

Diet

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Introduction

```

set.seed(123)

source("Baseline/utils.R")

#####
## Packages ##
#####

library(plyr) # Used for mapping values
suppressPackageStartupMessages(library(tidyverse)) # ggplot2, dplyr, and magrittr
library(readxl) # Read in Excel files
library(lubridate) # Handle dates
library(datefixR) # Standardise dates
library(patchwork) # Arrange ggplots

# Generate tables
suppressPackageStartupMessages(library(table1))
library(knitr)
library(pander)

# Generate flowchart of cohort derivation
library(DiagrammeR)
library(DiagrammeRsvg)

# paths to PRDiCCt data
if (file.exists("/docker")) { # If running in docker
  data.path <- "data/final/20221004/"
  redcap.path <- "data/final/20231030/"
  upf.path <- "data/final/20240924/"
  prefix <- "data/end-of-follow-up/"
  outdir <- "data/processed/"
} else { # Run on OS directly
  data.path <- "/Volumes/igmm/cvallejo-predicct/predicct/final/20221004/"
  redcap.path <- "/Volumes/igmm/cvallejo-predicct/predicct/final/20231030/"
  upf.path <- "/Volumes/igmm/cvallejo-predicct/predicct/final/20240924/"
  prefix <- "/Volumes/igmm/cvallejo-predicct/predicct/end-of-follow-up/"
  outdir <- "/Volumes/igmm/cvallejo-predicct/predicct/processed/"
}

```

```

}

demo <- readRDS(paste0(outdir, "demo-biochem.RDS"))

FFQ <- read_xlsx(paste0(
  prefix,
  "predicct ffq_nutrientfood groupDQI all foods_data (n1092)Nov2022.xlsx"
))

FFQ$meat_overall <- rowSums(FFQ[, paste0("meat7", letters[1:12], "_grams")])

FFQ$fish_overall <- rowSums(FFQ[, paste0("fish8", letters[1:13], "_grams")])

FFQ$ParticipantNo <- FFQ$participantno
demo <- merge(demo,
  FFQ[, c(
    "ParticipantNo",
    "Meat_sum",
    "meat_overall",
    "fish_overall",
    "fibre",
    "PUFA_percEng",
    "NOVAScore_cat",
    "dqi_tot"
  )],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE
)

cat_theme <- function(gg) {
  p <- gg +
    scale_fill_manual(values = c("#DA4167", "#F4D35E", "#083D77")) +
    scale_color_manual(values = colorspace::darken(c("#DA4167",
                                                    "#F4D35E",
                                                    "#083D77"),
                                                0.2))
  ) +
  theme_minimal()
  p
}

```

```

# library(writexl)
# FFQ <- merge(FFQ,
#   demo[, c("ParticipantNo", "FC", "Sex", "diagnosis2")],
#   by = "ParticipantNo",
#   all.x = TRUE,
#   all.y = FALSE
# )

# FFQ <- subset(FFQ, !is.na(FC))
# write_xlsx(FFQ, paste0("/Volumes/igmm/cvallejo-predicct/predicct/processed/", "FFQ-FC.xlsx"))

```

PREDiCCt has collected data on diet via food frequency questionnaires (FFQs) and food diaries. This dietary data has been analysed by staff at the [University of Aberdeen](#), primarily by [Dr Janet Kyle](#), [Dr Graham Horgan](#), and [Professor Alex Johnstone](#).

Whilst data for many dietary variables have been collected, this report will focus on the data outlined in the SAP.

1. Protein from animal-sources
2. Dietary fibre
3. Polyunsaturated fatty acids (PUFAs)
4. Nova intake score

The data for these variables were extracted from the FFQs. As reported associations between dietary data and IBD are often specific to a form of IBD rather than IBD as a whole, these data will be presented stratified by disease type.

Protein from meat sources

Figure 1 suggests there are relatively few vegetarians in the PREDiCCt cohort. Whilst some extreme values were observed for protein from meat sources, they remain plausible.

```

demo %>%
  drop_na(Meat_sum) %>%
  ggplot(aes(x = Meat_sum, color = diagnosis2, fill = diagnosis2)) +
  geom_histogram(bins = 25) +
  theme_minimal() +
  theme(legend.position = "none") +
  labs(
    x = "Protein from meat sources (g)",
    y = "Frequency",
    color = "IBD type",

```

```

    fill = "IBD type"
) +
scale_fill_manual(
  labels = c("UC/IBDU", "Crohn's"),
  values = c("#CDEDF6", "#FF6B6B")
) +
scale_color_manual(
  labels = c("UC/IBDU", "Crohn's"),
  values = c("#5EB1BF", "#C24343")
) +
facet_grid(rows = vars(diagnosis2))

```

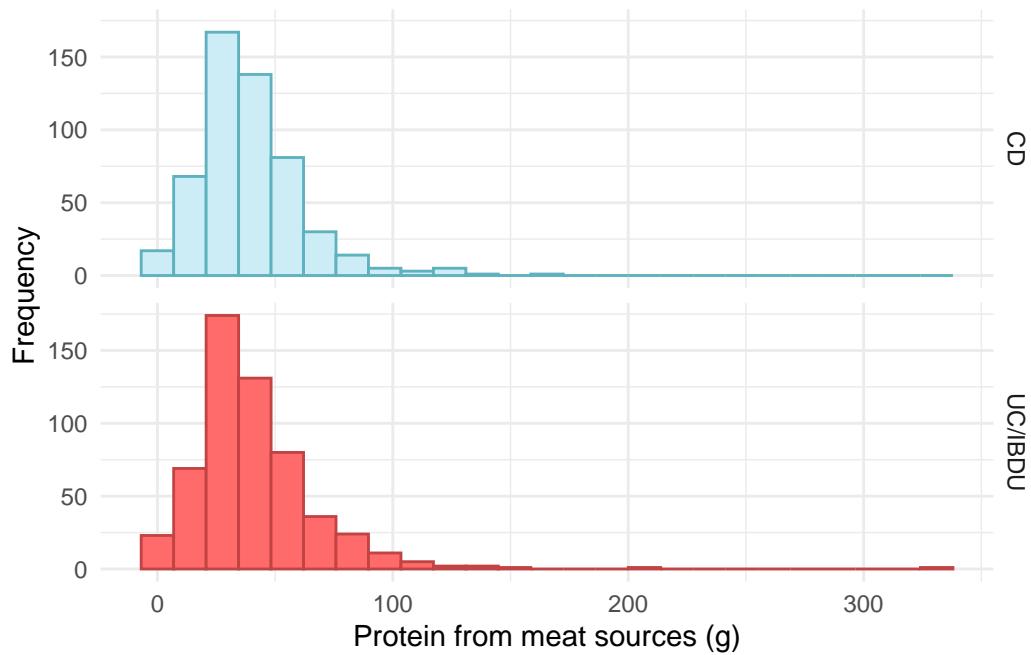


Figure 1: Distribution of protein intake from meat.

No association was observed between protein intake from meat and FC in either CD or UC.

```

demo %>%
  filter(diagnosis2 == "CD") %>%
  aov(formula = Meat_sum ~ cat) %>%
  summary() %>%
  pander()

```

Table 1: ANOVA between protein intake from meat and FC groups in Crohn's disease.

Table 1: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|--------|
| cat | 2 | 237.6 | 118.8 | 0.2419 | 0.7852 |
| Residuals | 494 | 242579 | 491.1 | NA | NA |

```
demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = Meat_sum ~ cat) %>%
  summary() %>%
  pander()
```

Table 2: ANOVA between protein intake from meat and FC groups in UC/IBDU.

Table 2: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|---------|
| cat | 2 | 3350 | 1675 | 2.814 | 0.06088 |
| Residuals | 512 | 304730 | 595.2 | NA | NA |

Overall meat intake

```
demo %>%
  drop_na(meat_overall) %>%
  ggplot(aes(x = meat_overall, color = diagnosis2, fill = diagnosis2)) +
  geom_histogram(bins = 25) +
  theme_minimal() +
  theme(legend.position = "none") +
  labs(
    x = "Meat intake (g)",
    y = "Frequency",
    color = "IBD type",
    fill = "IBD type"
  ) +
  scale_fill_manual(
    labels = c("UC/IBDU", "Crohn's"),
    values = c("#CDEDF6", "#FF6B6B")
```

```

) +
scale_color_manual(
  labels = c("UC/IBDU", "Crohn's"),
  values = c("#5EB1BF", "#C24343")
) +
facet_grid(rows = vars(diagnosis2))

```

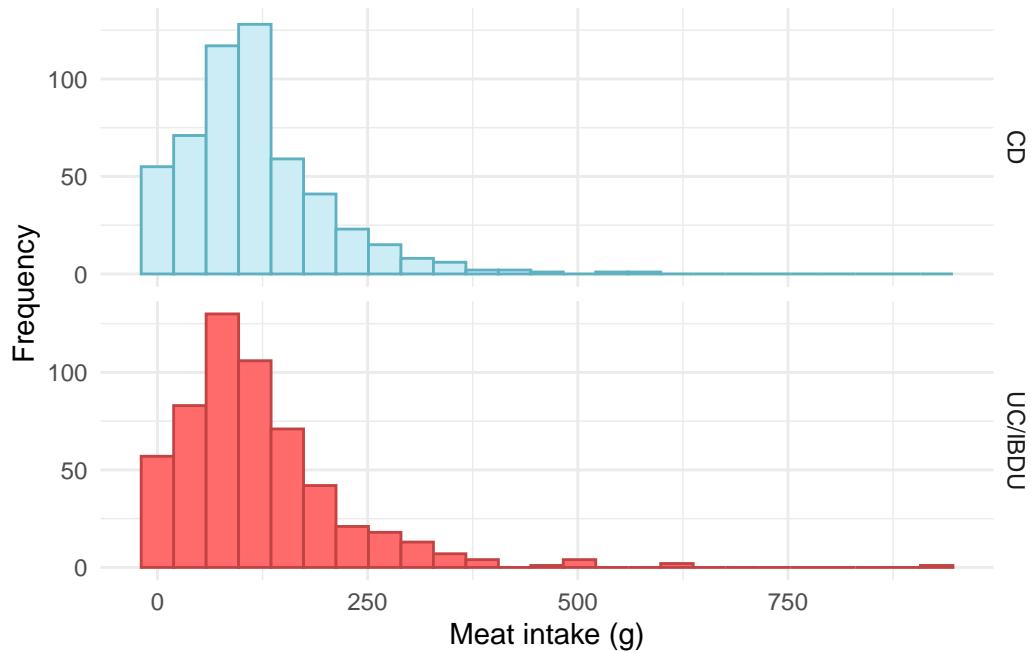


Figure 2: Distribution of overall meat intake.

No association was observed between meat intake and FC in CD. However, a significant association was observed between meat intake and FC in UC/IBDU Table 4.

```

demo %>%
  filter(diagnosis2 == "CD") %>%
  aov(formula = meat_overall ~ cat) %>%
  summary() %>%
  pandar()

```

Table 3: ANOVA between meat intake and FC groups in Crohn's disease.

Table 3: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|---------|---------|---------|--------|
| cat | 2 | 730.4 | 365.2 | 0.05301 | 0.9484 |
| Residuals | 494 | 3403211 | 6889 | NA | NA |

```
demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = meat_overall ~ cat) %>%
  summary() %>%
  pander()
```

Table 4: ANOVA between meat intake and FC groups in UC/IBDU.

Table 4: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|---------|---------|---------|---------|
| cat | 2 | 69131 | 34565 | 4.373 | 0.01309 |
| Residuals | 512 | 4046939 | 7904 | NA | NA |

```
p <- demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  drop_na(cat, meat_overall) %>%
  mutate(cat = fct_rev(cat)) %>%
  ggplot(aes(x = meat_overall, fill = cat, color = cat)) +
  geom_density() +
  facet_grid(rows = vars(cat)) +
  labs(x = "Meat intake",
       y = "Density",
       fill = "FC group",
       color = "FC group")
cat_theme(p)
```

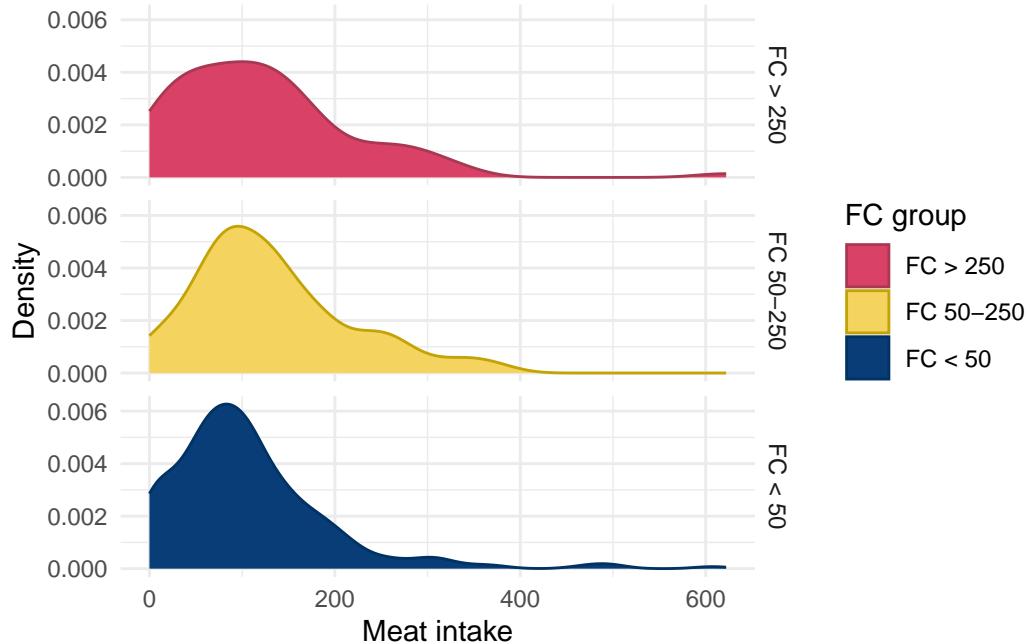


Figure 3: Distribution of meat intake by FC in UC.

Overall fish intake

```
demo %>%
  drop_na(fish_overall) %>%
  ggplot(aes(x = fish_overall, color = diagnosis2, fill = diagnosis2)) +
  geom_histogram(bins = 25) +
  theme_minimal() +
  theme(legend.position = "none") +
  labs(
    x = "Fish intake (g)",
    y = "Frequency",
    color = "IBD type",
    fill = "IBD type"
  ) +
  scale_fill_manual(
    labels = c("UC/IBDU", "Crohn's"),
    values = c("#CDEDF6", "#FF6B6B")
  ) +
  scale_color_manual(
```

```

labels = c("UC/IBDU", "Crohn's"),
values = c("#5EB1BF", "#C24343")
) +
facet_grid(rows = vars(diagnosis2))

```

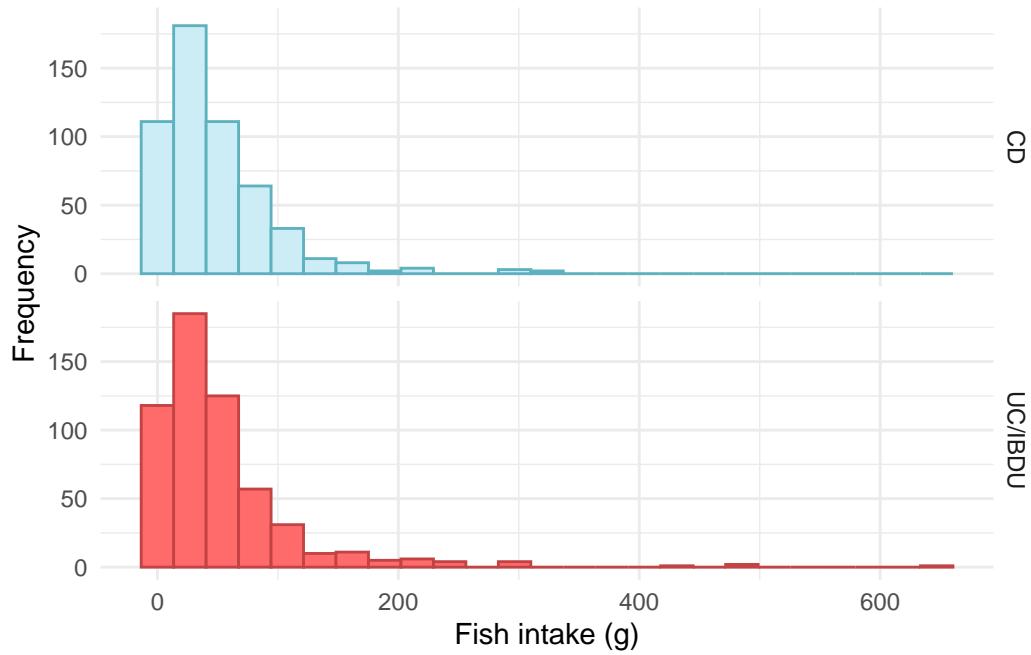


Figure 4: Distribution of overall fish intake.

No association was observed between meat intake and FC in CD. However, a significant association was observed between meat intake and FC in UC/IBDU Table 4.

```

demo %>%
filter(diagnosis2 == "CD") %>%
aov(formula = fish_overall ~ cat) %>%
summary() %>%
pander()

```

Table 5: ANOVA between fish intake and FC groups in Crohn's disease.

Table 5: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|---------|---------|---------|--------|
| cat | 2 | 4855 | 2427 | 1.085 | 0.3388 |
| Residuals | 494 | 1105599 | 2238 | NA | NA |

```
demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = fish_overall ~ cat) %>%
  summary() %>%
  pander()
```

Table 6: ANOVA between fish intake and FC groups in UC/IBDU.

Table 6: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|---------|---------|---------|--------|
| cat | 2 | 1986 | 992.9 | 0.2838 | 0.753 |
| Residuals | 512 | 1791051 | 3498 | NA | NA |

Dietary fibre

Fibre has frequently investigated as a potential factor in IBD pathogenesis, particularly in CD.

A study of 170,776 women across 26 years found fibre intake, particularly fibre derived from fruits, to be low for incident CD patients (Ananthakrishnan et al. 2013).

A US study of 1,130 CD subjects found CD patients who reported that they did not avoid high-fibre foods were approximately 40% less likely to have a disease flare in a 6-month period than those who avoided high-fibre foods (Brotherton et al. 2016).

There is less evidence of a relationship between UC and dietary fibre.

There does not appear to be substantial differences in fibre between CD and UC/IBDU PREDiCCt participants.

```

demo %>%
  drop_na(fibre) %>%
  ggplot(aes(x = fibre, color = diagnosis2, fill = diagnosis2)) +
  geom_histogram(bins = 25) +
  theme_minimal() +
  theme(legend.position = "none") +
  labs(
    x = "Dietary fibre",
    y = "Frequency",
    color = "IBD type",
    fill = "IBD type"
  ) +
  scale_fill_manual(
    values = c("#CDEDF6", "#FF6B6B")
  ) +
  scale_color_manual(
    values = c("#5EB1BF", "#C24343")
  ) +
  facet_grid(rows = vars(diagnosis2))

```

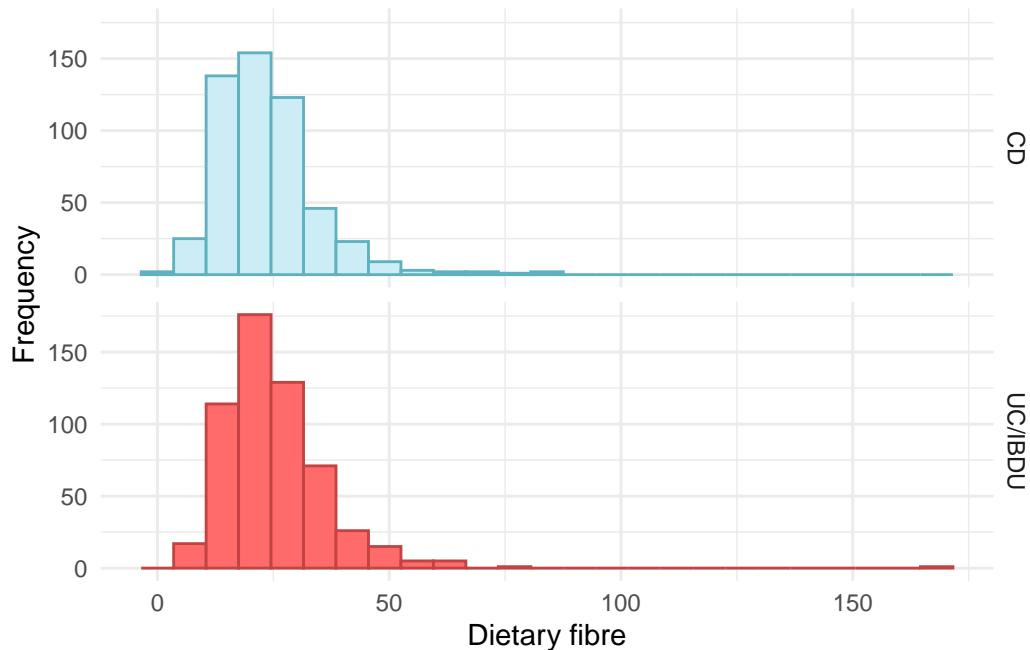


Figure 5: Distribution of dietary fibre.

No association was found between dietary fibre intake and FC.

```
demo %>%
  filter(diagnosis2 == "CD") %>%
  aov(formula = fibre ~ cat) %>%
  summary() %>%
  pandar()
```

Table 7: ANOVA between dietary fibre and FC groups in Crohn's disease.

Table 7: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|--------|
| cat | 2 | 333.4 | 166.7 | 1.496 | 0.2251 |
| Residuals | 494 | 55046 | 111.4 | NA | NA |

```
demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = fibre ~ cat) %>%
  summary() %>%
  pandar()
```

Table 8: ANOVA between dietary fibre and FC groups in UC/IBDU.

Table 8: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|--------|
| cat | 2 | 80.2 | 40.1 | 0.3739 | 0.6882 |
| Residuals | 512 | 54910 | 107.2 | NA | NA |

Polyunsaturated fatty acids

PUFAs exhibit anti-inflammatory properties and there is evidence of a relationship between PUFAs and UC incidence (Marion-Letellier et al. 2013). Research suggests that a diet with a poor balance of n-3 and n-6 PUFAs, commonly seen in “Western” diets is associated with IBD risk.

The PREdiCCt SAP states n-6 PUFAs will be examined. However, the data obtained from the FFQs describes PUFAs as a whole (including n-3 PUFAs).

```

demo %>%
  drop_na(cat) %>%
  ggplot(aes(x = PUFA_percEng, color = diagnosis2, fill = diagnosis2)) +
  geom_histogram(bins = 25) +
  theme_minimal() +
  theme(legend.position = "none") +
  labs(
    x = "PUFA intake",
    y = "Frequency",
    color = "IBD type",
    fill = "IBD type"
  ) +
  scale_fill_manual(
    values = c("#CDEDF6", "#FF6B6B")
  ) +
  scale_color_manual(
    values = c("#5EB1BF", "#C24343")
  ) +
  facet_grid(rows = vars(diagnosis2))

```

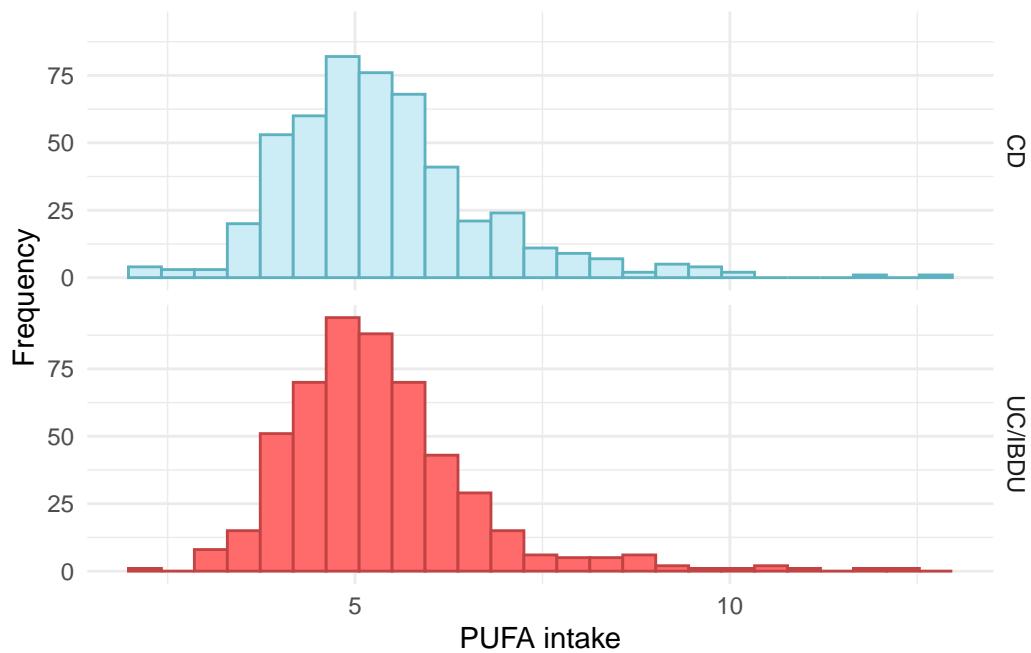


Figure 6: Distribution of polyunsaturated fatty acids.

A significant association was not seen between PUFA intake and FC.

```
demo %>%
  filter(diagnosis2 == "CD") %>%
  aov(formula = PUFA_percEng ~ cat) %>%
  summary() %>%
  pander()
```

Table 9: ANOVA between polyunsaturated fatty acids and FC groups in Crohn's disease.

Table 9: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|--------|
| cat | 2 | 0.9349 | 0.4674 | 0.2489 | 0.7798 |
| Residuals | 494 | 927.9 | 1.878 | NA | NA |

```
demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = PUFA_percEng ~ cat) %>%
  summary() %>%
  pander()
```

Table 10: ANOVA between polyunsaturated fatty acids and FC groups in UC/IBDU.

Table 10: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|---------|
| cat | 2 | 10.72 | 5.359 | 3.378 | 0.03487 |
| Residuals | 512 | 812.1 | 1.586 | NA | NA |

```
p <- demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  drop_na(cat, PUFA_percEng) %>%
  mutate(cat = fct_rev(cat)) %>%
  ggplot(aes(x = PUFA_percEng, fill = cat, color = cat)) +
  geom_density() +
  facet_grid(rows = vars(cat)) +
  labs(x = "PUFA intake",
       y = "Density",
       fill = "FC group",
```

```

color = "FC group")
cat_theme(p)

```

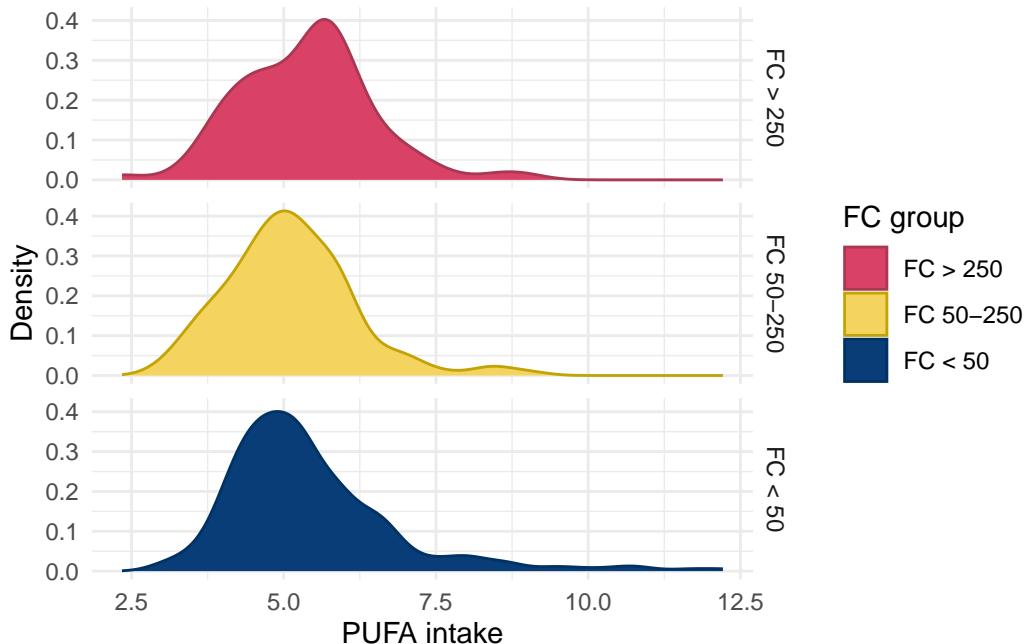


Figure 7: Distribution of polyunsaturated fatty acid intake by FC in UC.

Diet quality index

Diet quality index (DQI) is a measure of overall diet quality ranging from 0 to 100. A higher DQI indicates a diverse diet likely meeting recommended daily intakes but reflecting moderation whilst low values indicate the converse. We used Diet Quality Index-International (DQI-I) which has been validated for use in diverse populations (Kim et al. 2003). It should be noted DQI does not necessarily relate to ultra-processed food intake.

```

demo %>%
drop_na(cat) %>%
ggplot(aes(x = dqi_tot, color = diagnosis2, fill = diagnosis2)) +
geom_histogram(bins = 25) +
theme_minimal() +
theme(legend.position = "none") +
labs(
  x = "Diet quality index",

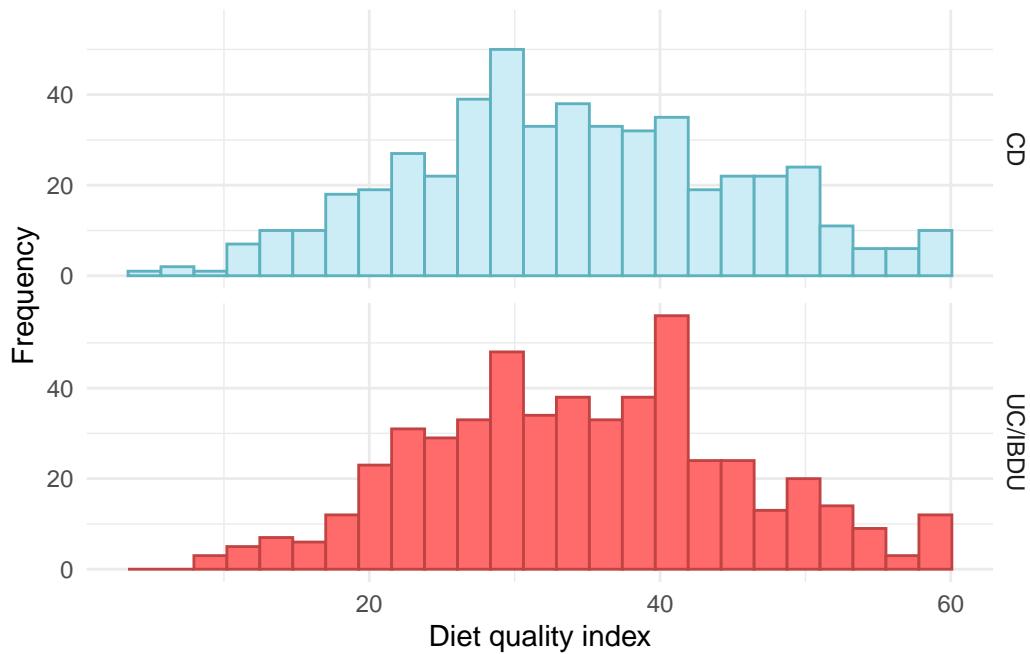
```

```

y = "Frequency",
color = "IBD type",
fill = "IBD type"
) +
scale_fill_manual(
  values = c("#CDEDF6", "#FF6B6B")
) +
scale_color_manual(
  values = c("#5EB1BF", "#C24343")
) +
facet_grid(rows = vars(diagnosis2))

```

Warning: Removed 1132 rows containing non-finite outside the scale range
(`stat_bin()`).



```

demo %>%
  filter(diagnosis2 == "CD") %>%
  aov(formula = dqi_tot ~ cat) %>%
  summary() %>%
  pander()

```

Table 11: ANOVA between diet quality index and FC groups in Crohn's disease.

Table 11: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|--------|
| cat | 2 | 121.6 | 60.8 | 0.4786 | 0.62 |
| Residuals | 494 | 62761 | 127 | NA | NA |

```
demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = dqi_tot ~ cat) %>%
  summary() %>%
  pander()
```

Table 12: ANOVA between diet quality index and FC groups in UC/IBDU.

Table 12: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|---------|
| cat | 2 | 769.2 | 384.6 | 3.393 | 0.03436 |
| Residuals | 512 | 58031 | 113.3 | NA | NA |

```
p <- demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  drop_na(cat, dqi_tot) %>%
  mutate(cat = fct_rev(cat)) %>%
  ggplot(aes(x = dqi_tot, fill = cat, color = cat)) +
  geom_density() +
  facet_grid(rows = vars(cat)) +
  labs(x = "Diet quality index",
       y = "Density",
       fill = "FC group",
       color = "FC group")
cat_theme(p)
```

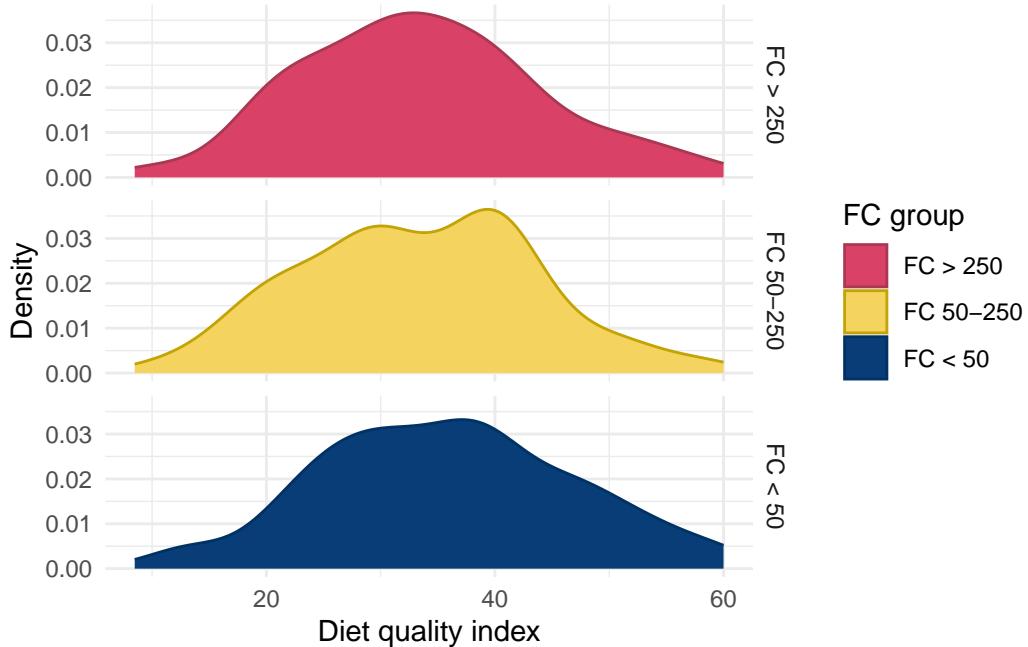


Figure 8: Distribution of diet quality index by FC in UC.

Nova intake score

There has been a great deal of recent research interest in ultra processed food (UPF) and IBD. For example, Narula et al. (2021) found UPF intake to be positively associated with IBD risk.

The Nova score is a popular approach for classifying UPFs (Monteiro et al. 2017). Food is classified as either unprocessed, processed culinary, processed food, or ultra-processed via the Nova score. The University of Aberdeen have developed an extension of the Nova score, the Nova intake score, which can be used to categorise individuals and their diets instead of individual food items.

The following definition of the Nova intake score was written by Liam McAdie during a 5th year medical elective in which he worked on the PREdiCCt dietary data. The formulae have received minor modifications, but otherwise the definitions remain unchanged from McAdie's work.

Definition

When completing the FFQ, participants were asked to report (a) portion size normally consumed, (b) number of times this portion is consumed in one day and (c) number of days per

week food type is consumed. Participant's daily average consumption (in grams) of a food and drink type (x) was calculated by:

$$x = \frac{c}{7}(a + b)$$

Standardised number of portions consumed daily for food and drink type (y) was calculated by dividing consumption (x) by the Foods Standard Agency average UK-portion size (z).

$$y = \frac{x}{z}$$

Nova intake scores (N) were calculated by multiplying the number of standardised portions consumed (y) by their corresponding Nova score (M) assigned in the database. This process is repeated for all 169 food and drink types and totalled to give one overall Nova intake score. This score is a marker representative of UPF intake.

$$N = \sum_{i=1}^{169} (y_i M_i)$$

Results

The distribution of Nova intake score appears to be uniform across the cohort, as such, it seems likely that these data have been mapped to quantiles and are no longer describing Nova Score categories.

```
demo$NOVAScore_cat <- factor(demo$NOVAScore_cat,
  levels = 1:4,
  labels = c(
    "Unprocessed",
    "Processed culinary",
    "Processed food",
    "Ultra-processed"
  )
)

demo %>%
  drop_na(NOVAScore_cat) %>%
  ggplot(aes(x = NOVAScore_cat, color = diagnosis2, fill = diagnosis2)) +
  geom_bar() +
  theme_minimal() +
  theme(legend.position = "none") +
```

```

  labs(
    x = "Nova intake score",
    y = "Frequency",
    color = "IBD type",
    fill = "IBD type"
  ) +
  scale_fill_manual(
    values = c("#CDEDF6", "#FF6B6B")
  ) +
  scale_color_manual(
    values = c("#5EB1BF", "#C24343")
  ) +
  facet_grid(rows = vars(diagnosis2))

```

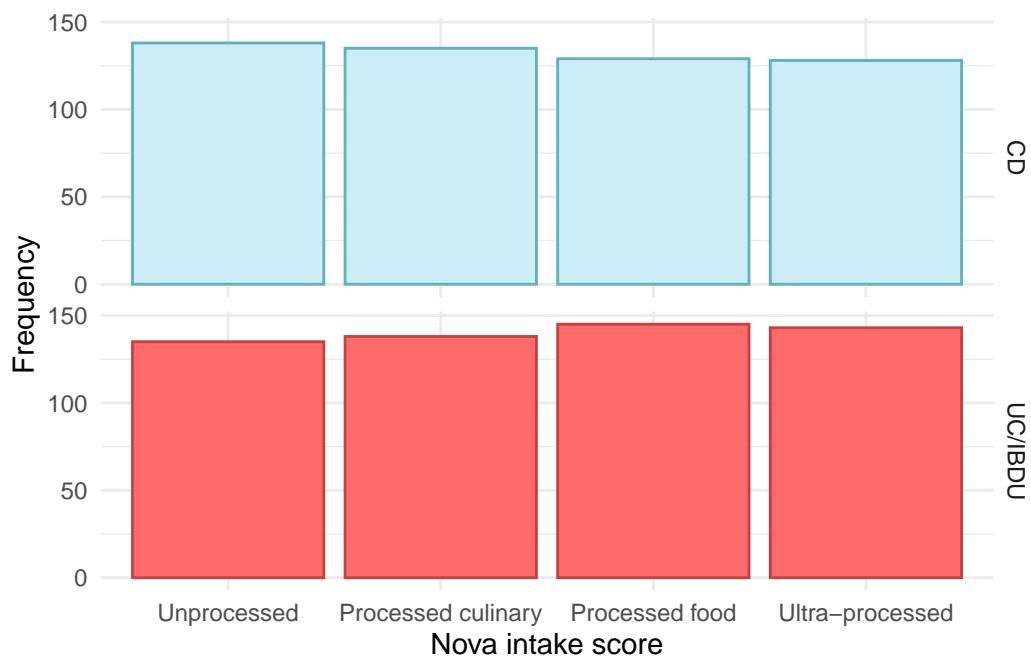


Figure 9: Distribution of Nova intake scores.

No significant association was observed between Nova intake scores and FC groups.

```

temp <- demo %>%
  filter(diagnosis2 == "CD")

pander(chisq.test(temp$NOVAScore_cat, temp$cat))

```

Table 13: Chi-squared test between Nova intake score and FC groups in Crohn's disease.

| Test statistic | df | P value |
|----------------|----|---------|
| 11.12 | 6 | 0.08488 |

```
temp <- demo %>%
  filter(diagnosis2 == "UC/IBDU")

pander(chisq.test(temp$NOVAScore_cat, temp$cat))
```

Table 14: Chi-squared test between Nova intake score and FC groups in UC/IBDU.

| Test statistic | df | P value |
|----------------|----|---------|
| 4.197 | 6 | 0.6501 |

Processed food subgroups

In addition to exploring UPF intake as a whole, we also explore UPF intake by subcategories. This approach is based on the methodology used by Cordova et al. (2023). The following categories have been identified by Dr Maiara Brusco De Freitas using FFQ groupings.

Animal-based products (processed meat) is the only subgroup considered which we found to be significantly associated with FC.

Breads and cereals

```
FFQ$breadIntake <- with(FFQ,
  (bread1a_grams +
   bread1b_grams +
   bread1c_grams +
   bread1d_grams +
   cereal2a_grams +
   cereal2b_grams +
   cereal2c_grams +
   cereal2d_grams +
   cereal2e_grams) /
  EnergykCAL) * 100

demo <- merge(demo,
```

```

FFQ[, c("ParticipantNo", "breadIntake")],
by = "ParticipantNo",
all.x = TRUE,
all.y = FALSE)

demo %>%
  drop_na(breadIntake) %>%
  ggplot(aes(x = breadIntake)) +
  geom_histogram(bins = 25, color = "#5C738F", fill = "#759EB8") +
  theme_minimal() +
  xlab("Processed bread and cereal intake / energy intake (g/kcal)") +
  ylab("Frequency")

```

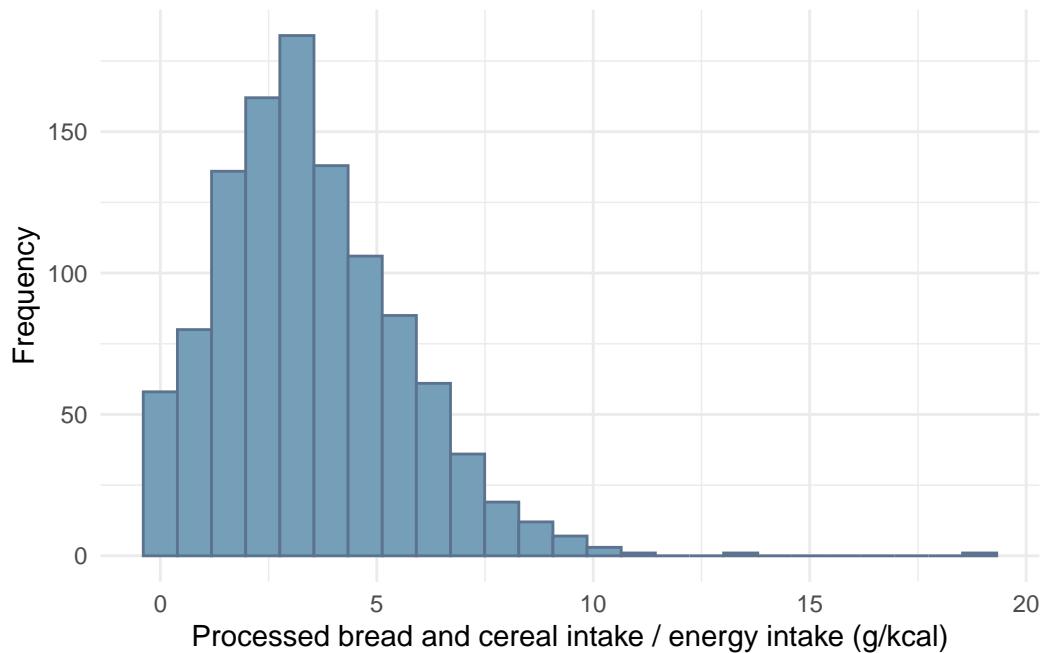


Figure 10: Distribution of processed bread and cereal intake divided by daily energy intake.

```
pander(summary(aov(breadIntake ~ cat, data = demo)))
```

Table 15: ANOVA between processed bread/cereal intake and FC groups.

Table 15: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|-----------|------|--------|---------|---------|--------|
| cat | 2 | 15.73 | 7.867 | 1.718 | 0.1799 |
| Residuals | 1009 | 4620 | 4.579 | NA | NA |

Sweets and desserts/snack foods

```
FFQ$sweetIntake <- with(FFQ,
  (Puddings13a_grams +
   Puddings13b_grams +
   Puddings13c_grams +
   Puddings13d_grams +
   Puddings13e_grams +
   Puddings13f_grams +
   Puddings13g_grams +
   Puddings13h_grams +
   Chocsetc14a_grams +
   Chocsetc14b_grams +
   Chocsetc14c_grams +
   Chocsetc14d_grams +
   Chocsetc14g_grams +
   Chocsetc14h_grams +
   Chocsetc14i_grams +
   Biscuits15a_grams +
   Biscuits15b_grams +
   Biscuits15c_grams +
   Biscuits15d_grams +
   Biscuits15e_grams +
   Biscuits15g_grams +
   Cakes16a_grams +
   Cakes16b_grams +
   Cakes16c_grams +
   Cakes16d_grams +
   Cakes16e_grams) /
   EnergykCAL) * 100

demo <- merge(demo,
  FFQ[, c("ParticipantNo", "sweetIntake")],
```

```

    by = "ParticipantNo",
    all.x = TRUE,
    all.y = FALSE)

demo %>%
  drop_na(sweetIntake) %>%
  ggplot(aes(x = sweetIntake)) +
  geom_histogram(bins = 25, color = "#B25966", fill = "#FFA3AF") +
  theme_minimal() +
  xlab("Sweet/dessert/snack intake / energy intake (g/kcal)") +
  ylab("Frequency")

```



Figure 11: Distribution of Sweet and dessert/snack intake divided by daily energy intake.

```

#| label: tbl-sweetintake-uc
#| tbl-cap: "ANOVA between sweet/dessert/snack intake and FC for UC/IBDU."

demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = sweetIntake ~ cat) %>%
  summary() %>%
  pander()

```

Table 16: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|--------|
| cat | 2 | 28.62 | 14.31 | 2.053 | 0.1294 |
| Residuals | 512 | 3569 | 6.971 | NA | NA |

```
#| label: tbl-sweetIntake
#| tbl-cap: "ANOVA between sweet/dessert/snack intake and FC groups."
pander(summary(aov(sweetIntake ~ cat, data = demo)))
```

Table 17: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|--------|
| cat | 2 | 1.351 | 0.6754 | 0.09064 | 0.9134 |
| Residuals | 1009 | 7518 | 7.451 | NA | NA |

Artificially and sugar-sweetened beverages

```
FFQ$drinkIntake <- with(FFQ,
  (Beverages18h_grams +
   Beverages18i_grams +
   Beverages18j_grams +
   Beverages18k_grams +
   Beverages18n_grams +
   Beverages18o_grams) /
  EnergykCAL) * 100

demo <- merge(demo,
  FFQ[, c("ParticipantNo", "drinkIntake")],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE)

demo %>%
  drop_na(drinkIntake) %>%
  ggplot(aes(x = drinkIntake)) +
  geom_histogram(bins = 25, color = "#C58500", fill = "#F4AC45") +
  theme_minimal() +
```

```
xlab("Artificial/sugar-sweetened beverage intake / energy intake (g/kcal)") +
ylab("Frequency")
```

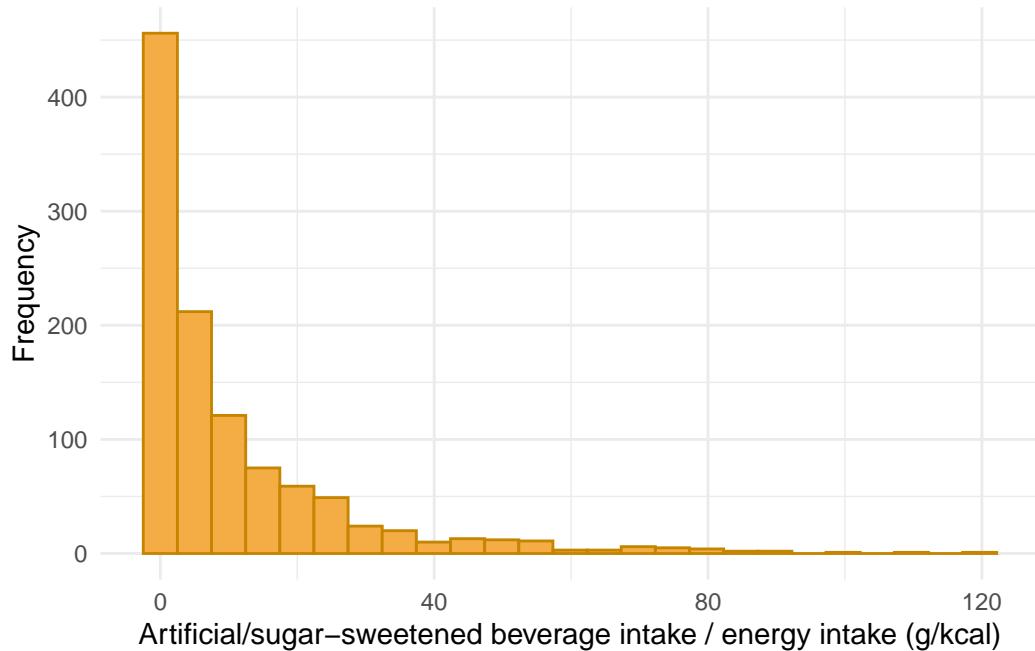


Figure 12: Distribution of artificially and sugar-sweetened drink intake divided by daily energy intake.

```
pander(summary(aov(sweetIntake ~ cat, data = demo)))
```

Table 18: ANOVA between artificial/sugar-sweetened beverage intake and FC groups.

Table 18: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|--------|
| cat | 2 | 1.351 | 0.6754 | 0.09064 | 0.9134 |
| Residuals | 1009 | 7518 | 7.451 | NA | NA |

Animal-based products (processed meat)

```

FFQ$processedMeatIntake <- with(FFQ,
  (meat7b_grams +
   meat7c_grams +
   meat7g_grams +
   meat7i_grams +
   meat7j_grams +
   meat7k_grams +
   meat7l_grams +
   fish8a_grams +
   fish8e_grams +
   fish8k_grams) /
  EnergykCAL) * 100

demo <- merge(demo,
  FFQ[, c("ParticipantNo", "processedMeatIntake")],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE)

demo %>%
  drop_na(processedMeatIntake) %>%
  ggplot(aes(x = processedMeatIntake)) +
  geom_histogram(bins = 25, color = "#BC0019", fill = "#FF4C55") +
  theme_minimal() +
  xlab("Processed animal-based product intake / energy intake (g/kcal)") +
  ylab("Frequency")

```

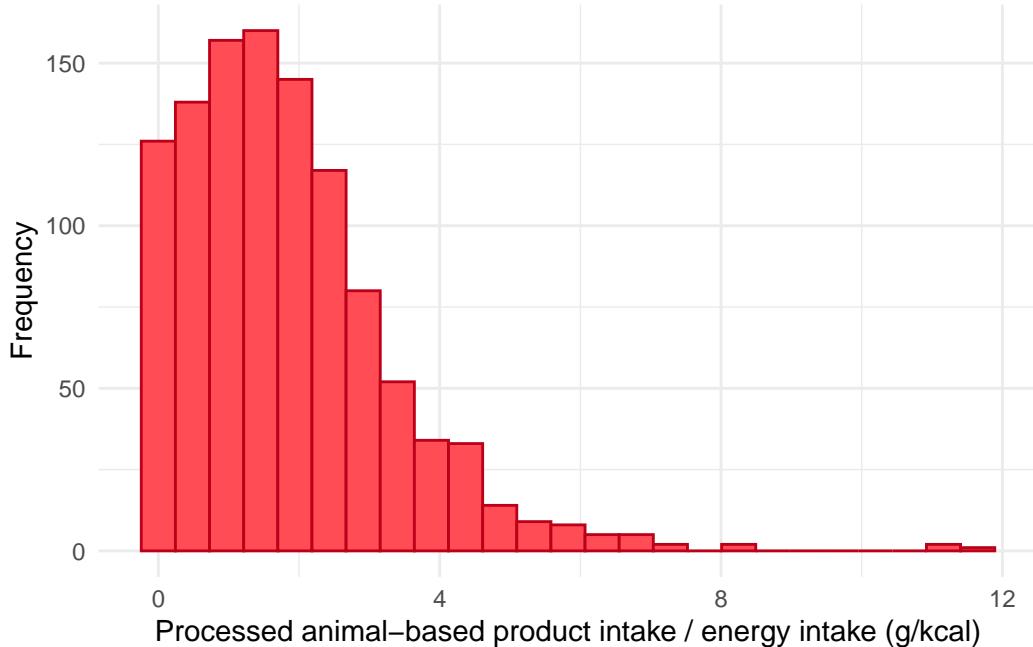


Figure 13: Distribution of processed animal-based product intake divided by daily energy intake.

```
pander(summary(aov(processedMeatIntake ~ cat, data = demo)))
```

Table 19: ANOVA between processed meat intake and FC groups.

Table 19: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|----------|
| cat | 2 | 27.23 | 13.62 | 6.328 | 0.001857 |
| Residuals | 1009 | 2171 | 2.152 | NA | NA |

From Figure 14, it appears subjects with FC<50 g/g at recruitment were more likely to consume no, or low levels of, processed meat.

```
demo %>%
  drop_na(processedMeatIntake, cat) %>%
  ggplot(aes(x = processedMeatIntake)) +
  geom_histogram(bins = 25, color = "#BC0019", fill = "#FF4C55") +
  theme_minimal()
```

```

xlab("Processed animal-based product intake / energy intake (g/kcal)") +
ylab("Frequency") +
facet_grid(rows = vars(cat))

```

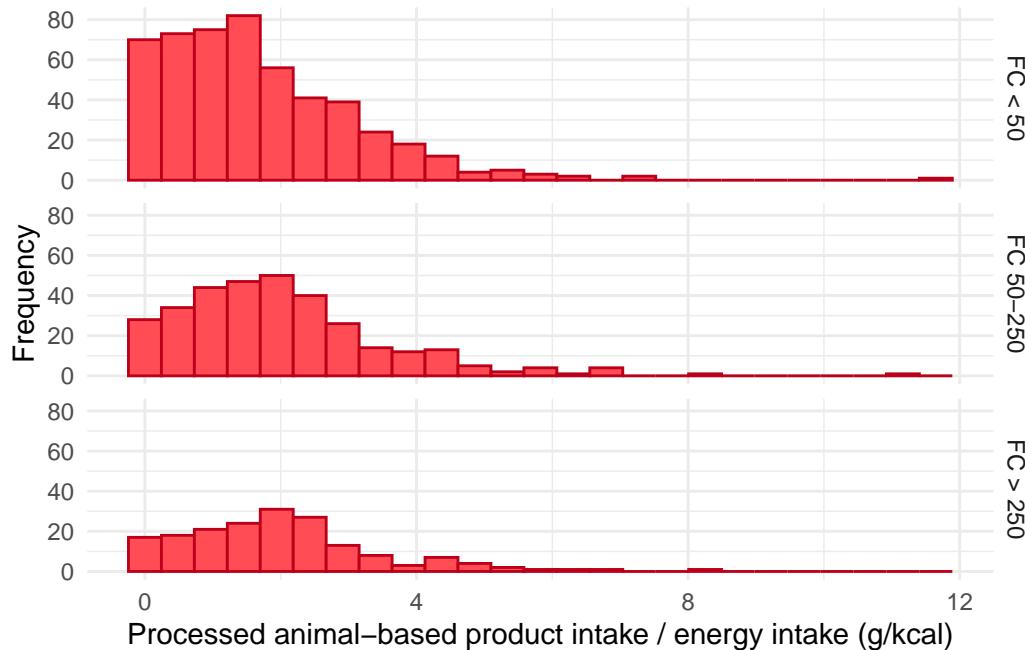


Figure 14: Distribution of processed animal-based product intake, divided by daily energy intake, and stratified by faecal calprotectin category.

Plant-based alternatives

As one would likely expect, consumption of processed plant-based alternatives is low.

```

FFQ$processedPlantIntake <- with(FFQ,
                                    (Milk3d_grams +
                                     Sav_etc10d_grams +
                                     Sav_etc10e_grams +
                                     Sav_etc10f_grams) /
                                    EnergykCAL) * 100

demo <- merge(demo,
                FFQ[, c("ParticipantNo", "processedPlantIntake")],
                by = "ParticipantNo",

```

```

    all.x = TRUE,
    all.y = FALSE)

demo %>%
  drop_na(processedPlantIntake) %>%
  ggplot(aes(x = processedPlantIntake)) +
  geom_histogram(bins = 25, color = "#069E79", fill = "#08C99B") +
  theme_minimal() +
  xlab("Processed plant-based alternative intake / energy intake (g/kcal)") +
  ylab("Frequency")

```

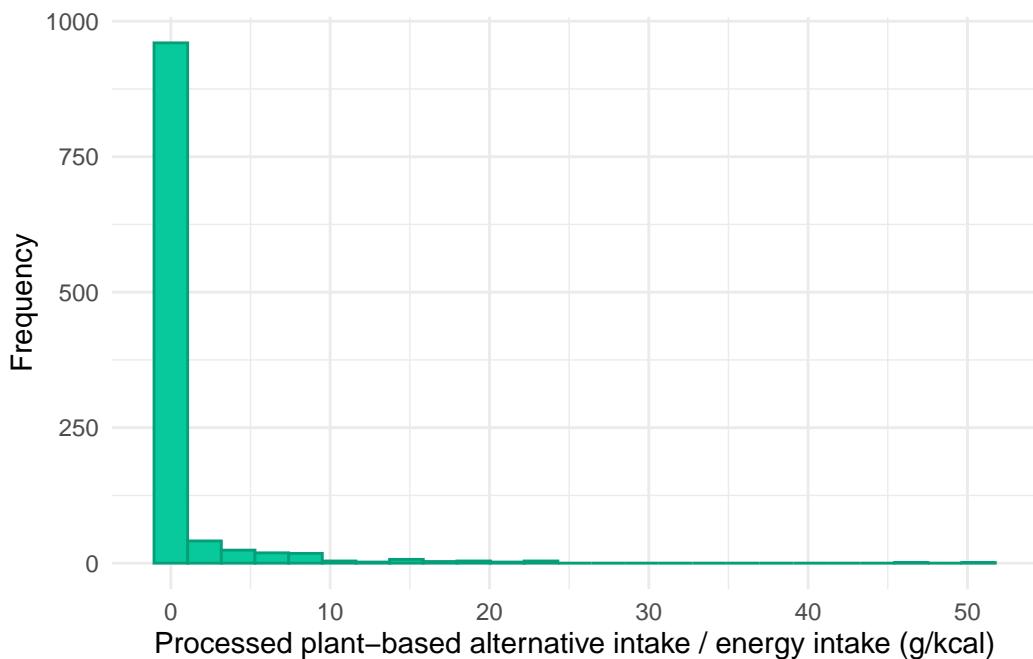


Figure 15: Distribution of processed plant-based alternatives divided by daily energy intake.

```
pander(summary(aov(processedPlantIntake ~ cat, data = demo)))
```

Table 20: ANOVA between processed plant-based alternatives intake and FC groups.

Table 20: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|-----|----|--------|---------|---------|--------|
| cat | 2 | 11.35 | 5.675 | 0.4328 | 0.6488 |

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|--------|
| Residuals | 1009 | 13230 | 13.11 | NA | NA |

Un-processed/minimally processed food subgroups

Fruit

```
FFQ$fruitIntake <- with(FFQ,
  (fruit12a_grams +
   fruit12b_grams +
   fruit12c_grams +
   fruit12c_grams +
   fruit12f_grams +
   fruit12g_grams +
   fruit12h_grams +
   fruit12i_grams +
   fruit12j_grams) /
  EnergykCAL) * 100

demo <- merge(demo,
  FFQ[, c("ParticipantNo", "fruitIntake")],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE)

demo %>%
  drop_na(fruitIntake) %>%
  ggplot(aes(x = fruitIntake)) +
  geom_histogram(bins = 25, color = "#C58901", fill = "#FFD639") +
  theme_minimal() +
  xlab("Fruit intake / energy intake (g/kcal)") +
  ylab("Frequency")
```

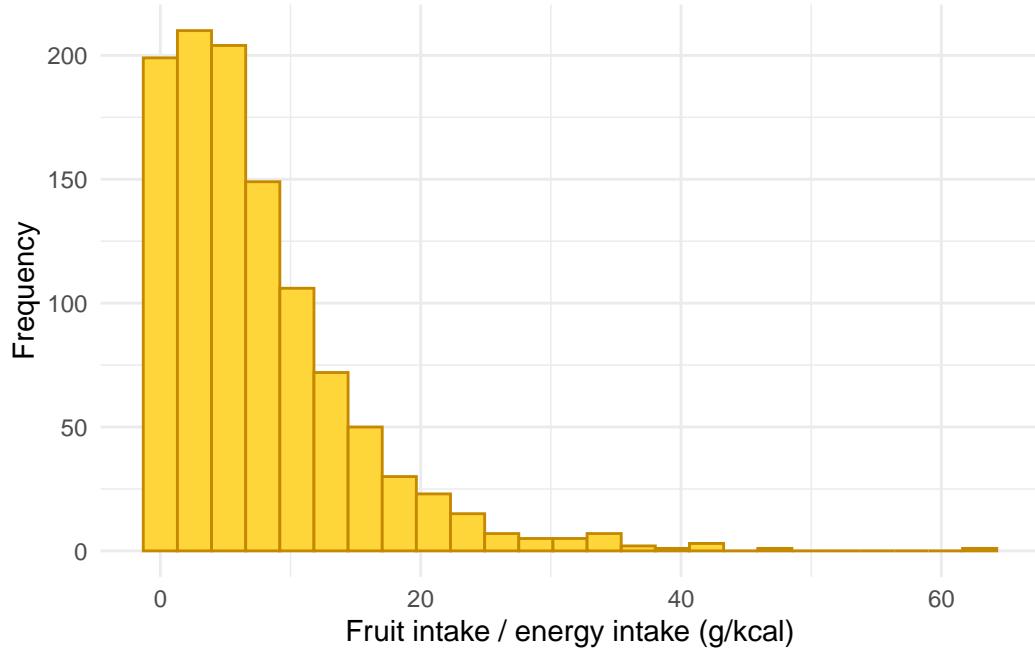


Figure 16: Distribution of fruit intake divided by daily energy intake.

```
pander(summary(aov(fruitIntake ~ cat, data = demo)))
```

Table 21: ANOVA between fruit intake and FC groups.

Table 21: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|--------|
| cat | 2 | 193.2 | 96.59 | 1.821 | 0.1624 |
| Residuals | 1009 | 53513 | 53.04 | NA | NA |

Vegetable and legumes

```
FFQ$vegIntake <- with(FFQ,
  (Veg11a_grams +
  Veg11b_grams +
  Veg11c_grams +
  Veg11d_grams +
  Veg11e_grams +
```

```

Veg11f_grams +
Veg11g_grams +
Veg11h_grams +
Veg11i_grams +
Veg11j_grams +
Veg11k_grams +
Veg11l_grams +
Veg11m_grams +
Veg11n_grams +
Veg11o_grams +
Veg11p_grams +
Pulses) /
EnergykCAL) * 100

demo <- merge(demo,
  FFQ[, c("ParticipantNo", "vegIntake")],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE)

demo %>%
  drop_na(vegIntake) %>%
  ggplot(aes(x = vegIntake)) +
  geom_histogram(bins = 25, color = "#662E9B", fill = "#A57CD9") +
  theme_minimal() +
  xlab("Vegetable and legume intake / energy intake (g/kcal)") +
  ylab("Frequency")

```

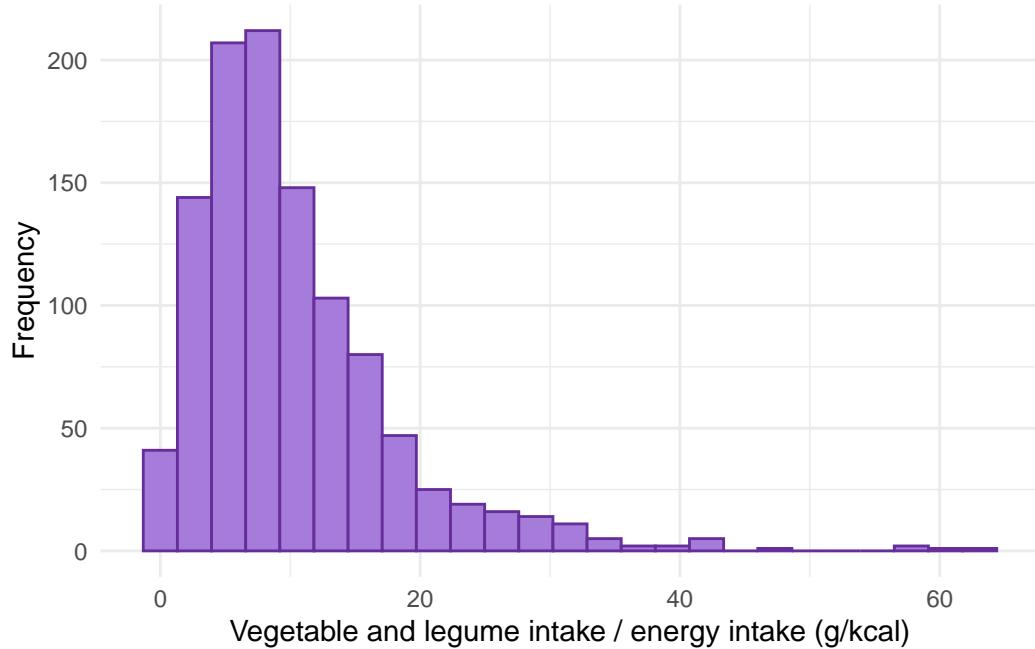


Figure 17: Distribution of vegetable and legume intake divided by daily energy intake.

```
pander(summary(aov(vegIntake ~ cat, data = demo)))
```

Table 22: ANOVA between vegetable/legume intake and FC groups.

Table 22: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|---------|
| cat | 2 | 335.3 | 167.6 | 2.71 | 0.06702 |
| Residuals | 1006 | 62228 | 61.86 | NA | NA |

Red meat

```
FFQ$redMeatIntake <- with(FFQ,
  (meat7d_grams +
   meat7e_grams +
   meat7h_grams) /
  EnergykCAL) * 100
demo <- merge(demo,
```

```

FFQ[, c("ParticipantNo", "redMeatIntake")],
by = "ParticipantNo",
all.x = TRUE,
all.y = FALSE)

demo %>%
  drop_na(redMeatIntake) %>%
  ggplot(aes(x = redMeatIntake)) +
  geom_histogram(bins = 25, color = "#93250B", fill = "#F34213") +
  theme_minimal() +
  xlab("VRed meat intake / energy intake (g/kcal)") +
  ylab("Frequency")

```

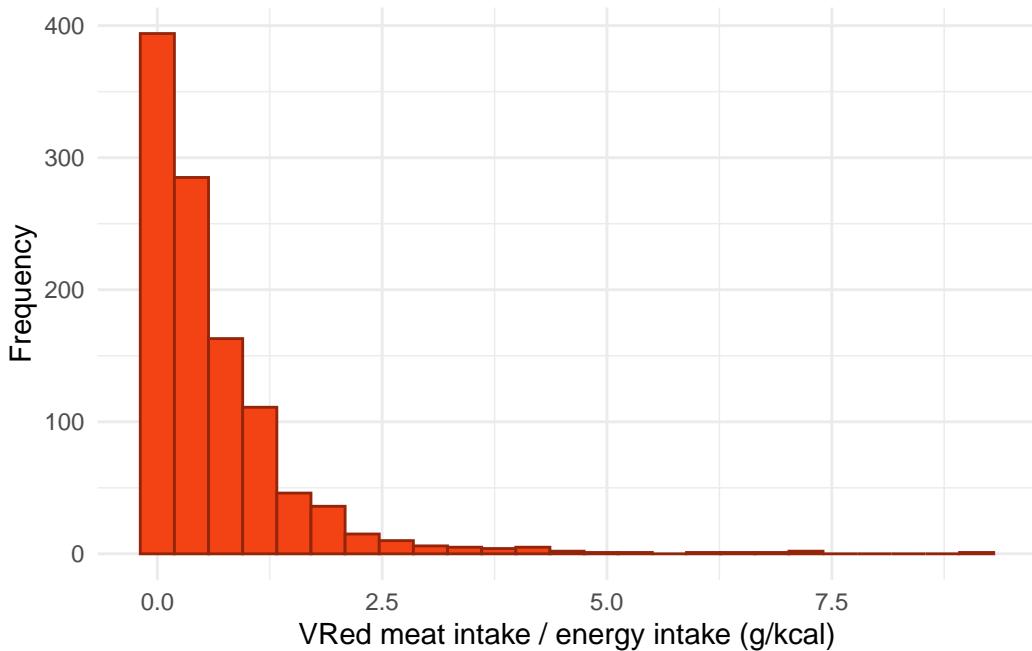


Figure 18: Distribution of red meat intake divided by daily energy intake.

```
pander(summary(aov(redMeatIntake ~ cat, data = demo)))
```

Table 23: ANOVA between red meat intake and FC groups.

Table 23: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|-----------|------|--------|---------|---------|--------|
| cat | 2 | 0.2782 | 0.1391 | 0.1716 | 0.8424 |
| Residuals | 1009 | 818 | 0.8107 | NA | NA |

White meat

```
FFQ$whiteMeatIntake <- with(FFQ,
                               meat7f_grams /
                               EnergykCAL) * 100
demo <- merge(demo,
               FFQ[, c("ParticipantNo", "whiteMeatIntake")],
               by = "ParticipantNo",
               all.x = TRUE,
               all.y = FALSE)

demo %>%
  drop_na(whiteMeatIntake) %>%
  ggplot(aes(x = whiteMeatIntake)) +
  geom_histogram(bins = 25, color = "#829399", fill = "#545F66") +
  theme_minimal() +
  xlab("White meat intake / energy intake (g/kcal)") +
  ylab("Frequency")
```

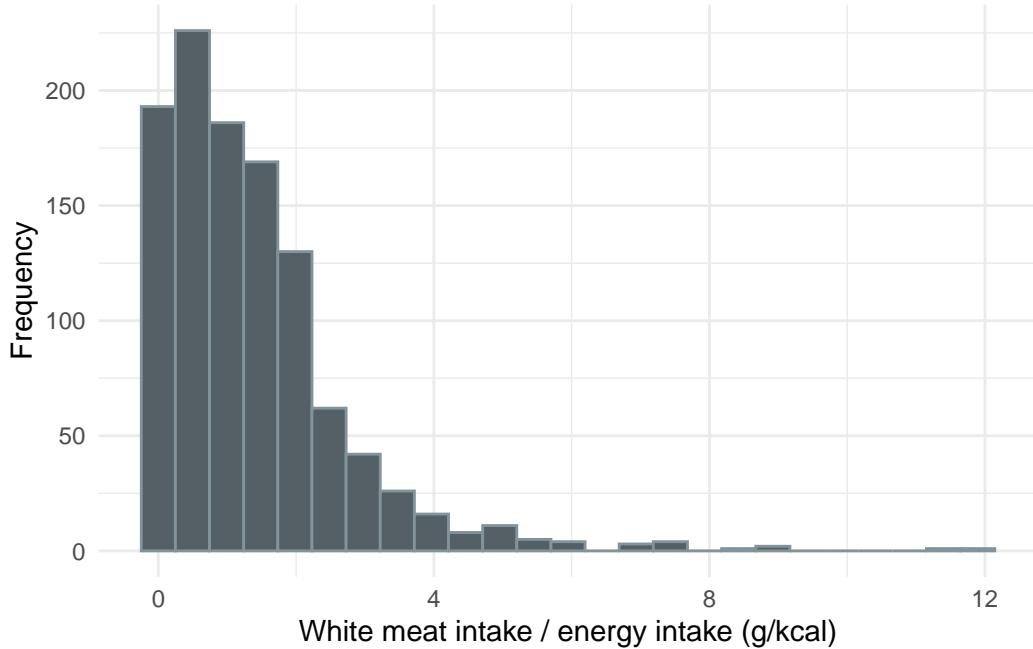


Figure 19: Distribution of white/oily fish intake divided by daily energy intake.

```
pander(summary(aov(whiteMeatIntake ~ cat, data = demo)))
```

Table 24: ANOVA between white meat intake and FC groups.

Table 24: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|--------|
| cat | 2 | 3.262 | 1.631 | 0.8655 | 0.4212 |
| Residuals | 1009 | 1901 | 1.884 | NA | NA |

Fish (white and oily)

```
FFQ$whiteFishIntake <- with(FFQ,
  (WhiteFish +
   OilyFish) /
  EnergykCAL) * 100
demo <- merge(demo,
  FFQ[, c("ParticipantNo", "whiteFishIntake")],
```

```

    by = "ParticipantNo",
    all.x = TRUE,
    all.y = FALSE)

demo %>%
  drop_na(whiteFishIntake) %>%
  ggplot(aes(x = whiteFishIntake)) +
  geom_histogram(bins = 25, color = "#003559", fill = "#006DAA") +
  theme_minimal() +
  xlab("White fish intake / energy intake (g/kcal)") +
  ylab("Frequency")

```

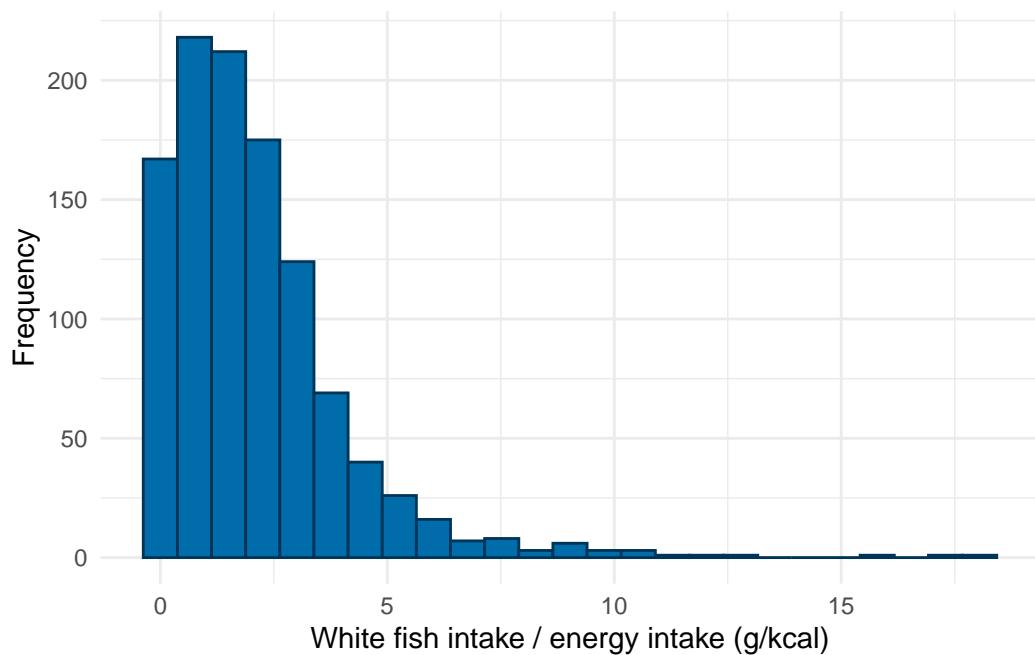


Figure 20: Distribution of white/oily fish intake divided by daily energy intake.

```
pander(summary(aov(whiteFishIntake ~ cat, data = demo)))
```

Table 25: ANOVA between fish (white and oily) intake and FC groups.

Table 25: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|--------|
| cat | 2 | 8.924 | 4.462 | 1.089 | 0.3369 |
| Residuals | 1003 | 4109 | 4.097 | NA | NA |

Percentage of energy intake

```

nova4 <- read_xlsx(paste0(upf.path, "NOVA4Scores.xlsx"))
colnames(nova4)[c(1, 6)] <- c("ParticipantNo", "UPF_perc")
demo <- merge(demo,
  nova4[, c("ParticipantNo", "UPF_perc")],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE
)

```

As an alternative to the above analyses, we have also explored the percentage of daily energy intake which is derived from ultra processed (UPF4) groups.

```

demo %>%
  drop_na(cat) %>%
  ggplot(aes(x = UPF_perc, color = diagnosis2, fill = diagnosis2)) +
  geom_histogram(bins = 25) +
  theme_minimal() +
  theme(legend.position = "none") +
  labs(
    x = "% of energy intake attributed to Nova 4 food and drink",
    y = "Frequency",
    color = "IBD type",
    fill = "IBD type"
  ) +
  scale_fill_manual(
    values = c("#CDEDF6", "#FF6B6B")
  ) +
  scale_color_manual(
    values = c("#5EB1BF", "#C24343")
  )

```

```
) +
  facet_grid(rows = vars(diagnosis2))
```

Warning: Removed 1132 rows containing non-finite outside the scale range
(`stat_bin()`).

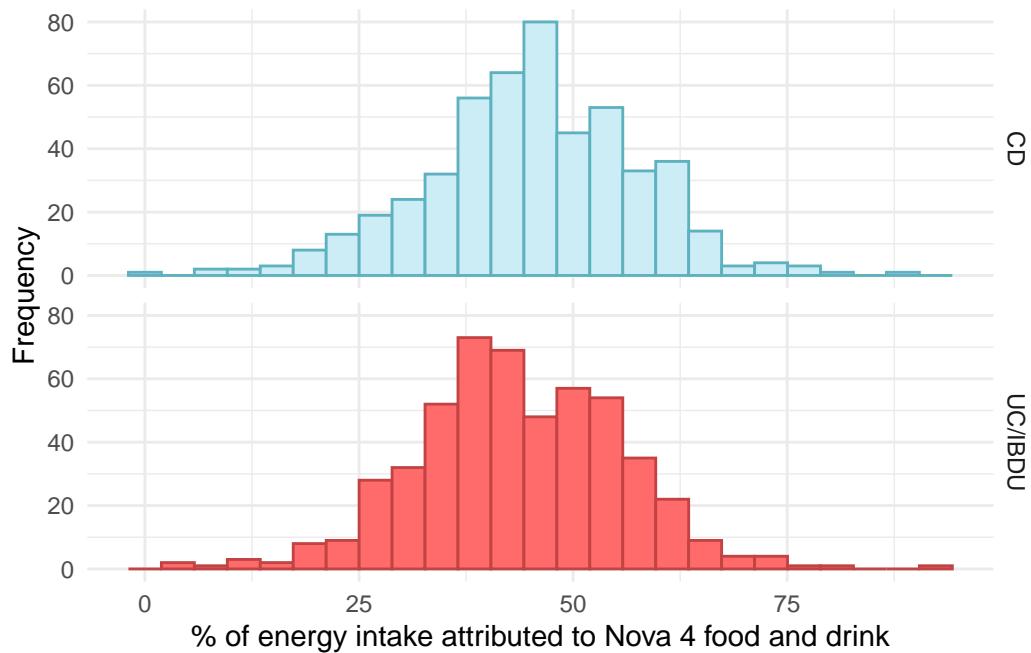


Figure 21: Distribution of the percentage of daily energy intake sourced from UPF (Nova score 4) food and drink.

```
demo %>%
  filter(diagnosis2 == "CD") %>%
  aov(formula = UPF_perc ~ cat) %>%
  summary() %>%
  pander()
```

Table 26: ANOVA between Nova 4 food as a percentage of energy intake and FC for Crohn's disease.

Table 26: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|--------|
| cat | 2 | 242.9 | 121.4 | 0.7854 | 0.4565 |
| Residuals | 494 | 76379 | 154.6 | NA | NA |

```
demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  aov(formula = UPF_perc ~ cat) %>%
  summary() %>%
  pander()
```

Table 27: ANOVA between Nova 4 food as a percentage of energy intake and FC for UC/IBDU.

Table 27: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|-----|--------|---------|---------|----------|
| cat | 2 | 1357 | 678.4 | 4.822 | 0.008423 |
| Residuals | 512 | 72042 | 140.7 | NA | NA |

```
p <- demo %>%
  filter(diagnosis2 == "UC/IBDU") %>%
  drop_na(cat, UPF_perc) %>%
  mutate(cat = fct_rev(cat)) %>%
  ggplot(aes(x = UPF_perc, fill = cat, color = cat)) +
  geom_density() +
  facet_grid(rows = vars(cat)) +
  labs(x = "Nova 4 food as a percentage of energy intake",
       y = "Density",
       fill = "FC group",
       color = "FC group")
cat_theme(p)
```

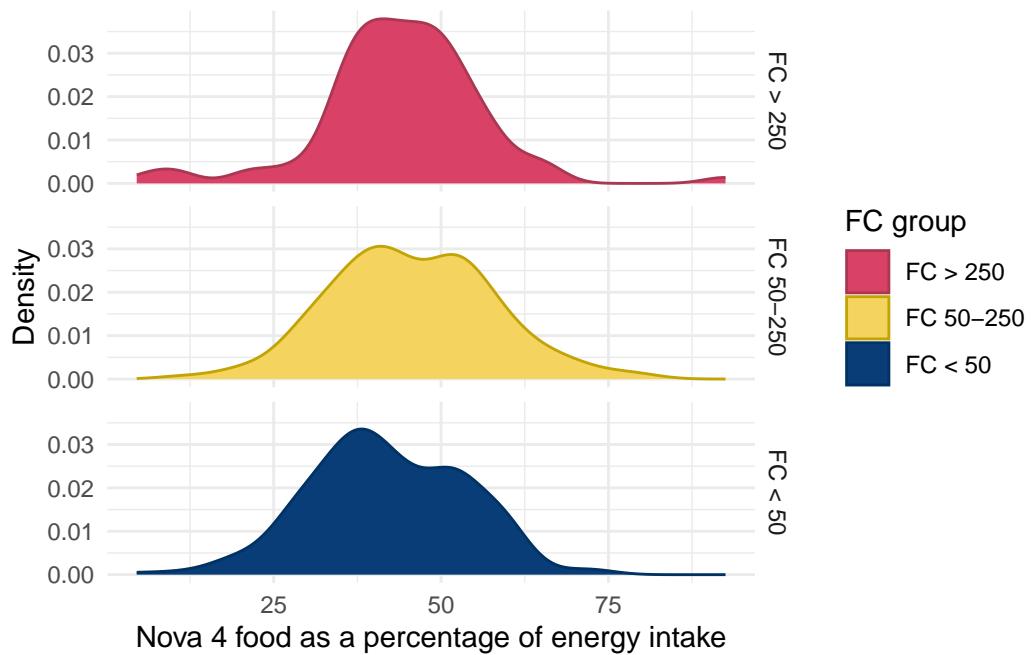


Figure 22: Distribution of Nova 4 food as a percentage of energy intake by FC in UC.

Alcohol use

```
demo <- merge(demo,
                 FFQ[, c("ParticipantNo", "Alcohol_percEng")],
                 by = "ParticipantNo",
                 all.x = TRUE,
                 all.y = FALSE)

demo %>%
  drop_na(Alcohol_percEng) %>%
  ggplot(aes(x = Alcohol_percEng, color = Sex, fill = Sex)) +
  geom_histogram(bins = 20) +
  facet_grid(cols = vars(Sex)) +
  theme_minimal() +
  labs(x = "Alcohol intake per energy",
       y = "Frequency",
       color = "Diagnosis",
       fill = "Diagnosis") +
```

```
scale_fill_manual(values = c("#FF966E", "#6A90A3")) +
scale_color_manual(values = c("#D16014", "#114B5F"))
```

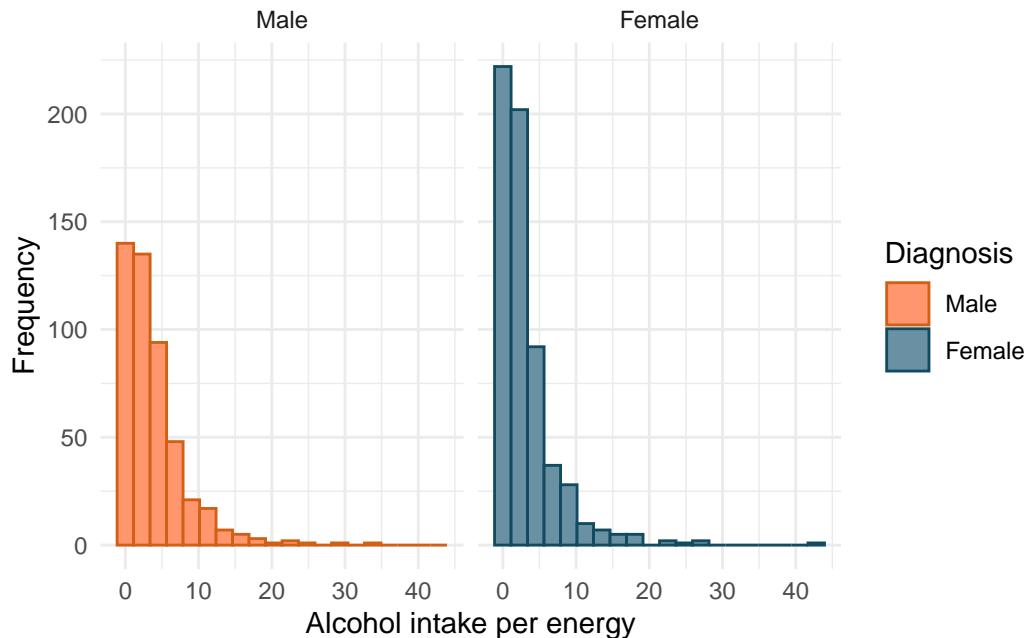


Figure 23: Distribution of alcohol per energy intake, stratified by sex.

```
pander(summary(aov(Alcohol_percEng ~ cat, data = demo)))
```

Table 28: ANOVA between alcohol intake and FC groups.

Table 28: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|--------|
| cat | 2 | 60.53 | 30.26 | 1.624 | 0.1977 |
| Residuals | 1009 | 18806 | 18.64 | NA | NA |

Diet quality index

```
demo %>%
  drop_na(dqi_tot) %>%
```

```

ggplot(aes(x = dqi_tot, color = diagnosis2, fill = diagnosis2)) +
  geom_histogram(bins = 20) +
  facet_grid(cols = vars(diagnosis2)) +
  theme_minimal() +
  labs(x = "Diet quality index",
       y = "Frequency",
       color = "Diagnosis",
       fill = "Diagnosis") +
  scale_fill_manual(values = c("#86DEB7", "#FC5A66")) +
  scale_color_manual(values = c("#529176", "#AC353F"))

```

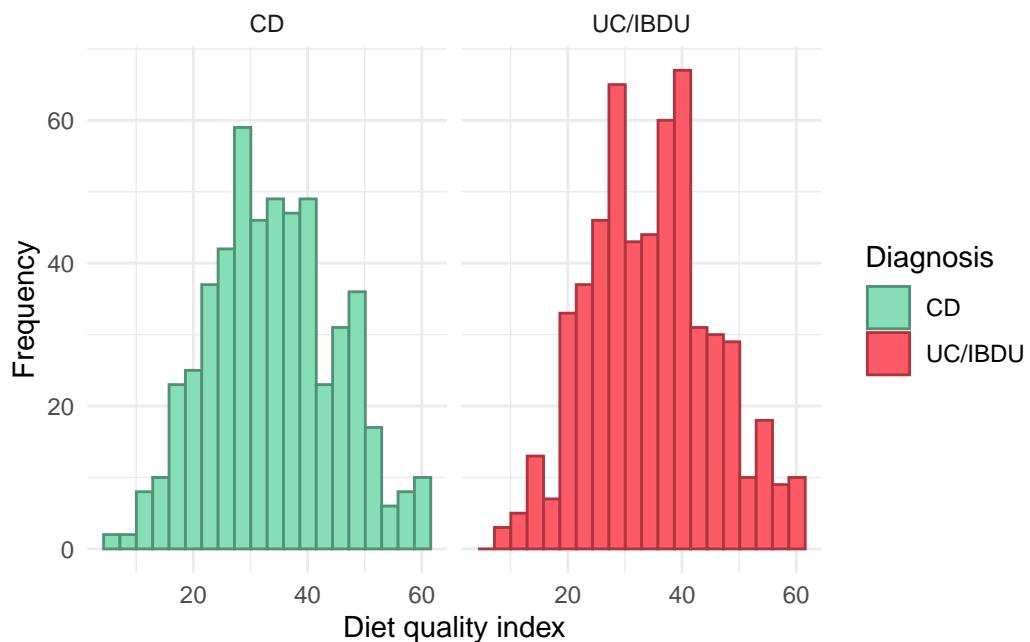


Figure 24: Distribution of diet quality index, stratified by IBD type.

```

demo %>%
  drop_na(dqi_tot, cat) %>%
  pull(dqi_tot) %>%
  quantile() %>%
  knitr::kable(digits = 2,
    caption = "Diet quality index quantiles for the FFQ subcohort.",
    col.names = c("Quantile", "DQI"))
)

```

Table 29: Diet quality index quantiles for the FFQ subcohort.

| Quantile | DQI |
|----------|-------|
| 0% | 5.59 |
| 25% | 26.60 |
| 50% | 33.99 |
| 75% | 41.36 |
| 100% | 60.00 |

```
pander(summary(aov(dqi_tot ~ cat, data = demo)))
```

Table 30: ANOVA between diet quality index and FC groups.

Table 30: Analysis of Variance Model

| | Df | Sum Sq | Mean Sq | F value | Pr(>F) |
|------------------|------|--------|---------|---------|---------|
| cat | 2 | 676.6 | 338.3 | 2.818 | 0.06019 |
| Residuals | 1009 | 121118 | 120 | NA | NA |

```
saveRDS(demo, paste0(outdir, "demo-diet.RDS"))
```

Comparison

Figure 25 presents macronutrient, PUFA and UPF intake as percentages of total energy intake.

```
FFQ$Prot_percEng <- ((FFQ$Protng * 4) / FFQ$EnergykCAL) * 100

FFQ <- merge(FFQ,
  nov4[, c("ParticipantNo", "UPF_perc")],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE
)

comparison <- reshape2::melt(FFQ,
  id.vars = "ParticipantNo",
  measure.vars = c(
```

```

    "CHO_percEng",
    "Fat_percEng",
    "Prot_percEng",
    "SatFat_percEng",
    "PUFA_percEng",
    "UPF_perc"
)
)

comparison <- merge(comparison,
  demo[, c("ParticipantNo", "Sex", "diagnosis2")],
  by = "ParticipantNo",
  all.x = TRUE,
  all.y = FALSE
)

comparison$variable <- factor(comparison$variable,
  levels = c(
    "CHO_percEng",
    "Fat_percEng",
    "Prot_percEng",
    "SatFat_percEng",
    "PUFA_percEng",
    "UPF_perc"
),
  labels = c(
    "Carbohydrate",
    "Fat",
    "Protein",
    "Saturated fat",
    "Polyunsaturated fatty acids",
    "Ultra-processed food"
))
)

p <- ggplot(
  comparison,
  aes(color = variable, fill = variable, y = value, x = Sex)
) +
  geom_violin() +
  facet_grid(~diagnosis2,
    scales = "free_x",
    space = "free_x",

```

```

    switch = "x"
) +
theme_minimal() +
theme(
  strip.placement = "outside",
  strip.background = element_rect(fill = "white"),
  strip.clip = "on",
  axis.title.x = element_blank(),
  legend.position = "bottom"
) +
scale_fill_manual(
  values = c(
    "#4F359B",
    "#FFED49",
    "#2EC4B6",
    "#E71D36",
    "#FF9F1C",
    "#80BF56"
  )
) +
scale_color_manual(
  values = c(
    "#392376",
    "#ADA009",
    "#00877C",
    "#9F1C29",
    "#B06B01",
    "#568238"
  )
) +
labs(
  y = "% of total energy intake",
  color = "",
  fill = ""
) + guides(
  colour = guide_legend(nrow = 1),
  fill = guide_legend(nrow = 1))
ggsave("plots/baseline/diet.png", p, width = 12 * 0.8, height = 7 * 0.8)
ggsave("plots/baseline/diet.pdf", p, width = 12 * 0.8, height = 7 * 0.8)
p

```

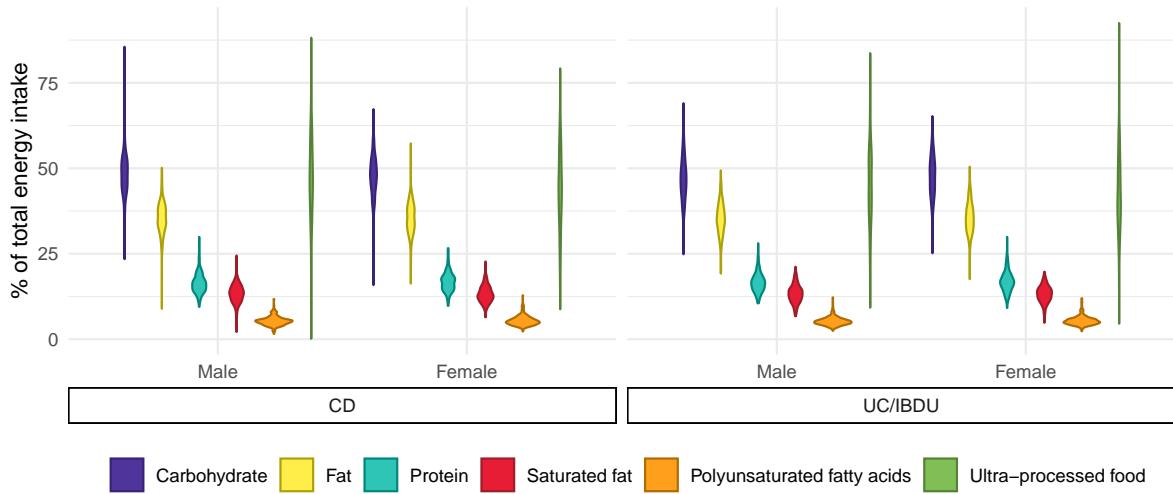


Figure 25: Dietary distribution of the FFQ subcohort expressed as percentages of energy intake and stratified by sex and diagnosis of either Crohn's disease or ulcerative colitis/inflammatory bowel disease unclassified.

Missingness

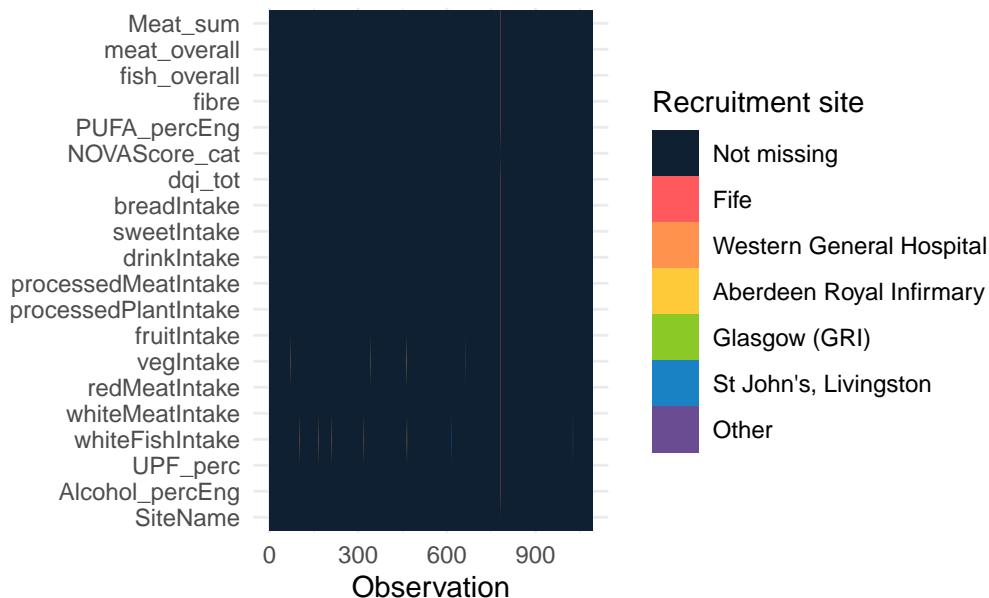
```
demo %>%
  filter(ParticipantNo %in% FFQ$ParticipantNo) %>%
  select(
    Meat_sum,
    meat_overall,
    fish_overall,
    fibre,
    PUFA_percEng,
    NOVAScore_cat,
    dqi_tot,
    breadIntake,
    sweetIntake,
    drinkIntake,
    processedMeatIntake,
    processedPlantIntake,
    fruitIntake,
    vegIntake,
    redMeatIntake,
    whiteMeatIntake,
```

```

whiteFishIntake,
UPF_perc,
Alcohol_percEng,
SiteName
) %>%
missing_plot2(title = "Disease phenotyping missingness")

```

Disease phenotyping missingness



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: *DiagrammeRsvg(v.0.1)*, *DiagrammeR(v.1.0.11)*, *pander(v.0.6.5)*, *knitr(v.1.47)*, *table1(v.1.4.3)*, *patchwork(v.1.2.0)*, *datefixR(v.1.6.1)*, *readxl(v.1.4.3)*, *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)*, *tidyrr(v.1.3.1)*, *tibble(v.3.2.1)*, *ggplot2(v.3.5.1)*, *tidyverse(v.2.0.0)* and *plyr(v.1.8.9)*

loaded via a namespace (and not attached): *shape(v.1.4.6.1)*, *gtable(v.0.3.5)*, *xfun(v.0.44)*, *htmlwidgets(v.1.6.4)*, *visNetwork(v.2.1.2)*, *lattice(v.0.22-6)*, *tzdb(v.0.4.0)*, *vctrs(v.0.6.5)*, *tools(v.4.4.0)*, *generics(v.0.1.3)*, *curl(v.5.2.1)*, *fansi(v.1.0.6)*, *pan(v.1.9)*, *jomo(v.2.7-6)*, *pkgconfig(v.2.0.3)*, *Matrix(v.1.7-0)*, *RColorBrewer(v.1.1-3)*, *lifecycle(v.1.0.4)*, *compiler(v.4.4.0)*, *farver(v.2.1.2)*, *textshaping(v.0.4.0)*, *munsell(v.0.5.1)*, *codetools(v.0.2-20)*, *htmltools(v.0.5.8.1)*, *yaml(v.2.3.8)*, *finalfit(v.1.0.7)*, *glmnet(v.4.1-8)*, *Formula(v.1.2-5)*, *mice(v.3.16.0)*, *nloptr(v.2.0.3)*, *pillar(v.1.9.0)*, *MASS(v.7.3-60.2)*, *iterators(v.1.0.14)*, *rpart(v.4.1.23)*, *boot(v.1.3-30)*, *mitml(v.0.4-5)*, *foreach(v.1.5.2)*, *nlme(v.3.1-164)*, *tidyselect(v.1.2.1)*, *digest(v.0.6.35)*, *stringi(v.1.8.4)*, *reshape2(v.1.4.4)*, *splines(v.4.4.0)*, *labeling(v.0.4.3)*, *fastmap(v.1.2.0)*, *grid(v.4.4.0)*, *colorspace(v.2.1-0)*, *cli(v.3.6.2)*, *magrittr(v.2.0.3)*, *survival(v.3.5-8)*, *utf8(v.1.2.4)*, *broom(v.1.0.6)*, *withr(v.3.0.0)*, *scales(v.1.3.0)*, *backports(v.1.5.0)*, *timechange(v.0.3.0)*, *rmarkdown(v.2.27)*, *nnet(v.7.3-19)*, *lme4(v.1.1-35.3)*, *cellranger(v.1.1.0)*, *ragg(v.1.3.2)*, *hms(v.1.1.3)*, *evaluate(v.0.23)*, *V8(v.4.4.2)*, *rlang(v.1.1.3)*, *Rcpp(v.1.0.12)*, *glue(v.1.7.0)*, *minqa(v.1.2.7)*, *jsonlite(v.1.8.8)*, *R6(v.2.5.1)* and *systemfonts(v.1.3.1)*

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