

Controlled variables

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Introduction

```
source("Survival/utils.R")

# Setup analysis environment
analysis_setup <- setup_analysis()
paths <- analysis_setup$paths
demo <- analysis_setup$demo

flare.df <- readRDS(paste0(paths$outdir, "flares-overview.RDS"))
flare.cd.df <- subset(flare.df, diagnosis2 == "CD")
flare.uc.df <- subset(flare.df, diagnosis2 == "UC/IBDU")
```

The variables being controlled for in later cox models analyses are first investigated.

Although smoking status was originally planned to be controlled for, the [high degree of missingness](#) for these data and the [lack of significant associations with time to flare](#) has resulted in smoking status not being controlled for in later analyses.

Of the variables considered here, only sex is associated with disease flare.

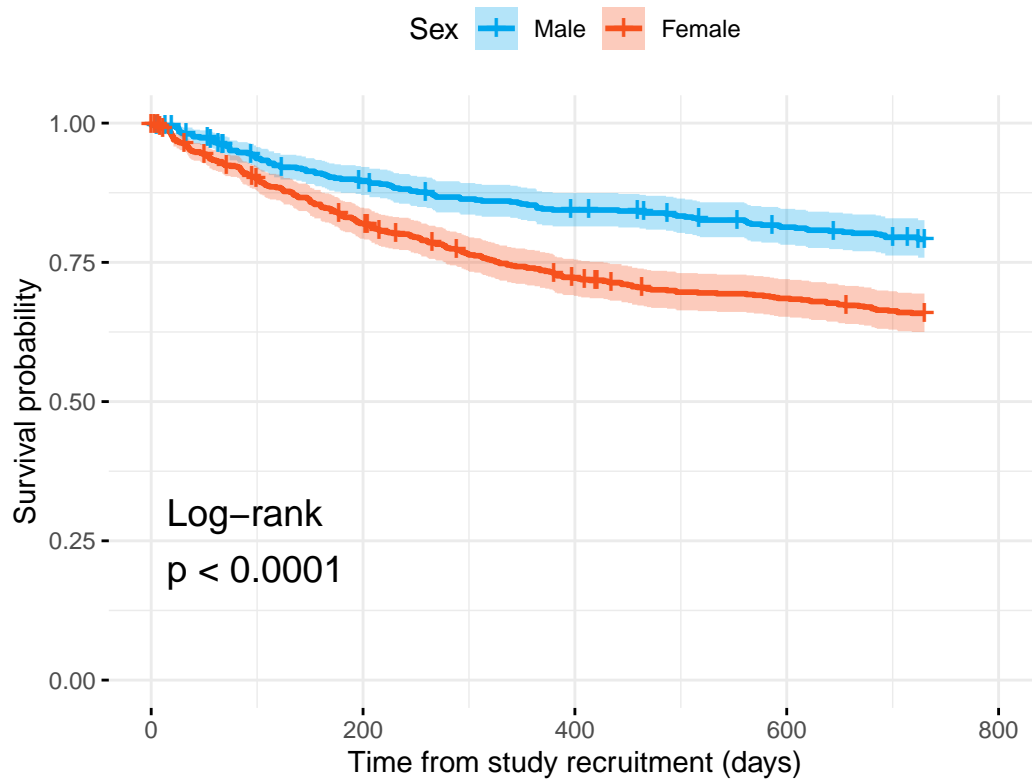
Sex

Crohn's disease

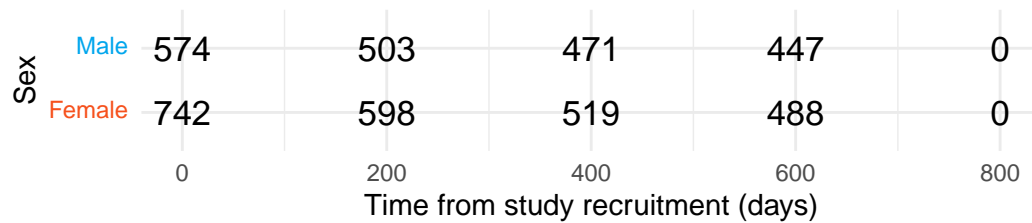
Patient-reported flare

```
generate_survival_plot(  
  data = flare.cd.df,  
  formula = Surv(softflare_time, softflare) ~ Sex,  
  legend_title = "Sex",  
  legend_labs = c("Male", "Female"),  
  palette = c("#00A6ED", "#F6511D"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to clinical flare",  
  break_time_by = 200,  
  plot_path = "plots/cd/soft-flare/controlled/sex"  
)
```

Time to clinical flare



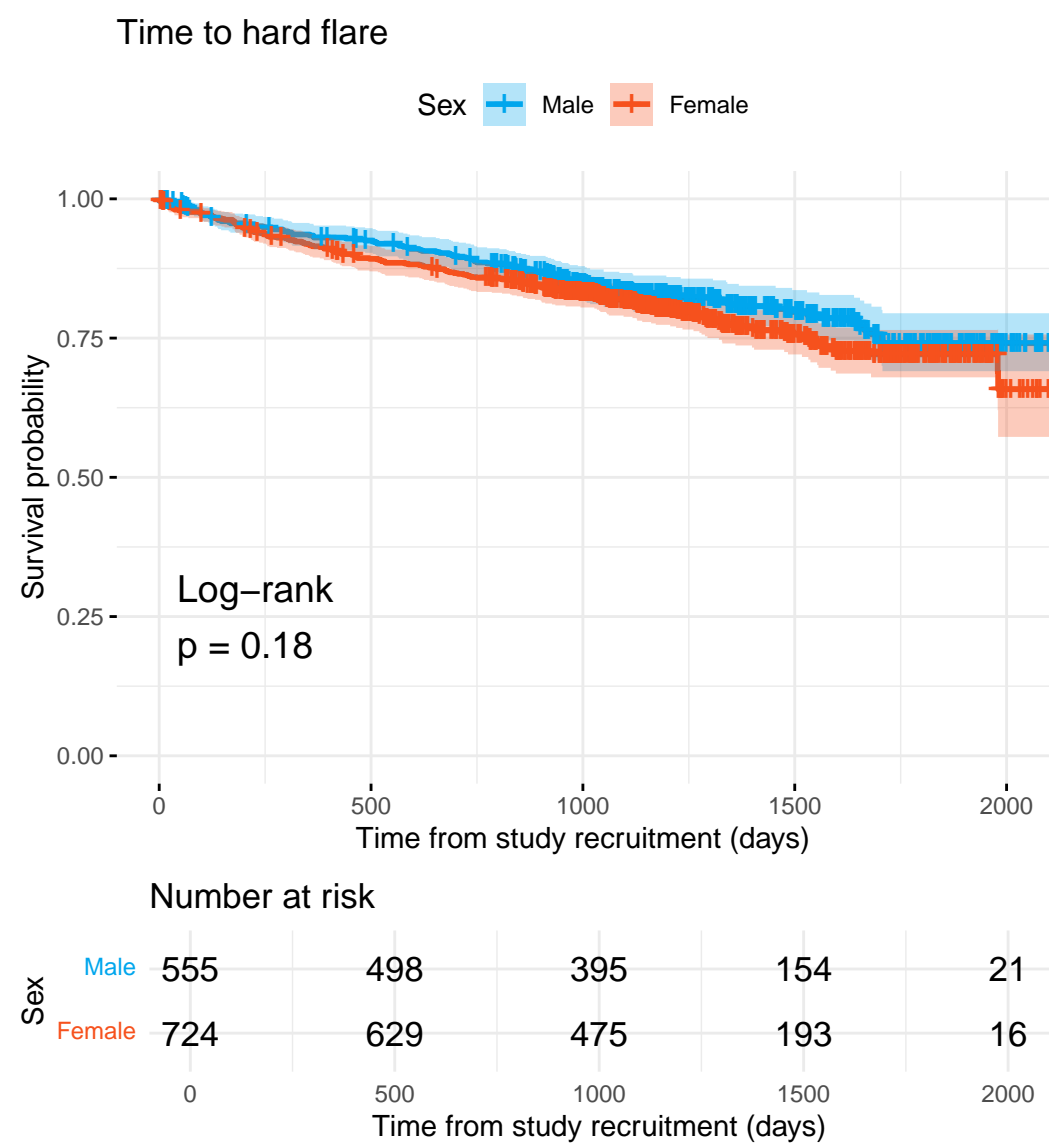
Number at risk



Hard flare

```
generate_survival_plot(
  data = flare.cd.df,
  formula = Surv(hardflare_time, hardflare) ~ Sex,
  legend_title = "Sex",
  legend_labs = c("Male", "Female"),
  palette = c("#00A6ED", "#F6511D"),
  xlab = "Time from study recruitment (days)",
```

```
title = "Time to hard flare",
break_time_by = 500,
plot_path = "plots/cd/hard-flare/controlled/sex"
)
```

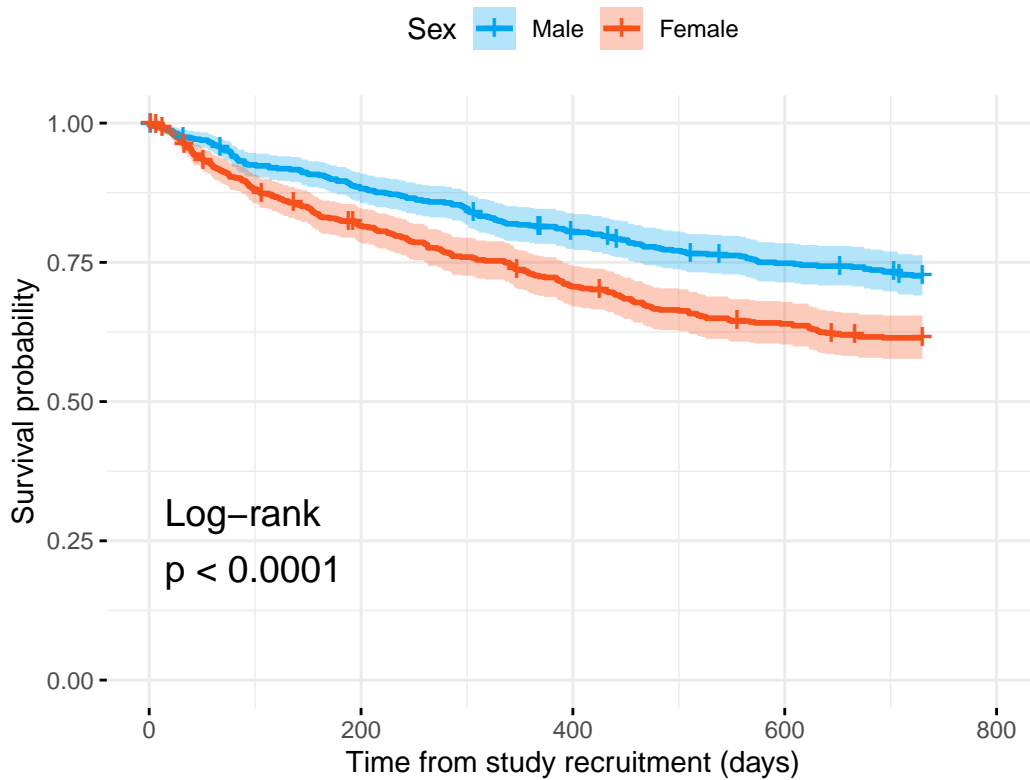


Ulcerative colitis

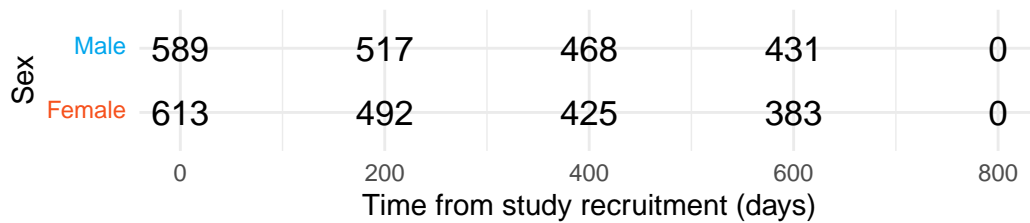
Patient-reported flare

```
generate_survival_plot(  
  data = flare.uc.df,  
  formula = Surv(softflare_time, softflare) ~ Sex,  
  legend_title = "Sex",  
  legend_labs = c("Male", "Female"),  
  palette = c("#00A6ED", "#F6511D"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to clinical flare",  
  break_time_by = 200,  
  plot_path = "plots/uc/soft-flare/controlled/sex"  
)
```

Time to clinical flare



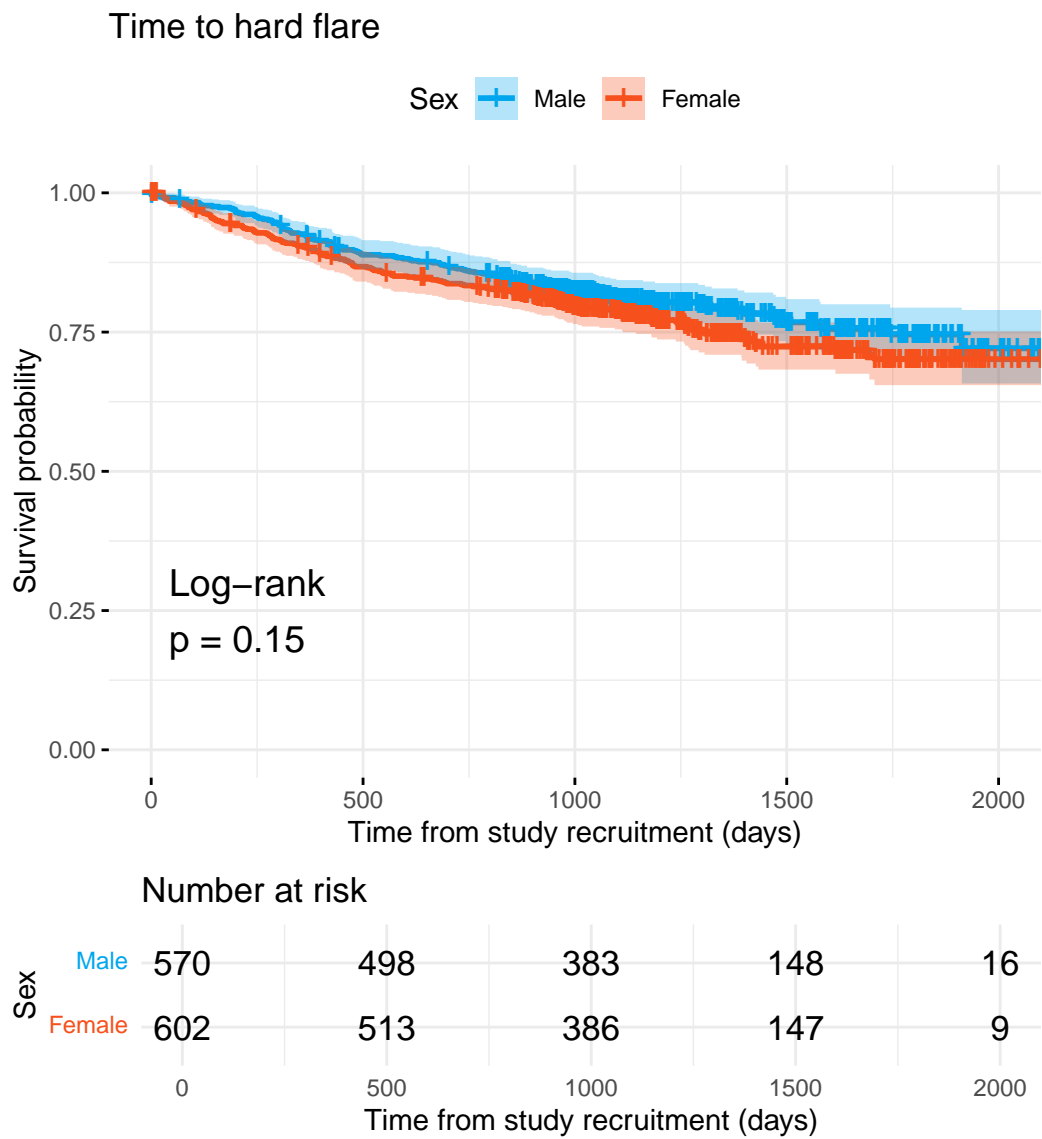
Number at risk



Hard flare

```
generate_survival_plot(
  data = flare.uc.df,
  formula = Surv(hardflare_time, hardflare) ~ Sex,
  legend_title = "Sex",
  legend_labs = c("Male", "Female"),
  palette = c("#00A6ED", "#F6511D"),
  xlab = "Time from study recruitment (days)",
```

```
title = "Time to hard flare",
break_time_by = 500,
plot_path = "plots/uc/hard-flare/controlled/sex"
)
```



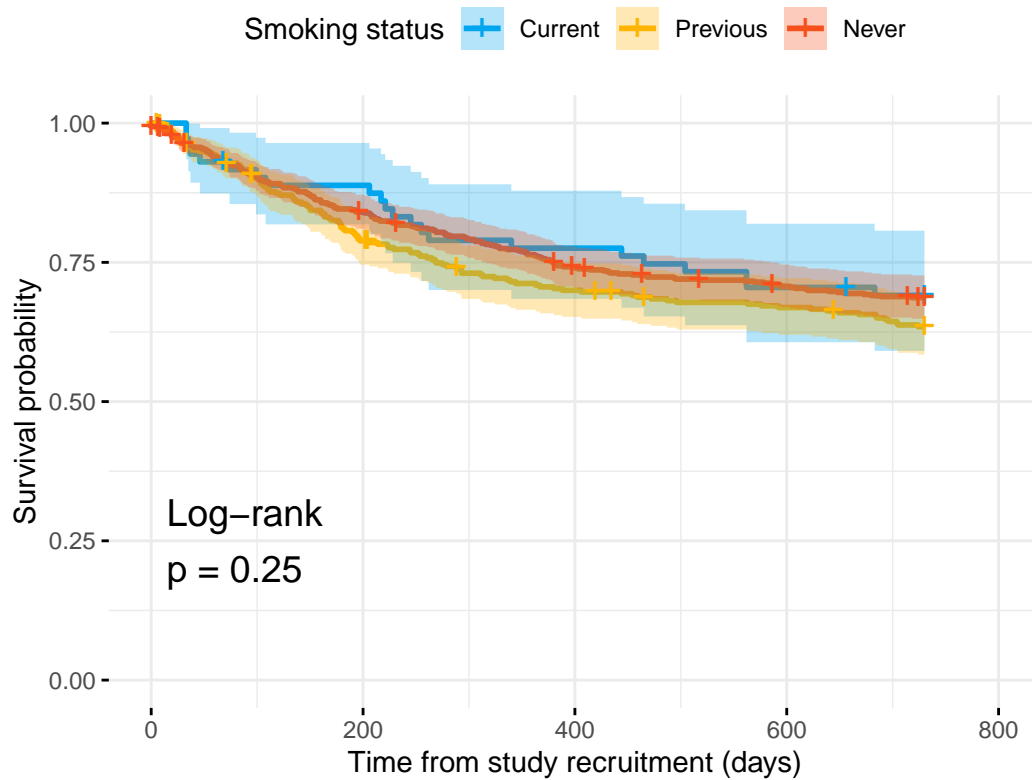
Smoking status

Crohn's disease

Patient-reported flare

```
generate_survival_plot(  
  data = flare.cd.df,  
  formula = Surv(softflare_time, softflare) ~ Smoke,  
  legend_title = "Smoking status",  
  legend_labs = c("Current", "Previous", "Never"),  
  palette = c("#00A6ED", "#FFB400", "#F6511D"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to clinical flare",  
  break_time_by = 200,  
  plot_path = "plots/cd/soft-flare/controlled/smoke"  
)
```

Time to clinical flare



Number at risk

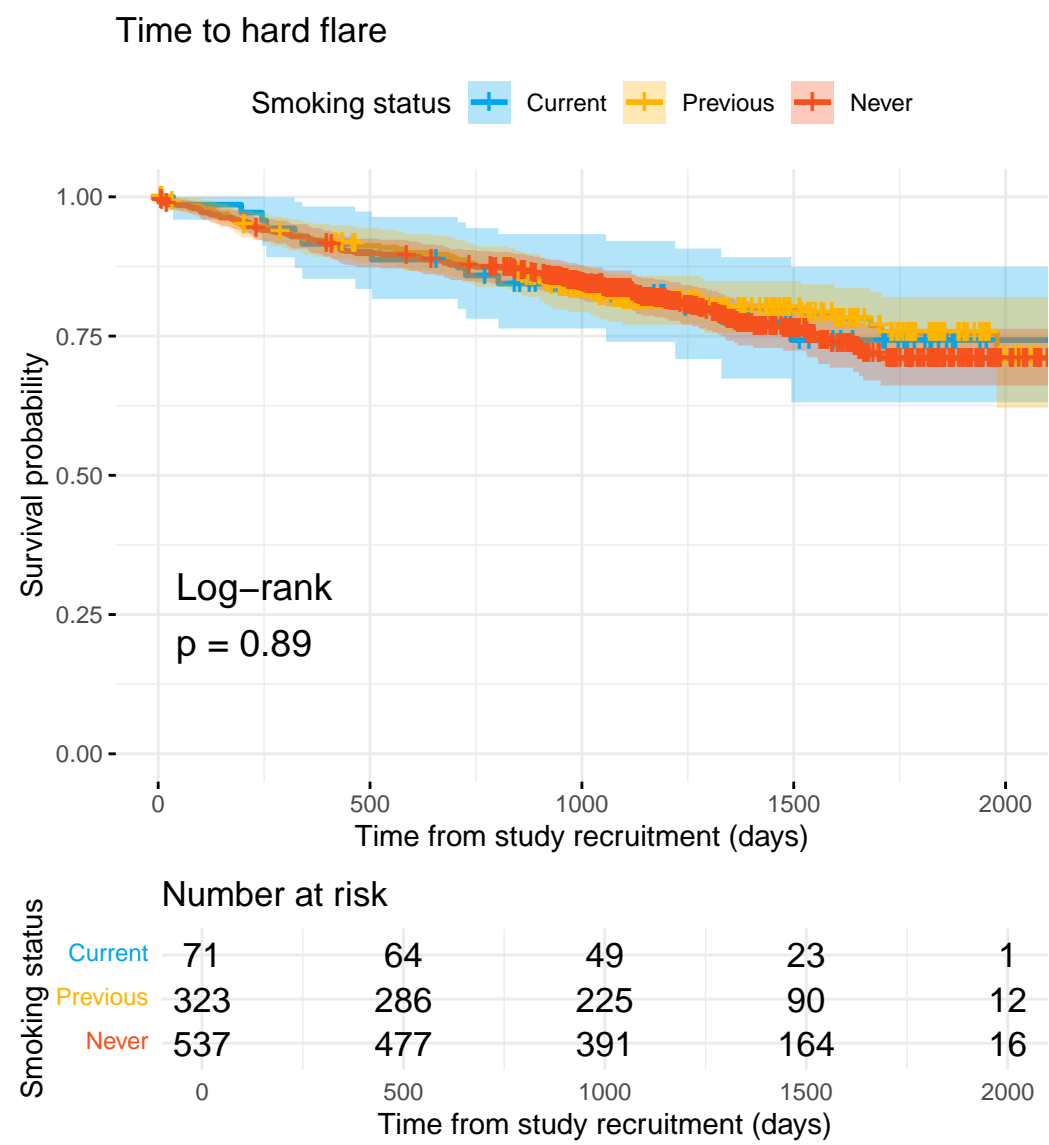
Smoking status	0	200	400	600	800
Current	72	63	55	50	0
Previous	336	260	228	215	0
Never	556	462	404	382	0

Time from study recruitment (days)

Hard flare

```
generate_survival_plot(
  data = flare.cd.df,
  formula = Surv(hardflare_time, hardflare) ~ Smoke,
  legend_title = "Smoking status",
  legend_labels = c("Current", "Previous", "Never"),
  palette = c("#00A6ED", "#FFB400", "#F6511D"),
  xlab = "Time from study recruitment (days)",
```

```
title = "Time to hard flare",
break_time_by = 500,
plot_path = "plots/cd/hard-flare/controlled/smoke"
)
```

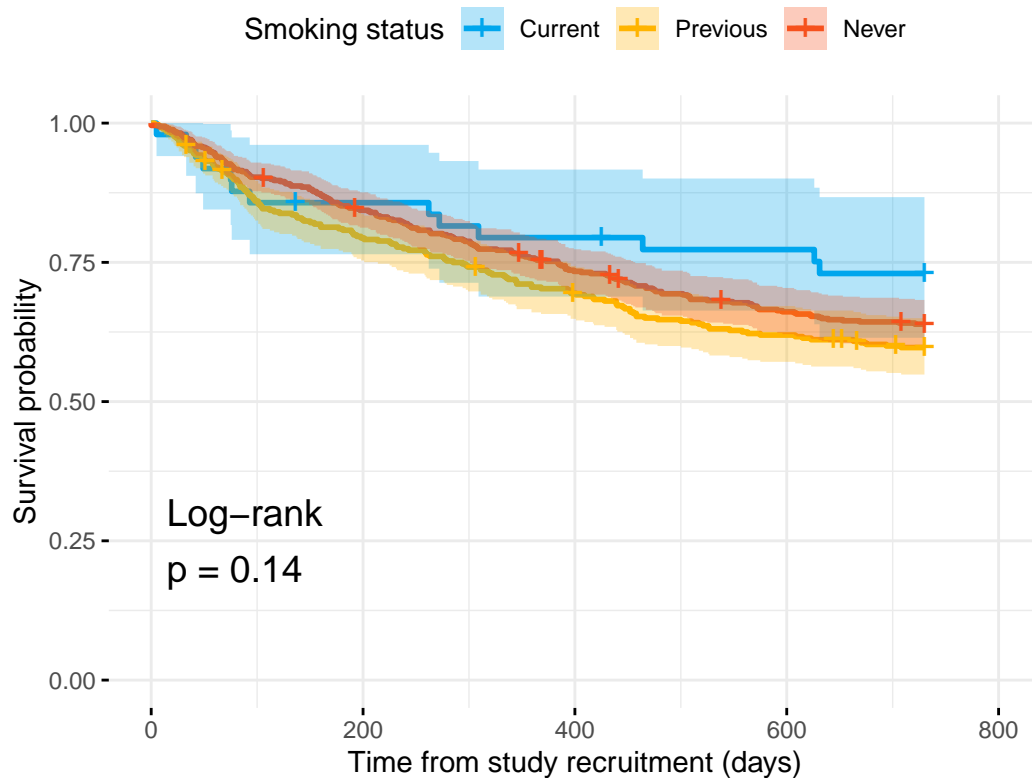


Ulcerative colitis

Patient-reported flare

```
generate_survival_plot(  
  data = flare.uc.df,  
  formula = Surv(softflare_time, softflare) ~ Smoke,  
  legend_title = "Smoking status",  
  legend_labs = c("Current", "Previous", "Never"),  
  palette = c("#00A6ED", "#FFB400", "#F6511D"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to clinical flare",  
  break_time_by = 200,  
  plot_path = "plots/uc/soft-flare/controlled/smoke"  
)
```

Time to clinical flare



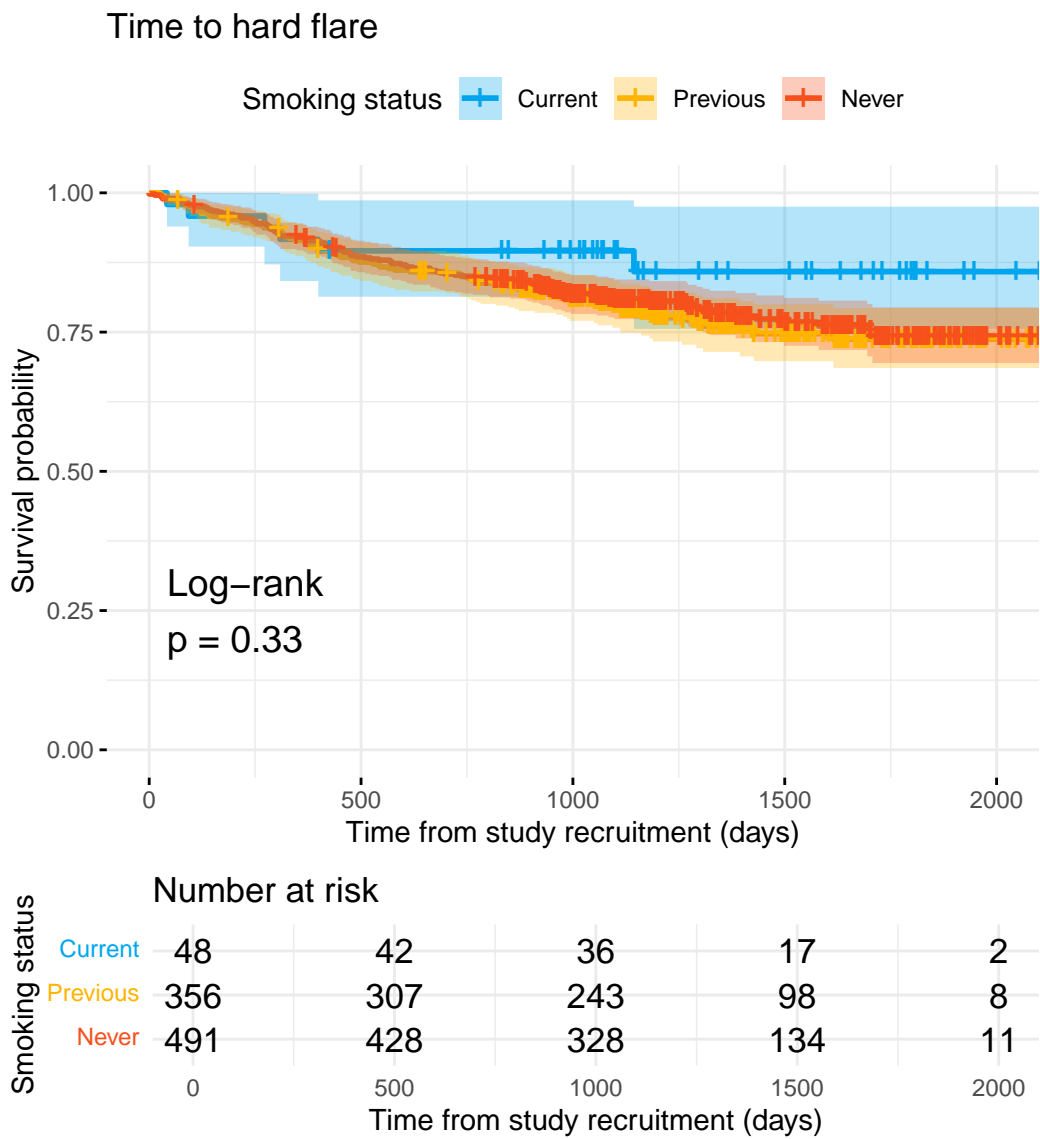
Number at risk

Smoking status					
Current	49	41	38	36	0
Previous	366	288	250	223	0
Never	505	424	366	327	0
	0	200	400	600	800
	Time from study recruitment (days)				

Hard flare

```
generate_survival_plot(
  data = flare.uc.df,
  formula = Surv(hardflare_time, hardflare) ~ Smoke,
  legend_title = "Smoking status",
  legend_labs = c("Current", "Previous", "Never"),
  palette = c("#00A6ED", "#FFB400", "#F6511D"),
  xlab = "Time from study recruitment (days)",
```

```
title = "Time to hard flare",
break_time_by = 500,
plot_path = "plots/uc/hard-flare/controlled/smoke"
)
```



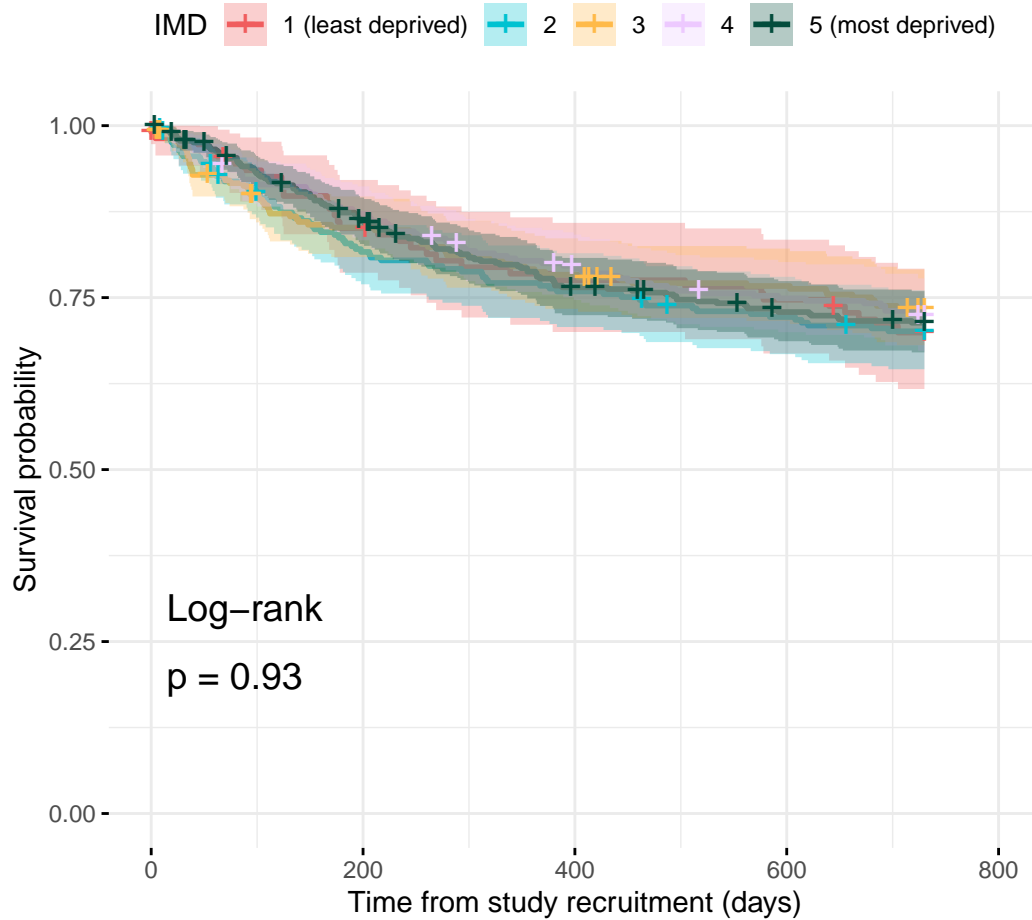
Social deprivation

Crohn's disease

Patient-reported flare

```
generate_survival_plot(  
  data = flare.cd.df,  
  formula = Surv(softflare_time, softflare) ~ IMD,  
  legend_title = "IMD",  
  legend_labs = c("1 (least deprived)", "2", "3", "4", "5 (most deprived)"),  
  palette = c("#F05D5E", "#00C2D1", "#FFBA49", "#EDC9FF", "#034C3C"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to clinical flare",  
  break_time_by = 200,  
  plot_path = "plots/cd/soft-flare/controlled/imd"  
)
```

Time to clinical flare



Number at risk

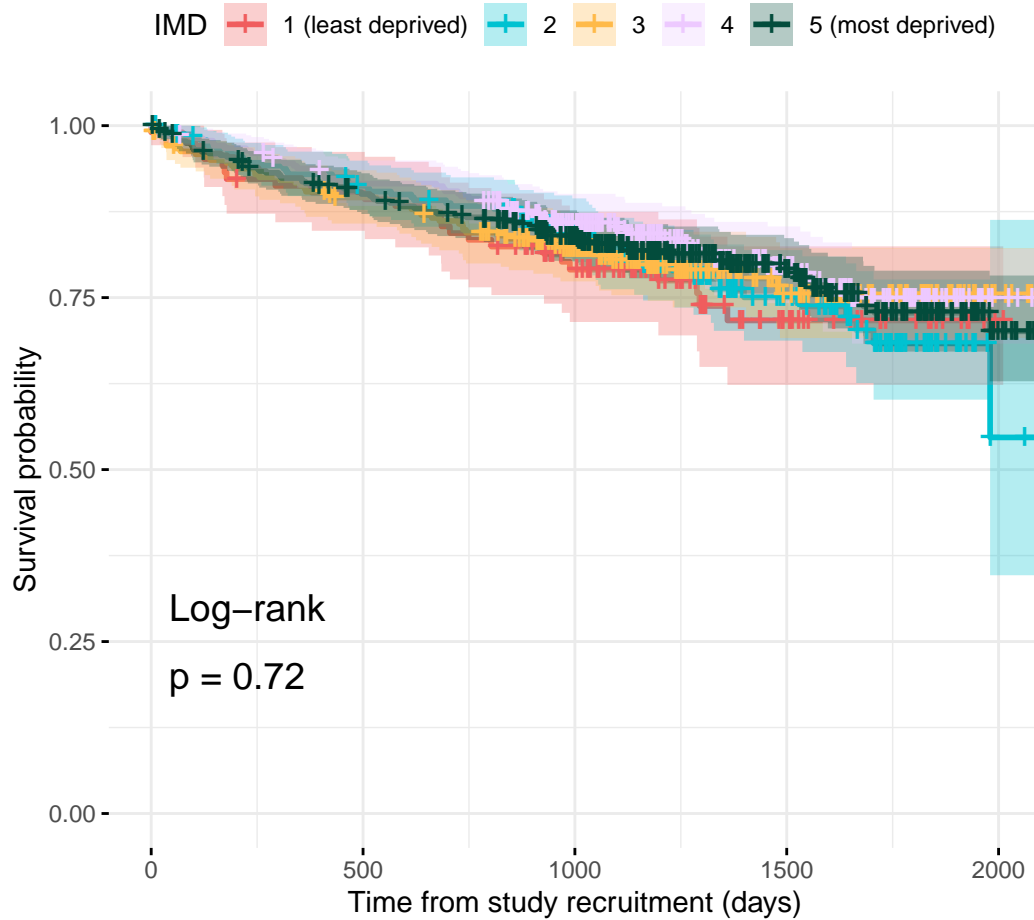
IMD		0	200	400	600	800
1 (least deprived)	109	91	82	79	0	
2	249	199	185	174	0	
3	254	211	194	186	0	
4	281	244	218	205	0	
5 (most deprived)	409	344	301	282	0	

Time from study recruitment (days)

Hard flare


```
generate_survival_plot(  
  data = flare.cd.df,  
  formula = Surv(hardflare_time, hardflare) ~ IMD,  
  legend_title = "IMD",  
  legend_labs = c("1 (least deprived)", "2", "3", "4", "5 (most deprived)"),  
  palette = c("#F05D5E", "#00C2D1", "#FFBA49", "#EDC9FF", "#034C3C"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to hard flare",  
  break_time_by = 500,  
  plot_path = "plots/cd/hard-flare/controlled/imd"  
)
```

Time to hard flare



Number at risk

IMD	1 (least deprived)	103	92	69	24	1
	2	245	217	160	60	3
	3	243	211	161	60	6
	4	275	248	191	78	5
	5 (most deprived)	399	347	282	122	21
		0	500	1000	1500	2000
		Time from study recruitment (days)				

Ulcerative colitis

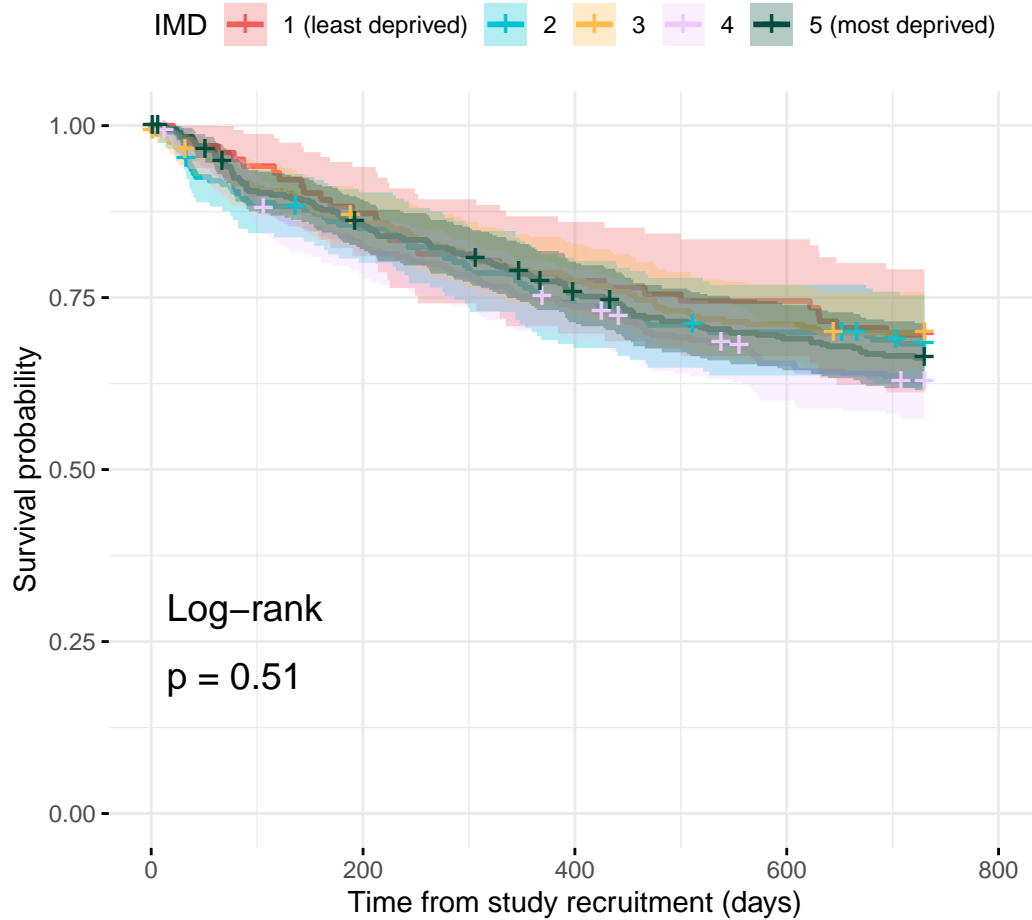
Patient-reported flare

```

generate_survival_plot(
  data = flare.uc.df,
  formula = Surv(softflare_time, softflare) ~ IMD,
  legend_title = "IMD",
  legend_labs = c("1 (least deprived)", "2", "3", "4", "5 (most deprived)"),
  palette = c("#F05D5E", "#00C2D1", "#FFBA49", "#EDC9FF", "#034C3C"),
  xlab = "Time from study recruitment (days)",
  title = "Time to clinical flare",
  break_time_by = 200,
  plot_path = "plots/uc/soft-flare/controlled/imd"
)

```

Time to clinical flare



Number at risk

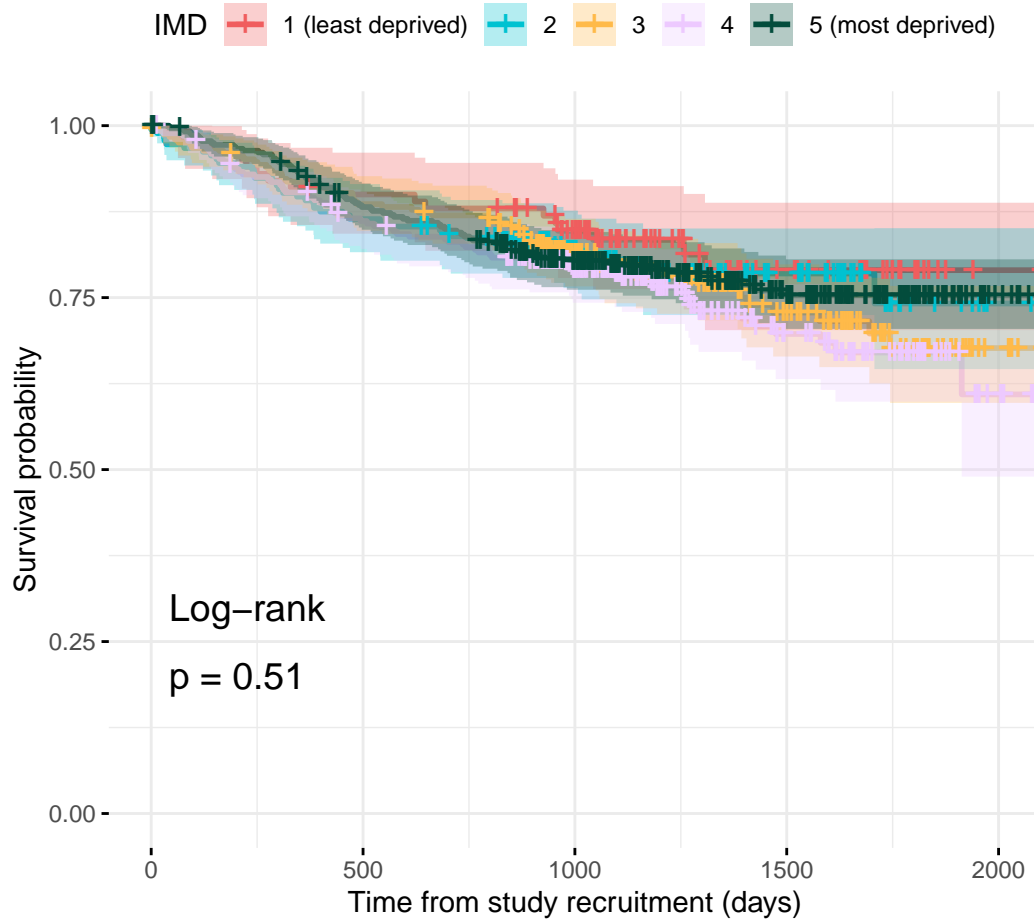
IMD					
1 (least deprived)	102	89	79	76	0
2	188	158	137	129	0
3	255	216	195	179	0
4	275	224	200	174	0
5 (most deprived)	371	313	273	248	0
	0	200	400	600	800

Time from study recruitment (days)

Hard flare

```
generate_survival_plot(  
  data = flare.uc.df,  
  formula = Surv(hardflare_time, hardflare) ~ IMD,  
  legend_title = "IMD",  
  legend_labs = c("1 (least deprived)", "2", "3", "4", "5 (most deprived)"),  
  palette = c("#F05D5E", "#00C2D1", "#FFBA49", "#EDC9FF", "#034C3C"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to hard flare",  
  break_time_by = 500,  
  plot_path = "plots/uc/hard-flare/controlled/imd"  
)
```

Time to hard flare



IMD	0	500	1000	1500	2000
1 (least deprived)	100	89	72	26	1
2	184	159	118	38	3
3	247	217	167	64	6
4	270	227	171	58	6
5 (most deprived)	360	309	233	106	8

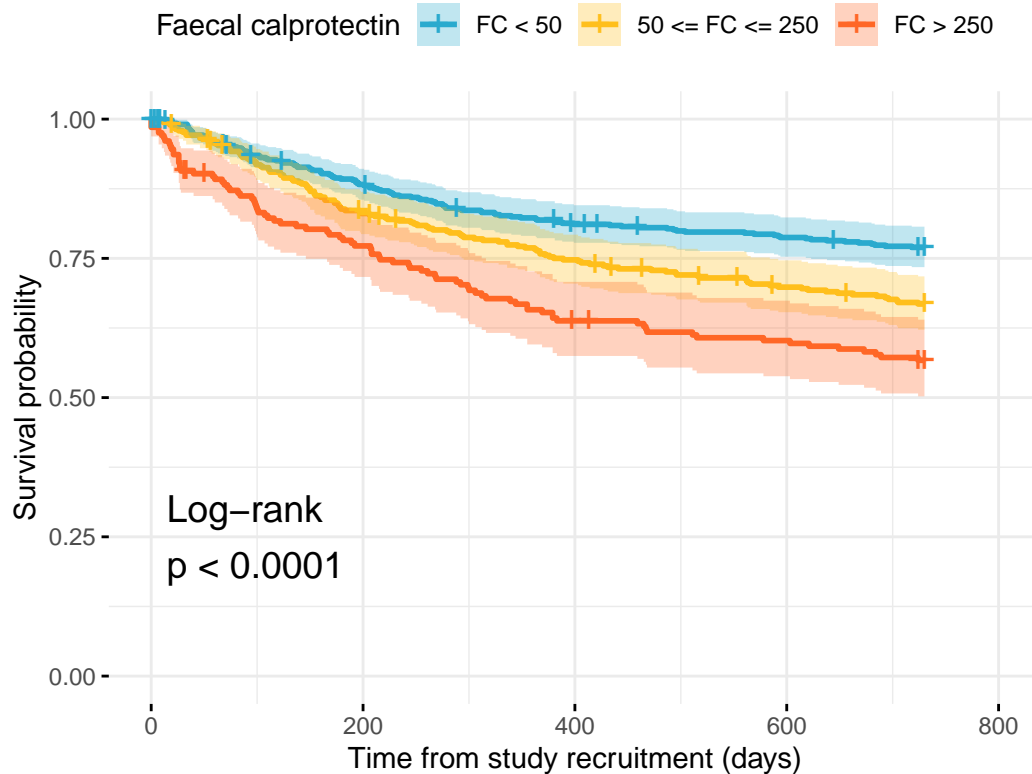
Faecal calprotectin

Crohn's disease

Patient-reported flare

```
p <- generate_survival_plot(  
  data = flare.cd.df,  
  formula = Surv(softflare_time, softflare) ~ cat,  
  legend_title = "Faecal calprotectin",  
  legend_labs = c("FC < 50", "50 FC 250", "FC > 250"),  
  palette = c("#2AAACE", "#FFBF1C", "#FF6726"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to clinical flare",  
  break_time_by = 200,  
  plot_path = "plots/cd/soft-flare/controlled/fc"  
)  
  
saveRDS(p, paste0(paths$outdir, "fc-cd-soft.RDS"))  
  
print(p, newpage = FALSE)
```

Time to clinical flare



Faecal calprotectin

Number at risk

FC < 50	527	457	416	401	0
50 ≤ FC ≤ 250	381	312	278	254	0
FC > 250	204	155	127	119	0

Time from study recruitment (days)

Hard flare

```
p <- generate_survival_plot(
  data = flare.cd.df,
  formula = Surv(hardflare_time, hardflare) ~ cat,
  legend_title = "Faecal calprotectin",
  legend_labels = c("FC < 50", "50 ≤ FC ≤ 250", "FC > 250"),
  palette = c("#2AAACE", "#FFBF1C", "#FF6726"),
  xlab = "Time from study recruitment (days)",
```



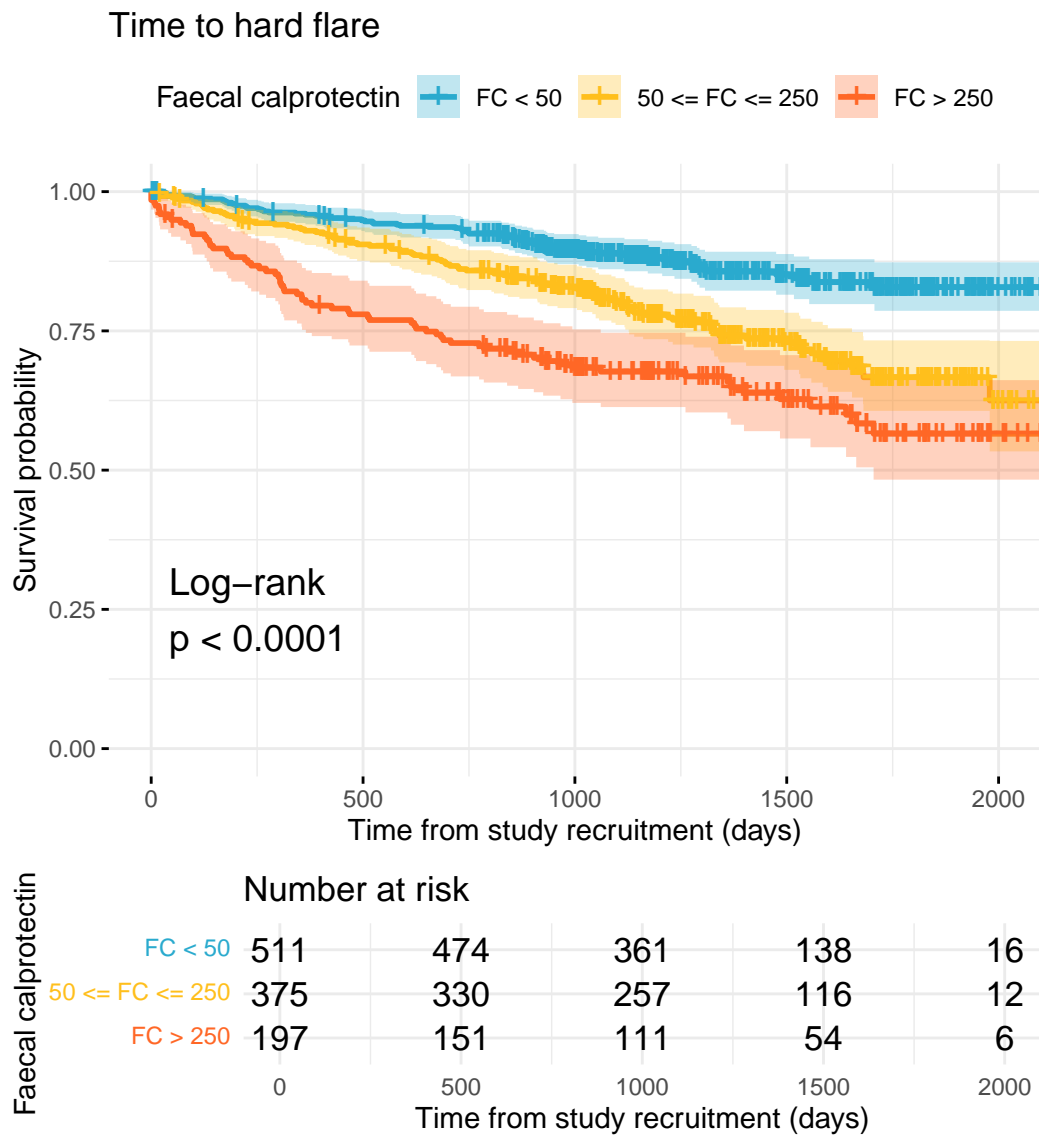
```

title = "Time to hard flare",
break_time_by = 500,
plot_path = "plots/cd/hard-flare/controlled/fc"
)

saveRDS(p, paste0(paths$outdir, "fc-cd-hard.RDS"))

print(p, newpage = FALSE)

```

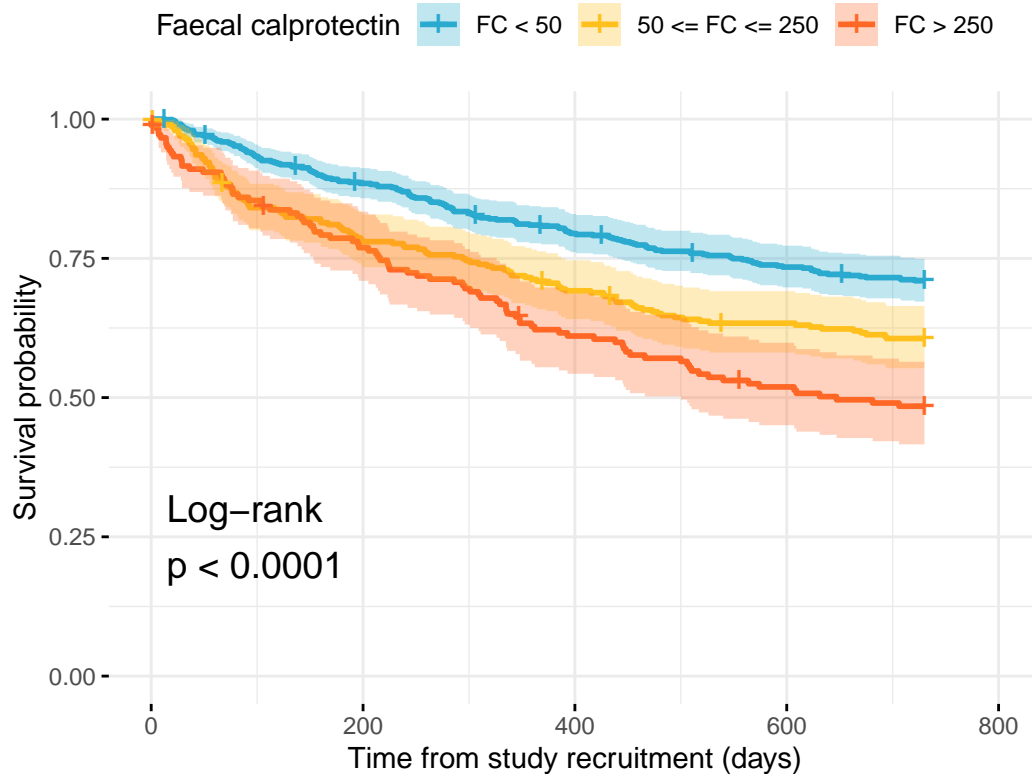


Ulcerative colitis

Patient-reported flare

```
p <- generate_survival_plot(  
  data = flare.uc.df,  
  formula = Surv(softflare_time, softflare) ~ cat,  
  legend_title = "Faecal calprotectin",  
  legend_labs = c("FC < 50", "50 FC 250", "FC > 250"),  
  palette = c("#2AAACE", "#FFBF1C", "#FF6726"),  
  xlab = "Time from study recruitment (days)",  
  title = "Time to clinical flare",  
  break_time_by = 200,  
  plot_path = "plots/uc/soft-flare/controlled/fc"  
)  
  
saveRDS(p, paste0(paths$outdir, "fc-uc-soft.RDS"))  
  
print(p, newpage = FALSE)
```

Time to clinical flare



Faecal calprotectin

Number at risk

FC < 50	539	473	423	389	0
50 ≤ FC ≤ 250	297	230	203	184	0
FC > 250	179	136	107	90	0

Time from study recruitment (days)

Hard flare

```
p <- generate_survival_plot(
  data = flare.uc.df,
  formula = Surv(hardflare_time, hardflare) ~ cat,
  legend_title = "Faecal calprotectin",
  legend_labels = c("FC < 50", "50 ≤ FC ≤ 250", "FC > 250"),
  palette = c("#2AAACE", "#FFBF1C", "#FF6726"),
  xlab = "Time from study recruitment (days)",
```

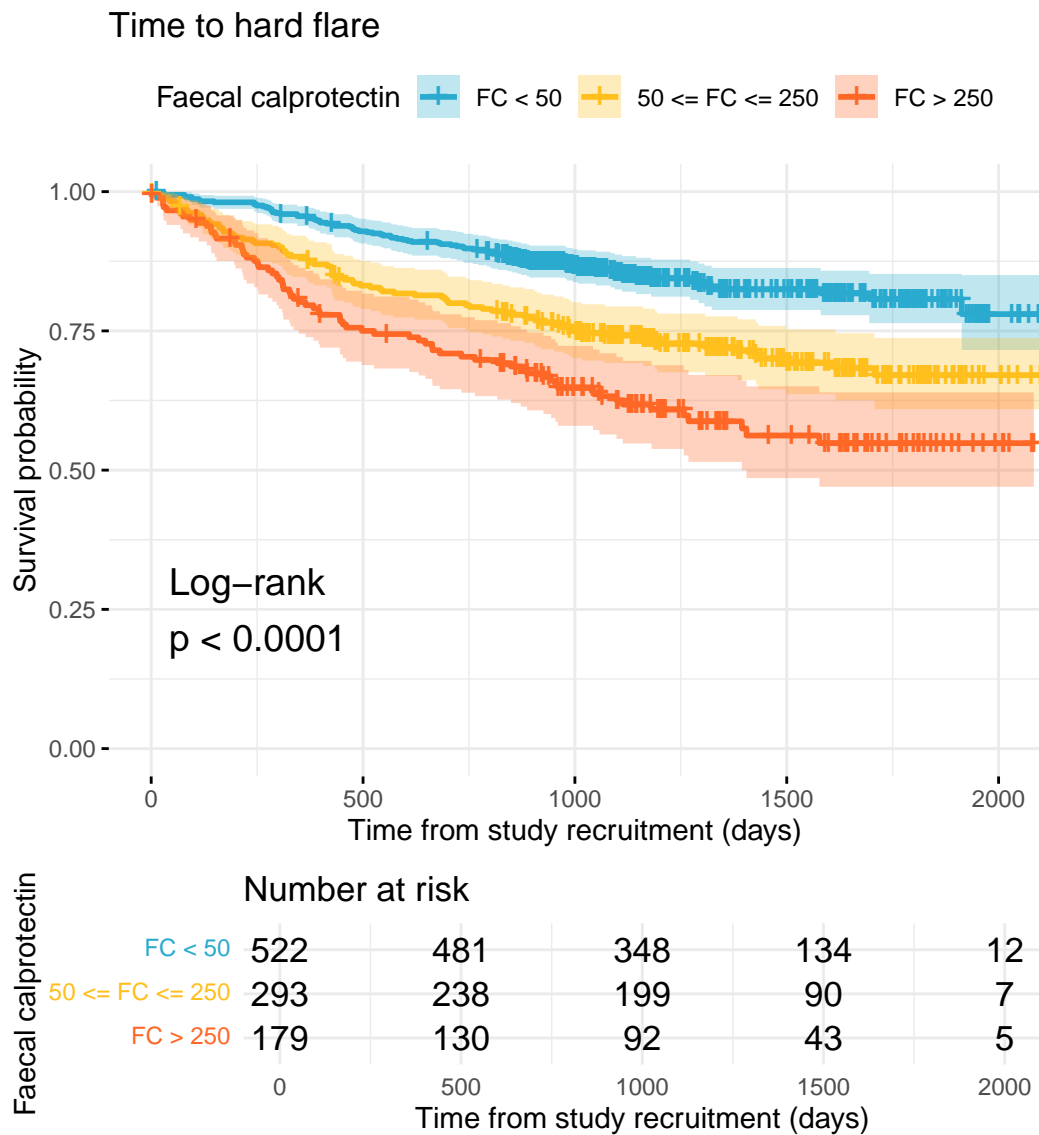
```

title = "Time to hard flare",
break_time_by = 500,
plot_path = "plots/uc/hard-flare/controlled/fc"
)

saveRDS(p, paste0(paths$outdir, "fc-uc-hard.RDS"))

print(p, newpage = FALSE)

```



Cox models

Crohn's disease

Patient-reported flare

```
fit.me <- coxph(  
  Surv(softflare_time, softflare) ~  
    Sex + IMD + cat + Smoke + frailty(SiteNo),  
  control = coxph.control(outer.max = 20),  
  data = flare.cd.df,  
  model = TRUE  
)  
  
cd.clin.forest <- get_HR(  
  fit.me,  
  c("SmokePrevious", "SmokeNever")  
)  
  
fit.me <- coxph(  
  Surv(softflare_time, softflare) ~  
    Sex + IMD + cat + frailty(SiteNo),  
  control = coxph.control(outer.max = 20),  
  data = flare.cd.df,  
  model = TRUE  
)  
  
cd.clin.forest <- rbind(  
  cd.clin.forest,  
  get_HR(  
    fit.me,  
    c(  
      "SexFemale",  
      paste0("IMD", seq(2, 5)),  
      "catFC 50-250",  
      "catFC > 250"  
    )  
  )  
)
```

```
invisible(cox_summary(fit.me))
```

Cox model summary:

Variable	HR	Lower 95%	Upper 95%	P-value
SexFemale	1.9989	1.5753	2.5364	0.0000
IMD2	0.9364	0.5970	1.4686	0.7746
IMD3	0.8868	0.5609	1.4021	0.6074
IMD4	0.9417	0.6062	1.4631	0.7894
IMD5	0.9857	0.6443	1.5078	0.9469
catFC 50-250	1.5844	1.2278	2.0445	0.0004
catFC > 250	2.4138	1.8192	3.2028	0.0000

Diagnostics:

Proportional hazards assumption test

	Chi-squared statistic	DF	P-value
Sex	0.3091	0.9923	0.5750
IMD	5.8397	3.9497	0.2063
cat	2.3232	1.9815	0.3093
GLOBAL	8.4076	13.9400	0.8643

DF betas

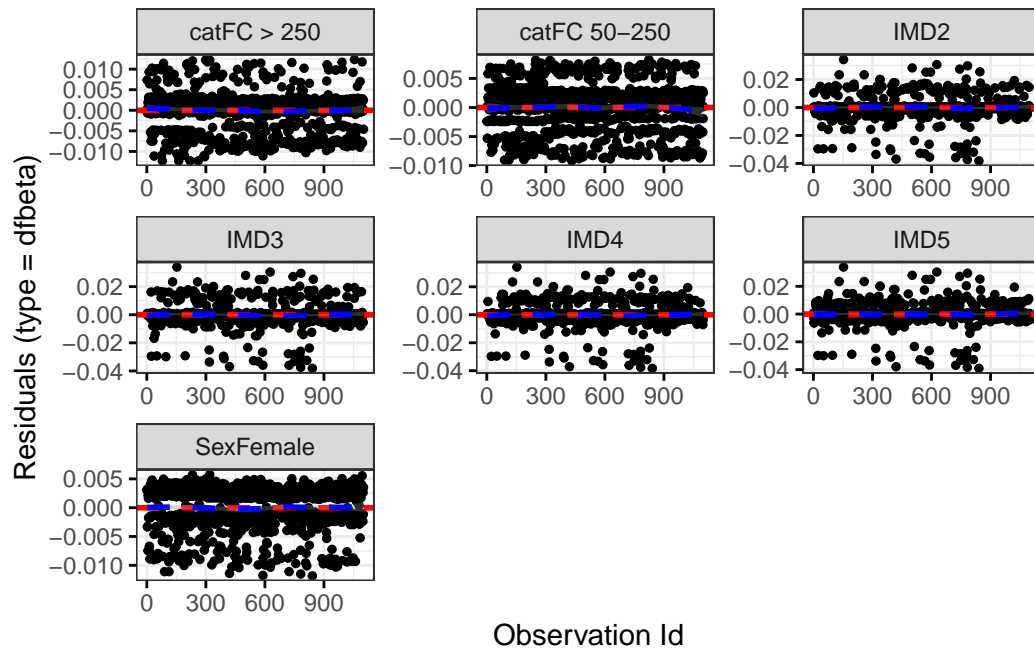
Warning: `gather_()` was deprecated in tidyr 1.2.0.

i Please use `gather()` instead.

i The deprecated feature was likely used in the survminer package.

Please report the issue at <<https://github.com/kassambara/survminer/issues>>.

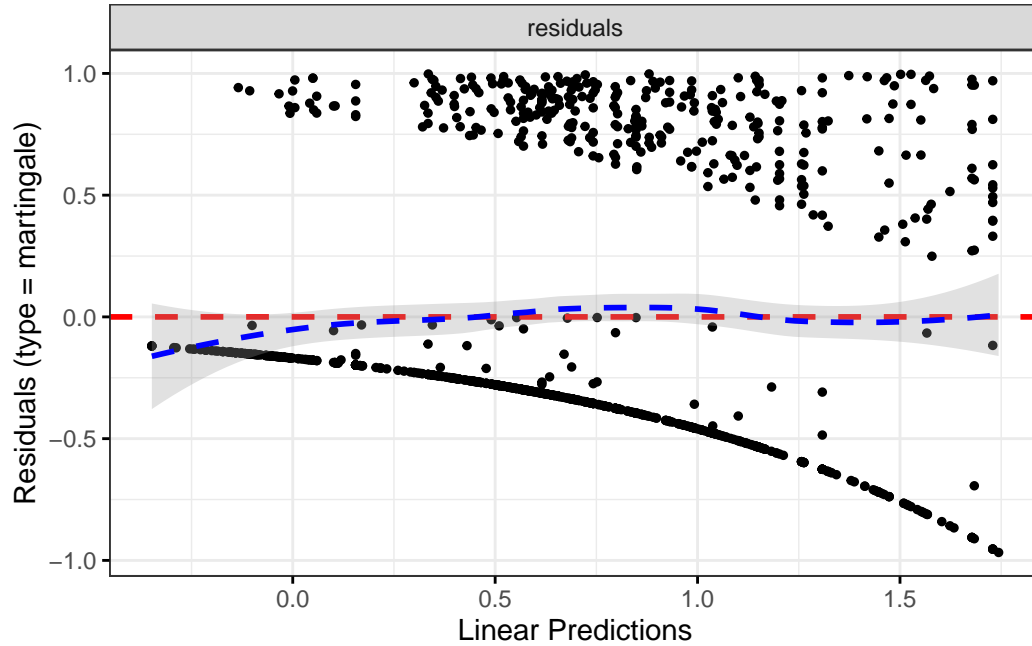
`geom_smooth()` using formula = 'y ~ x'



#####

Martingale residuals

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



Hard flare

```
fit.me <- coxph(  
  Surv(hardflare_time, hardflare) ~  
    Sex + IMD + cat + Smoke + frailty(SiteNo),  
  control = coxph.control(outer.max = 20),  
  data = flare.cd.df  
)  
  
cd.hard.forest <- get_HR(  
  fit.me,  
  c("SmokePrevious", "SmokeNever")  
)  
  
fit.me <- coxph(  
  Surv(hardflare_time, hardflare) ~  
    Sex + IMD + cat + frailty(SiteNo),  
  control = coxph.control(outer.max = 20),  
  data = flare.cd.df  
)  
  
cd.hard.forest <- rbind(  
  cd.hard.forest,  
  get_HR(  
    fit.me,  
    c(  
      "SexFemale",  
      paste0("IMD", seq(2, 5)),  
      "catFC > 250"  
    )  
  )  
)  
  
invisible(cox_summary(fit.me))
```

Cox model summary:

Variable	HR	Lower 95%	Upper 95%	P-value
SexFemale	1.3887	1.0579	1.8227	0.0180
IMD2	0.9220	0.5365	1.5844	0.7688

Variable	HR	Lower 95%	Upper 95%	P-value
IMD3	0.9675	0.5566	1.6817	0.9068
IMD4	0.8950	0.5222	1.5338	0.6864
IMD5	0.9035	0.5370	1.5199	0.7021
catFC 50-250	2.0217	1.4730	2.7750	0.0000
catFC > 250	3.3366	2.3693	4.6989	0.0000

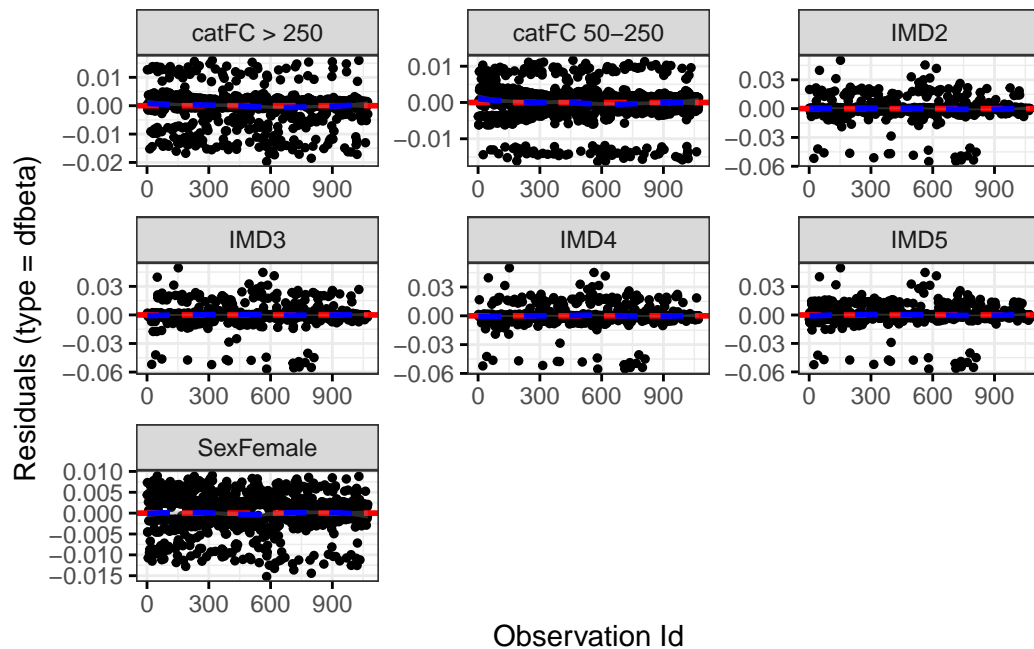
Diagnostics:

Proportional hazards assumption test

	Chi-squared statistic	DF	P-value
Sex	0.2571	0.9863	0.6064
IMD	4.2174	3.9407	0.3689
cat	8.8712	1.9847	0.0116
GLOBAL	13.9394	19.6668	0.8190

DF betas

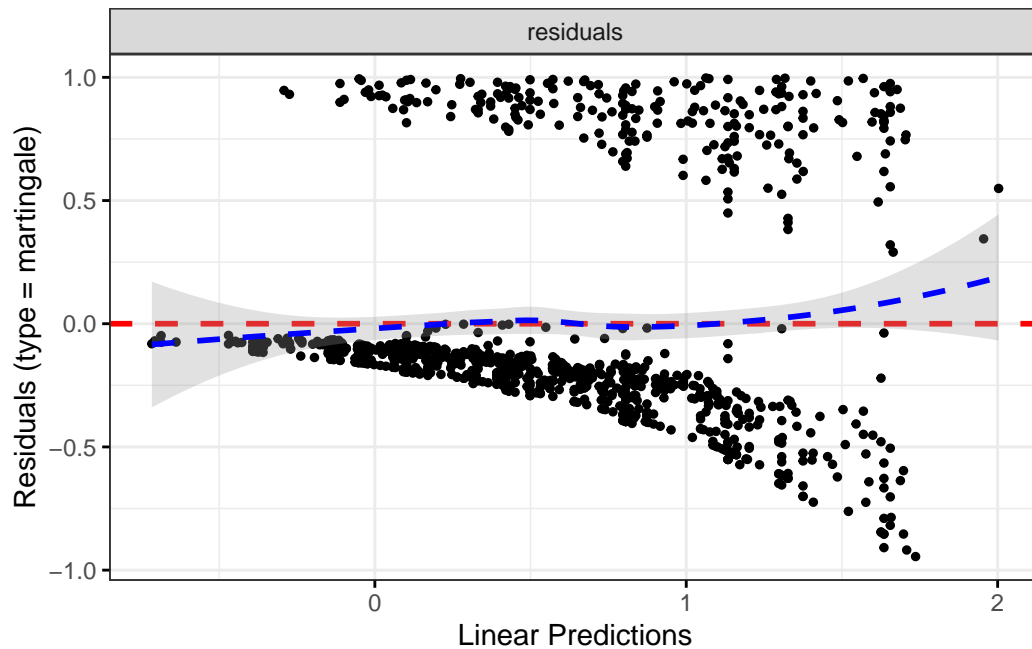
`geom_smooth()` using formula = 'y ~ x'



#####

Martingale residuals

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



Ulcerative colitis

Patient-reported flare

```
fit.me <- coxph(  
  Surv(softflare_time, softflare) ~  
    Sex + IMD + cat + Smoke + frailty(SiteNo),  
  control = coxph.control(outer.max = 20),  
  data = flare.uc.df  
)  
  
uc.clin.forest <- get_HR(  
  fit.me,  
  c("SmokePrevious", "SmokeNever")  
)
```

```

fit.me <- coxph(
  Surv(softflare_time, softflare) ~
    Sex + IMD + cat + frailty(SiteNo),
  control = coxph.control(outer.max = 20),
  data = flare.uc.df
)

uc.clin.forest <- rbind(
  uc.clin.forest,
  get_HR(
    fit.me,
    c(
      "SexFemale",
      paste0("IMD", seq(2, 5)),
      "catFC > 250"
    )
  )
)

invisible(cox_summary(fit.me))

```

Cox model summary:

Variable	HR	Lower 95%	Upper 95%	P-value
SexFemale	1.5438	1.2475	1.9104	0.0001
IMD2	1.2433	0.7856	1.9678	0.3525
IMD3	1.1010	0.7025	1.7255	0.6748
IMD4	1.4420	0.9388	2.2151	0.0946
IMD5	1.1988	0.7858	1.8290	0.4002
catFC 50-250	1.5688	1.2269	2.0058	0.0003
catFC > 250	2.1447	1.6433	2.7991	0.0000

Diagnostics:

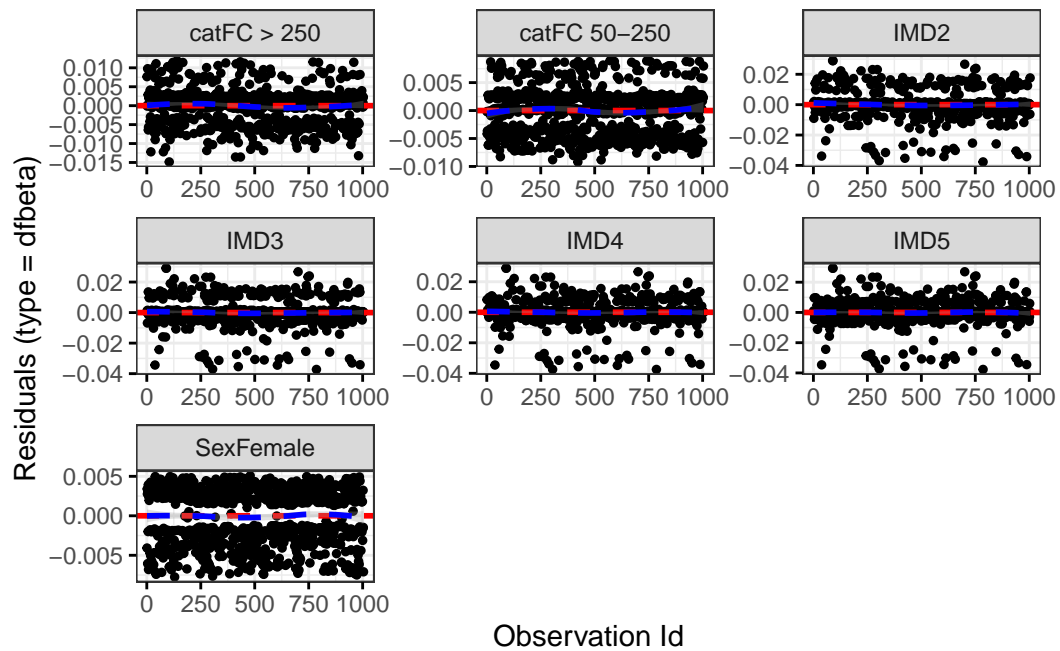
Proportional hazards assumption test

	Chi-squared statistic	DF	P-value
Sex	1.3013	0.9907	0.2514
IMD	4.0189	3.9418	0.3949

	Chi-squared statistic	DF	P-value
cat	5.7453	1.9706	0.0550
GLOBAL	11.3236	18.7016	0.9037

DF betas

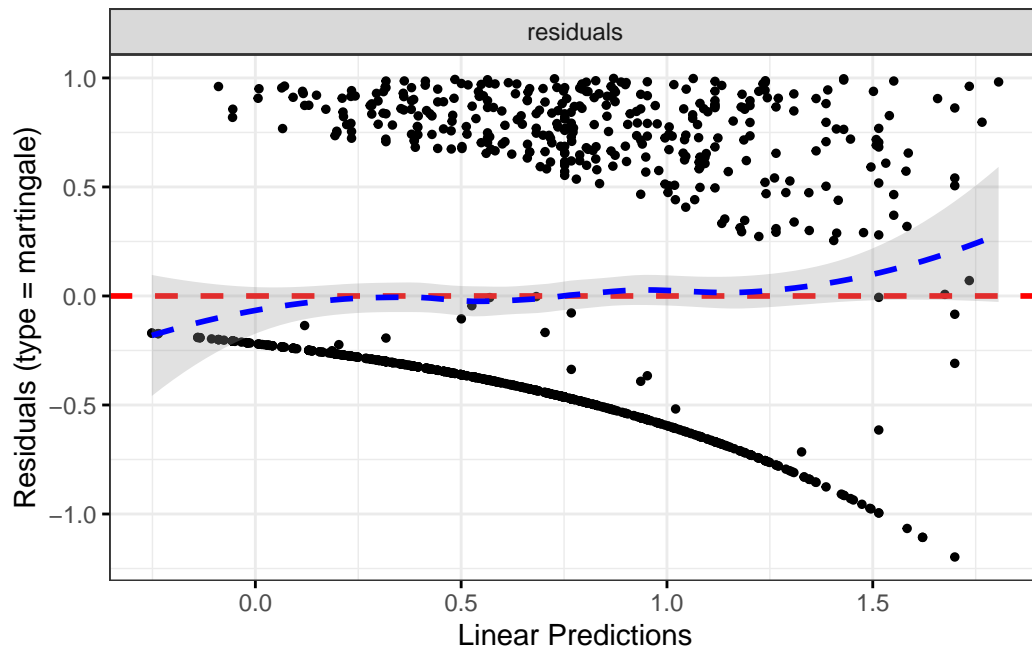
``geom_smooth()`` using formula = 'y ~ x'



#####

Martingale residuals

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



Hard flare

```
fit.me <- coxph(
  Surv(hardflare_time, hardflare) ~
    Sex + IMD + cat + frailty(SiteNo),
  control = coxph.control(outer.max = 20),
  data = flare.uc.df
)

uc.hard.forest <- get_HR(
  fit.me,
  c("SmokePrevious", "SmokeNever")
)

fit.me <- coxph(
  Surv(hardflare_time, hardflare) ~
    Sex + IMD + cat + frailty(SiteNo),
  control = coxph.control(outer.max = 20),
  data = flare.uc.df
)
```

```
uc.hard.forest <- rbind(
  uc.hard.forest,
  get_HR(
    fit.me,
    c(
      "SexFemale",
      paste0("IMD", seq(2, 5)),
      "catFC 50-250",
      "catFC > 250"
    )
  )
)

invisible(cox_summary(fit.me))
```

Cox model summary:

Variable	HR	Lower 95%	Upper 95%	P-value
SexFemale	1.3259	1.0208	1.7221	0.0345
IMD2	1.4092	0.7861	2.5260	0.2494
IMD3	1.3774	0.7835	2.4213	0.2659
IMD4	1.7484	1.0130	3.0174	0.0448
IMD5	1.2989	0.7566	2.2298	0.3430
catFC 50-250	2.0322	1.4885	2.7744	0.0000
catFC > 250	3.2203	2.3245	4.4614	0.0000

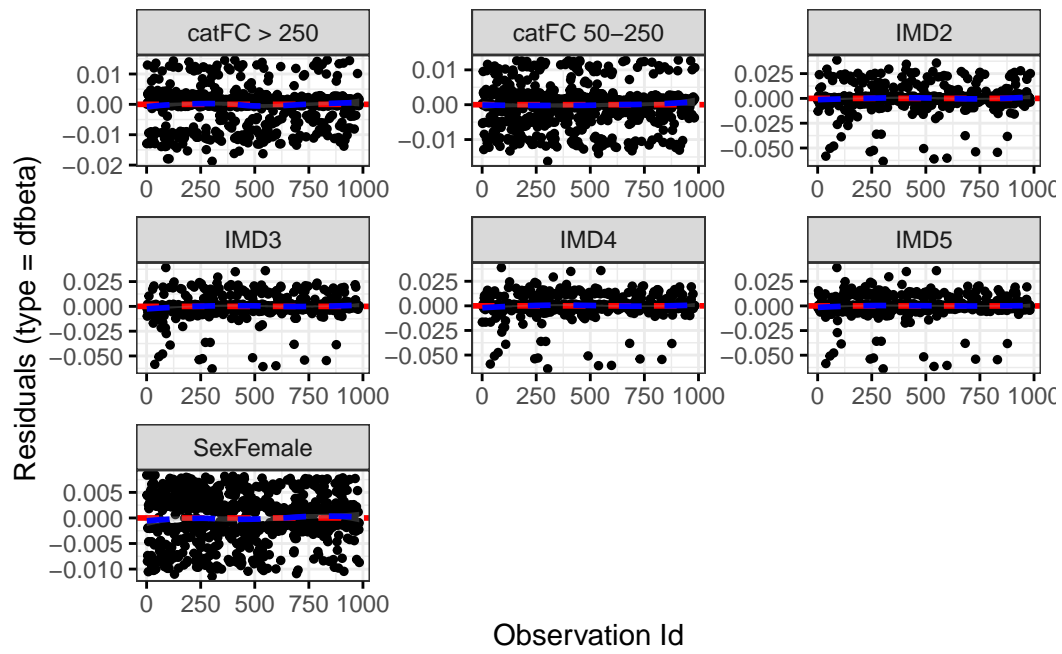
Diagnostics:

Proportional hazards assumption test

	Chi-squared statistic	DF	P-value
Sex	0.1461	0.9849	0.6962
IMD	2.6145	3.9368	0.6145
cat	4.3647	1.9671	0.1096
GLOBAL	7.4355	23.5846	0.9994

DF betas

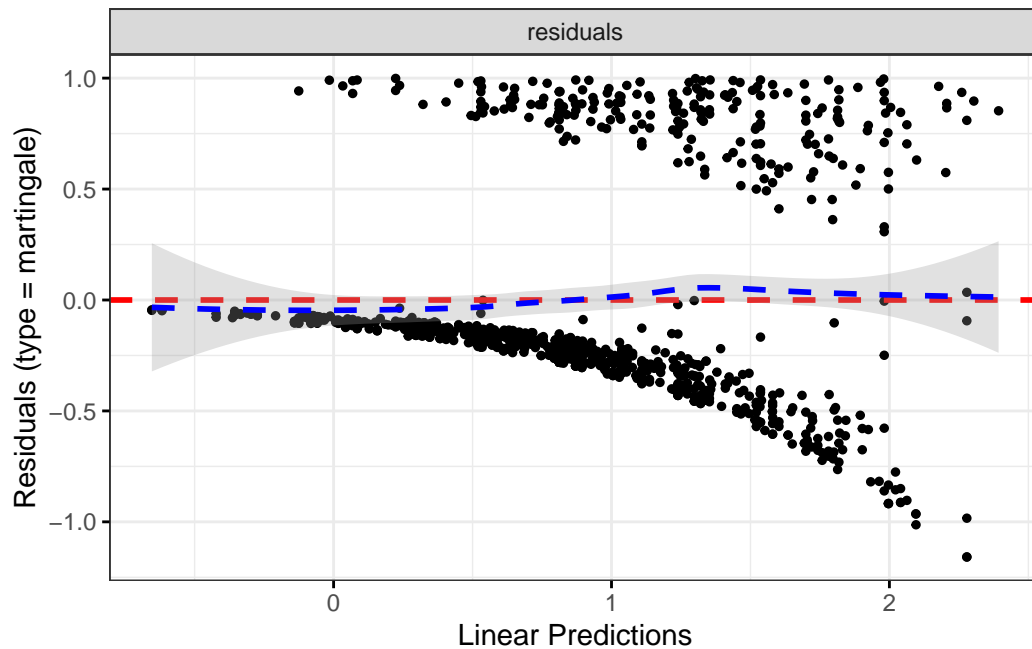
```
`geom_smooth()` using formula = 'y ~ x'
```



#####

Martingale residuals

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



Across IBD

Patient-reported flare

```
fit.me <- coxph(
  Surv(softflare_time, softflare) ~
    Sex + IMD + cat + frailty(SiteNo),
  control = coxph.control(outer.max = 20),
  data = flare.df
)

invisible(cox_summary(fit.me))
```

Cox model summary:

Variable	HR	Lower 95%	Upper 95%	P-value
SexFemale	1.7183	1.4676	2.0119	0.0000
IMD2	1.0417	0.7555	1.4364	0.8032
IMD3	0.9689	0.7027	1.3360	0.8474
IMD4	1.1549	0.8490	1.5712	0.3590
IMD5	1.0554	0.7814	1.4255	0.7252

Variable	HR	Lower 95%	Upper 95%	P-value
catFC 50-250	1.5194	1.2743	1.8117	0.0000
catFC > 250	2.2203	1.8303	2.6934	0.0000

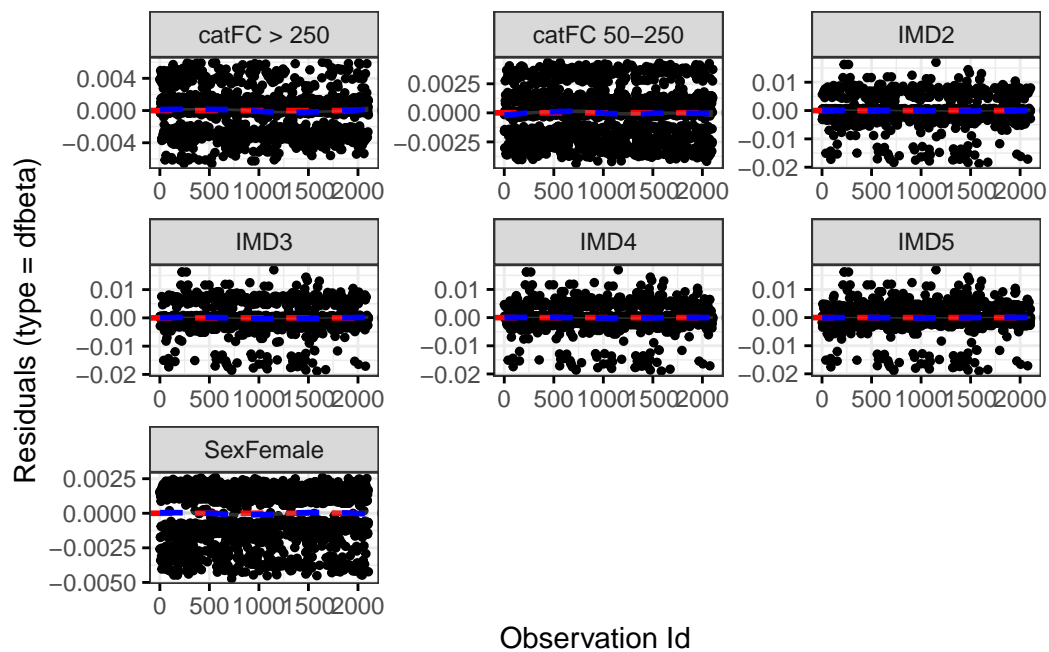
Diagnostics:

Proportional hazards assumption test

	Chi-squared statistic	DF	P-value
Sex	1.9368	0.9936	0.1627
IMD	8.9273	3.9484	0.0609
cat	1.1234	1.9824	0.5659
GLOBAL	12.1742	22.3691	0.9594

DF betas

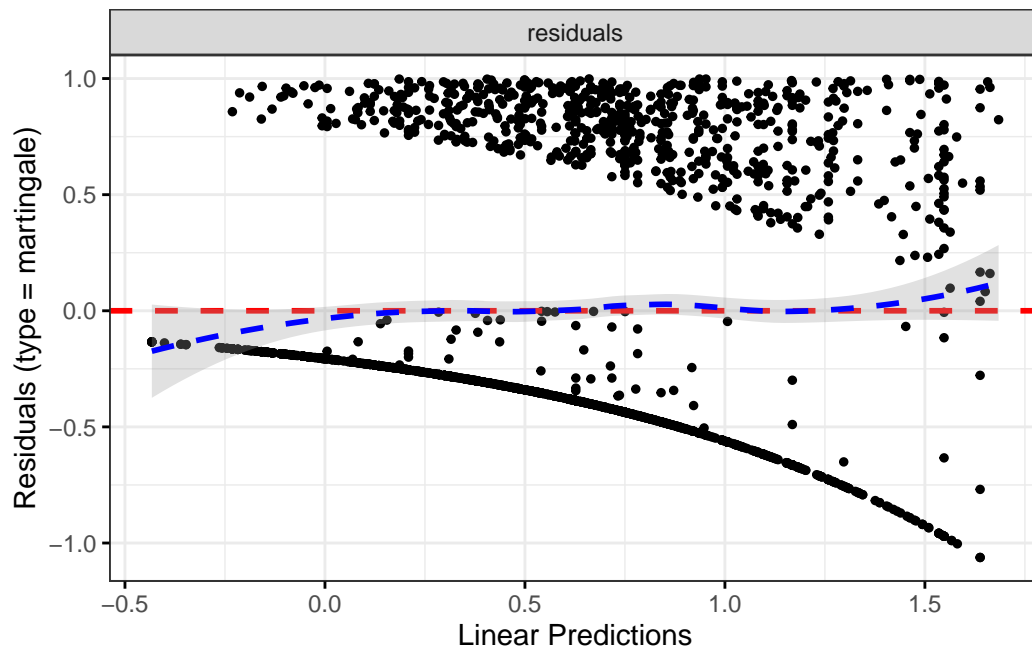
``geom_smooth()`` using formula = 'y ~ x'



#####

Martingale residuals

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



Hard flare

```
fit.me <- coxph(  
  Surv(hardflare_time, hardflare) ~  
    Sex + IMD + cat + frailty(SiteNo),  
  control = coxph.control(outer.max = 20),  
  data = flare.df  
)  
  
invisible(cox_summary(fit.me))
```

Cox model summary:

Variable	HR	Lower 95%	Upper 95%	P-value
SexFemale	1.3310	1.1037	1.6051	0.0028
IMD2	1.1029	0.7416	1.6402	0.6286
IMD3	1.1157	0.7525	1.6542	0.5858
IMD4	1.2392	0.8452	1.8169	0.2720
IMD5	1.0508	0.7220	1.5293	0.7959

Variable	HR	Lower 95%	Upper 95%	P-value
catFC 50-250	1.9760	1.5846	2.4641	0.0000
catFC > 250	3.2506	2.5702	4.1112	0.0000

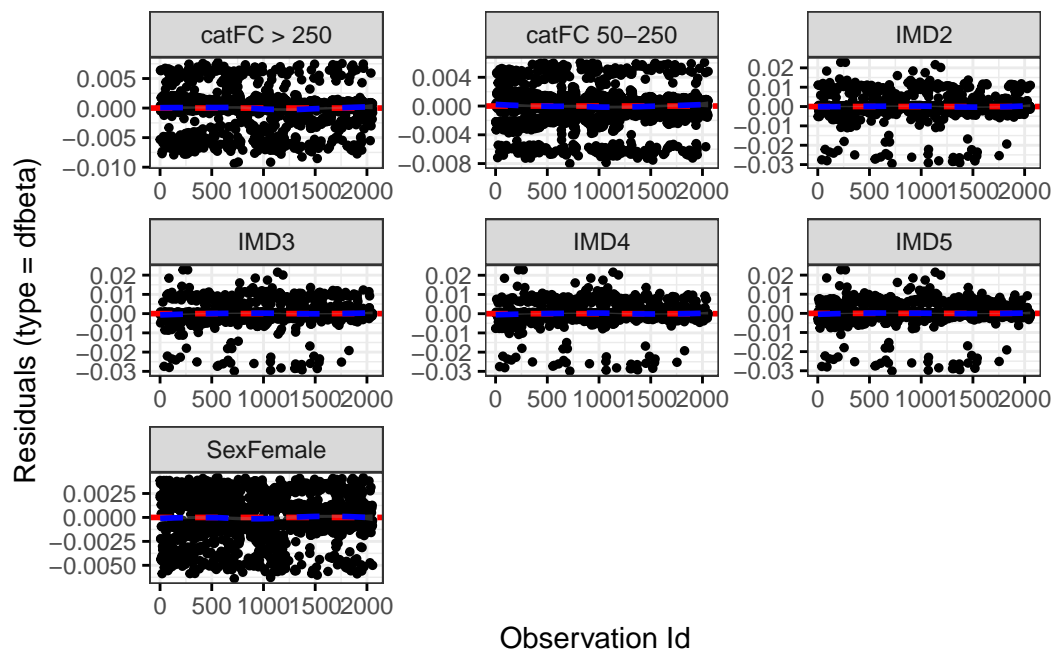
Diagnostics:

Proportional hazards assumption test

	Chi-squared statistic	DF	P-value
Sex	0.2285	0.9928	0.6297
IMD	0.8488	3.9546	0.9289
cat	8.4343	1.9867	0.0145
GLOBAL	9.9289	29.8504	0.9998

DF betas

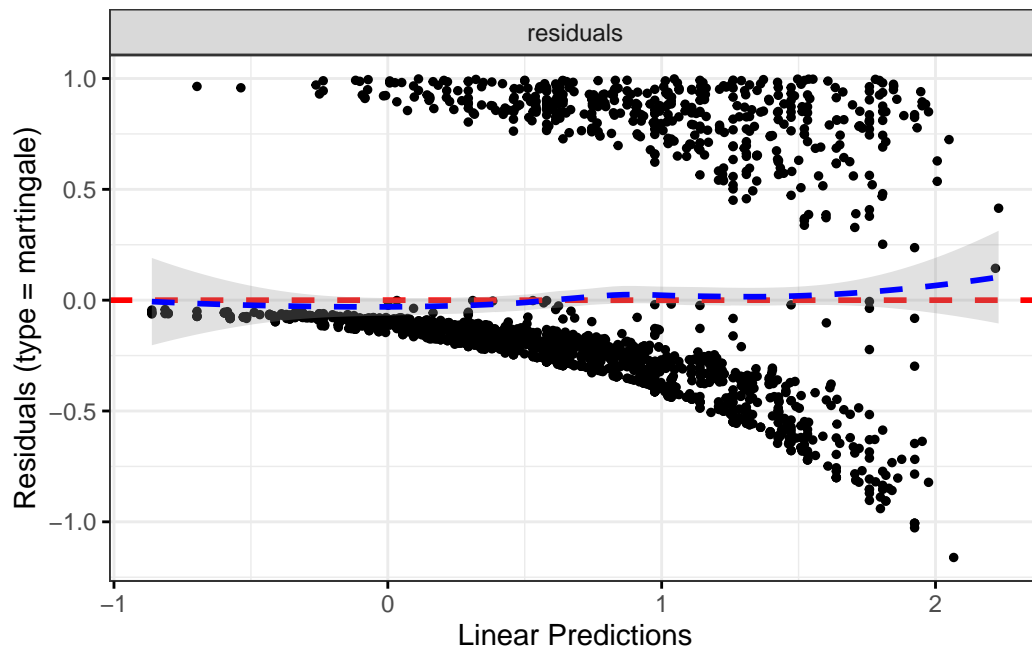
``geom_smooth()`` using formula = 'y ~ x'



#####

Martingale residuals

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



```
saveRDS(flare.df, paste0(paths$outdir, "flares-controlled.RDS"))
saveRDS(flare.cd.df, paste0(paths$outdir, "flares-controlled-cd.RDS"))
saveRDS(flare.uc.df, paste0(paths$outdir, "flares-controlled-uc.RDS"))

saveRDS(cd.clin.forest, paste0(paths$outdir, "cd-clin-controlled.RDS"))
saveRDS(cd.hard.forest, paste0(paths$outdir, "cd-hard-controlled.RDS"))
saveRDS(uc.clin.forest, paste0(paths$outdir, "uc-clin-controlled.RDS"))
saveRDS(uc.hard.forest, paste0(paths$outdir, "uc-hard-controlled.RDS"))
```

Reproduction and reproducibility

Session info

R version 4.4.0 (2024-04-24)

Platform: aarch64-unknown-linux-gnu

locale: LC_CTYPE=en_US.UTF-8, LC_NUMERIC=C, LC_TIME=en_US.UTF-8, LC_COLLATE=en_US.UTF-8, LC_MONETARY=en_US.UTF-8, LC_MESSAGES=en_US.UTF-8, LC_PAPER=en_US.UTF-8, LC_NAME=C, LC_ADDRESS=C, LC_TELEPHONE=C, LC_MEASUREMENT=en_US.UTF-8 and LC_IDENTIFICATION=C

attached base packages: *stats*, *graphics*, *grDevices*, *utils*, *datasets*, *methods* and *base*

other attached packages: *gtsummary*(v.1.7.2), *DescTools*(v.0.99.54), *finalfit*(v.1.0.7), *corme*(v.2.2-20), *bdsmatrix*(v.1.3-7), *pander*(v.0.6.5), *survminer*(v.0.4.9), *ggpubr*(v.0.6.0), *survival*(v.3.5-8), *datefixR*(v.1.6.1), *lubridate*(v.1.9.3), *forcats*(v.1.0.0), *stringr*(v.1.5.1), *dplyr*(v.1.1.4), *purrr*(v.1.0.2), *readr*(v.2.1.5), *tidyr*(v.1.3.1), *tibble*(v.3.2.1), *ggplot2*(v.3.5.1), *tidyverse*(v.2.0.0) and *readxl*(v.1.4.3)

loaded via a namespace (and not attached): *gridExtra*(v.2.3), *gld*(v.2.6.6), *rlang*(v.1.1.3), *magrittr*(v.2.0.3), *e1071*(v.1.7-14), *compiler*(v.4.4.0), *mgcv*(v.1.9-1), *vc-
trs*(v.0.6.5), *pkgconfig*(v.2.0.3), *shape*(v.1.4.6.1), *fastmap*(v.1.2.0), *backports*(v.1.5.0), *labeling*(v.0.4.3), *KMsurv*(v.0.1-5), *utf8*(v.1.2.4), *rmarkdown*(v.2.27), *markdown*(v.1.12), *tzdb*(v.0.4.0), *nloptr*(v.2.0.3), *xfun*(v.0.44), *glmnet*(v.4.1-8), *jomo*(v.2.7-6), *jsonlite*(v.1.8.8), *pan*(v.1.9), *broom*(v.1.0.6), *R6*(v.2.5.1), *stringi*(v.1.8.4), *car*(v.3.1-2), *boot*(v.1.3-30), *rpart*(v.4.1.23), *cellranger*(v.1.1.0), *Rcpp*(v.1.0.12), *iterators*(v.1.0.14), *knitr*(v.1.47), *zoo*(v.1.8-12), *Matrix*(v.1.7-0), *splines*(v.4.4.0), *nnet*(v.7.3-19), *timechange*(v.0.3.0), *tidyselect*(v.1.2.1), *rstudioapi*(v.0.16.0), *abind*(v.1.4-5), *yaml*(v.2.3.8), *ggtext*(v.0.1.2), *codetools*(v.0.2-20), *lattice*(v.0.22-6), *withr*(v.3.0.0), *evaluate*(v.0.23), *proxy*(v.0.4-27), *xml2*(v.1.3.6), *survMisc*(v.0.5.6), *pillar*(v.1.9.0), *carData*(v.3.0-5), *mice*(v.3.16.0), *foreach*(v.1.5.2), *generics*(v.0.1.3), *hms*(v.1.1.3), *commonmark*(v.1.9.1), *munsell*(v.0.5.1), *scales*(v.1.3.0), *rootSolve*(v.1.8.2.4), *minqa*(v.1.2.7), *xtable*(v.1.8-4), *class*(v.7.3-22), *glue*(v.1.7.0), *lmom*(v.3.0), *tools*(v.4.4.0), *data.table*(v.1.15.4), *lme4*(v.1.1-35.3), *ggsig-
nif*(v.0.6.4), *Exact*(v.3.2), *mvtnorm*(v.1.2-5), *grid*(v.4.4.0), *colorspace*(v.2.1-0), *nlme*(v.3.1-
164), *cli*(v.3.6.2), *km.ci*(v.0.5-6), *fansi*(v.1.0.6), *expm*(v.0.999-9), *broom.helpers*(v.1.15.0), *gt*(v.0.10.1), *gtable*(v.0.3.5), *rstatix*(v.0.7.2), *digest*(v.0.6.35), *farver*(v.2.1.2), *html-
tools*(v.0.5.8.1), *lifecycle*(v.1.0.4), *httr*(v.1.4.7), *mitml*(v.0.4-5), *gridtext*(v.0.1.5) and *MASS*(v.7.3-60.2)

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