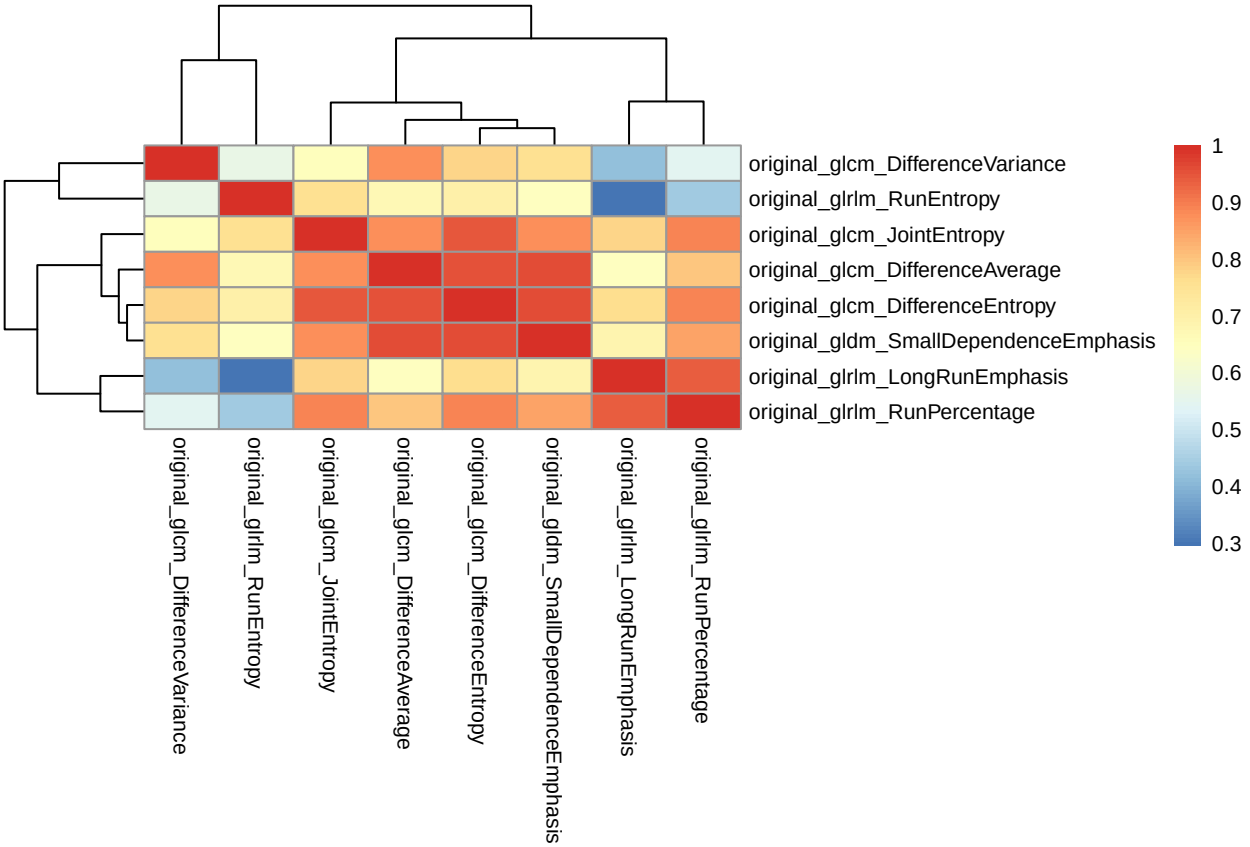
Radiomics

Loading Everything

Project Plan

What features to take?

- Not sure to take Zone Entropy or not
- Run Entropy and Zone Entropy do not follow the same patter on biplot



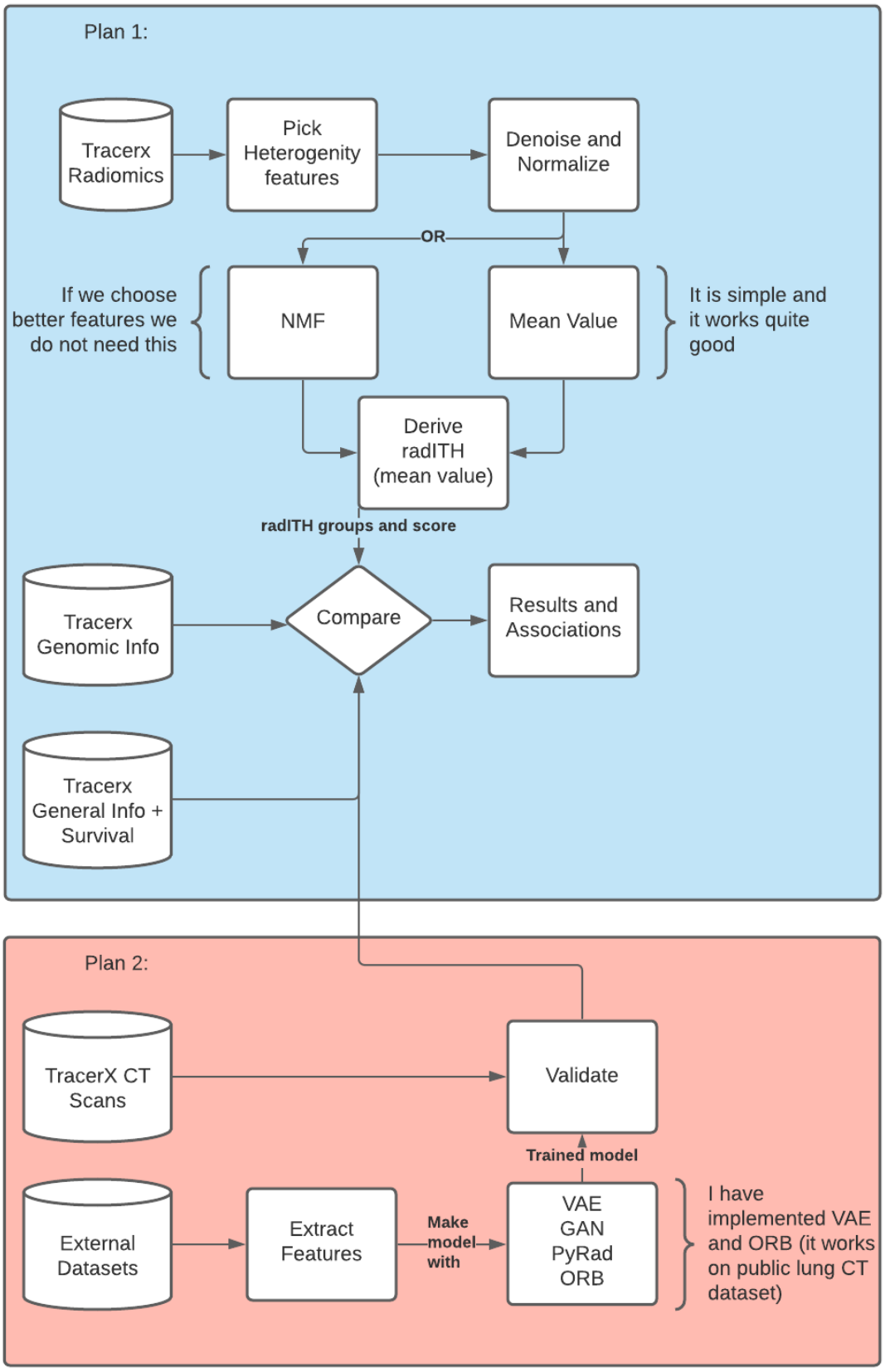
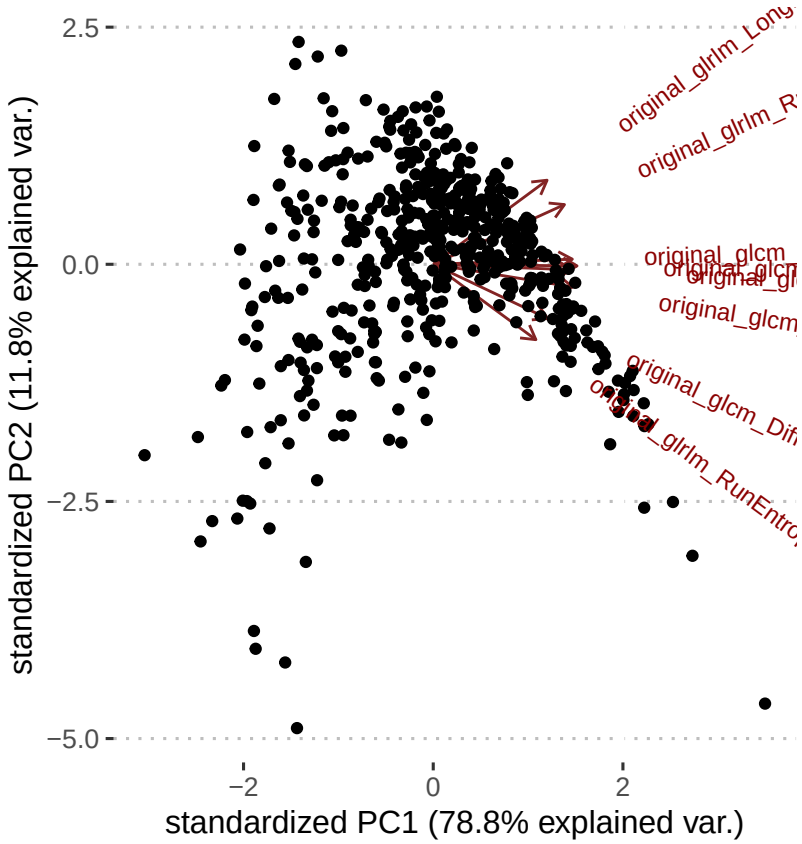


Figure 1: Project Plan



Important measures to check

- We will compare diameter to volume to ITH

```
pyrad$volume = as.numeric(pyrad$original_shape_MeshVolume)
pyrad$volume_from_pyrad = as.numeric(pyrad$original_shape_MeshVolume)
pyrad$diameter = as.numeric(pyrad$original_shape_Maximum2DDiameterSlice)
```

how to define radITH

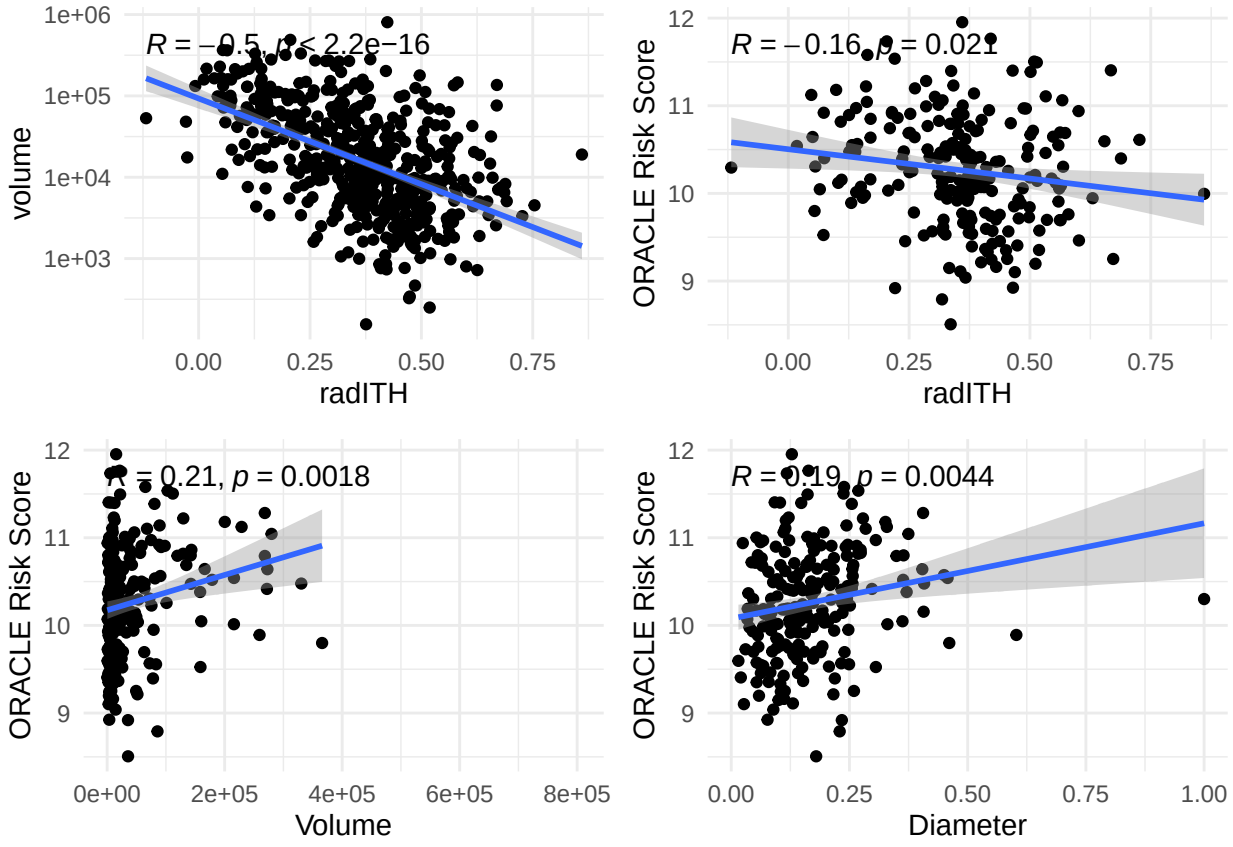
- Do we need to normalize something by volume?
- Numbers were a bit wierd when divided by volume therefore I did not divide anything with volume

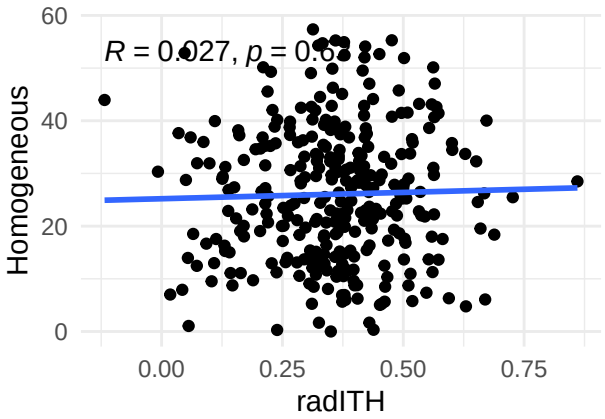
```
# weighted mean
w = 1-abs(cor(pyrad[,features_of_interest], pyrad[,"volume"]))
pyrad$radITH = apply(pyrad[,features_of_interest],1, function(x){
  weighted.mean(x[features_of_interest], w = w)
})
```

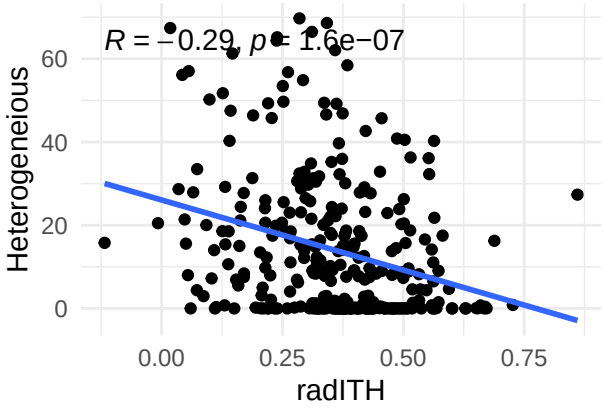
```r
#pyrad$radITH = rowMeans(pyrad[,features_of_interest], na.rm = T)
Q = 3


pyrad$volume_group = gtools::quantcut(pyrad$volume, q=Q, na.rm=TRUE)
pyrad$diameter_group = gtools::quantcut(pyrad$diameter, q=Q, na.rm=TRUE)
pyrad$radITH_group = gtools::quantcut(pyrad$radITH, q=Q, na.rm=TRUE)
```

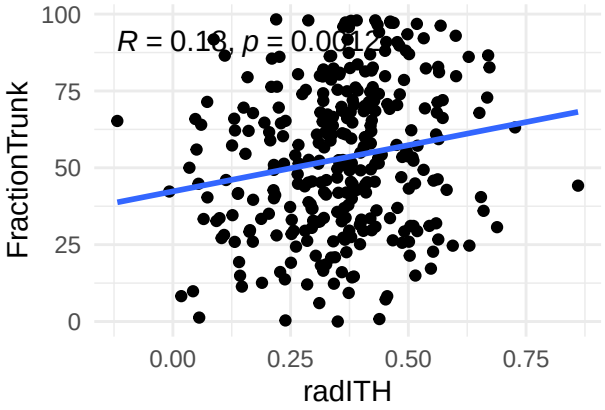
Expected correlations

- Negative cor radITH to volume









Mutations

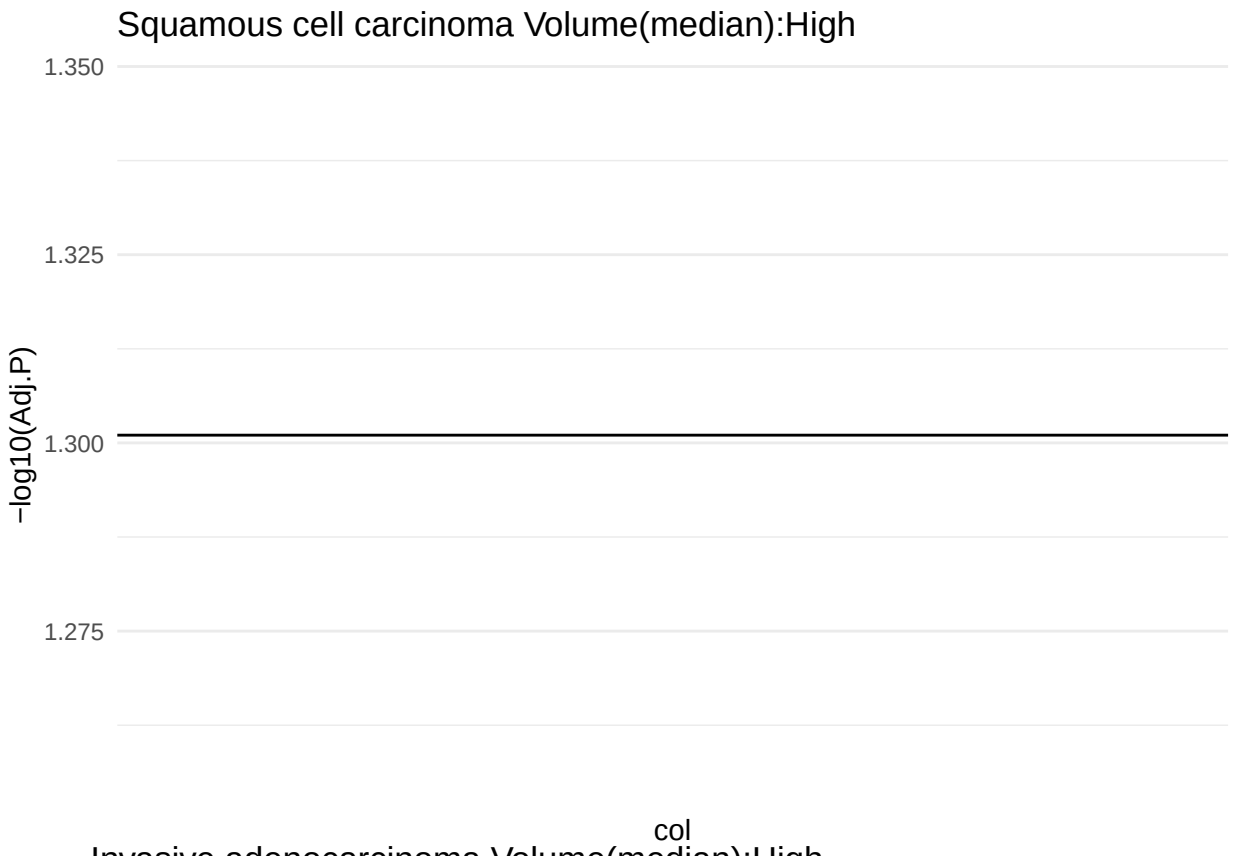
Let's group DRIVER mutations by Sanchez Vega def

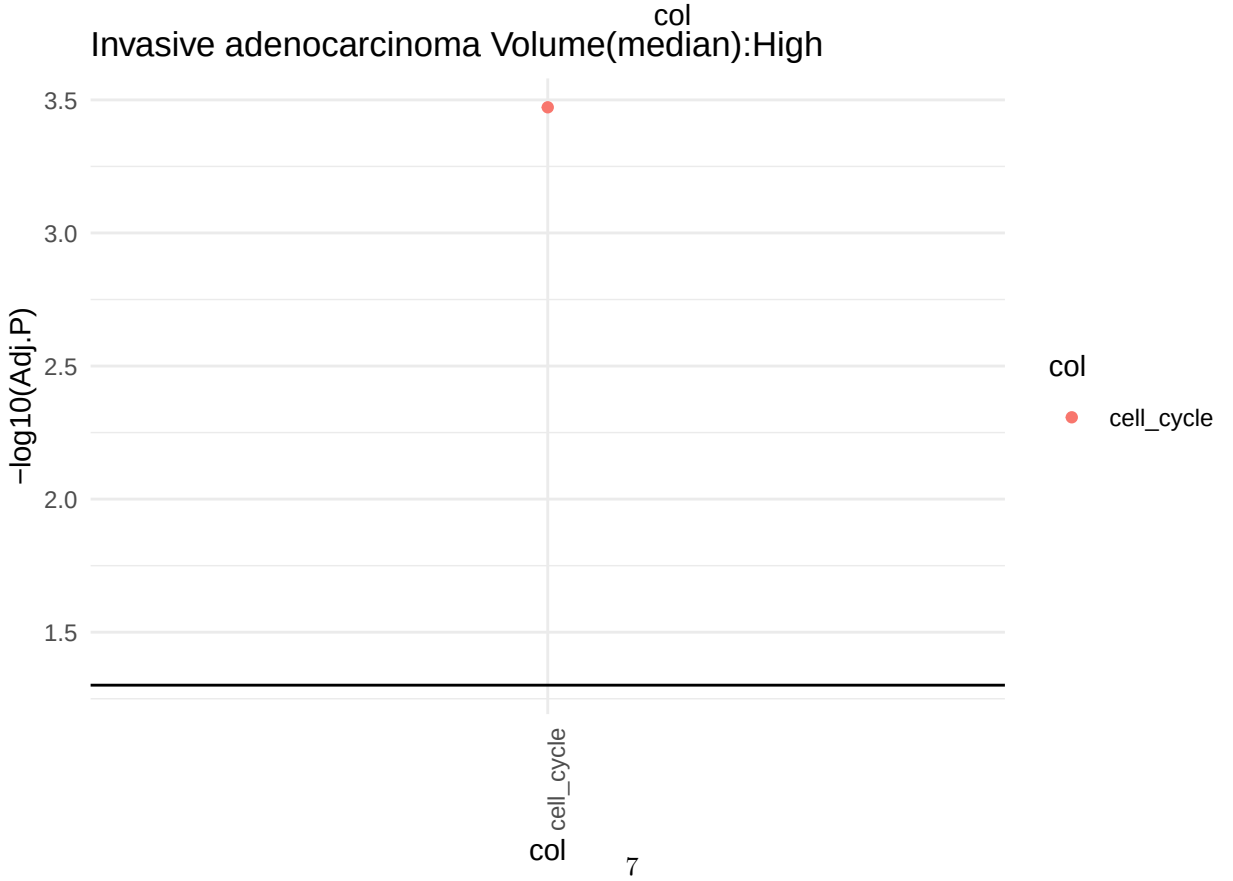
Let's test Sanchez Vega Muts vs radITH groups (q =3)

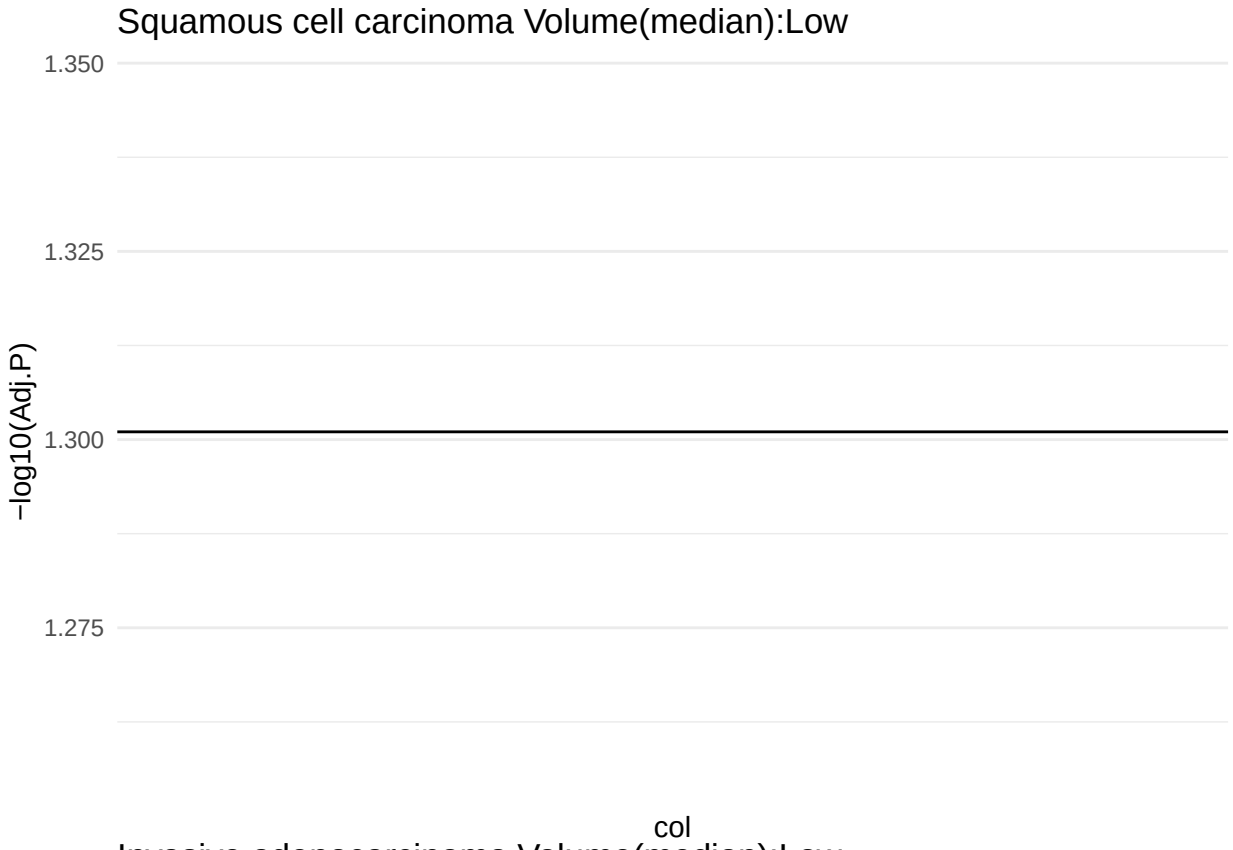
```
## [1] "Adeno fisher test results"

## [1] "nrf2"
##
##  Fisher's Exact Test for Count Data
##
## data:  table(tmp$radITH_group, tmp[, col])
## p-value = 0.03115
## alternative hypothesis: two.sided
##
## [1] "pi3k"
##
##  Fisher's Exact Test for Count Data
##
## data:  table(tmp$radITH_group, tmp[, col])
## p-value = 0.01356
```

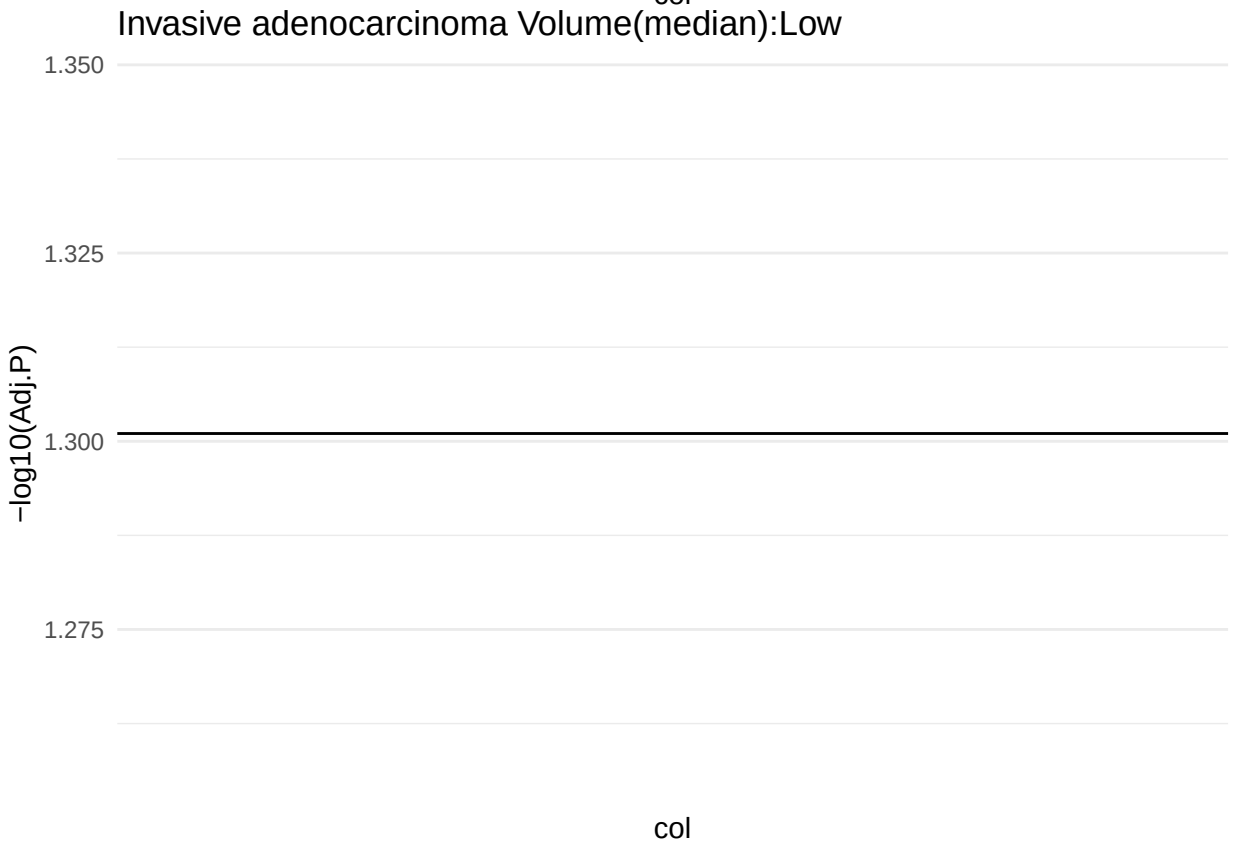
```
## alternative hypothesis: two.sided
##
## [1] "cell_cycle"
##
##  Fisher's Exact Test for Count Data
##
## data:  table(tmp$radITH_group, tmp[, col])
## p-value = 0.000566
## alternative hypothesis: two.sided

## [1] "Squamous fisher test results"

## [1] "rtk_kras"
##
##  Fisher's Exact Test for Count Data
##
## data:  table(tmp$radITH_group, tmp[, col])
## p-value = 0.02937
## alternative hypothesis: two.sided
##
## [1] "pi3k"
##
##  Fisher's Exact Test for Count Data
##
## data:  table(tmp$radITH_group, tmp[, col])
## p-value = 0.04171
## alternative hypothesis: two.sided
```

SanchezVega vs radITH groups (q = 3) vs pathology vs volume (Median)






Squamous cell carcinoma Volume(median):Low
1.350
1.325
1.300
1.275
−log10(Adj.P)
col


Invasive adenocarcinoma Volume(median):Low
1.350
1.325
1.300
1.275
−log10(Adj.P)
col

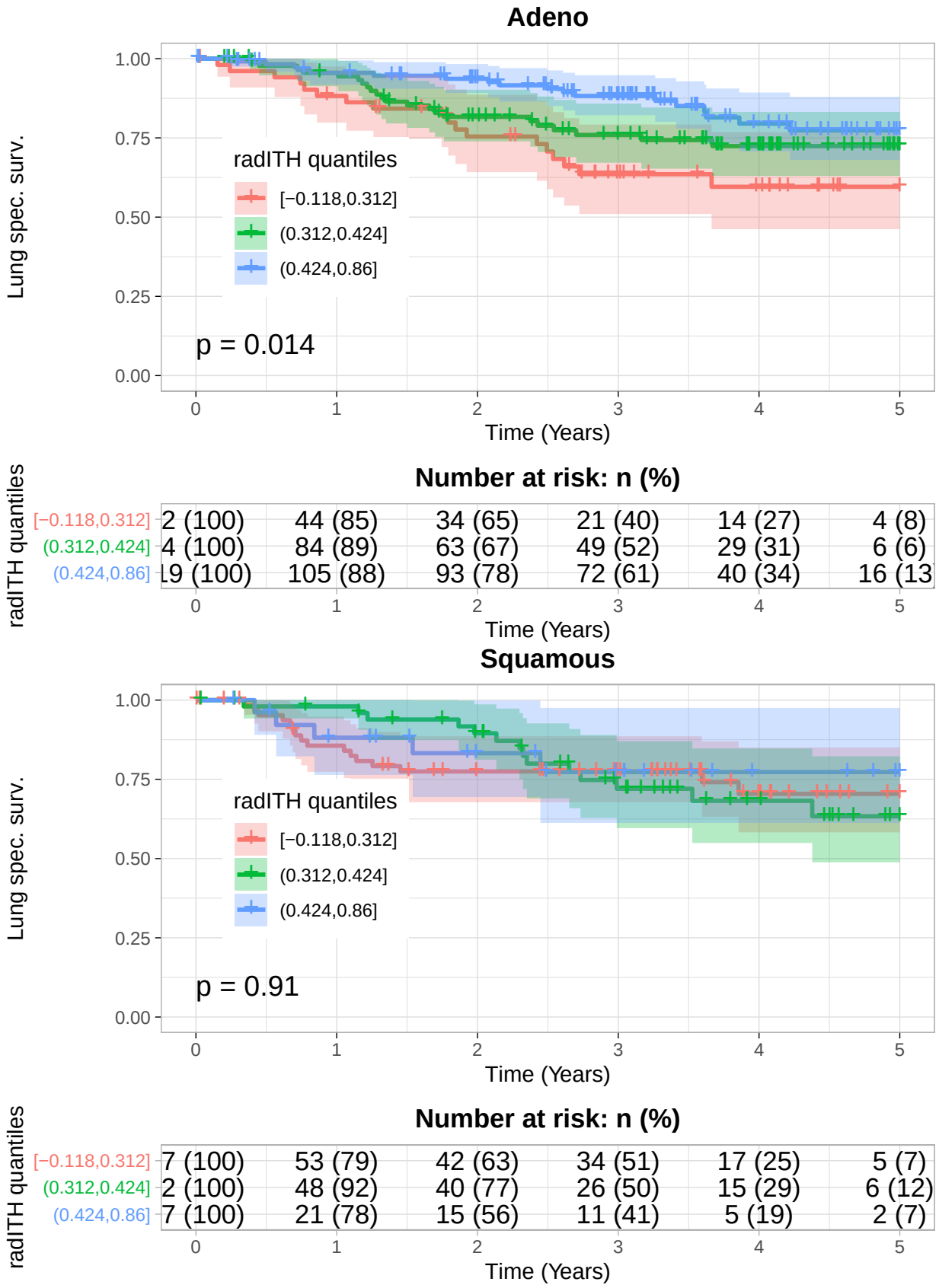
Does Volume or diameter predict biology?

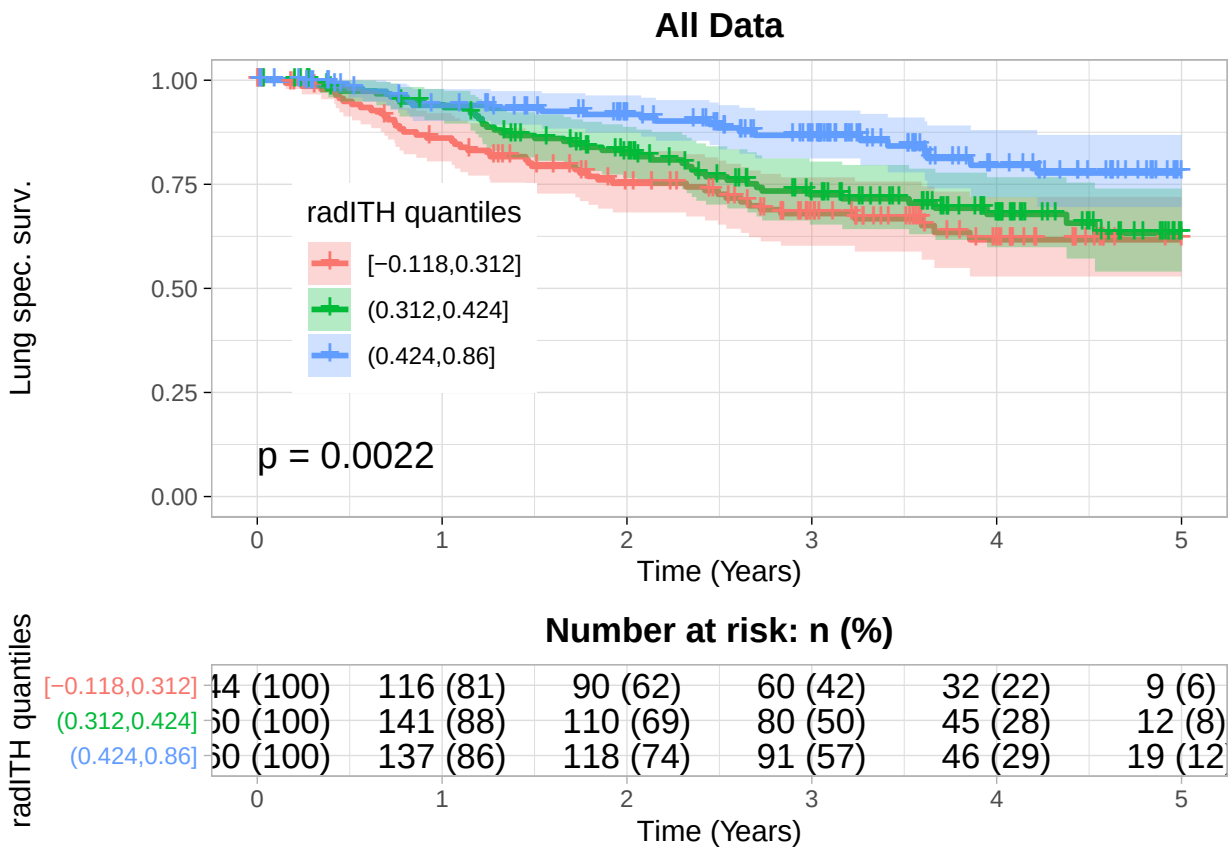
- Diameter is not associated at all
- Volume is associated with HIPPO

```
## [1] "Adeno fisher test results"
```

```
## [1] "Squamous fisher test results"
```

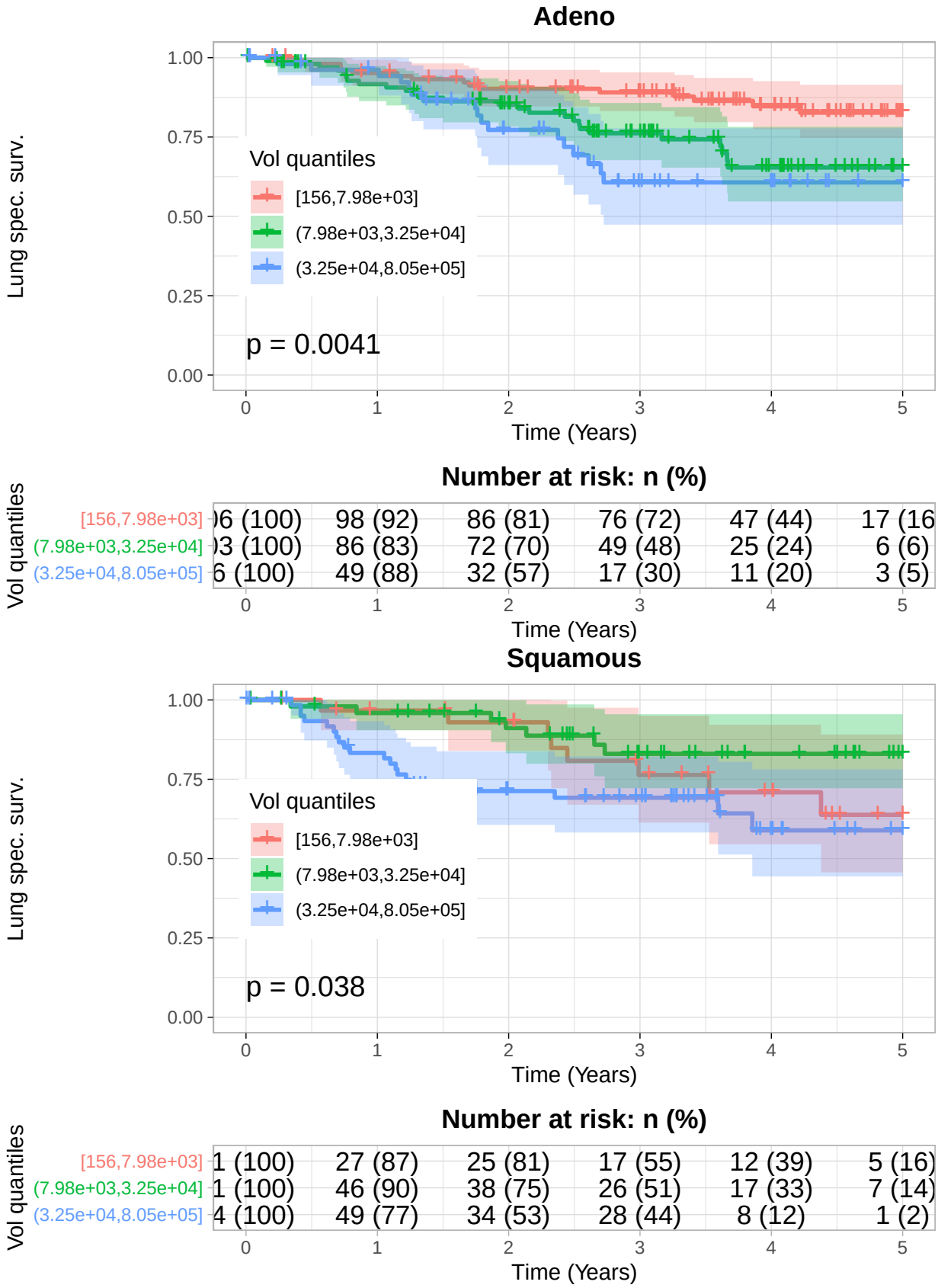
How does radITH associate with survival?

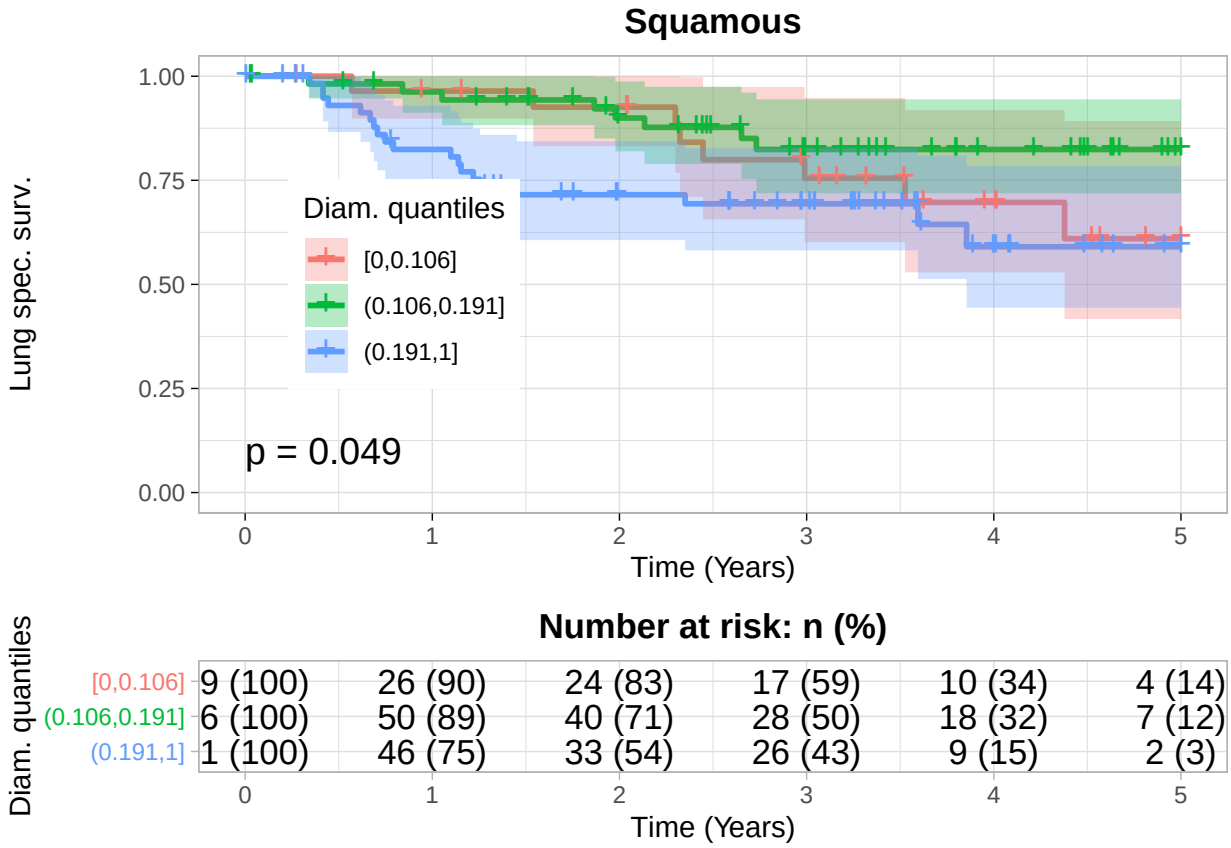



All Data
Lung spec. surv.
1.00
0.75
0.50
0.25
0.00
radITH quantiles
[−0.118,0.312]
(0.312,0.424]
(0.424,0.86]
p = 0.0022
0
1
2
3
4
5
Time (Years)

Number at risk: n (%)
radITH quantiles
[−0.118,0.312]
(0.312,0.424]
(0.424,0.86]
44 (100)
116 (81)
90 (62)
60 (42)
32 (22)
9 (6)
60 (100)
141 (88)
110 (69)
80 (50)
45 (28)
12 (8)
60 (100)
137 (86)
118 (74)
91 (57)
46 (29)
19 (12
0
1
2
3
4
5
Time (Years)

How does volume (diameter) associate to survival?

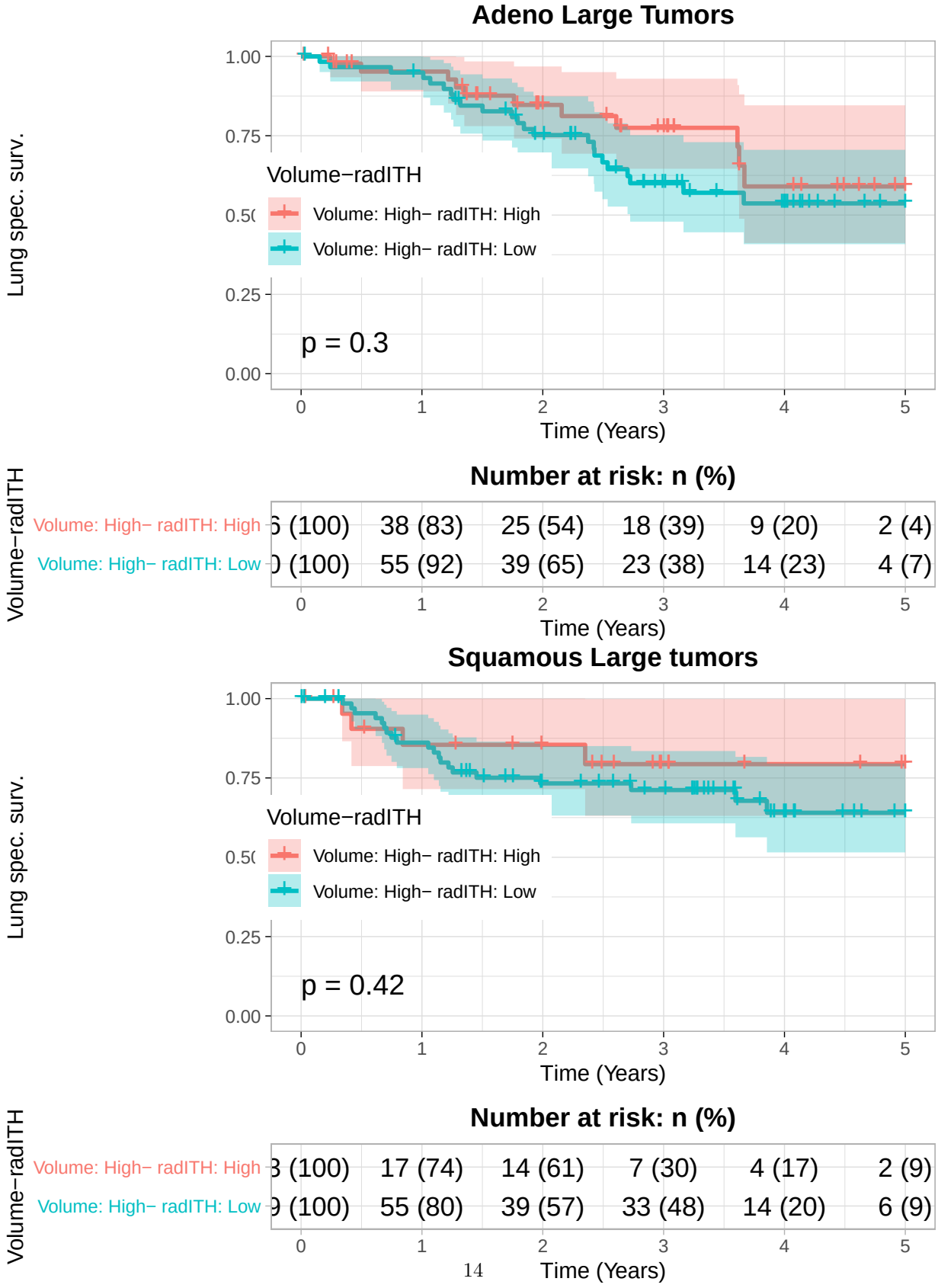


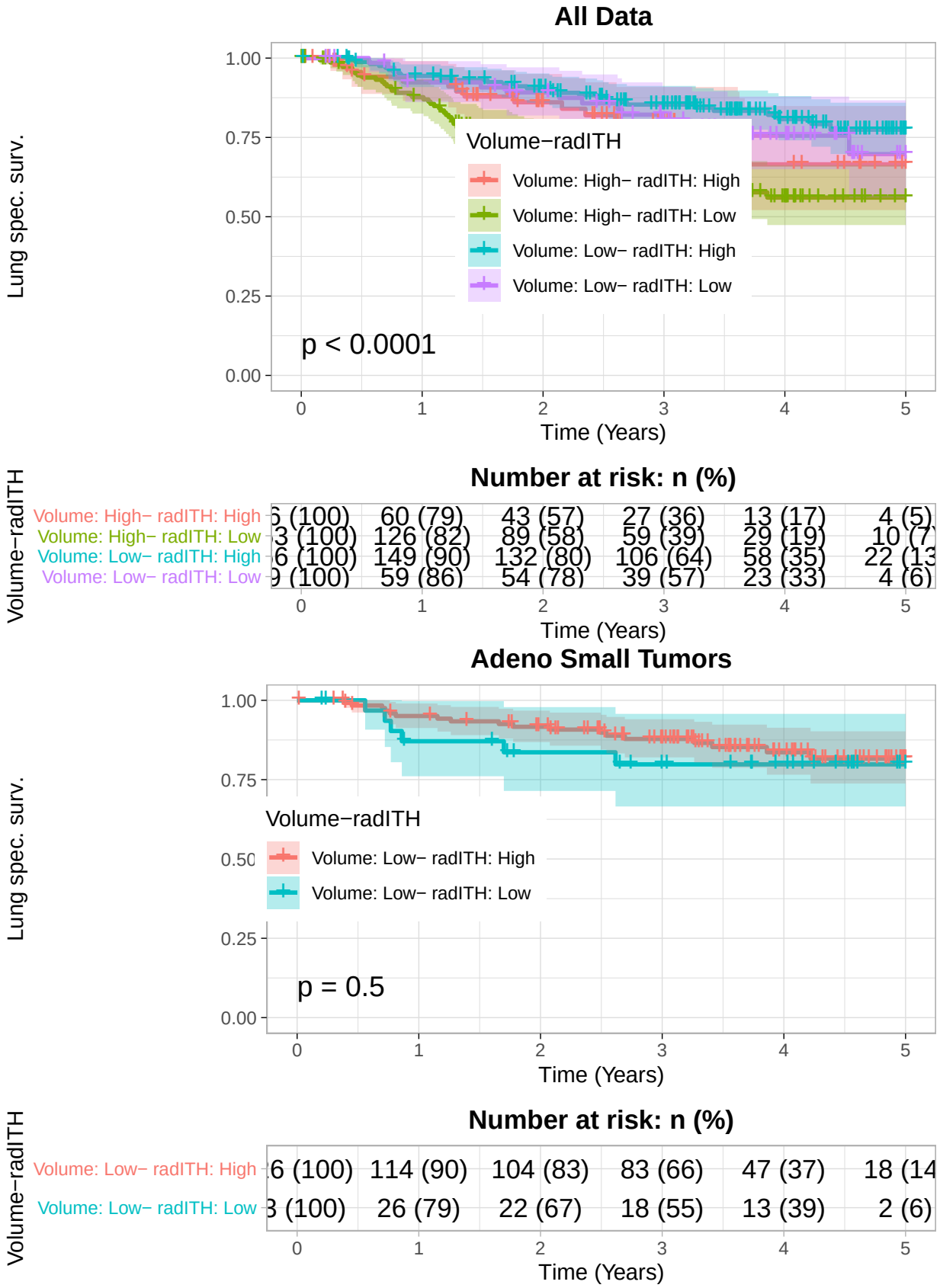

Squamous
Lung spec. surv.
1.00
0.75
0.50
0.25
0.00
Diam. quantiles
[0,0.106]
(0.106,0.191]
(0.191,1]
p = 0.049
0
1
2
3
4
5
Time (Years)

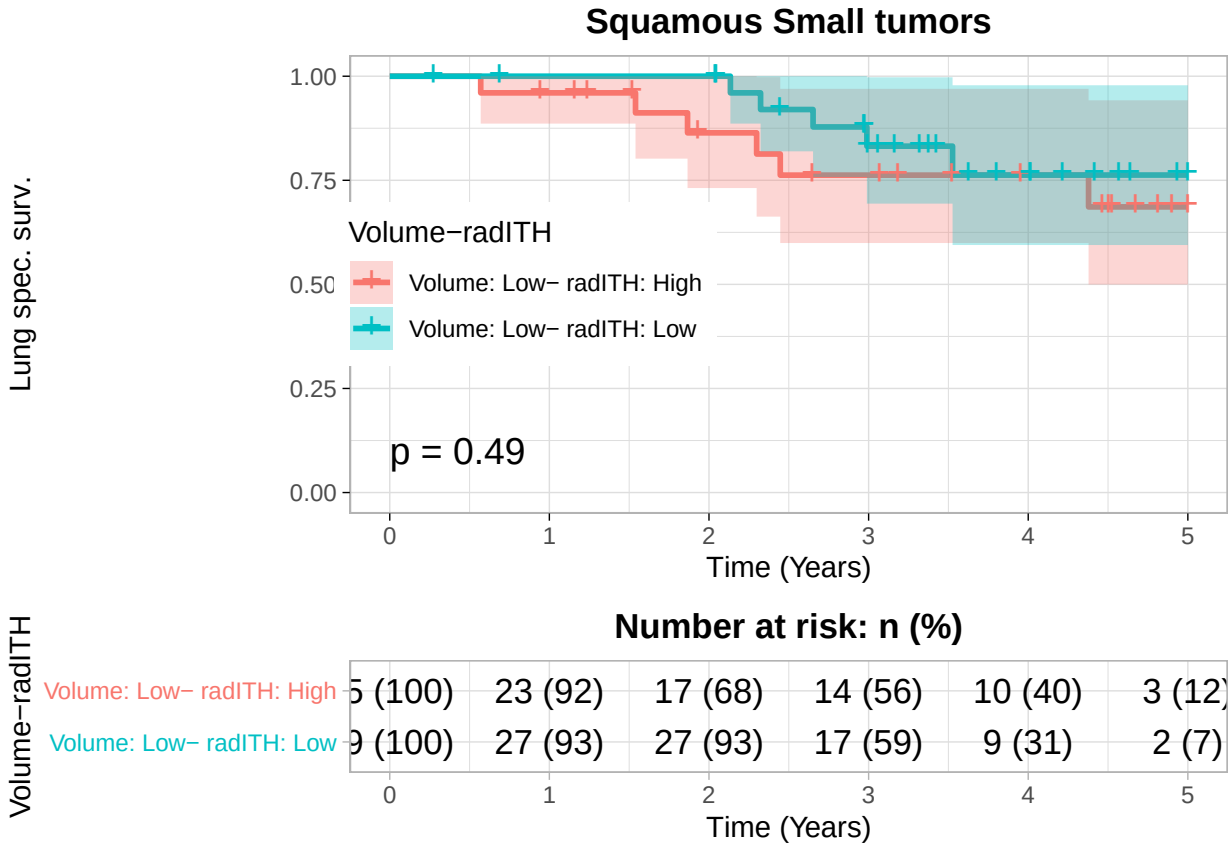
Number at risk: n (%)
Diam. quantiles
[0,0.106]
(0.106,0.191]
(0.191,1]
9 (100)
26 (90)
24 (83)
17 (59)
10 (34)
4 (14)
6 (100)
50 (89)
40 (71)
28 (50)
18 (32)
7 (12)
1 (100)
46 (75)
33 (54)
26 (43)
9 (15)
2 (3)
0
1
2
3
4
5
Time (Years)

Can we overlap radITH and Volume groups and check survival?

In order to increase group sizes, all measures will be split by median (Q=2)

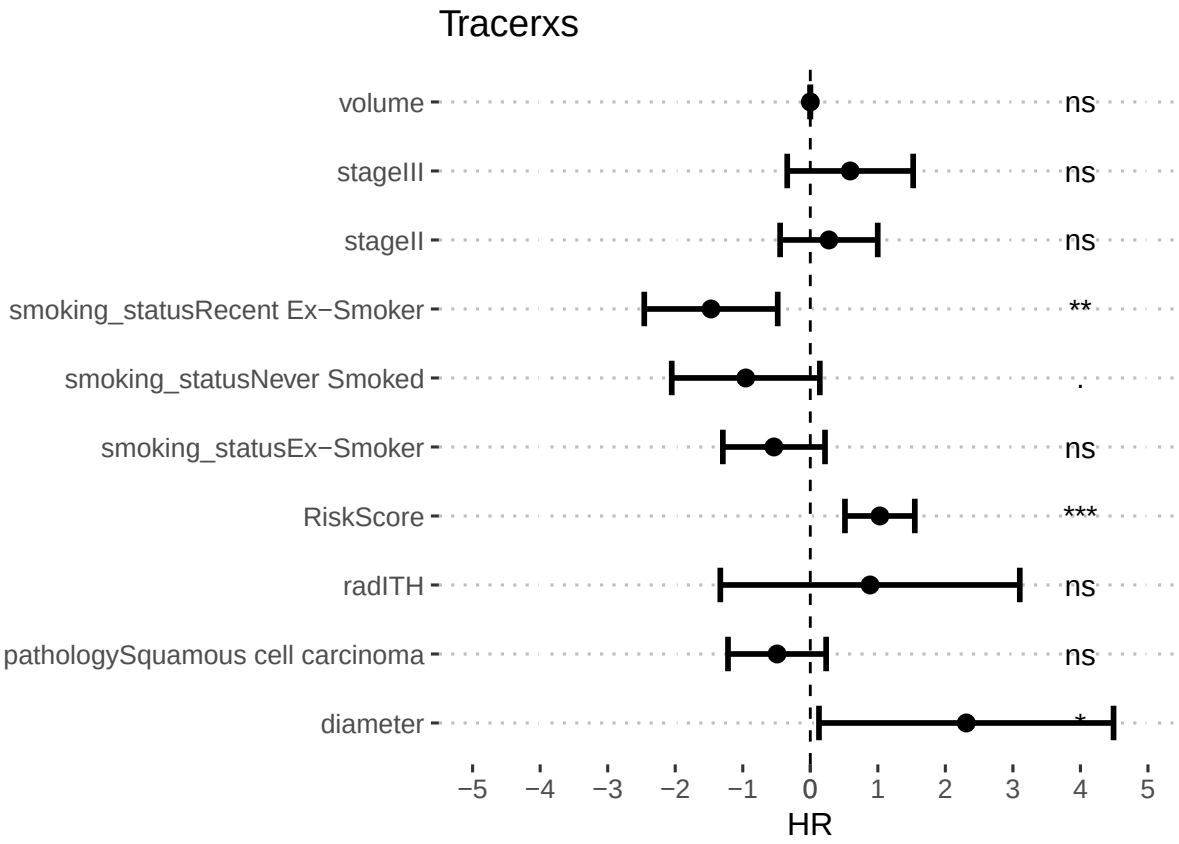



All Data
Lung spec. surv.
1.00
0.75
0.50
0.25
0.00
Volume−radITH
Volume: High− radITH: High
Volume: High− radITH: Low
Volume: Low− radITH: High
Volume: Low− radITH: Low
p < 0.0001
0
1
2
3
4
5
Time (Years)
Number at risk: n (%)
Volume−radITH
Volume: High− radITH: High
Volume: High− radITH: Low
Volume: Low− radITH: High
Volume: Low− radITH: Low
6 (100)
60 (79)
43 (57)
27 (36)
13 (17)
4 (5)
3 (100)
126 (82)
89 (58)
59 (39)
29 (19)
10 (7
6 (100)
149 (90)
132 (80)
106 (64)
58 (35)
22 (13
9 (100)
59 (86)
54 (78)
39 (57)
23 (33)
4 (6)
0
1
2
3
4
5
Time (Years)
Adeno Small Tumors
Lung spec. surv.
1.00
0.75
0.50
0.25
0.00
Volume−radITH
Volume: Low− radITH: High
Volume: Low− radITH: Low
p = 0.5
0
1
2
3
4
5
Time (Years)
Number at risk: n (%)
Volume−radITH
Volume: Low− radITH: High
Volume: Low− radITH: Low
6 (100)
114 (90)
104 (83)
83 (66)
47 (37)
18 (14
3 (100)
26 (79)
22 (67)
18 (55)
13 (39)
2 (6)
0
1
2
3
4
5
Time (Years)



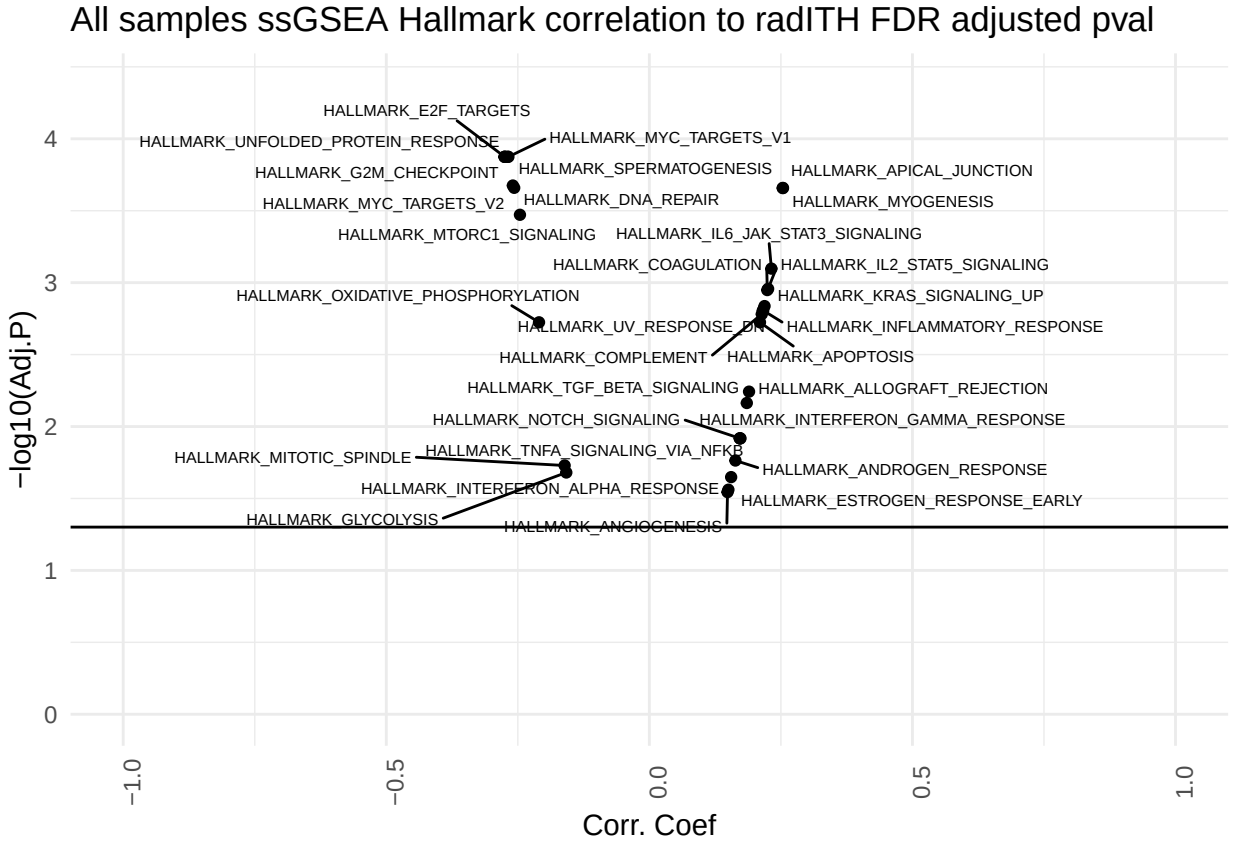
Coxph Model

- radITH does not help improve cox ph model

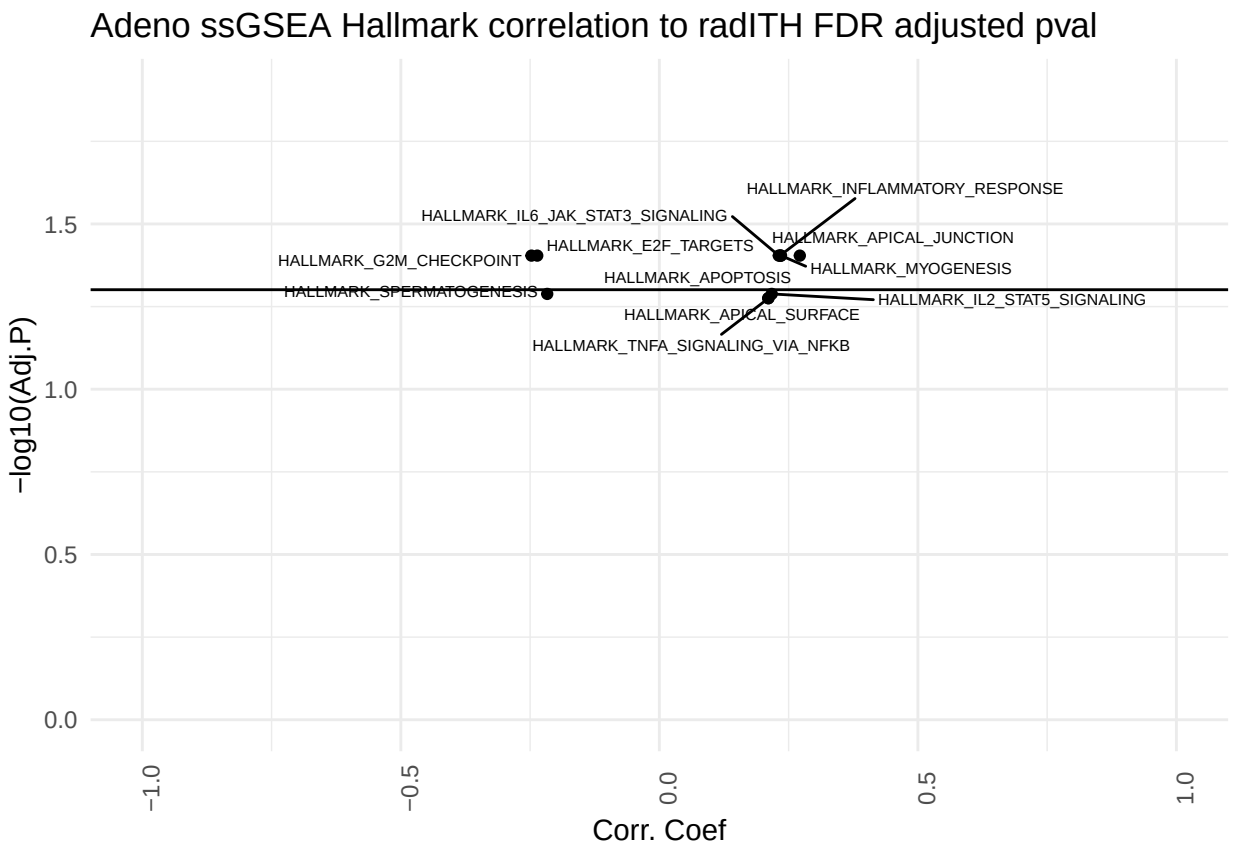


Hallmarks all samples

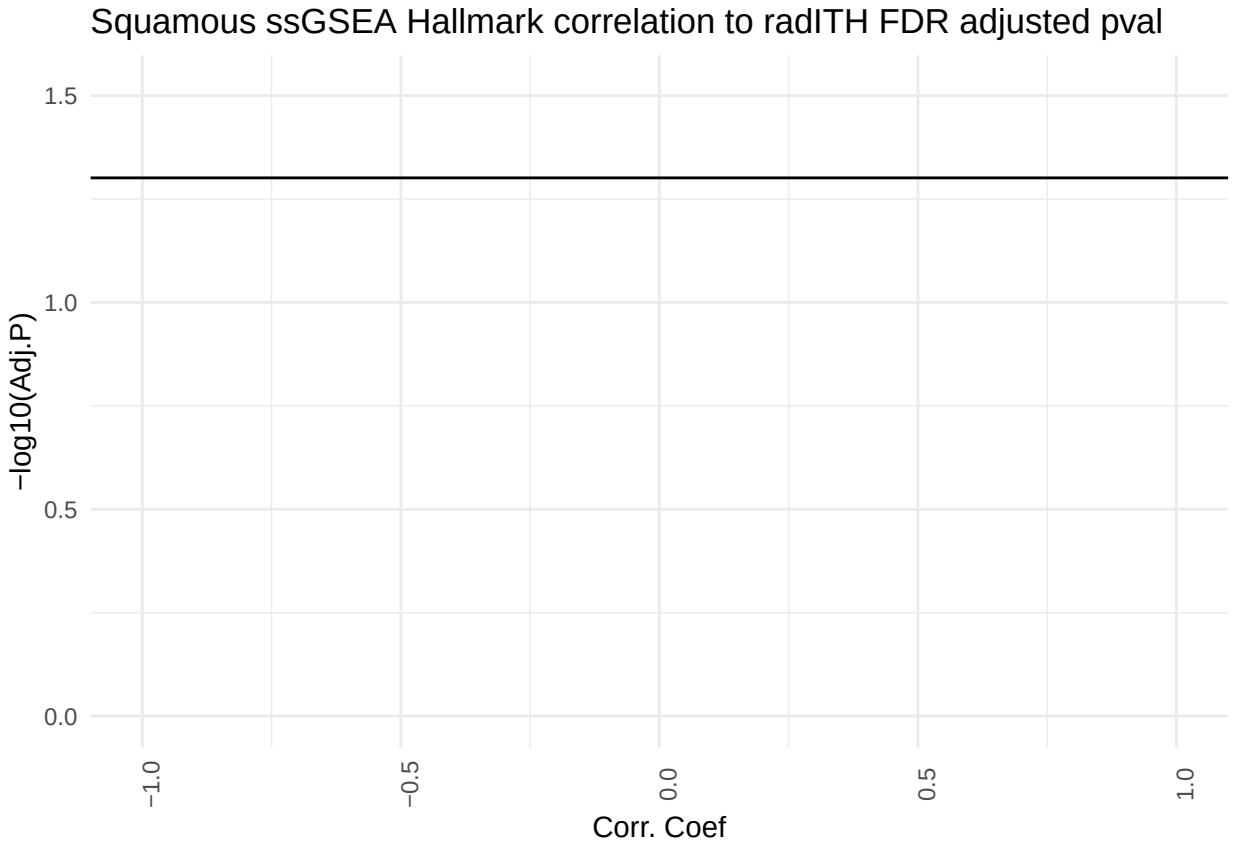
- Association (cor) of radITH with hallmarks
- Hallmarks computed with SS-GSEA
- P values are adjusted using FDR


All samples ssGSEA Hallmark correlation to radITH FDR adjusted pval
HALLMARK_E2F_TARGETS
HALLMARK_UNFOLDED_PROTEIN_RESPONSE
HALLMARK_MYC_TARGETS_V1
HALLMARK_G2M_CHECKPOINT
HALLMARK_SPERMATOGENESIS
HALLMARK_APICAL_JUNCTION
HALLMARK_MYC_TARGETS_V2
HALLMARK_DNA_REPAIR
HALLMARK_MYOGENESIS
HALLMARK_MTORC1_SIGNALING
HALLMARK_IL6_JAK_STAT3_SIGNALING
HALLMARK_COAGULATION
HALLMARK_IL2_STAT5_SIGNALING
HALLMARK_OXIDATIVE_PHOSPHORYLATION
HALLMARK_KRAS_SIGNALING_UP
HALLMARK_UV_RESPONSE_DN
HALLMARK_INFLAMMATORY_RESPONSE
HALLMARK_COMPLEMENT
HALLMARK_APOPTOSIS
HALLMARK_TGF_BETA_SIGNALING
HALLMARK_ALLOGRAFT_REJECTION
HALLMARK_NOTCH_SIGNALING
HALLMARK_INTERFERON_GAMMA_RESPONSE
HALLMARK_MITOTIC_SPINDLE
HALLMARK_TNFA_SIGNALING_VIA_NFKB
HALLMARK_ANDROGEN_RESPONSE
HALLMARK_INTERFERON_ALPHA_RESPONSE
HALLMARK_ESTROGEN_RESPONSE_EARLY
HALLMARK_GLYCOLYSIS
HALLMARK_ANGIOGENESIS
−log10(Adj.P)
4
3
2
1
0
−1.0
−0.5
0.0
0.5
1.0
Corr. Coef

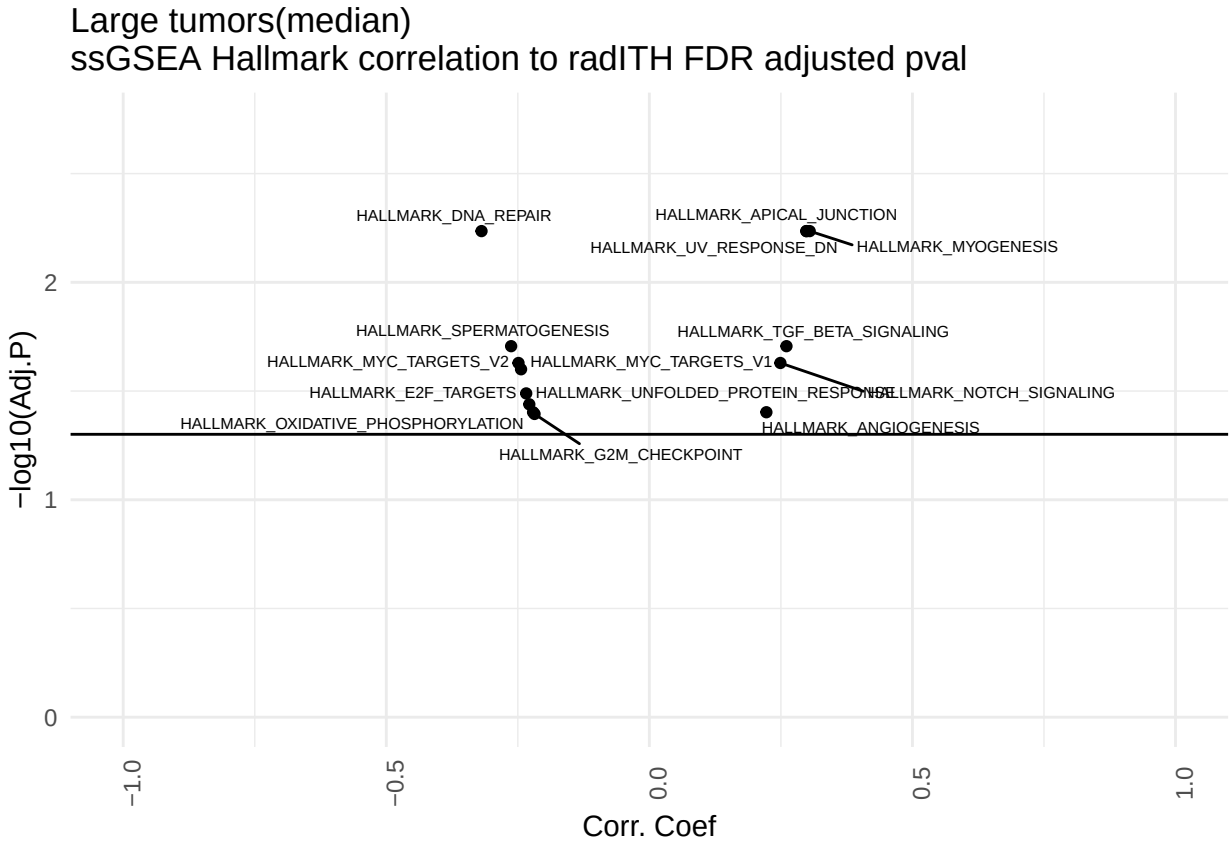
Hallmarks Adeno

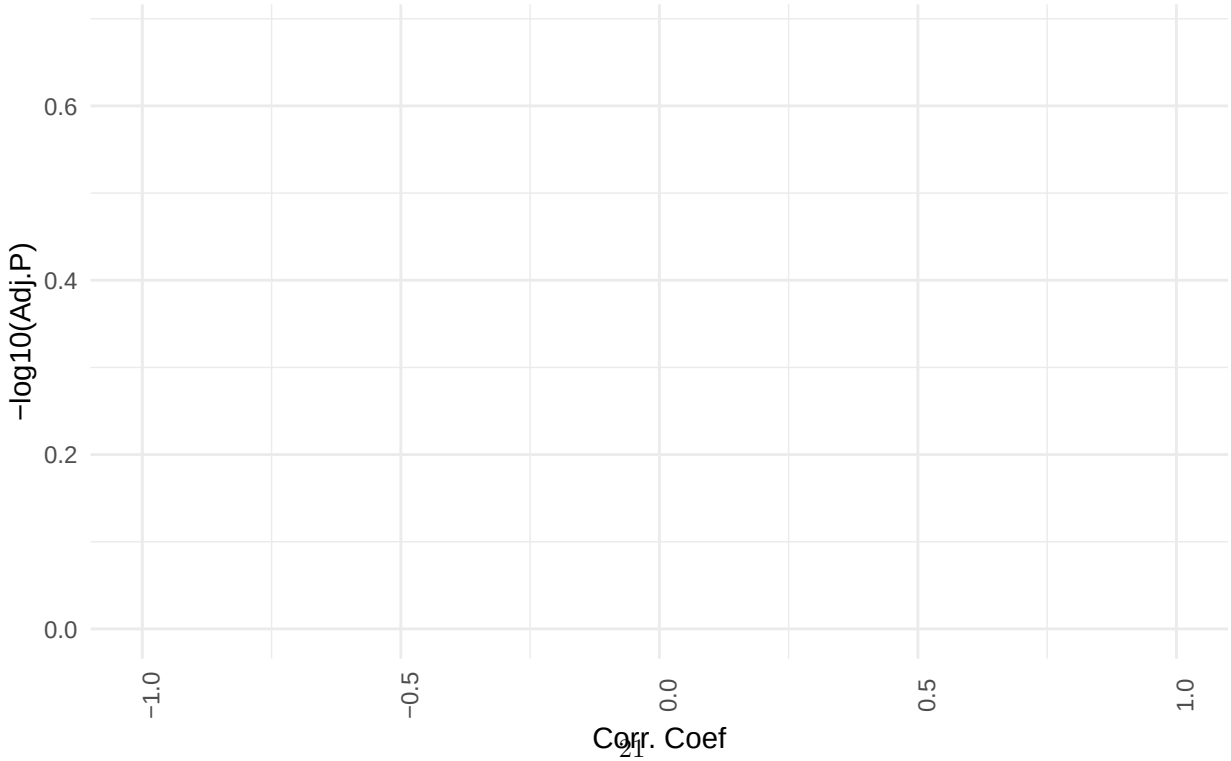


Hallmarks Squamous

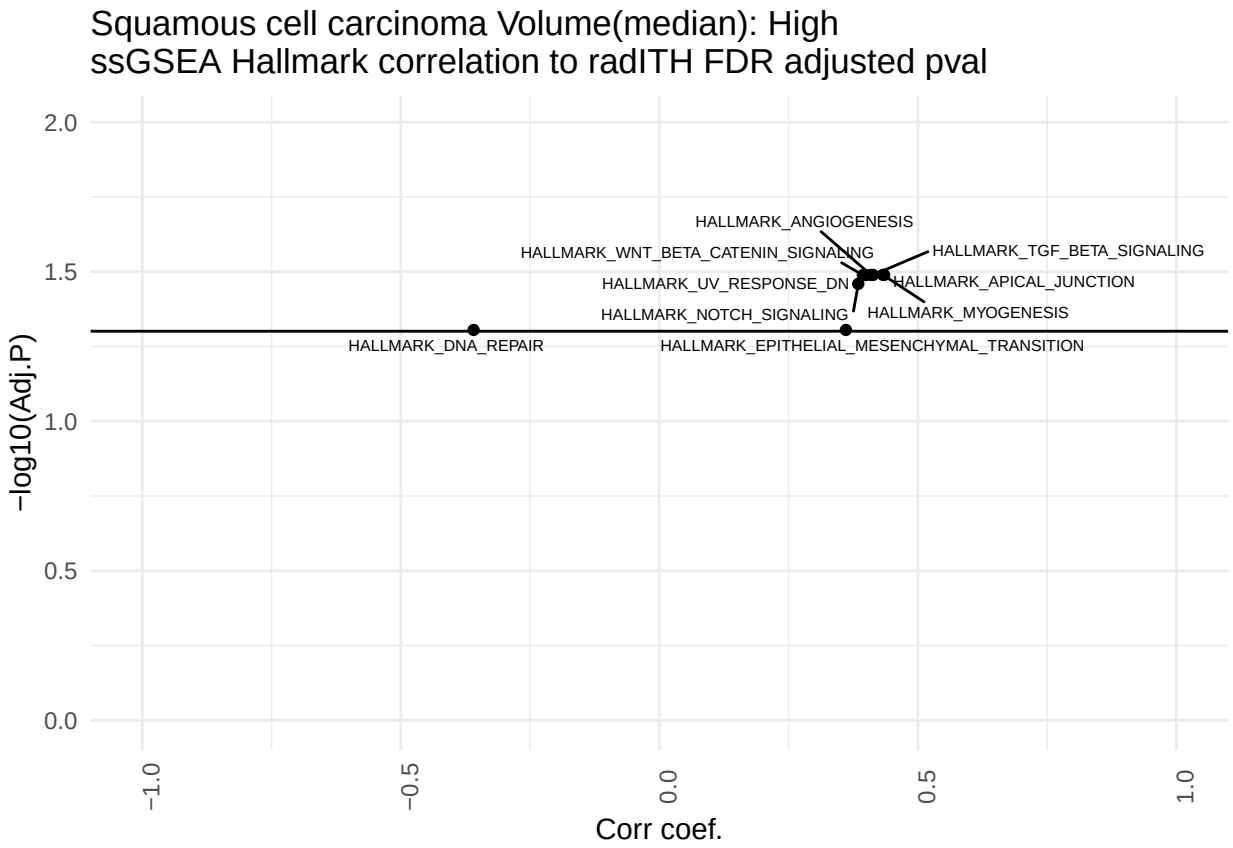


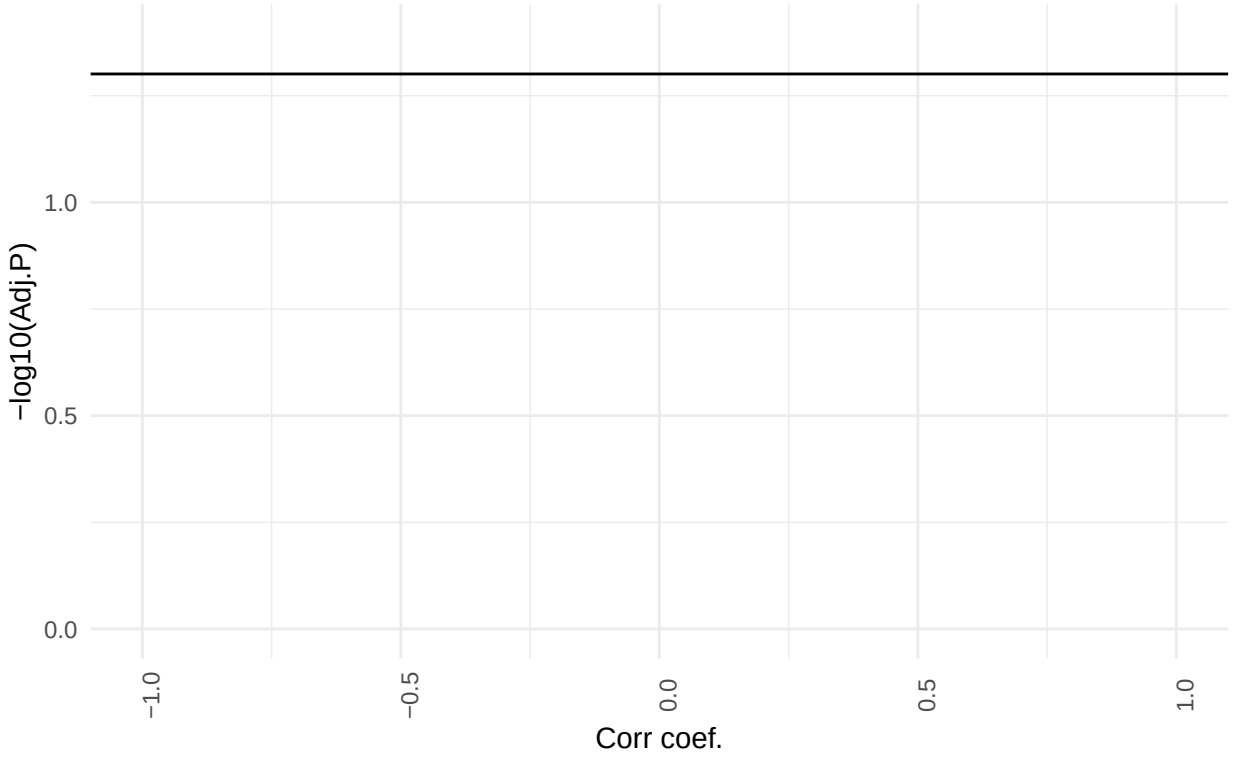
Hallmark expression-radITH Correlation in Large vs Small tumors (all samples)

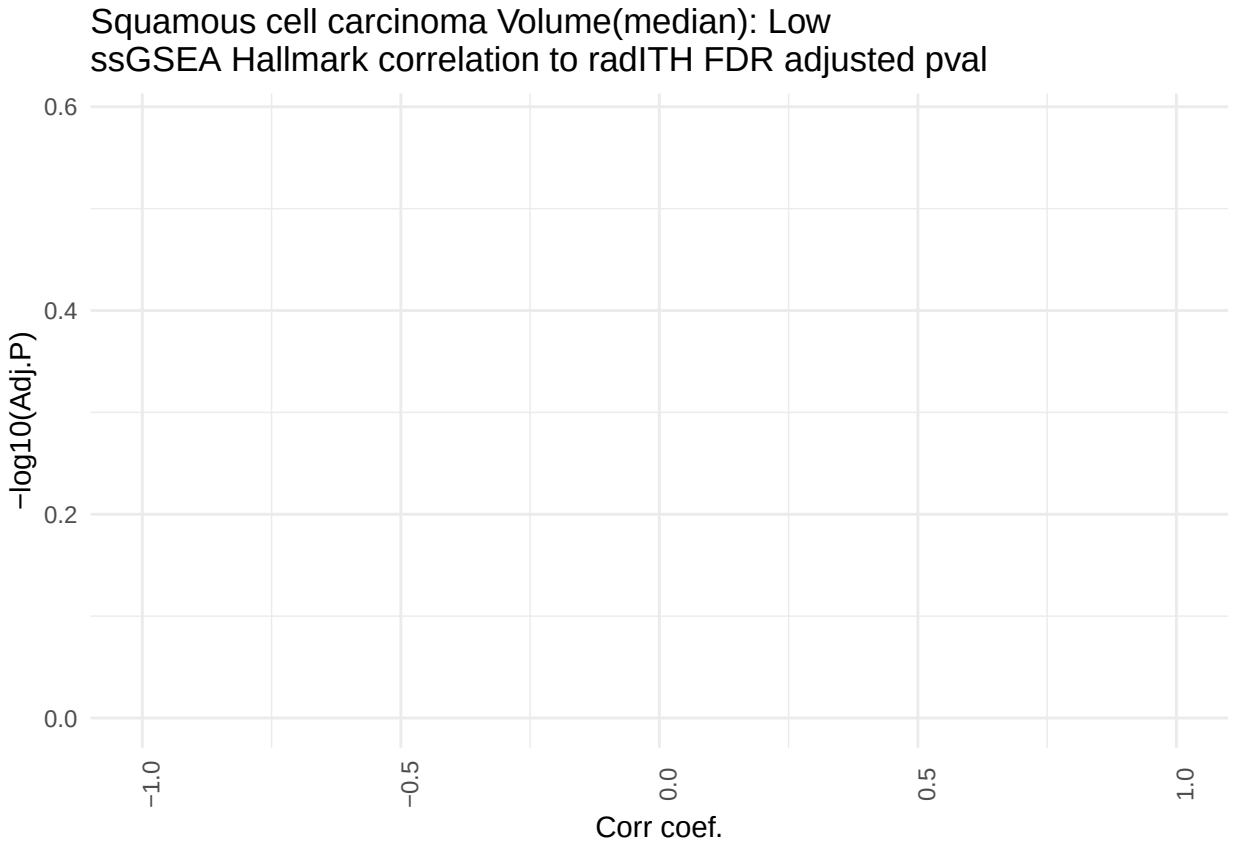


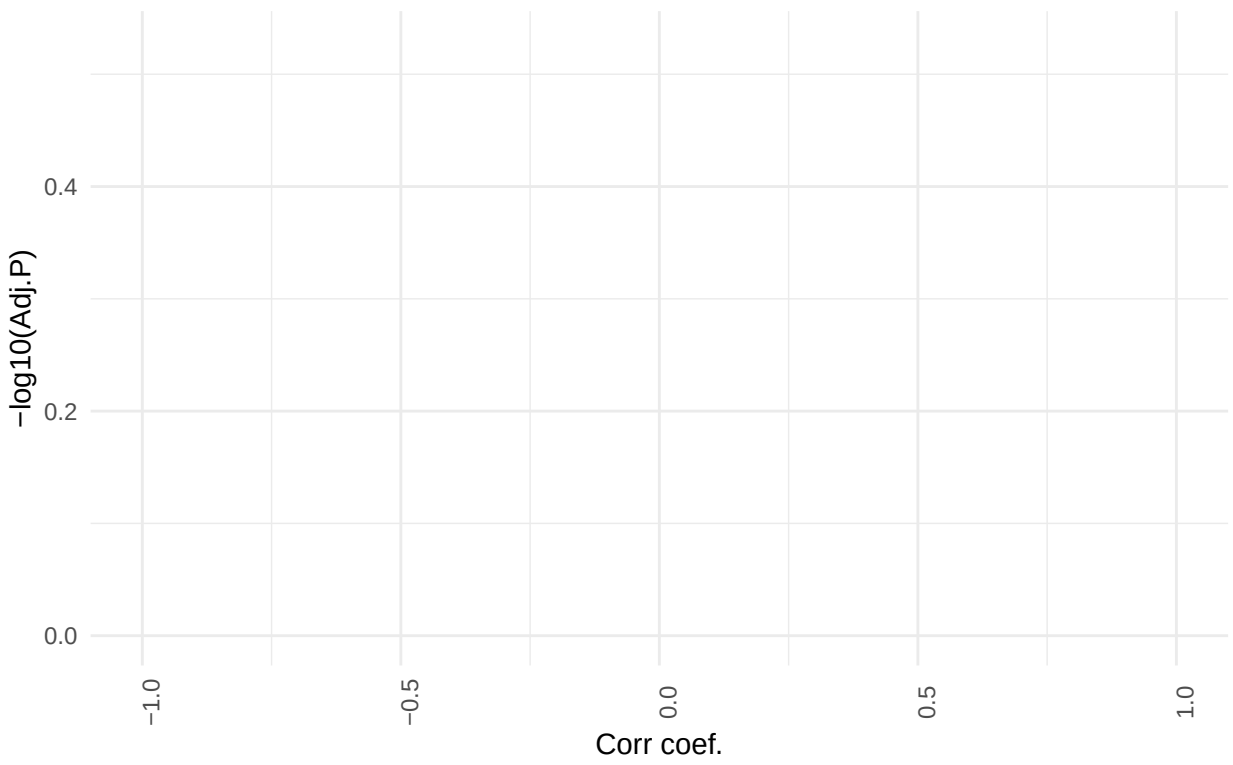


Let's split by Size and Pathology and repeat



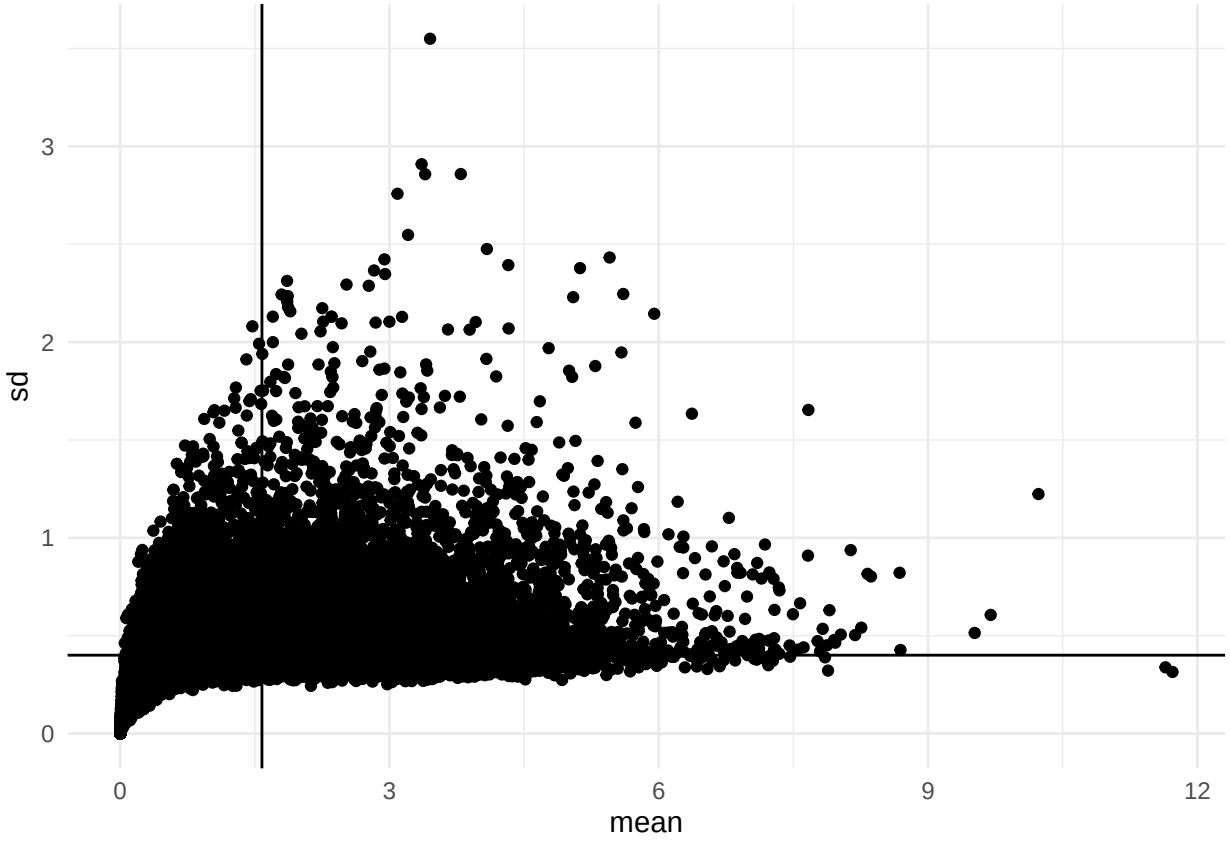



Squamous cell carcinoma Volume(median): Low
ssGSEA Hallmark correlation to radITH FDR adjusted pval
0.6
0.4
0.2
0.0
−log10(Adj.P)
−1.0
−0.5
0.0
0.5
1.0
Corr coef.


Invasive adenocarcinoma Volume(median): Low
ssGSEA Hallmark correlation to radITH FDR adjusted pval
0.4
0.2
0.0
−log10(Adj.P)
−1.0
−0.5
0.0
0.5
1.0
Corr coef.

Picking genes for Gene Expression Analysis

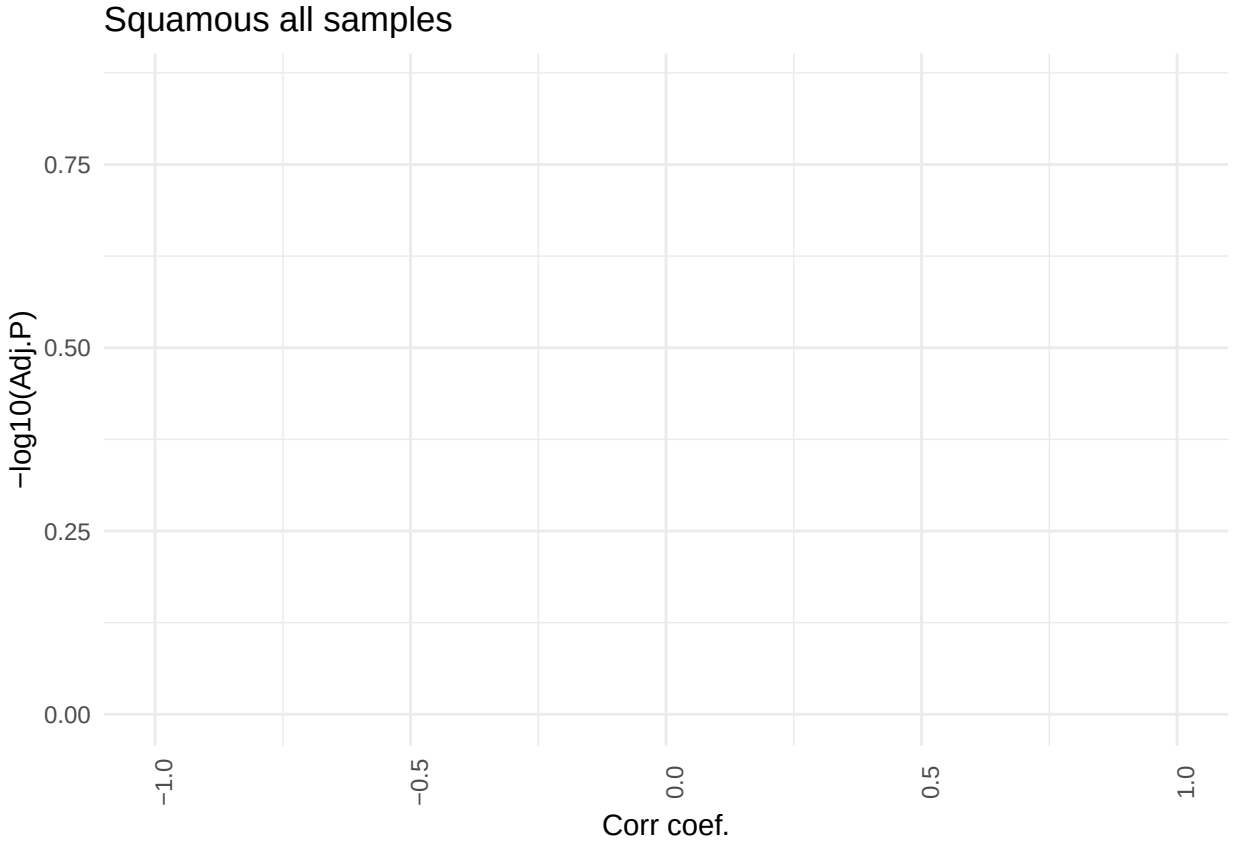
- Mean and SD value based on entire cohort

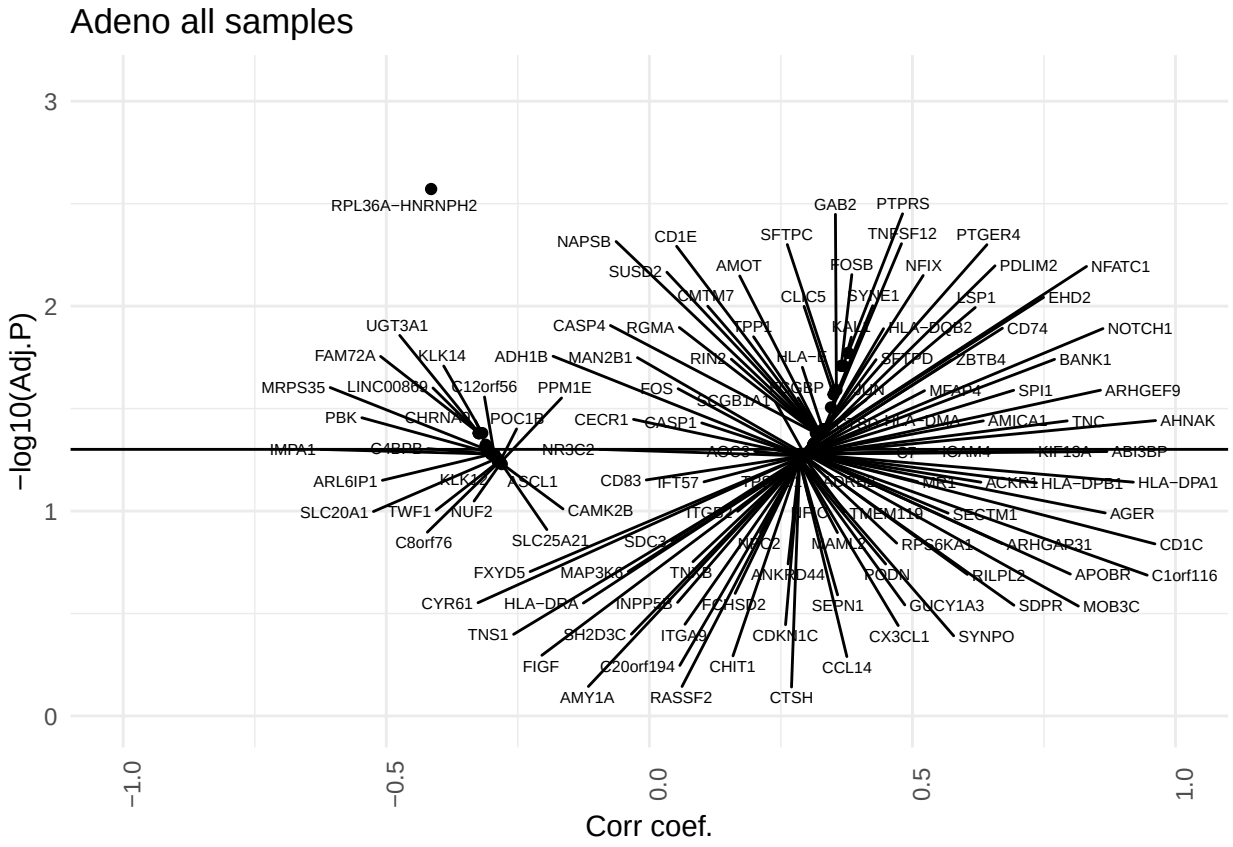



```
## Number of Genes after cutoff:  10332
```

Gene Expression Analysis without volume

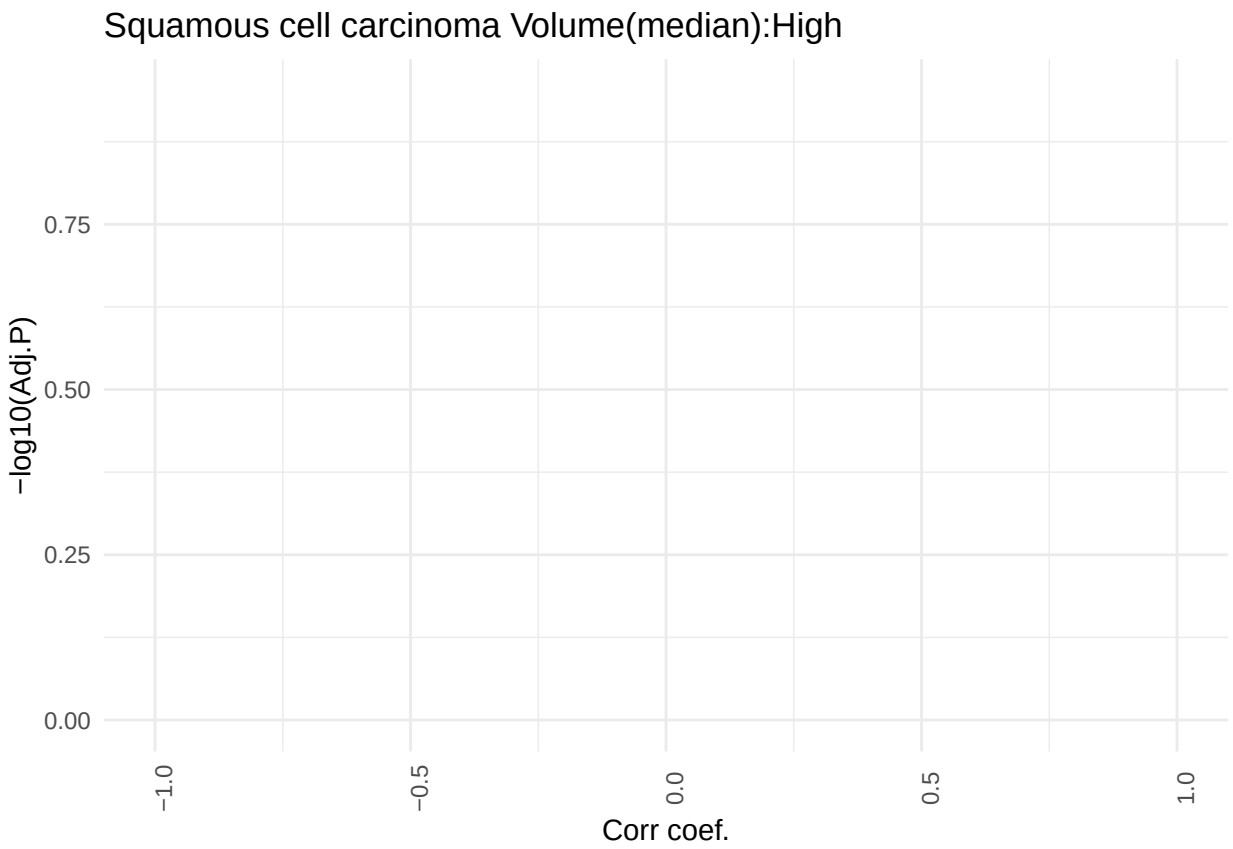
- Genes that were picked for analysis were based on mean and SD (entire cohort)

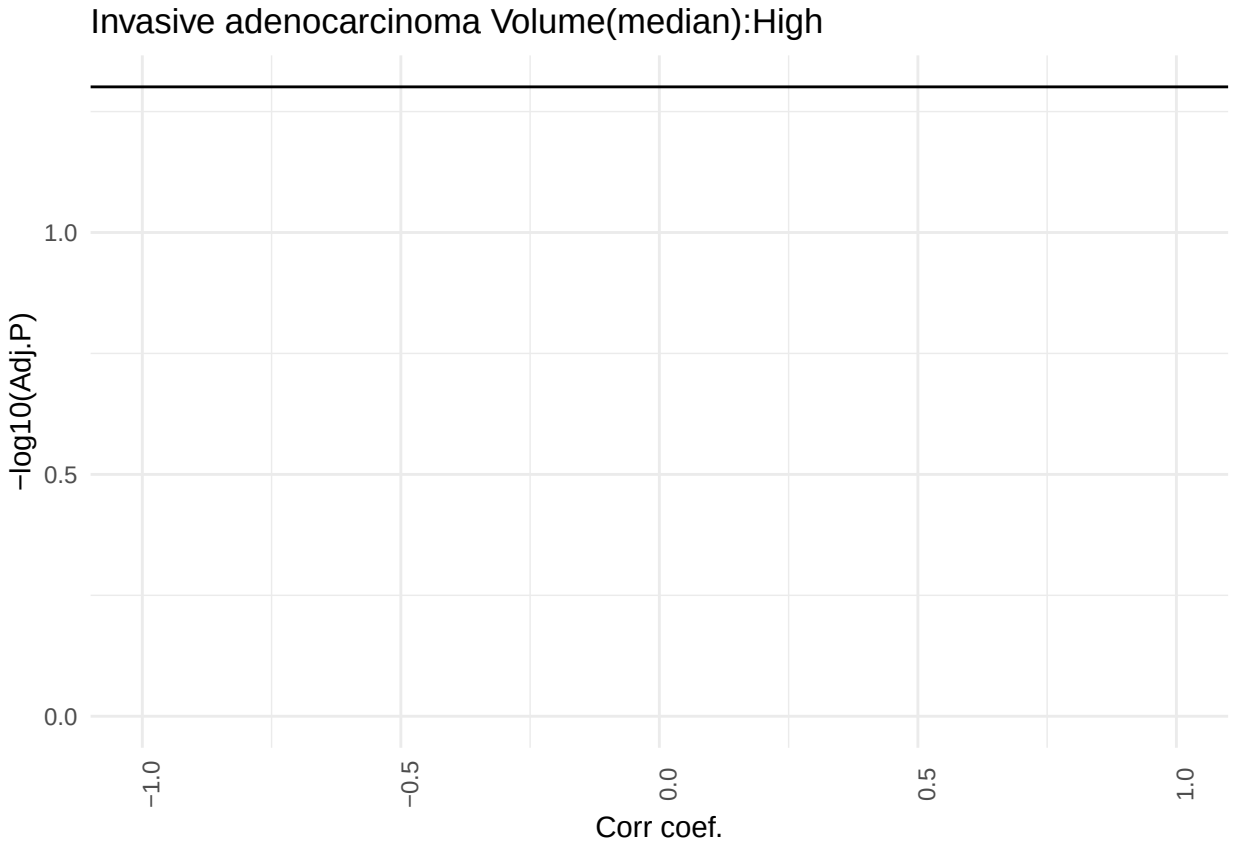

Squamous all samples
0.75
0.50
0.25
0.00
−log10(Adj.P)
−1.0
−0.5
0.0
0.5
1.0
Corr coef.

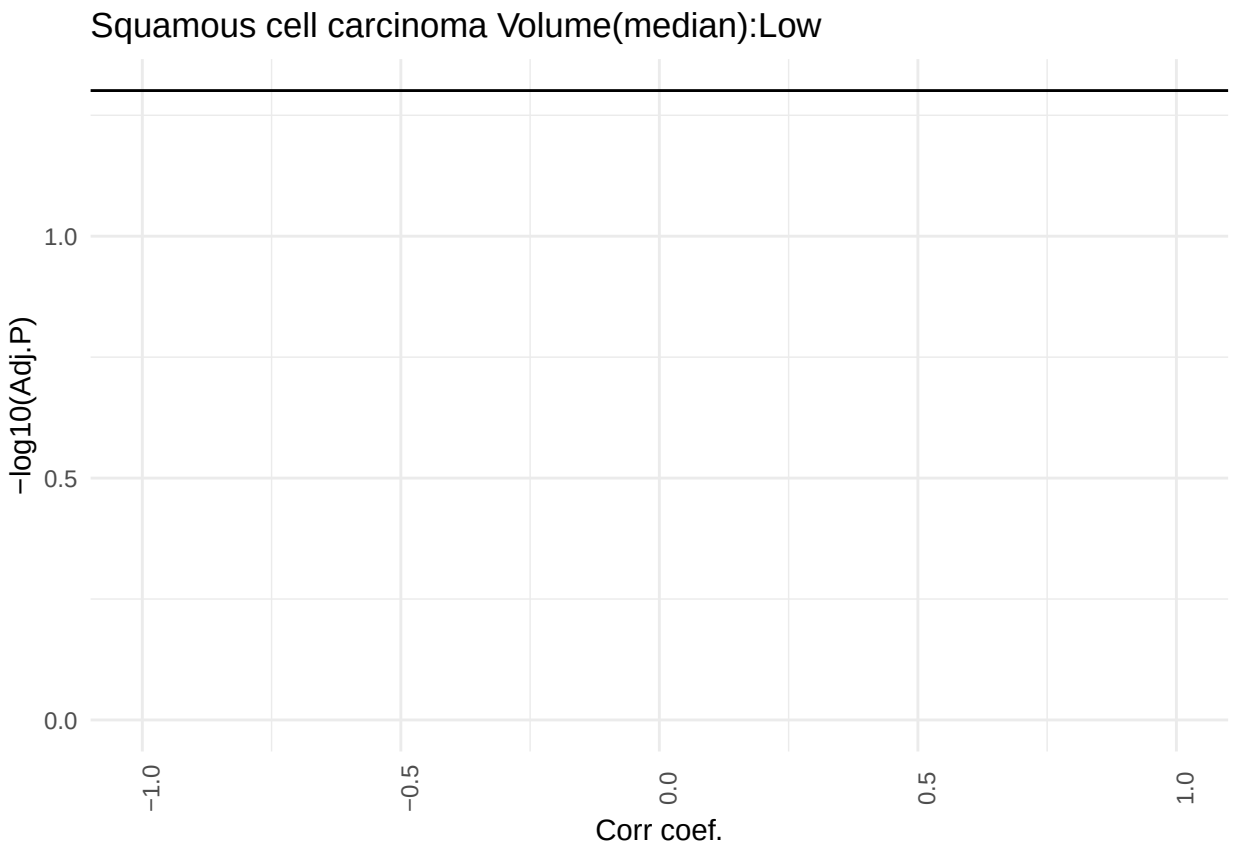

Adeno all samples
3
2
1
0
−log10(Adj.P)
RPL36A−HNRNPH2
GAB2
PTPRS
NAPSB
CD1E
SFTPC
TNFSF12
PTGER4
SUSD2
AMOT
FOSB
NFIX
PDLIM2
NFATC1
CMTM7
CLIC5
SYNE1
LSP1
EHD2
UGT3A1
CASP4
RGMA
TPP1
HLA−DQB2
CD74
NOTCH1
FAM72A
KLK14
ADH1B
MAN2B1
RIN2
HLA−E
SFTPD
ZBTB4
BANK1
MRPS35
LINC00869
C12orf56
PPM1E
EOS
SCGB1A1
MFAP4
SPI1
ARHGEF9
PBK
CHRNA1
POC1B
CECR1
CASP1
HLA−DMA
AMICA1
TNC
AHNAK
IMPA1
C4BPB
NR3C2
AGC1
ICAM1
KIF13A
ABI3BP
ARL6IP1
KLK1
CCL1
CD83
IFT57
ACKR1
HLA−DPB1
HLA−DPA1
SLC20A1
TWF1
NUF2
CAMK2B
ITGB4
TMEM110
SECTM1
AGER
C8orf76
SLC25A21
SDC3
RPS6KA1
ARHGAP31
CD1C
FXYD5
MAP3K6
TNNC2
ANKRD44
PODN
RILPL2
APOBR
C1orf116
CYR61
HLA−DRA
INPP5D
FCHSD2
SEPN1
GUCY1A3
SDPR
MOB3C
TNS1
SH2D3C
ITGA9
CDKN1C
CX3CL1
SYNPO
FIGF
C20orf194
CHIT1
CCL14
AMY1A
RASSF2
CTSH
−1.0
−0.5
0.0
0.5
1.0
Corr coef.

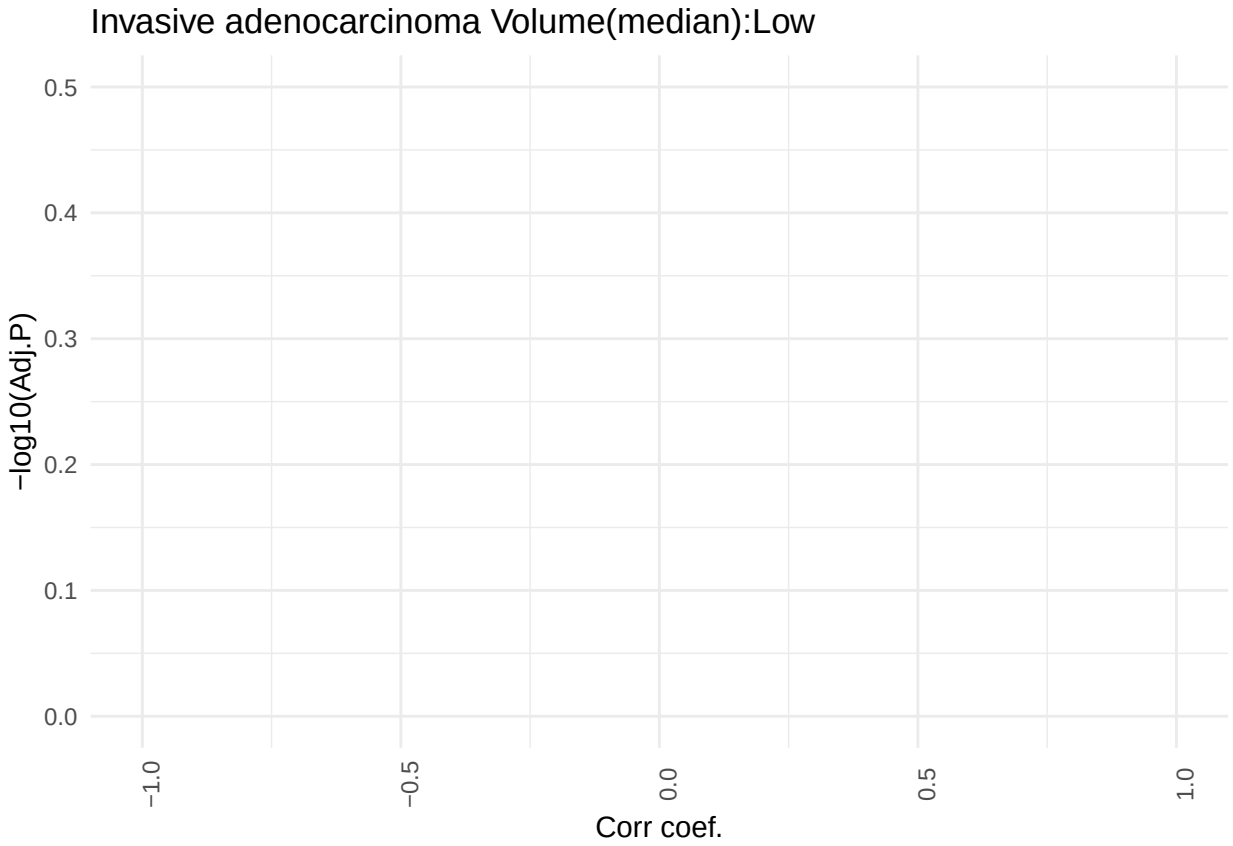
Gene Expression Analysis by volume group and cancer type

- Genes that were picked for analysis were based on mean and SD (entire cohort)

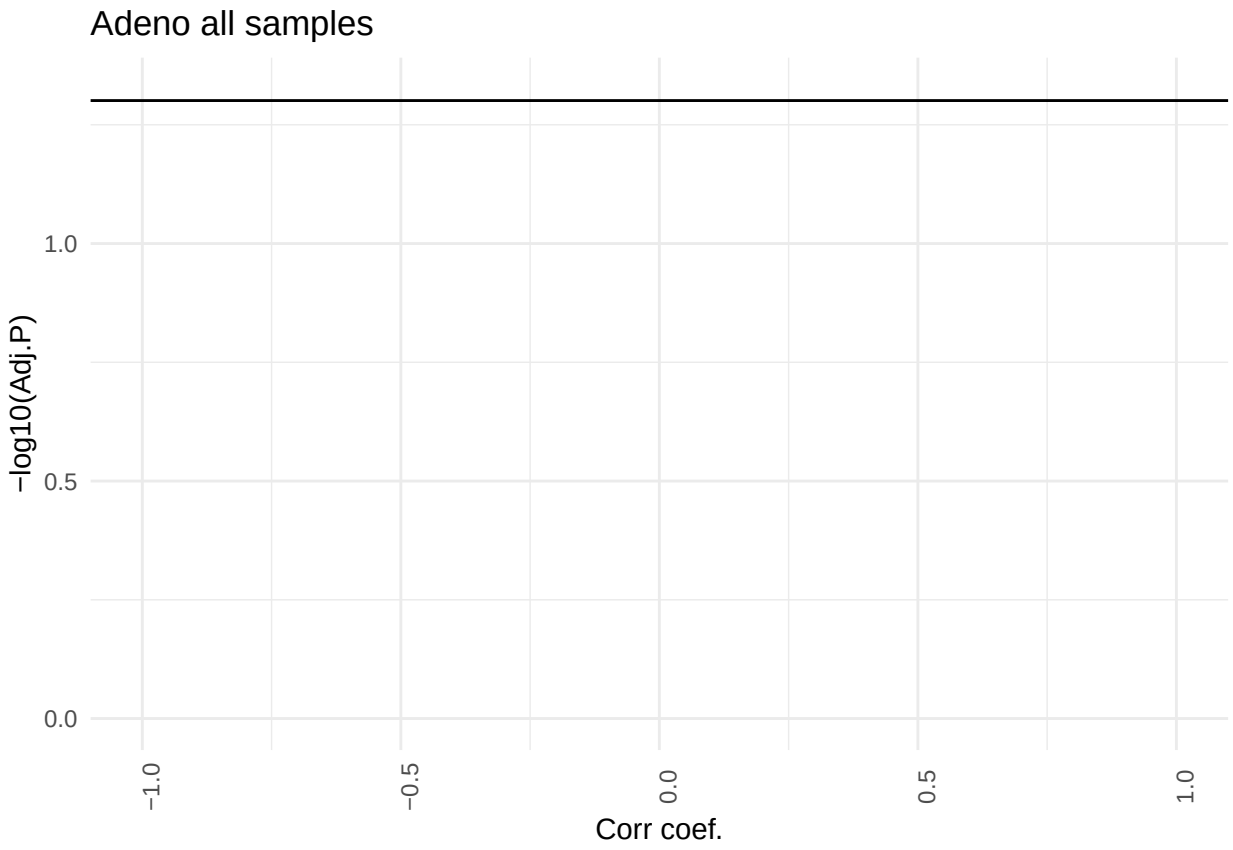


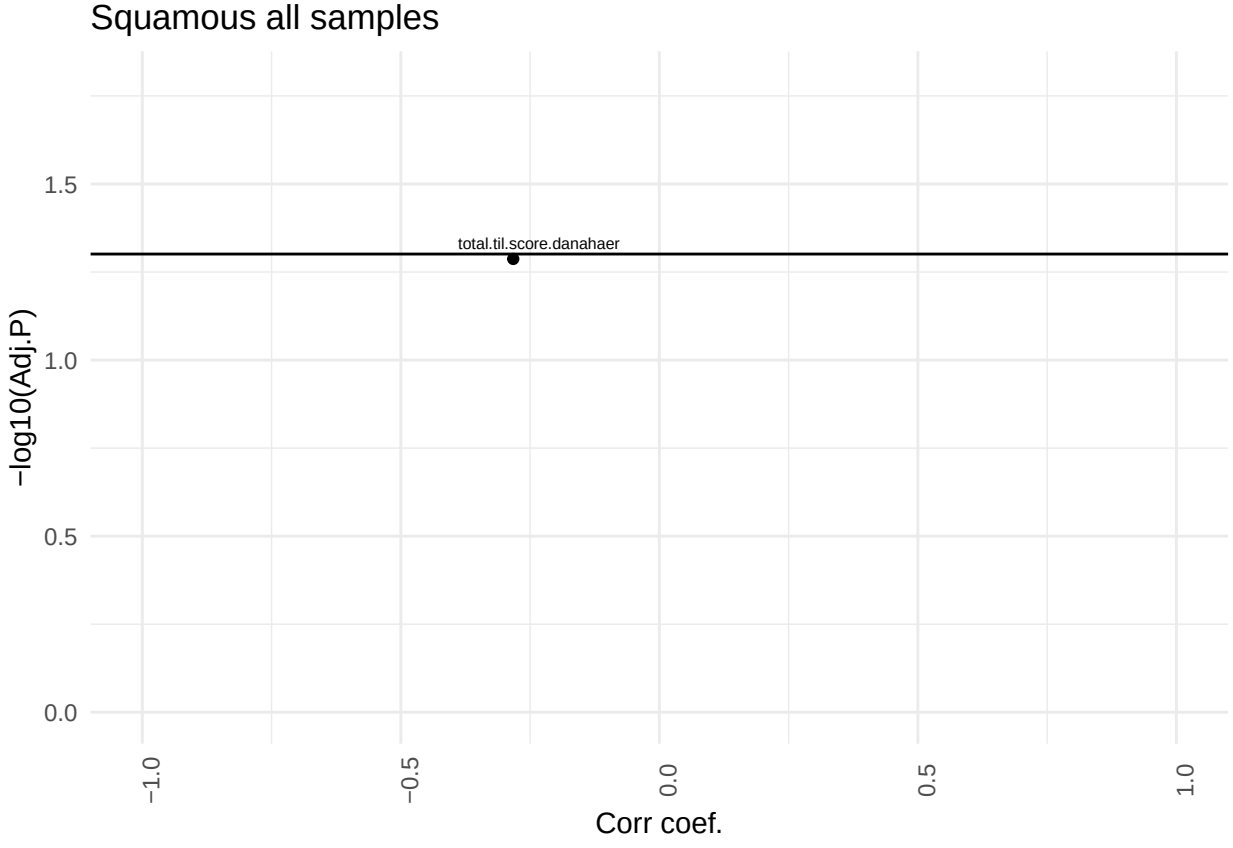

Invasive adenocarcinoma Volume(median):High
−log10(Adj.P)
1.0
0.5
0.0
−1.0
−0.5
0.0
0.5
1.0
Corr coef.

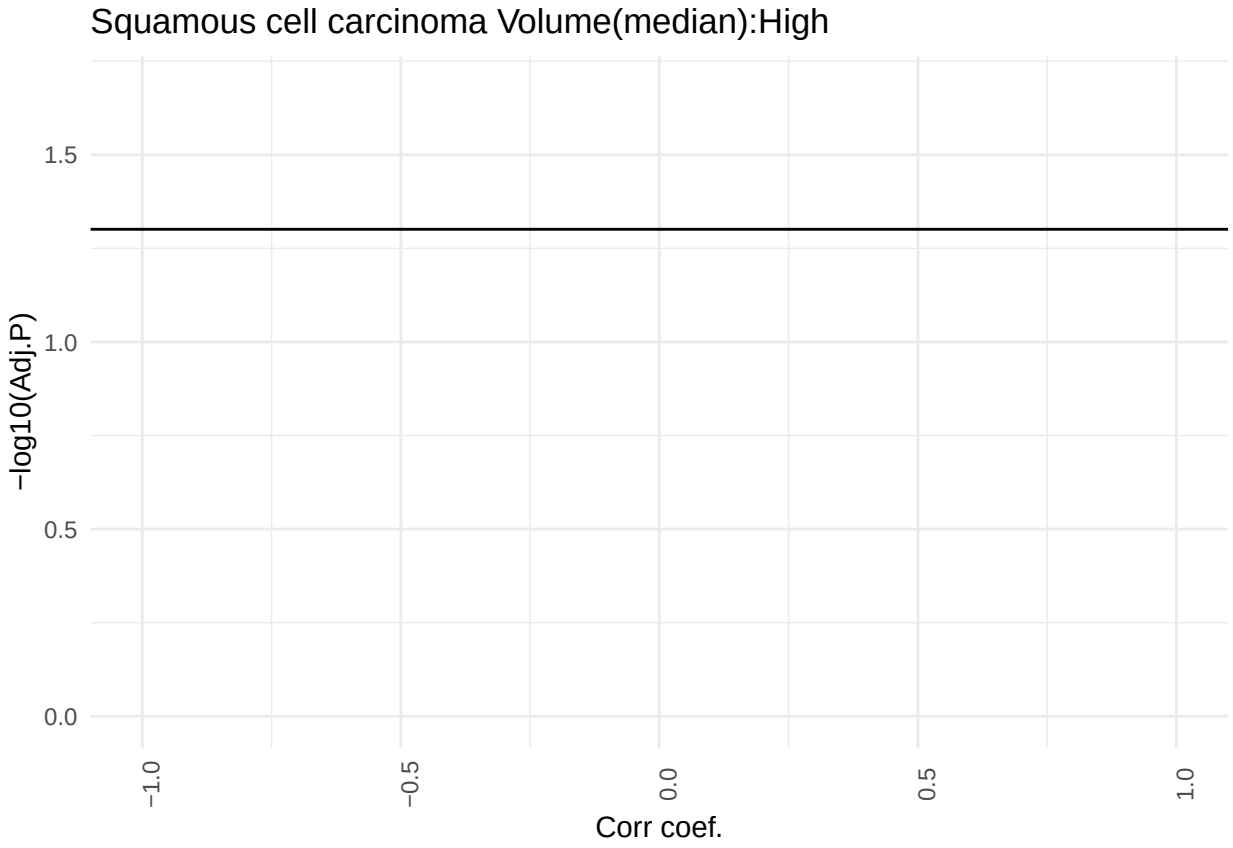

Squamous cell carcinoma Volume(median):Low
−log10(Adj.P)
1.0
0.5
0.0
−1.0
−0.5
0.0
0.5
1.0
Corr coef.

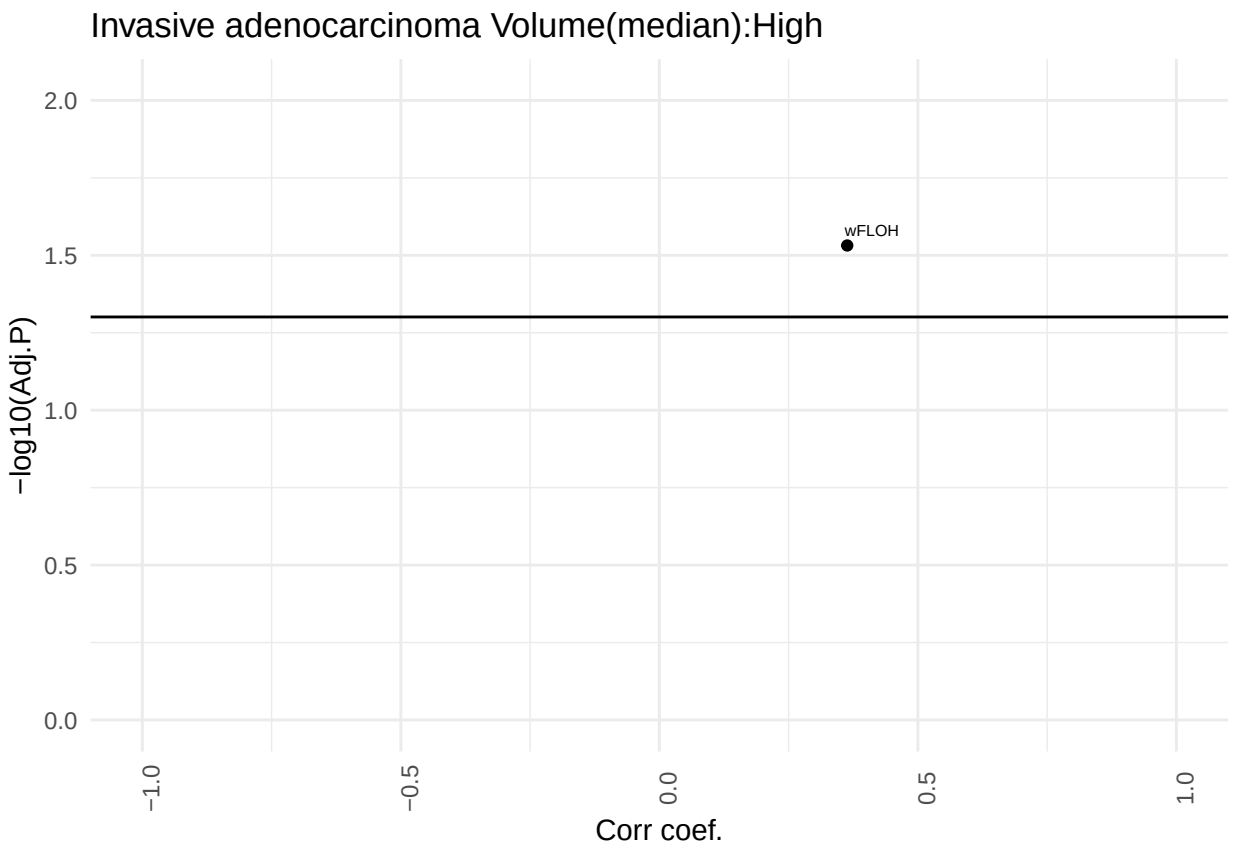

Invasive adenocarcinoma Volume(median):Low
0.5
0.4
0.3
0.2
0.1
0.0
−log10(Adj.P)
−1.0
−0.5
0.0
0.5
1.0
Corr coef.

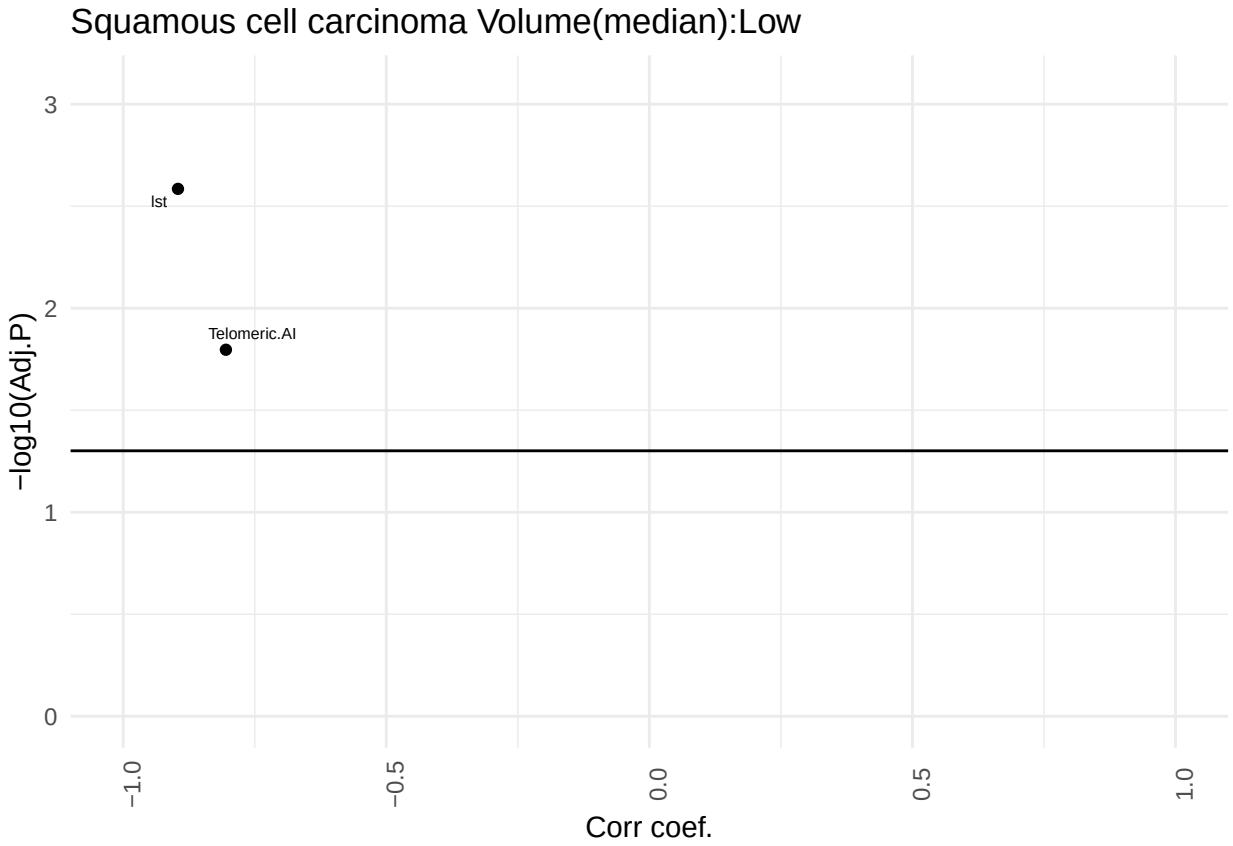
Chr Instability and TIL

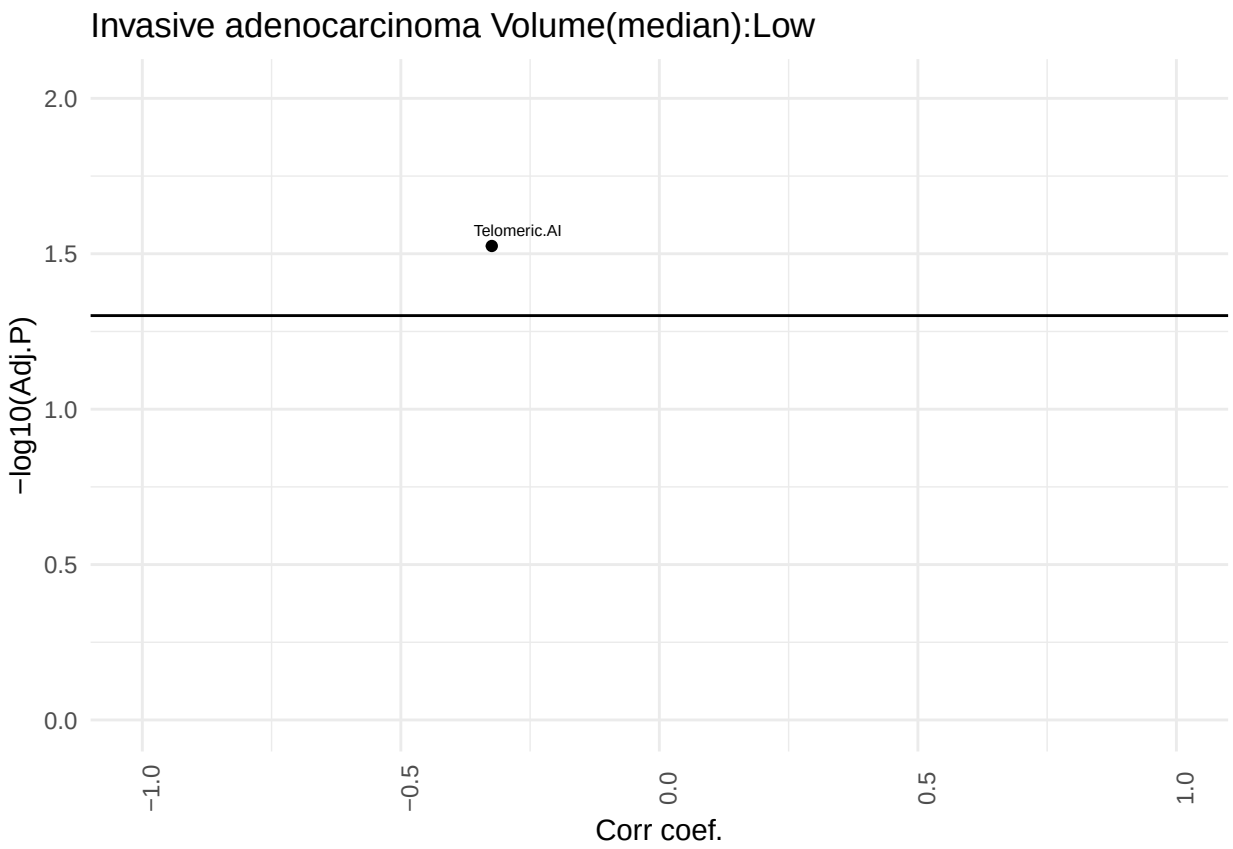





Squamous cell carcinoma Volume(median):High
1.5
1.0
0.5
0.0
−log10(Adj.P)
−1.0
−0.5
0.0
0.5
1.0
Corr coef.


Invasive adenocarcinoma Volume(median):High
2.0
1.5
1.0
0.5
0.0
−log10(Adj.P)
wFLOH
−1.0
−0.5
0.0
0.5
1.0
Corr coef.


Squamous cell carcinoma Volume(median):Low
3
2
1
0
lst
Telomeric.AI
−log10(Adj.P)
−1.0
−0.5
0.0
0.5
1.0
Corr coef.


Invasive adenocarcinoma Volume(median):Low
2.0
1.5
1.0
0.5
0.0
Telomeric.AI
−log10(Adj.P)
−1.0
−0.5
0.0
0.5
1.0
Corr coef.