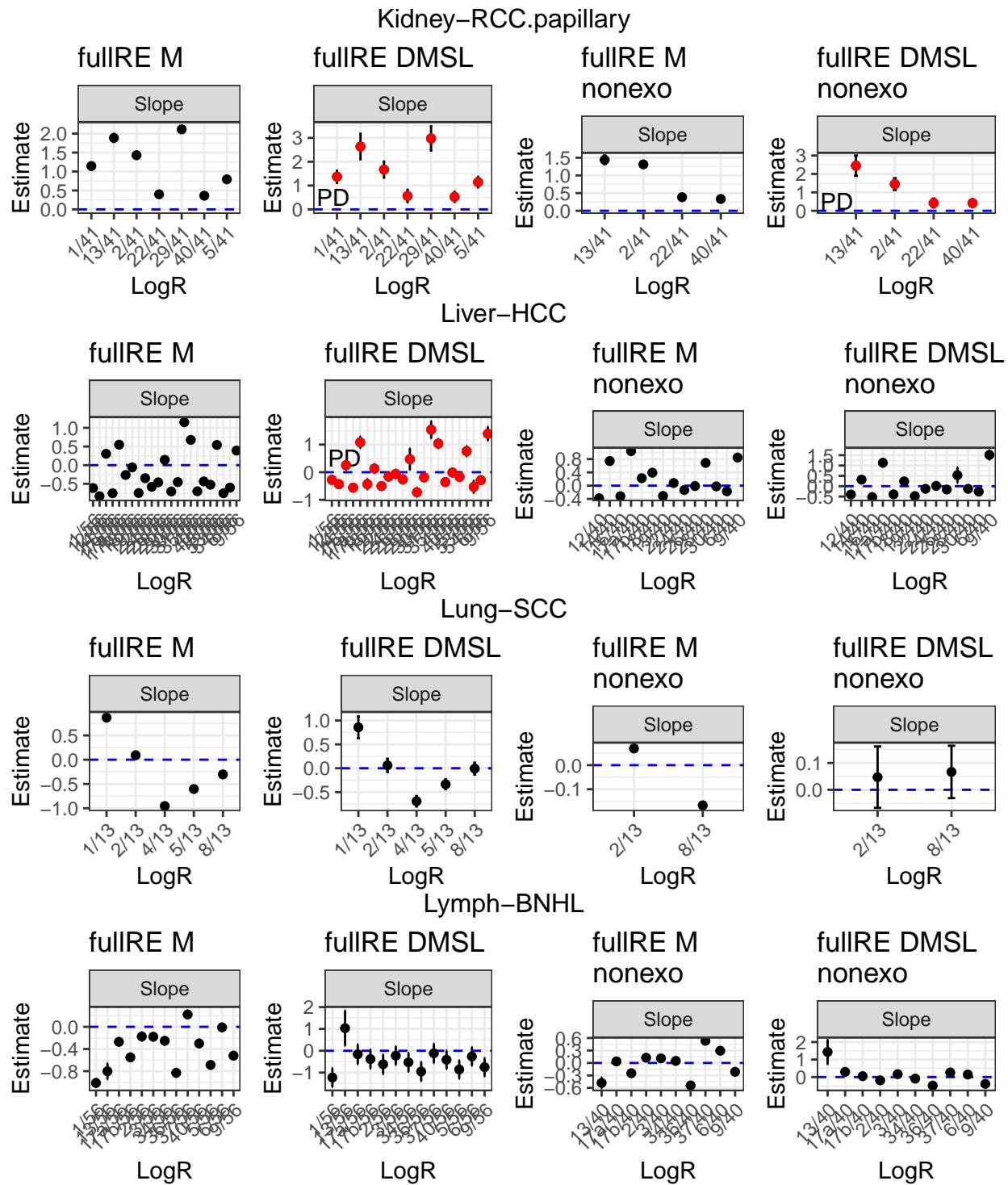
- kidney rcc.clearcell: very similar, although I have more SBS29
- kidney papillary: only I have it
- liver hcc: different. I have a lot of SBS40 and SBS12, they have mostly SBS5 ***
- lung adenoca: very similar
- lung SCC: very similar, though I have more SBS8
- lymph BNHL: very similar
- Lymph CLL: very similar, althpugh theirs are much more sparse
- myeloid AML: very similar, although I don't have any SBS60 and they seem to have
- myeloid MDS: I don't have it
- myeloid MPN: similar, although mine is much more sparse
- ovary adenoca: different. I have a lot of SBS40, which in their case is rare, and they have much more of SBS3 than I do ***
- panc-adenoca: different. I have a lot of SBS8 that they don't have. ***
- panc-endocrine: sort of similar. I have more SBS8 than they and they have more SBS5
- Prost-adenoca: sort of similar, I have more SBS8
- skin-melanoma.acral: they don't have this category. They have "skin-melanoma", which might be both together? (!!!) Similar exposures...
- softtissue-leiomyo: very similar exposures
- softtissue-liposarc: very similar exposures
- stomach adenoca: very similar, mine seem to be more homogeneous
- thy-adenoca: very similar
- uterus-adenoca: very similar

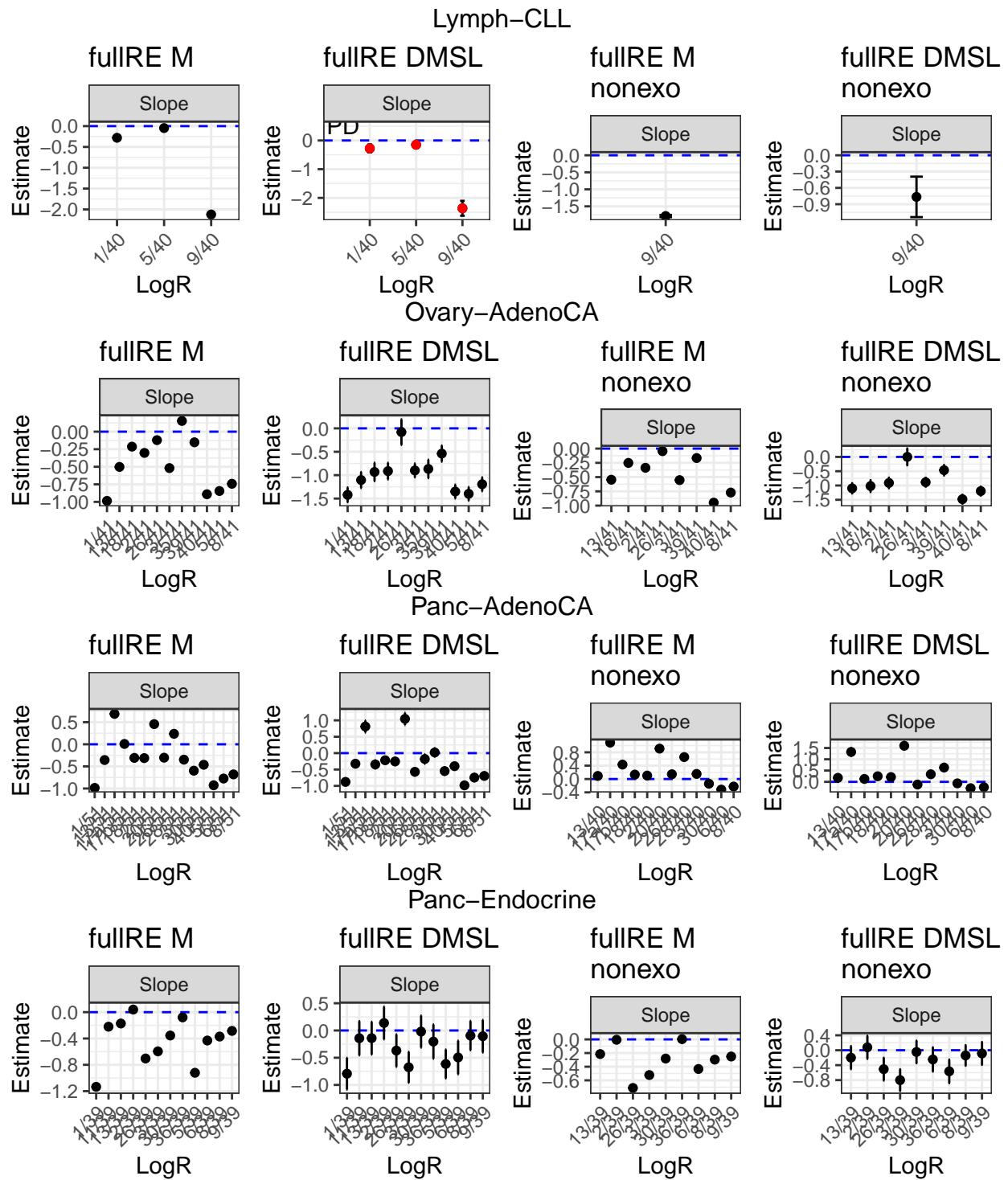
Betas from PCAWG subset of signatures



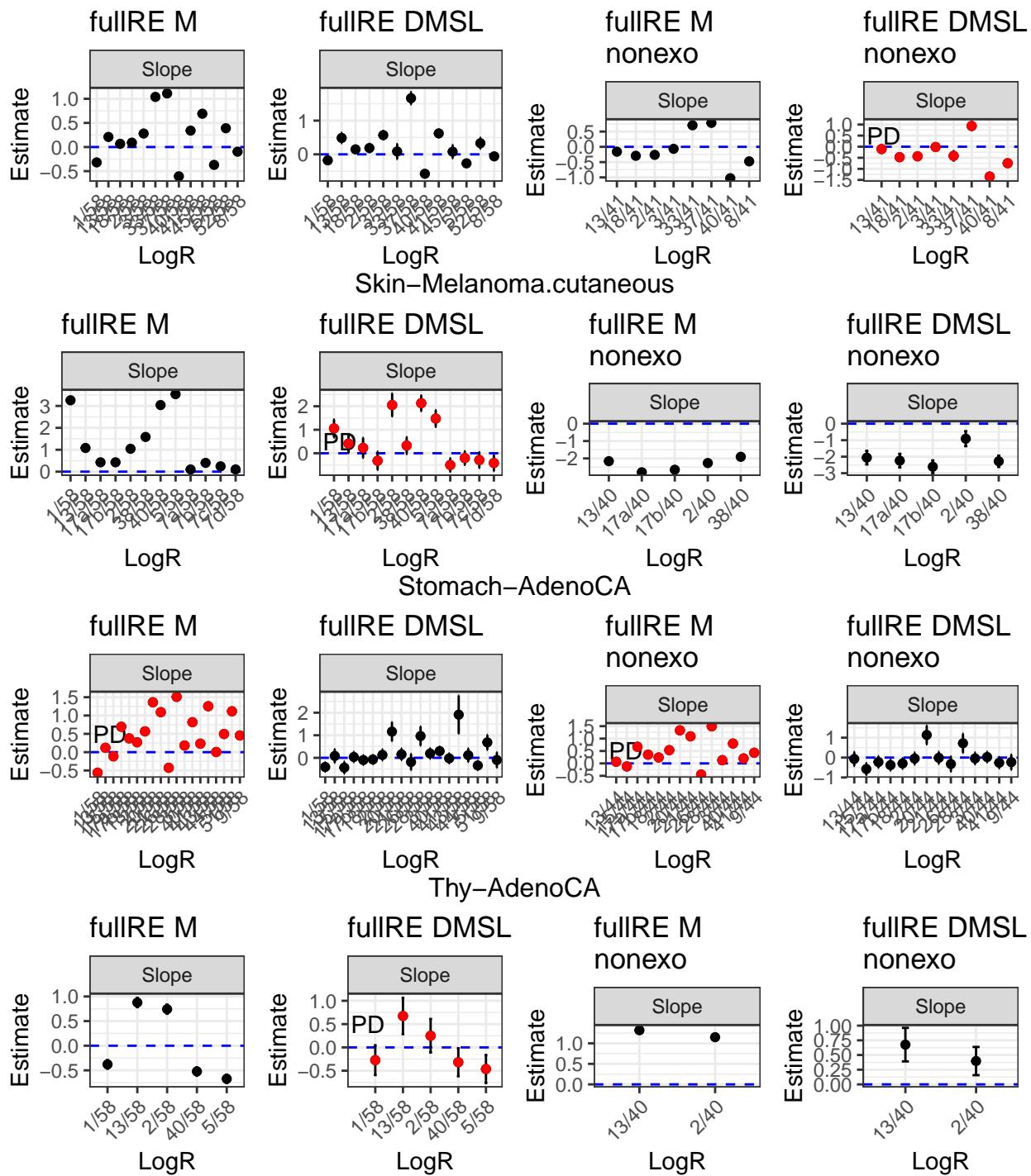


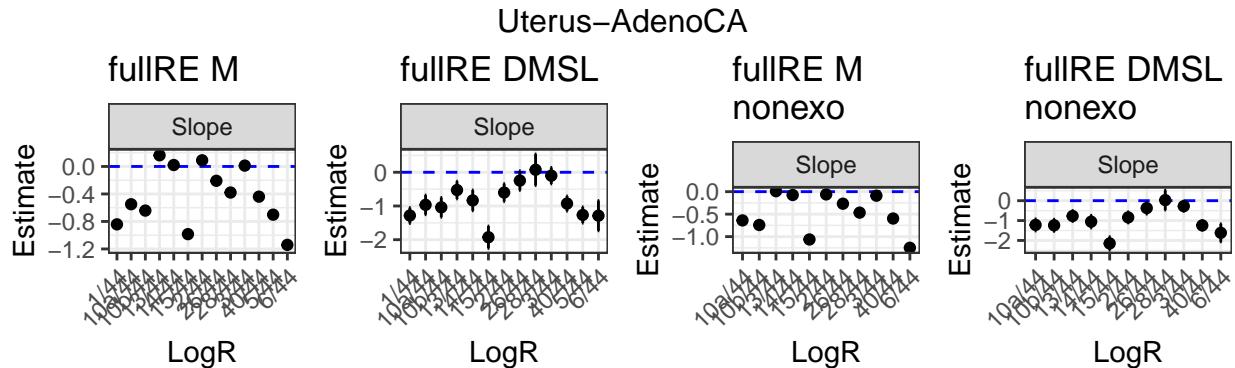






Prost–AdenoCA





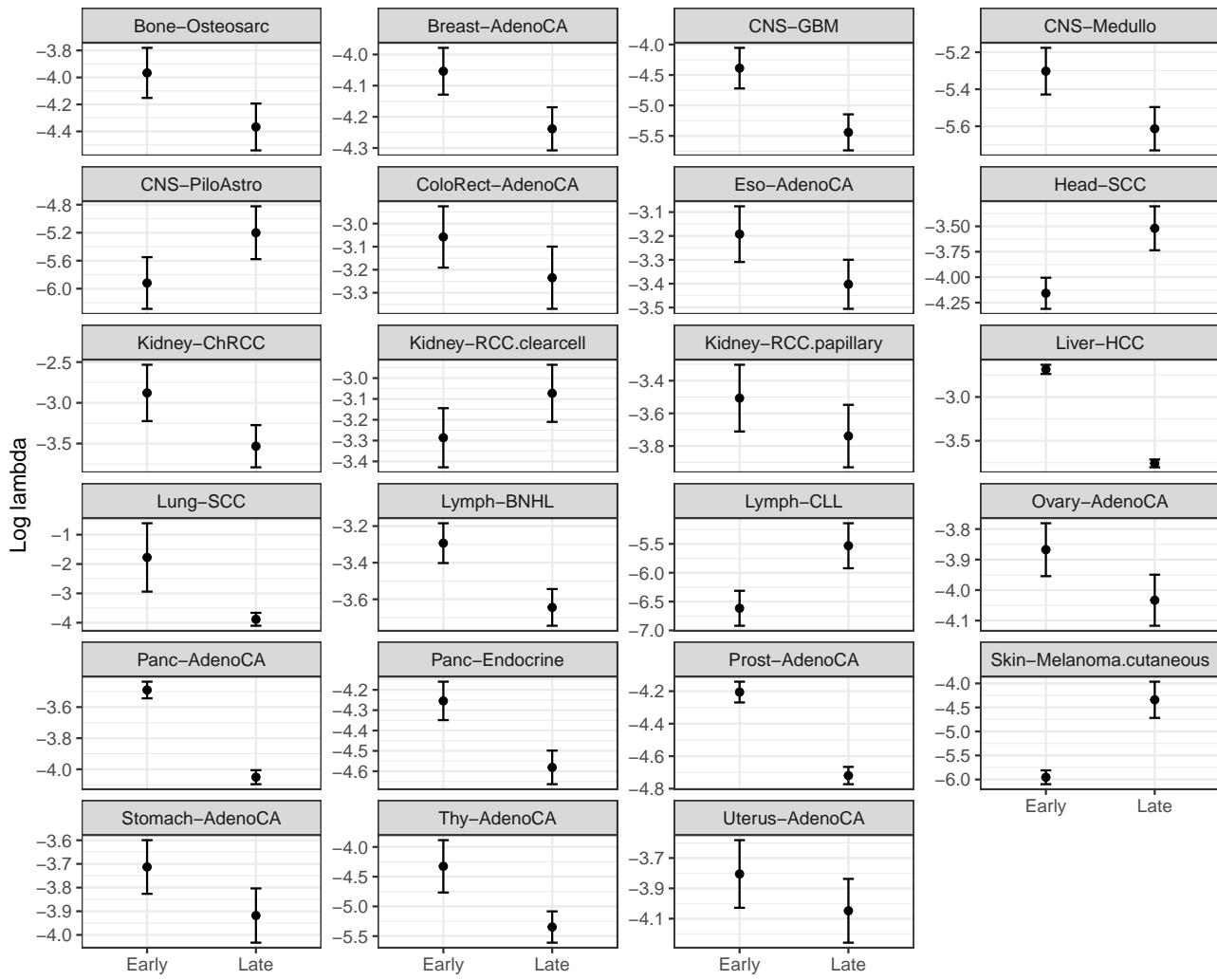
Overdispersion parameters in double-lambda DM

```

ovrdisp <- do.call('rbind.data.frame', lapply(1:length(diagRE_DMDL_nonexo_SP), try(function(idx){
  if(diagRE_DMDL_nonexo_SP[[idx]]$pdHess){
    cbind.data.frame( plot_lambdas(diagRE_DMDL_nonexo_SP[[idx]], return_df=T, plot=F), ct=names(diagRE_DMDL_nonexo_SP))
  } else{
    c(NA, NA)
  }
})))
ovrdisp[ovrdisp$name == 'Lambda 1', 'name'] = 'Early'
ovrdisp[ovrdisp$name == 'Lambda 2', 'name'] = 'Late'

ggplot(ovrdisp, aes(x=name, y=Estimate))+
  geom_point()+
  geom_errorbar(aes(ymin=Estimate-Std..Error,
                     ymax=Estimate+Std..Error), width=.1)+
  theme_bw()+
  facet_wrap(~ct, scales = "free_y", nrow=6)+
  labs(x=' ', y='Log lambda')

```



Test for differential precision (1/overdispersion) parameter

```
differential_precision <- p.adjust(sapply(diagRE_DMDL_nonexo_SP, wald_TMB_wrapper_overdisp), method = 'fdr')
names(differential_precision) <- names(diagRE_DMDL_nonexo_SP)
sort(differential_precision)
```

##	Liver-HCC	Panc-AdenoCA	Skin-Melanoma.cutaneous
##	5.160159e-58	7.096293e-18	9.923539e-09
##	Prost-AdenoCA	Lung-SCC	Head-SCC
##	1.219769e-07	1.139987e-05	8.968677e-02
##	Panc-Endocrine	CNS-GBM	Lymph-CLL
##	8.968677e-02	1.094428e-01	1.257732e-01
##	Thy-AdenoCA	Lymph-BNHL	CNS-Medullo
##	1.332616e-01	1.707526e-01	2.670091e-01
##	Breast-AdenoCA	Kidney-ChRCC	CNS-PiloAstro
##	3.645074e-01	3.883654e-01	4.524310e-01
##	Stomach-AdenoCA	Uterus-AdenoCA	Bone-Osteosarc
##	4.524310e-01	4.524310e-01	4.745719e-01
##	Eso-AdenoCA	Ovary-AdenoCA	Kidney-RCC.clearcell
##	4.815932e-01	4.979627e-01	5.431631e-01

```

##          ColoRect-AdenoCA      Kidney-RCC.papillary
##          6.589716e-01      6.806308e-01


```

Liver-HCC Lung-SCC Panc-AdenoCA
5.160159e-58 1.139987e-05 7.096293e-18
Prost-AdenoCA Skin-Melanoma.cutaneous
1.219769e-07 9.923539e-09
```



```

ovrdisp$differentially_abundant = ifelse(ovrdisp$ct %in% names(differential_precision[(differential_precision <= 0.05)]), differential_precision[(differential_precision <= 0.05)], 0)
ovrdisp$differentially_abundant
```



```

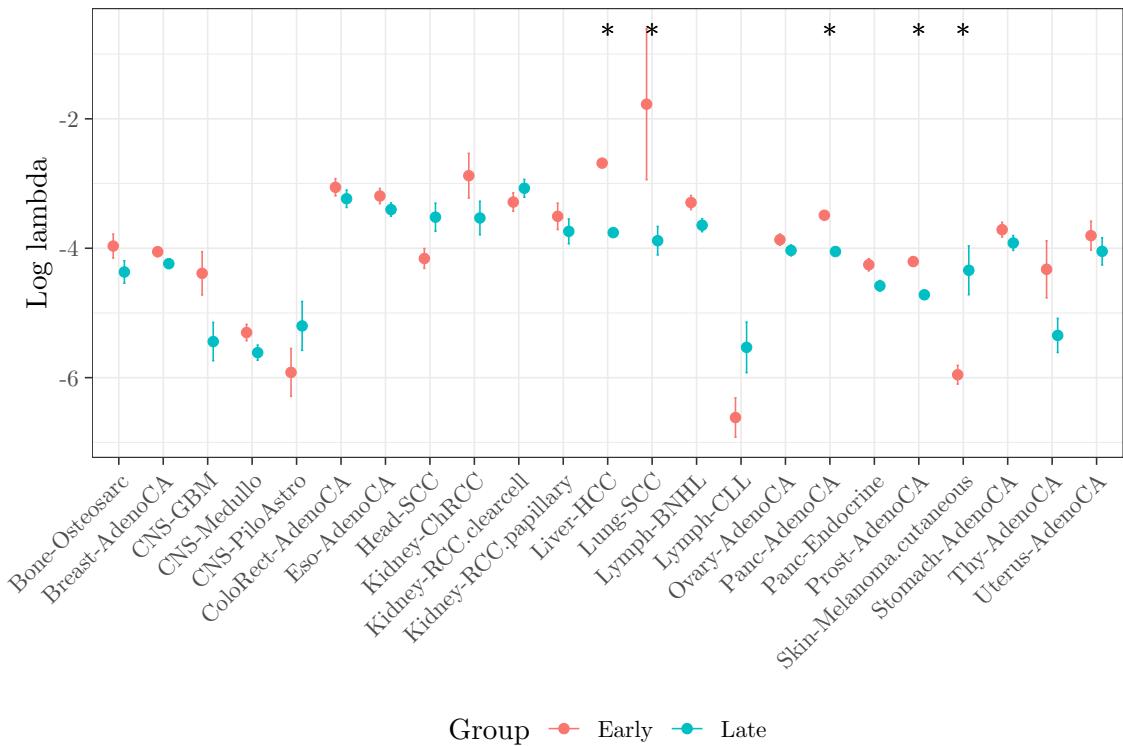
[1] ""
[20] "*"
[39] "*"
```



```

ggplot(ovrdisp, aes(x=ct, y=Estimate, group=name, col=name))+
 geom_point(position=position_dodge(width=0.5))+
 geom_errorbar(aes(ymin=Estimate-Std..Error,
 ymax=Estimate+Std..Error), width=.1, position=position_dodge(width=0.5))+
 theme_bw()+
 geom_text(aes(y=Inf, label=differentially_abundant, vjust=1.8), col='black')+
 theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+
 labs(x='', y='Log lambda', col='Group')+theme(legend.position = "bottom")+
 theme(
 legend.margin=margin(0,0,0,0),
 legend.box.margin=margin(-10,-10,-10,-10),
 plot.margin = unit(c(1,1,1,1), "cm"))
```


```



Group —●— Early —●— Late

Test for differential precision (1/overdispersion) parameter

```
differential_precision_2 <- p.adjust(sapply(diagRE_DMDL_nonexo_SP, ttest_TMB_wrapper_overdisp), method = names(differential_precision_2) <- names(diagRE_DMDL_nonexo_SP)
sort(differential_precision_2)
```

##	Liver-HCC	Panc-AdenoCA	Prost-AdenoCA
##	8.145123e-24	2.860615e-07	1.126237e-04
##	Skin-Melanoma.cutaneous	CNS-GBM	Head-SCC
##	1.723631e-02	2.834265e-01	2.834265e-01
##	Lymph-BNHL	Panc-Endocrine	Lung-SCC
##	2.834265e-01	2.834265e-01	3.053481e-01
##	Lymph-CLL	Thy-AdenoCA	Breast-AdenoCA
##	3.053481e-01	3.147768e-01	3.578140e-01
##	CNS-Medullo	Bone-Osteosarc	Kidney-ChRCC
##	3.578140e-01	4.331744e-01	4.331744e-01
##	CNS-PiloAstro	Eso-AdenoCA	Ovary-AdenoCA
##	4.352908e-01	4.352908e-01	4.352908e-01
##	Stomach-AdenoCA	Kidney-RCC.clearcell	ColoRect-AdenoCA
##	4.502790e-01	5.128995e-01	5.601231e-01
##	Kidney-RCC.papillary	Uterus-AdenoCA	
##	5.770837e-01	5.770837e-01	

```
table(differential_precision_2 <= 0.05)
```

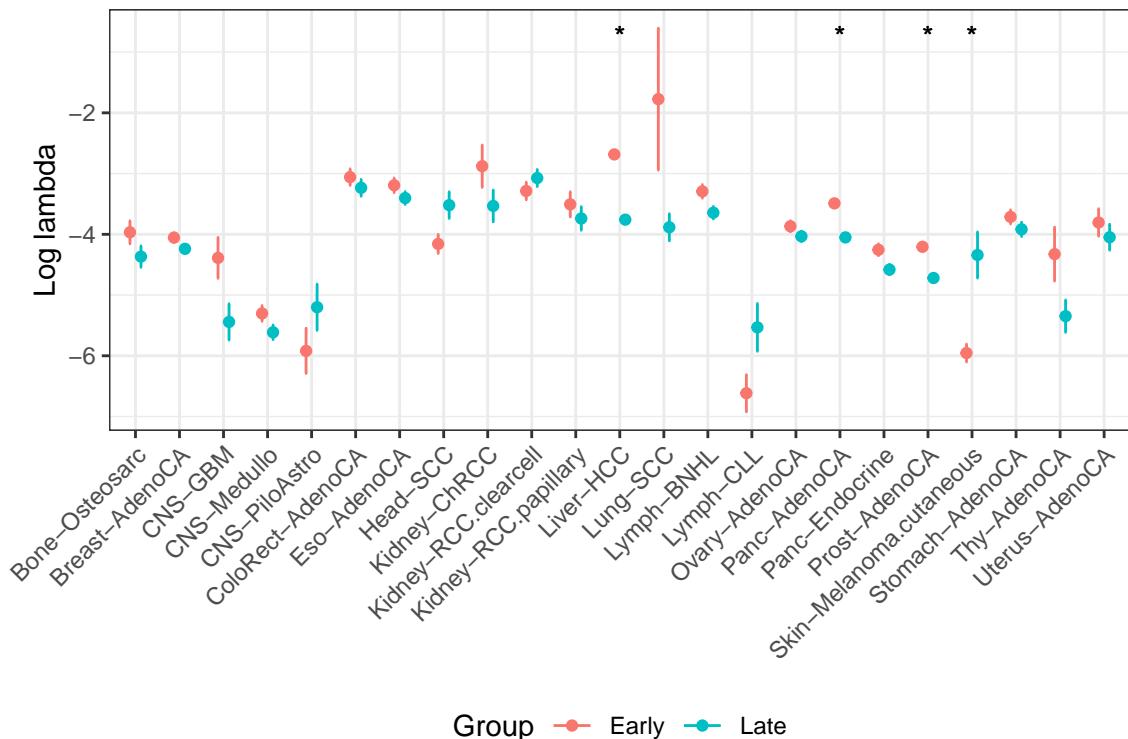
```
##  
## FALSE TRUE  
## 19 4
```

```
differential_precision_2[(differential_precision_2 <= 0.05)]
```

```
##          Liver-HCC      Panc-AdenoCA      Prost-AdenoCA
## 8.145123e-24 2.860615e-07 1.126237e-04
## Skin-Melanoma.cutaneous
## 1.723631e-02

ovrdisp$differential_precision_2 = ifelse(ovrdisp$ct %in% names(differential_precision_2)[(differential_precision_2 <= 0.05)], 1, 0)

ggplot(ovrdisp, aes(x=ct, y=Estimate, group=name, col=name))+
  geom_point(position=position_dodge(width=0.5))+
  geom_errorbar(aes(ymin=Estimate-Std..Error,
                     ymax=Estimate+Std..Error), width=.1, position=position_dodge(width=0.5))+
  theme_bw()+
  geom_text(aes(y=Inf, label=differential_precision_2, vjust=1.8), col='black')+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+
  labs(x='', y='Log lambda', col='Group')+theme(legend.position = "bottom")+
  theme(
    legend.margin=margin(0,0,0,0),
    legend.box.margin=margin(-10,-10,-10,-10),
    plot.margin = unit(c(1,1,1,1), "cm"))
```



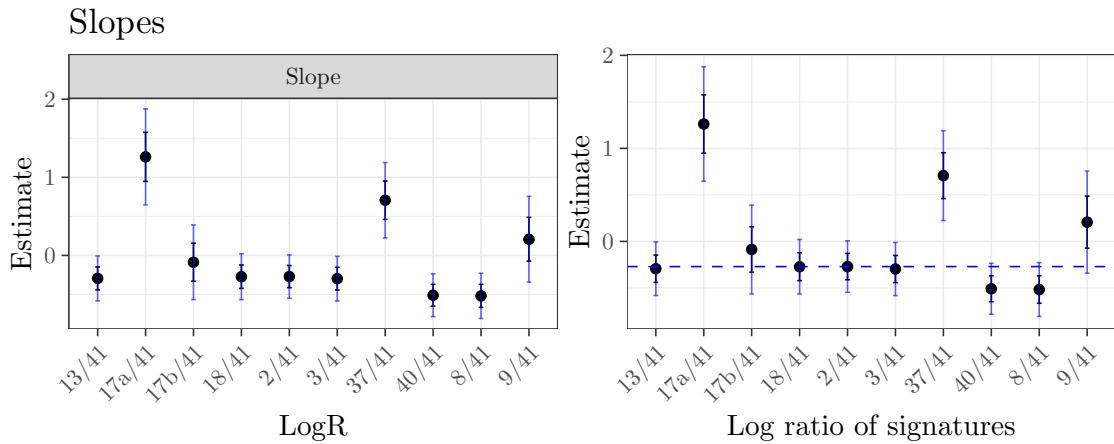
Minimal perturbation

Note: this is using the original, non SP, signatures (hence not the best version).

```
minimalpert_L2 <- function(i){
  sum(i)/sum(i^2)
}
```

```

#
# betas_breast <- data.frame(plot_betas(diagRE_DMSL_nonexo[["Breast-AdenoCA"]], names_cats= logR_nonexo_r
#                               return_df=T, plot=F))
#
# .slopes_minpert <- betas_breast %>% dplyr::filter(type_beta == "Slope") %>% dplyr::select(Estimate) %>%
# #
# # minimalpert_L2(softmax(c(.slopes_minpert, 0)))
# median(c(.slopes_minpert, 0))
#
# aa <- plot_betas(diagRE_DMSL_nonexo[["Breast-AdenoCA"]], names_cats= logR_nonexo_notsorted[["Breast-AdenoCA"]]
#                   return_df=F, plot=F, only_slope = T, line_zero=F)
# # aa <- geom_hline(yintercept = 0)+geom_vline(xintercept = 1)+geom_hline(yintercept = median(c(.slopes_minpert, 0)))
# aa + geom_hline(yintercept = median(c(.slopes_minpert, 0)), lty='dashed', col='blue')+geom_hline(yintercept = mean(c(.slopes_minpert, 0)), lty='dashed', col='red')
# 
```



For the thesis:

```

pdf("../results/results_TMB/pcawg/minimalperturbation_SP_all.pdf", width = 4, height = 3)
for(ct in names(diagRE_DMDL_nonexo_SP)){
  .betas_ct_it <- data.frame(plot_betas(TMB_obj = diagRE_DMDL_nonexo_SP[[ct]],
                                         names_cats= logR_nonexo_notsorted_SP[[ct]],
                                         return_df=T, plot=F))
  .slopes_minpert <- .betas_ct_it %>% dplyr::filter(type_beta == "Slope") %>% dplyr::select(Estimate) %>%
  print(aaa <- plot_betas(TMB_obj = diagRE_DMDL_nonexo_SP[[ct]], names_cats= logR_nonexo_notsorted_SP[[ct]],
                           return_df=F, plot=F, only_slope = T, line_zero=F, add_confint = T, return_ggplot=TRUE)
  +
  geom_hline(yintercept = median(c(.slopes_minpert, 0)), lty='dashed', col='blue')+ggtitle(ct))
}
dev.off()

## pdf
## 2

```

```

\subsection{Minimal perturbation in diagRE_DMDL_nonexo_S}

perturbed_betas_diagRE_DMDL_nonexo_SP <- lapply(names(diagRE_DMDL_nonexo_SP), try(give_min_pert))

perturbed_betas_diagRE_DMDL_nonexo_SP_vec <- do.call('c', sapply(perturbed_betas_diagRE_DMDL_nonexo_SP, f

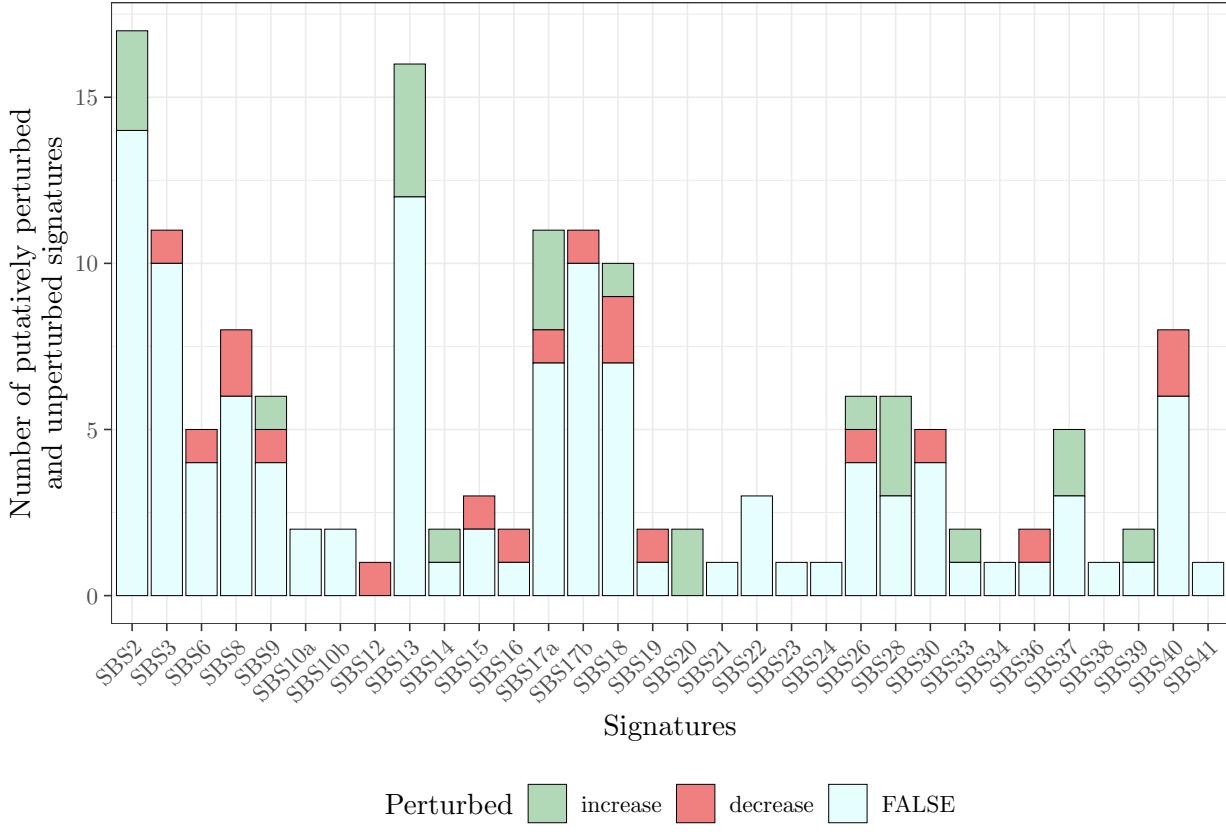
perturbed_betas_diagRE_DMDL_nonexo_SP_df <- cbind.data.frame(sig=gsub("betas_perturbed.", "", 
  names(perturbed_betas_diagRE_DMDL_nonexo_SP_vec))

```

```

perturbed=perturbed_betas_diagRE_DMDL_nonexo_SP_df
ggplot(perturbed_betas_diagRE_DMDL_nonexo_SP_df, aes(x=factor(sig, levels=gtools::mixedsort(unique(sig))), fill=factor(perturbed, levels=c('increase', 'decrease'))))
  geom_bar(col='black', size=0.001)+theme_bw()+
  scale_fill_manual(values=c( '#b1d8b7', '#f08080', '#e7feff'))+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1), legend.position = "bottom")+
  labs(x='Signatures', y='Number of putatively perturbed\nand unperturbed signatures', fill='Perturbed')

```



Minimal perturbation per signature

```

names(perturbed_betas_diagRE_DMDL_nonexo_SP) <- names(diagRE_DMDL_nonexo_SP)
ggplot(reshape2::melt(lapply(perturbed_betas_diagRE_DMDL_nonexo_SP, `[, 'betas_perturbed'])),
  aes(x=L1, fill=factor(value, levels=c('increase', 'decrease', 'FALSE'))))+geom_bar(col='black', size=0.001)+scale_fill_manual(values=c('#b1d8b7', '#f08080', '#e7feff'))+theme(legend.position = "bottom")+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+labs(x='Cancer type',
  y='Number of putatively perturbed and unperturbed signatures', fill='Perturbed')

```

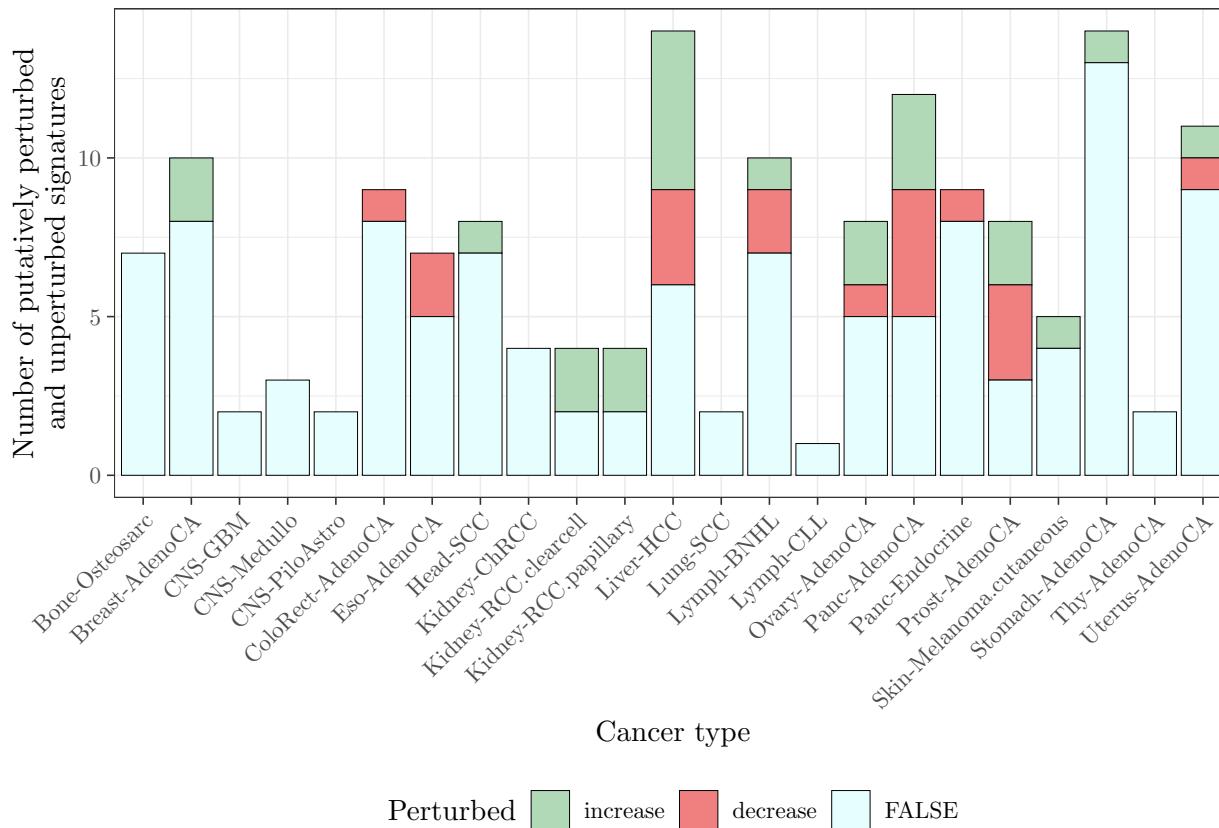


Table of perturbed signatures

```

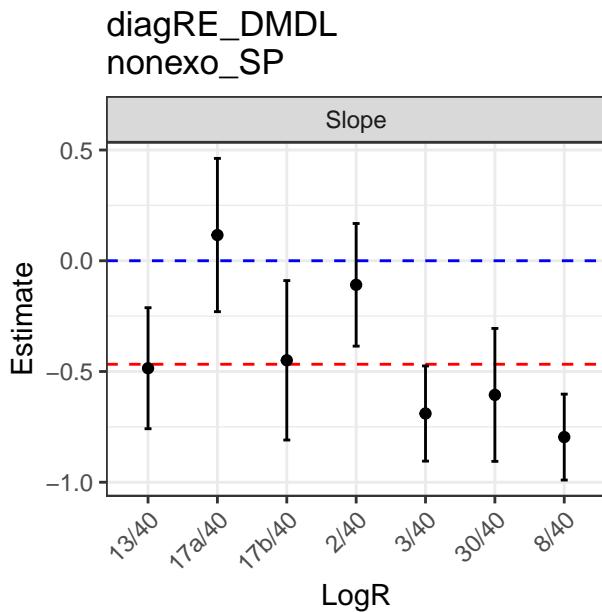
relevel_perturbation <- cbind(c('increase', 'decrease'), c('+', '-'))

write("", ".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt", append = F)
# for(i in names(perturbed_betas_diagRE_DMDL_nonexo_SP)){
#   write(paste0(i, '&', paste0(names(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed)[perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed], collapse = ", ")), file = ".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt")
# }

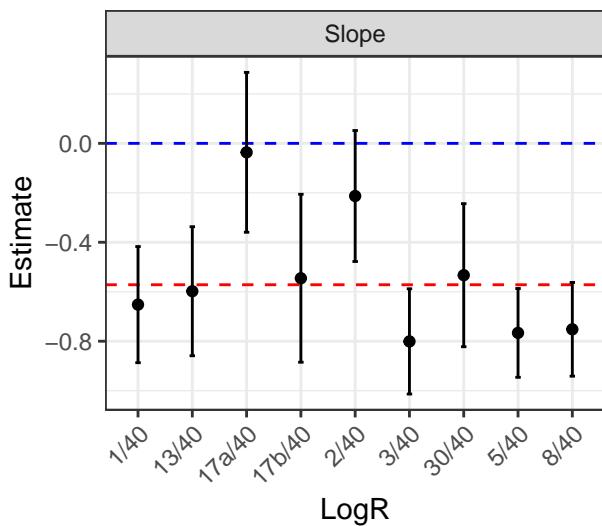
for(i in names(perturbed_betas_diagRE_DMDL_nonexo_SP)){
  # write(x = paste0(i, '&', paste0(sapply(which(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed), function(x){x}), collapse = ", ", sep = '')), file = ".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt")
  # write(x = paste0(i, '&', paste0(names(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed)[j], '(', relevel_perturbation, ')'), collapse = ', ', sep = '')), file = ".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt")
  # write(x = paste0(paste0(i, '&', paste0(sapply(which(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed), function(x){x}), collapse = ", ", sep = ''))), file = ".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt")
  # write(x = paste0(paste0(i, '&', paste0(names(perturbed_betas_diagRE_DMDL_nonexo_SP[[i]]$betas_perturbed)[j], '(', relevel_perturbation, ')')), collapse = ', ', sep = '')), file = ".../results/results_TMB/pcawg/minimal_perturbation_sigs.txt")
}

```

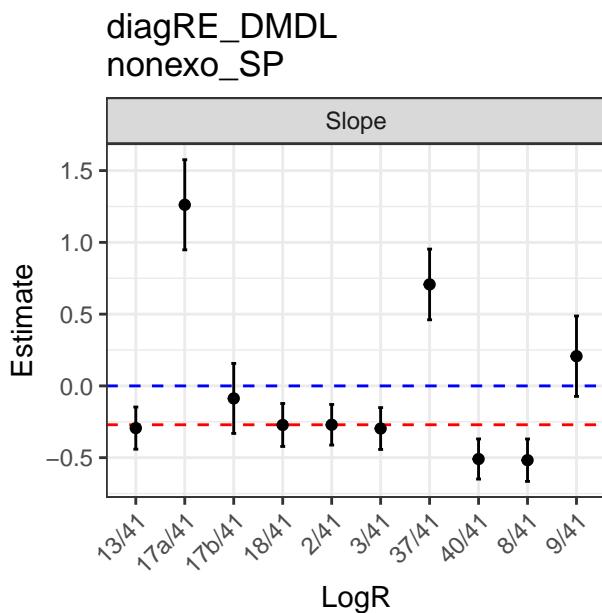
Bone–Osteosarc



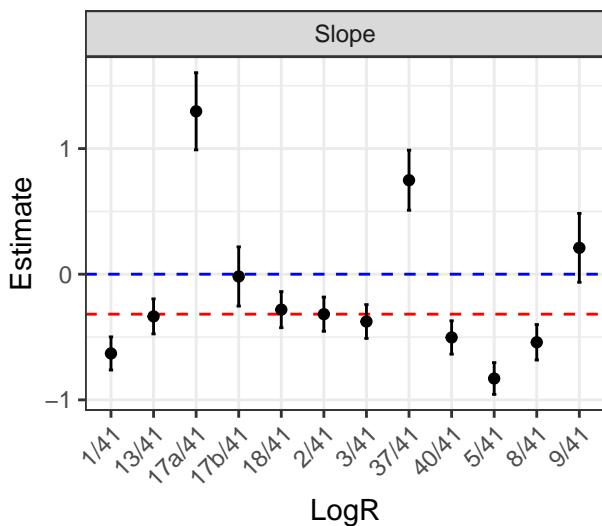
**diagRE_DMDL
nonexowSBS1SBS5_SP**



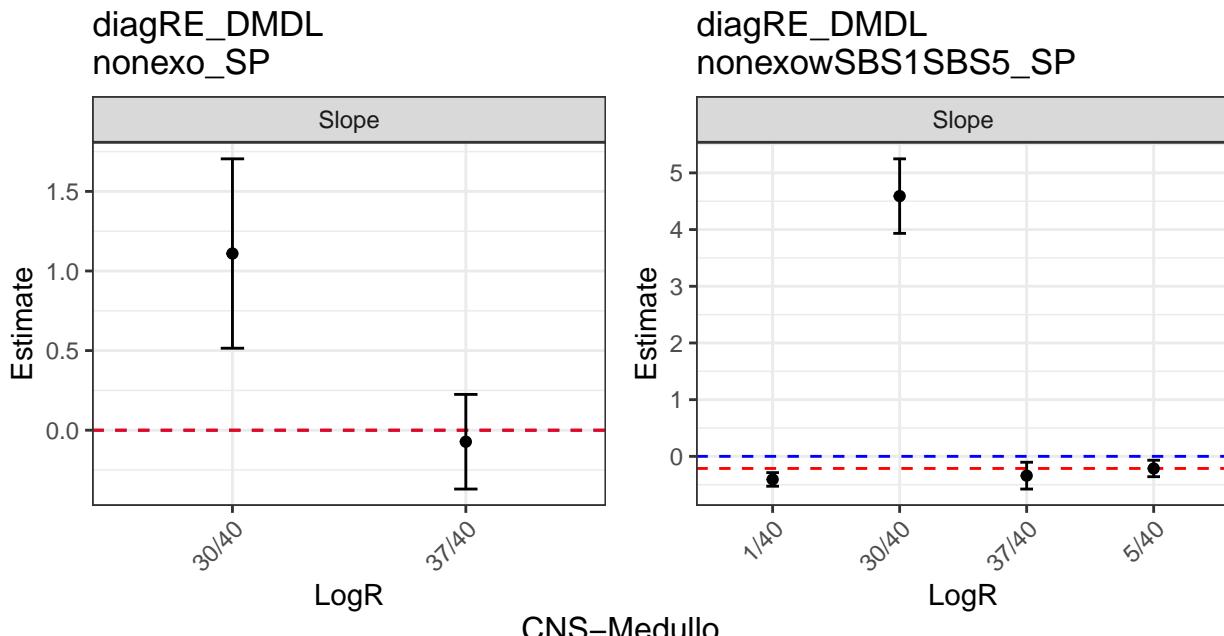
Breast–AdenoCA



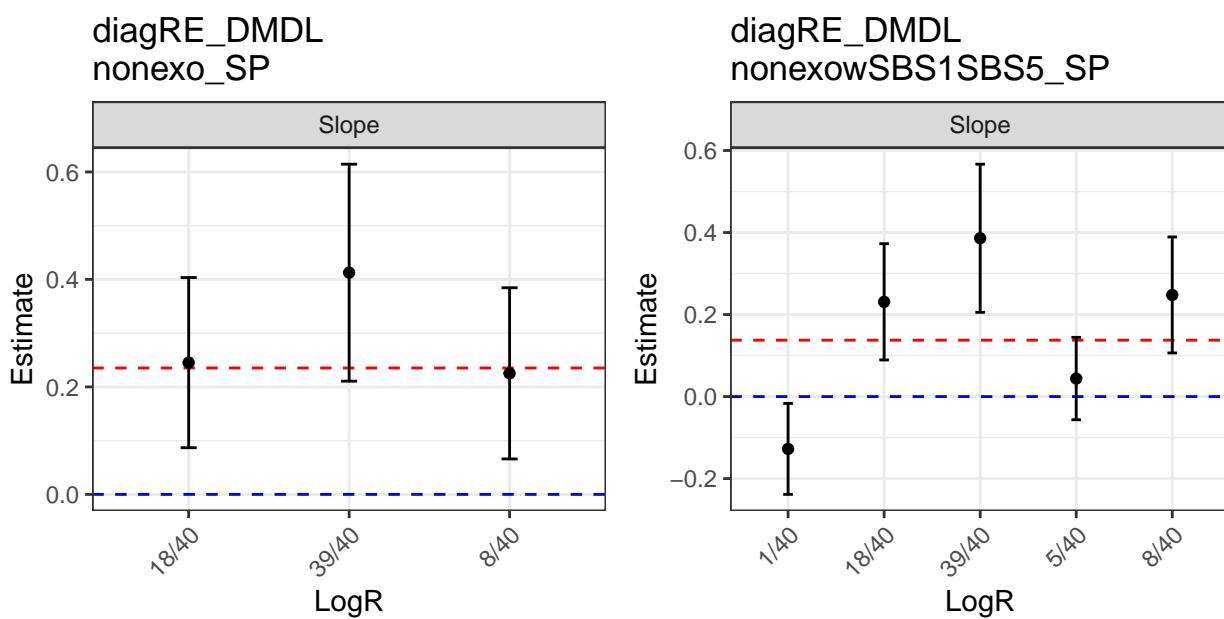
**diagRE_DMDL
nonexowSBS1SBS5_SP**



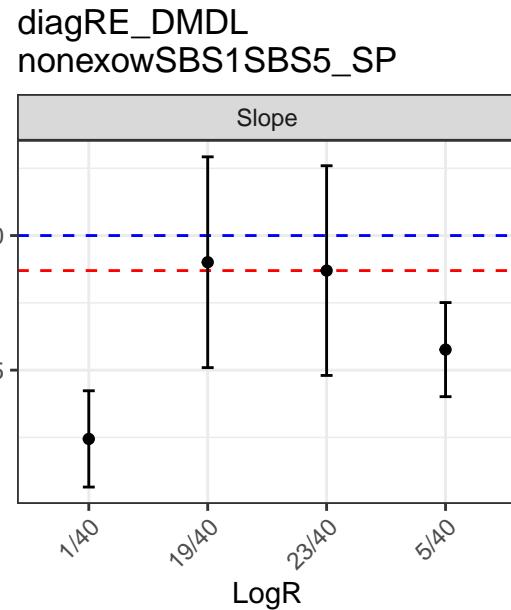
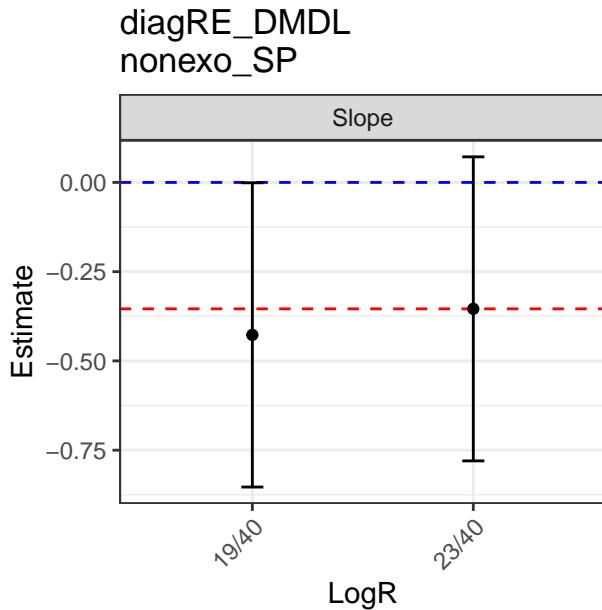
CNS–GBM



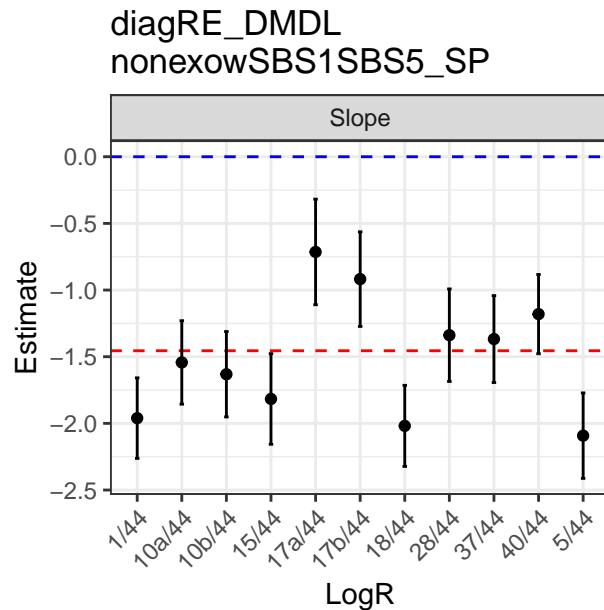
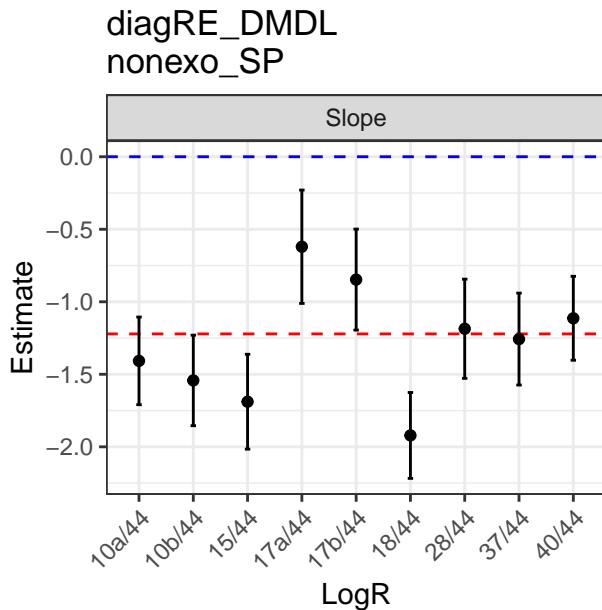
CNS–Medullo



CNS–PiloAstro

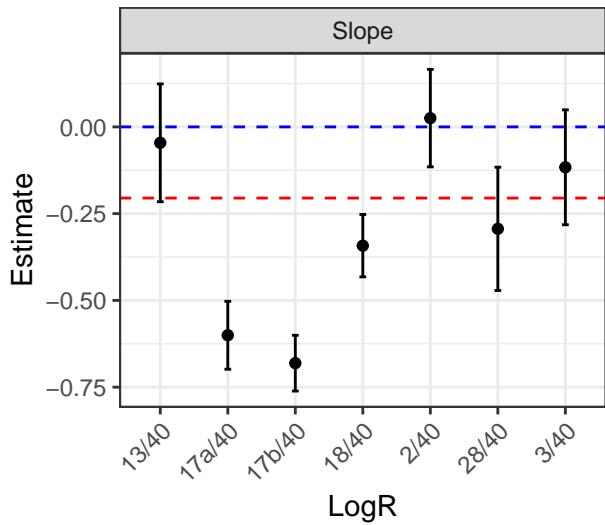


ColoRect–AdenoCA

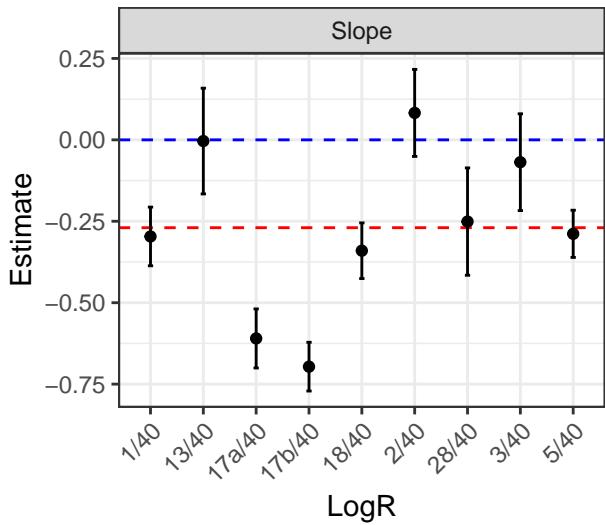


Eso-AdenoCA

diagRE_DMDL
nonexo_SP

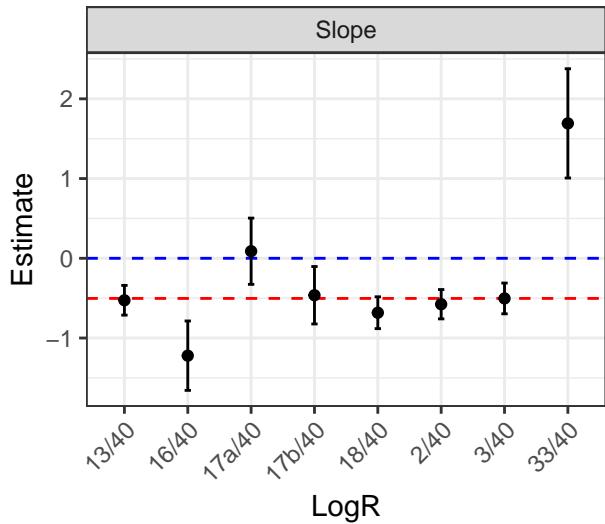


diagRE_DMDL
nonexowSBS1SBS5_SP

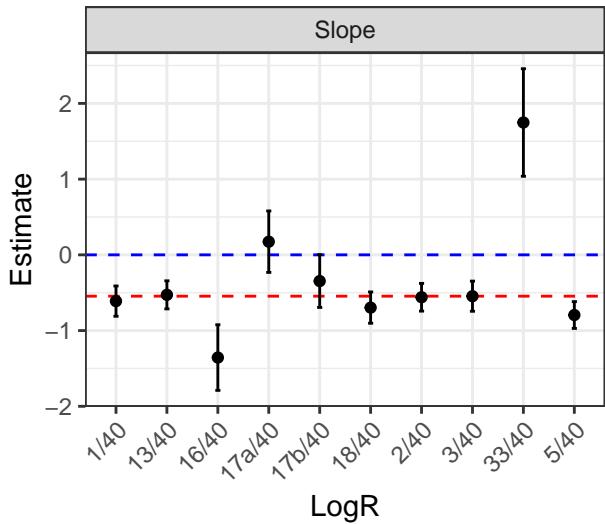


Head-SCC

diagRE_DMDL
nonexo_SP

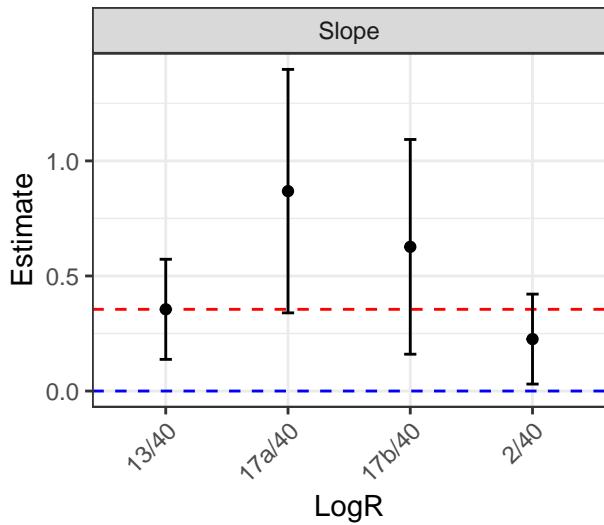


diagRE_DMDL
nonexowSBS1SBS5_SP

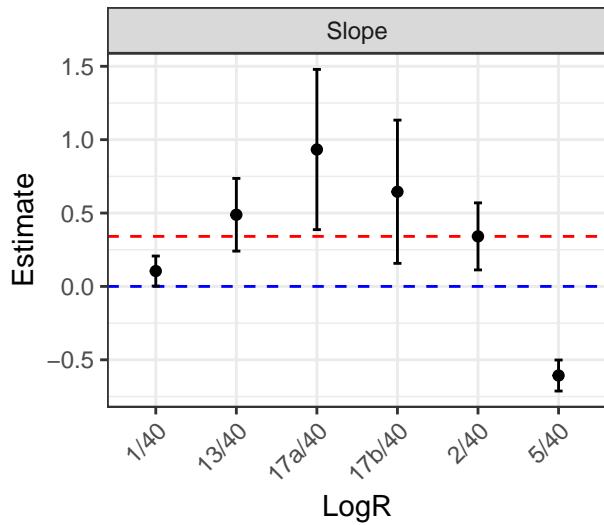


Kidney–ChRCC

diagRE_DMDL
nonexo_SP

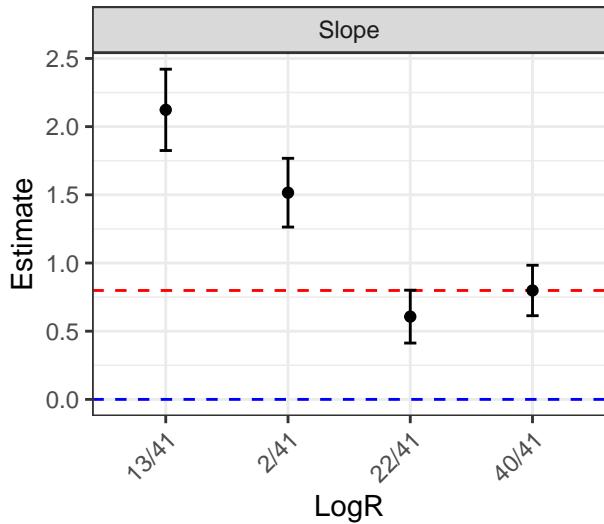


diagRE_DMDL
nonexowSBS1SBS5_SP

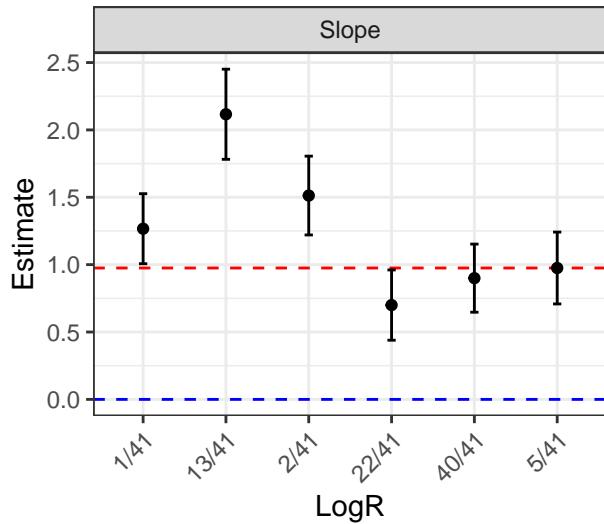


Kidney–RCC.clearcell

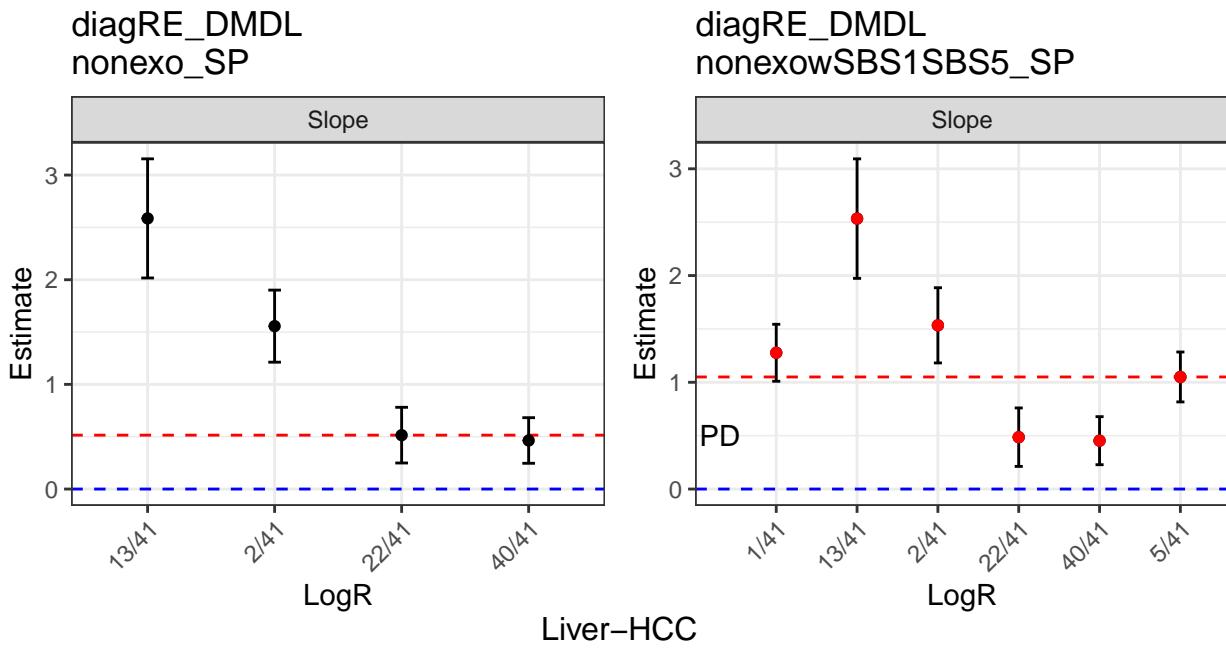
diagRE_DMDL
nonexo_SP



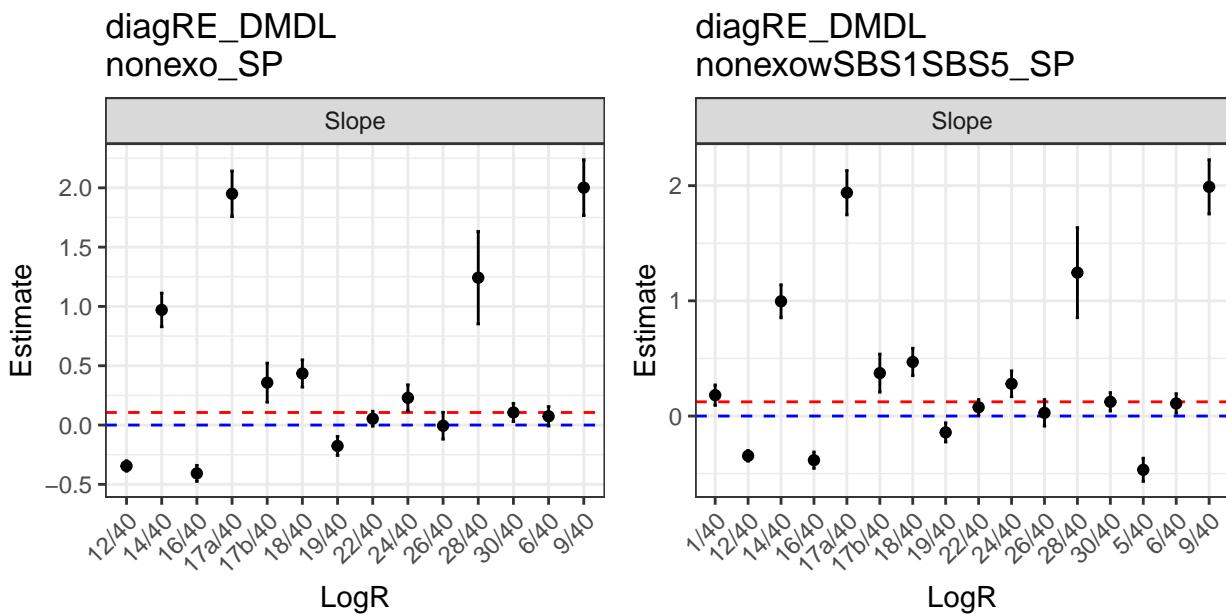
diagRE_DMDL
nonexowSBS1SBS5_SP



Kidney–RCC.papillary

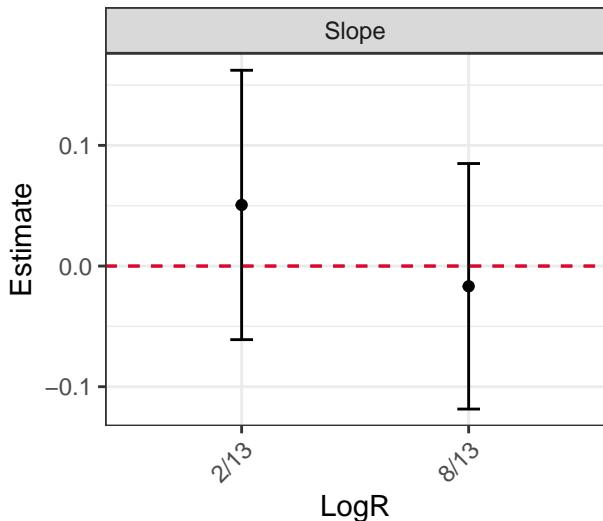


Liver–HCC

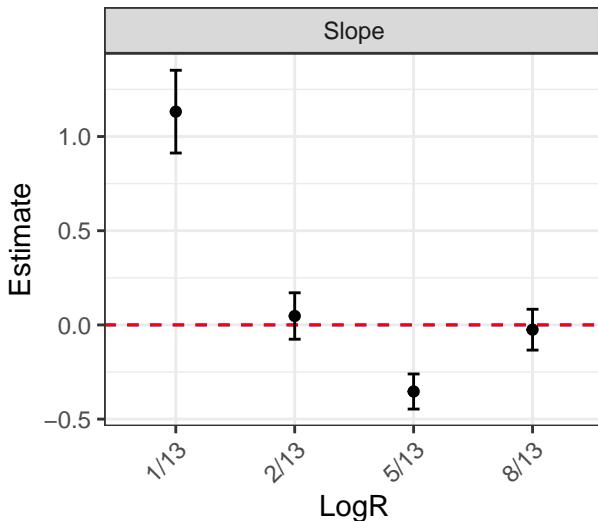


Lung-SCC

diagRE_DMDL
nonexo_SP

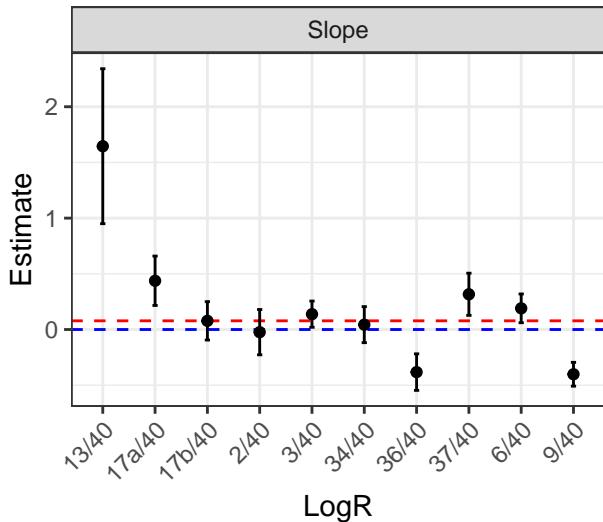


diagRE_DMDL
nonexowSBS1SBS5_SP

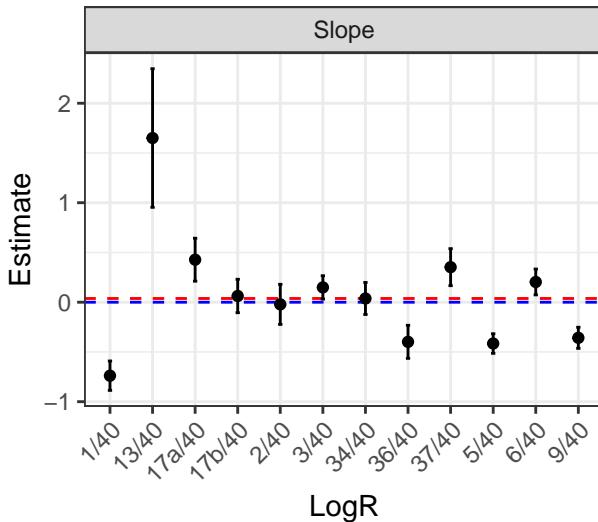


Lymph-BNHL

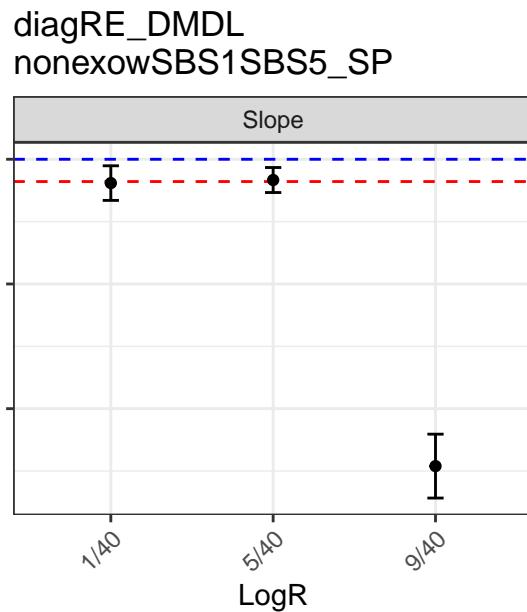
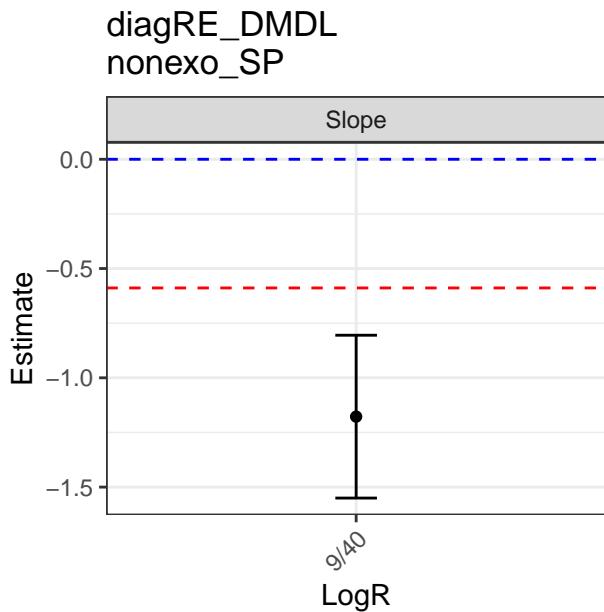
diagRE_DMDL
nonexo_SP



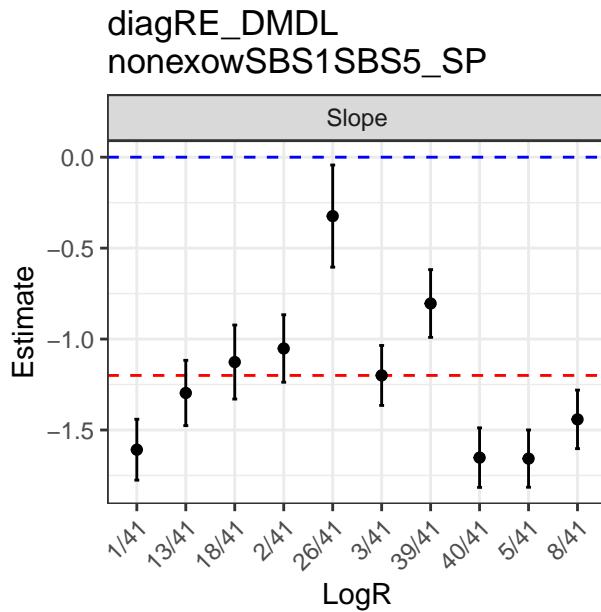
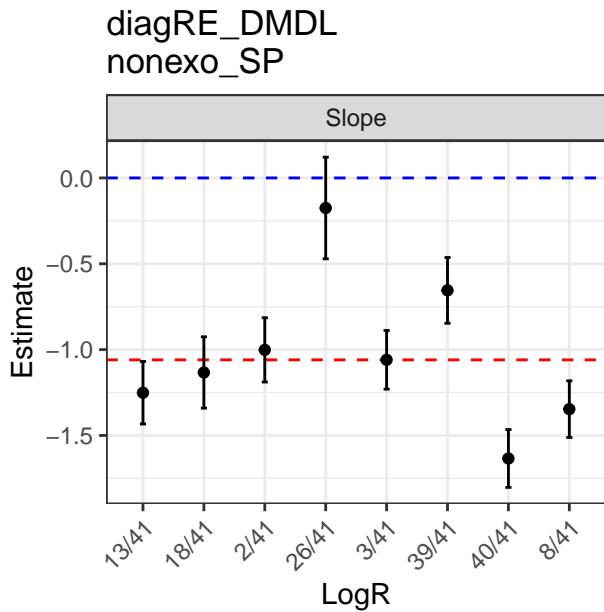
diagRE_DMDL
nonexowSBS1SBS5_SP



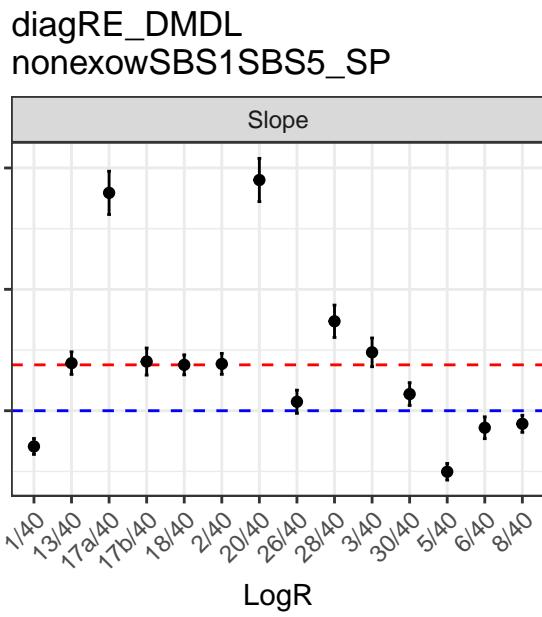
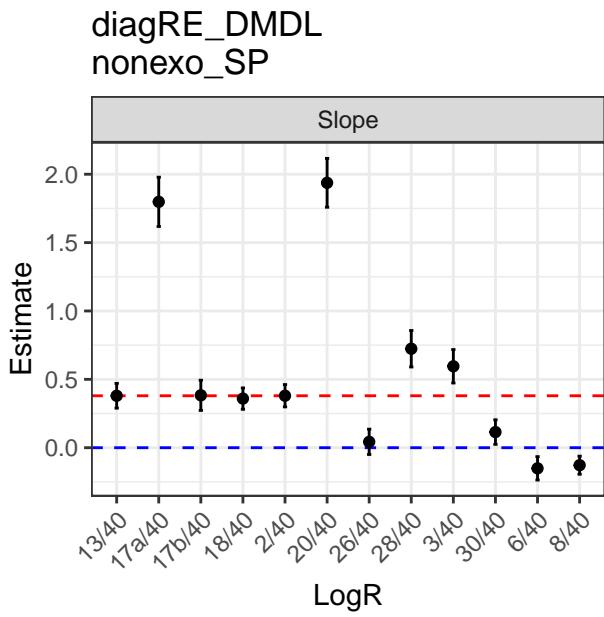
Lymph-CLL



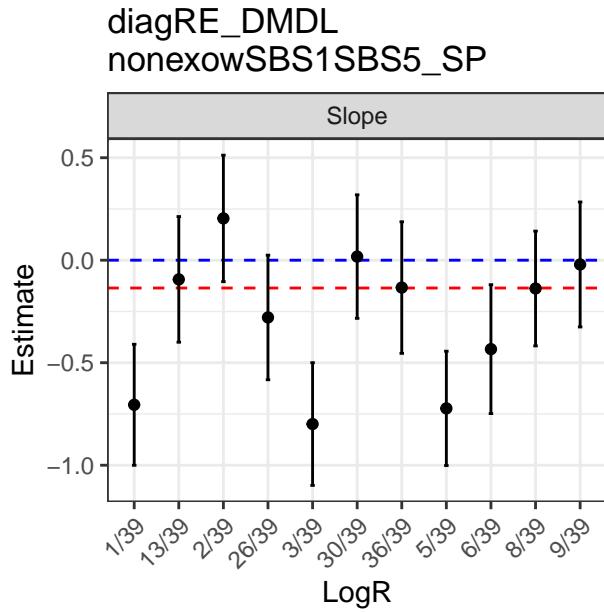
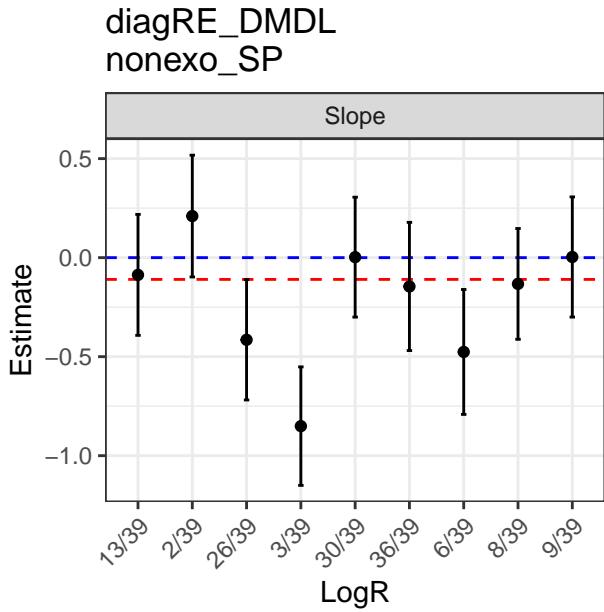
Ovary-AdenoCA



Panc–AdenoCA

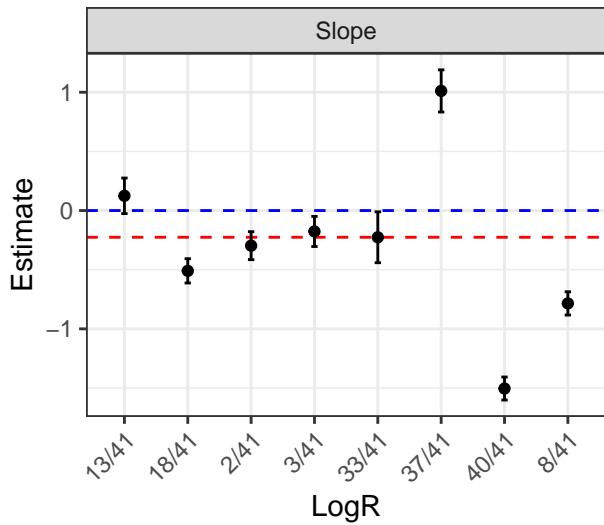


Panc–Endocrine

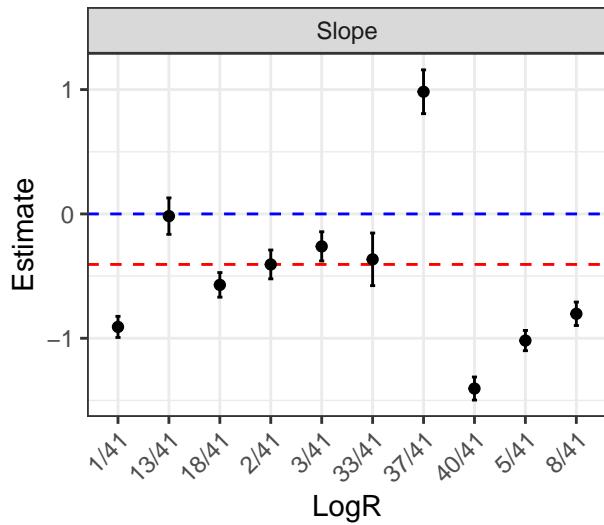


Prost–AdenoCA

diagRE_DMDL
nonexo_SP

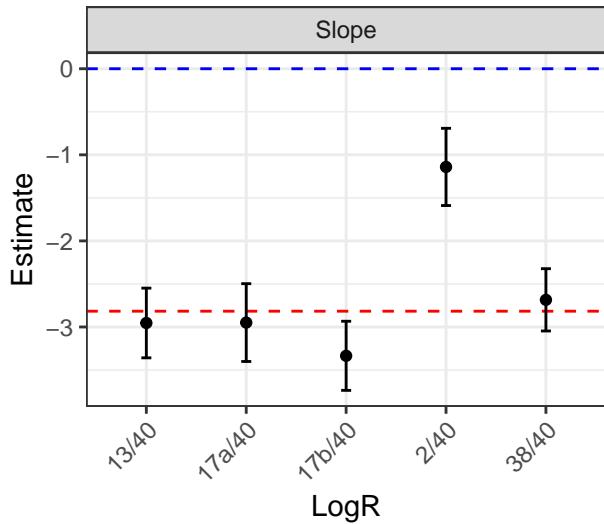


diagRE_DMDL
nonexowSBS1SBS5_SP

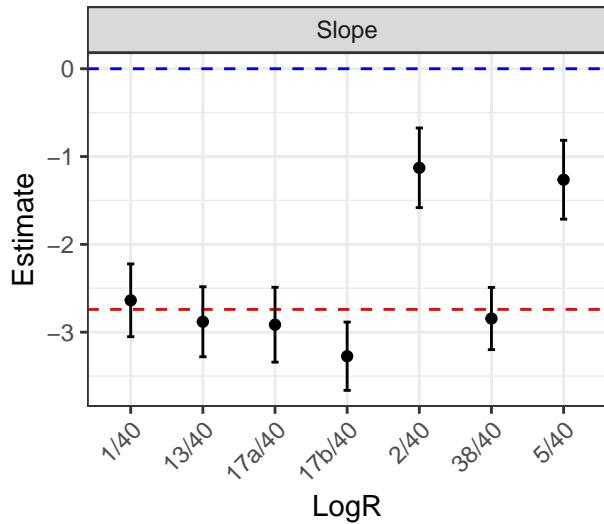


Skin–Melanoma.cutaneous

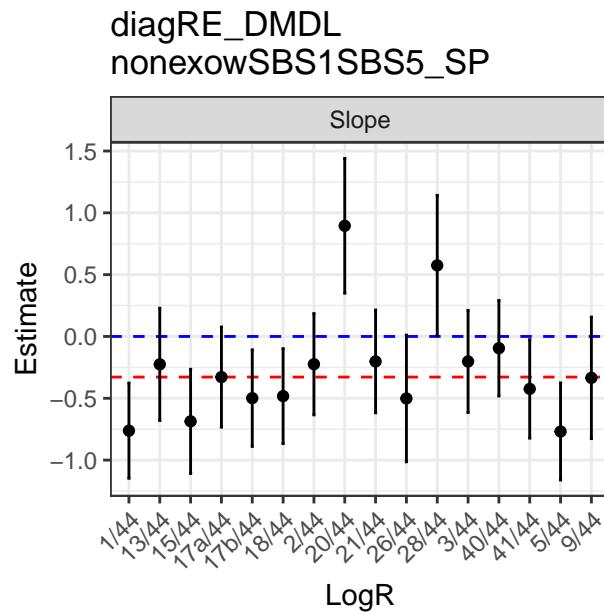
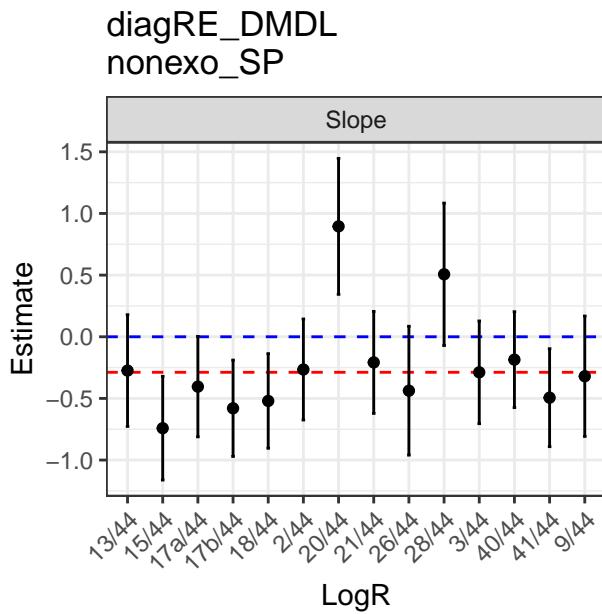
diagRE_DMDL
nonexo_SP



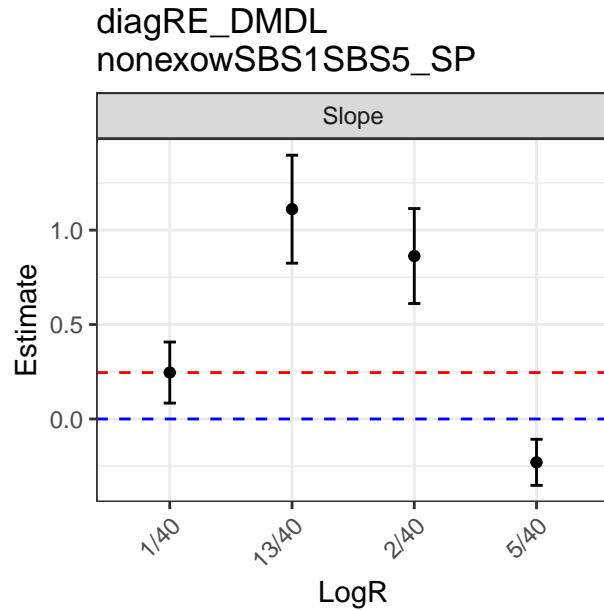
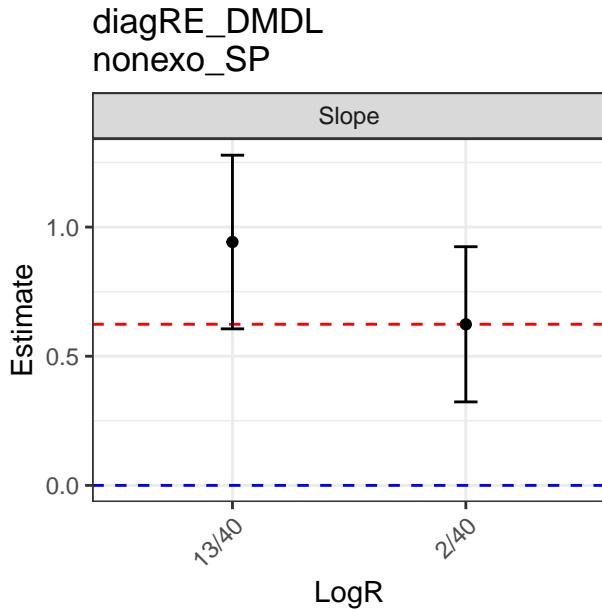
diagRE_DMDL
nonexowSBS1SBS5_SP



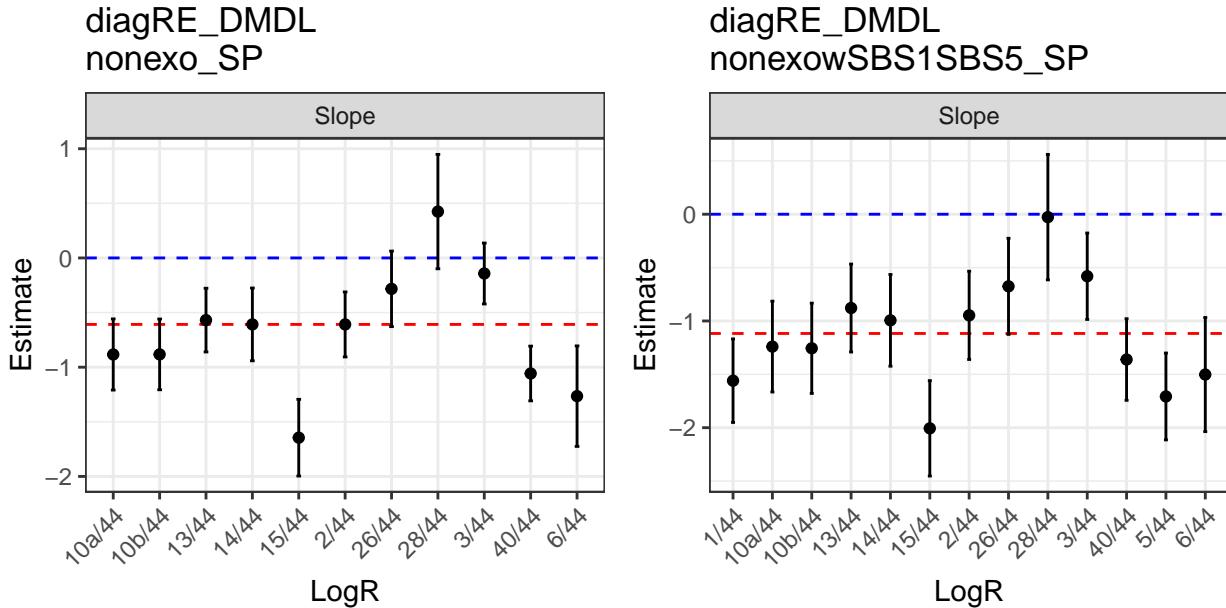
Stomach–AdenoCA



Thy–AdenoCA



Uterus–AdenoCA



Comparing the s1/s5 baseline to the minimal perturbation results

```

##      [,1]     [,2]     [,3]     [,4]     [,5]     [,6]     [,7]
## SBS1 "FALSE" "decrease" "FALSE" "decrease" "decrease" "FALSE" "FALSE"
## SBS5 "FALSE" "decrease" "FALSE" "FALSE"   "FALSE"   "decrease" "FALSE"
##      [,8]     [,9]     [,10]    [,11]    [,12]    [,13]    [,14]
## SBS1 "FALSE" "decrease" "FALSE" "FALSE"   "FALSE"   "increase" "decrease"
## SBS5 "FALSE" "decrease" "FALSE" "FALSE"   "decrease" "decrease" "decrease"
##      [,15]    [,16]    [,17]    [,18]    [,19]    [,20]    [,21]
## SBS1 "FALSE" "decrease" "decrease" "FALSE"   "decrease" "FALSE" "FALSE"
## SBS5 "FALSE" "decrease" "decrease" "decrease" "decrease" "increase" "FALSE"
##      [,22]    [,23]
## SBS1 "FALSE"   "FALSE"
## SBS5 "decrease" "FALSE"

## [1] 2 23

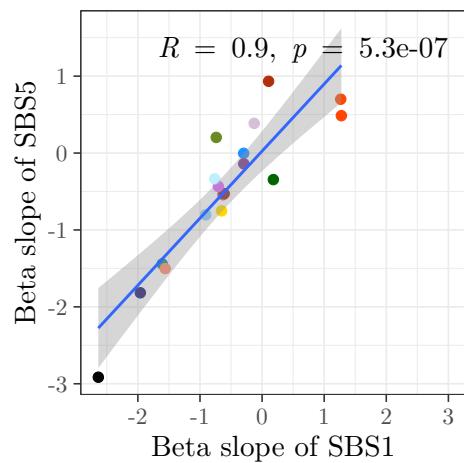
## [1] "Ct for which SBS1 and SBS5 are not DA"
## [1] 9

## [1] "Ct for which SBS1 and SBS5 both decrease"
## [1] 6

```

Plotting the betas of SBS1 and SBS5, and their correlation

```
## `geom_smooth()` using formula 'y ~ x'
```



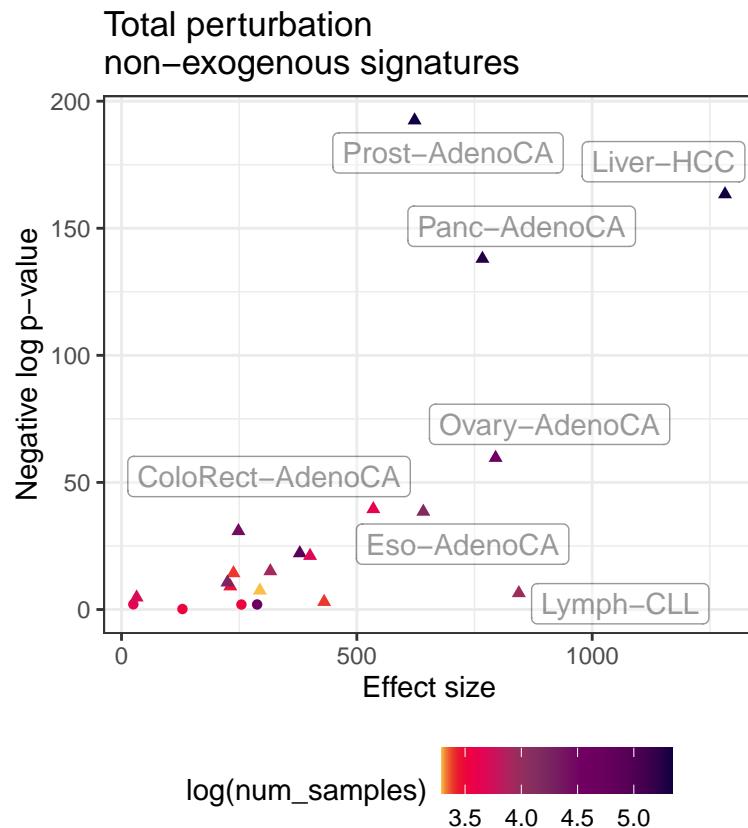
```
## [1] 27 8
## [1] 27 8
## [1] 136 11
## [1] 136 11
## [1] 34 3
## [1] 34 3
## [1] 106 4
## [1] 106 4
## [1] 41 3
## [1] 41 3
## [1] 37 10
## [1] 37 10
## [1] 65 8
## [1] 65 8
## [1] 32 9
## [1] 32 9
## [1] 38 5
## [1] 38 5
## [1] 86 5
## [1] 86 5
## [1] 30 5
## [1] 30 5
## [1] 207 15
## [1] 207 15
## [1] 34 3
## [1] 34 3
## [1] 51 11
## [1] 51 11
## [1] 53 2
## [1] 53 2
## [1] 97 9
## [1] 97 9
## [1] 193 13
## [1] 193 13
## [1] 70 10
## [1] 70 10
## [1] 208 9
```

```

## [1] 208   9
## [1] 29   6
## [1] 29   6
## [1] 30 15
## [1] 30 15
## [1] 41   3
## [1] 41   3
## [1] 40 12
## [1] 40 12

##          Bone-Osteosarc      Breast-AdenoCA      CNS-GBM
##                      8                  11                  3
##          CNS-Medullo      CNS-PiloAstro      ColoRect-AdenoCA
##                      4                  3                  10
##          Eso-AdenoCA        Head-SCC       Kidney-ChRCC
##                      8                  9                  5
##          Kidney-RCC.clearcell Kidney-RCC.papillary      Liver-HCC
##                      5                  5                  15
##          Lung-SCC           Lymph-BNHL      Lymph-CLL
##                      3                  11                  2
##          Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
##                      9                  13                  10
##          Prost-AdenoCA     Skin-Melanoma.cutaneous      Stomach-AdenoCA
##                      9                  6                  15
##          Thy-AdenoCA        Uterus-AdenoCA
##                      3                  12
## Error in apply(pert, 1, function(i) sqrt(sum((i - 1/(ncol(exposures_cancertype_obj$Y)))^2))) :
##   dim(X) must have a positive length
## Error in apply(pert, 1, function(i) sqrt(sum((i - 1/(ncol(exposures_cancertype_obj$Y)))^2))) :
##   dim(X) must have a positive length
## Warning: NAs introduced by coercion
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
## Warning: Removed 2 rows containing missing values (geom_point).
## Warning: Removed 2 rows containing missing values (geom_label_repel).
## Warning: ggrepel: 14 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



##	Bone-Osteosarc	Breast-AdenoCA	CNS-GBM
##	320.02704	469.29125	524.08517
##	CNS-Medullo	CNS-PiloAstro	ColoRect-AdenoCA
##	217.31161	27.02067	1031.46320
##	Eso-AdenoCA	Head-SCC	Kidney-ChRCC
##	522.66804	221.26052	103.16727
##	Kidney-RCC.clearcell	Kidney-RCC.papillary	Liver-HCC
##	247.53963	156.30958	1332.22216
##	Lung-SCC	Lymph-BNHL	Lymph-CLL
##	86.07143	345.88535	442.78303
##	Ovary-AdenoCA	Panc-AdenoCA	Panc-Endocrine
##	755.21919	829.19711	220.55650
##	Prost-AdenoCA	Skin-Melanoma.cutaneous	Stomach-AdenoCA
##	459.55271	1017.96421	540.50633
##	Thy-AdenoCA	Uterus-AdenoCA	
##	82.57481	458.24059	
##	Bone-Osteosarc	Breast-AdenoCA	CNS-GBM
##	1.080828e-04	2.239756e-28	3.390137e-03
##	CNS-Medullo	CNS-PiloAstro	ColoRect-AdenoCA
##	8.431463e-03	5.615238e-04	6.356131e-26
##	Eso-AdenoCA	Head-SCC	Kidney-ChRCC
##	5.329093e-21	4.975610e-05	1.562125e-09
##	Kidney-RCC.clearcell	Kidney-RCC.papillary	Liver-HCC
##	4.027485e-18	NA	4.747822e-107
##	Lung-SCC	Lymph-BNHL	Lymph-CLL

```

##          7.747310e-22      3.908637e-19      6.611927e-20
## Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
##          8.965185e-38      4.096402e-119     3.987099e-10
## Prost-AdenoCA Skin-Melanoma.cutaneous Stomach-AdenoCA
##          6.474116e-99      9.272113e-25     1.715150e-06
## Thy-AdenoCA       Uterus-AdenoCA
##          8.821583e-06      4.819867e-10

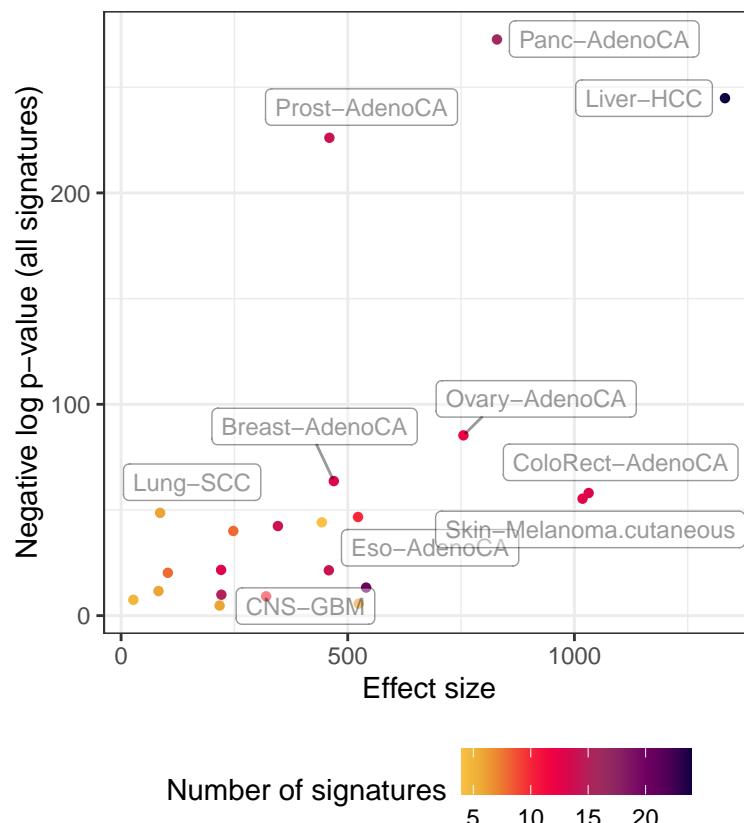
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 1 rows containing missing values (geom_point).

## Warning: Removed 1 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 12 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



```

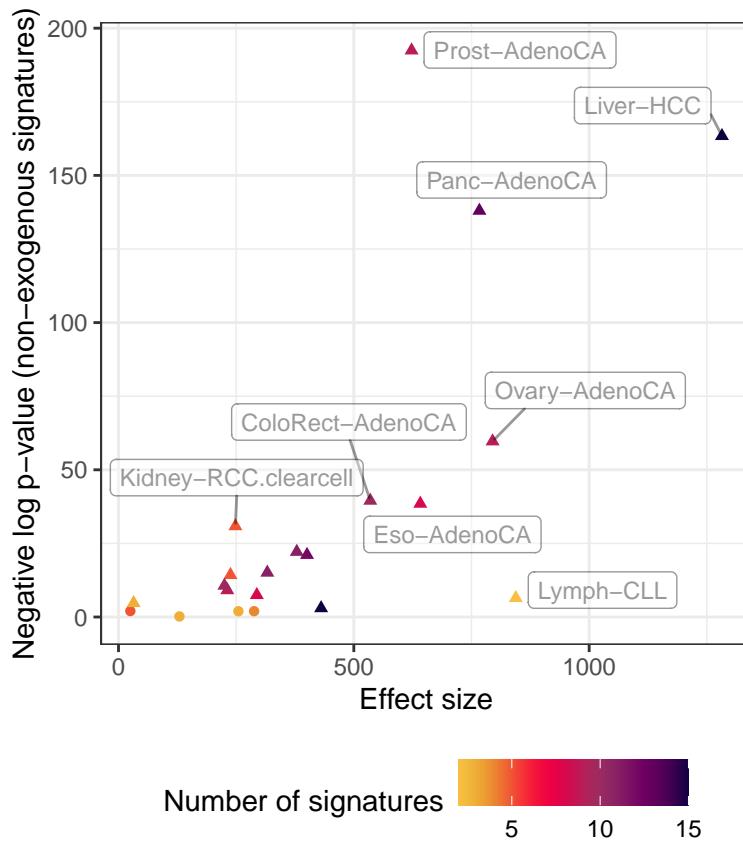
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 2 rows containing missing values (geom_point).

## Warning: Removed 2 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 13 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps

```



HMP

Simple HMP tests to see what is differentially abundant

```
## Error in signatures_PCAWG_it["x"][[1]][, 2] :
##   incorrect number of dimensions

## Error in signature_roo_it[[2]] : subscript out of bounds

## Warning in loglikDM(data, gamma.MoM): full precision may not have been achieved
## in 'lgamma'

## Error in rowSums(sig_obj$Y) :
##   'x' must be an array of at least two dimensions
## Error in rowSums(sig_obj$Y) :
##   'x' must be an array of at least two dimensions
## Error : $ operator is invalid for atomic vectors

## [1] "Biliary-AdenoCA.p value"           "Bladder-TCC.p value"
## [3] "Bone-Benign.p value"                "Bone-Epith.p value"
## [5] "Bone-Osteosarc.p value"             "Breast-AdenoCA.p value"
## [7] "Breast-DCIS.p value"                "Breast-LobularCA.p value"
## [9] "Cervix-AdenoCA.p value"              "Cervix-SCC.p value"
## [11] "CNS-GBM.p value"                   "CNS-Medullo.p value"
## [13] "CNS-Oligo.p value"                 "CNS-PiloAstro.p value"
## [15] "ColoRect-AdenoCA.p value"            "Eso-AdenoCA.p value"
```

```

## [17] "Head-SCC.p value"           "Kidney-ChRCC.p value"
## [19] "Kidney-RCC.clearcell.p value" "Kidney-RCC.papillary.p value"
## [21] "Liver-HCC.p value"          "Lung-AdenoCA.p value"
## [23] "Lung-SCC.p value"          "Lymph-BNHL.p value"
## [25] "Lymph-CLL.p value"          "Myeloid-AML.p value"
## [27] "Myeloid-MPN.p value"        "Ovary-AdenoCA.p value"
## [29] "Panc-AdenoCA.p value"       "Panc-Endocrine.p value"
## [31] "Prost-AdenoCA.p value"      "Skin-Melanoma.acral.p value"
## [33] "Skin-Melanoma.cutaneous.p value" "Skin-Melanoma.mucosal"
## [35] "SoftTissue-Leiomyo.p value"   "SoftTissue-Liposarc.p value"
## [37] "Stomach-AdenoCA.p value"     "Thy-AdenoCA.p value"
## [39] "Uterus-AdenoCA.p value"

## [1] "Bone-Osteosarc"            "Breast-AdenoCA"
## [3] "CNS-GBM"                  "CNS-Medullo"
## [5] "CNS-PiloAstro"            "ColoRect-AdenoCA"
## [7] "Eso-AdenoCA"              "Head-SCC"
## [9] "Kidney-ChRCC"             "Kidney-RCC.clearcell"
## [11] "Kidney-RCC.papillary"     "Liver-HCC"
## [13] "Lung-SCC"                 "Lymph-BNHL"
## [15] "Lymph-CLL"                "Ovary-AdenoCA"
## [17] "Panc-AdenoCA"             "Panc-Endocrine"
## [19] "Prost-AdenoCA"            "Skin-Melanoma.cutaneous"
## [21] "Stomach-AdenoCA"          "Thy-AdenoCA"
## [23] "Uterus-AdenoCA"

##      Bone-Osteosarc.p value      Breast-AdenoCA.p value
##                      6.918553e-01 1.000000e+00
##      CNS-GBM.p value           CNS-Medullo.p value
##                      1.000000e+00 3.245284e-01
##      CNS-PiloAstro.p value    ColoRect-AdenoCA.p value
##                      1.000000e+00 1.000000e+00
##      Eso-AdenoCA.p value       Head-SCC.p value
##                      1.000000e+00 1.000000e+00
##      Kidney-ChRCC.p value     Kidney-RCC.clearcell.p value
##                      1.000000e+00 1.000000e+00
##      Kidney-RCC.papillary.p value Liver-HCC.p value
##                      1.000000e+00 1.000000e+00
##      Lung-SCC.p value          Lymph-BNHL.p value
##                      1.000000e+00 1.000000e+00
##      Lymph-CLL.p value         Ovary-AdenoCA.p value
##                      1.000000e+00 1.000000e+00
##      Panc-AdenoCA.p value     Panc-Endocrine.p value
##                      1.000000e+00 1.000000e+00
##      Prost-AdenoCA.p value    Skin-Melanoma.cutaneous.p value
##                      1.000000e+00 1.000000e+00
##      Stomach-AdenoCA.p value   Thy-AdenoCA.p value
##                      1.000000e+00 1.000000e+00
##      Uterus-AdenoCA.p value    7.559522e-10

##      Bone-Osteosarc.p value      Breast-AdenoCA.p value
##                      0.8538039 0.8538039

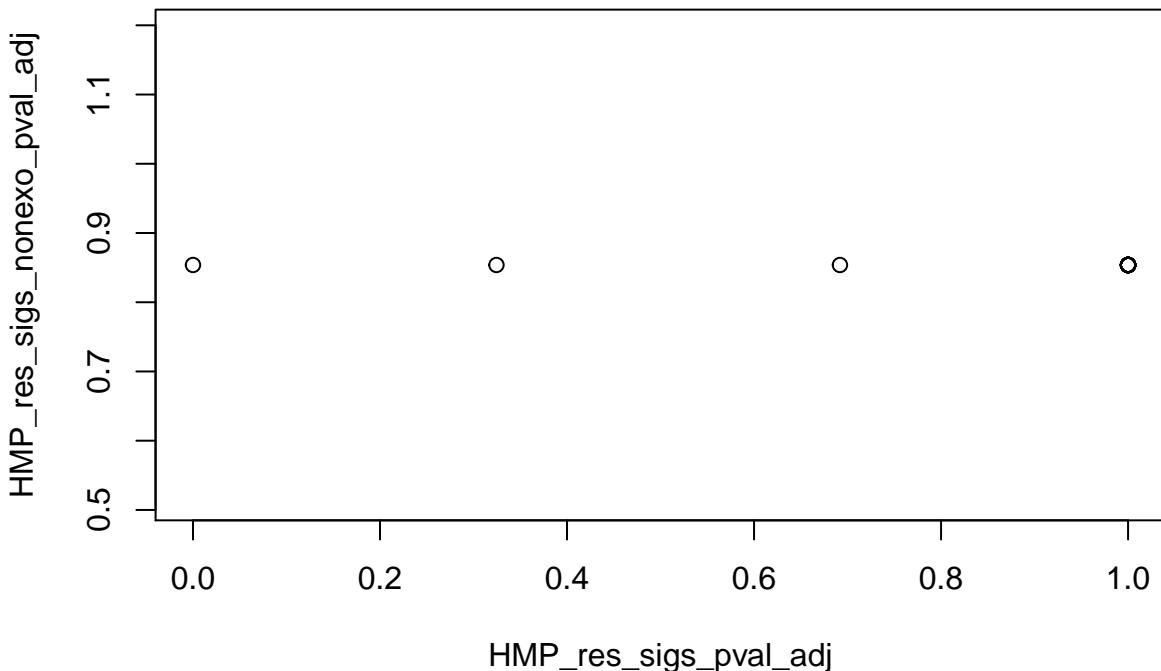
```

```

##          CNS-GBM.p value          CNS-Medullo.p value
##          0.8538039          0.8538039
##          CNS-PiloAstro.p value    ColoRect-AdenoCA.p value
##          0.8538039          0.8538039
##          Eso-AdenoCA.p value     Head-SCC.p value
##          0.8538039          0.8538039
##          Kidney-ChRCC.p value   Kidney-RCC.clearcell.p value
##          0.8538039          0.8538039
##          Kidney-RCC.papillary.p value Liver-HCC.p value
##          0.8538039          0.8538039
##          Lung-SCC.p value       Lymph-BNHL.p value
##          0.8538039          0.8538039
##          Lymph-CLL.p value      Ovary-AdenoCA.p value
##          0.8538039          0.8538039
##          Panc-AdenoCA.p value   Panc-Endocrine.p value
##          0.8538039          0.8538039
##          Prost-AdenoCA.p value  Skin-Melanoma.cutaneous.p value
##          0.8538039          0.8538039
##          Stomach-AdenoCA.p value Thy-AdenoCA.p value
##          0.8538039          0.8538039
##          Uterus-AdenoCA.p value
##          0.8538039

## Uterus-AdenoCA.p value
## 7.559522e-10

```



```

pvals_diagRE_DMDL_SP_adj <- p.adjust(pvals_diagRE_DMDL_SP, 'fdr')
pvals_diagRE_DMDL_nonexo_SP_adj <- p.adjust(pvals_diagRE_DMDL_nonexo_SP, 'fdr')
pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations_adj <- p.adjust(pvals_fullREDMnoscaling_SP_no
pvals_fullRE_M_nonexo_SP_adj <- p.adjust(pvals_fullRE_M_nonexo_SP, 'fdr')
pvals_fullRE_DMSL_nonexo_SP_adj <- p.adjust(pvals_fullRE_DMSL_nonexo_SP, 'fdr')

```

```

names(pvals_diagRE_DMDL_SP_adj) <- names(pvals_diagRE_DMDL_nonexo_SP_adj) <- names(pvals_fullRE_M_nonexo_)

table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05,
      fullRE_DMSL_DA=pvals_fullRE_DMSL_nonexo_SP_adj <= 0.05)

##          fullRE_DMSL_DA
## diagRE_DMDL_DA FALSE TRUE
##      FALSE      5     1
##      TRUE       1    11

names(pvals_diagRE_DMDL_nonexo_SP_adj)[which((pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05) & (fullRE_DMSL_DA=0.05))

## [1] "Lymph-CLL"

names(pvals_diagRE_DMDL_nonexo_SP_adj)[which((pvals_diagRE_DMDL_nonexo_SP_adj > 0.05) & (fullRE_DMSL_DA=0.05))

## [1] "Stomach-AdenoCA"

table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05,
      fullRE_M_DA=pvals_fullRE_M_nonexo_SP_adj <= 0.05)

##          fullRE_M_DA
## diagRE_DMDL_DA TRUE
##      FALSE      5
##      TRUE     17

# table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj <= 0.05,
#       HMP_DA=HMP_res_sigs_pval_adj <= 0.05)

# table(diagRE_DMDL_DA=pvals_diagRE_DMDL_nonexo_SP_adj < 0.05, HMP_res_sigs_DA=HMP_res_sigs < 0.05)

p.adjust(pvals_diagRE_DMDL_SP, method = "BH")

##          Bone-Osteosarc      Breast-AdenoCA          CNS-GBM
##      1.251484e-04      9.854928e-28      3.551572e-03
##          CNS-Medullo      CNS-PiloAstro      ColoRect-AdenoCA
##      8.431463e-03      6.176762e-04      2.330581e-25
##          Eso-AdenoCA      Head-SCC          Kidney-ChRCC
##      1.302667e-20      6.081301e-05      2.291117e-09
##      Kidney-RCC.clearcell      Kidney-RCC.papillary      Liver-HCC
##      7.383723e-18                  NA      5.222605e-106
##          Lung-SCC      Lymph-BNHL          Lymph-CLL
##      2.130510e-21      7.817274e-19      1.454624e-19
##          Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
##      4.930852e-37      9.012085e-118      6.747398e-10
##          Prost-AdenoCA      Skin-Melanoma.cutaneous      Stomach-AdenoCA
##      4.747685e-98      2.914093e-24      2.358331e-06
##          Thy-AdenoCA      Uterus-AdenoCA
##      1.141617e-05      7.574077e-10

p.adjust(pvals_diagRE_DMDL_nonexo_SP, method = "BH")

##          Bone-Osteosarc      Breast-AdenoCA          CNS-GBM
##      8.712593e-04      6.123721e-10      1.557247e-01

```

```

##          CNS-Medullo      CNS-PiloAstro    ColoRect-AdenoCA
## 1.557247e-01      5.270878e-01   3.141298e-17
##          Eso-AdenoCA        Head-SCC       Kidney-ChRCC
## 7.328650e-17      1.788732e-04   1.557247e-01
## Kidney-RCC.clearcell Kidney-RCC.papillary   Liver-HCC
## 1.137607e-13      1.190455e-06   1.263498e-70
##          Lung-SCC         Lymph-BNHL     Lymph-CLL
## 8.301558e-01      5.881884e-07   2.256505e-03
##          Ovary-AdenoCA     Panc-AdenoCA   Panc-Endocrine
## 6.973340e-26      8.893577e-60   4.169125e-05
##          Prost-AdenoCA Skin-Melanoma.cutaneous Stomach-AdenoCA
## 6.044387e-83      9.919659e-17   6.320633e-02
##          Thy-AdenoCA       Uterus-AdenoCA
## 1.170750e-02      1.568961e-09

df_pvals_DMDL_SP <- cbind.data.frame(pvals_DM=pvals_diagRE_DMDL_SP_adj,
                                         pvals_DMnonexo=pvals_diagRE_DMDL_nonexo_SP_adj,
                                         num_samples=as.numeric(num_samples_all_SP),
                                         num_sigs_nonexo=as.numeric(num_sigs_nonexo_SP),
                                         ct=enough_samples,
                                         pvals_DM_censored=sapply(-log(pvals_diagRE_DMDL_SP_adj),
                                                       function(i) min(i, 25)),
                                         pvals_DMnonexo_censored=sapply(-log(pvals_diagRE_DMDL_nonexo_SP_adj),
                                                       function(i) min(i, 25)),
                                         bool_censored=(( -log(pvals_diagRE_DMDL_nonexo_SP_adj) > 25 ) | ( -log(pvals_diagRE_))

ggplot(df_pvals_DMDL_SP,
       aes(x=pvals_DM_censored, y=pvals_DMnonexo_censored,
            # size=num_samples,
            label=ct, size=bool_censored))+geom_point(aes (col=ct))+geom_hline(yintercept = -log(0.05), lty='dashed')+geom_vline(xintercept = -log(0.05), lty='dashed')+geom_label_repel(size=3.2, alpha=0.6, max.overlaps = 30)+ theme_bw()+
theme(legend.position = "bottom", legend.text=element_text(size=8))+labs(x='- Log p-value all signatures', y='- Log p-value nonexogenous signatures')+guides(size=FALSE, col=FALSE)+ #, col=guide_legend(ncol=4),
scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
lims(x=c(0, 30), y=c(0,30))

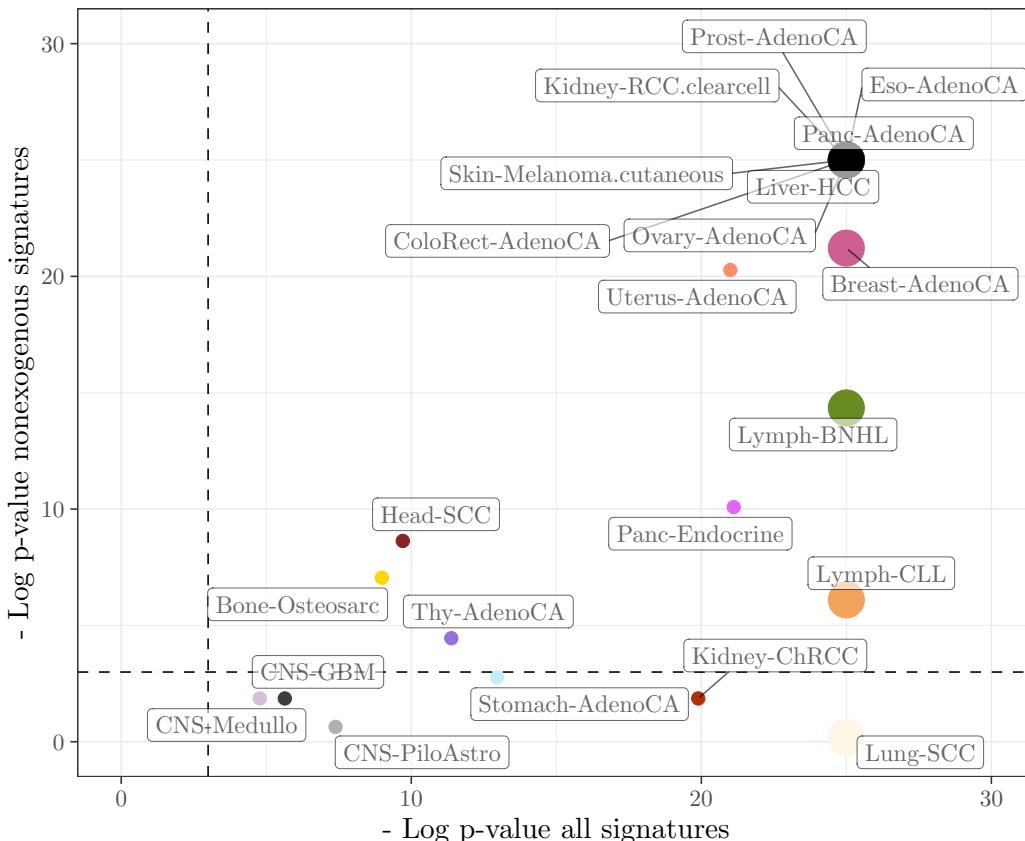
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.

## Warning: Using size for a discrete variable is not advised.

## Warning: Removed 1 rows containing missing values (geom_point).

## Warning: Removed 1 rows containing missing values (geom_label_repel).

```



```
t.test(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, 'num_samples'],
       df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05, 'num_samples'])
```

```
##
```

```
## Welch Two Sample t-test
```

```
##
```

```
## data: df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, "num_samples"] and df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05, "num_samples"]
## t = 1.8016, df = 19.213, p-value = 0.08733
```

```
## alternative hypothesis: true difference in means is not equal to 0
```

```
## 95 percent confidence interval:
```

```
## -5.663104 76.055261
```

```
## sample estimates:
```

```
## mean of x mean of y
```

```
## 82.52941 47.33333
```

```
t.test(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, 'num_sigs_nonexo'],
       df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05, 'num_sigs_nonexo'])
```

```
##
```

```
## Welch Two Sample t-test
```

```
##
```

```
## data: df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, "num_sigs_nonexo"] and df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05, "num_sigs_nonexo"]
## t = 1.466, df = 7.0453, p-value = 0.1858
```

```
## alternative hypothesis: true difference in means is not equal to 0
```

```
## 95 percent confidence interval:
```

```
## -1.886557 8.063027
```

```

## sample estimates:
## mean of x mean of y
## 8.588235 5.500000
mean(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05, 'num_sigs_nonexo'])

## [1] 8.588235
mean(df_pvals_DMDL_SP[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05, 'num_sigs_nonexo'])

## [1] 5.5

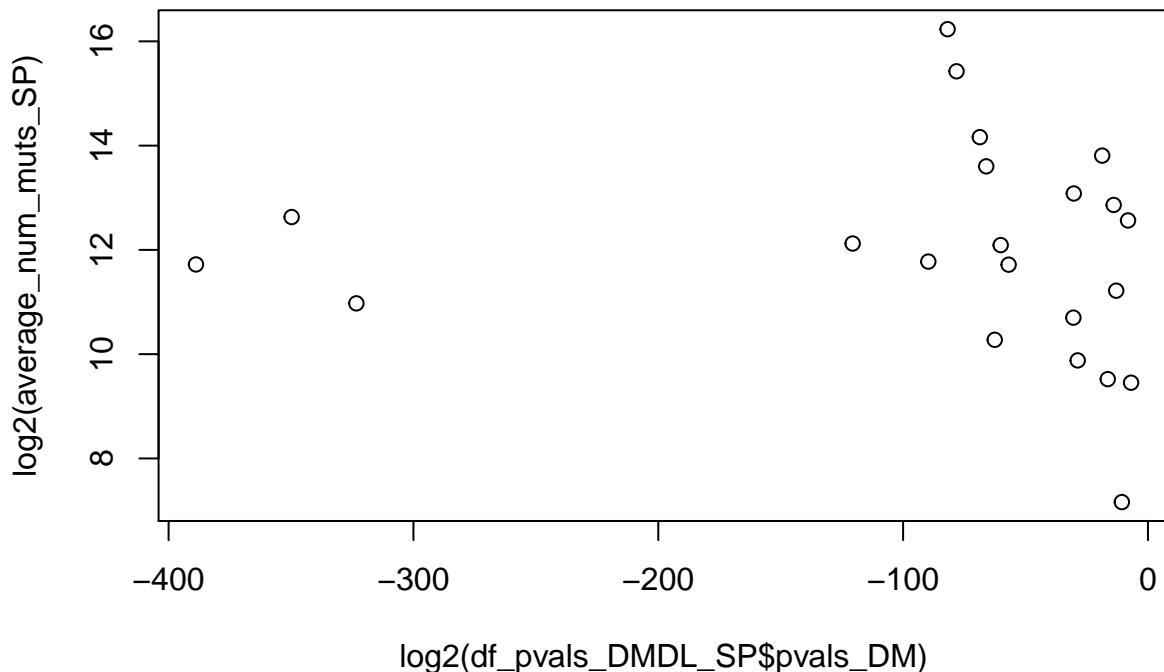
Does DA or not scale with the average number of mutations in the observed exposures (i.e. per patient and group) of the relevant ct?

average_num_muts_SP <- sapply(enough_samples, function(ct){
  .xx <- all_objects_SP[[ct]]
  try(mean(rowSums(.xx$Y)))
})

average_num_muts_SP

##          Bone-Osteosarc      Breast-AdenoCA      CNS-GBM
##                2382.1852        3507.5588       6057.6618
##          CNS-Medullo      CNS-PiloAstro  ColoRect-AdenoCA
##                  700.8915        143.3452       77035.7838
##          Eso-AdenoCA      Head-SCC           Kidney-ChRCC
##                 12439.3692       7445.4219       942.5263
## Kidney-RCC.clearcell Kidney-RCC.papillary      Liver-HCC
##                   3365.9477        2740.9833       6340.5121
##          Lung-SCC          Lymph-BNHL      Lymph-CLL
##                 18340.1471        4367.0392       1239.9057
##          Ovary-AdenoCA      Panc-AdenoCA      Panc-Endocrine
##                   4458.4691        3376.0415       1664.5857
## Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
##                  2011.8966        43998.4833      14345.9667
##          Thy-AdenoCA      Uterus-AdenoCA
##                   734.8902        8670.1125
plot(log2(df_pvals_DMDL_SP$pvals_DM), log2(average_num_muts_SP))

```



`log2(average_num_mutations_SP)`

```
t.test(log2(average_num_mutations_SP)[df_pvals_DMDL_SP$pvals_DMnonexo <= 0.05],
       log2(average_num_mutations_SP)[df_pvals_DMDL_SP$pvals_DMnonexo > 0.05])
```

##

Welch Two Sample t-test

##

data: log2(average_num_mutations_SP)[df_pvals_DMDL_SP\$pvals_DMnonexo <= 0.05] and log2(average_num_mutations_SP)[df_pvals_DMDL_SP\$pvals_DMnonexo > 0.05]

t = 0.85052, df = 6.3966, p-value = 0.4257

alternative hypothesis: true difference in means is not equal to 0

95 percent confidence interval:

-1.88287 3.93586

sample estimates:

mean of x mean of y

12.19856 11.17207

```
pcawg_palette <- pcawg.colour.palette(gsub("\\.*", "", enough_samples), scheme = "tumour.subtype")
names(pcawg_palette) <- enough_samples
```

`pvals_diagRE_DMDL_nonexo_SP_adj`

##	Bone-Osteosarc	Breast-AdenoCA	CNS-GBM
##	8.712593e-04	6.123721e-10	1.557247e-01
##	CNS-Medullo	CNS-PiloAstro	ColoRect-AdenoCA
##	1.557247e-01	5.270878e-01	3.141298e-17
##	Eso-AdenoCA	Head-SCC	Kidney-ChRCC
##	7.328650e-17	1.788732e-04	1.557247e-01
##	Kidney-RCC.clearcell	Kidney-RCC.papillary	Liver-HCC
##	1.137607e-13	1.190455e-06	1.263498e-70
##	Lung-SCC	Lymph-BNHL	Lymph-CLL
##	8.301558e-01	5.881884e-07	2.256505e-03
##	Ovary-AdenoCA	Panc-AdenoCA	Panc-Endocrine

```

##          6.973340e-26          8.893577e-60          4.169125e-05
## Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
##          6.044387e-83          9.919659e-17          6.320633e-02
## Thy-AdenoCA           Uterus-AdenoCA
##          1.170750e-02          1.568961e-09

pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations_adj

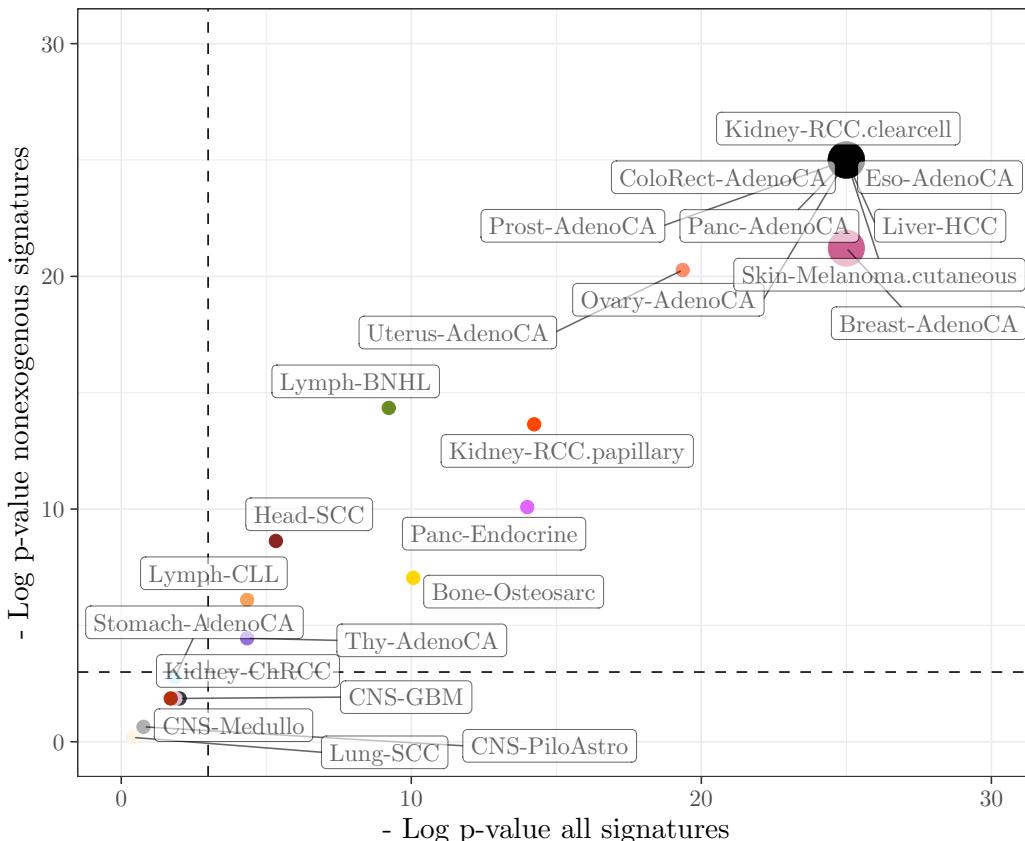
##          Bone-Osteosarc      Breast-AdenoCA          CNS-GBM
##          4.248457e-05          7.759783e-12          1.336685e-01
##          CNS-Medullo        CNS-PiloAstro       ColoRect-AdenoCA
##          1.538381e-01          4.648237e-01          1.023484e-15
##          Eso-AdenoCA          Head-SCC            Kidney-ChRCC
##          3.759670e-18          4.834276e-03          1.814391e-01
## Kidney-RCC.clearcell    Kidney-RCC.papillary      Liver-HCC
##          3.652385e-14          6.557344e-07          3.704923e-63
##          Lung-SCC             Lymph-BNHL            Lymph-CLL
##          6.693019e-01          9.868396e-05          1.303426e-02
##          Ovary-AdenoCA        Panc-AdenoCA       Panc-Endocrine
##          1.231778e-22          7.710539e-59          8.327076e-07
##          Prost-AdenoCA Skin-Melanoma.cutaneous      Stomach-AdenoCA
##          6.572758e-67          3.732926e-14          1.576047e-01
##          Thy-AdenoCA          Uterus-AdenoCA
##          1.303426e-02          3.911013e-09

df_pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations <- cbind.data.frame(pvals_DMnonexo_nonscal-
                                         pvals_DMnonexo=pvals_diagRE_DMDL_nonexo_SP_adj,
                                         num_samples=as.numeric(num_samples_all_SP),
                                         num_sigs_nonexo=as.numeric(num_sigs_nonexo_SP),
                                         ct=enough_samples,
                                         pvals_DM_nonscaling_censored=sapply(-log(pvals_fullREDMnoscaling_SP_nonexo_subset
                                             function(i) min(i, 25)),
                                         pvals_DMnonexo_censored=sapply(-log(pvals_diagRE_DMDL_nonexo_SP_adj),
                                             function(i) min(i, 25)),
                                         bool_censored=(( -log(pvals_diagRE_DMDL_nonexo_SP_adj) > 25 ) | ( -log(pvals_fullRE
ggplot(df_pvals_fullREDMnoscaling_SP_nonexo_subsets_and_amalgamations,
  aes(x=pvals_DM_nonscaling_censored, y=pvals_DMnonexo_censored,
      # size=num_samples,
      label=ct, size=bool_censored))+geom_point(aes (col=ct))+
  geom_hline(yintercept = -log(0.05), lty='dashed')+geom_vline(xintercept = -log(0.05), lty='dashed')+#
  geom_label_repel(size=3.2, alpha=0.6, max.overlaps = 30)+ theme_bw()+
  theme(legend.position = "bottom", legend.text=element_text(size=8))+#
  labs(x=' - Log p-value all signatures', y=' - Log p-value nonexogenous signatures')+#
  guides(size=FALSE, col=FALSE)+ #, col=guide_legend(ncol=4),
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
  lims(x=c(0, 30), y=c(0,30))

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Using size for a discrete variable is not advised.

```



See script PCAWG_HMP_and_alternative_methods.R for the analyses of PCAWG data using alternative models.

Tracksig

```

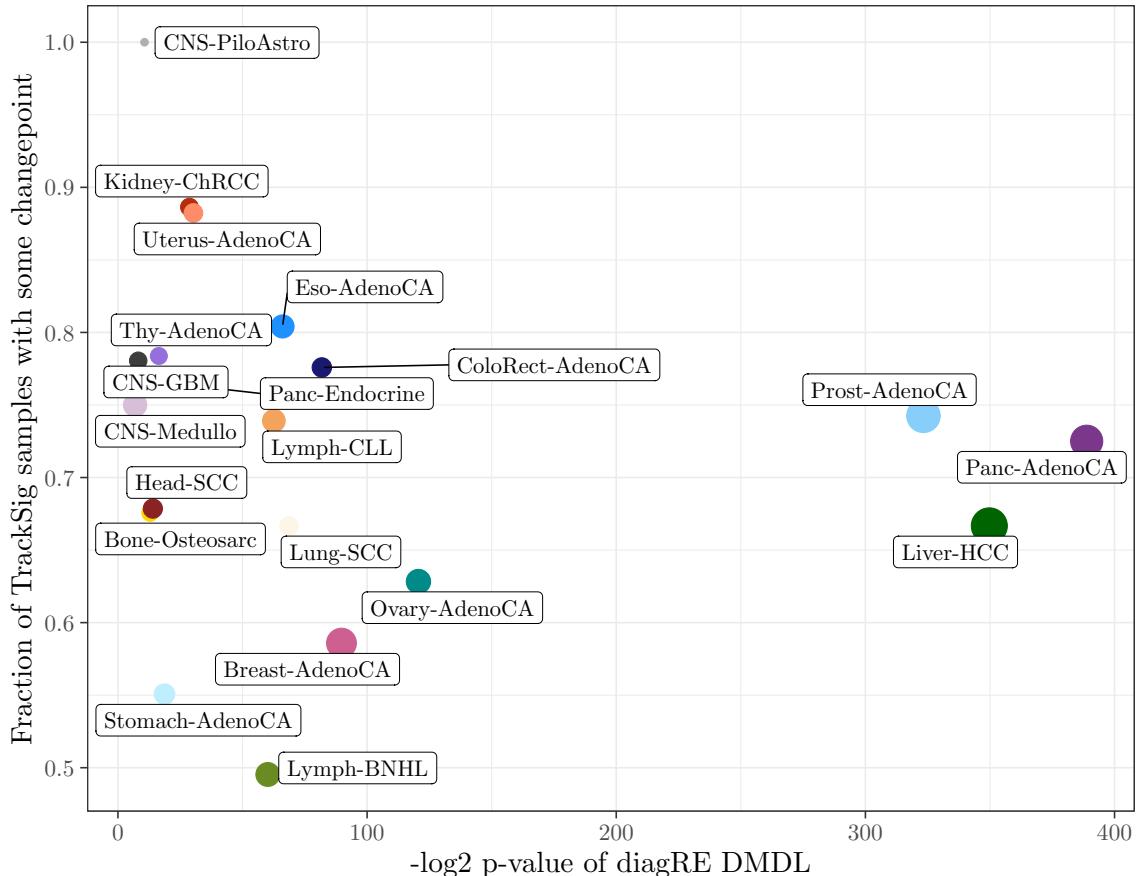
tracksig = read.csv("../data/restricted/tracksig/changepoints_stats_tracksig.csv", stringsAsFactors =
tracksig = tracksig %>% group_by(type) %>%
  dplyr::summarize(count = n(), bool_changepoints=sum(n_changepoints > 0)) %>%
  mutate(tracksig_frac= bool_changepoints/count)
tracksig = cbind.data.frame(pvals_diagRE_DMDL_SP_adj,
                           tracksig[match(names(pvals_diagRE_DMDL_SP_adj), tracksig$type),],
                           effect_size3_SP=effect_size3_SP[match(names(pvals_diagRE_DMDL_SP_adj), names(effect_size3_SP))])
tracksig$ct = rownames(tracksig)
tracksig$minpvals = -log2(tracksig$pvals_diagRE_DM)

pcawg_palette <- pcawg.colour.palette(gsub("\\\\..*", "", tracksig$ct), scheme = "tumour.subtype")
names(pcawg_palette) <- tracksig$ct

ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_SP_adj), y=tracksig_frac, label=ct, size=count))+geom_point()
  labs(x='-log2 p-value of diagRE DMDL', y='Fraction of TrackSig samples with some changepoint')+ 
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
  # scale_x_continuous(trans = "log2")+
  theme_bw() + theme(legend.position = "bottom")

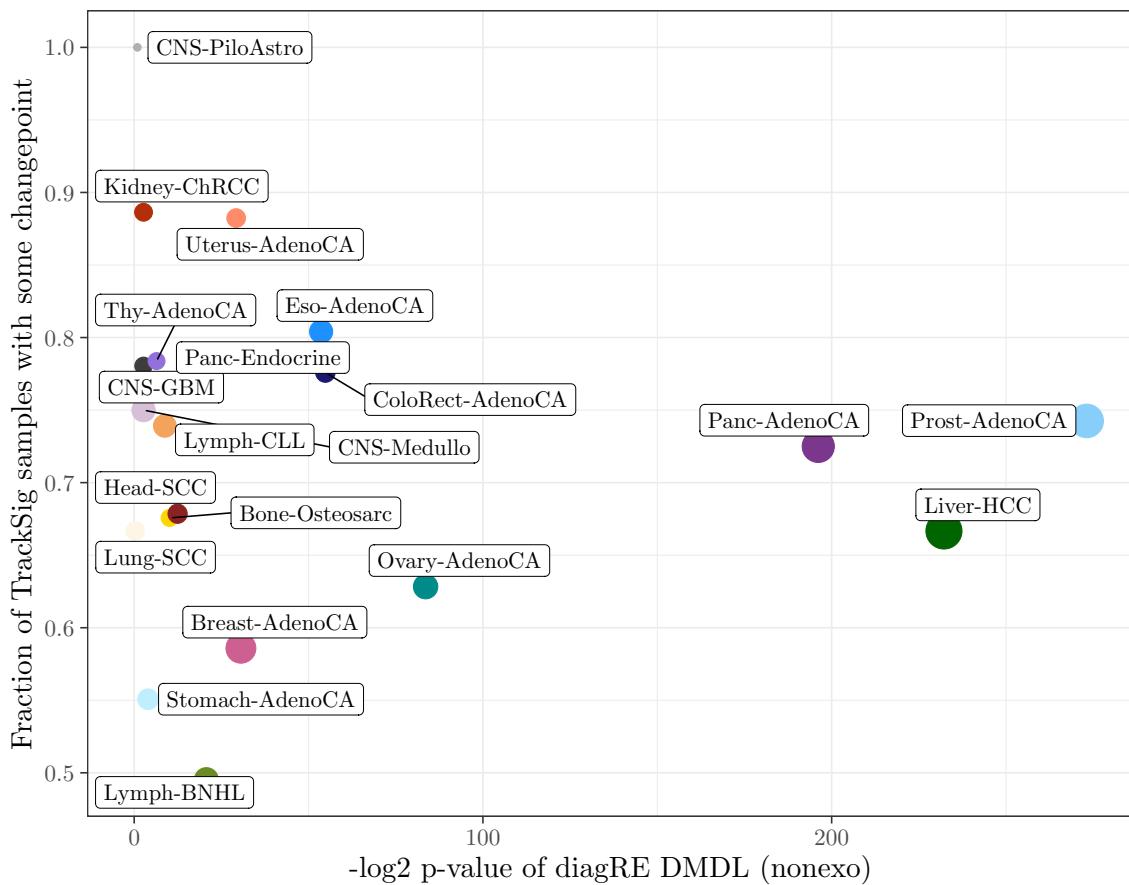
```

```
## Warning: Removed 3 rows containing missing values (geom_point).
## Warning: Removed 3 rows containing missing values (geom_label_repel).
```



```
ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_nonexo_SP_adj), y=tracksig_frac, label=ct, size=count))+
  geom_point()+
  labs(x='-\log2 p-value of diagRE DMDL (nonexo)', y='Fraction of TrackSig samples with some changepoint')+
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
  theme_bw()+theme(legend.position = "bottom")
```

```
## Warning: Removed 3 rows containing missing values (geom_point).
## Warning: Removed 3 rows containing missing values (geom_label_repel).
```



```

  300      ● Bone-Osteosarc   ● ColoRect-AdenoCA   ● Kidney-RCC.papillary   ● Ovary-Aden
ct      ● Breast-AdenoCA   ● Eso-AdenoCA       ● Liver-HCC                 ● Panc-Adeno
      ● CNS-GBM           ● Head-SCC          ● Lung-SCC                  ● Panc-Endoc
      ● CNS-Medullo        ● Kidney-ChRCC       ● Lymph-BNHL                ● Prost-Adenc
      ● CNS-PiloAstro      ● Kidney-RCC.clearcell ● Lymph-CLL                 ● Skin-Melan

```

```

ggplot(tracksig, aes(x=effect_size3_SP, y=tracksig_frac, label=ct, col=ct))+  

  geom_point(aes(size=minpvals))+geom_label_repel(max.overlaps = 5)+  

  labs(x='Effect size', y='Fraction of TrackSig samples with some changepoint', col="")  

  +theme_bw()  

  +scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")  

  +guides(col=guide_legend(ncol=4), size=FALSE)

```

```

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  

## "none")` instead.  

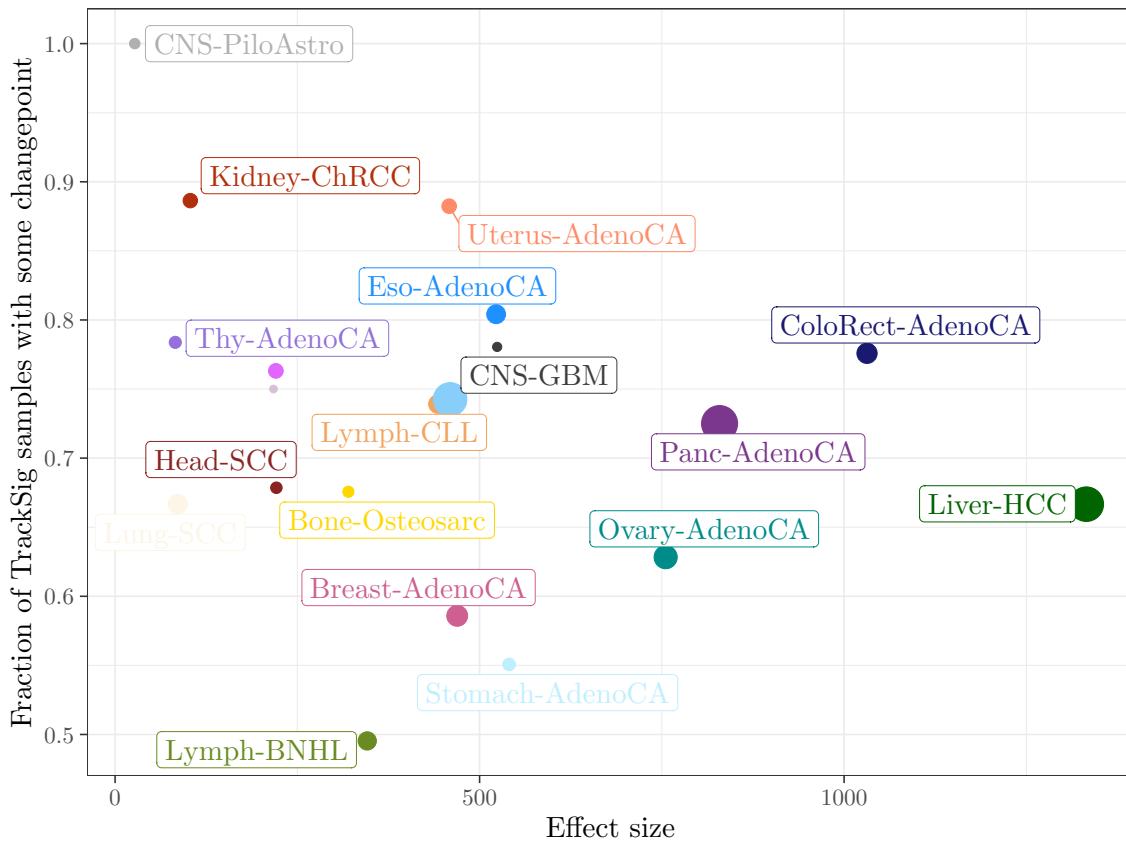
## Warning: Removed 3 rows containing missing values (geom_point).  

## Warning: Removed 3 rows containing missing values (geom_label_repel).  

## Warning: ggrepel: 3 unlabeled data points (too many overlaps). Consider  

## increasing max.overlaps

```



a	Bone-Osteosarc	a	Eso-AdenoCA	a	Lung-SCC	a	Prost-AdenoCA
a	Breast-AdenoCA	a	Head-SCC	a	Lymph-BNHL	a	Skin-Melanoma.cutaneo
a	CNS-GBM	a	Kidney-ChRCC	a	Lymph-CLL	a	Stomach-AdenoCA
a	CNS-Medullo	a	Kidney-RCC.clearcell	a	Ovary-AdenoCA	a	Thy-AdenoCA
a	CNS-PiloAstro	a	Kidney-RCC.papillary	a	Panc-AdenoCA	a	Uterus-AdenoCA
a	ColoRect-AdenoCA	a	Liver-HCC	a	Panc-Endocrine		

Same plots, but smaller, for images

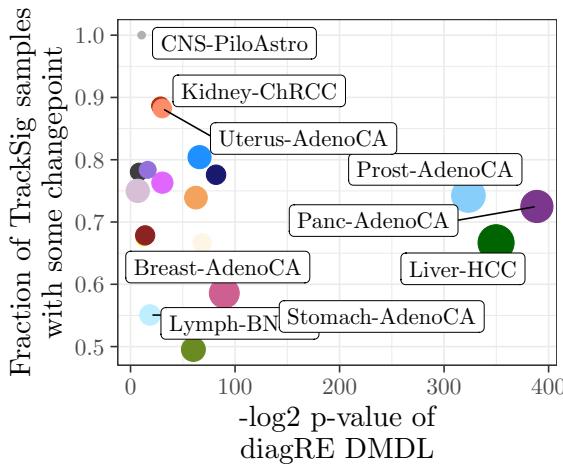
```
ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_SP_adj), y=tracksig_frac, label=ct, size=count))+geom_point()
  labs(x='-log2 p-value of\n diagRE DMDL', y='Fraction of TrackSig samples\n with some changepoint')+ 
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
  # scale_x_continuous(trans = "log2")+
  theme_bw()+theme(legend.position = "bottom")+guides(col=FALSE)+labs(size='N. obs')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

## Warning: Removed 3 rows containing missing values (geom_point).

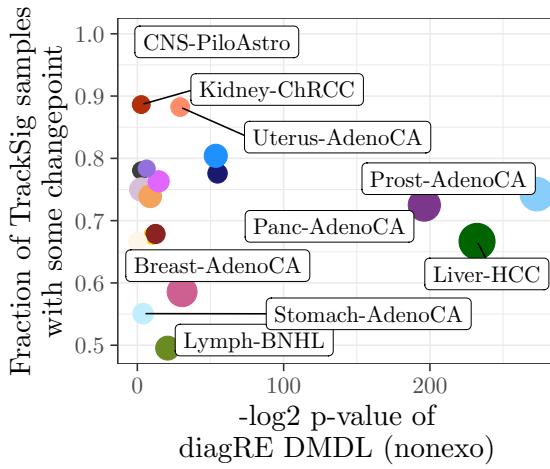
## Warning: Removed 3 rows containing missing values (geom_label_repel).

## Warning: ggrepel: 11 unlabeled data points (too many overlaps). Consider
## increasing max.overlaps
```



```
ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_nonexo_SP_adj), y=tracksig_frac, label=ct, size=count))+
  geom_label_repel(size=3, col='black', max.overlaps = 4) +
  labs(x='-\log2 p-value of\n diagRE DMDL (nonexo)', y='Fraction of TrackSig samples\n with some changepoint') +
  scale_color_manual(values = pcawg_palette) + theme(legend.position = "bottom") +
  theme_bw() + theme(legend.position = "bottom") + guides(col=FALSE) + labs(size='N. obs')
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.  
  
## Warning: Removed 3 rows containing missing values (geom_point).  
  
## Warning: Removed 3 rows containing missing values (geom_label_repel).  
  
## Warning: ggrepel: 11 unlabeled data points (too many overlaps). Consider  
## increasing max.overlaps
```



```
plot_for_ct_legend <- ggplot(tracksig, aes(x=-log2(pvals_diagRE_DMDL_nonexo_SP_adj), y=tracksig_frac, label=ct, size=count))+
  geom_label_repel(size=3, col='black', max.overlaps = 2) +
```

```

labs(x='-log2 p-value of\n diagRE DMDL (nonexo)', y='Fraction of TrackSig samples\n with some changepoi
  scale_color_manual(values = pcawg_palette)+theme(legend.position = "bottom")+
theme_bw()+theme(legend.position = "bottom")+labs(size='N. observations')+guides(size=FALSE)+labs(col='')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

legend_ct <- (cowplot::get_legend(plot_for_ct_legend))

## Warning: Removed 3 rows containing missing values (geom_point).

## Warning: Removed 3 rows containing missing values (geom_label_repel).

# pdf("../results/results_TMB/pcawg/legend_cts.pdf", height = 1, width = 6.5)
grid.newpage()
grid.draw(legend_ct)

● Bone-Osteosarc      ● ColoRect-AdenoCA      ● Kidney-RCC.papillary      ● Ovary-AdenoCA      ● Stomach-AdenoCA
● Breast-AdenoCA     ● Eso-AdenoCA        ● Liver-HCC            ● Panc-AdenoCA       ● Thy-AdenoCA
● CNS-GBM             ● Head-SCC          ● Lung-SCC           ● Panc-Endocrine    ● Uterus-AdenoCA
● CNS-Medullo         ● Kidney-ChRCC        ● Lymph-BNHL          ● Prost-AdenoCA
● CNS-PiloAstro        ● Kidney-RCC.clearcell ● Lymph-CLL           ● Skin-Melanoma.cutaneous

# dev.off()

gerstung_changing_sigs_early_late <- readxl::read_excel("/Users/morril01/Documents/PhD/GlobalDA/data/rest

## New names:
## * ` ` -> ...1

gerstung_changing_sigs_clonal_subclonal <- readxl::read_excel("/Users/morril01/Documents/PhD/GlobalDA/dat

## New names:
## * ` ` -> ...1

# gerstung_changing_sigs <- readxl::read_excel("/Users/morril01/Documents/PhD/GlobalDA/data/restricted/p
# gerstung_changing_sigs <- readxl::read_excel("/Users/morril01/Documents/PhD/GlobalDA/data/restricted/p
# gerstung_constant_sigs <- readxl::read_excel("/Users/morril01/Documents/PhD/GlobalDA/data/restricted/p
# gerstung_changing_sigs
# gerstung_constant_sigs

gerstung_changing_sigs_earlylate <- gerstung_changing_sigs_early_late #gerstung_changing_sigs[gerstung_ch
gerstung_changing_sigs_clonalsubclonal <- gerstung_changing_sigs_clonal_subclonal #gerstung_changing_sigs

gerstung_changing_sigs_earlylate$signature[(gerstung_changing_sigs_earlylate$signature == "SBS6.14.15.20.
gerstung_changing_sigs_clonalsubclonal$signature[(gerstung_changing_sigs_clonalsubclonal$signature == "SE
gerstung_changing_sigs_earlylate$signature <- gsub("_", ".", gerstung_changing_sigs_earlylate$signature)
gerstung_changing_sigs_clonalsubclonal$signature <- gsub("_", ".", gerstung_changing_sigs_clonalsubclonal

# df_changes_el <- gerstung_changing_sigs_earlylate %>% group_by(signature) %>% dplyr::summarise(median(
# df_changes_cs <- gerstung_changing_sigs_clonalsubclonal %>% group_by(signature) %>% dplyr::summarise(m
df_changes_el <- gerstung_changing_sigs_earlylate %>% group_by(signature) %>% dplyr::summarise(median(log(
df_changes_cs <- gerstung_changing_sigs_clonalsubclonal %>% group_by(signature) %>% dplyr::summarise(medi

```

```

# grid.arrange(ggplot(gerstung_changing_sigs_earlylate, aes(x=factor(signature, levels=df_changes_el$signature),
#                                         y=mean_change, group=signature, col=histology_abbreviation))+geom_boxplot()
#                                         geom_hline(yintercept = 0, lty='dashed')+guides(col=FALSE)+theme_bw())
#     theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late'),
# ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=factor(signature, levels=df_changes_cs$signature,
#                                         y=mean_change, group=signature, col=histology_abbreviation))+geom_boxplot()+
#     geom_jitter()+guides(col=FALSE)+theme_bw())
#     theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Clonal vs subclonal'),
# nrow=2)

## removing cancer types where there aren't many observations
select_self <- function(i) i[i]
gerstung_changing_sigs_earlylate <- gerstung_changing_sigs_earlylate %>% dplyr::filter(signature %in% names(select_self))
gerstung_changing_sigs_clonalsubclonal <- gerstung_changing_sigs_clonalsubclonal %>% dplyr::filter(signature %in% names(select_self))

pcawg_palette <- pcawg.colour.palette(x = gsub("-", ".", tolower(gsub("\\\\..*", "", sort(unique(gerstung_changing_sigs_earlylate$tumour_type)))))

## Warning in pcawg.colour.palette(x = gsub("-", ".", tolower(gsub("\\\\..*", :, :
## Unrecognized input value for x. Default to fill.colour.
names(pcawg_palette) <- sort(unique(gerstung_changing_sigs_earlylate$tumour_type))

unique(gerstung_changing_sigs_clonal_subclonal$signature)

## [1] "DBS2"                  "DBS5"                  "ID1"
## [4] "ID2"                   "ID8"                   "n_unassigned"
## [7] "SBS1"                   "SBS2.13"                "SBS3"
## [10] "SBS40"                 "SBS4"                  "SBS16"
## [13] "SBS4"                   "SBS5"                  "SBS6"
## [16] "DBS9"                   "DBS10"                 "DBS3"
## [19] "SBS10"                 "SBS28"                 "DBS11"
## [22] "SBS18"                 "SBS12"                 "SBS17"
## [25] "DBS7"                   "SBS37"                 "SBS9"
## [28] "SBS8"                   "SBS41"                 "SBS35"
## [31] "DBS1"                   "ID13"                  "SBS7"
## [34] "SBS54"                 "DBS8"                  "SBS38"
## [37] "SBS22"                 "SBS34"                 "SBS56"
## [40] "SBS29"                 "SBS6.14.15.20.21.26.44" "SBS36"
## [43] "SBS30"                 "SBS31"                 "SBS33"
## [46] "SBS39"                 "SBS24"                 "SBS11"
## [49] "SBS19"                 "SBS23"                 "SBS23"

gerstung_changing_sigs_earlylate$signature <- factor(gerstung_changing_sigs_earlylate$signature,
                                                       levels=df_changes_el$signature[order(df_changes_el$signature)])
gerstung_changing_sigs_clonalsubclonal$signature <- factor(gerstung_changing_sigs_clonalsubclonal$signature,
                                                               levels=df_changes_cs$signature[order(df_changes_cs$signature)])

# grid.arrange(ggplot(gerstung_changing_sigs_earlylate, aes(x=signature,
#                                         y=log2fc_earlyLate, group=signature, col=tumor_type)))

```

```

# geom_hline(yintercept = 0, lty='dashed')+  

# guides(col=FALSE)+theme_bw()+
# theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late')  

# scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between early  

# ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=signature,  

# y=log2fc_clonalSubclonal, group=signature)  

# geom_hline(yintercept = 0, lty='dashed')+  

# geom_boxplot()+ geom_jitter(alpha=0.2)+guides(col=FALSE)+theme_bw()+
# theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Clonal vs subclonal')  

# scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between clonal vs  

# nrow=2)  

ggplot(gerstung_changing_sigs_earlylate, aes(x=signature,  

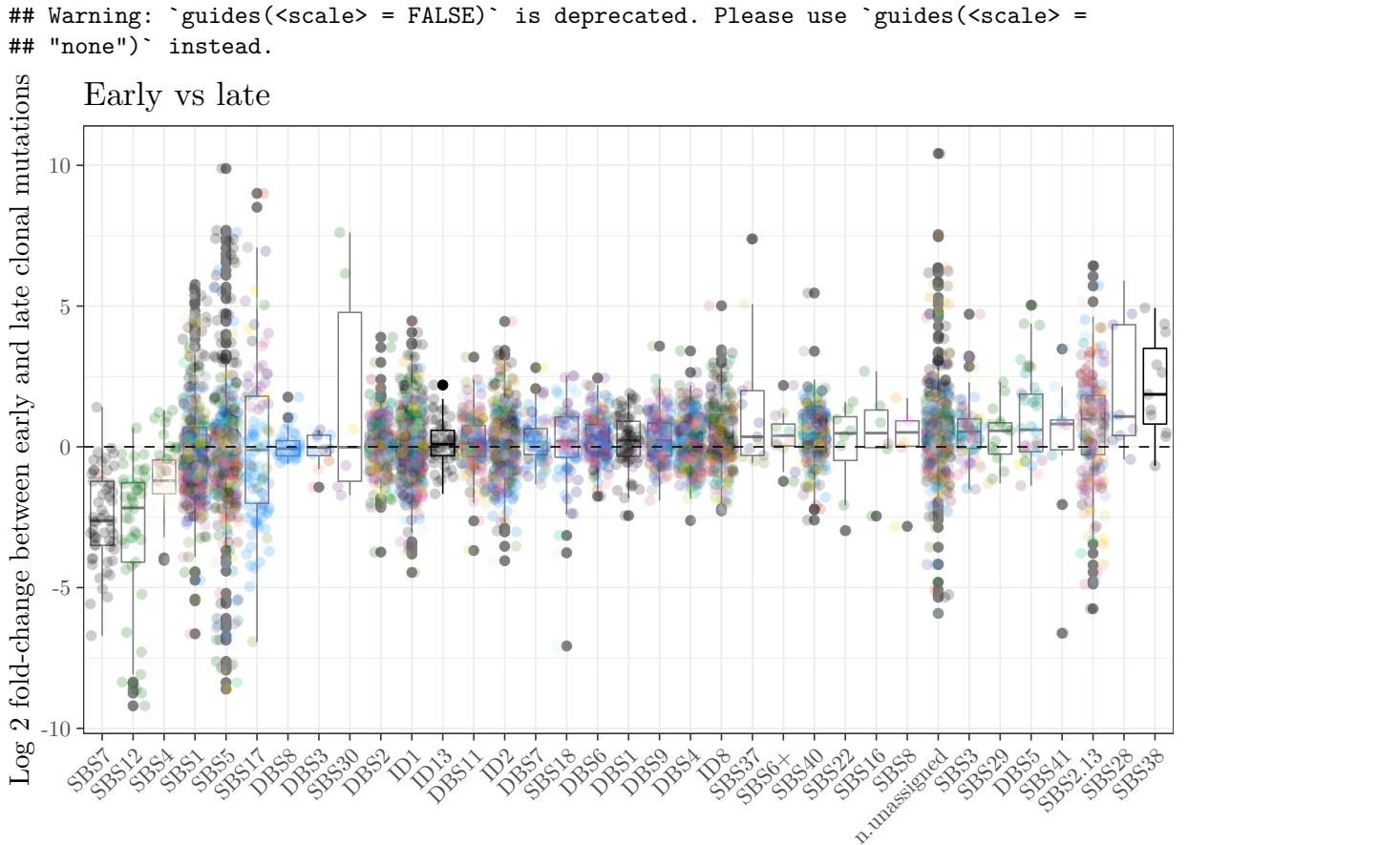
y=log2fc_earlyLate, group=signature,col=tumour)  

geom_hline(yintercept = 0, lty='dashed')+  

guides(col=FALSE)+theme_bw()+
theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late')  

scale_color_manual(values = pcawg_palette)+labs(x='signature', y='Log 2 fold-change between early and late clonal mutations')

```



```

ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=signature,  

y=log2fc_clonalSubclonal, group=signature)  

geom_hline(yintercept = 0, lty='dashed')+  

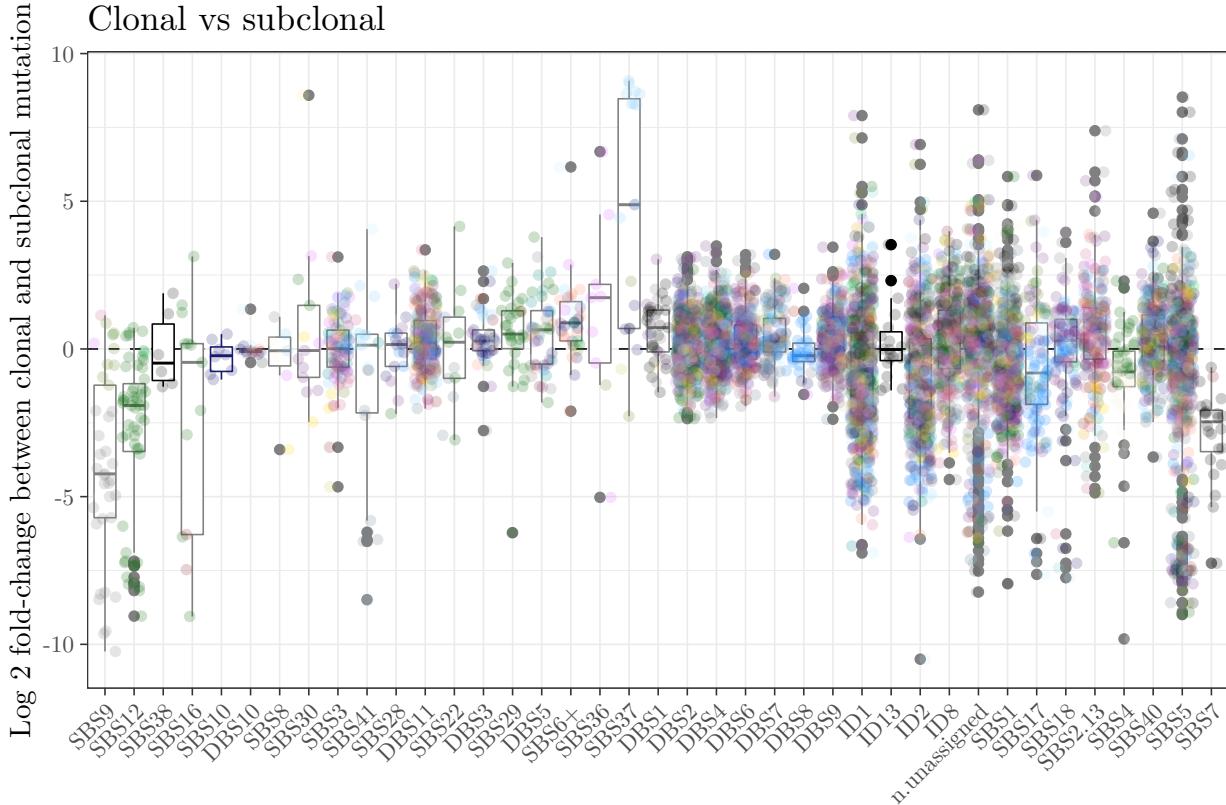
geom_boxplot()+ geom_jitter(alpha=0.2)+guides(col=FALSE)+theme_bw()+
theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Clonal vs subclonal')

```

```

  scale_color_manual(values = pcawg_palette)+labs(x=' ', y='Log 2 fold-change between clonal
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
## Warning: Removed 38 rows containing non-finite values (stat_boxplot).
## Warning: Removed 38 rows containing missing values (geom_point).

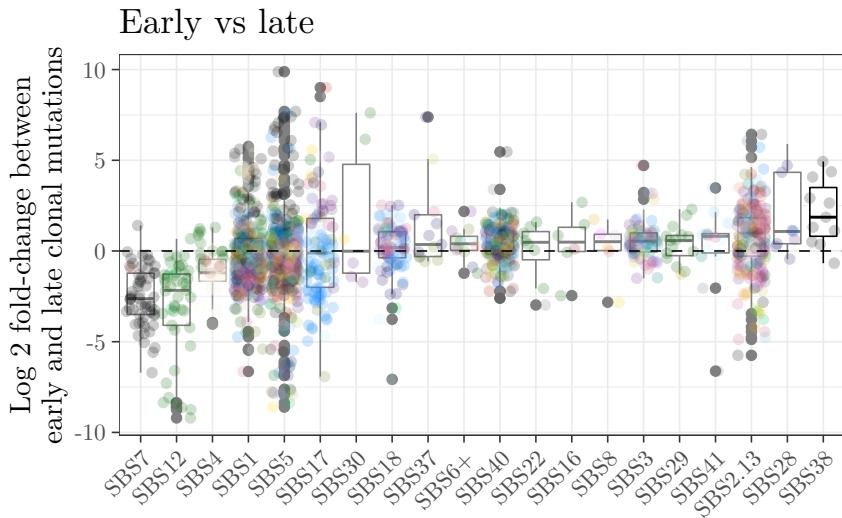
```



```

ggplot(gerstung_changing_sigs_earlylate[grepl('SBS', gerstung_changing_sigs_earlylate$signature),], aes(x=
y=log2fc_earlyLate, group=signature,col=tumour_
geom_hline(yintercept = 0, lty='dashed')+guides(col=FALSE)+theme_bw()+
theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Early vs late')+scale_color_manual(values = pcawg_palette)+labs(x=' ', y='Log 2 fold-change between \nearly
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

```

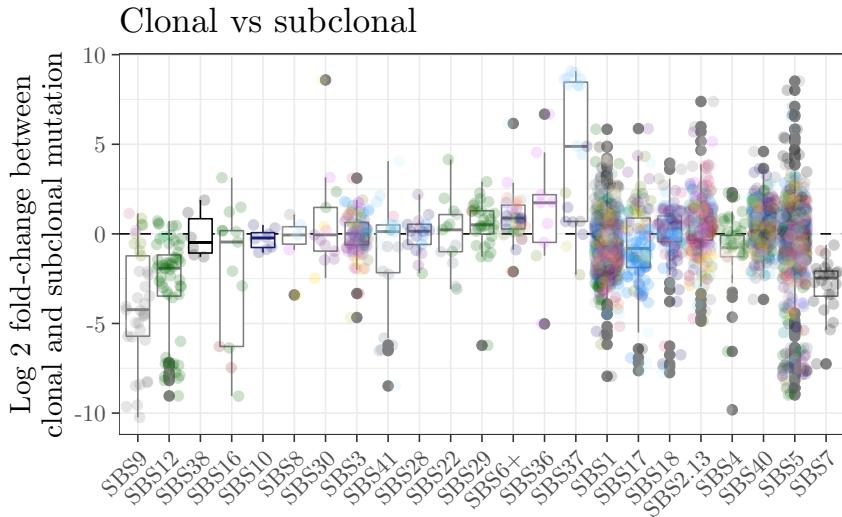


```
ggplot(gerstung_changing_sigs_clonalsubclonal[grep('SBS', gerstung_changing_sigs_clonalsubclonal$signature),
                                               y=log2fc_clonalSubclonal, group=signature]) +
  geom_hline(yintercept = 0, lty='dashed') +
  geom_boxplot() + geom_jitter(alpha=0.2)+guides(col=FALSE)+theme_bw()+
  theme(axis.text.x=element_text(angle = 45, hjust = 1, vjust=1))+ggtitle('Clonal vs subclonal')
  scale_color_manual(values = pcawg_palette)+labs(x=' ', y='Log 2 fold-change between \nclonal\nand subclonal')

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.

## Warning: Removed 13 rows containing non-finite values (stat_boxplot).

## Warning: Removed 13 rows containing missing values (geom_point).
```



```
df_changes_el_persample <- gerstung_changing_sigs_earlylate %>% group_by(samplename) %>% dplyr:::summarise()
df_changes_cs_persample <- gerstung_changing_sigs_clonalsubclonal %>% group_by(samplename) %>% dplyr:::summarise()
gerstung_changing_sigs_earlylate$samplename <- factor(gerstung_changing_sigs_earlylate$samplename,
                                                       levels=df_changes_el_persample$samplename[order])
gerstung_changing_sigs_clonalsubclonal$samplename <- factor(gerstung_changing_sigs_clonalsubclonal$samplename,
                                                               levels=df_changes_cs_persample$samplename[order])
```

```

table(is.na(gerstung_changing_sigs_earlylate$samplename))

##
## FALSE
## 5347

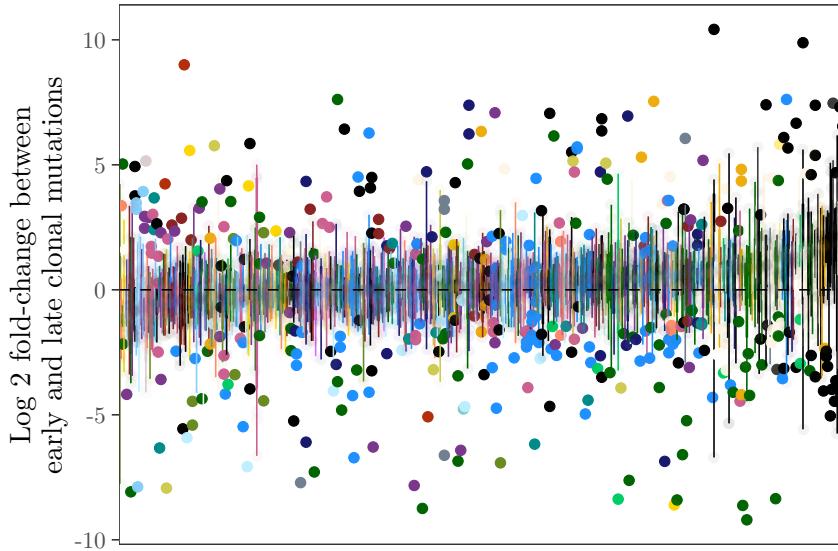
table(is.na(gerstung_changing_sigs_clonalsubclonal$samplename))

##
## FALSE
## 7216

ggplot(gerstung_changing_sigs_earlylate, aes(x=samplename,
                                               y=log2fc_earlyLate, group=samplename, col=tumour_type))+
  geom_hline(yintercept = 0, lty='dashed')+
  guides(col=FALSE)+theme_bw()+
  theme(axis.title.x=element_blank(),
        axis.text.x=element_blank(),
        axis.ticks.x=element_blank())+
  scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between\nnearly and late clonal mutations')+
  theme(panel.grid.major = element_blank(), panel.grid.minor = element_blank())

```

Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.



```

ggplot(gerstung_changing_sigs_clonalsubclonal, aes(x=samplename,
                                                       y=log2fc_clonalSubclonal, group=samplename, col=tumour_type))+
  geom_hline(yintercept = 0, lty='dashed')+
  geom_boxplot()+
  geom_jitter(alpha=0.05)+guides(col=FALSE)+theme_bw()+
  theme(axis.title.x=element_blank(),
        axis.text.x=element_blank(),
        axis.ticks.x=element_blank())+ggtitle('Clonal vs subclonal')+
  scale_color_manual(values = pcawg_palette)+labs(x='', y='Log 2 fold-change between\nnclonal and subclonal mutations')+
  theme(panel.grid.major = element_blank(), panel.grid.minor = element_blank())

```

Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.

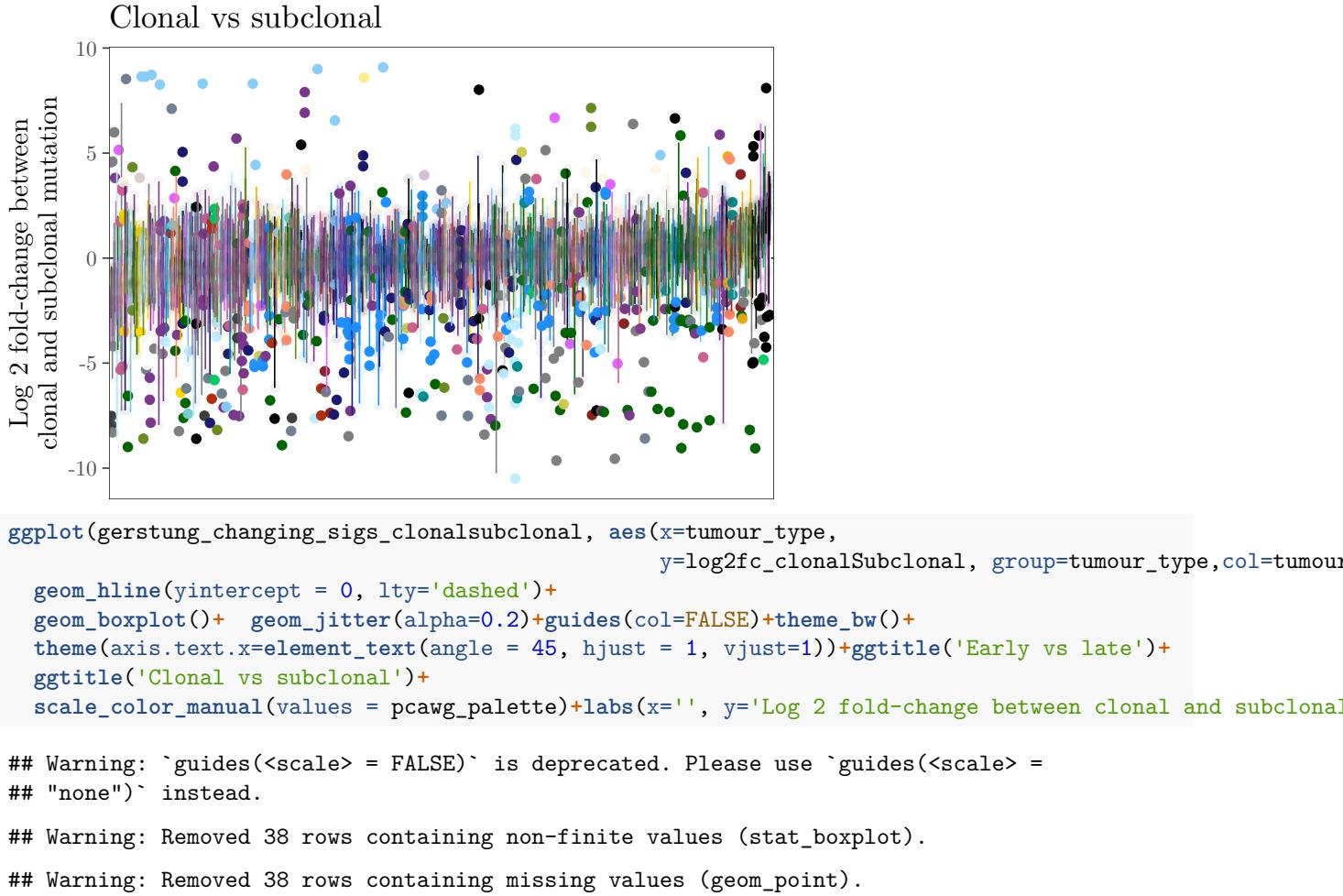
```

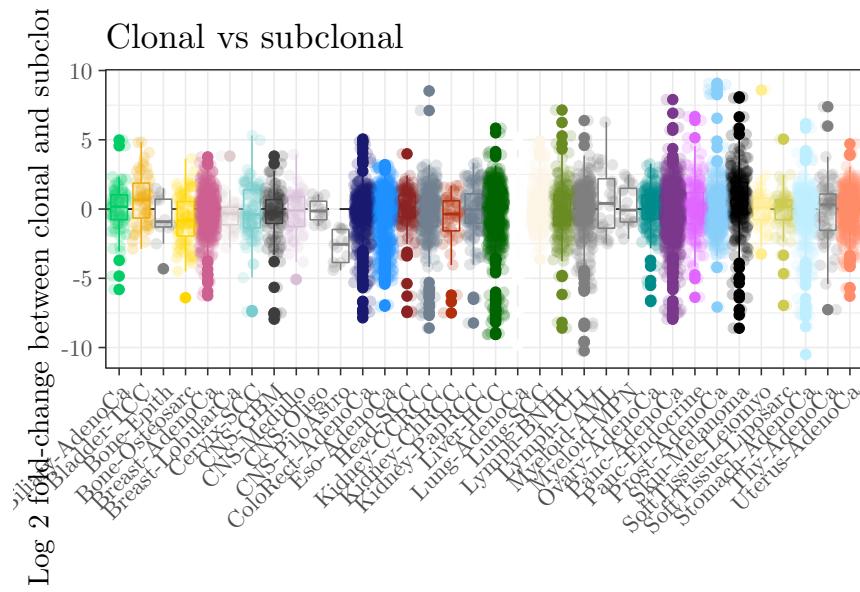
## "none")` instead.

## Warning: Removed 38 rows containing non-finite values (stat_boxplot).

## Warning: Removed 38 rows containing missing values (geom_point).

```





```

gerstung_changing_sigs_clonalsubclonal_var <- gerstung_changing_sigs_clonalsubclonal %>%
  dplyr::group_by(tumour_type) %>% summarise(varlog2=var(log2fc_clonalSubclonal), count=n())
ggplot(gerstung_changing_sigs_clonalsubclonal_var,
       aes(x=varlog2, y=count, label=tumour_type, col=tumour_type)) + geom_point() +
  scale_color_manual(values = pcawg_palette) + guides(col=FALSE) + theme_bw() + geom_label_repel(max.overlaps =

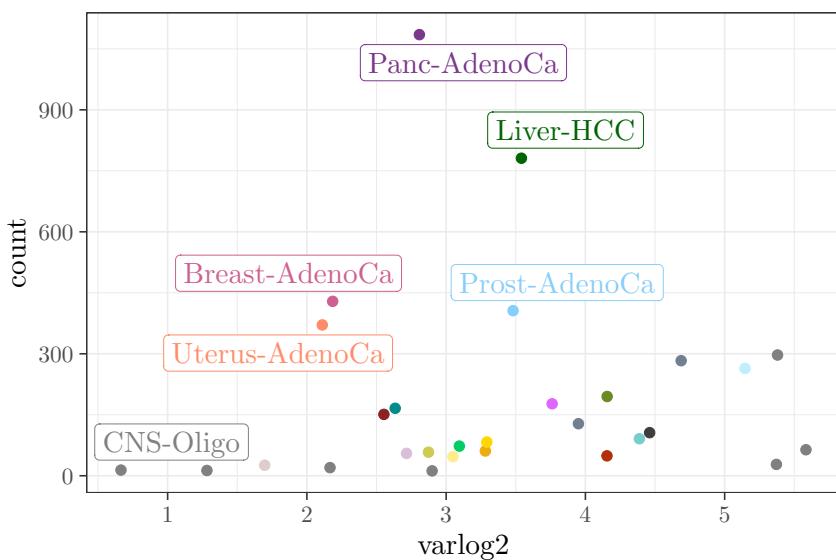
```

Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> = "none")` instead.

Warning: Removed 4 rows containing missing values (geom_point).

Warning: Removed 4 rows containing missing values (geom_label_repel).

Warning: ggrepel: 24 unlabeled data points (too many overlaps). Consider increasing max.overlaps



```

  labs(x='Variance of log2 fold change in cancer type', y='Number of observations')

## $x
## [1] "Variance of log2 fold change in cancer type"
##
## $y
## [1] "Number of observations"
##
## attr(,"class")
## [1] "labels"

perturbed_betas_diagRE_DMDL_nonexo_SP_df_summary <- perturbed_betas_diagRE_DMDL_nonexo_SP_df %>% dplyr::g
  summarise(meanperturbed=mean( !(perturbed == 'FALSE')))

perturbed_betas_diagRE_DMDL_nonexo_SP_df_summary

## # A tibble: 32 x 2
##       sig   meanperturbed
##   <chr>      <dbl>
## 1 SBS10a      0
## 2 SBS10b      0
## 3 SBS12      1
## 4 SBS13     0.25
## 5 SBS14     0.5
## 6 SBS15    0.333
## 7 SBS16     0.5
## 8 SBS17a    0.364
## 9 SBS17b    0.0909
## 10 SBS18     0.3
## # ... with 22 more rows

comparison_with_gerstung_earlylate <- cbind.data.frame(perturbed_betas_diagRE_DMDL_nonexo_SP_df_summary,
                                                       df_changes_el[match(perturbed_betas_diagRE_DM
                                                       df_changes_el$signature),

comparison_with_gerstung_earlylate

##       sig meanperturbed signature median(log2fc_earlyLate)
## 1 SBS10a 0.000000000 <NA>          NA
## 2 SBS10b 0.000000000 <NA>          NA
## 3 SBS12 1.000000000 SBS12 -2.16839553
## 4 SBS13 0.250000000 <NA>          NA
## 5 SBS14 0.500000000 <NA>          NA
## 6 SBS15 0.333333333 <NA>          NA
## 7 SBS16 0.500000000 SBS16 0.48743401
## 8 SBS17a 0.36363636 <NA>          NA
## 9 SBS17b 0.09090909 <NA>          NA
## 10 SBS18 0.30000000 SBS18 0.19987446
## 11 SBS19 0.50000000 SBS19 -1.96353701
## 12 SBS2 0.17647059 <NA>          NA
## 13 SBS20 1.00000000 <NA>          NA
## 14 SBS21 0.00000000 <NA>          NA
## 15 SBS22 0.00000000 SBS22 0.47923554
## 16 SBS23 0.00000000 <NA>          NA

```

```

## 17 SBS24 0.00000000 SBS24 -10.24985022
## 18 SBS26 0.33333333 <NA> NA
## 19 SBS28 0.50000000 SBS28 1.07561394
## 20 SBS3 0.09090909 SBS3 0.53915013
## 21 SBS30 0.20000000 SBS30 -0.01377077
## 22 SBS33 0.50000000 <NA> NA
## 23 SBS34 0.00000000 SBS34 -0.20973256
## 24 SBS36 0.50000000 SBS36 0.99203837
## 25 SBS37 0.40000000 SBS37 0.35693398
## 26 SBS38 0.00000000 SBS38 1.86314214
## 27 SBS39 0.50000000 SBS39 -0.28583208
## 28 SBS40 0.25000000 SBS40 0.46436260
## 29 SBS41 0.00000000 SBS41 0.80987484
## 30 SBS6 0.20000000 <NA> NA
## 31 SBS8 0.25000000 SBS8 0.51226887
## 32 SBS9 0.33333333 SBS9 1.61493581

```

```

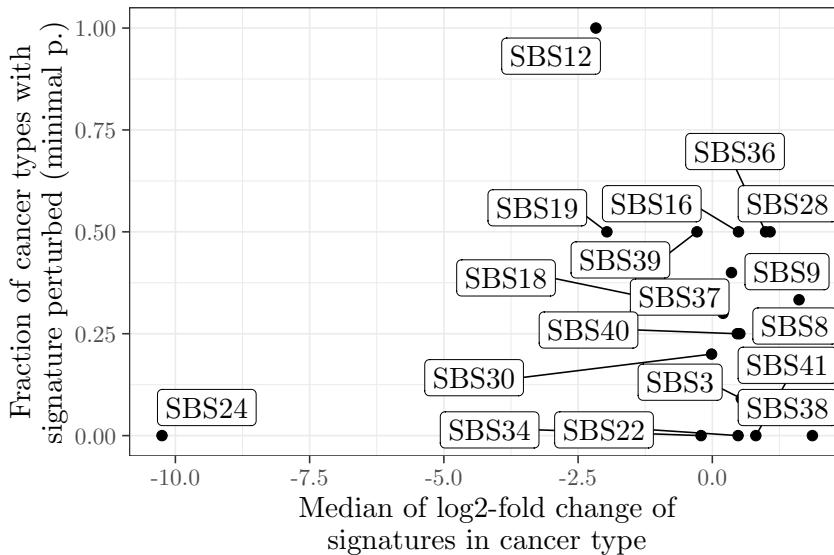
comparison_with_gerstung_earlylate$medianlog2fcearlylate = comparison_with_gerstung_earlylate$`median(log2fc)`

ggplot(comparison_with_gerstung_earlylate, aes(x=medianlog2fcearlylate, y=meanperturbed, label=signature))
  labs(x='Median of log2-fold change of\nsignatures in cancer type', y='Fraction of cancer types with\nsignatures')

## Warning: Removed 14 rows containing missing values (geom_point).

## Warning: Removed 14 rows containing missing values (geom_label_repel).

```



Barplots of cancer types with and without differential abundance

```

give_barplot_from_obj(obj = signatures_PCAWG[['CNS-Medullo']], legend_on = F,
                      nrow=1, verbose=F,
                      only_normalised=T)

```

```

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

```

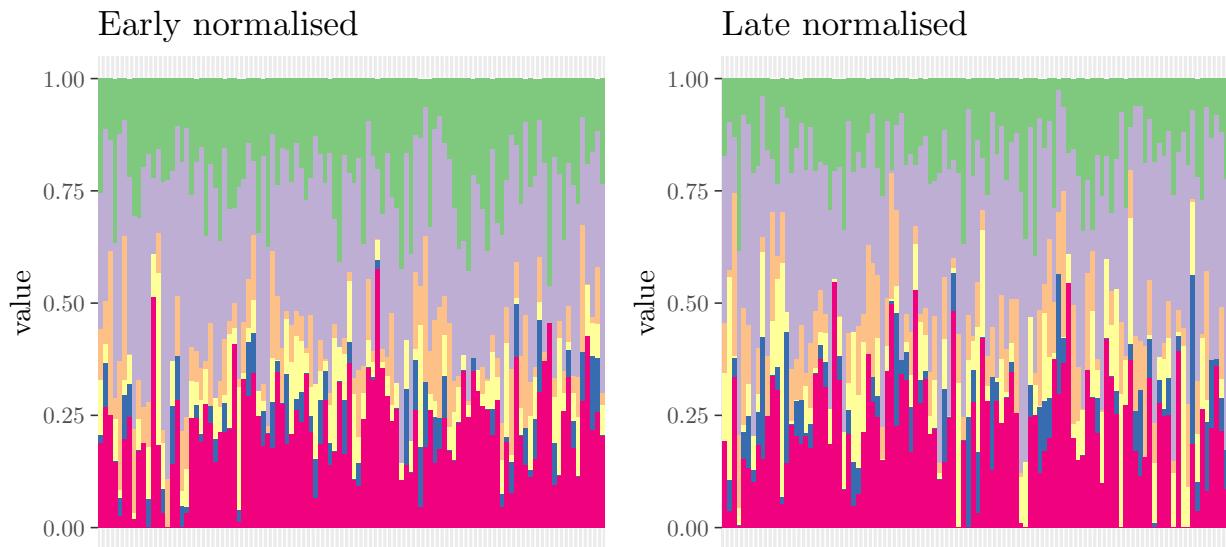
```

## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.

```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.
```



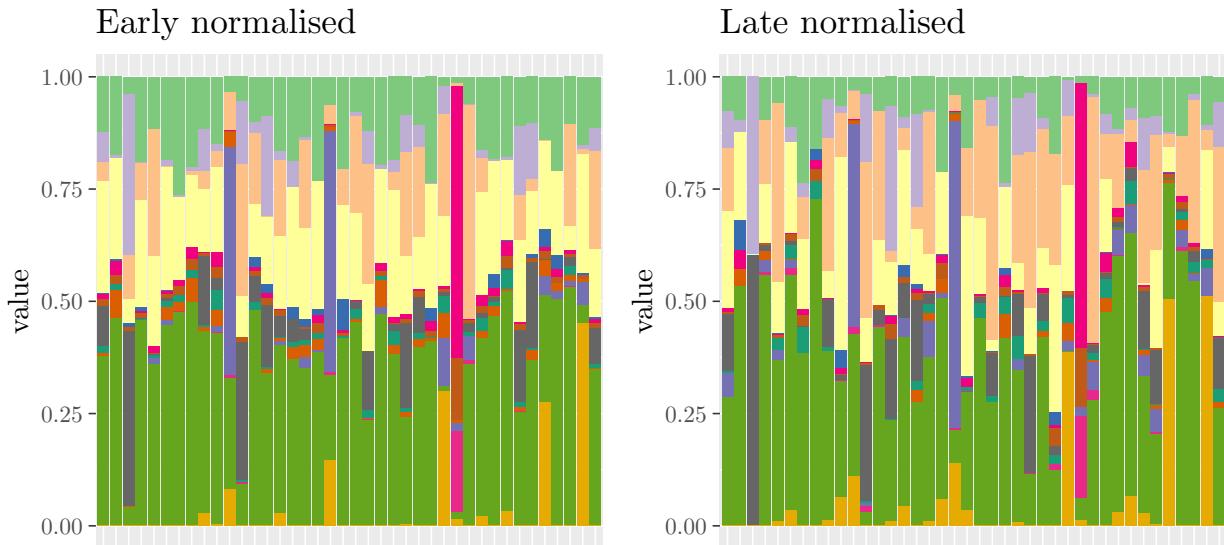
```
give_barplot_from_obj(obj = signatures_PCAWG[['Uterus-AdenoCA']], legend_on = F,  
                      nrow=1, verbose=F,  
                      only_normalised=T)
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =  
## "none")` instead.
```



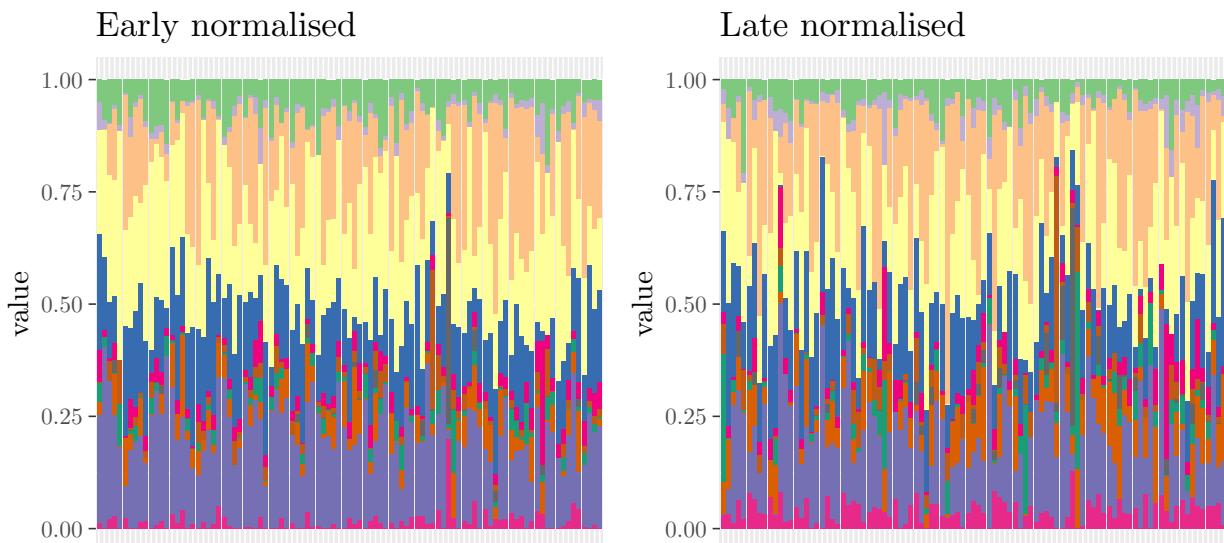
```
give_barplot_from_obj(obj = signatures_PCAWG[['Ovary-AdenoCA']], legend_on = F,
                      nrow=1, verbose=F,
                      only_normalised=T)
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```

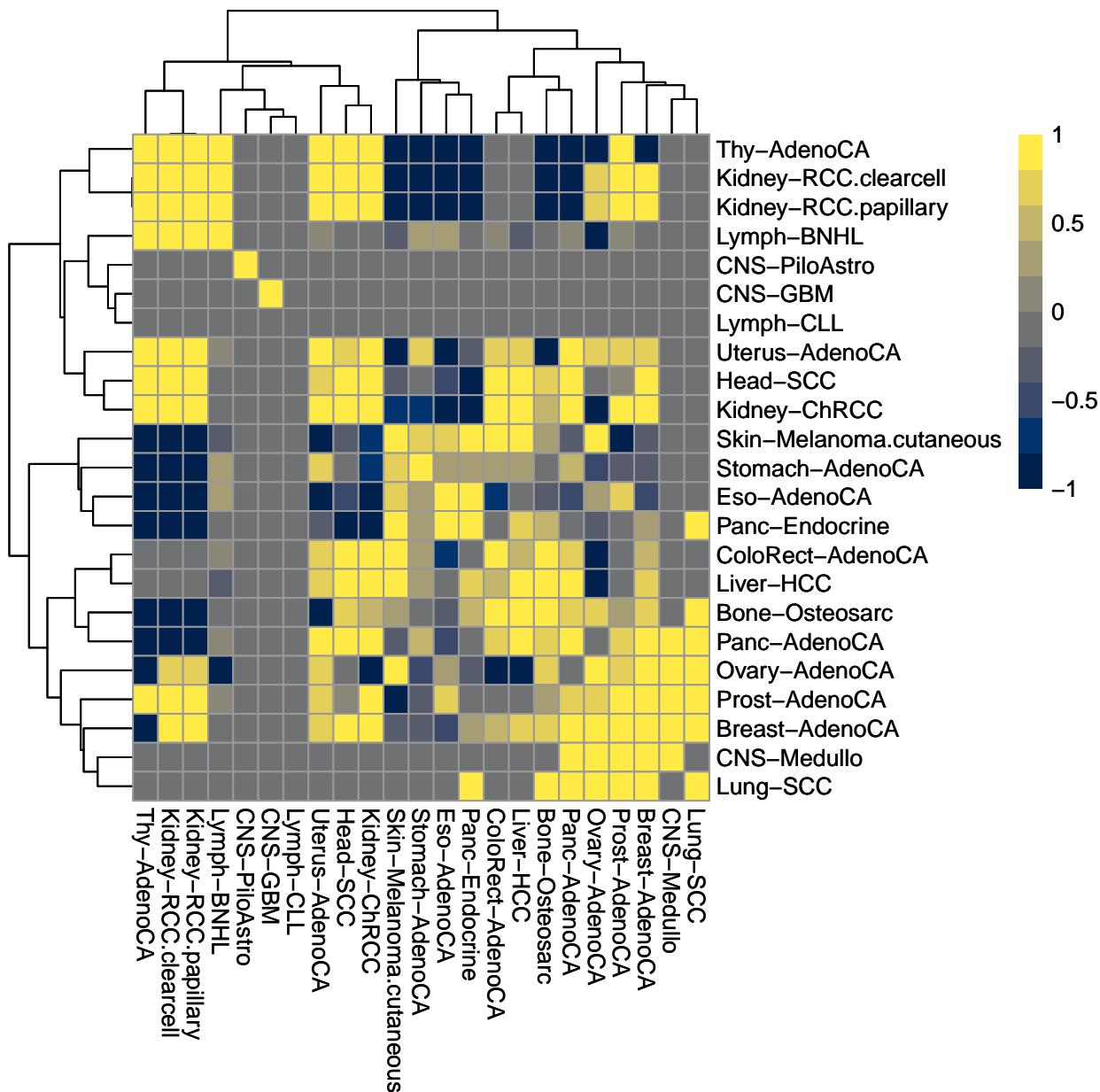
```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```

```
## Warning: `guides(<scale> = FALSE)` is deprecated. Please use `guides(<scale> =
## "none")` instead.
```



Correlations of cancer types and of signatures based on betas



```
## null device
##      1
## null device
##      1
```

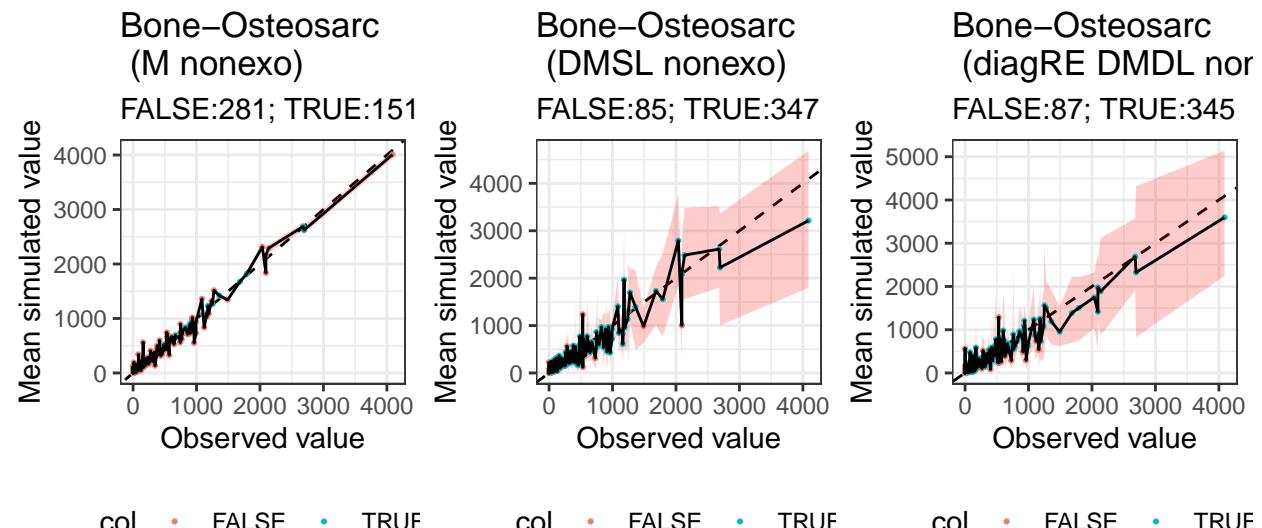
Ranked plots

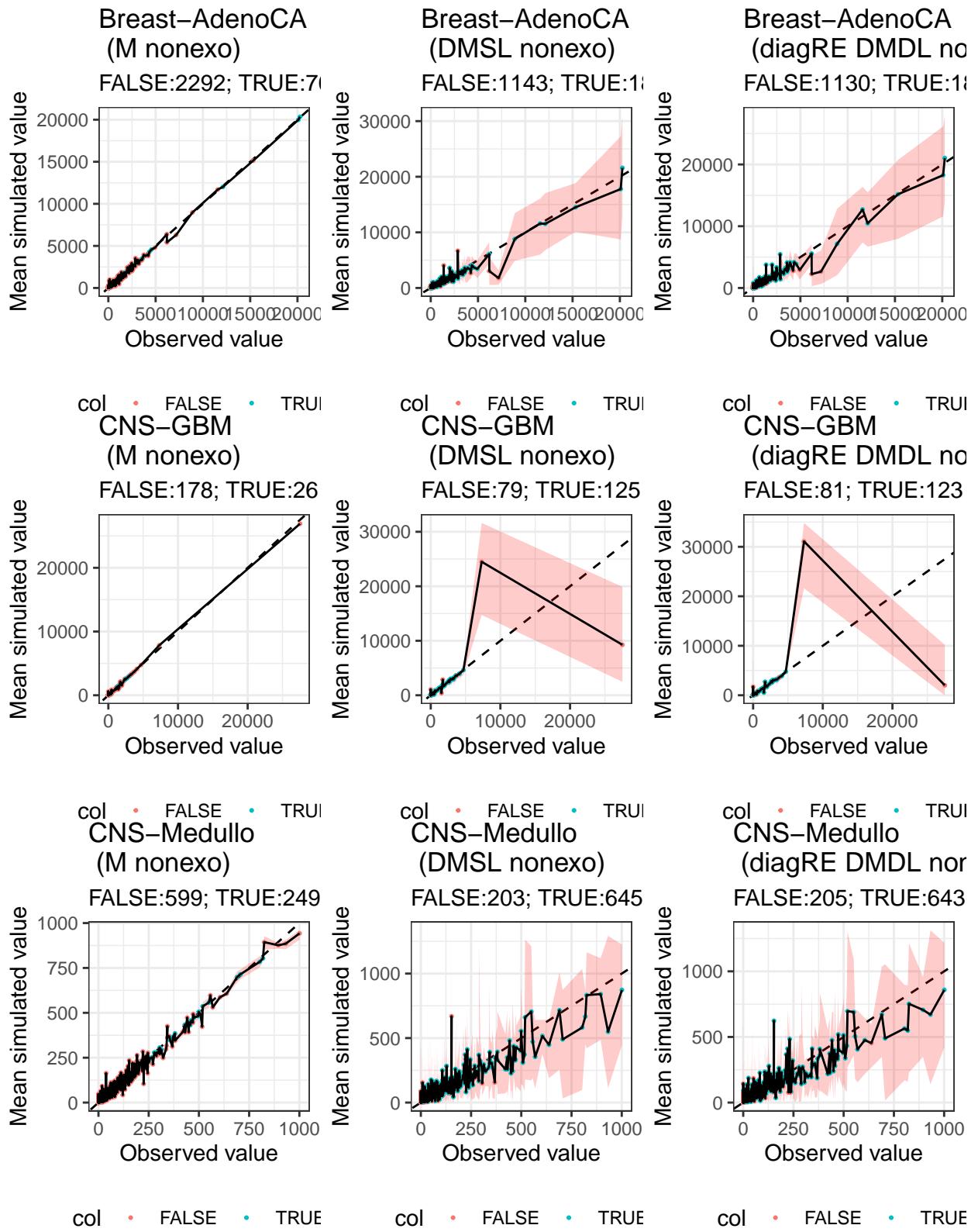
```
for(ct in enough_samples){
  integer_overdispersion_param_DMSL <- 1
  grid.arrange(give_interval_plots_2(df_rank = lapply(list(give_ranked_plot_simulation(tmb_fit_object =
    data_object = all_objects_nonexo_SP[[ct]]),
```

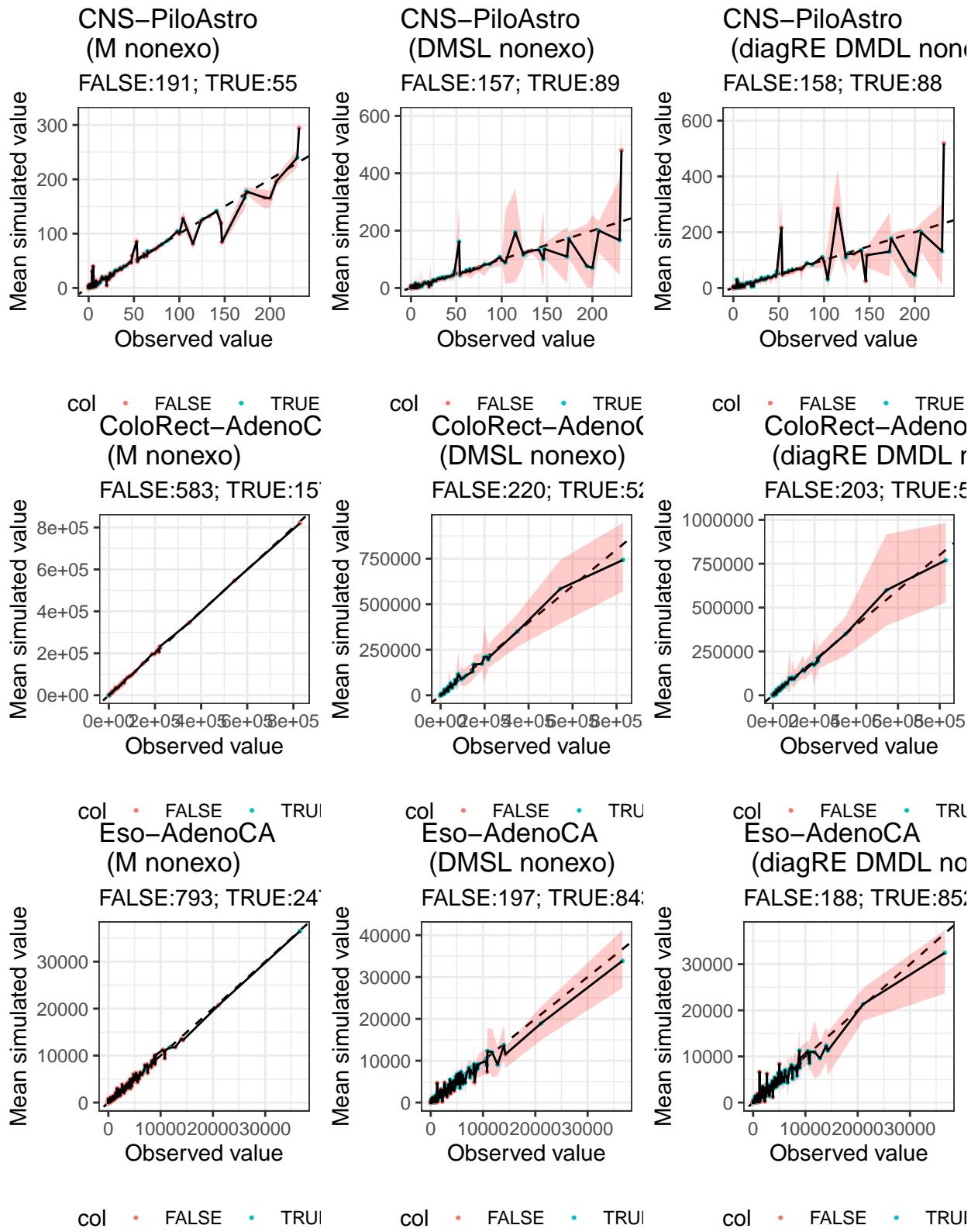
```

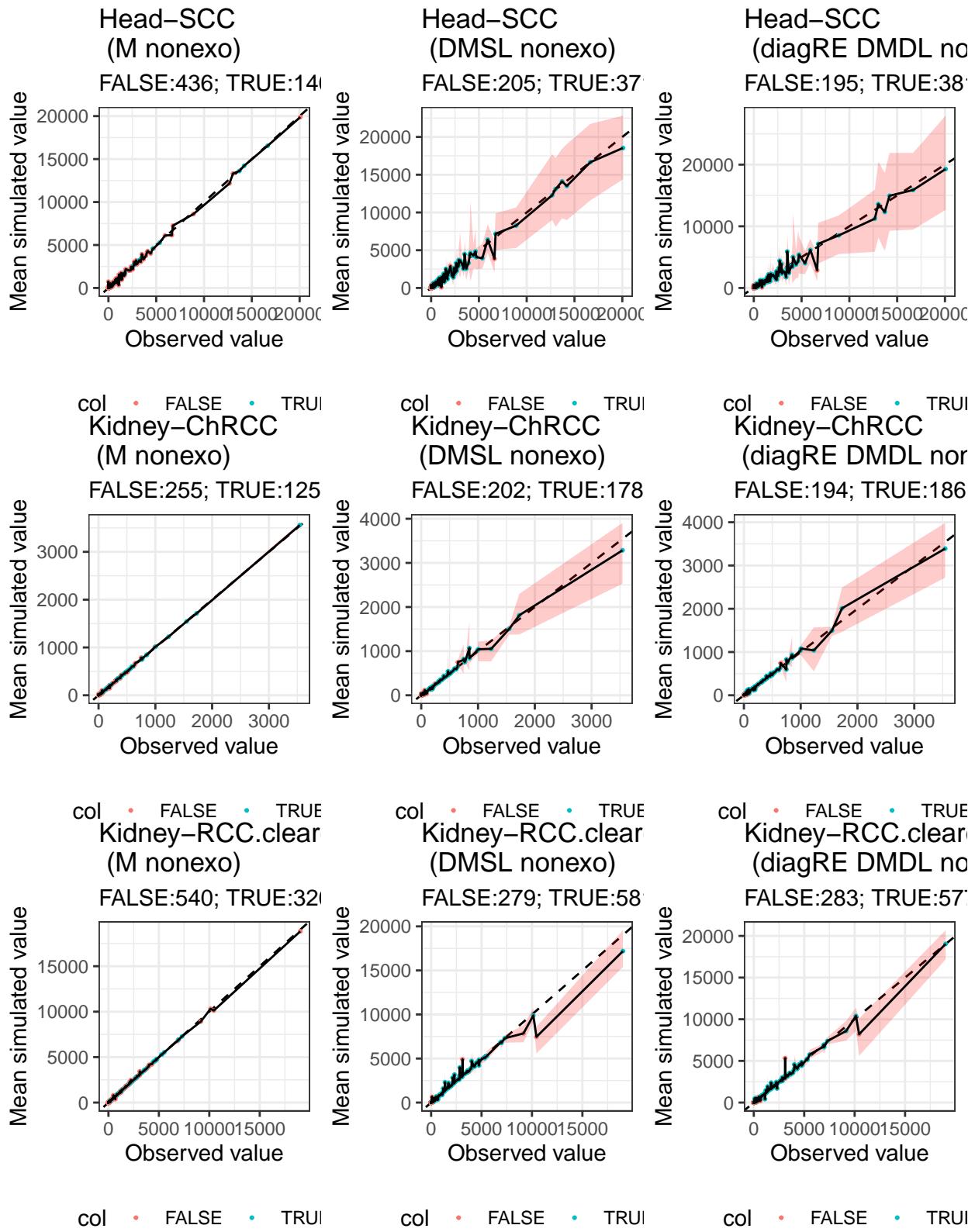
print_plot = F, nreps = 20, model = "M")), function(i){
  lapply(i, function(j) cbind.data.frame(sorted_value=as.vector(j),
                                         rank_number=1:length(j)) )}[[1]],
  data_object = all_objects_nonexo_SP[[ct]],
  loglog = F, title = paste0(ct, '\n (M nonexo)'), 
give_interval_plots_2(df_rank = lapply(list(give_ranked_plot_simulation(tmb_fit_object = fullRE_DMSL_r
  data_object = all_objects_nonexo_SP[[ct]],
  print_plot = F, nreps = 20, model = "DMSL", integer_overdispersion_param = integer_ove
    lapply(i, function(j) cbind.data.frame(sorted_value=as.vector(j),
                                           rank_number=1:length(j)) )}[[1]],
  data_object = all_objects_nonexo_SP[[ct]],
  loglog = F, title = paste0(ct, '\n (DMSL nonexo)'), 
give_interval_plots_2(df_rank = lapply(list(give_ranked_plot_simulation(tmb_fit_object = diagRE_DMDL_r
  data_object = all_objects_nonexo_SP[[ct]],
  print_plot = F, nreps = 20, model = "DM", integer_overdispersion_param = 1000)), funct
    lapply(i, function(j) cbind.data.frame(sorted_value=as.vector(j),
                                           rank_number=1:length(j)) )}[[1]],
  data_object = all_objects_nonexo_SP[[ct]],
  loglog = F, title = paste0(ct, '\n (diagRE DMDL nonexo)'), ncol=3)
}

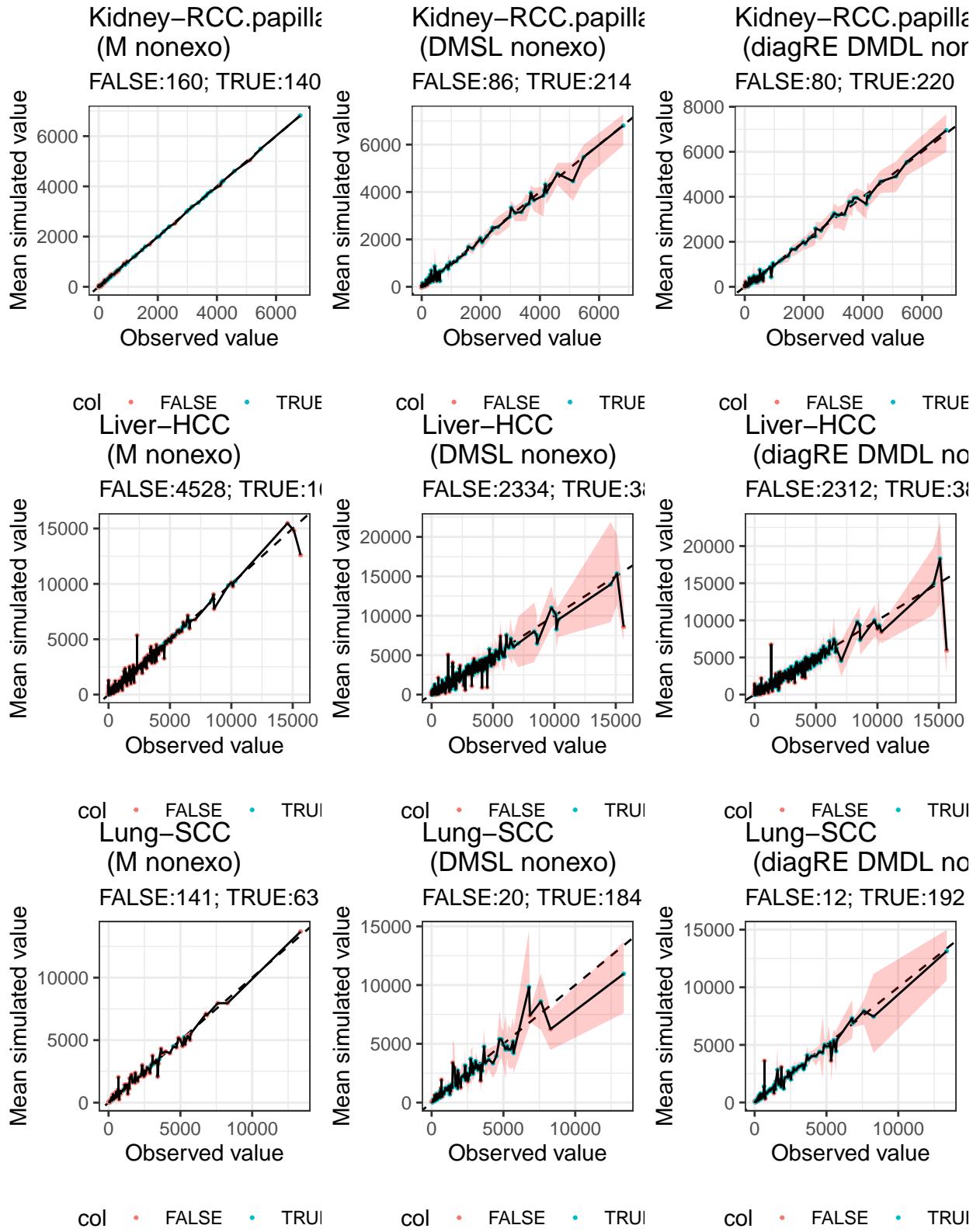
```

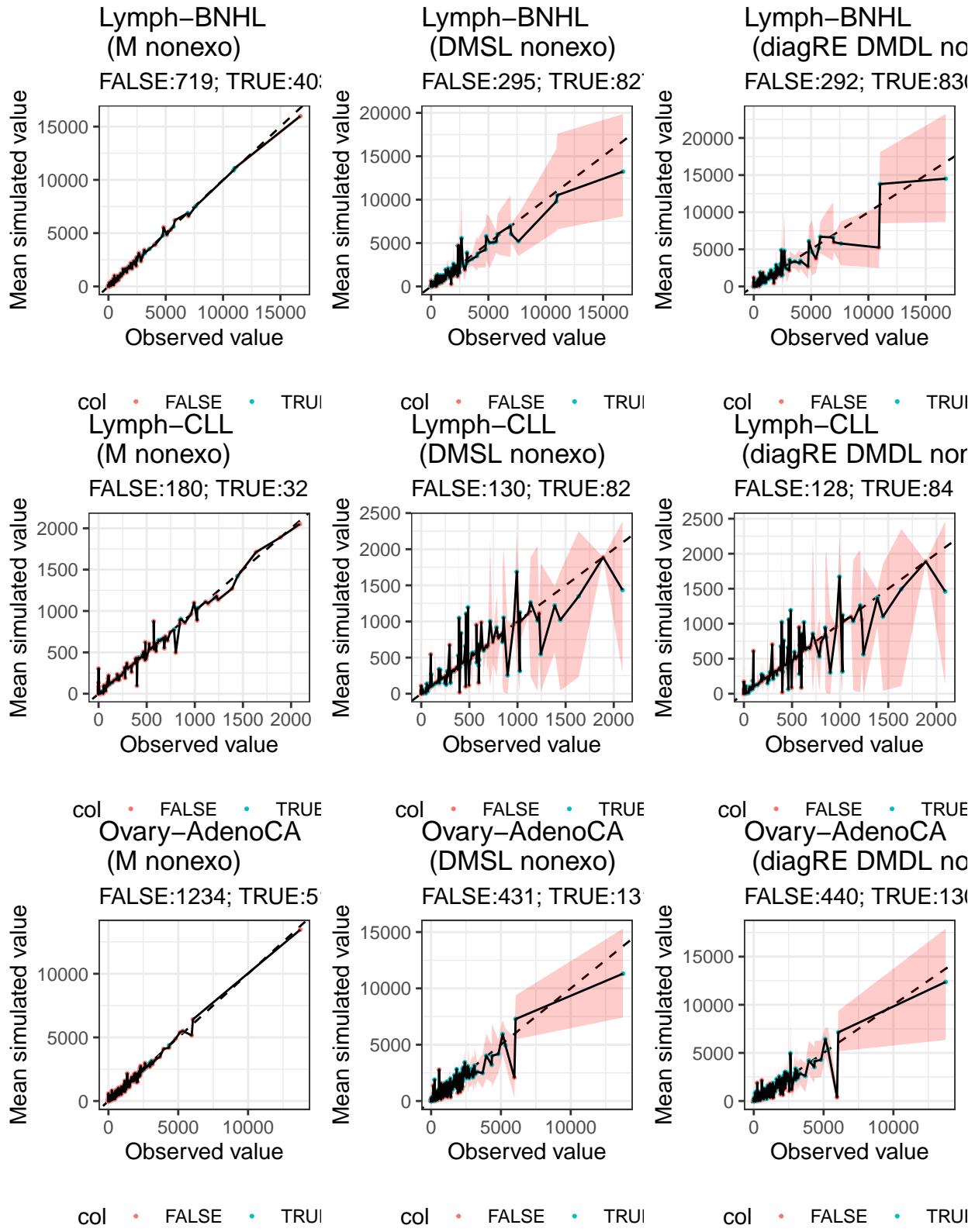


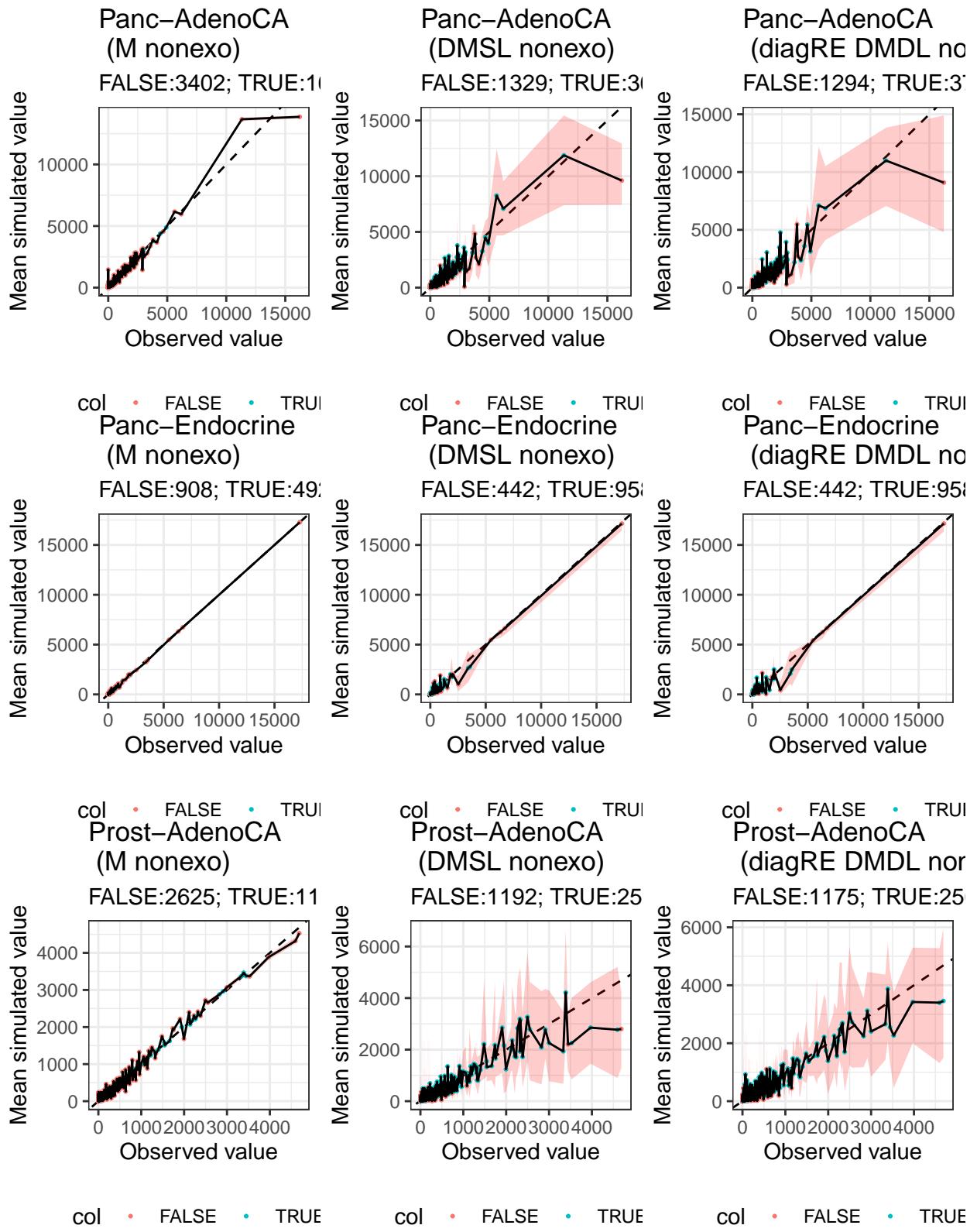


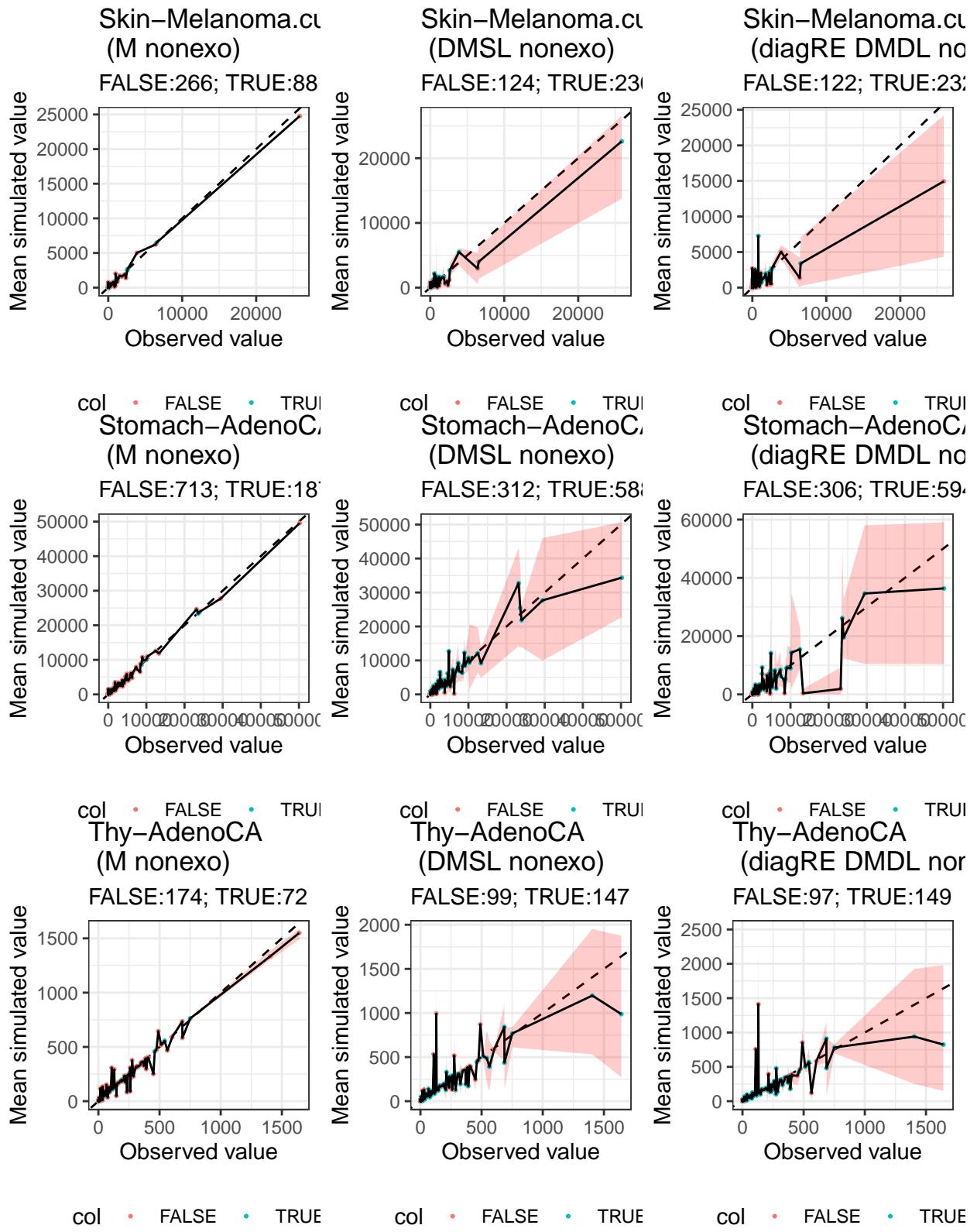


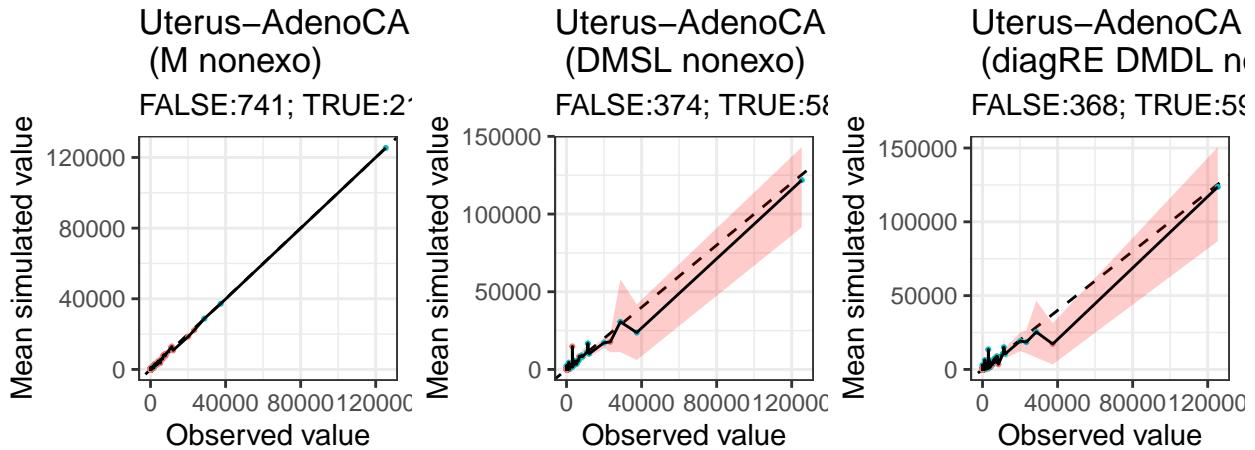












col • FALSE • TRUE

col • FALSE • TRUE

col • FALSE • TRUE

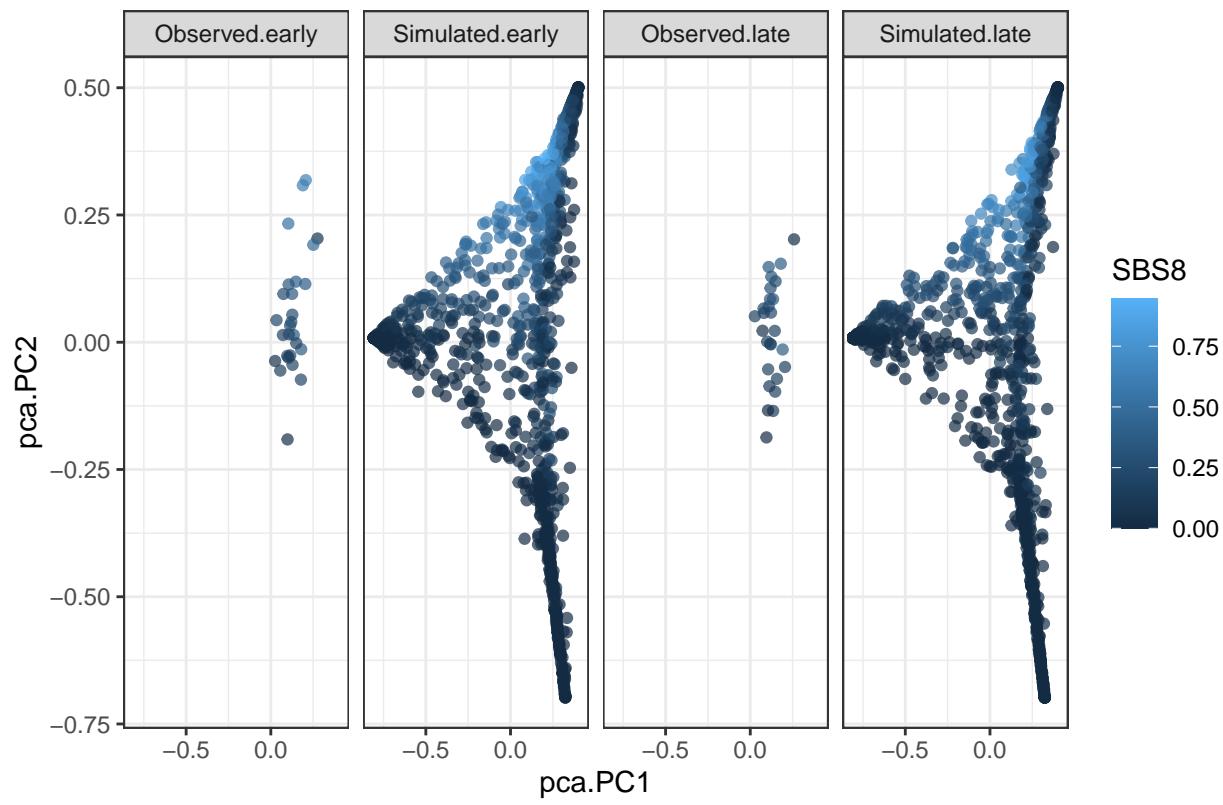
```
ct <- "Bone-Osteosarc"
.sim <- give_sim_from_estimates(tmb_object = fullRE_DMSL_nonexo_SP[[ct]], ct=ct, typedata="signatures",
                                    sigs_to_remove=unique(nonexogenous$V1),
                                    bool_give_PCA = T, path_to_data= ".../.../data/",
                                    obj_data=all_objects_nonexo_SP[[ct]],
                                    bool_nonexo=T,
                                    model="fullRE_DM", nrow_pca_plot=1)

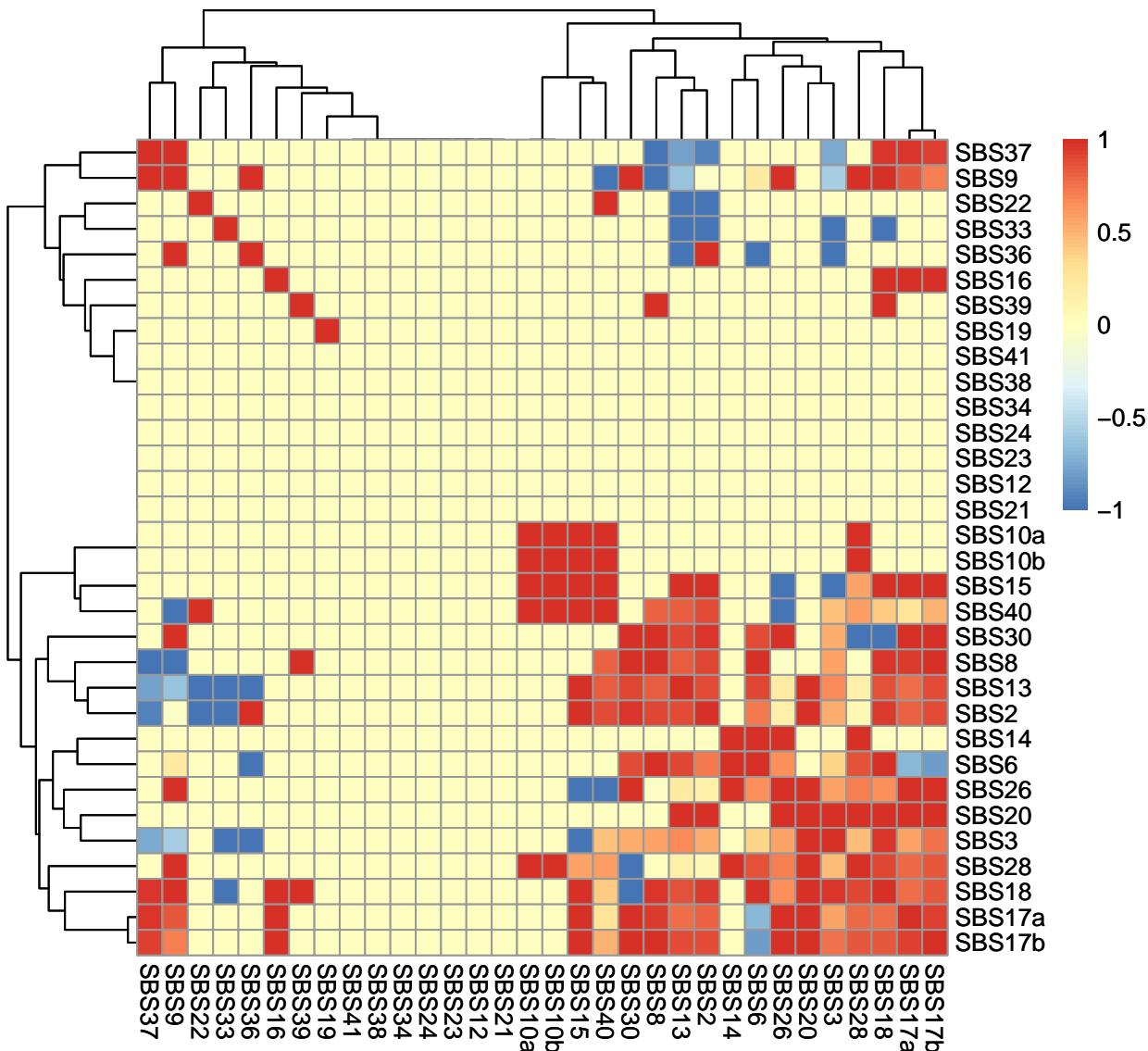
## Warning in fill_covariance_matrix(arg_d = dmin1, arg_entries_var = var_vec, :
## This function had been incorrect until now (30 july 2021)

## Warning in fill_covariance_matrix(arg_d = dmin1, arg_entries_var = var_vec_v2, :
## This function had been incorrect until now (30 july 2021)

## Warning in mvtnorm::rmvnorm(n = n_sim, mean = rep(0, dmin1), sigma = cov_mat):
## sigma is numerically not positive semidefinite
.sim[[2]]+ggtitle(paste0('Simulation of ', ct))
```

Simulation of Bone–Osteosarc





```

## null device
##      1

## null device
##      1

##      Bone-Osteosarc Breast-AdenoCA      CNS-GBM CNS-Medullo CNS-PiloAstro
## 10a          NA        NA          NA        NA        NA
## 10b          NA        NA          NA        NA        NA
## 12           NA        NA          NA        NA        NA
## 13     -0.4851852   -0.29393557        NA        NA        NA
## 14           NA        NA          NA        NA        NA
## 15           NA        NA          NA        NA        NA
## 16           NA        NA          NA        NA        NA
## 17a      0.1160637    1.26176677        NA        NA        NA
## 17b     -0.4495100   -0.08718682        NA        NA        NA

```

## 18		NA	-0.27226387	NA	0.2451783	NA
## 19		NA	NA	NA	NA	-0.4272079
## 2	-0.1086854		-0.27064004	NA	NA	NA
## 20		NA	NA	NA	NA	NA
## 21		NA	NA	NA	NA	NA
## 22		NA	NA	NA	NA	NA
## 23		NA	NA	NA	NA	-0.3541996
## 24		NA	NA	NA	NA	NA
## 26		NA	NA	NA	NA	NA
## 28		NA	NA	NA	NA	NA
## 3	-0.6897242		-0.29703844	NA	NA	NA
## 30	-0.6056439		NA	1.10972619	NA	NA
## 33		NA	NA	NA	NA	NA
## 34		NA	NA	NA	NA	NA
## 36		NA	NA	NA	NA	NA
## 37		NA	0.70695540	-0.07243086	NA	NA
## 38		NA	NA	NA	NA	NA
## 39		NA	NA	0.4125790	NA	
## 40		NA	-0.50926622	NA	NA	NA
## 41		NA	NA	NA	NA	NA
## 6		NA	NA	NA	NA	NA
## 8	-0.7960993		-0.51749527	NA	0.2251997	NA
## 9		NA	0.20693966	NA	NA	NA
## 10a	ColoRect-AdenoCA	Eso-AdenoCA		Head-SCC	Kidney-ChRCC	Kidney-RCC.clearcell
## 10b	-1.4074471	NA		NA	NA	NA
## 12	-1.5422385	NA	NA	NA	NA	NA
## 13		NA	-0.04596199	-0.52635385	0.3550827	2.1230383
## 14		NA	NA	NA	NA	NA
## 15	-1.6889979	NA	NA	NA	NA	NA
## 16		NA	NA	-1.22120425	NA	NA
## 17a	-1.9215061	-0.6204530	-0.60042854	0.08862915	0.8686071	NA
## 17b	-0.8469961	-0.8469961	-0.68081851	-0.46340155	0.6265696	NA
## 18		-0.34228548	-0.34228548	-0.68255609	NA	NA
## 19		NA	NA	NA	NA	NA
## 20		NA	0.02518066	-0.57582551	0.2256605	1.5155703
## 21		NA	NA	NA	NA	NA
## 22		NA	NA	NA	NA	0.6067726
## 23		NA	NA	NA	NA	NA
## 24		NA	NA	NA	NA	NA
## 26		NA	NA	NA	NA	NA
## 28		-1.1859091	-1.1859091	-0.29377455	NA	NA
## 30		NA	-0.11644857	-0.50324912	NA	NA
## 33		NA	NA	1.69184650	NA	NA
## 34		NA	NA	NA	NA	NA
## 36		NA	NA	NA	NA	NA
## 37		-1.2572104	-1.2572104	NA	NA	NA
## 38		NA	NA	NA	NA	NA
## 39		NA	NA	NA	NA	NA

## 40	-1.1136927	NA	NA	NA	0.7985707
## 41	NA	NA	NA	NA	NA
## 6	NA	NA	NA	NA	NA
## 8	NA	NA	NA	NA	NA
## 9	NA	NA	NA	NA	NA
##	Kidney-RCC.papillary	Liver-HCC	Lung-SCC	Lymph-BNHL	Lymph-CLL
## 10a	NA	NA	NA	NA	NA
## 10b	NA	NA	NA	NA	NA
## 12	NA	-0.345207420	NA	NA	NA
## 13	2.5859030	NA	NA	1.64560251	NA
## 14	NA	0.970507228	NA	NA	NA
## 15	NA	NA	NA	NA	NA
## 16	NA	-0.407429345	NA	NA	NA
## 17a	NA	1.949623968	NA	0.43754125	NA
## 17b	NA	0.357684393	NA	0.07786144	NA
## 18	NA	0.434727115	NA	NA	NA
## 19	NA	-0.176304092	NA	NA	NA
## 2	1.5564367	NA	0.05062637	-0.02400179	NA
## 20	NA	NA	NA	NA	NA
## 21	NA	NA	NA	NA	NA
## 22	0.5148814	0.053234843	NA	NA	NA
## 23	NA	NA	NA	NA	NA
## 24	NA	0.229396587	NA	NA	NA
## 26	NA	-0.005989797	NA	NA	NA
## 28	NA	1.242332222	NA	NA	NA
## 3	NA	NA	NA	0.13776447	NA
## 30	NA	0.105869335	NA	NA	NA
## 33	NA	NA	NA	NA	NA
## 34	NA	NA	NA	0.04350633	NA
## 36	NA	NA	NA	-0.38252264	NA
## 37	NA	NA	NA	0.31621429	NA
## 38	NA	NA	NA	NA	NA
## 39	NA	NA	NA	NA	NA
## 40	0.4639053	NA	NA	NA	NA
## 41	NA	NA	NA	NA	NA
## 6	NA	0.073980394	NA	0.19005491	NA
## 8	NA	NA	-0.01677345	NA	NA
## 9	NA	2.001518345	NA	-0.40180524	-1.177635
##	Ovary-AdenoCA	Panc-AdenoCA	Panc-Endocrine	Prost-AdenoCA	
## 10a	NA	NA	NA	NA	
## 10b	NA	NA	NA	NA	
## 12	NA	NA	NA	NA	
## 13	-1.2512015	0.37995820	-0.087086745	0.1246728	
## 14	NA	NA	NA	NA	
## 15	NA	NA	NA	NA	
## 16	NA	NA	NA	NA	
## 17a	NA	1.79812084	NA	NA	
## 17b	NA	0.38336742	NA	NA	
## 18	-1.1331678	0.35916034	NA	-0.5098650	
## 19	NA	NA	NA	NA	
## 2	-1.0015169	0.38030698	0.209990497	-0.2967570	

## 20	NA	1.93713597	NA	NA
## 21	NA	NA	NA	NA
## 22	NA	NA	NA	NA
## 23	NA	NA	NA	NA
## 24	NA	NA	NA	NA
## 26	-0.1750862	0.04310237	-0.414887355	NA
## 28	NA	0.72385281	NA	NA
## 3	-1.0594838	0.59560835	-0.850836395	-0.1768158
## 30	NA	0.11446597	0.002470565	NA
## 33	NA	NA	NA	-0.2259301
## 34	NA	NA	NA	NA
## 36	NA	NA	-0.145465514	NA
## 37	NA	NA	NA	1.0113497
## 38	NA	NA	NA	NA
## 39	-0.6548442	NA	NA	NA
## 40	-1.6340751	NA	NA	-1.5045199
## 41	NA	NA	NA	NA
## 6	NA	-0.15079533	-0.476148963	NA
## 8	-1.3466732	-0.12777479	-0.132613541	-0.7850431
## 9	NA	NA	0.003342611	NA
##	Skin-Melanoma.cutaneous	Stomach-AdenoCA	Thy-AdenoCA	Uterus-AdenoCA
## 10a	NA	NA	NA	-0.8837555
## 10b	NA	NA	NA	-0.8828957
## 12	NA	NA	NA	NA
## 13	-2.953469	-0.2741750	0.9422149	-0.5688807
## 14	NA	NA	NA	-0.6083201
## 15	NA	-0.7414961	NA	-1.6452513
## 16	NA	NA	NA	NA
## 17a	-2.948658	-0.4043640	NA	NA
## 17b	-3.334771	-0.5799258	NA	NA
## 18	NA	-0.5205178	NA	NA
## 19	NA	NA	NA	NA
## 2	-1.140634	-0.2655205	0.6236426	-0.6087296
## 20	NA	0.8952101	NA	NA
## 21	NA	-0.2079586	NA	NA
## 22	NA	NA	NA	NA
## 23	NA	NA	NA	NA
## 24	NA	NA	NA	NA
## 26	NA	-0.4374430	NA	-0.2829108
## 28	NA	0.5066307	NA	0.4243581
## 3	NA	-0.2882412	NA	-0.1422257
## 30	NA	NA	NA	NA
## 33	NA	NA	NA	NA
## 34	NA	NA	NA	NA
## 36	NA	NA	NA	NA
## 37	NA	NA	NA	NA
## 38	-2.684604	NA	NA	NA
## 39	NA	NA	NA	NA
## 40	NA	-0.1855569	NA	-1.0576199
## 41	NA	-0.4939740	NA	NA
## 6	NA	NA	NA	-1.2651810

```
## 8      NA      NA      NA      NA
## 9      NA -0.3200956      NA      NA
```