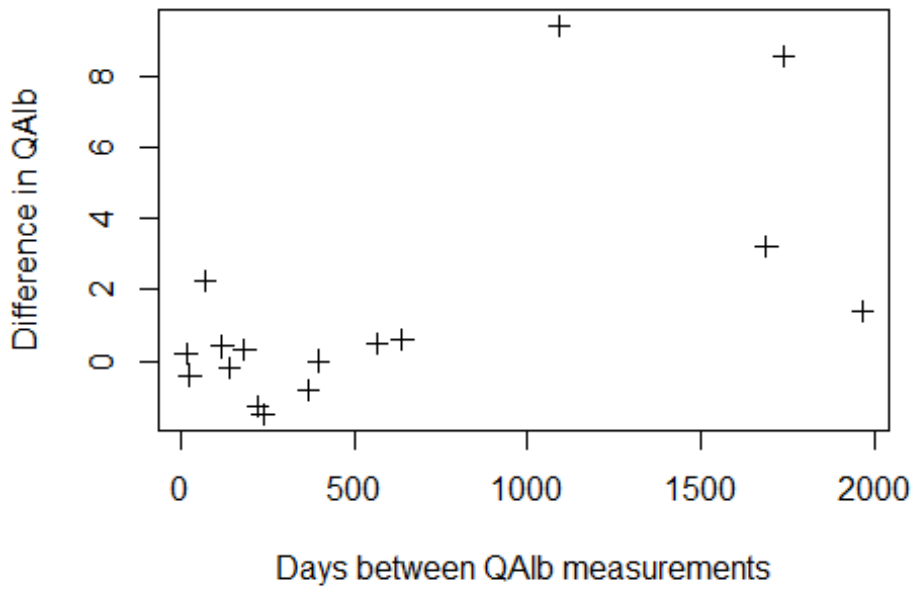
Supplementary Material

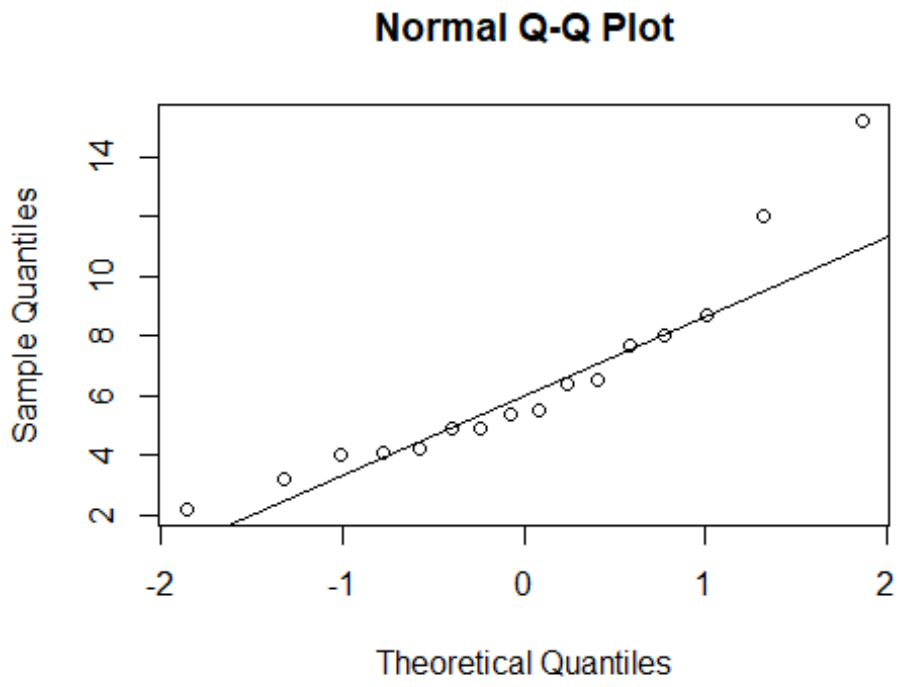
Progression of Blood-Brain Barrier Leakage in Patients with Alzheimer's Disease as Measured with the Cerebrospinal Fluid/Plasma Albumin Ratio Over Time

Analysis

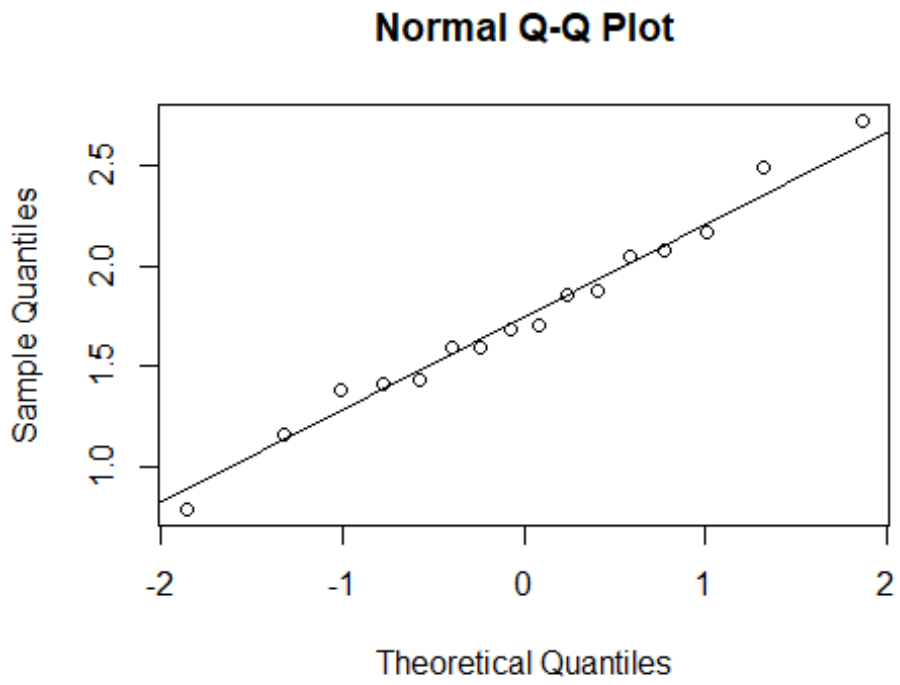
```
# One-sample t-test
res <- t.test(BBH$Alb_diff)
res
##
##  One Sample t-test
##
## data:  BBH$Alb_diff
## t = 1.7717, df = 15, p-value = 0.09675
## alternative hypothesis: true mean is not equal to 0
## 95 percent confidence interval:
##  -0.2873134  3.1172177
## sample estimates:
## mean of x
##  1.414952
res$p.value
## [1] 0.096753
res$conf.int
## [1] -0.2873134  3.1172177
## attr(,"conf.level")
## [1] 0.95
plot(BBH$Time_diff,BBH$Alb_diff,pch = c(3), xlab = "Days between QAlb
measurements", ylab = "Difference in QAlb")
```



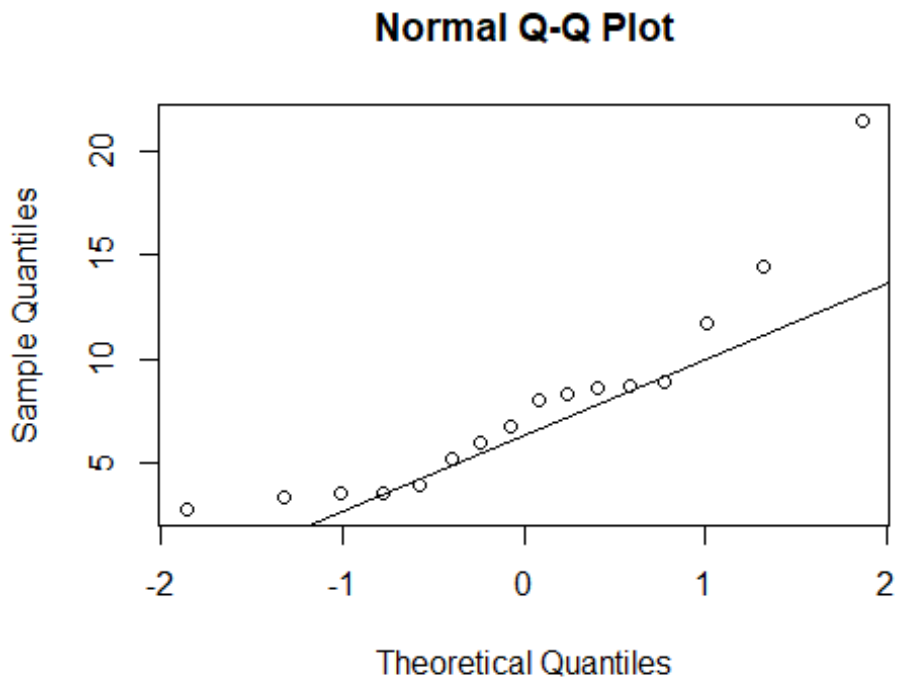

```r
#Paired t-test - for stats
qqnorm(BBH$`Cerebrospinal fluids_Albumin ratio`)
qqline(BBH$`Cerebrospinal fluids_Albumin ratio`)
```



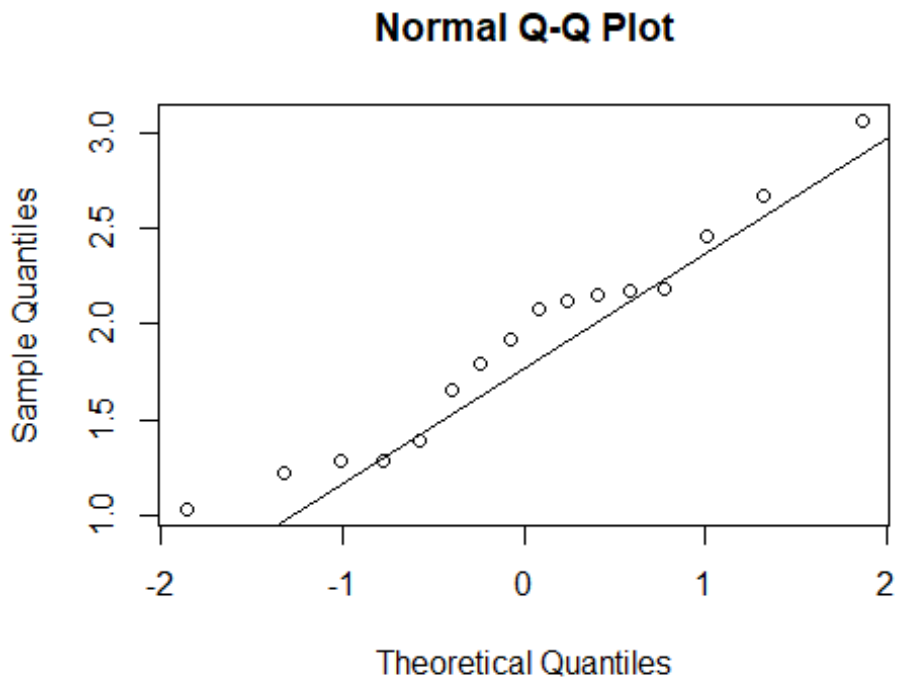

```
qqnorm( log(BBH$`Cerebrospinal fluids_Albumin ratio`) )
qqline( log(BBH$`Cerebrospinal fluids_Albumin ratio`) )
```




```
qqnorm(BBH$`Cerebrospinal fluids_Albumin ratio2`)
qqline(BBH$`Cerebrospinal fluids_Albumin ratio2`)
```

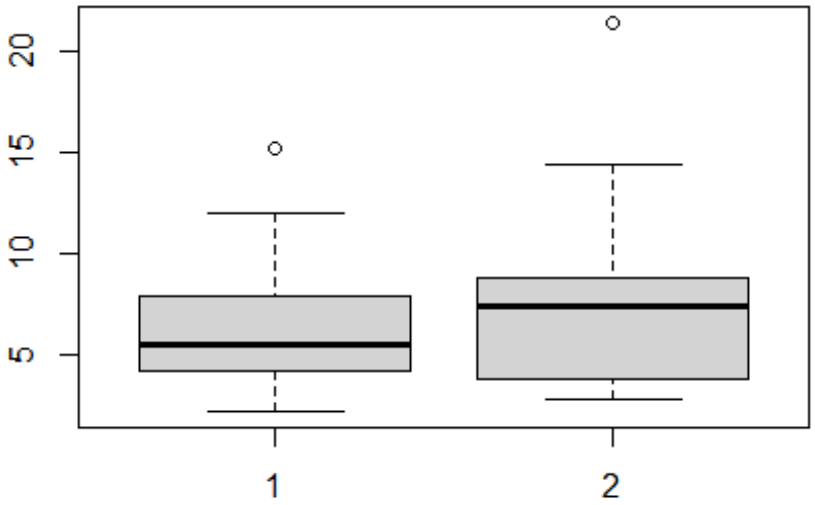



```
qqnorm( log(BBH$`Cerebrospinal fluids_Albumin ratio2`) )
qqline( log(BBH$`Cerebrospinal fluids_Albumin ratio2`) )
```




```
# When using paired t-tests, it seems to help with log-transform of the data

boxplot(BBH$`Cerebrospinal fluids_Albumin ratio`, BBH$`Cerebrospinal
fluids_Albumin ratio2`)
```

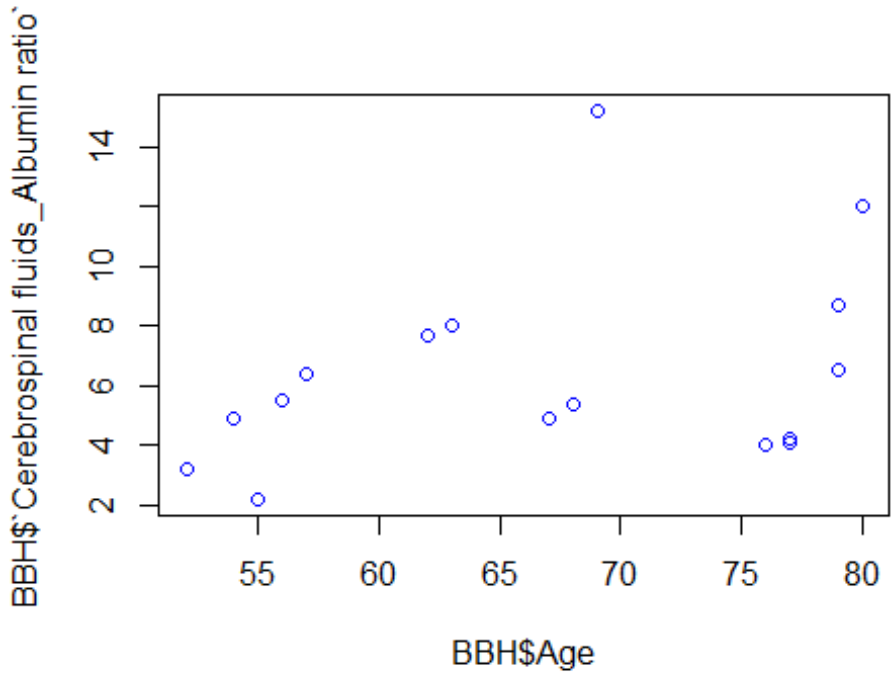



```
res <- t.test(BBH$`Cerebrospinal fluids_Albumin ratio`, BBH$`Cerebrospinal
fluids_Albumin ratio2`, paired = TRUE, alternative = "two.sided")
res$p.value
## [1] 0.096753
res$conf.int
## [1] -3.1172177  0.2873134
## attr(,"conf.level")
## [1] 0.95
res <- t.test(log(BBH$`Cerebrospinal fluids_Albumin ratio`),
log(BBH$`Cerebrospinal fluids_Albumin ratio2`), paired = TRUE, alternative =
"two.sided")
res$p.value
## [1] 0.1493965
res$conf.int
## [1] -0.37401526  0.06267315
## attr(,"conf.level")
## [1] 0.95
# Comparing <1 year and >1 year
wilcox.test(BBH$Alb_diff_procent~as.factor(BBH$Group_year))
##
##  Wilcoxon rank sum exact test
##
## data:  BBH$Alb_diff_procent by as.factor(BBH$Group_year)
## W = 53, p-value = 0.02813
## alternative hypothesis: true location shift is not equal to 0
```

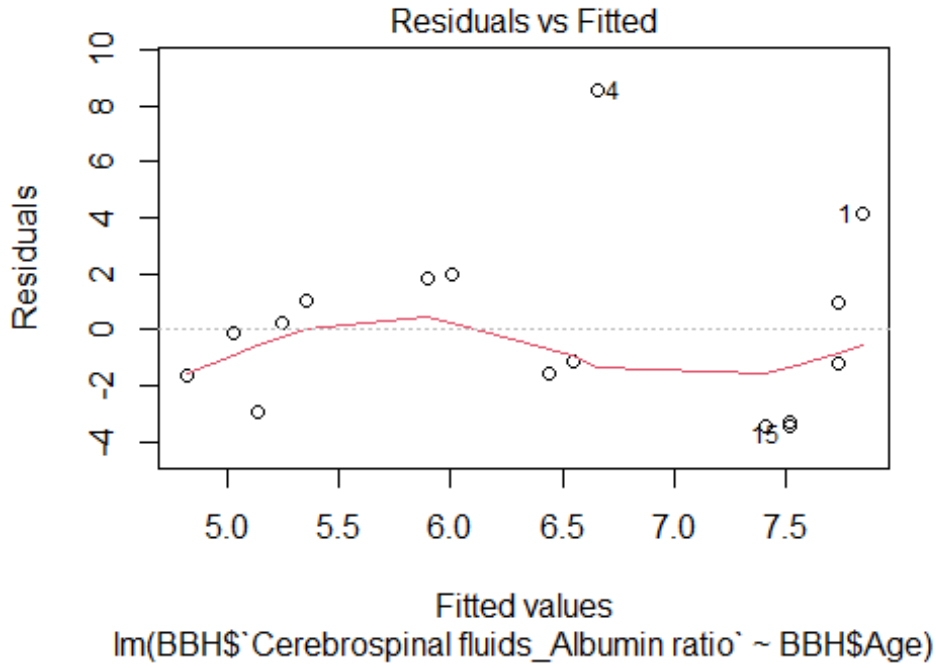
Correlations

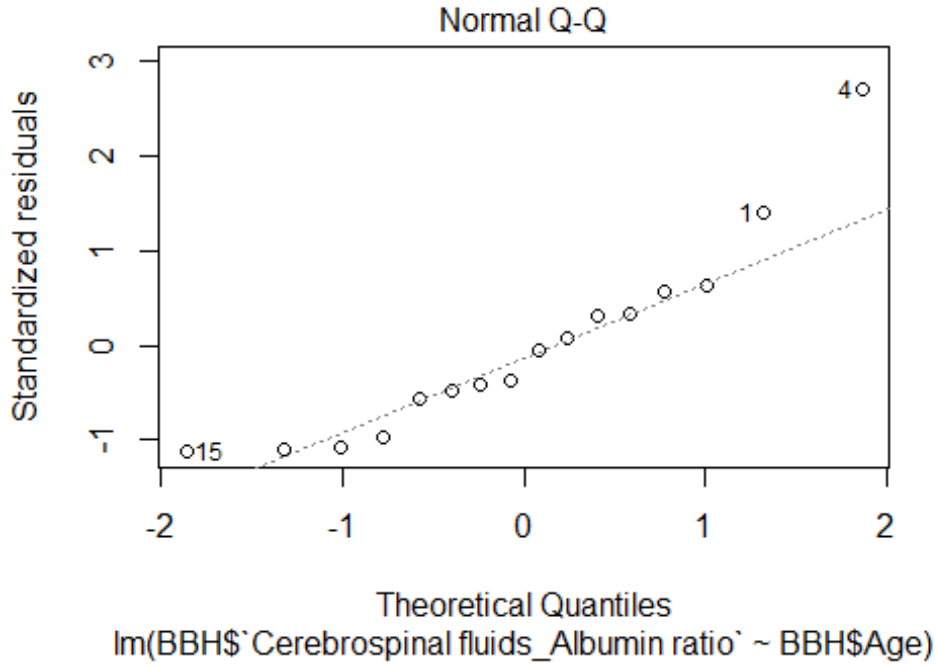
```
# Age
model.linreg <- lm(BBH$`Cerebrospinal fluids_Albumin ratio`~ BBH$Age)
summary(model.linreg)
##
## Call:
## lm(formula = BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$Age)
##
## Residuals:
```

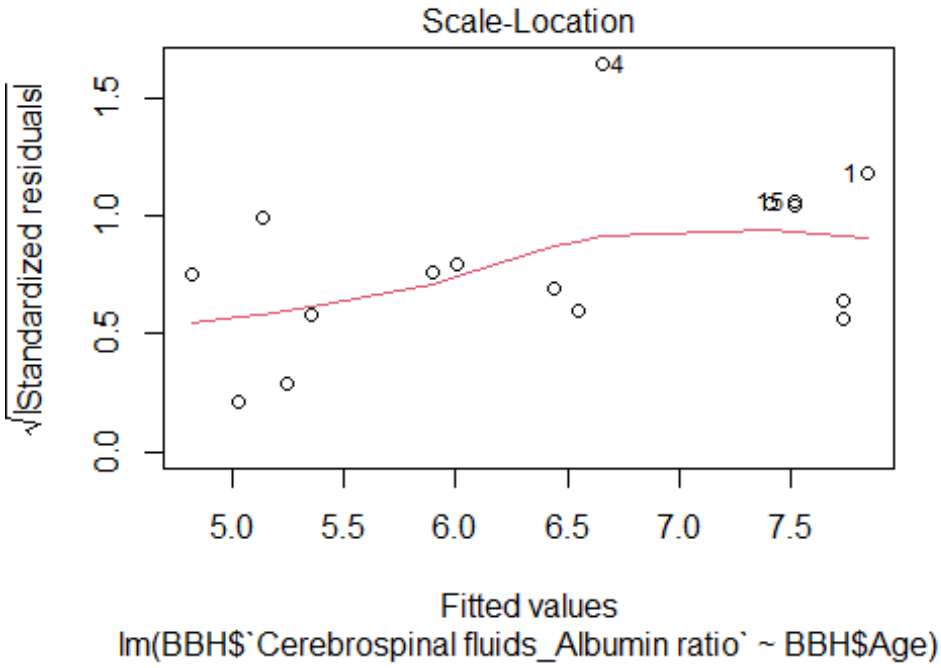
```
##     Min      1Q  Median      3Q     Max
## -3.4179 -1.9600 -0.6382  1.2341  8.5469
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept) -0.80632    5.64707  -0.143    0.888
## BBH$Age      0.10811    0.08347   1.295    0.216
##
## Residual standard error: 3.279 on 14 degrees of freedom
## Multiple R-squared:  0.107,  Adjusted R-squared:  0.04321
## F-statistic: 1.677 on 1 and 14 DF,  p-value: 0.2162
confint(model.linreg)
##                    2.5 %     97.5 %
## (Intercept) -12.91807253 11.3054321
## BBH$Age      -0.07091763  0.2871323
plot(BBH$`Cerebrospinal fluids_Albumin ratio`~ BBH$Age, col = "blue")
```

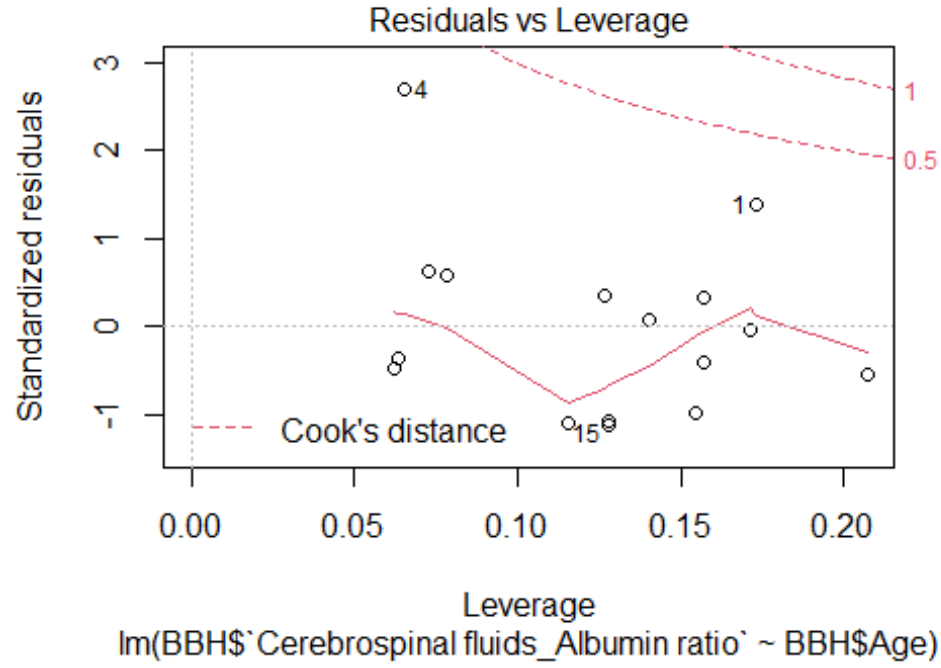



```
plot(model.linreg)
```

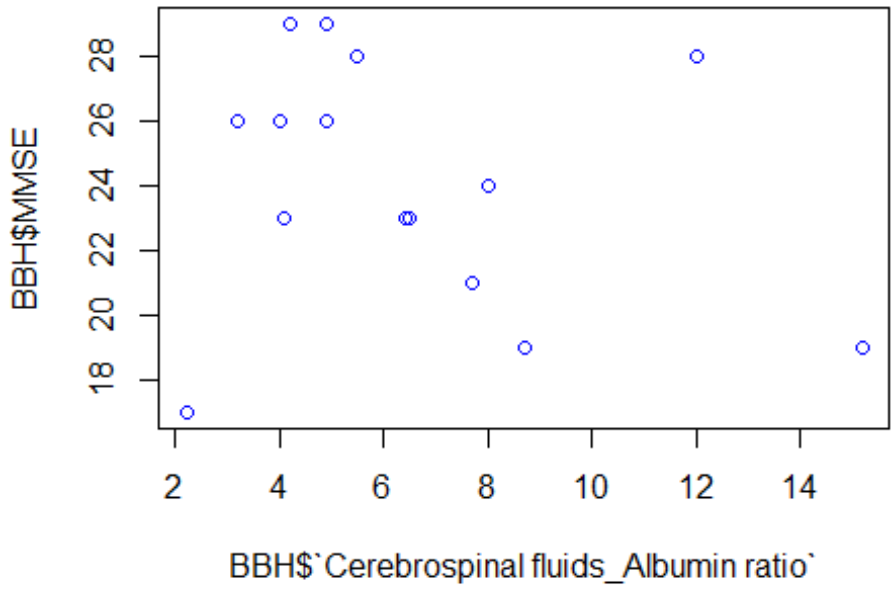

Residuals vs Fitted
Residuals
Fitted values
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$Age)


Normal Q-Q
Standardized residuals
Theoretical Quantiles
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$Age)

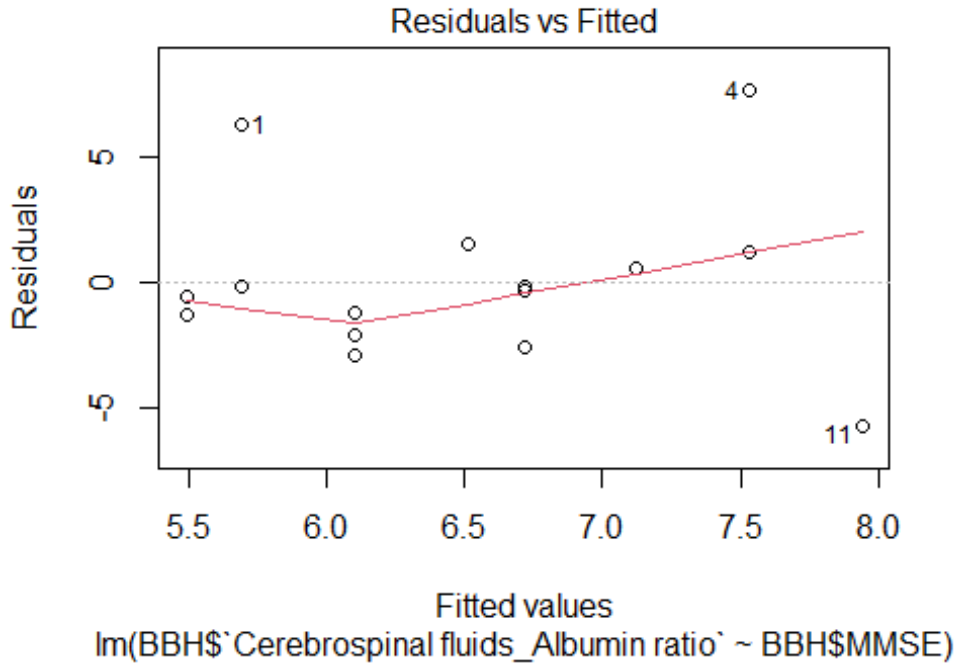

Scale-Location
√|Standardized residuals|
0.0
0.5
1.0
1.5
4
1
15
5.0
5.5
6.0
6.5
7.0
7.5
Fitted values
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$Age)

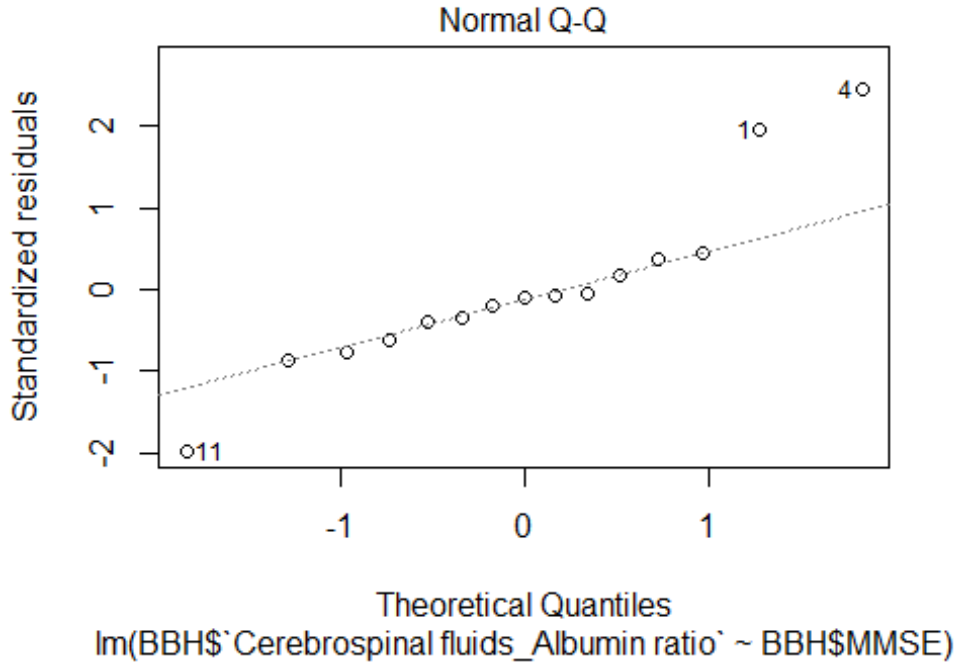

Residuals vs Leverage
Standardized residuals
-1
0
1
2
3
4
1
0.5
1
Cook's distance
15
0.00
0.05
0.10
0.15
0.20
Leverage
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$Age)

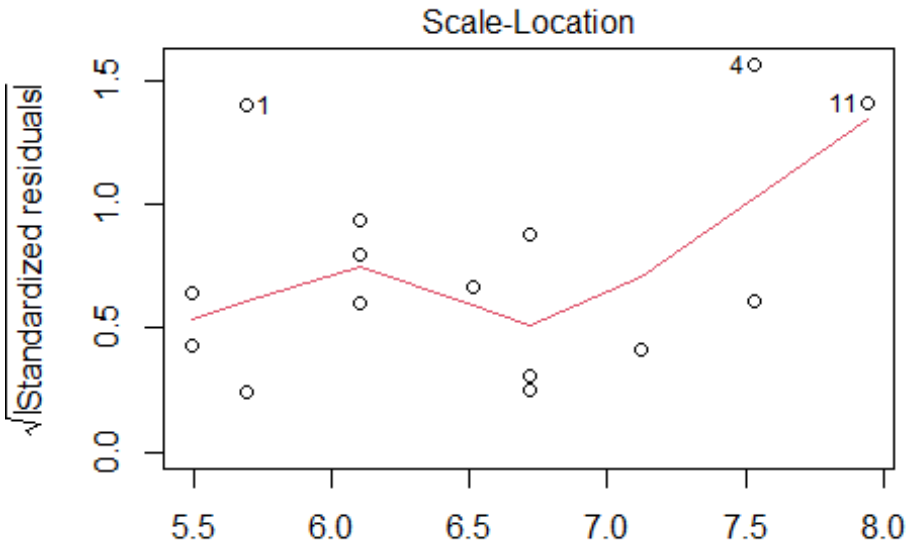
```r
# MMSE
model.linreg <- lm(BBH$`Cerebrospinal fluids_Albumin ratio`~ BBH$MMSE)
summary(model.linreg)
##
## Call:
## lm(formula = BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$MMSE)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -5.7414 -1.6979 -0.3165  0.8710  7.6669
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  11.4118     5.9458   1.919   0.0772 .
## BBH$MMSE     -0.2041     0.2442  -0.836   0.4183
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.496 on 13 degrees of freedom
##   (1 observation deleted due to missingness)
## Multiple R-squared:  0.05102,    Adjusted R-squared:  -0.02198
## F-statistic: 0.6989 on 1 and 13 DF,  p-value: 0.4183
confint(model.linreg)
##                   2.5 %    97.5 %
## (Intercept) -1.4332850 24.256814
## BBH$MMSE    -0.7316826  0.323402
plot(BBH$`Cerebrospinal fluids_Albumin ratio`, BBH$MMSE, col = "blue")
```

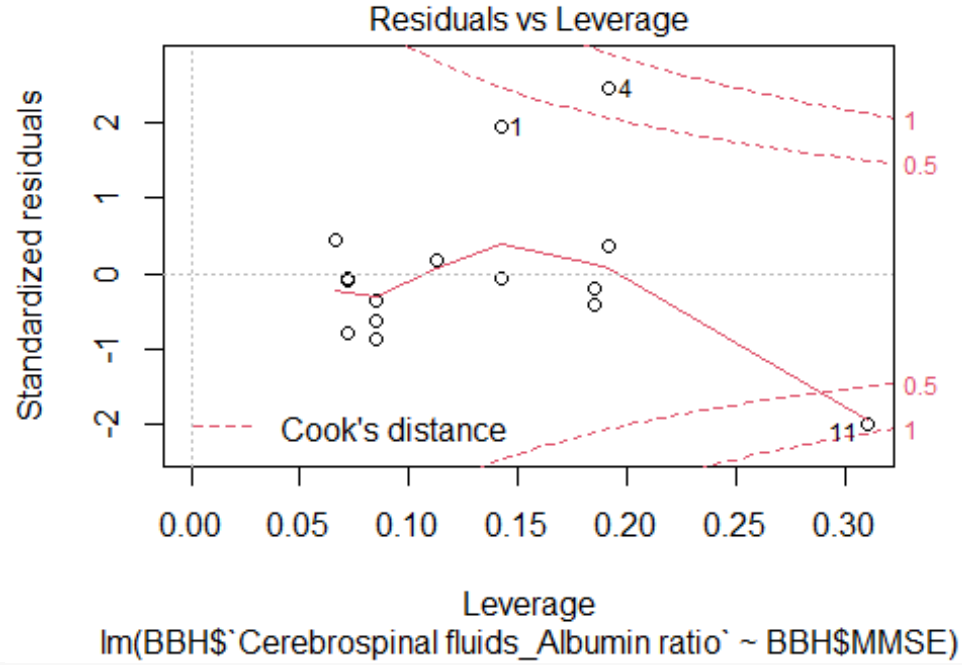



```
plot(model.linreg)
```

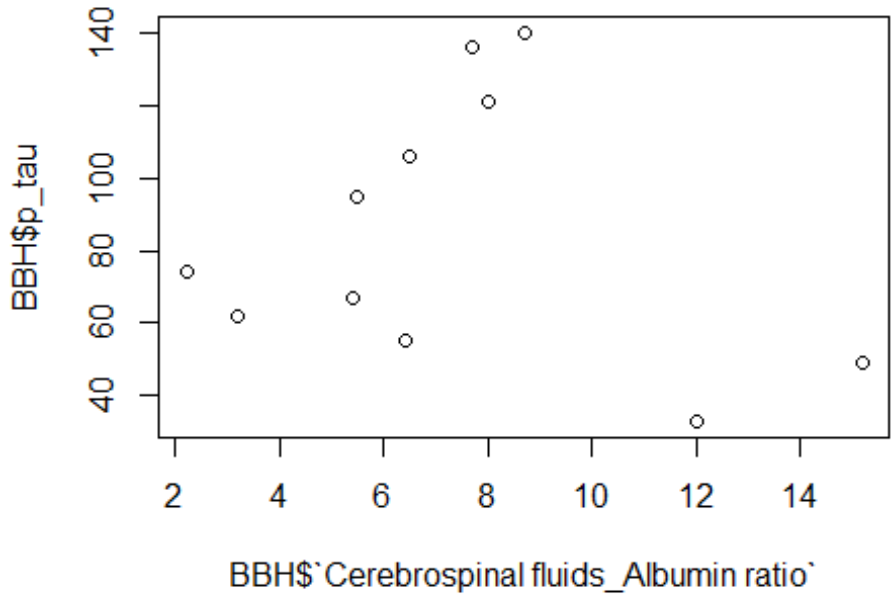

Residuals vs Fitted
Residuals
Fitted values
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$MMSE)


Normal Q-Q
Standardized residuals
Theoretical Quantiles
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$MMSE)

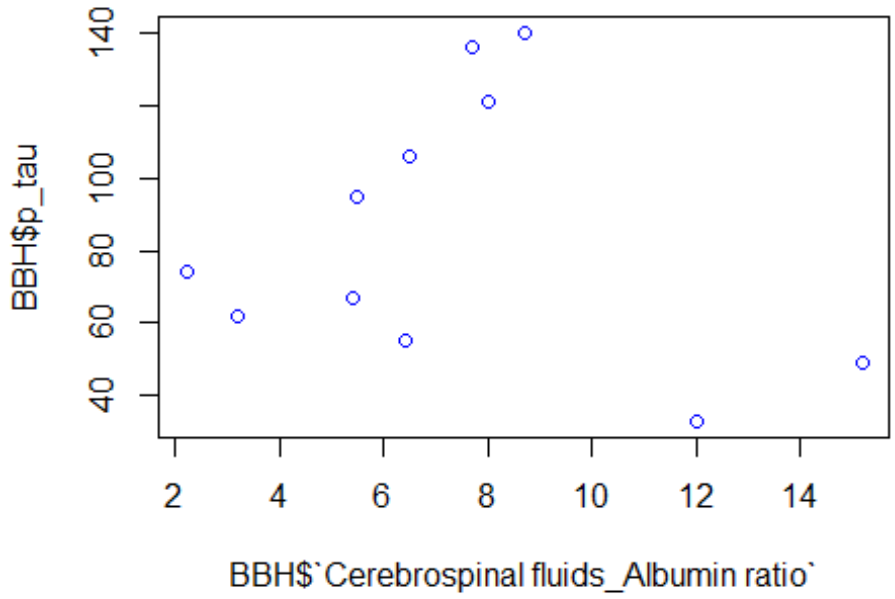




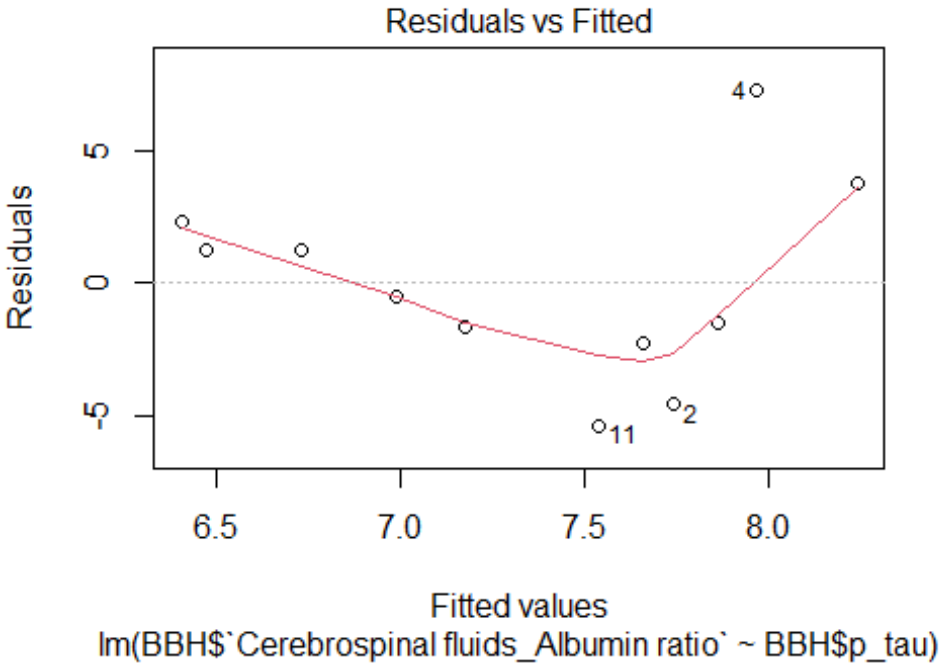

```r
# Amyloid
mean(BBH$Amyloid, na.rm=TRUE)
## [1] 370.7273
sd(BBH$Amyloid, na.rm=TRUE)
## [1] 165.5096
# p-tau
mean(BBH$p_tau, na.rm=TRUE)
## [1] 85.27273
sd(BBH$p_tau, na.rm=TRUE)
## [1] 36.51874
plot(BBH$`Cerebrospinal fluids_Albumin ratio`, BBH$p_tau)
```

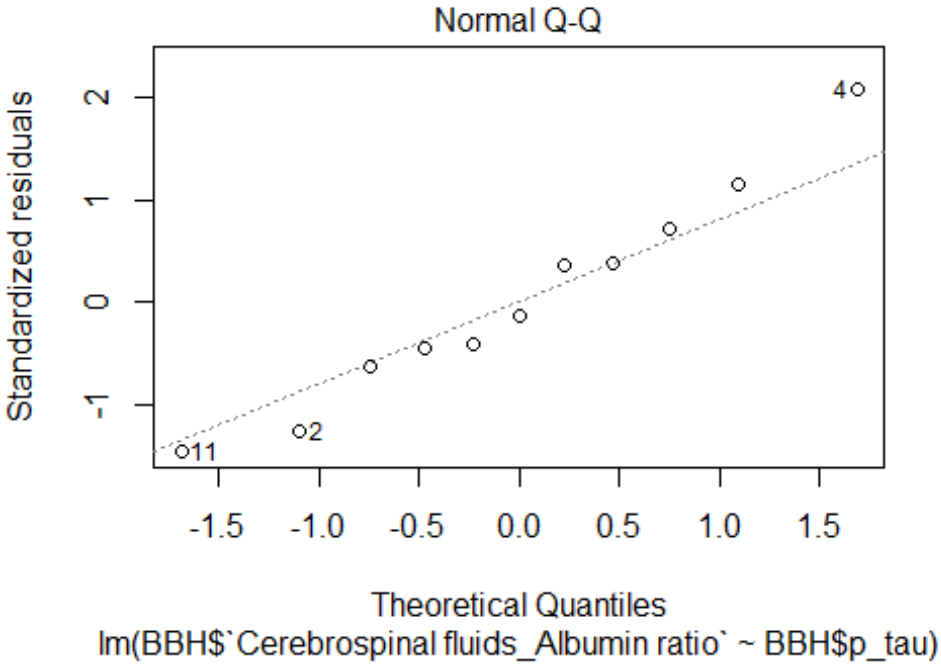


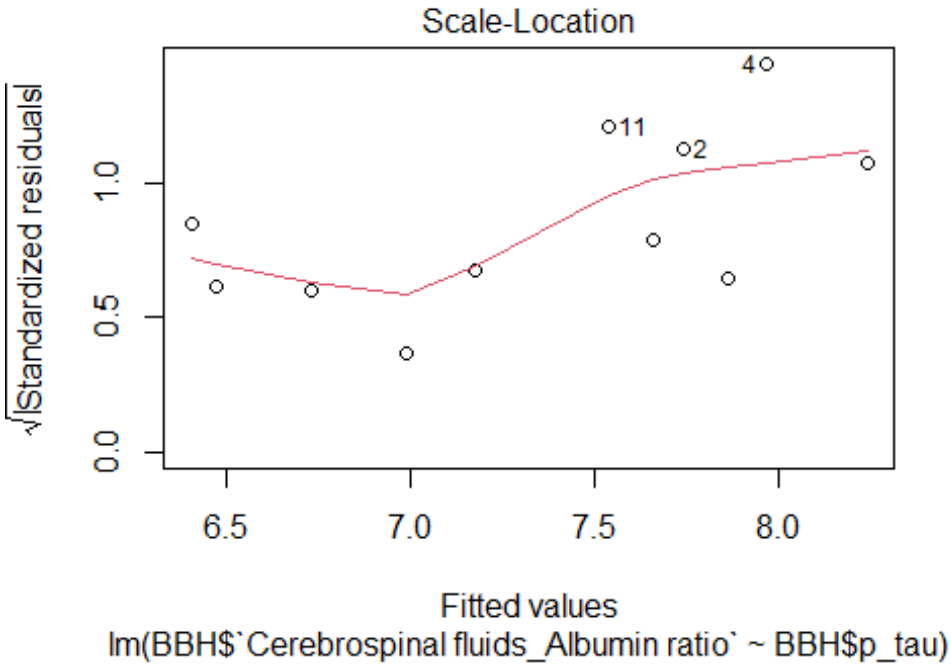

```
model.linreg <- lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$p_tau)
summary(model.linreg)
##
## Call:
## lm(formula = BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$p_tau)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -5.3375 -1.9672 -0.4877  1.7832  7.2330
##
## Coefficients:
##             Estimate Std. Error t value Pr(>|t|)
## (Intercept)  8.80877    3.08244   2.858   0.0189 *
## BBH$p_tau   -0.01718    0.03347  -0.513   0.6201
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 3.865 on 9 degrees of freedom
##   (5 observations deleted due to missingness)
## Multiple R-squared:  0.02845,    Adjusted R-squared:  -0.0795
## F-statistic: 0.2635 on 1 and 9 DF,  p-value: 0.6201
confint(model.linreg)
##                   2.5 %     97.5 %
## (Intercept)  1.83581581 15.7817280
## BBH$p_tau   -0.09288424  0.0585246
plot(BBH$`Cerebrospinal fluids_Albumin ratio`, BBH$p_tau, col = "blue")
```

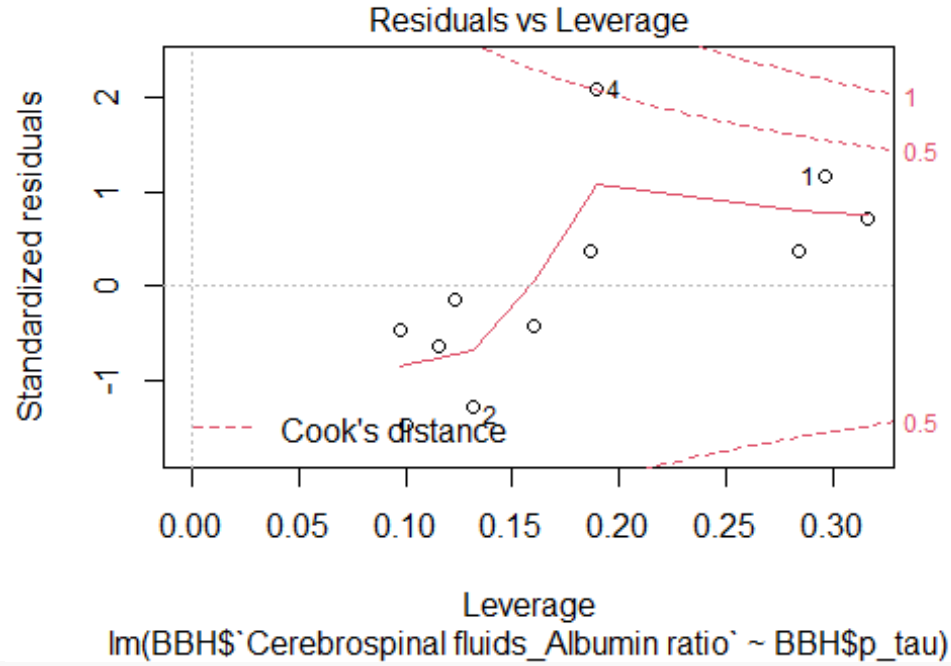



```
plot(model.linreg)
```

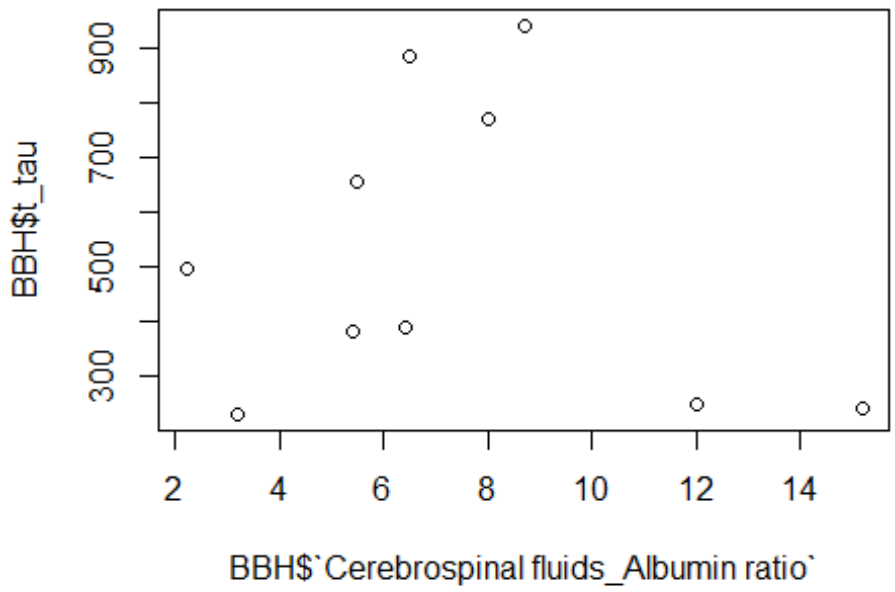

Residuals vs Fitted
Residuals
5
0
-5
4
11
2
6.5
7.0
7.5
8.0
Fitted values
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$p_tau)


Normal Q-Q
Standardized residuals
2
1
0
-1
4
2
11
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
Theoretical Quantiles
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$p_tau)

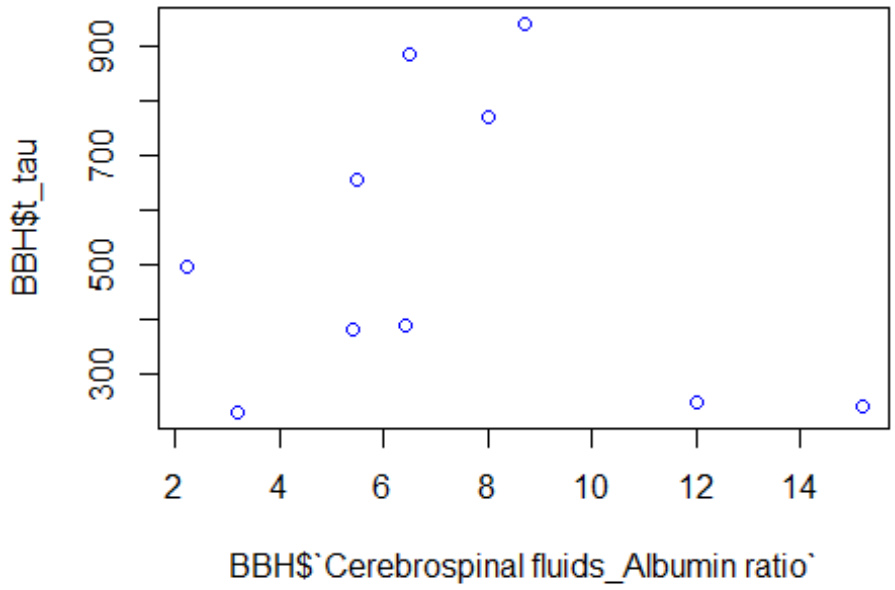




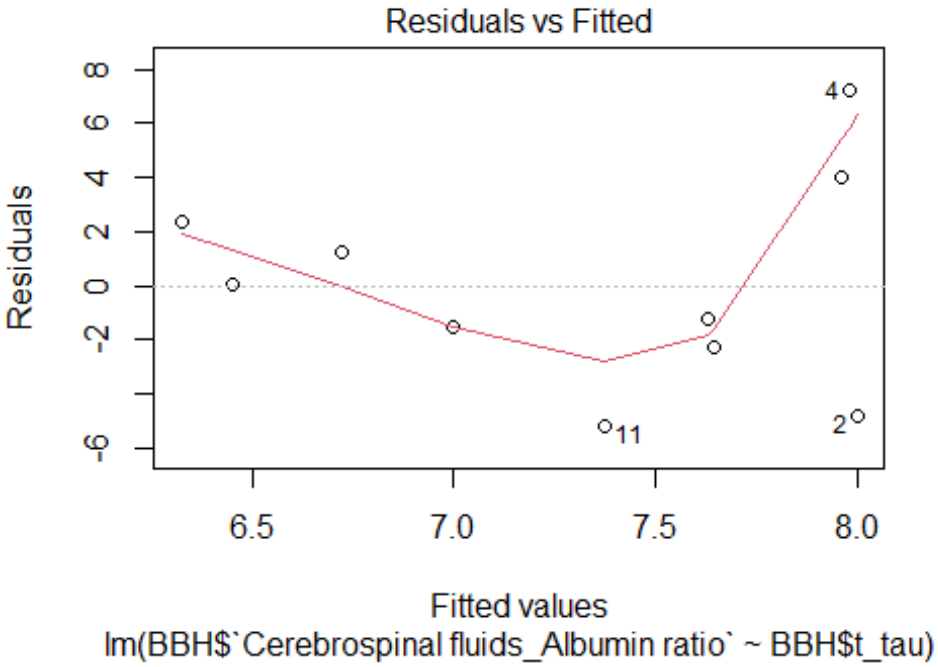

```r
# t-tau
mean(BBH$t_tau, na.rm=TRUE)
## [1] 524.3
sd(BBH$t_tau, na.rm=TRUE)
## [1] 271.3399
plot(BBH$`Cerebrospinal fluids_Albumin ratio`, BBH$t_tau)
```

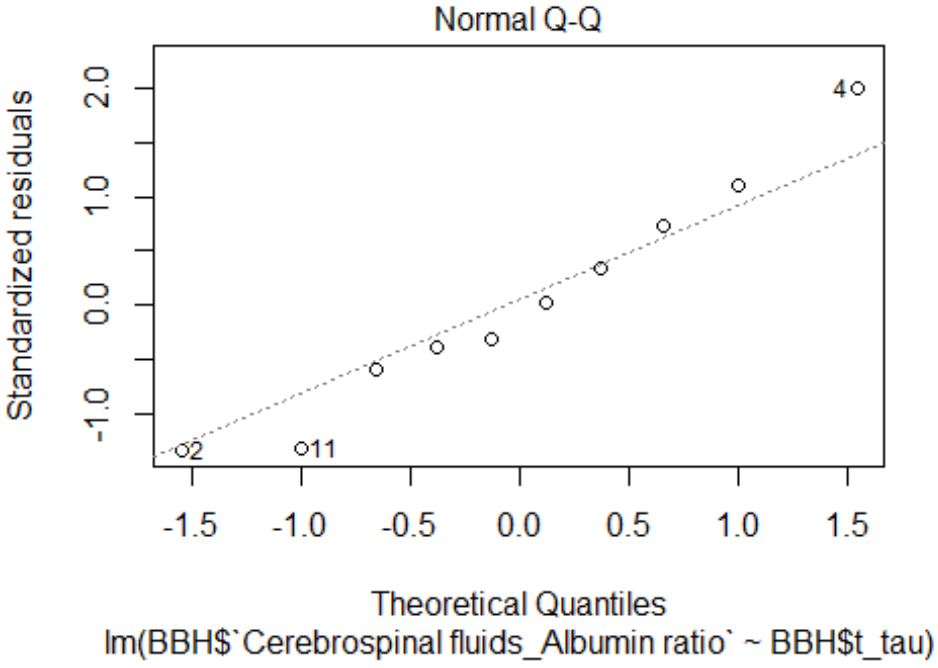


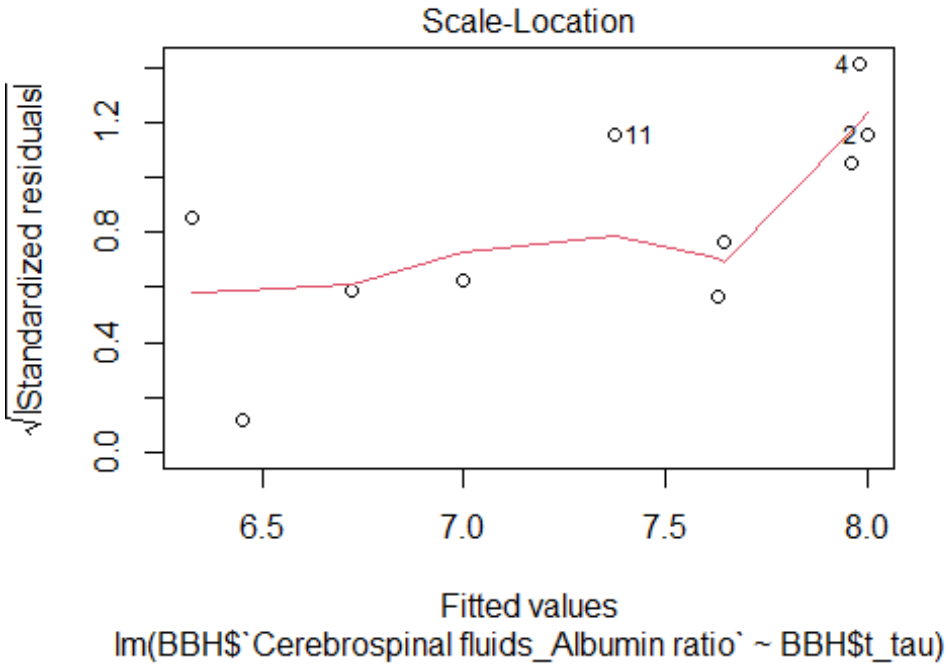

```
model.linreg <- lm(BBH$`Cerebrospinal fluids_Albumin ratio`~ BBH$t_tau)
summary(model.linreg)
##
## Call:
## lm(formula = BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$t_tau)
##
## Residuals:
##     Min      1Q  Median      3Q     Max
## -5.1728 -2.0579 -0.5902  2.1009  7.2212
##
## Coefficients:
##              Estimate Std. Error t value Pr(>|t|)
## (Intercept)  8.549338   2.942150   2.906   0.0197 *
## BBH$t_tau   -0.002367   0.005037  -0.470   0.6509
## ---
## Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
##
## Residual standard error: 4.1 on 8 degrees of freedom
##   (6 observations deleted due to missingness)
## Multiple R-squared:  0.02687,    Adjusted R-squared:  -0.09478
## F-statistic: 0.2209 on 1 and 8 DF,  p-value: 0.6509
confint(model.linreg)
##                   2.5 %       97.5 %
## (Intercept)  1.76472872 15.333947642
## BBH$t_tau   -0.01398309  0.009248561
plot(BBH$`Cerebrospinal fluids_Albumin ratio`, BBH$t_tau, col = "blue")
```

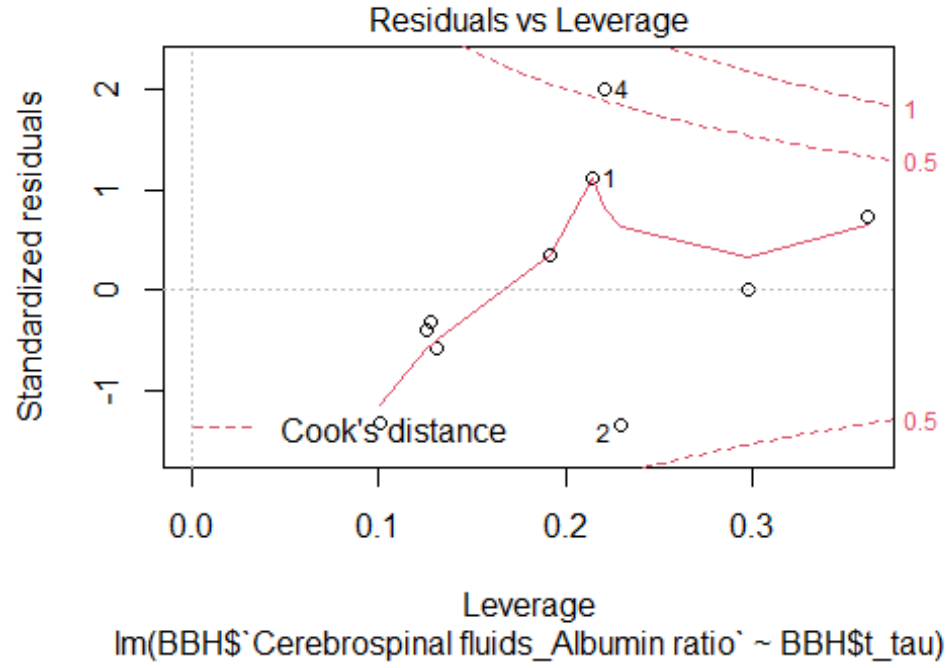



```
plot(model.linreg)
```


Residuals vs Fitted
Residuals
8
6
4
2
0
-2
-6
4
11
2
6.5
7.0
7.5
8.0
Fitted values
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$t_tau)


Normal Q-Q
Standardized residuals
2.0
1.0
0.0
-1.0
4
2
11
-1.5
-1.0
-0.5
0.0
0.5
1.0
1.5
Theoretical Quantiles
lm(BBH$`Cerebrospinal fluids_Albumin ratio` ~ BBH$t_tau)

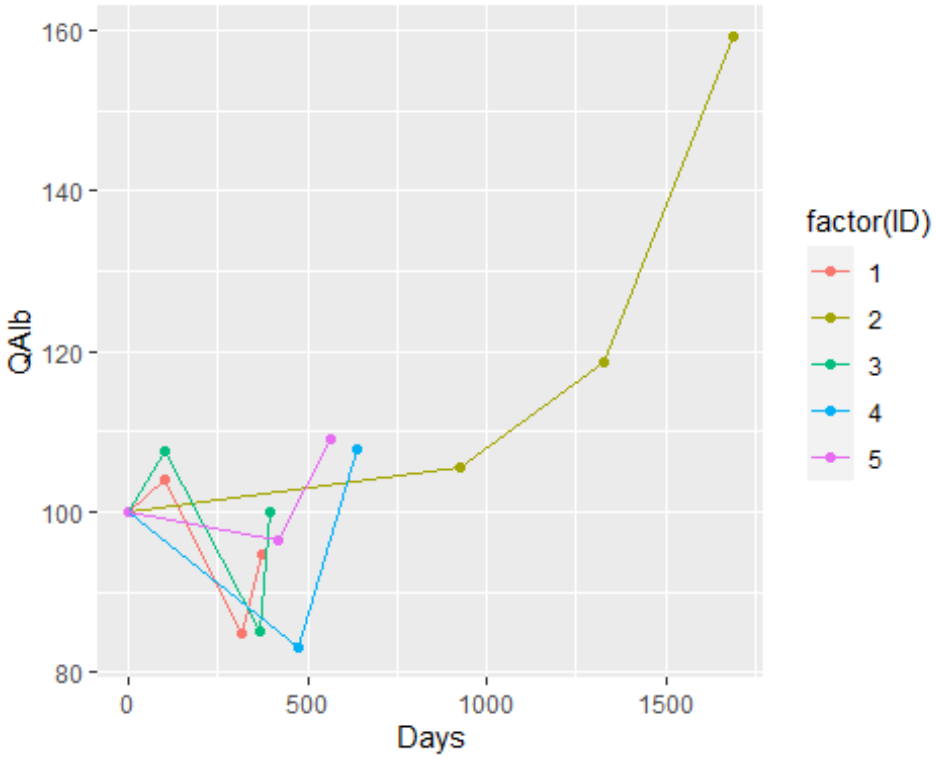




More than 2 lumbar punctures performed

```
T_mult <- read_excel("Data2.xlsx")

library("ggplot2")
df <- data.frame(ID=c(T_mult$ID), QAlb=c(T_mult$`Percentage value`),
Days=c(T_mult$Days))
ggplot(df,aes(x=Days,y=QAlb,
              group=ID,color=factor(ID)))+
  geom_point()+geom_line()
```


160
140
120
100
80
QAlb
0
500
1000
1500
Days
factor(ID)
1
2
3
4
5