

Elukestvusanalüüs III

Probleemid Cox'i mudeliga

Võrdeliste riskide eeldus

- Kas saame aru, mida antud eeldus tähendab?
- Kuidas ikkagi kontrollida?
- Mida teha, kui eeldus on rikutud?

Vasakult kärpimine (left truncation)

- ajas muutuvad riskitegurid

Kes vastutab ehk võistlevad riskid

Võrdeliste riskide eeldusest

	riskifunktsioon					
Mehed (0)	$h_0(t)$					
Naised (1)	$h_0(t) \cdot \exp(-0,357) = 0,7 h_0(t)$					
	$t=1$	$t=2$	$t=3$	$t=4$...	
Mehed	0,1	0,2	0,1	0,3	...	
Naised	0,07	0,14	0,07	0,21	...	eeldus täidetud
Naised	0,07	0,15	0,08	0,27	...	eeldus pole täidetud

Võrdeliste riskide eeldusest

	riskifunktsioon
Mehed	$h_0(t)$
Mehed+harjumus	$h_0(t) \cdot \exp(0,182) = h_0(t) \cdot 1,2$
Naised	$h_0(t) \cdot \exp(-0,357) = h_0(t) \cdot 0,7$
Naised+harjumus	$h_0(t) \cdot \exp(-0,357+0.182) = h_0(t) \cdot 0,7 \cdot 1,2$

```
> m=coxph(Surv(aeg, status)~sugu+ harjumus)
```

```
> m
```

	coef	exp(coef)	se(coef)	z	p
sugu	-0.357	0.74891	0.01253	-23.09	<2e-16
harjumus	0.182	1.21218	0.01252	15.37	<2e-16

Võrdeliste riskide eeldusest

	riskifunktsioon
Mehed	$h_0(t)$
Mehed+harjumus	$h_0(t) \cdot \exp(0,182) = h_0(t) \cdot 1,2$
Naised	$h_0(t) \cdot \exp(-0,357) = h_0(t) \cdot 0,7$
Naised+harjumus	$h_0(t) \cdot \exp(-0,357+0.182) = h_0(t) \cdot 0,7 \cdot 1,2$

```
> m=coxph(Surv(aeg, status)~sugu+ harjumus)
```

```
> m
```

	coef	exp(coef)	se(coef)	z	
sugu	-0.357	0.74891	0.01253	-23.09	<2e-16
harjumus	0.182	1.21218	0.01252	15.37	<2e-16

```
> cox.zph(m)
```

	chisq	df	p
sugu	24.70	1	6.7e-07
harjumus	5.65	1	0.017
GLOBAL	26.39	2	1.9e-06

Võrdeliste riskide eeldusest

```
> m3=coxph(Surv(aeg, status)~strata(sugu)+harjumus)
```

```
> m3
```

	coef	exp(coef)	se(coef)	z	p
harjumus	0.19161	1.21120	0.01252	15.3	<2e-16

```
> cox.zph(m3)
```

	chisq	df	p
harjumus	1.71	1	0.19
GLOBAL	1.71	1	0.19

Mehed

riskifunktsioon

$h_0(t)$

Naised

$h_1(t)$

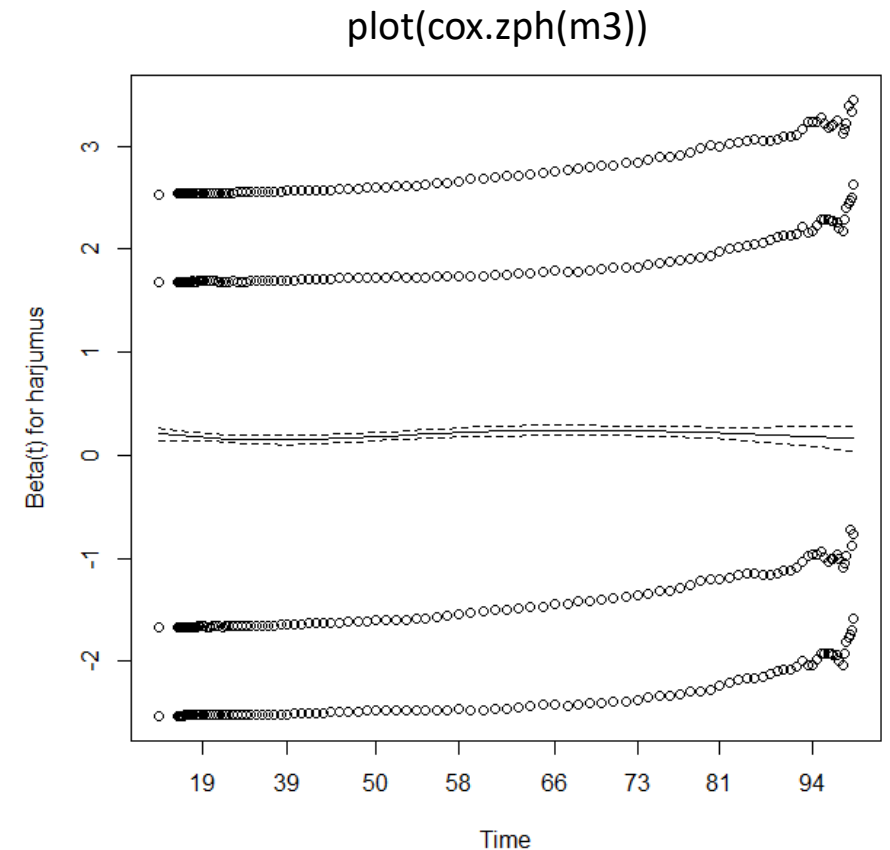
Mehed+harjumus

$h_0(t) \cdot \exp(0,19) = h_0(t) \cdot 1,2$

Naised+harjumus

$h_1(t) \cdot \exp(0,19) = h_1(t) \cdot 1,2$

Lahendus1: hindame eraldi riskifunktsioonid meestele ja naistele (meeste surmarisk ei pea alati olema sama arv kordi suurem naiste surmariskist, erinevus võib ajas muutuda)



Võrdeliste riskide eeldusest

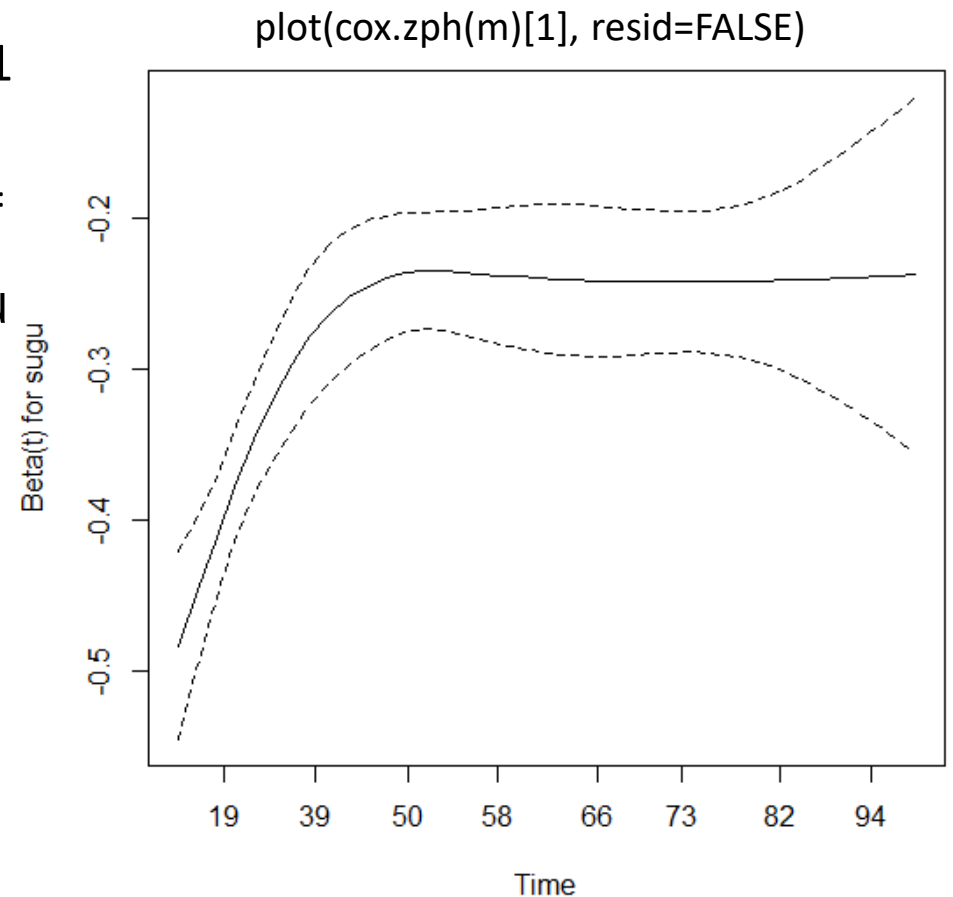
Lahendus2: Proovime leida mudeli, mis kirjeldab, kuidas riskide erinevus ajas muutub...

	riskifunktsioon
Mehed	$h_0(t)$
Mehed+harjumus	$h_0(t) \cdot \exp(0,182) = h_0(t) \cdot 1$
Naised	$h_0(t) \cdot \exp(-0,357) = h_0(t) \cdot$
Naised+harjumus	$h_0(t) \cdot \exp(-0,357+0.182) =$

```
> m=coxph(Surv(aeg, status)~sugu+ harjumu
```

```
> m
```

	coef	exp(coef)	se(coef)	
sugu	-0.357	0.74891	0.01253	-23.
harjumus	0.182	1.21218	0.01252	15.



Võrdeliste riskide eeldusest

Lahendus2: Proovime leida mudeli, mis kirjeldab, kuidas riskide erinevus ajas muutub...

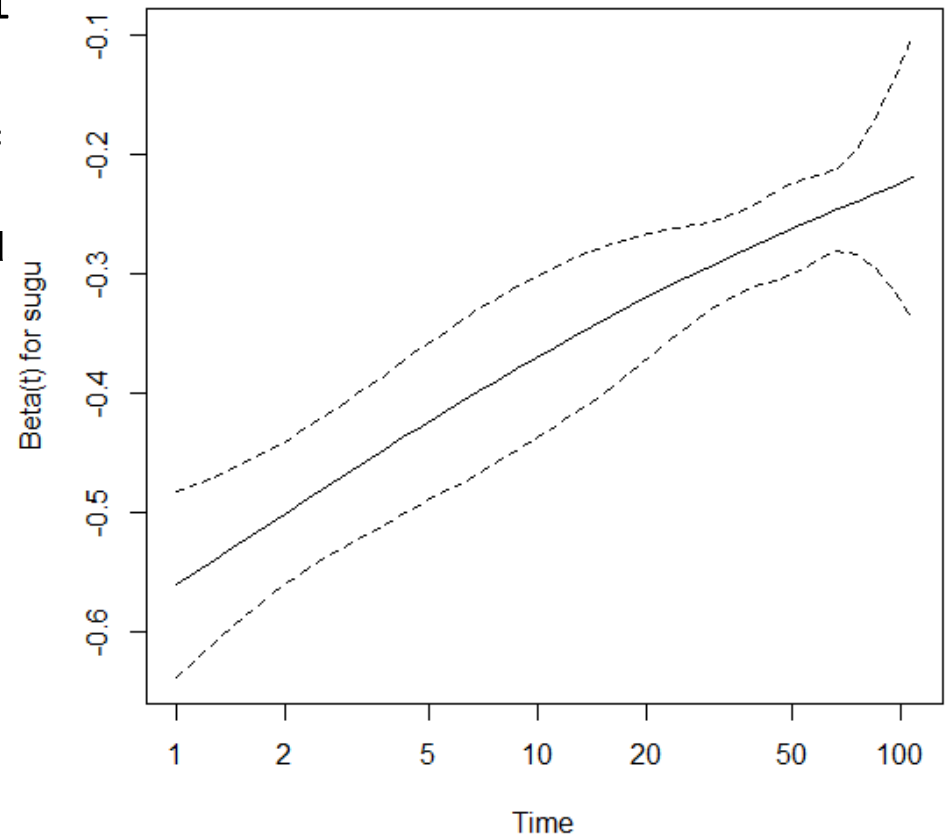
	riskifunktsioon
Mehed	$h_0(t)$
Mehed+harjumus	$h_0(t) \cdot \exp(0,182) = h_0(t) \cdot 1$
Naised	$h_0(t) \cdot \exp(-0,357) = h_0(t) \cdot$
Naised+harjumus	$h_0(t) \cdot \exp(-0,357+0.182) =$

```
> m=coxph(Surv(aeg, status)~sugu+ harjumu
```

```
> m
```

	coef	exp(coef)	se(coef)	
sugu	-0.357	0.74891	0.01253	-23.
harjumus	0.182	1.21218	0.01252	15.

```
plot(cox.zph(m, transform="log")[1],  
      resid=FALSE)
```

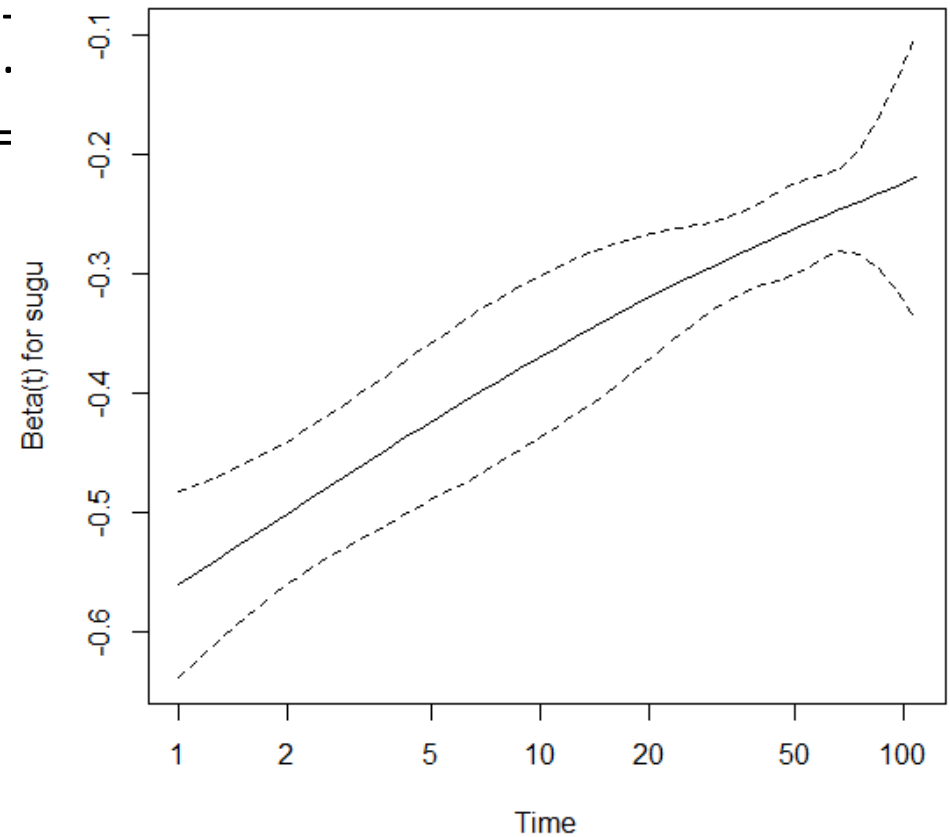


Võrdeliste riskide eeldusest

Lahendus2: Proovime leida mudeli, mis kirjeldab, kuidas riskide erinevus ajas muutub...

	riskifunktsioon
Mehed	$h_0(t)$
Mehed+harjumus	$h_0(t) \cdot \exp(0,182) = h_0(t) \cdot \dots$
Naised	$h_0(t) \cdot \exp(-0,357) = h_0(t) \cdot \dots$
Naised+harjumus	$h_0(t) \cdot \exp(-0,357+0.182) = \dots$

```
> m=coxph(Surv(aeg, status)~sugu+ harjumus)
> plot(cox.zph(m, transform="log")[1],
       resid=FALSE)
> m2=coxph(Surv(aeg, status)~sugu+harjumus+ tt(sugu),
+         tt=function(x,t,...) x*log(t) )
> m2
coef exp(coef) se(coef)      z      p
sugu   -0.518119  0.595640  0.034974 -14.815 < 2e-16
harjumus  0.191675  1.211277  0.012520  15.310 < 2e-16
tt(sugu)  0.068252  1.070635  0.009714   7.026 2.12e-12
```



Lahendus2: Proovime leida mudeli, mis kirjeldab, kuidas riskide erinevus ajas muutub...

Võrdeliste riskide eeldusest

	riskifunktsioon
Mehed	$h_0(t)$
Naised	$h_0(t) \cdot \exp(-0,518 + 0,068 \cdot \log(t)) = h_0(t) \cdot 0,6 \cdot 1,07^{\log(t)}$
Mehed+harjumus	$h_0(t) \cdot \exp(0,19) = h_0(t) \cdot 1,2$
Naised+harjumus	$h_0(t) \cdot \exp(-0,518 + 0,068 \cdot \log(t) + 0,19) = h_0(t) \cdot 0,6 \cdot 1,07^{\log(t)} \cdot 1,2$

```
> m=coxph(Surv(aeg, status)~sugu+ harjumus)
> plot(cox.zph(m, transform="log")[1],
       resid=FALSE)
> m2=coxph(Surv(aeg, status)~sugu+harjumus+ tt(sugu),
+         tt=function(x,t,...) x*log(t) )
> m2
coef exp(coef) se(coef)      z      p
sugu      -0.518119  0.595640  0.034974 -14.815 < 2e-16
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tt(sugu)   0.068252  1.070635  0.009714   7.026 2.12e-12
```

Võrdeliste riskide eeldusest

	riskifunktsioon
Mehed	$h_0(t)$
Naised	$h_0(t) \cdot \exp(-0,518 + 0,068 \cdot \log(t)) = h_0(t) \cdot 0,6 \cdot 1,07^{\log(t)}$
Mehed+harjumus	$h_0(t) \cdot \exp(0,19) = h_0(t) \cdot 1,2$
Naised+harjumus	$h_0(t) \cdot \exp(-0,518 + 0,068 \cdot \log(t) + 0,19) = h_0(t) \cdot 0,6 \cdot 1,07^{\log(t)} \cdot 1,2$

```
> m=coxph(Surv(aeg, status)~sugu+ harjumus)
```

```
> plot(cox.zph(m, transform="log")[1],  
      resid=FALSE)
```

```
> m2=coxph(Surv(aeg, status)~sugu+harjumus+ tt(sugu),  
+         tt=function(x,t,...) x*log(t) )
```

```
> m2
```

coef	exp(coef)	se(coef)	z	p
sugu	-0.518119	0.595640	0.034974	-14.815 < 2e-16
harjumus	0.191675	1.211277	0.012520	15.310 < 2e-16
tt(sugu)	0.068252	1.070635	0.009714	7.026 2.12e-12

```
m3=coxph(Surv(aeg, status)~sugu+ tt(sugu),  
         tt=function(x,t,...) cbind(x*log(t), x*log(t)**2) )
```

Kärpimine (*Truncation*)

Ideaalsed vaatlused (ideal observations):

6.87 12.32 5.82 4.71 17.96 5.90 26.42

Tsenseerimine (*Censoring*):

6.87 10.00+ 5.82 4.71 10.00+ 5.90 10.00+

Kärpimine (*Truncation*):

6.87 5.82 4.71 5.90

Kärpimine

Ideaalsed vaatlused (ideal observations):

6.87 **12.32** 5.82 4.71 **17.96** 5.90 **26.42**

Tsenseerimine (*Censoring*):

6.87 **10.00+** 5.82 4.71 **10.00+** 5.90 **10.00+**

Kärpimine (*Truncation*):

6.87 5.82 4.71 5.90



Kärpimine

Ideaalsed vaatlused (ideal observations):

6.87 **12.32** 5.82 4.71 **17.96** 5.90 **26.42**

$$L = P(Y = y_1) \cdot \dots \cdot P(Y = y_k)$$

Tsenseerimine (*Censoring*):

6.87 **10.00+** 5.82 4.71 **10.00+** 5.90 **10.00+**

$$L = P(Y = y_1) \cdot \dots \cdot P(Y = y_k) \cdot P(Y \geq 10) \cdot \dots \cdot P(Y \geq 10)$$

Kärpimine (*Truncation*):

6.87 5.82 4.71 5.90

$$L = P(Y = y_1 | Y \leq 10) \cdot \dots \cdot P(Y = y_k | Y \leq 10)$$

Vasakult kärpimine

Ideaalsed vaatlused (ideal observations):

6.87 **12.32** 5.82 4.71 **17.96** 5.90 **26.42**

Paremalt tsenseerimine (*Censoring*):

6.87 **10.00+** 5.82 4.71 **10.00+** 5.90 **10.00+**

Vasakult kärpimine (puuduvad mingist väärtusest väiksemad eluead)

Ideaalsed vaatlused (ideal observations):

6.87 **12.32** **5.82** **4.71** 17.96 **5.90** 26.42

Paremalt tsenseerimine (*Censoring*):

6.87 **10.00+** 5.82 4.71 **10.00+** 5.90 **10.00+**

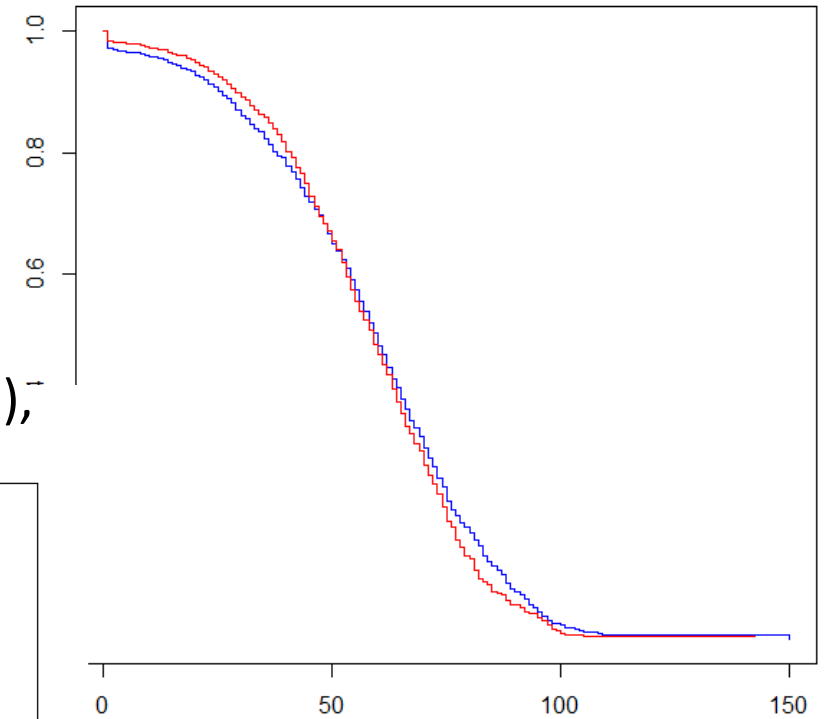
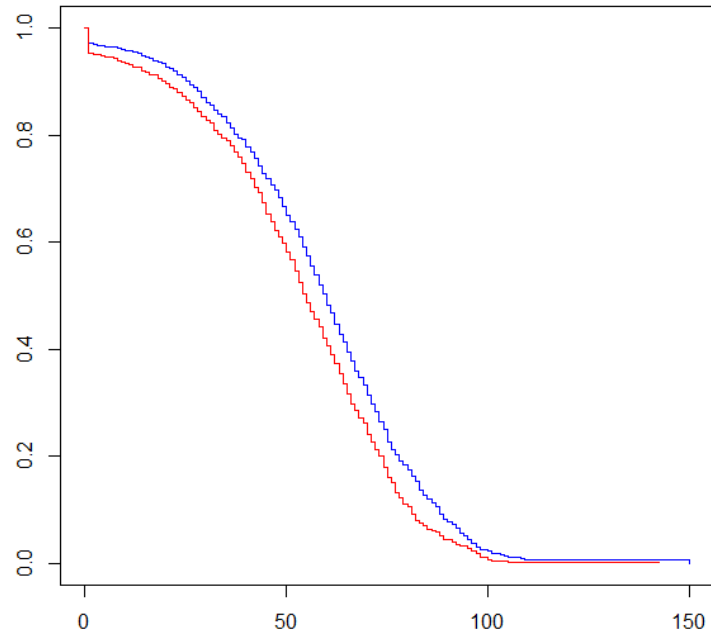
Vasakult kärpimine + paremalt tsenseerimine

6.87 **10.00+** **10.00+** **10.00+**



Kärpimine

```
plot(survfit(Surv(aeg, status)~sugu, data=andmed),  
     col=c("blue","red"))  
plot(survfit(Surv(algusaeg, aeg, status)~sugu, data=andmed),  
     col=c("blue","red"))
```



Kärpimine

```
> coxph(Surv(aeg, status)~sugu, data=andmed)
```

	coef	exp(coef)	se(coef)	z	p
sugu	0.03038	1.03084	0.03721	0.816	0.414

```
> coxph(Surv(algusaeg, aeg, status)~sugu, data=andmed)
```

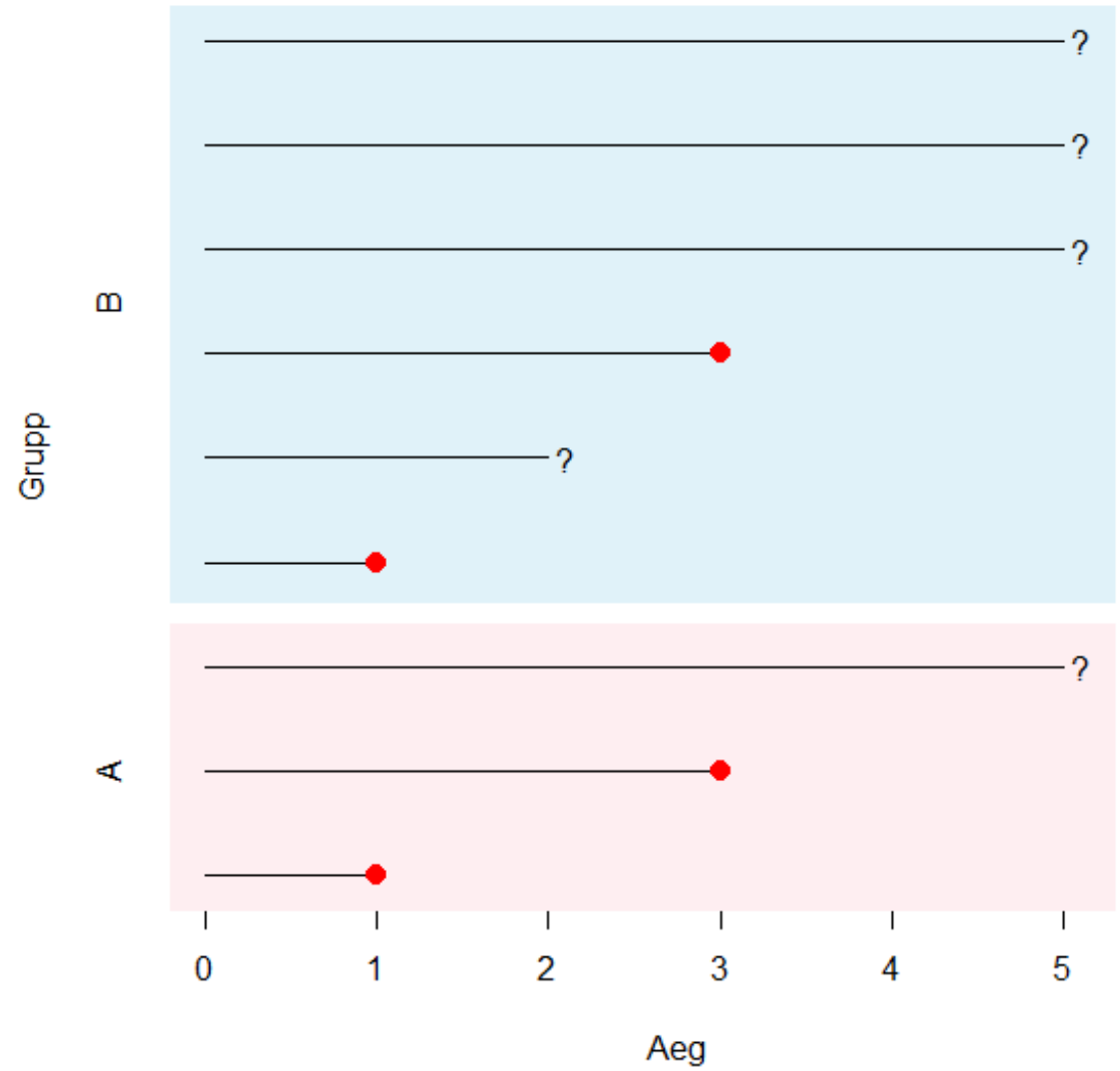
	coef	exp(coef)	se(coef)	z	p
sugu	0.22398	1.25104	0.03751	5.972	2.35e-09

Andmed

id	grupp	vanus	suri
1	A	1	1
2	A	3	1
3	A	5	0
4	B	1	1
5	B	2	0
6	B	3	1
7	B	5	0
8	B	5	0
9	B	5	0

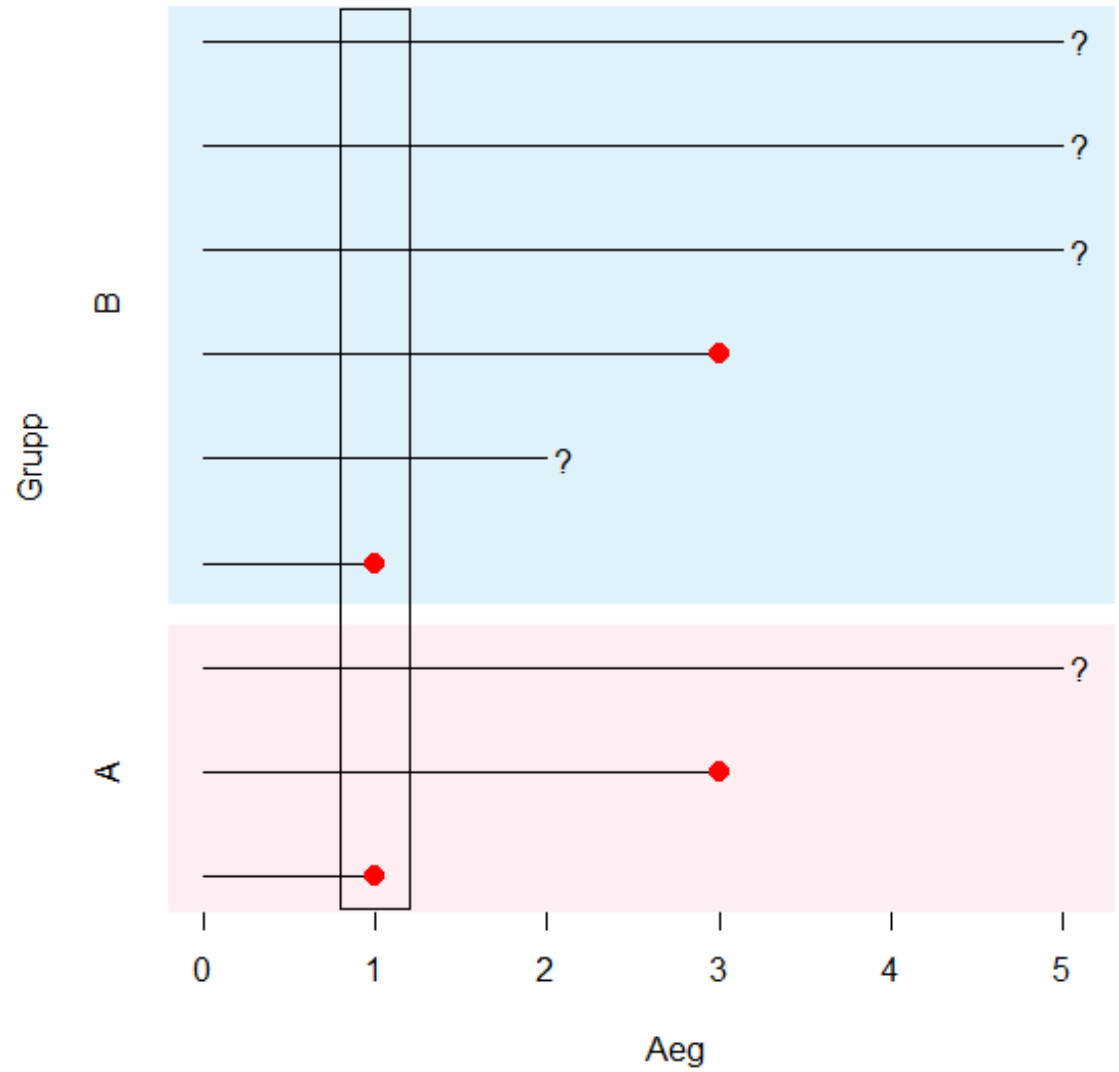
Andmed

id	grupp	vanus	suri
1	A	1	1
2	A	3	1
3	A	5	0
4	B	1	1
5	B	2	0
6	B	3	1
7	B	5	0
8	B	5	0
9	B	5	0



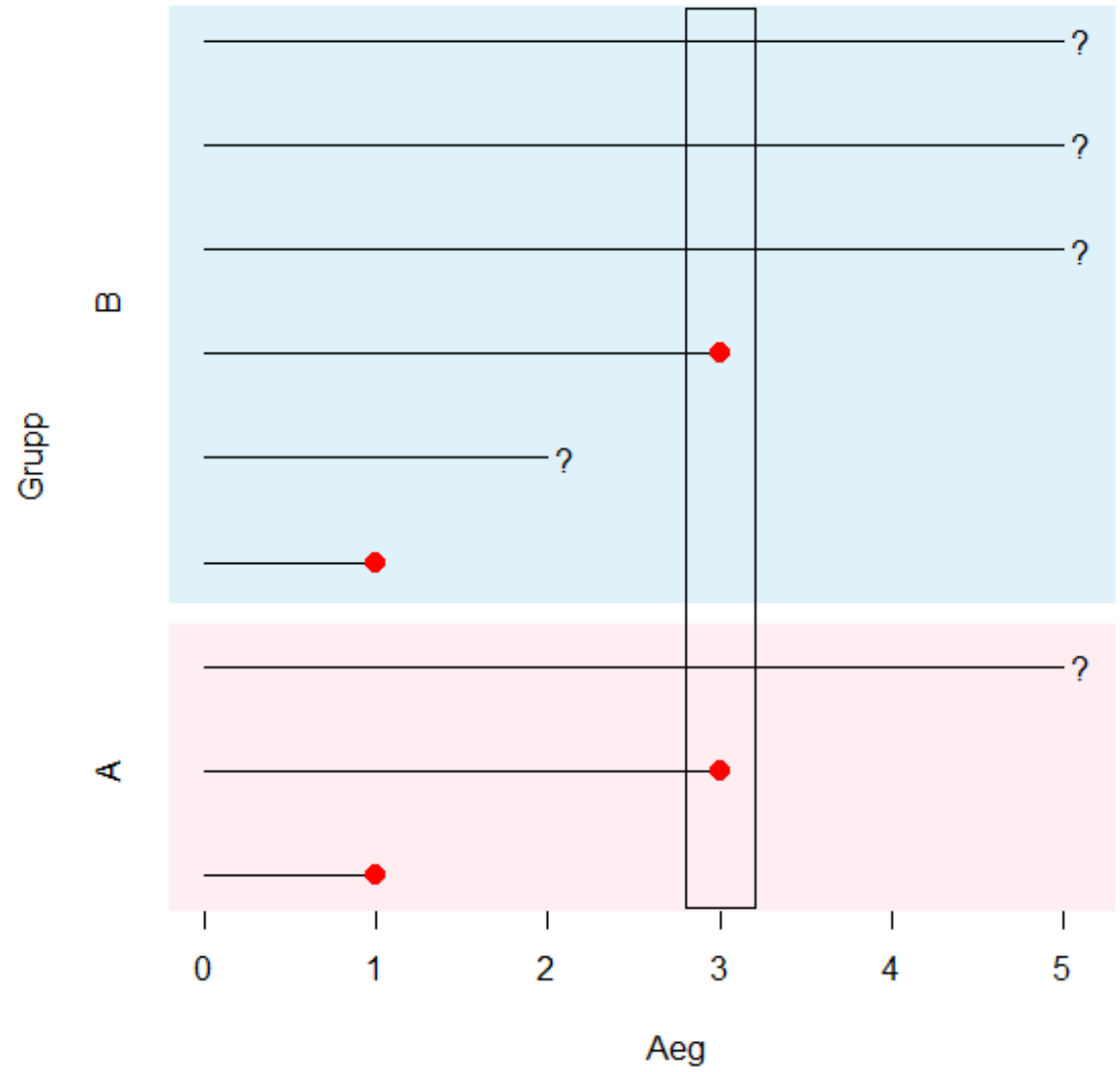
Andmed

id	grupp	vanus	suri
1	A	1	1
2	A	3	1
3	A	5	0
4	B	1	1
5	B	2	0
6	B	3	1
7	B	5	0
8	B	5	0
9	B	5	0



Andmed

id	grupp	vanus	suri
1	A	1	1
2	A	3	1
3	A	5	0
4	B	1	1
5	B	2	0
6	B	3	1
7	B	5	0
8	B	5	0
9	B	5	0



Andmed

id	grupp	vanus	suri
1	A	1	1
2	A	3	1
3	A	5	0
4	B	1	1
5	B	2	0
6	B	3	1
7	B	5	0
8	B	5	0
9	B	5	0

```
> m=coxph(Surv(vanus, suri)~relevel(factor(grupp), ref="B"), data=andmed,  
          ties="breslow")
```

```
> m
```

```
                coef exp(coef) se(coef)      z      p  
relevel(factor(grupp), ref = "B")A 0.6931    2.0000    1.0000 0.693 0.488
```

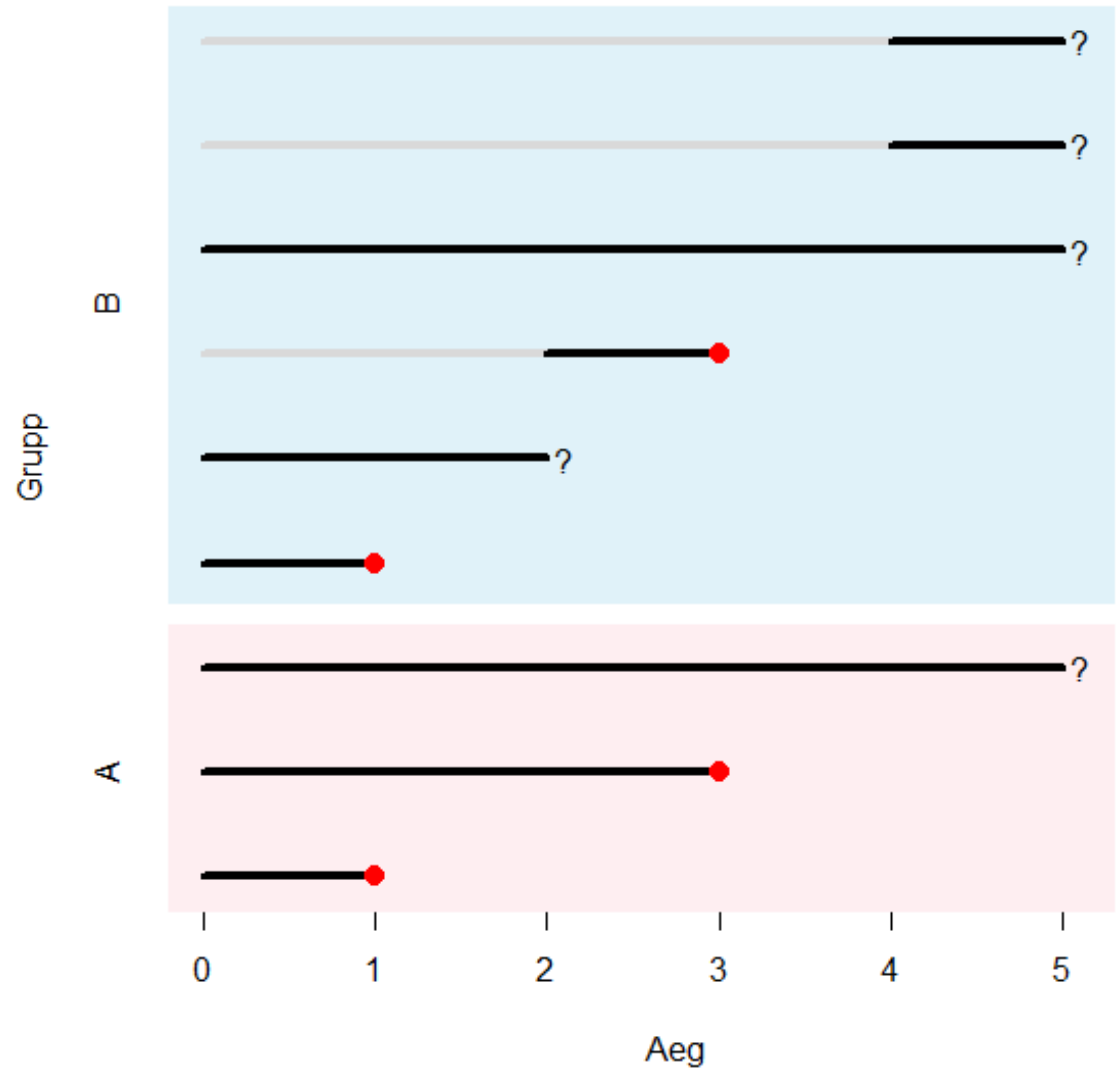
```
Likelihood ratio test=0.47 on 1 df, p=0.4925  
n= 9, number of events= 4
```

```
> cox.zph(m)
```

```
                chisq df p  
relevel(factor(grupp), ref = "B") 3.9e-33  1 1  
GLOBAL                3.9e-33  1 1
```

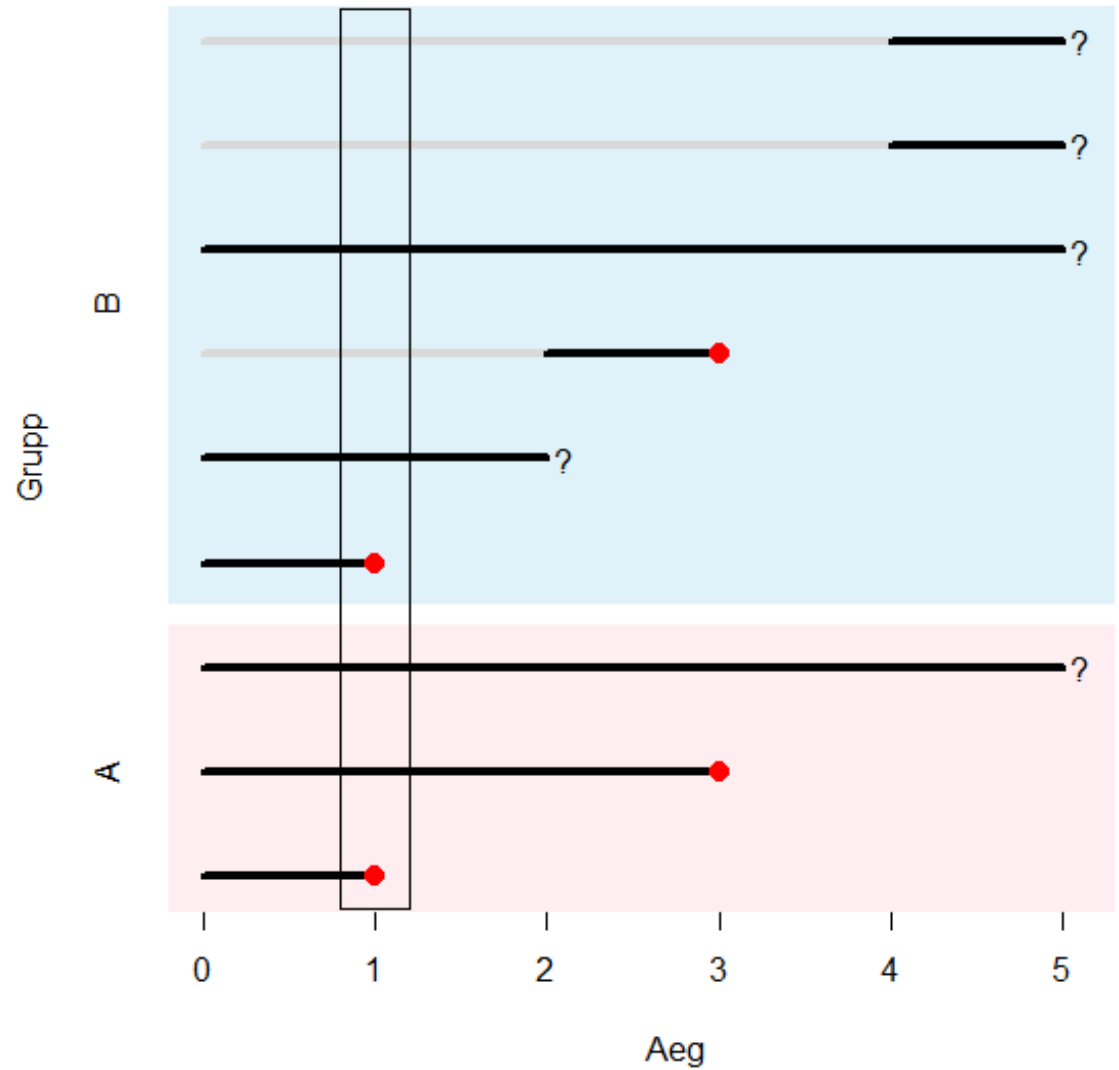
Andmed

id	grupp	vanus	suri	liitus
1	A	1	1	0
2	A	3	1	0
3	A	5	0	0
4	B	1	1	0
5	B	2	0	0
6	B	3	1	2
7	B	5	0	0
8	B	5	0	4
9	B	5	0	40



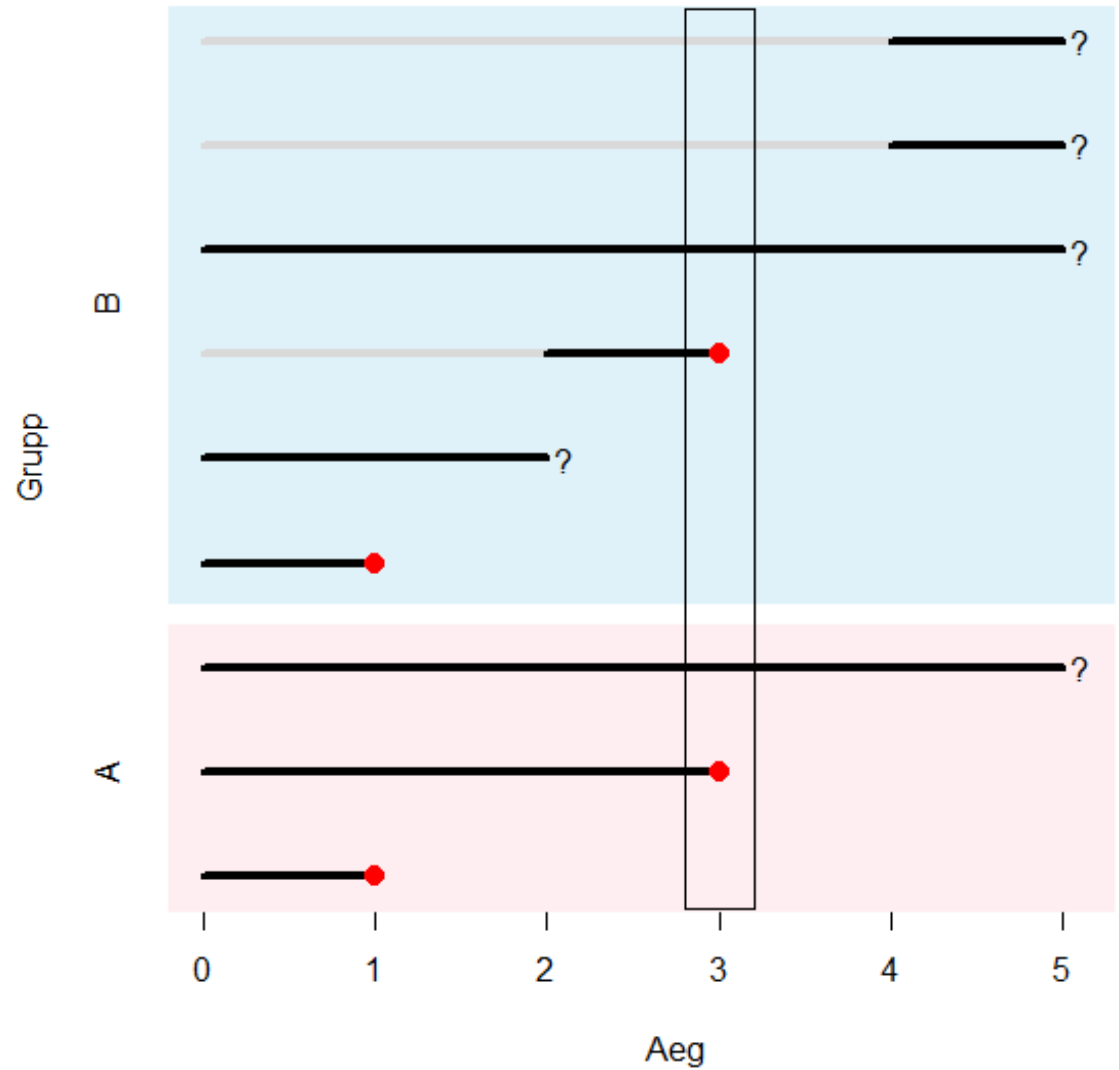
Andmed

id	grupp	vanus	suri	liitus
1	A	1	1	0
2	A	3	1	0
3	A	5	0	0
4	B	1	1	0
5	B	2	0	0
6	B	3	1	2
7	B	5	0	0
8	B	5	0	4
9	B	5	0	40



Andmed

id	grupp	vanus	suri	liitus
1	A	1	1	0
2	A	3	1	0
3	A	5	0	0
4	B	1	1	0
5	B	2	0	0
6	B	3	1	2
7	B	5	0	0
8	B	5	0	4
9	B	5	0	40



Andmed

id	grupp	vanus	suri	liitus
1	A	1	1	0
2	A	3	1	0
3	A	5	0	0
4	B	1	1	0
5	B	2	0	0
6	B	3	1	2
7	B	5	0	0
8	B	5	0	4
9	B	5	0	40

```
> m=coxph(Surv(liitus, vanus, suri)~grupp,  
           data=andmed, ties="breslow")
```

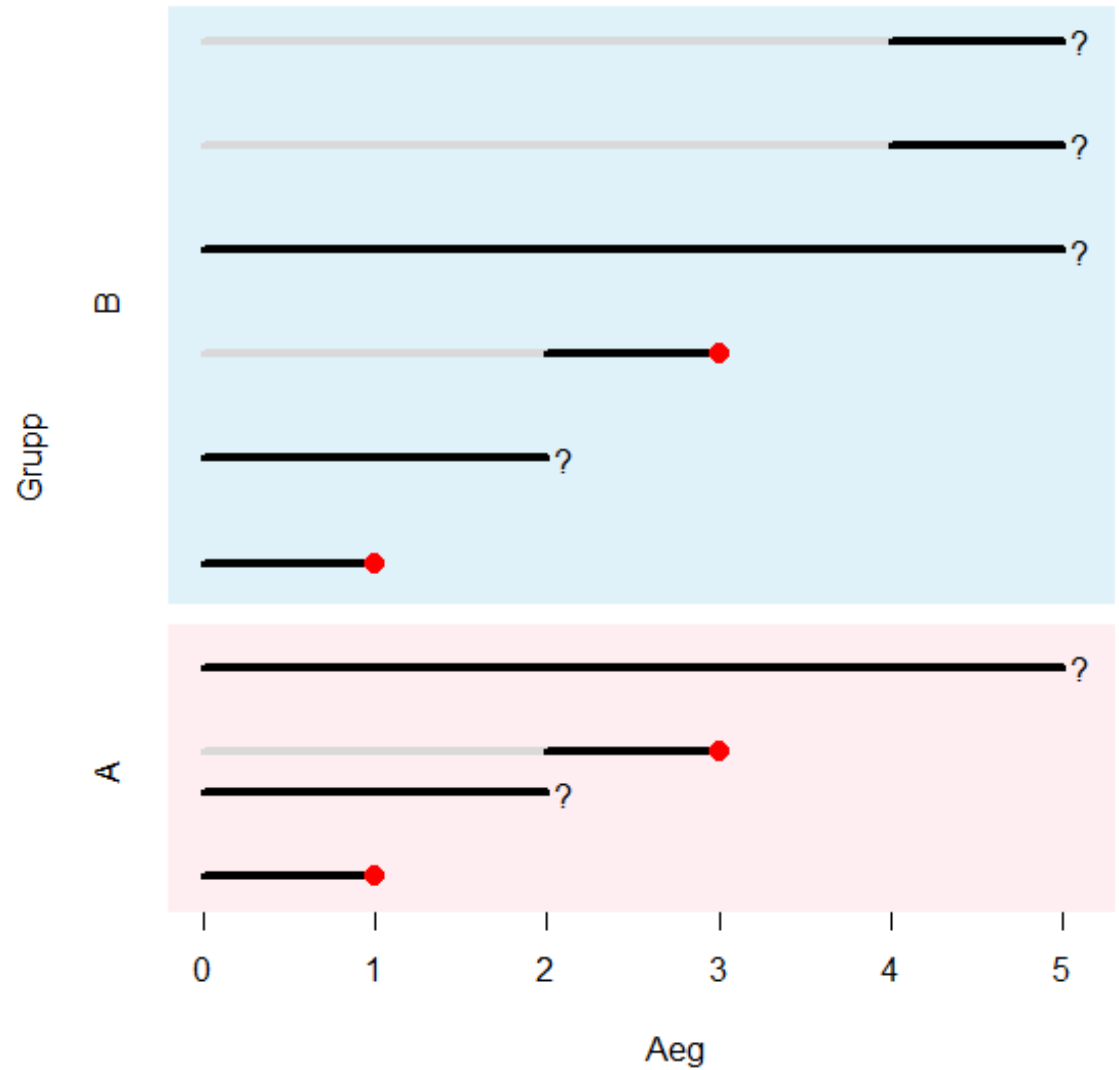
```
> m
```

```
           coef exp(coef) se(coef) z p  
gruppB      0           1       1 0 1
```

```
Likelihood ratio test=0 on 1 df, p=1  
n= 9, number of events= 4
```

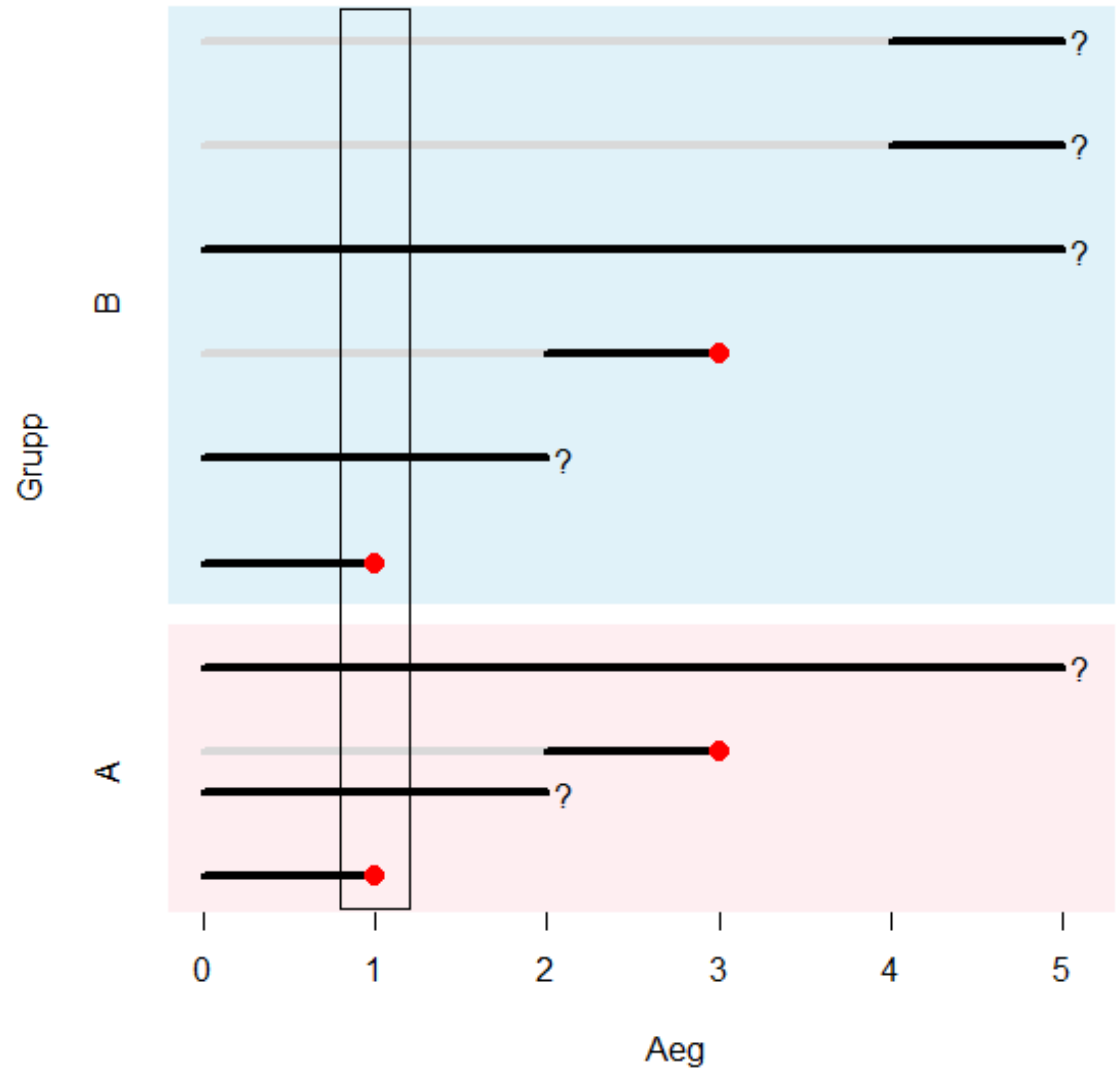
Andmed

id	grupp	vanus	suri	liitus
1	A	1	1	0
2	A	2	0	0
3	A	5	0	0
4	B	1	1	0
5	B	2	0	0
6	B	3	1	2
7	B	5	0	0
8	B	5	0	4
9	B	5	0	4
2	A	3	1	2



Andmed

id	grupp	vanus	suri	liitus
1	A	1	1	0
2	A	2	0	0
3	A	5	0	0
4	B	1	1	0
5	B	2	0	0
6	B	3	1	2
7	B	5	0	0
8	B	5	0	4
9	B	5	0	4
2	A	3	1	2



Andmed

id	grupp	vanus	suri	liitus
1	A	1	1	0
2	A	2	0	0
3	A	5	0	0
4	B	1	1	0
5	B	2	0	0
6	B	3	1	2
7	B	5	0	0
8	B	5	0	4
9	B	5	0	4
2	A	3	1	2

