

Controlled variables

Nathan Constantine-Cooke

2025-08-13

Table of contents

| | |
|----------------------------------|----|
| Introduction | 2 |
| Sex | 3 |
| Crohn's disease | 3 |
| Patient-reported flare | 3 |
| Hard flare | 4 |
| Ulcerative colitis | 5 |
| Patient-reported flare | 5 |
| Hard flare | 7 |
| Smoking status | 9 |
| Crohn's disease | 9 |
| Patient-reported flare | 9 |
| Hard flare | 10 |
| Ulcerative colitis | 11 |
| Patient-reported flare | 11 |
| Social deprivation | 15 |
| Crohn's disease | 15 |
| Patient-reported flare | 15 |
| Hard flare | 16 |
| Ulcerative colitis | 18 |
| Patient-reported flare | 18 |
| Hard flare | 20 |
| Faecal calprotectin | 23 |
| Crohn's disease | 23 |
| Patient-reported flare | 23 |
| Hard flare | 24 |
| Ulcerative colitis | 26 |
| Patient-reported flare | 26 |
| Hard flare | 27 |

| | |
|--|----|
| Cox models | 29 |
| Crohn's disease | 29 |
| Patient-reported flare | 29 |
| Proportional hazards assumption test | 30 |
| DF betas | 30 |
| Hard flare | 32 |
| Proportional hazards assumption test | 33 |
| DF betas | 33 |
| Ulcerative colitis | 34 |
| Patient-reported flare | 34 |
| Proportional hazards assumption test | 35 |
| DF betas | 36 |
| Hard flare | 37 |
| Proportional hazards assumption test | 38 |
| DF betas | 38 |
| Across IBD | 40 |
| Patient-reported flare | 40 |
| Proportional hazards assumption test | 41 |
| DF betas | 41 |
| Hard flare | 42 |
| Proportional hazards assumption test | 43 |
| DF betas | 43 |
| Reproduction and reproducibility | 44 |

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.

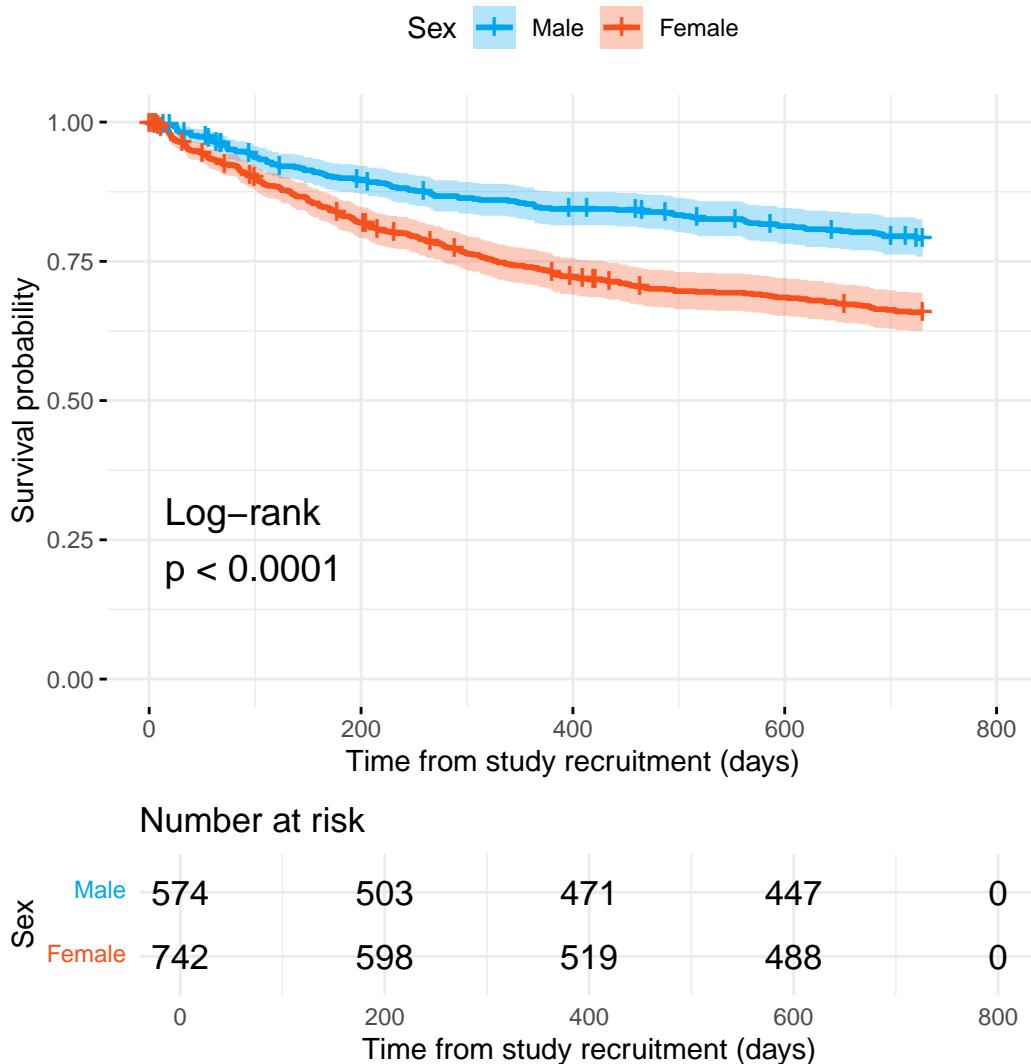
Sex

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



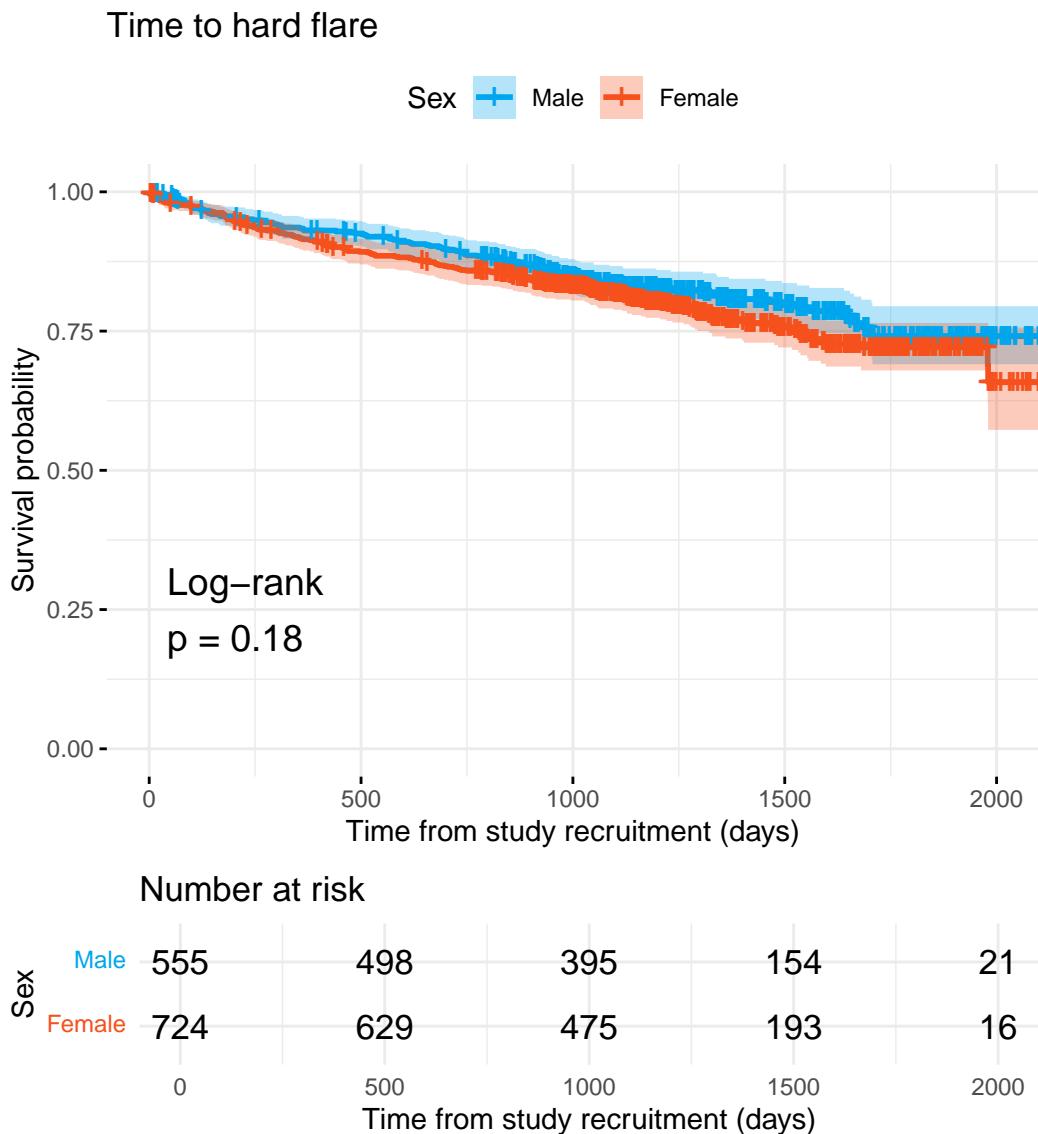
Hard flare

```
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"
)

```

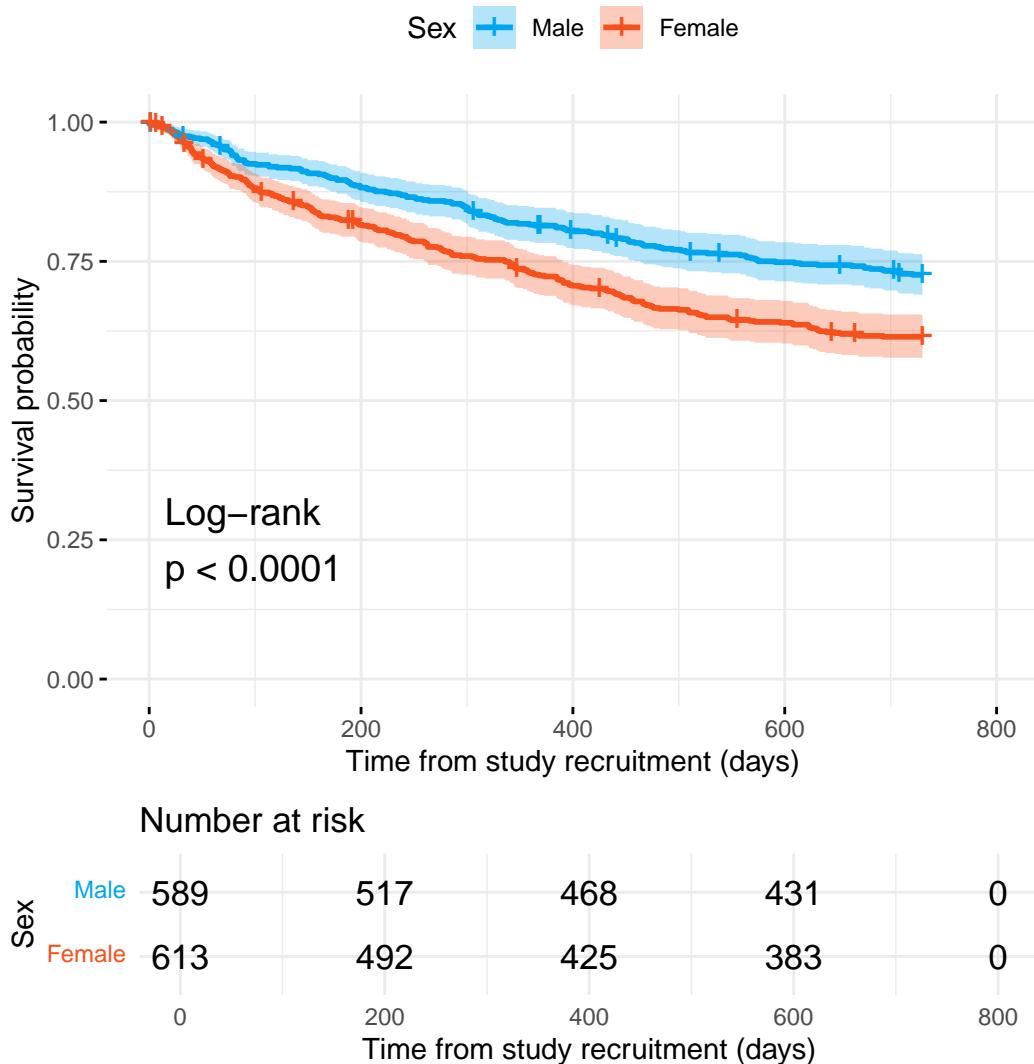


Ulcerative colitis

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"
)
```

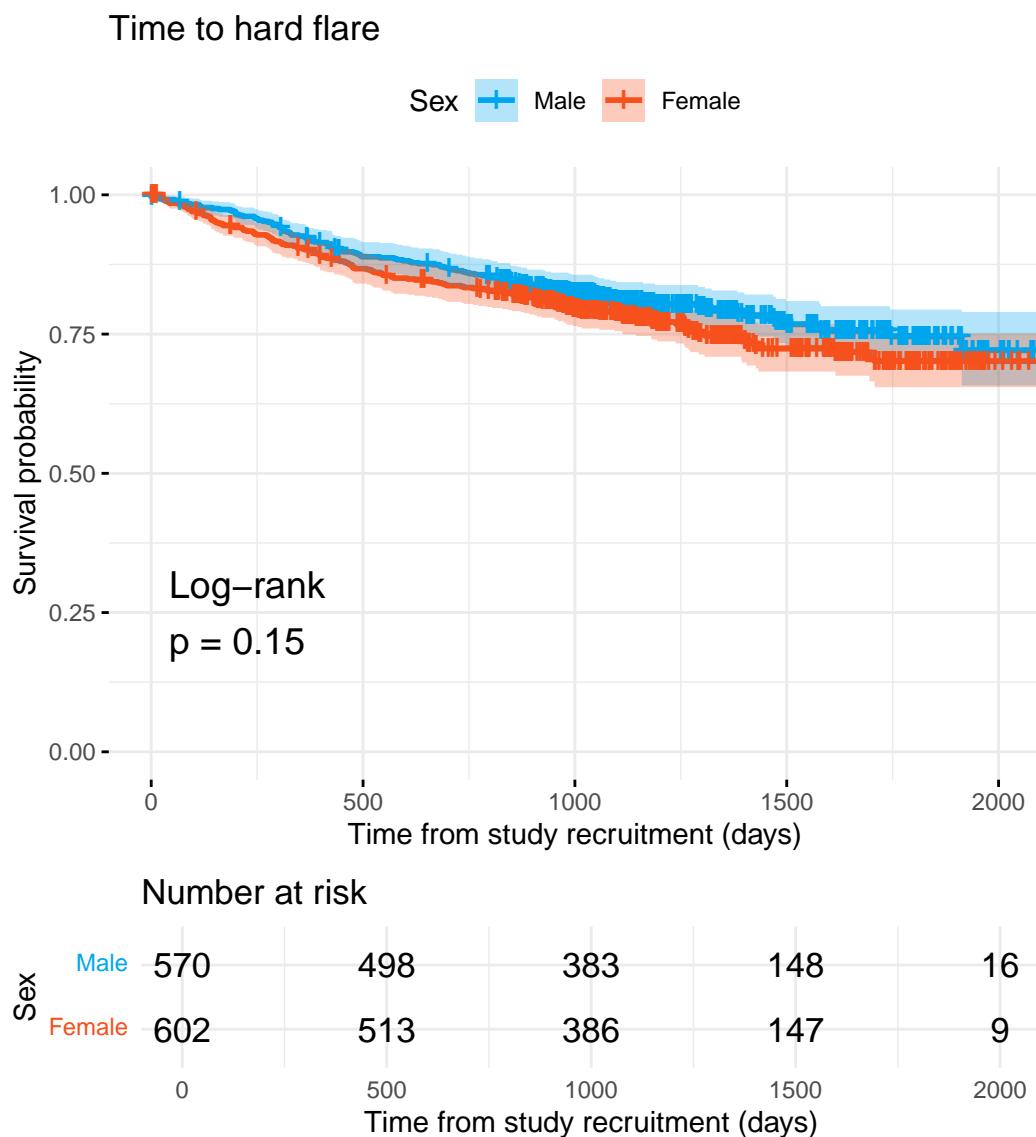
Time to clinical flare



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"
)
```



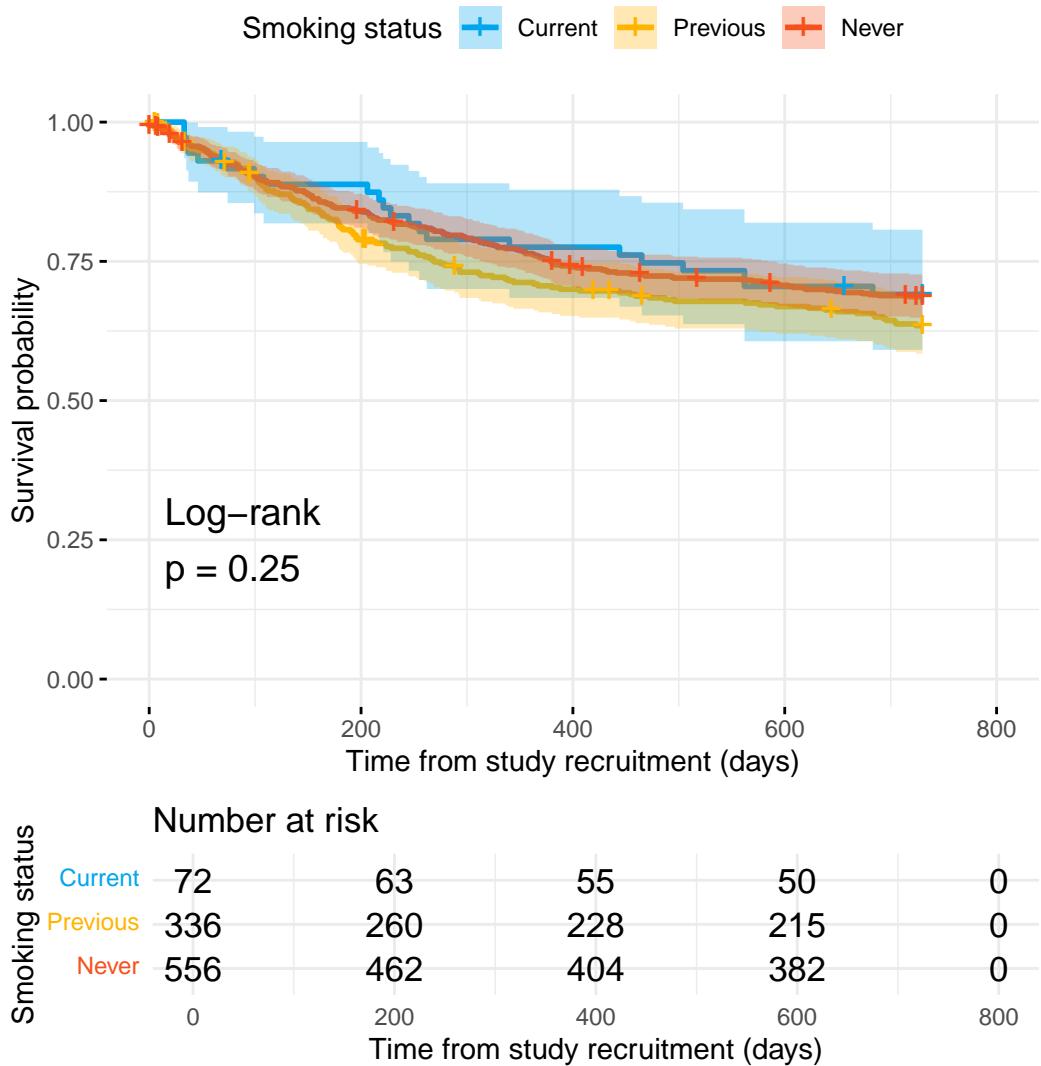
Smoking status

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



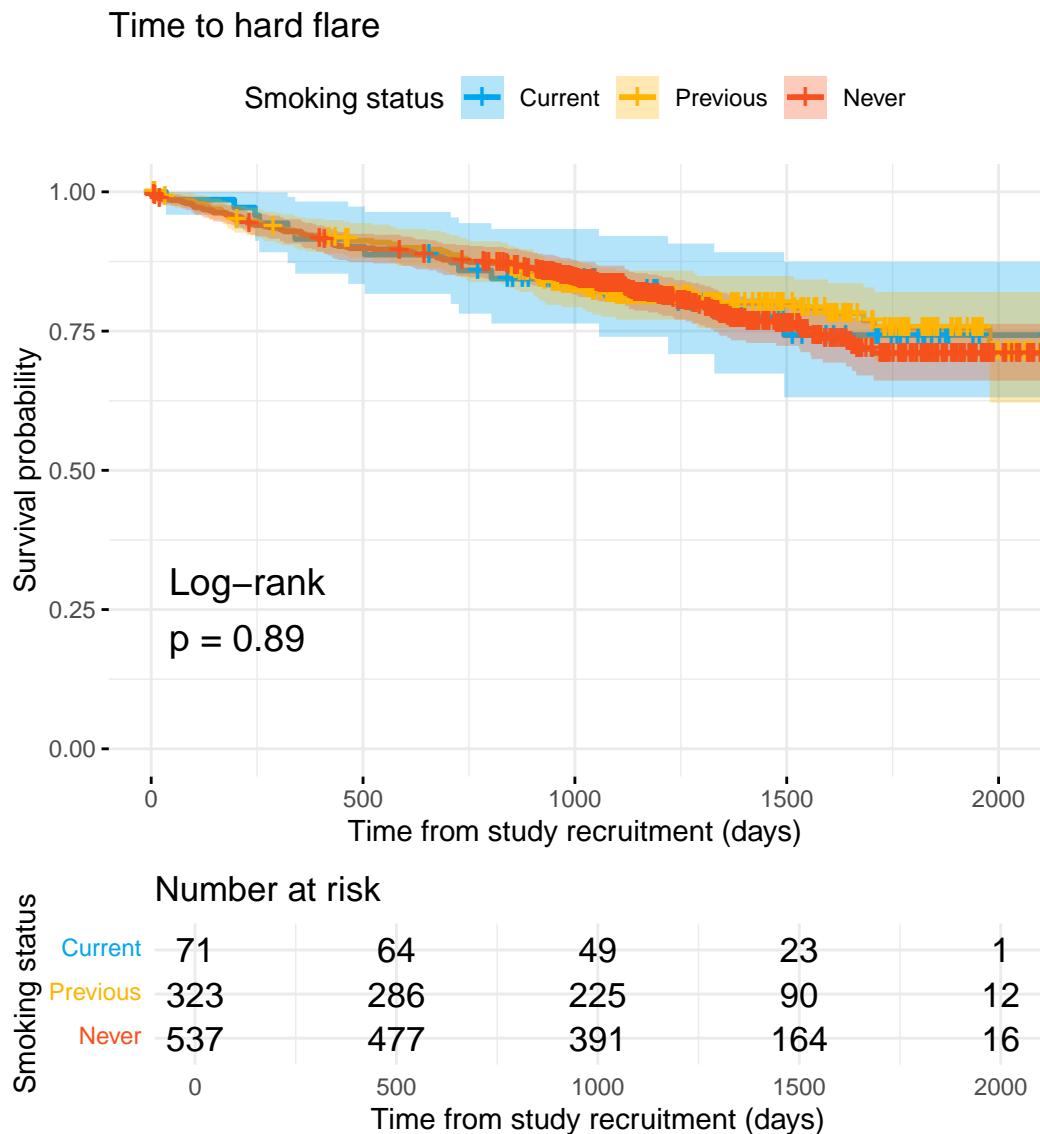
Hard flare

```
generate_survival_plot(
  data = flare.cd.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/cd/hard-flare/controlled/smoke"
)

```

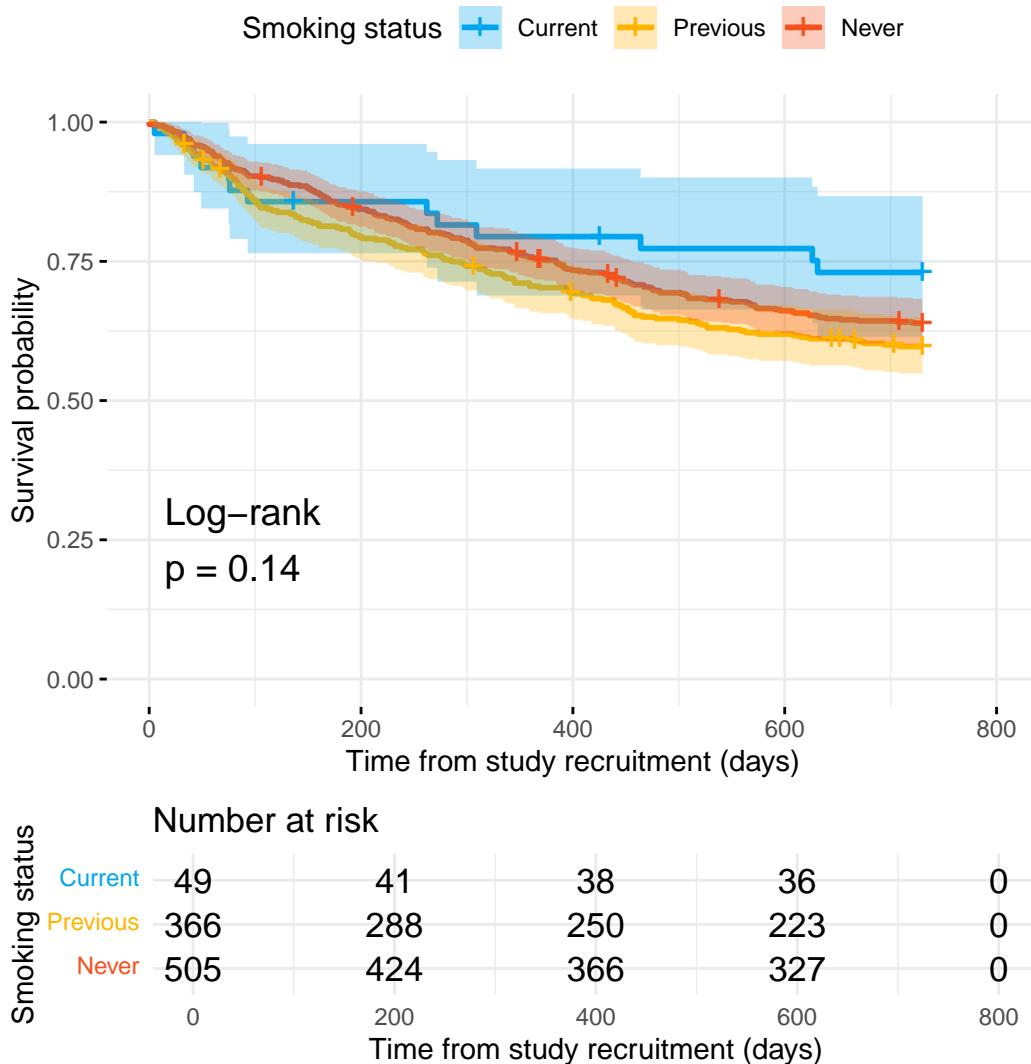


Ulcerative colitis

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



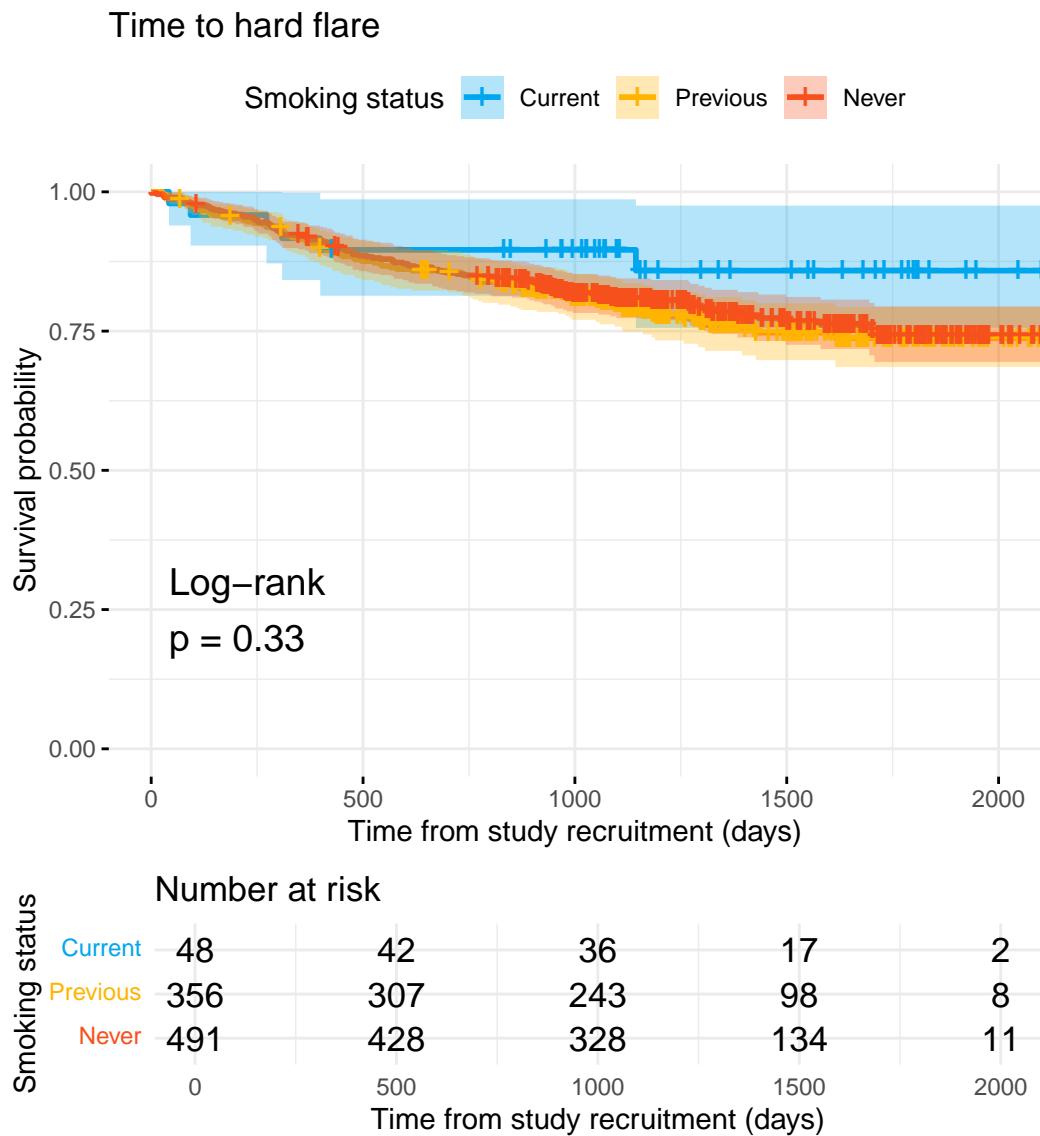
```
#### Hard flare
```

```
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"
)

```



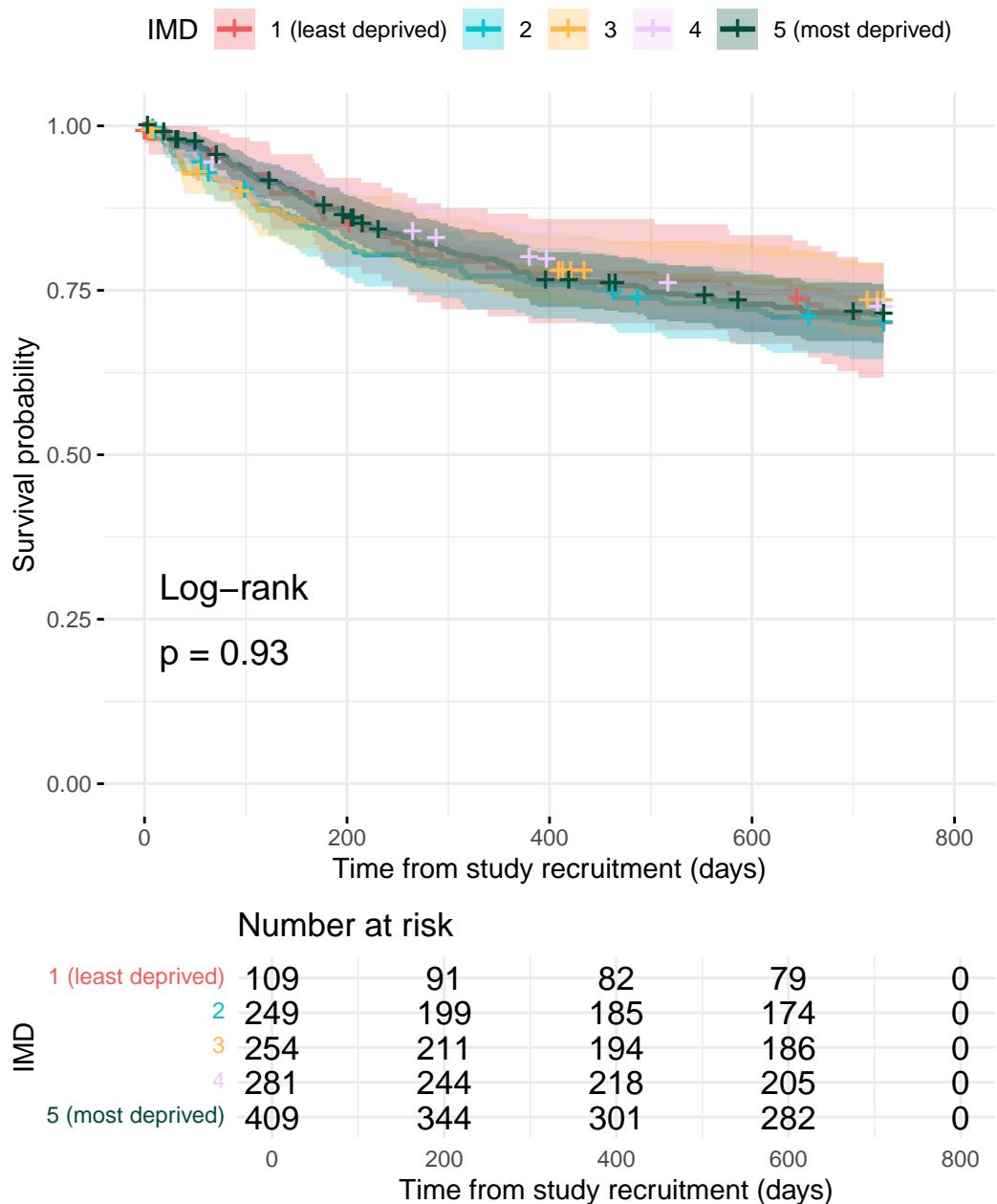
Social deprivation

Crohn's disease

Patient-reported flare

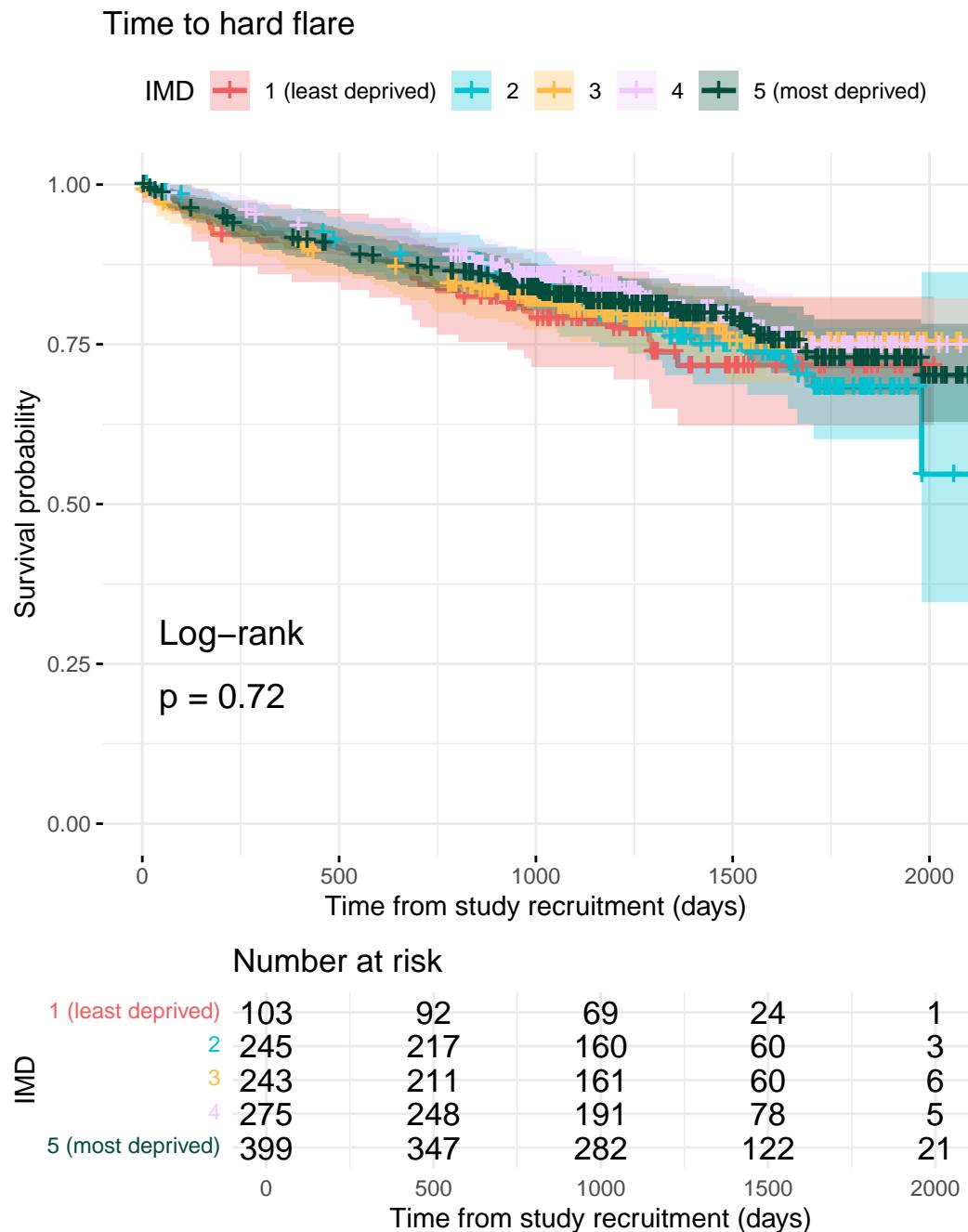
```
generate_survival_plot(
  data = flare.cd.df,
  formula = Surv(softflare_time, softflare) ~ IMD,
  legend_title = "IMD",
  legend_labs = c("1 (least deprived)", "2", "3", "4", "5 (most deprived)"),
  palette = c("#F05D5E", "#00C2D1", "#FFBA49", "#EDC9FF", "#034C3C"),
  xlab = "Time from study recruitment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

Time to clinical flare



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"
)
```

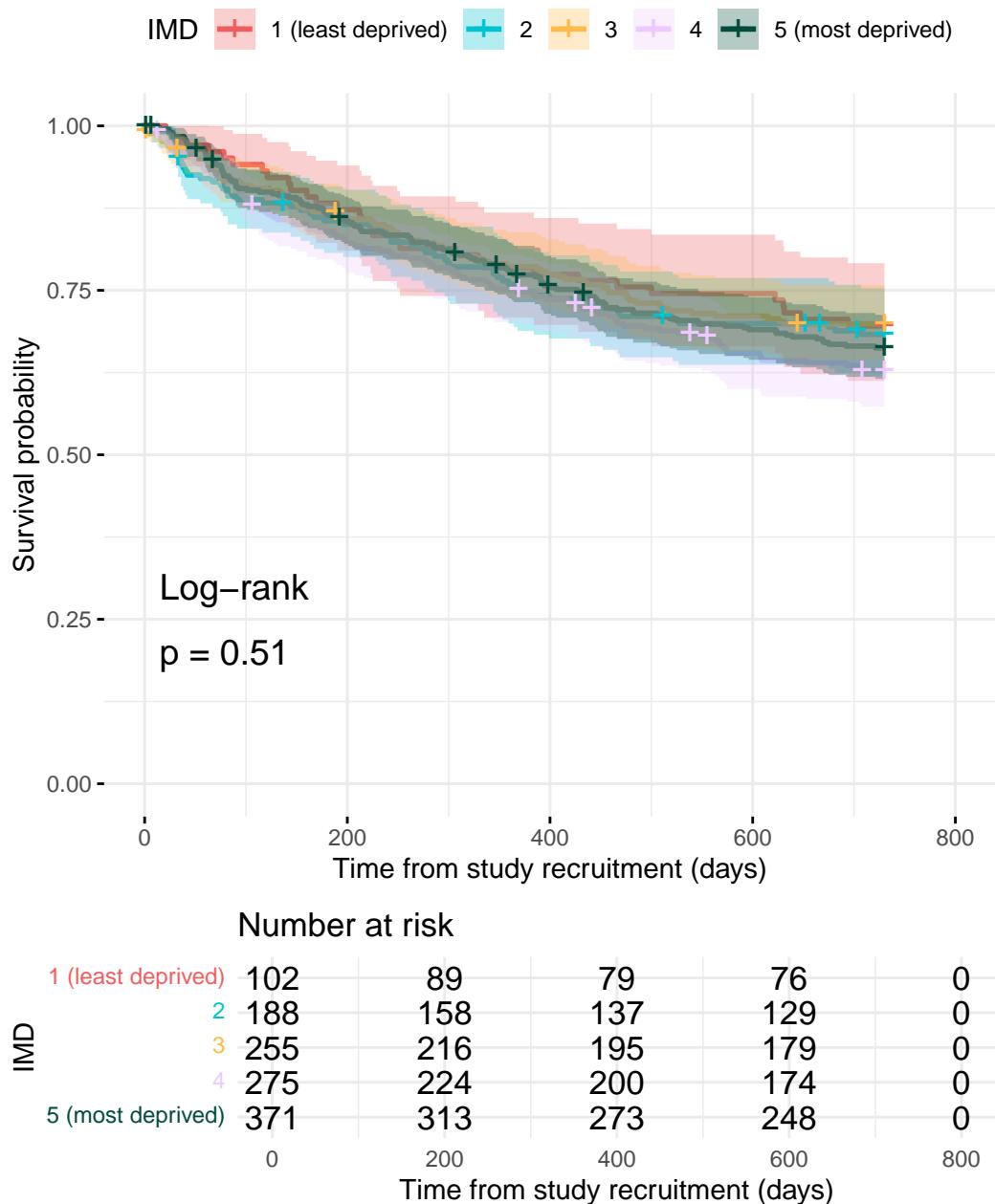


Ulcerative colitis

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"
)
```

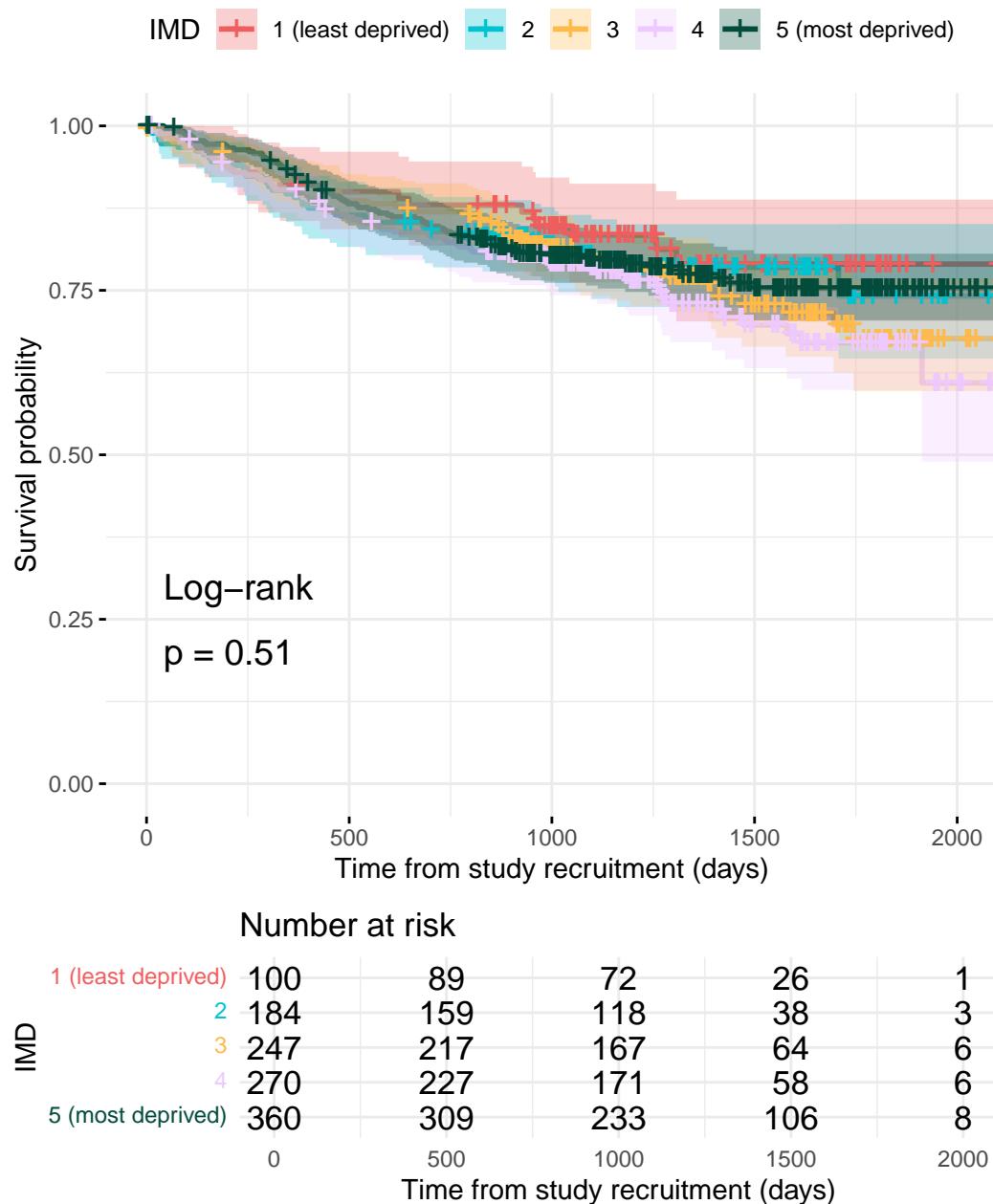
Time to clinical flare



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



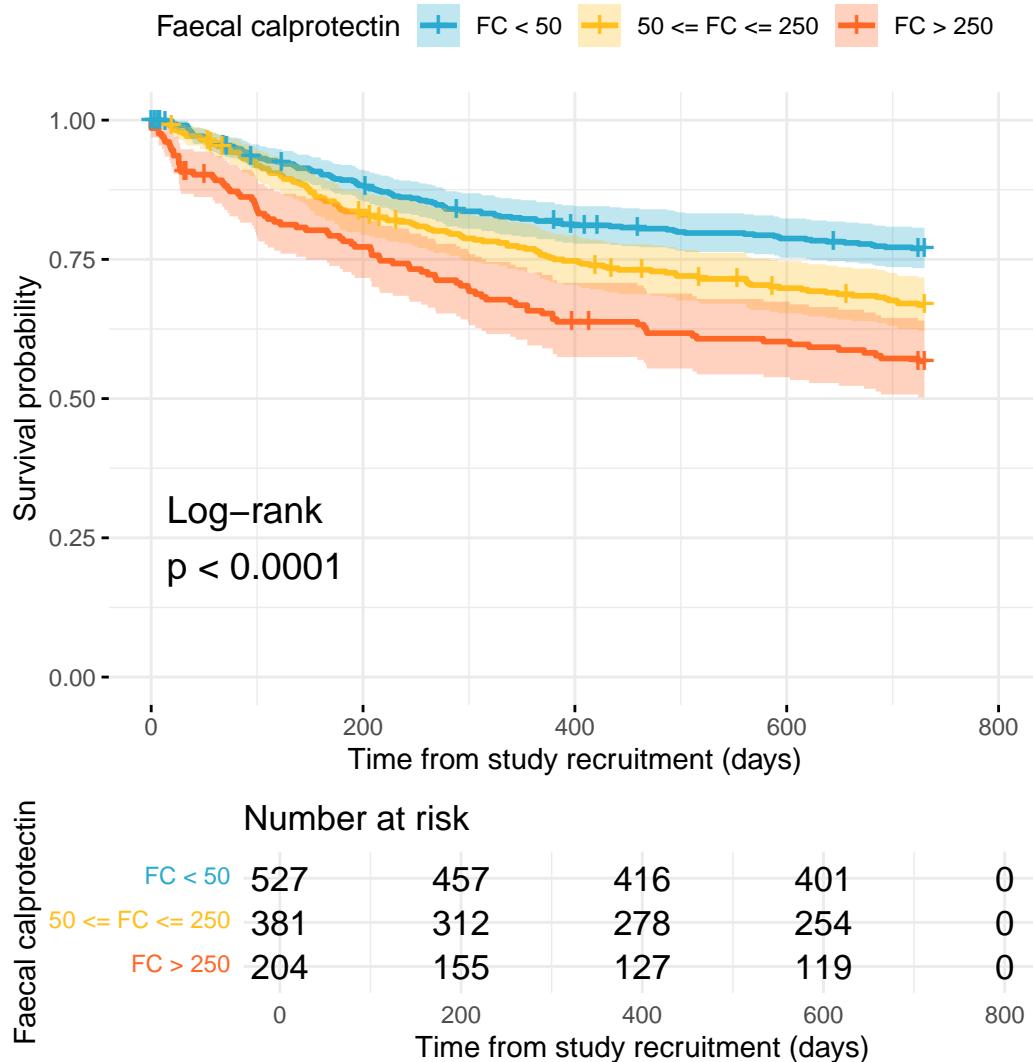
Faecal calprotectin

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



Hard flare

```
p <- generate_survival_plot(
  data = flare.cd.df,
  formula = Surv(hardflare_time, hardflare) ~ 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)",
```

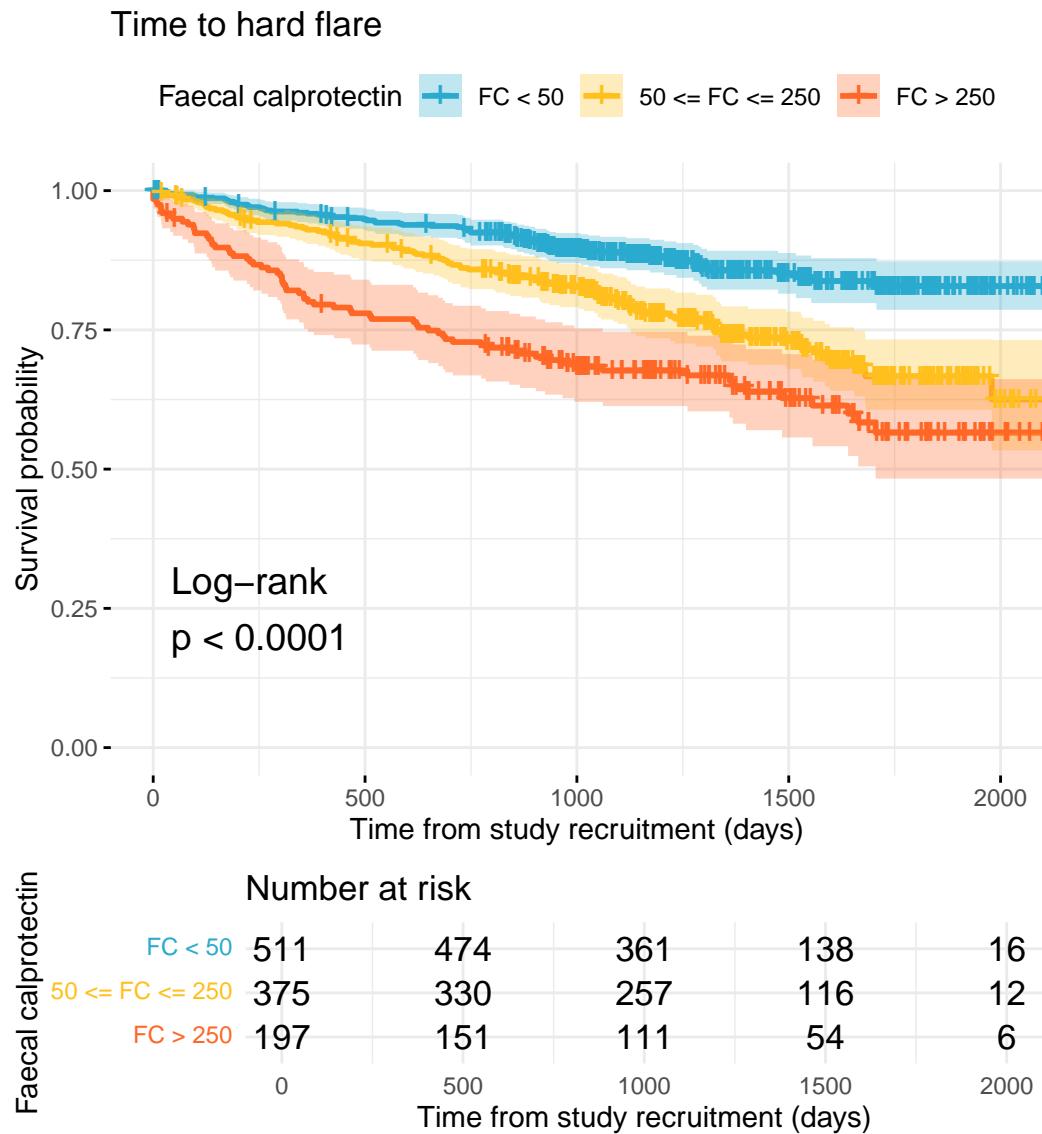
```

    title = "Time to 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)

```

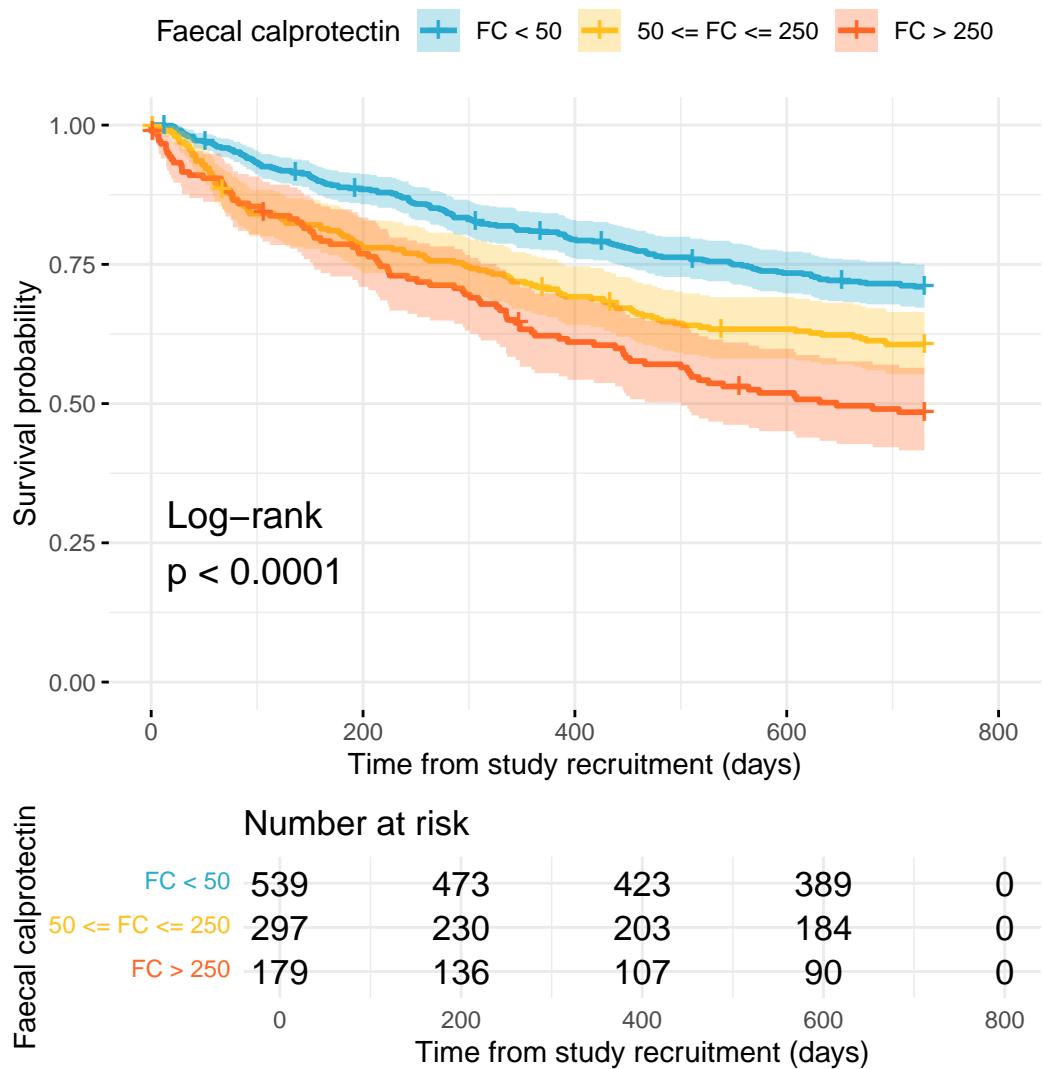


Ulcerative colitis

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



Hard flare

```
p <- generate_survival_plot(
  data = flare.uc.df,
  formula = Surv(hardflare_time, hardflare) ~ 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)",
```

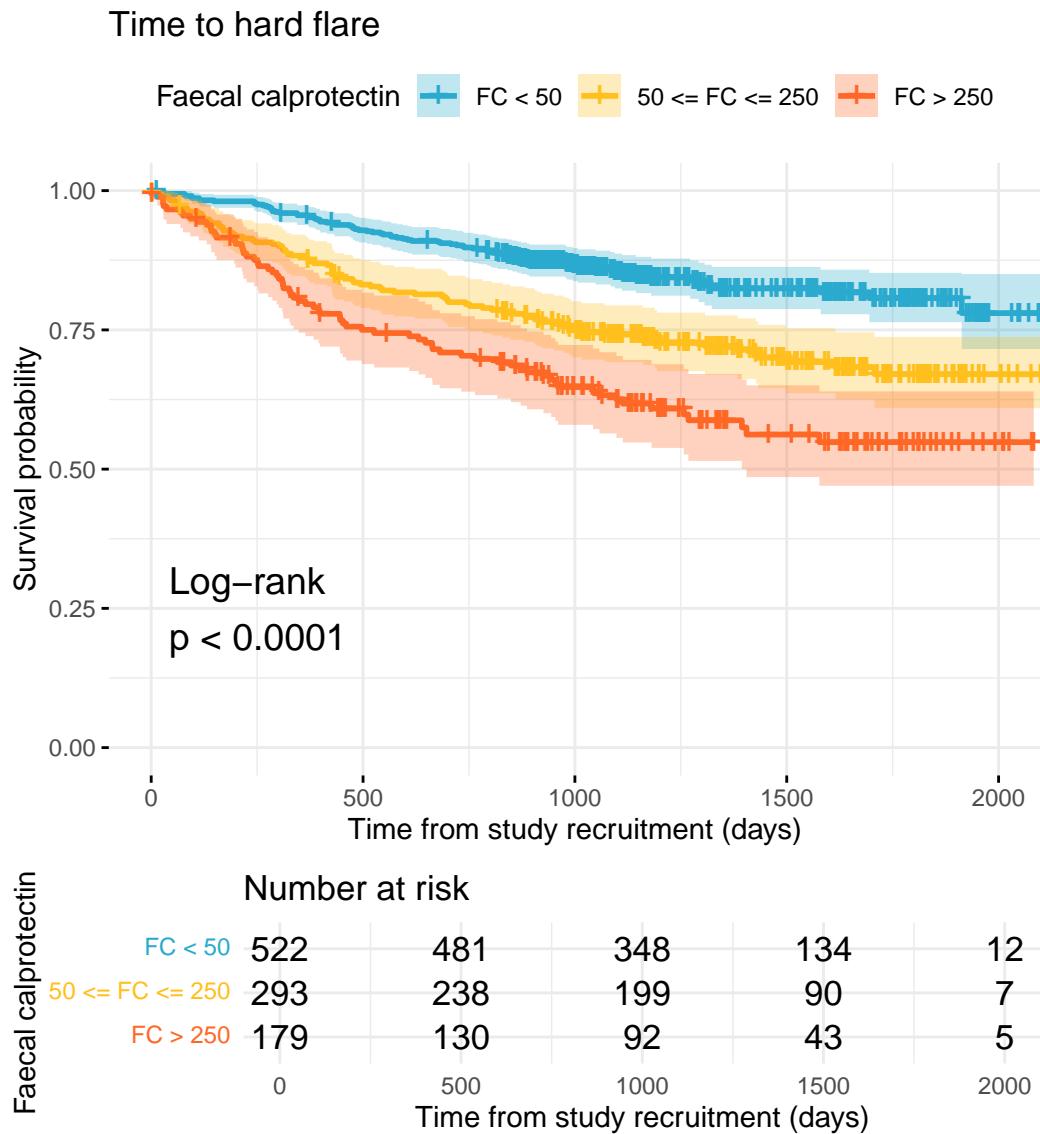
```

    title = "Time to 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:

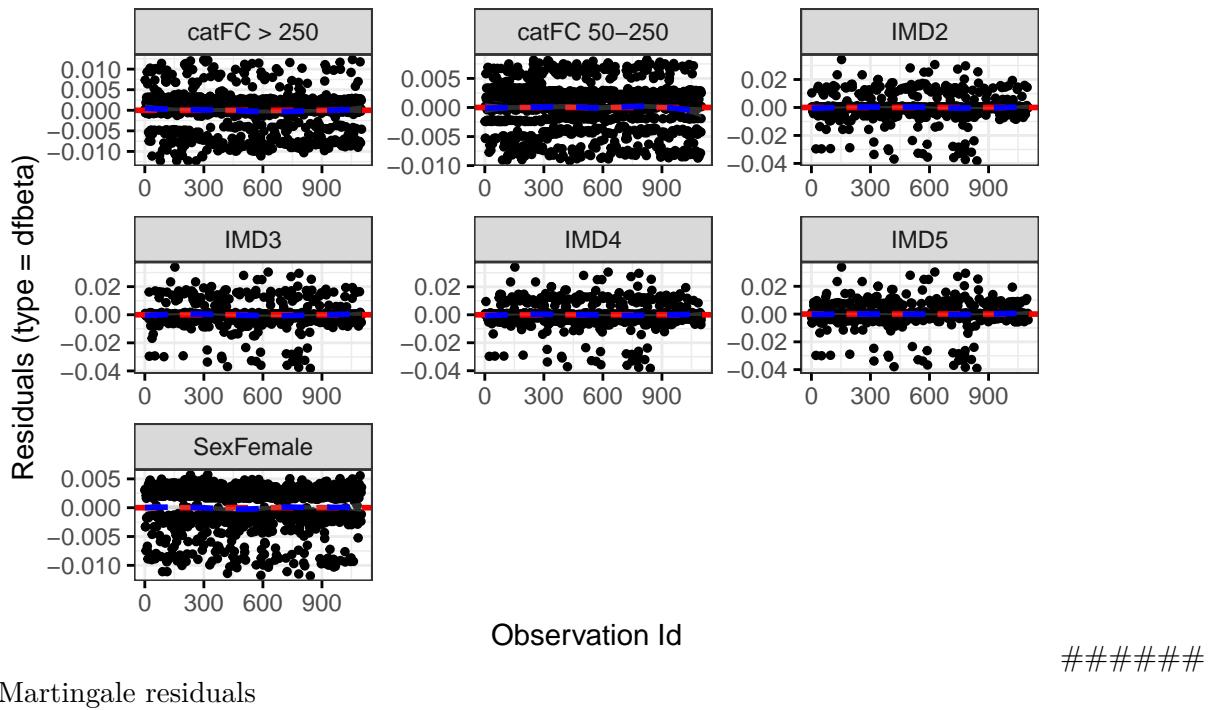
Proportional hazards assumption test

| | 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 |

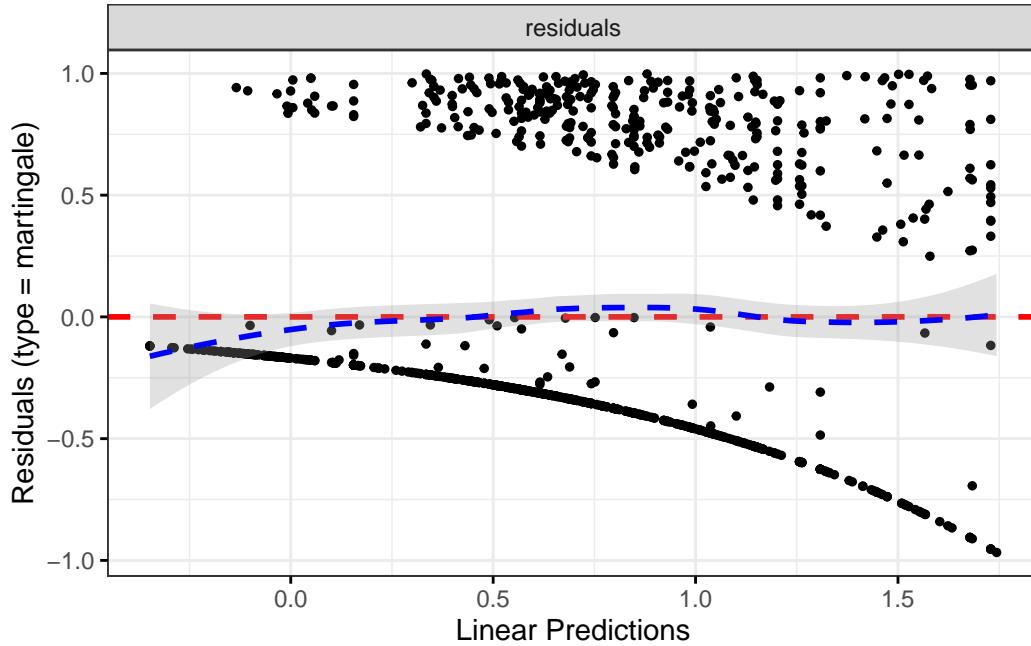
DF betas

```
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'
```



```
`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 |

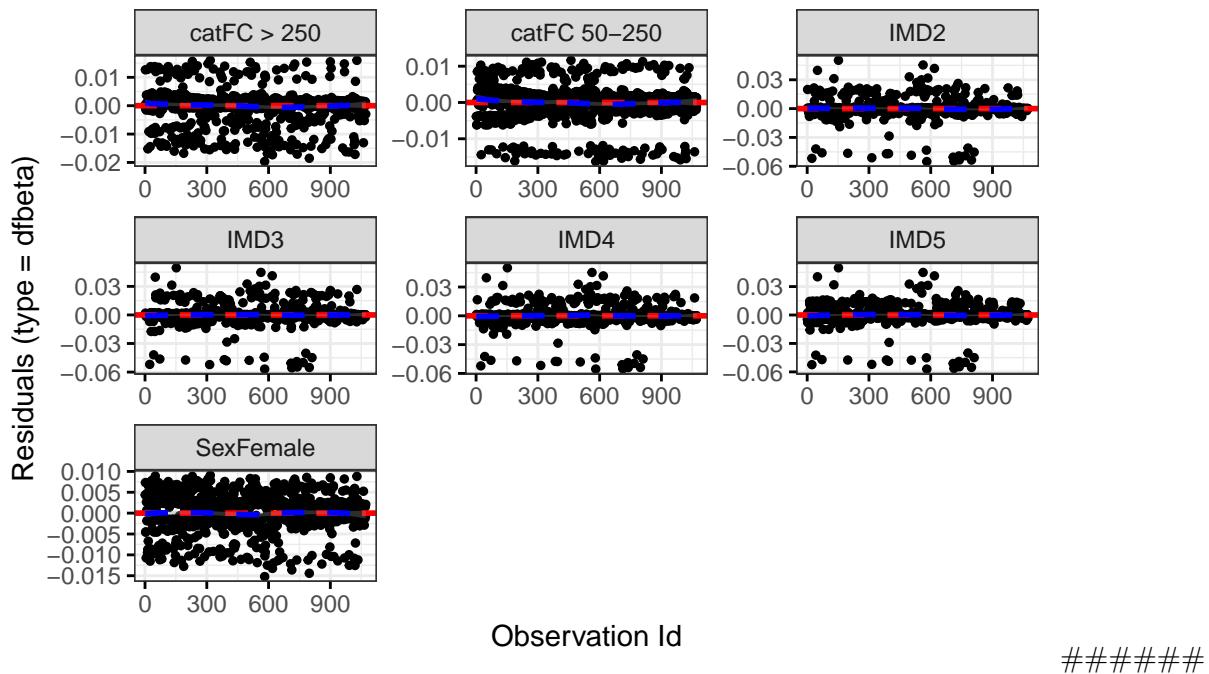
Diagnostics:

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 |

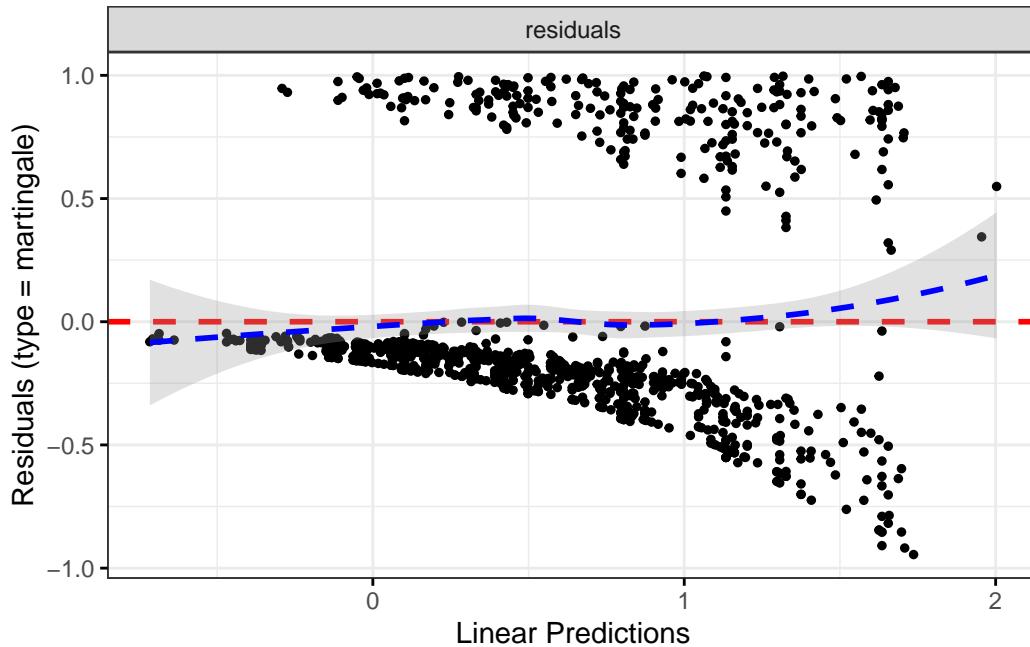
DF betas

`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:

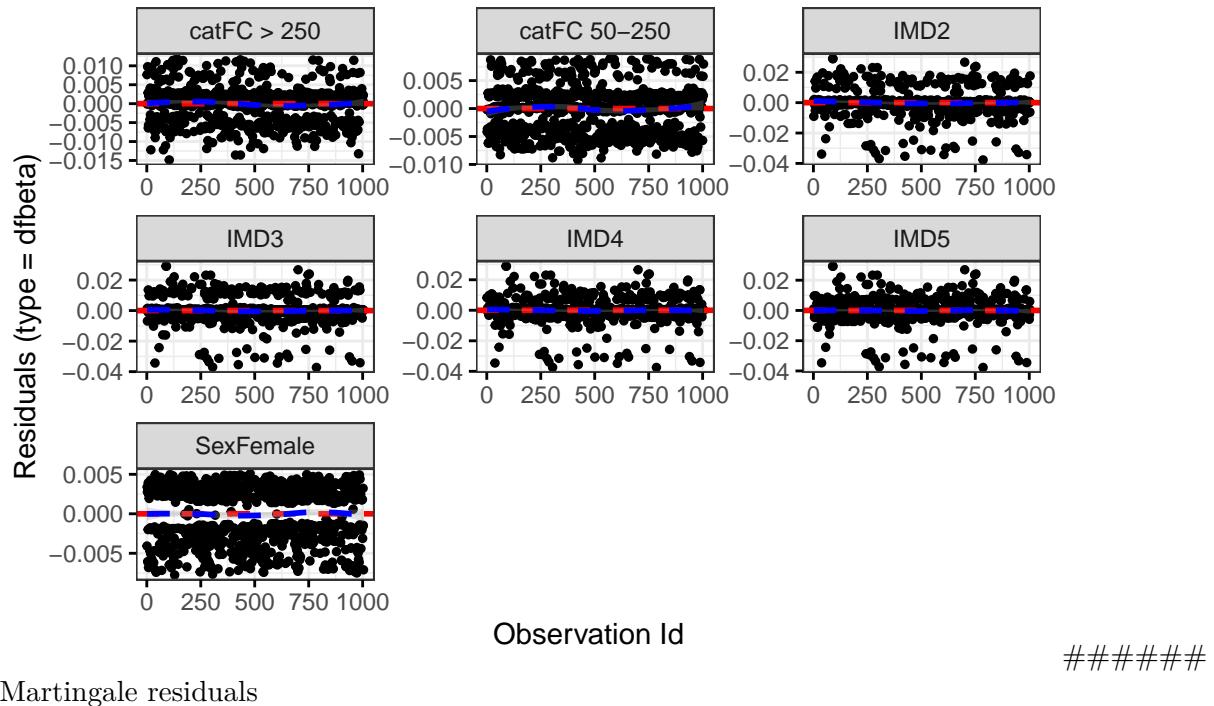
Proportional hazards assumption test

| | 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

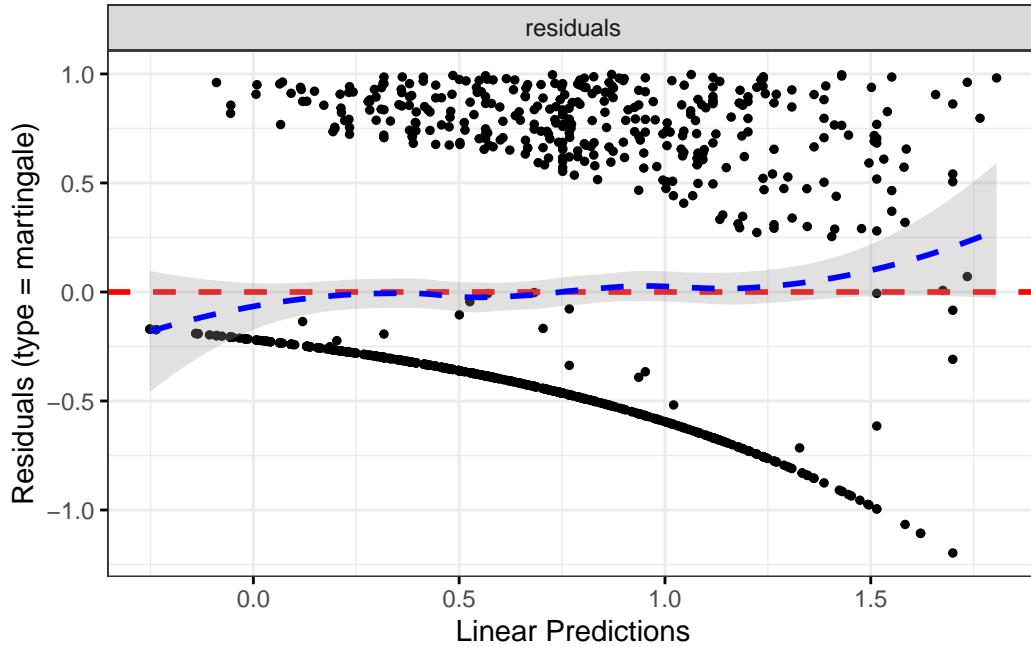
```
`geom_smooth()` using formula = 'y ~ x'
```



#####

Martingale residuals

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



Hard flare

```

fit.me <- coxph(
  Surv(hardflare_time, hardflare) ~
    Sex + IMD + cat + Smoke + 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 |

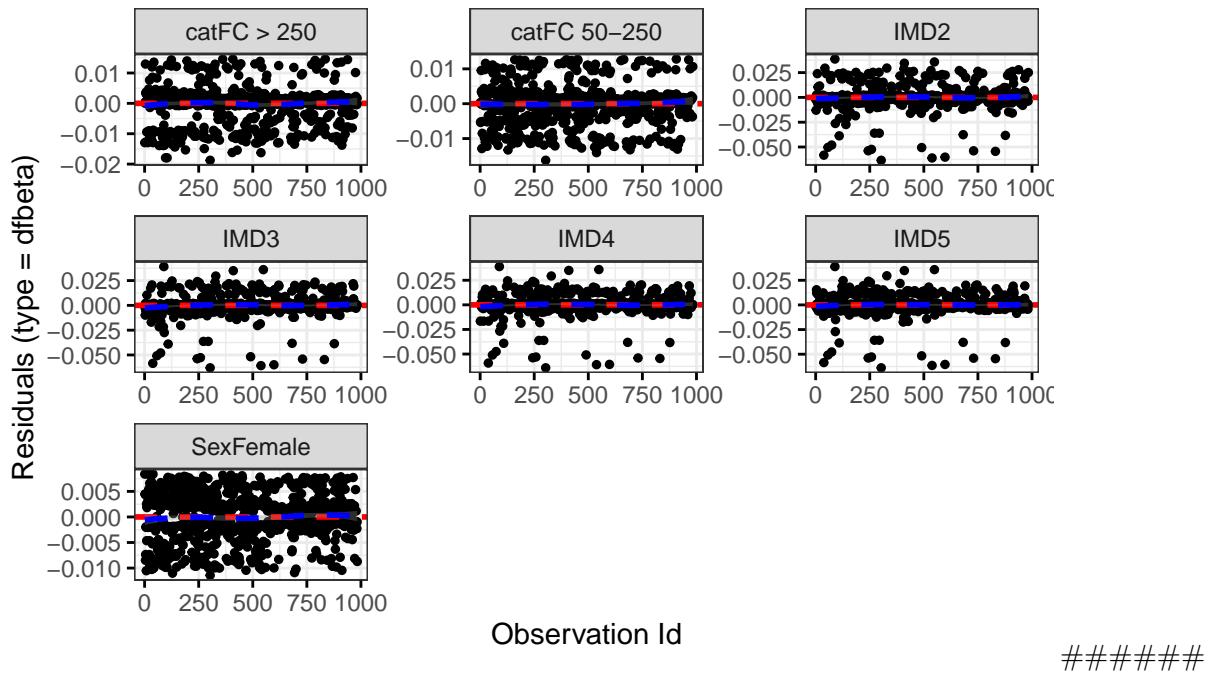
Diagnostics:

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 |

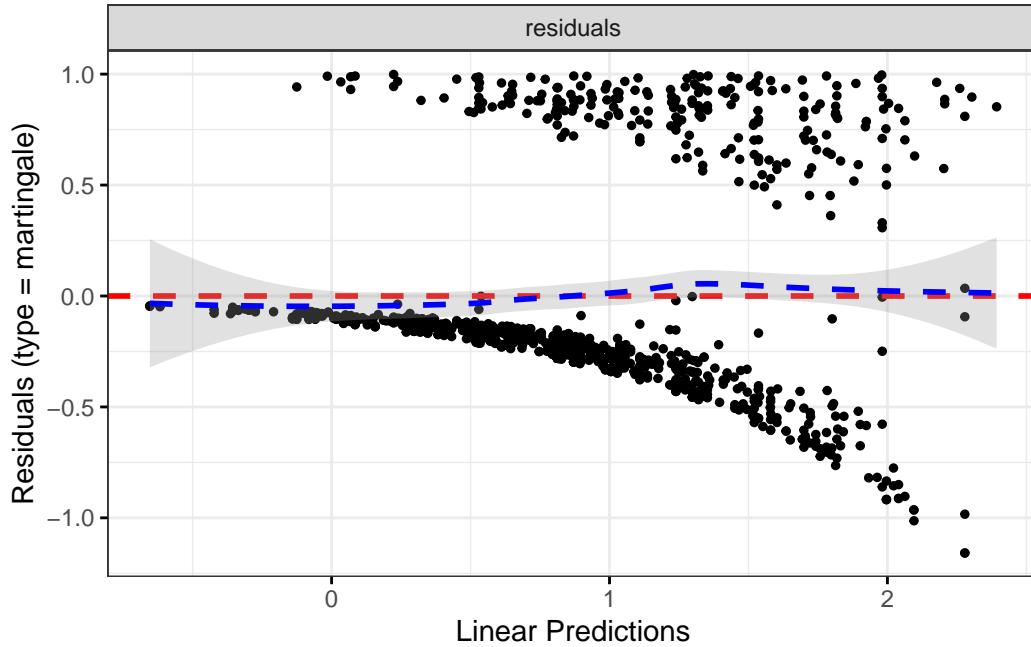
DF betas

```
`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 |

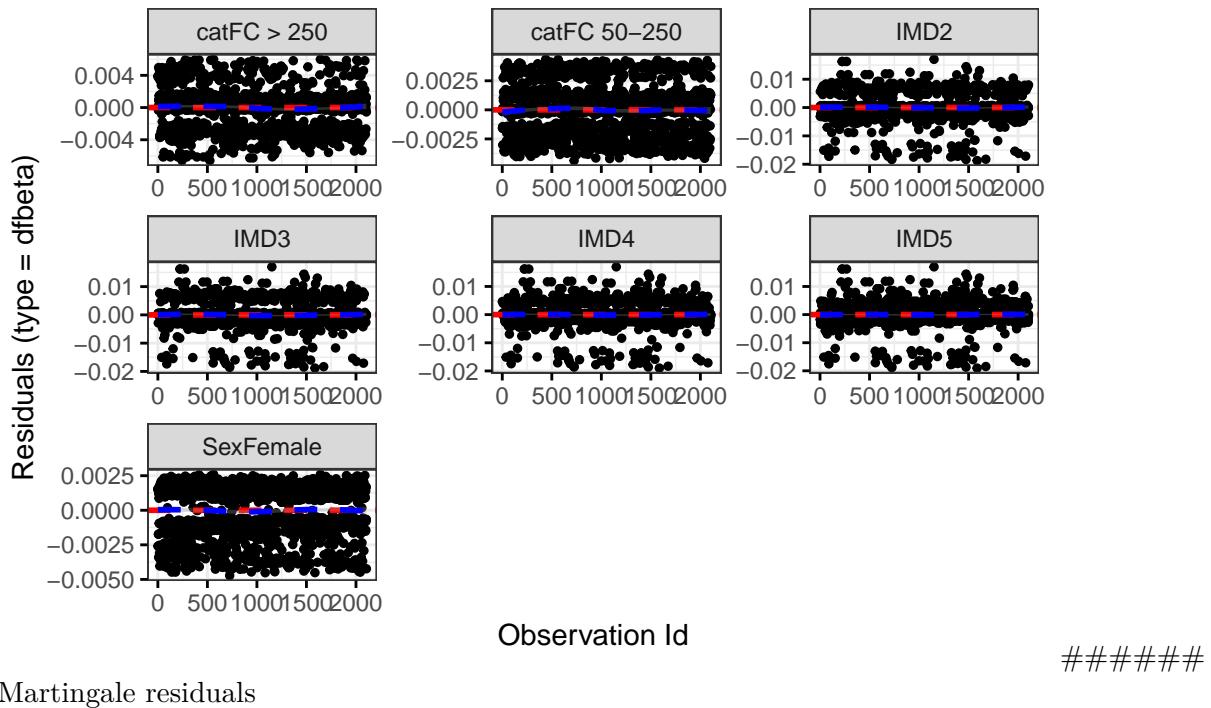
Diagnostics:

Proportional hazards assumption test

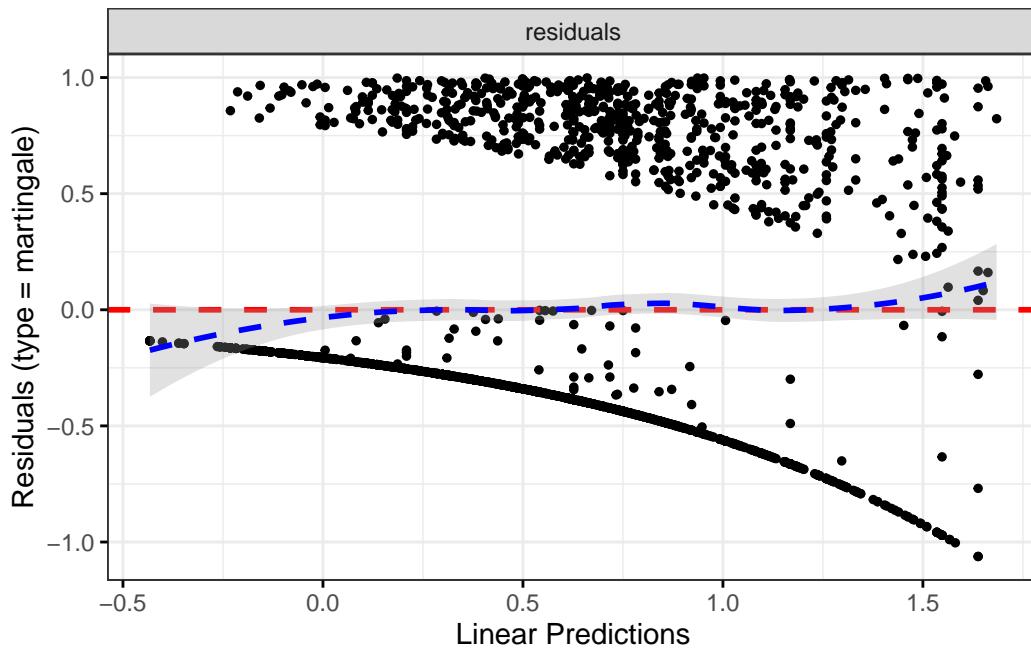
| | Chi-squared statistic | DF | P-value |
|--------|-----------------------|---------|---------|
| Sex | 1.9368 | 0.9936 | 0.1627 |
| IMD | 8.9273 | 3.9484 | 0.0609 |
| cat | 1.1234 | 1.9824 | 0.5659 |
| GLOBAL | 12.1742 | 22.3691 | 0.9594 |

DF betas

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



```
`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 |

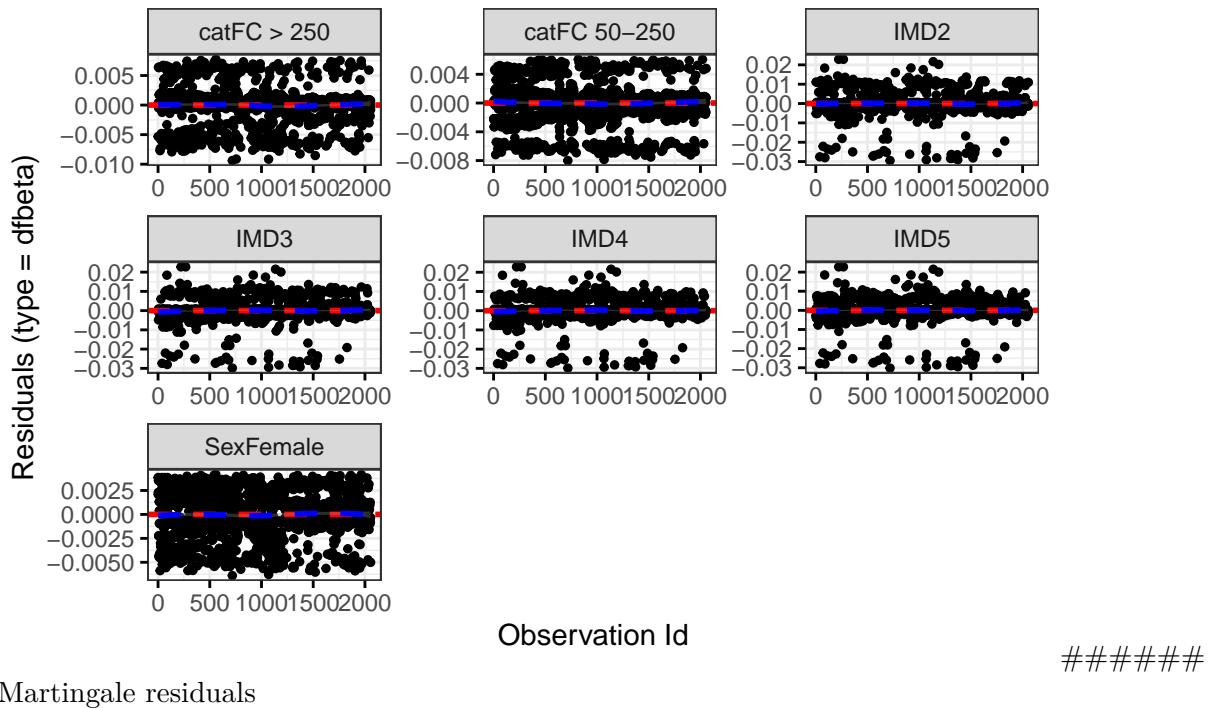
Diagnostics:

Proportional hazards assumption test

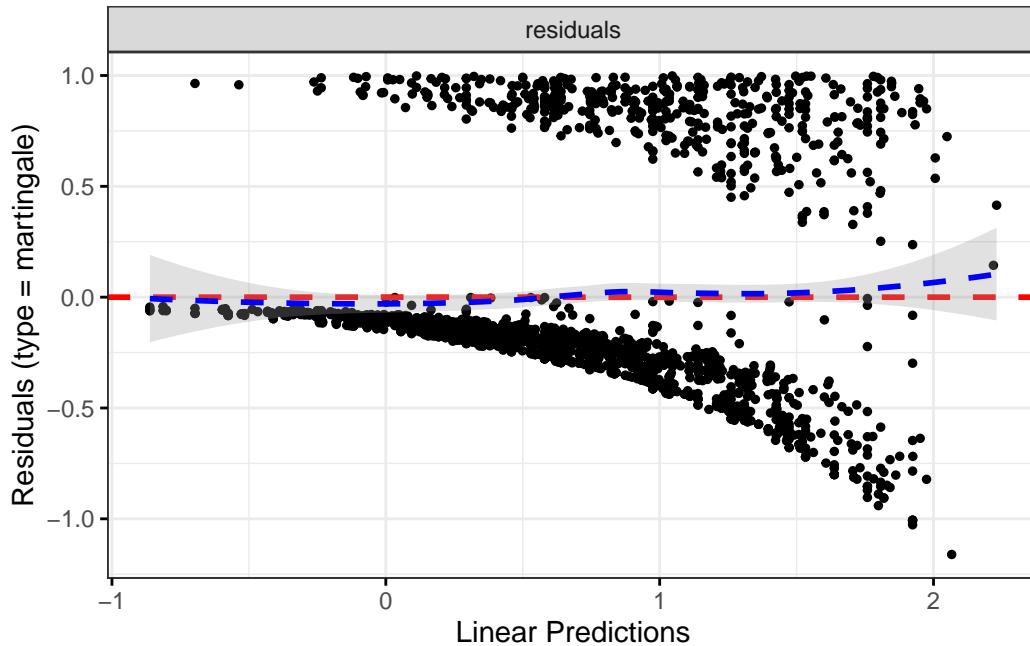
| | Chi-squared statistic | DF | P-value |
|--------|-----------------------|---------|---------|
| Sex | 0.2285 | 0.9928 | 0.6297 |
| IMD | 0.8488 | 3.9546 | 0.9289 |
| cat | 8.4343 | 1.9867 | 0.0145 |
| GLOBAL | 9.9289 | 29.8504 | 0.9998 |

DF betas

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



```
`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), coxme(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), vctrs(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), ggsignif(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), htmltools(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)*

Licensed by CC BY unless otherwise stated.