ICPSR 2017 "Advanced Maximum Likelihood": Survival Analysis

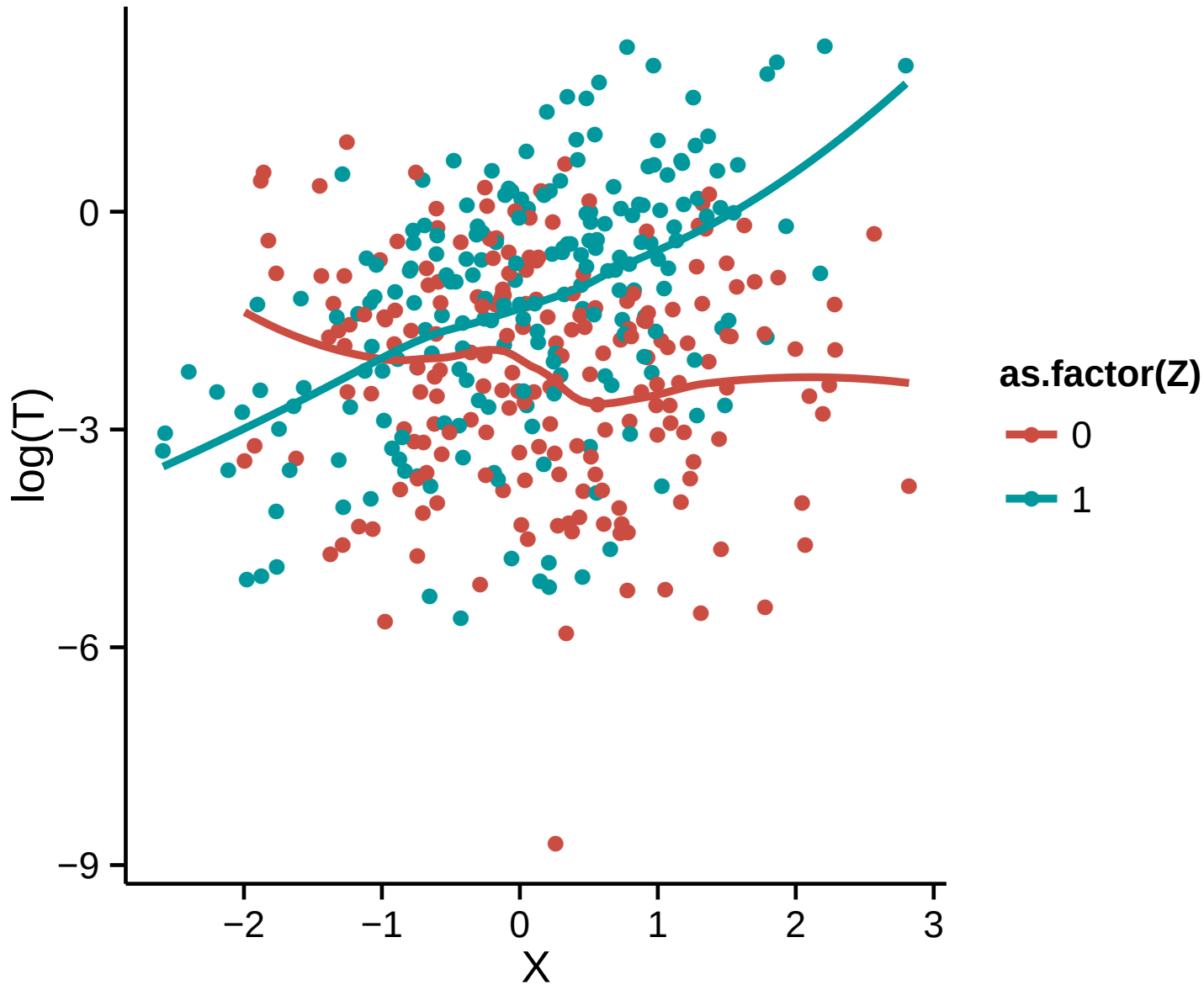
Interactions

June 24, 2017

Interactions: Binary $\times$ Continuous

```
set.seed(1122334)
N<-400
X<-rnorm(N)
W<- -X + rchisq(N,5) # X and W correlated
Z<-rbinom(N,1,0.5)
XB<-(-0.2+0.3*W+(0.5*X)-(0.5*Z)-(1*X*Z))
T<-abs(rexp(N,rate=exp(XB)))
C<-rbinom(N,1,0.8)
df<-data.frame(X=X,W=W,Z=Z,T=T,C=C)
S<-Surv(df$T,df$C)
```

A Plot



Interactions: Cox Results

```
coxFit<-coxph(S~W+X+Z+X*Z,df)
summary(coxFit)

  n= 400, number of events= 309

       coef exp(coef) se(coef)     z      Pr(>|z|)
W    0.3009    1.3511   0.0218 13.80       < 2e-16 ***
X    0.5746    1.7764   0.0845  6.80 0.00000000001 ***
Z   -0.6454    0.5245   0.1221 -5.29 0.00000012391 ***
X:Z -1.1074    0.3304   0.1217 -9.10       < 2e-16 ***
---
Signif. codes:  0 *** 0.001 ** 0.01 * 0.05 . 0.1   1

    exp(coef) exp(-coef) lower .95 upper .95
W       1.351      0.740     1.295     1.410
X       1.776      0.563     1.505     2.096
Z       0.524      1.907     0.413     0.666
X:Z     0.330      3.026     0.260     0.419

Concordance= 0.758  (se = 0.019 )
Rsquare= 0.471   (max possible= 1 )
Likelihood ratio test= 254  on 4 df,   p=0
Wald test            = 240  on 4 df,   p=0
Score (logrank) test = 261  on 4 df,   p=0
```

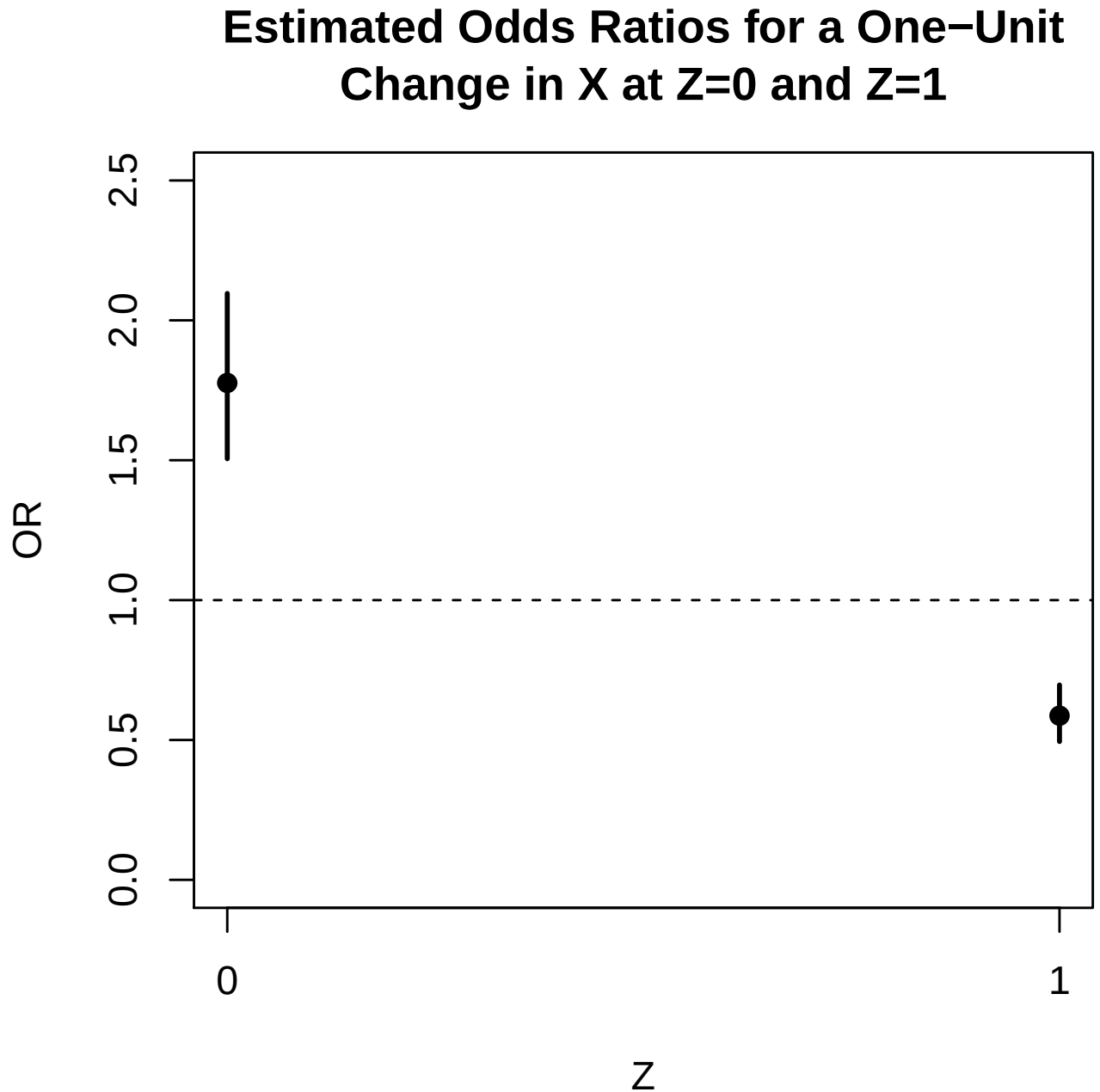
Interpretation: Hypothesis Tests

```
> library(car)
> linearHypothesis(coxFit,"Z+X:Z")
Linear hypothesis test

Hypothesis:
Z  + X:Z = 0

Model 1: restricted model
Model 2: S ~ W + X + Z + X * Z

  Res.Df Df Chisq Pr(>Chisq)
1    397
2    396  1   100     <2e-16 ***
---
Signif. codes:  0 *** 0.001 ** 0.01 * 0.05 . 0.1   1
```

Interpretation: Hazard Ratios

```
VCV<-vcov(coxFit)
coxOR<-data.frame(Z=c(0,1),
      B=c(coxFit$coefficients[2],coxFit$coefficients[2]+coxFit$coefficients[4])
      se=c(sqrt(VCV[2,2]),sqrt(VCV[2,2]+VCV[4,4]+2*(VCV[2,4]))))
z<-qnorm(0.975)
coxOR$OR<-exp(coxOR$B)
coxOR$UB<-exp(coxOR$B + z*coxOR$se)
coxOR$LB<-exp(coxOR$B - z*coxOR$se)

with(coxOR, plot(Z,OR,ylim=c(0,2.5),xaxt="n",pch=19,
   main="Estimated Odds Ratios for a One-unit\nChange in X at Z=0 and Z=1"))
with(coxOR, lines(c(0,0),c(UB[1],LB[1]),lwd=2))
with(coxOR, lines(c(1,1),c(UB[2],LB[2]),lwd=2))
abline(h=1,lwd=1,lty=2)
axis(1,at=c(0,1))
```

Interpretation: Hazard Ratios

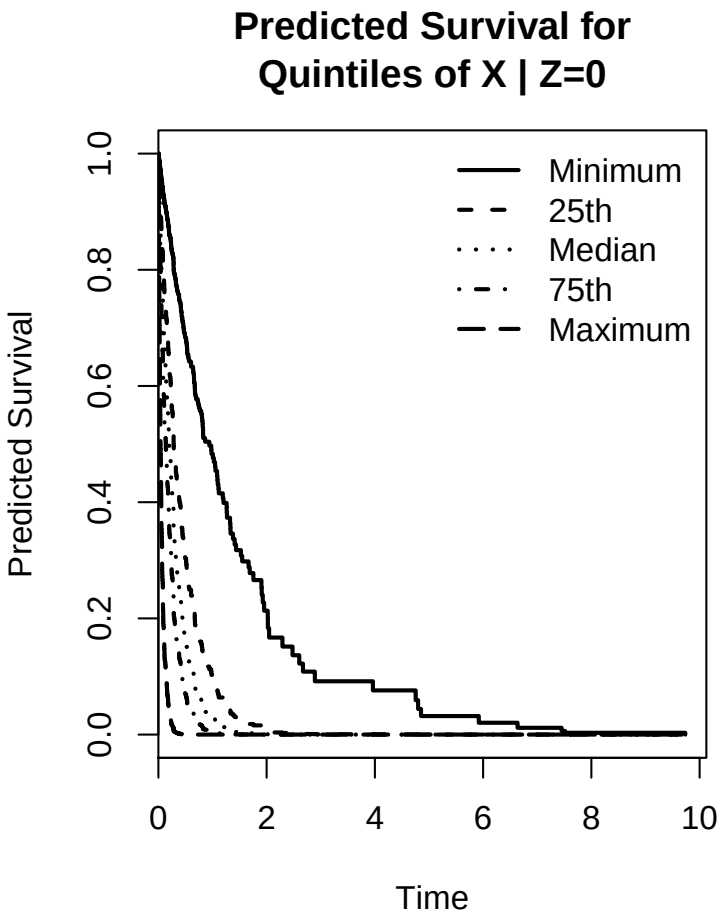


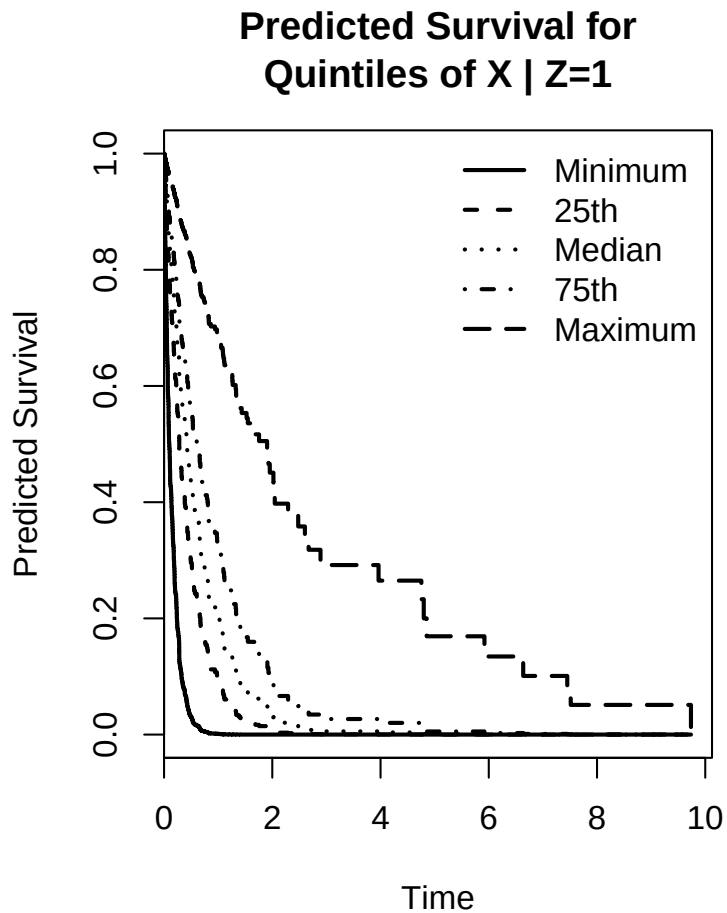
Interpretation: Predicted Survival

```
curves<-5
dfZ0<-data.frame(W=rep(mean(df$W),times=curves),
                 X=quantile(X,probs=seq(0,1,length=curves)),
                 Z=rep(0,times=curves))
SZ0<-survfit(coxFit,dfZ0)

plot(SZ0,mark.time=FALSE,lty=seq(1:5),lwd=2,
     main="Predicted Survival for\nQuintiles of X | Z=0",
     xlab="Time",ylab="Predicted Survival")
legend("topright",lty=seq(1:5),bty="n",lwd=2,
       legend=c("Minimum","25th","Median","75th","Maximum"))
```

(Repeat for $Z = 1$...)

Interpretation: Predicted Survival





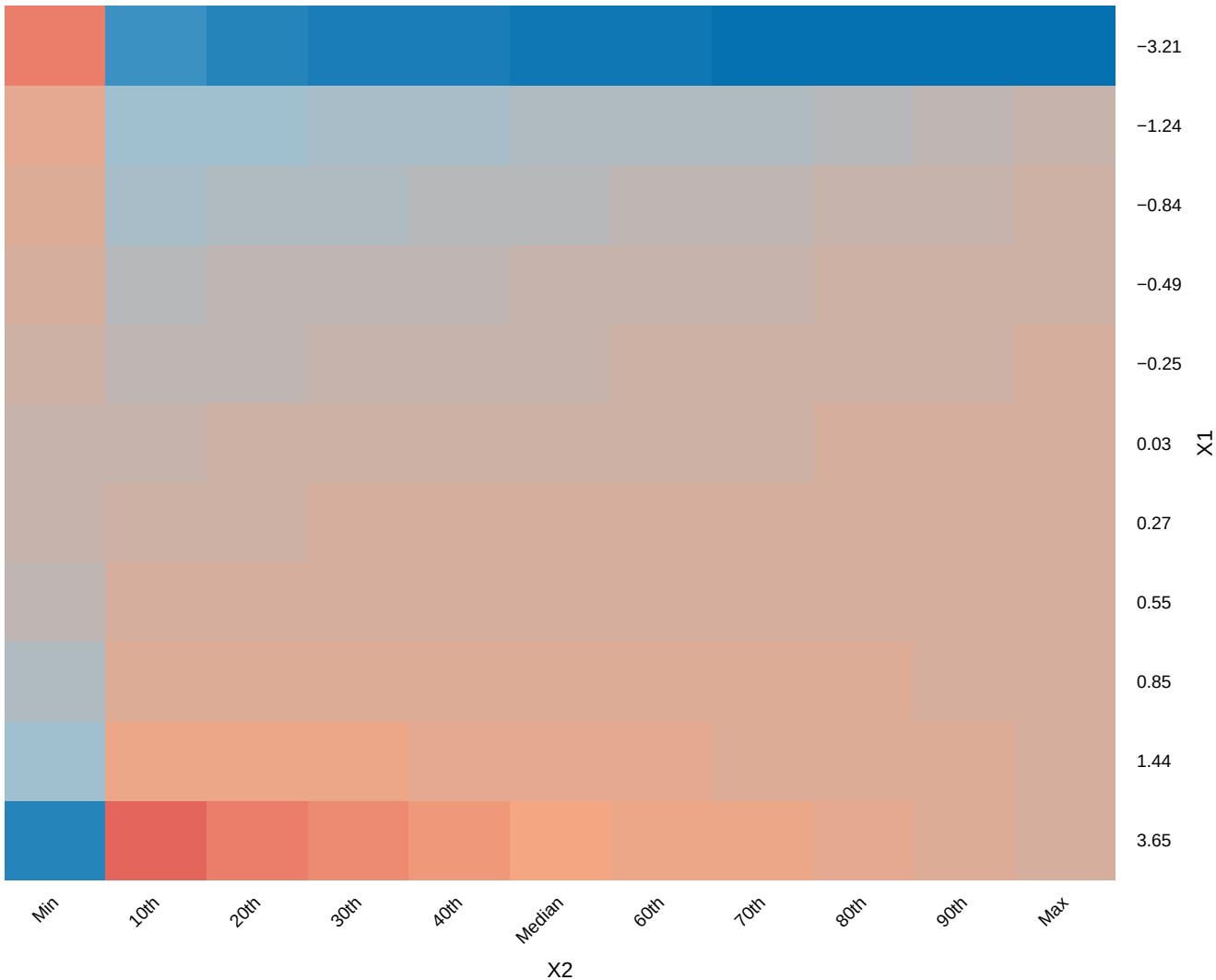
Interactions: Continuous $\times$ Continuous

```
set.seed(2719)
N<-400
X1<-rnorm(N)
W<- -X1 + rchisq(N,5) # X1 and W are correlated
X2<-rpois(N,20)
XB<-(-0.2 + 0.3*W + (0.5*X1) - (0.5*X2) - (1*X1*X2))
T<-abs(rexp(N,rate=exp(XB)))
C<-rbinom(N,1,0.8)
df2<-data.frame(W=W,X1=X1,X2=X2,T=T,C=C)
S2<-Surv(df2$T,df2$C)
```

Cox Model Fit

```
cox2<-coxph(S2~W+X1+X2+X1*X2,df2)
summary(cox2)

  n= 400, number of events= 318

         coef exp(coef) se(coef)      z Pr(>|z|)
W      0.3267    1.3864   0.0230  14.19   <2e-16 ***
X1     0.6872    1.9881   0.3459   1.99    0.047 *
X2    -0.5072    0.6022   0.0294 -17.26   <2e-16 ***
X1:X2 -1.0243    0.3590   0.0536 -19.13   <2e-16 ***
---
Signif. codes:  0 *** 0.001 ** 0.01 * 0.05 . 0.1   1

      exp(coef) exp(-coef) lower .95 upper .95
W         1.386      0.721     1.325     1.450
X1        1.988      0.503     1.009     3.916
X2        0.602      1.661     0.568     0.638
X1:X2     0.359      2.785     0.323     0.399

Concordance= 0.98  (se = 0.019 )
Rsquare= 0.988   (max possible= 1 )
Likelihood ratio test= 1756  on 4 df,   p=0
Wald test            = 413  on 4 df,   p=0
Score (logrank) test = 527  on 4 df,   p=0
```

Predicted Relative Risk: Heatmap



Predicted (log-)Relative Risk: Level Plot