ABG-VBG Analysis

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reminder: if rendering fails, consider deleting cached items: e.g. rm -rf ABG-VBG-analysis-2025-12-7_cache/

1 TODO:

- ☐ **High missingness in the 3-level CO categories.** pco2_cat_abg missing in 1,630/2,491; pco2_cat_vbg in 1,778/2,491; pco2_cat_calc in 2,200/2,491. This drives the complete-case drop noted above and will also affect any categorical CO models. Evidence: skim table. - evaluate if this is still a problem? **High apparent missingness in 3-level CO categories (complete-case drop).** The three-category sections trigger "Removed rows…" and show large sample loss. This is expected if many encounters lack PaCO /VBG CO (and you haven't switched those analyses over to MI or inverse-probability-of-observation). Flag it in the text or impute/weight appropriately.
- ☐ **ABG vs VBG IPW tuning asymmetry - these should be the same. Currently,** The VBG block shows different tuning prose ("changed trees and bag fraction"), implying divergence from the ABG settings; just document so readers don't infer drift as a bias. Evidence: the VBG section text notes altered tuning.
- ☐ **Shapley plots emit warnings. l**oess near-singularities and pseudo-inverse messages (often due to very flat x-ranges or duplicated x). "aesthetics dropped: colour" (stat layer not using mapped colour), "label cannot be a <element_blank> object."

  NOT YET ready for this one. Create Cohort Flow Diagram [New analysis/graphic needed]

  - ☐ • Show numbers at each step:
  - ☐ • Starting suspected-hypercapnia cohort.
  - ☐ • Exclusions (age <18, missing key data, etc.).
  - ☐ • Final analytic cohort.
  - ☐ • Split into ABG only, VBG only, both, and neither.
  - ☐ • This addresses STROBE's "participants" and flow requirements.

-

2 Data Pre-processing

This code pulls in the master database (a STATA file) and does some initial cleaning - this will only need to be run once, and then the data can be accessed in the usual way.

2.1 1) Seed escrow (reproducibility anchors)

Table 1: Seed escrow for MI, GBM, and SHAP runs

component	seed
Multiple imputation (mice)	20251206
ABG propensity GBM (non-MI)	42
VBG propensity GBM (non-MI)	42
SHAP (fastshap/shapviz)	123
MI GBM seeds (ABG per imputation)	20251206 + imputation index
MI GBM seeds (VBG per imputation)	30251206 + imputation index

Chunk seed-escrow runtime: 0.00 s

Chunk gt-pdf-helper runtime: 0.00 s

Converts the data from a STATA format to rdata if the rdata file does not exist. If it does already exist, it just loads that.

```
# data_dir_name <- '/Users/blocke/Box Sync/Residency Personal Files/Scholarly Work/Locke Research Projects/abg-vbg-project/data'
data_dir_name <- '/Users/reblocke/Research/abg-vbg-project/data'

rdata_file <- file.path(data_dir_name, "full_trinetx.rdata")
stata_file <- file.path(data_dir_name, "full_db.dta")

if (!dir.exists(data_dir_name)) {
  dir.create(data_dir_name)
  message("Directory 'data' created.")
} else {
  message("Directory 'data' already exists.")
}
```

```
Directory 'data' already exists.
```

```r
if (file.exists(rdata_file)) {
  load(rdata_file)
  message("Loaded existing dataset from 'full_trinetx.rdata'.")
} else {
  message("RData file not found. Reading Stata dataset...")
  stata_data <- read_dta(stata_file)

  message("Extracting variable labels...")
  var_label(stata_data)

  message("Extracting value labels...")
  sapply(stata_data, function(x) if (is.labelled(x)) val_labels(x))

  save(stata_data, file = rdata_file)
  message("Dataset saved as 'full_trinetx.rdata'.")

  load(rdata_file)
  message("Loaded newly saved dataset from 'full_trinetx.rdata'.")
}
```

```
Loaded existing dataset from 'full_trinetx.rdata'.
```

Chunk load-trinetx-data runtime: 7.08 s

```r
covars_gbm <- c(
  "age_at_encounter","sex","race_ethnicity","curr_bmi",
  "copd","asthma","osa","chf","acute_nmd","phtn","ckd","dm",
  "location","encounter_type","temp_new","sbp","dbp","hr","spo2",
  "sodium","serum_cr","serum_hco3","serum_cl","serum_lac","serum_k",
  "wbc","plt","bnp","serum_phos","serum_ca"
)

gbm_params <- list(
  n.trees           = 1500,
  interaction.depth = 3,
```

```
  shrinkage          = 0.01,
  bag.fraction       = 0.8,
  cv.folds           = 5,
  stop.method        = "es.mean",
  n.cores            = parallel::detectCores()
)

formula_abg      <- reformulate(covars_gbm, response = "has_abg")
formula_vbg      <- reformulate(covars_gbm, response = "has_vbg")
```

Chunk propensity-config runtime: 0.01 s

Creating subset_data

```
set.seed(123)
rows_to_keep <- round(nrow(stata_data) * 1) #1 for real run
subset_data <- stata_data[sample(nrow(stata_data), rows_to_keep), ]

subset_data <- subset_data %>%
  filter(encounter_type != 1)

table(subset_data$encounter_type)
```

```
     2      3
171727 343559
```

```
dim(subset_data)
```

```
[1] 515286    546
```

Chunk sample-subset-data runtime: 5.60 s

Generating Codebook for the Full Dataset

```r
message("Generating codebook for the dataset...")
```

```
Generating codebook for the dataset...
```

```r
study_codebook <- codebookr::codebook(
  stata_data,
  title = "Full TrinetX",
  subtitle = "Dataset Documentation",
  description = "This dataset contains patient-level records from the TrinetX database.
                 It has been processed and converted from the original Stata file."
)
codebook_file <- results_path("codebookr.docx")
print(study_codebook, codebook_file)
message("Codebook saved to: ", codebook_file)
```

```
Codebook saved to: /Users/reblocke/Research/abg-vbg-project/Results/codebookr.docx
```

Chunk codebook-export-full runtime: 95.53 s

New Variable - Death at 60 days

```r
subset_data <- subset_data %>%
  mutate(
    ## 1. Did the patient die?
    died = if_else(!is.na(death_date), 1L, 0L),

    ## 2. Absolute death date (if death_date is an offset)
    death_abs = if_else(!is.na(death_date),
                        encounter_date + death_date,
                        as.Date(NA)),

    ## 3. Year month (YM) for encounter and death
    enc_ym   = floor_date(encounter_date, unit = "month"),
    death_ym = floor_date(death_abs      , unit = "month"),
```

```r
    ## 4. Reference censoring date: 1 Jun 2024
    ref_ym = ymd("2024-06-01"),

    ## 5. Months from encounter to death or censoring
    months_death_or_cens = case_when(
      !is.na(death_ym) ~ interval(enc_ym, death_ym) %/% months(1),
      TRUE             ~ interval(enc_ym, ref_ym)   %/% months(1)
    ),

    ## 6. Remove impossible values
    months_death_or_cens = if_else(
      months_death_or_cens < 0 | months_death_or_cens > 16,
      NA_integer_, months_death_or_cens
    ),

    ## 7. Death within one or two months
    died_1mo = if_else(died == 1 & months_death_or_cens <  1, 1L, 0L),
    died_2mo = if_else(died == 1 & months_death_or_cens <= 1, 1L, 0L),

    ## 8. Month of death (missing if censored)
    death_time = if_else(died == 1, months_death_or_cens, NA_integer_),

    ## 9. Death within 60 days (new variable)
    death_60d = if_else(died == 1 & death_abs <= (encounter_date + days(60)), 1L, 0L)
  ) %>%
  select(-enc_ym, -death_ym)

subset_data <- subset_data %>%
  mutate(
    death_60d = if_else(died == 1 & death_abs <= (encounter_date + days(60)), 1L, 0L)
  )
```

Chunk derive-death-60d runtime: 1.73 s

```r
table(subset_data$death_60d, useNA = "ifany")
```

```
     0      1
461485  53801
```

```r
prop.table(table(subset_data$death_60d, useNA = "ifany"))
```

```
      0       1
0.89559 0.10441
```

```r
summary(subset_data$death_60d)
```

```
   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
 0.0000  0.0000  0.0000  0.1044  0.0000  1.0000
```

Chunk death-60d-summary runtime: 0.05 s

2.2 2) Baseline tables

2.2.1 2.1 Table 1A and 1B:

```r
# Robust derivation of analysis variables + helper for Table 1 production
# ------------------------------------------------------------------------

# helper: label binary 0/1 → "No"/"Yes"
bin_lab <- function(x) factor(x, levels = c(0, 1), labels = c("No", "Yes"))

subset_data <- subset_data %>%
  mutate(
```

```r
    ## ensure 0/1 numerics (avoids factor-level coercion)
    across(c(has_abg, has_vbg, hypercap_on_abg, hypercap_on_vbg),
           ~ as.numeric(as.character(.))),

    ## derive ABG / VBG hypercapnia groups
    abg_group
    = case_when(
      has_abg == 0                          ~ "No ABG",
      has_abg == 1 & hypercap_on_abg == 0   ~ "ABG_NoHypercapnia",
      has_abg == 1 & hypercap_on_abg == 1   ~ "ABG_Hypercapnia",
      TRUE                                  ~ "Missing"
    ),
    vbg_group = case_when(
      has_vbg == 0                          ~ "No VBG",
      has_vbg == 1 & hypercap_on_vbg == 0   ~ "VBG_NoHypercapnia",
      has_vbg == 1 & hypercap_on_vbg == 1   ~ "VBG_Hypercapnia",
      TRUE                                  ~ "Missing"
    ),

    ## factorise groups with explicit NA/Missing level
    abg_group = factor(
      abg_group,
      levels = c("No ABG", "ABG_NoHypercapnia", "ABG_Hypercapnia", "Missing")
    ),
    vbg_group = factor(
      vbg_group,
      levels = c("No VBG", "VBG_NoHypercapnia", "VBG_Hypercapnia", "Missing")
    ),

    ## labelled covariates
    sex_label      = factor(sex, levels = c(0, 1), labels = c("Female", "Male")),
    race_ethnicity_label     = factor(
      race_ethnicity,
      levels = c(0, 1, 2, 3, 4, 5, 6),
      labels = c("White", "Black or African American", "Hispanic",
                 "Asian", "American Indian", "Pacific Islander", "Unknown")
```

```
    ), location_label     = factor(
      location,
      levels = c(0, 1, 2, 3),
      labels = c("South", "Northeast" ,"Midwest", "West")
    ), encounter_type_label = factor(
      encounter_type,
      levels = c(2, 3),
      labels = c("Emergency", "Inpatient")
    ),
    osa_label      = bin_lab(osa),
    asthma_label   = bin_lab(asthma),
    copd_label     = bin_lab(copd),
    chf_label      = bin_lab(chf),
    nmd_label      = bin_lab(nmd),
    phtn_label     = bin_lab(phtn),
    ckd_label      = bin_lab(ckd),
    diabetes_label = bin_lab(dm)
  )

# variables to summarise
vars <- c(
  "age_at_encounter", "curr_bmi", "sex_label", "race_ethnicity_label", "location_label",
  "osa_label", "asthma_label", "copd_label", "chf_label", "nmd_label",
  "phtn_label", "ckd_label", "diabetes_label", "encounter_type_label", "vbg_co2", "paco2"
)

# Table 1 constructor
make_table1 <- function(data, group_var, caption = "") {
  group_sym <- rlang::sym(group_var)

  data %>%
    filter(!is.na(!!group_sym),                    # drop explicit NA
           !!group_sym != "Missing") %>%           # drop "Missing" cohort
    droplevels() %>%                               # trim empty factor levels
    select(all_of(c(group_var, vars))) %>%
    gtsummary::tbl_summary(
```

```
      by   = !!group_sym,
      type = list(sex_label ~ "categorical"),
      statistic = list(
        gtsummary::all_continuous()  ~ "{mean} ± {sd}; {N_miss}/{N_obs} missing ({p_miss}%)",
        gtsummary::all_categorical() ~ "{n} ({p}%)"
      ),
      digits   = list(gtsummary::all_continuous() ~ 1),
      missing  = "no"                                  # no gtsummary missing column/row
    ) %>%
    gtsummary::modify_header(label = "**Variable**") %>%
    gtsummary::modify_caption(caption)
}

# build tables
table1A <- make_table1(subset_data, "abg_group", caption = "Table 1A: ABG cohorts")
table1B <- make_table1(subset_data, "vbg_group", caption = "Table 1B: VBG cohorts")

table1A
```

```
table1B
```

Chunk derive-table1-cohorts runtime: 7.95 s

Generating Word Doc for Table 1A & 1B

```
ft_table1A <- as_flex_table(table1A)
ft_table1B <- as_flex_table(table1B)

doc <- read_docx() %>%
  body_add_par("Table 1A. Baseline Characteristics by ABG Group", style = "heading 1") %>%
  body_add_flextable(ft_table1A) %>%
  body_add_par("Table 1B. Baseline Characteristics by VBG Group", style = "heading 1") %>%
  body_add_flextable(ft_table1B)

print(doc, target = results_path("Table1_ABG_VBG.docx"))
```

Chunk export-table1a-table1b-word runtime: 0.65 s

Variable	**No ABG** N = 328,044[1]	**ABG_NoHypercapnia** N = 129,429[1]	**ABG_Hypercapnia** N =
Age (years)	58.1 ± 18.1; 0.0/328,044.0 missing (0.0%)	60.8 ± 17.1; 0.0/129,429.0 missing (0.0%)	62.1 ± 16.4; 0.0/57,813.0 mis
Current BMI kg/m2	32.3 ± 8.7; 184,223.0/328,044.0 missing (56.2%)	28.6 ± 6.9; 75,826.0/129,429.0 missing (58.6%)	29.8 ± 7.9; 33,496.0/57,813.0 m
sex_label			
Female	169,023 (52%)	57,767 (45%)	27,116 (47%)
Male	159,021 (48%)	71,662 (55%)	30,697 (53%)
race_ethnicity_label			
White	200,033 (61%)	81,357 (63%)	39,784 (69%)
Black or African American	62,418 (19%)	19,197 (15%)	8,082 (14%)
Hispanic	23,548 (7.2%)	7,464 (5.8%)	2,757 (4.8%)
Asian	4,880 (1.5%)	2,739 (2.1%)	789 (1.4%)
American Indian	1,971 (0.6%)	1,768 (1.4%)	316 (0.5%)
Pacific Islander	460 (0.1%)	162 (0.1%)	56 (<0.1%)
Unknown	34,734 (11%)	16,742 (13%)	6,029 (10%)
location_label			
South	138,843 (42%)	70,729 (55%)	32,694 (57%)
Northeast	93,209 (28%)	23,262 (18%)	12,975 (22%)
Midwest	22,924 (7.0%)	10,703 (8.3%)	4,844 (8.4%)
West	73,068 (22%)	24,735 (19%)	7,300 (13%)
osa_label	60,653 (18%)	17,709 (14%)	11,965 (21%)
asthma_label	48,456 (15%)	13,049 (10%)	8,268 (14%)
copd_label	60,214 (18%)	21,195 (16%)	18,846 (33%)
chf_label	59,770 (18%)	25,469 (20%)	16,219 (28%)
nmd_label	11,891 (3.6%)	5,861 (4.5%)	2,487 (4.3%)
phtn_label	23,854 (7.3%)	10,513 (8.1%)	7,347 (13%)
ckd_label	54,528 (17%)	24,849 (19%)	11,769 (20%)
diabetes_label	93,007 (28%)	37,426 (29%)	18,521 (32%)
encounter_type_label			
Emergency	142,713 (44%)	19,196 (15%)	9,818 (17%)
Inpatient	185,331 (56%)	110,233 (85%)	47,995 (83%)
VBG PCO2	45.5 ± 10.5; 233,430.0/328,044.0 missing (71.2%)	42.0 ± 11.2; 91,782.0/129,429.0 missing (70.9%)	57.4 ± 18.4; 40,411.0/57,813.0 m
Arterial PCO2	NA ± NA; 328,044.0/328,044.0 missing (100.0%)	35.5 ± 6.1; 0.0/129,429.0 missing (0.0%)	58.5 ± 20.4; 0.0/57,813.0 mis

[1]Mean ± SD; N Missing/No. obs. missing (% Missing); n (%)

Variable	**No VBG** N = 365,623[1]	**VBG_NoHypercapnia** N = 105,646[1]	**VBG_Hypercapnia** N =
Age (years)	59.4 ± 17.8; 0.0/365,623.0 missing (0.0%)	58.1 ± 17.8; 0.0/105,646.0 missing (0.0%)	61.0 ± 16.7; 0.0/44,017.0 mis
Current BMI kg/m2	31.8 ± 8.5; 192,892.0/365,623.0 missing (52.8%)	28.7 ± 7.2; 69,615.0/105,646.0 missing (65.9%)	29.3 ± 7.9; 31,038.0/44,017.0 m
sex_label			
Female	184,619 (50%)	48,931 (46%)	20,356 (46%)
Male	181,004 (50%)	56,715 (54%)	23,661 (54%)
race_ethnicity_label			
White	241,114 (66%)	55,100 (52%)	24,960 (57%)
Black or African American	61,814 (17%)	19,199 (18%)	8,684 (20%)
Hispanic	22,951 (6.3%)	8,354 (7.9%)	2,464 (5.6%)
Asian	5,439 (1.5%)	2,293 (2.2%)	676 (1.5%)
American Indian	2,128 (0.6%)	1,683 (1.6%)	244 (0.6%)
Pacific Islander	543 (0.1%)	110 (0.1%)	25 (<0.1%)
Unknown	31,634 (8.7%)	18,907 (18%)	6,964 (16%)
location_label			
South	196,774 (54%)	30,426 (29%)	15,066 (34%)
Northeast	65,537 (18%)	44,405 (42%)	19,504 (44%)
Midwest	24,891 (6.8%)	9,178 (8.7%)	4,402 (10%)
West	78,421 (21%)	21,637 (20%)	5,045 (11%)
osa_label	65,748 (18%)	15,634 (15%)	8,945 (20%)
asthma_label	49,810 (14%)	13,419 (13%)	6,544 (15%)
copd_label	70,950 (19%)	16,459 (16%)	12,846 (29%)
chf_label	68,964 (19%)	20,573 (19%)	11,921 (27%)
nmd_label	14,796 (4.0%)	3,754 (3.6%)	1,689 (3.8%)
phtn_label	27,731 (7.6%)	8,534 (8.1%)	5,449 (12%)
ckd_label	61,091 (17%)	21,290 (20%)	8,765 (20%)
diabetes_label	101,173 (28%)	33,665 (32%)	14,116 (32%)
encounter_type_label			
Emergency	124,405 (34%)	34,711 (33%)	12,611 (29%)
Inpatient	241,218 (66%)	70,935 (67%)	31,406 (71%)
VBG PCO2	NA ± NA; 365,623.0/365,623.0 missing (100.0%)	40.1 ± 6.6; 0.0/105,646.0 missing (0.0%)	60.2 ± 12.6; 0.0/44,017.0 mis
Arterial PCO2	42.4 ± 15.5; 233,430.0/365,623.0 missing (63.8%)	38.6 ± 15.4; 68,334.0/105,646.0 missing (64.7%)	52.7 ± 19.6; 26,280.0/44,017.0 m

[1]Mean ± SD; N Missing/No. obs. missing (% Missing); n (%)

2.2.2 2.2 Table 1 (Overall ABG/VBG status)

```
# Status factors (column labels are taken from factor levels)
subset_data <- subset_data %>%
  mutate(
    abg_status = factor(has_abg, levels = c(0, 1),
                        labels = c("Did not get ABG", "Did get ABG")),
    vbg_status = factor(has_vbg, levels = c(0, 1),
                        labels = c("Did not get VBG", "Did get VBG"))
  )

# ABG table with "Everyone" column first
tbl1_abg <- subset_data %>%
  select(all_of(vars), abg_status) %>%
  gtsummary::tbl_summary(
    by = abg_status,
    type = list(sex_label ~ "categorical"),
    statistic = list(
      gtsummary::all_continuous()  ~ "{mean} ± {sd}; {N_miss}/{N_obs} missing ({p_miss}%)",
      gtsummary::all_categorical() ~ "{n} ({p}%)"
    ),
    digits   = list(gtsummary::all_continuous() ~ 1),
    missing  = "no"
  ) %>%
  gtsummary::add_overall(last = FALSE, col_label = "Everyone") %>%
  gtsummary::modify_header(label = "**Variable**")

# VBG table (no "Everyone" here)
tbl1_vbg <- subset_data %>%
  select(all_of(vars), vbg_status) %>%
  gtsummary::tbl_summary(
    by = vbg_status,
    type = list(sex_label ~ "categorical"),
    statistic = list(
      gtsummary::all_continuous()  ~ "{mean} ± {sd}; {N_miss}/{N_obs} missing ({p_miss}%)",
```

```
      gtsummary::all_categorical() ~ "{n} ({p}%)"
    ),
    digits   = list(gtsummary::all_continuous() ~ 1),
    missing  = "no"
  ) %>%
  gtsummary::modify_header(label = "**Variable**")

library(gtsummary)

tbl1 <- tbl_merge(
  tbls = list(tbl1_abg, tbl1_vbg)
) %>%
  modify_caption("**Table 1. Baseline summary: Everyone, ABG status, and VBG status**")

tbl1
```

Chunk table1-everyone-abg-vbg runtime: 3.27 s

2.2.3 2.3 Table 2 (Hypercapnia within cohorts)

```
# Hypercapnia factors within measured cohorts
subset_data <- subset_data %>%
  mutate(
    hyper_abg = factor(hypercap_on_abg, levels = c(1, 0),
                       labels = c("Got ABG & Hypercapnia", "Got ABG & No hypercapnia")),
    hyper_vbg = factor(hypercap_on_vbg, levels = c(1, 0),
                       labels = c("Got VBG & Hypercapnia", "Got VBG & No hypercapnia"))
  )

# ABG cohort (has_abg == 1)
tbl2_abg <- subset_data %>%
  filter(has_abg == 1) %>%
  select(all_of(vars), hyper_abg) %>%
  gtsummary::tbl_summary(
```

Table 1

Variable	Everyone[1]	**Did not get ABG** N = 328,044[1]	**Did get ABG** N =
Age (years)	59.2 ± 17.7; 0.0/515,286.0 missing (0.0%)	58.1 ± 18.1; 0.0/328,044.0 missing (0.0%)	61.2 ± 16.9; 0.0/187,242.0
Current BMI kg/m2	31.1 ± 8.4; 293,545.0/515,286.0 missing (57.0%)	32.3 ± 8.7; 184,223.0/328,044.0 missing (56.2%)	29.0 ± 7.2; 109,322.0/187,242.
sex_label			
Female	253,906 (49%)	169,023 (52%)	84,883 (45%
Male	261,380 (51%)	159,021 (48%)	102,359 (55%
race_ethnicity_label			
White	321,174 (62%)	200,033 (61%)	121,141 (65%
Black or African American	89,697 (17%)	62,418 (19%)	27,279 (15%
Hispanic	33,769 (6.6%)	23,548 (7.2%)	10,221 (5.5%
Asian	8,408 (1.6%)	4,880 (1.5%)	3,528 (1.9%
American Indian	4,055 (0.8%)	1,971 (0.6%)	2,084 (1.1%
Pacific Islander	678 (0.1%)	460 (0.1%)	218 (0.1%)
Unknown	57,505 (11%)	34,734 (11%)	22,771 (12%
location_label			
South	242,266 (47%)	138,843 (42%)	103,423 (55%
Northeast	129,446 (25%)	93,209 (28%)	36,237 (19%
Midwest	38,471 (7.5%)	22,924 (7.0%)	15,547 (8.3%
West	105,103 (20%)	73,068 (22%)	32,035 (17%
osa_label	90,327 (18%)	60,653 (18%)	29,674 (16%
asthma_label	69,773 (14%)	48,456 (15%)	21,317 (11%
copd_label	100,255 (19%)	60,214 (18%)	40,041 (21%
chf_label	101,458 (20%)	59,770 (18%)	41,688 (22%
nmd_label	20,239 (3.9%)	11,891 (3.6%)	8,348 (4.5%)
phtn_label	41,714 (8.1%)	23,854 (7.3%)	17,860 (9.5%
ckd_label	91,146 (18%)	54,528 (17%)	36,618 (20%
diabetes_label	148,954 (29%)	93,007 (28%)	55,947 (30%
encounter_type_label			
Emergency	171,727 (33%)	142,713 (44%)	29,014 (15%
Inpatient	343,559 (67%)	185,331 (56%)	158,228 (85%
VBG PCO2	46.0 ± 12.7; 365,623.0/515,286.0 missing (71.0%)	45.5 ± 10.5; 233,430.0/328,044.0 missing (71.2%)	46.9 ± 15.6; 132,193.0/187,242
Arterial PCO2	42.6 ± 16.3; 328,044.0/515,286.0 missing (63.7%)	NA ± NA; 328,044.0/328,044.0 missing (100.0%)	42.6 ± 16.3; 0.0/187,242.0

[1]Mean ± SD; N Missing/No. obs. missing (% Missing); n (%)

```
    by = hyper_abg,
    type = list(sex_label ~ "categorical"),
    statistic = list(
      gtsummary::all_continuous()  ~ "{mean} ± {sd}; {N_miss}/{N_obs} missing ({p_miss}%)",
      gtsummary::all_categorical() ~ "{n} ({p}%)"
    ),
    digits   = list(gtsummary::all_continuous() ~ 1),
    missing  = "no"
  ) %>%
  gtsummary::modify_header(
    label  = "**Variable**",
    stat_1 = "**Got ABG & Hypercapnia**",
    stat_2 = "**Got ABG & No hypercapnia**"
  )

# VBG cohort (has_vbg == 1)
tbl2_vbg <- subset_data %>%
  filter(has_vbg == 1) %>%
  select(all_of(vars), hyper_vbg) %>%
  gtsummary::tbl_summary(
    by = hyper_vbg,
    type = list(sex_label ~ "categorical"),
    statistic = list(
      gtsummary::all_continuous()  ~ "{mean} ± {sd}; {N_miss}/{N_obs} missing ({p_miss}%)",
      gtsummary::all_categorical() ~ "{n} ({p}%)"
    ),
    digits   = list(gtsummary::all_continuous() ~ 1),
    missing  = "no"
  ) %>%
  gtsummary::modify_header(
    label  = "**Variable**",
    stat_1 = "**Got VBG & Hypercapnia**",
    stat_2 = "**Got VBG & No hypercapnia**"
  )

# Merge side-by-side (no spanners; 4 requested columns)
```

```r
table2 <- gtsummary::tbl_merge(
  tbls = list(tbl2_abg, tbl2_vbg),
  tab_spanner = c(NULL, NULL)
) %>%
  gtsummary::modify_caption("**Table 2. Baseline summary by hypercapnia within ABG and VBG cohorts**")

table2
```

Chunk table2-hypercapnia-cohorts runtime: 4.04 s

Chunk table2-outcome-panel runtime: 2.03 s

2.2.4 2.4 Generating Word Docs for New Table 1 and 2

```r
library(gtsummary)
library(flextable)
library(officer)

# gtsummary objects (example: table1, table2)
ft1 <- as_flex_table(tbl1)
ft2 <- as_flex_table(table2)

doc <- read_docx() %>%
  body_add_par("Table 1", style = "heading 1") %>%
  body_add_flextable(ft1) %>%
  body_add_par("Table 2", style = "heading 1") %>%
  body_add_flextable(ft2)

print(doc, target = results_path("Tables.docx"))
```

Chunk export-table1-table2-word runtime: 1.00 s

Table 1

Variable	Got ABG & Hypercapnia[1]	Got ABG & No hypercapnia[1]	Got VBG & Hypercap
Age (years)	62.1 ± 16.4; 0.0/57,813.0 missing (0.0%)	60.8 ± 17.1; 0.0/129,429.0 missing (0.0%)	61.0 ± 16.7; 0.0/44,017.0 missi
Current BMI kg/m2	29.8 ± 7.9; 33,496.0/57,813.0 missing (57.9%)	28.6 ± 6.9; 75,826.0/129,429.0 missing (58.6%)	29.3 ± 7.9; 31,038.0/44,017.0 mis
sex_label			
Female	27,116 (47%)	57,767 (45%)	20,356 (46%)
Male	30,697 (53%)	71,662 (55%)	23,661 (54%)
race_ethnicity_label			
White	39,784 (69%)	81,357 (63%)	24,960 (57%)
Black or African American	8,082 (14%)	19,197 (15%)	8,684 (20%)
Hispanic	2,757 (4.8%)	7,464 (5.8%)	2,464 (5.6%)
Asian	789 (1.4%)	2,739 (2.1%)	676 (1.5%)
American Indian	316 (0.5%)	1,768 (1.4%)	244 (0.6%)
Pacific Islander	56 (<0.1%)	162 (0.1%)	25 (<0.1%)
Unknown	6,029 (10%)	16,742 (13%)	6,964 (16%)
location_label			
South	32,694 (57%)	70,729 (55%)	15,066 (34%)
Northeast	12,975 (22%)	23,262 (18%)	19,504 (44%)
Midwest	4,844 (8.4%)	10,703 (8.3%)	4,402 (10%)
West	7,300 (13%)	24,735 (19%)	5,045 (11%)
osa_label	11,965 (21%)	17,709 (14%)	8,945 (20%)
asthma_label	8,268 (14%)	13,049 (10%)	6,544 (15%)
copd_label	18,846 (33%)	21,195 (16%)	12,846 (29%)
chf_label	16,219 (28%)	25,469 (20%)	11,921 (27%)
nmd_label	2,487 (4.3%)	5,861 (4.5%)	1,689 (3.8%)
phtn_label	7,347 (13%)	10,513 (8.1%)	5,449 (12%)
ckd_label	11,769 (20%)	24,849 (19%)	8,765 (20%)
diabetes_label	18,521 (32%)	37,426 (29%)	14,116 (32%)
encounter_type_label			
Emergency	9,818 (17%)	19,196 (15%)	12,611 (29%)
Inpatient	47,995 (83%)	110,233 (85%)	31,406 (71%)
VBG PCO2	57.4 ± 18.4; 40,411.0/57,813.0 missing (69.9%)	42.0 ± 11.2; 91,782.0/129,429.0 missing (70.9%)	60.2 ± 12.6; 0.0/44,017.0 missi
Arterial PCO2	58.5 ± 20.4; 0.0/57,813.0 missing (0.0%)	35.5 ± 6.1; 0.0/129,429.0 missing (0.0%)	52.7 ± 19.6; 26,280.0/44,017.0 mis

[1]Mean ± SD; N Missing/No. obs. missing (% Missing); n (%)

Table 2a. Crude outcomes by hypercapnia group

Cohort	Outcome	Hypercapnia	No hypercapnia
ABG	IMV	15373/57813 (26.6%)	32800/129429 (25.3%)
ABG	NIV	9246/57813 (16.0%)	9794/129429 (7.6%)
ABG	Death (60d)	10525/57813 (18.2%)	22193/129429 (17.1%)
ABG	Hypercapnic RF	13588/57813 (23.5%)	6688/129429 (5.2%)
VBG	IMV	8122/44017 (18.5%)	15095/105646 (14.3%)
VBG	NIV	5316/44017 (12.1%)	5383/105646 (5.1%)
VBG	Death (60d)	6697/44017 (15.2%)	13786/105646 (13.0%)
VBG	Hypercapnic RF	9391/44017 (21.3%)	3837/105646 (3.6%)

Counts and column percentages; denominator is non-missing records within each cohort.

3 Unweighted Binary Logistic Regressions

Unweighted, Hypercapnia (binary yes/no) Simple (1 predictor) Regressions:

Unweighted, ABG Group: hypercapnia treated as a binary (yes/no) predictor

3.0.1 3.1 ABG: Binary hypercapnia models

```
logit_intubated_abg <- glm(imv_proc ~ hypercap_on_abg, data = subset_data, family = binomial)
summary(logit_intubated_abg)
```

```
Call:
glm(formula = imv_proc ~ hypercap_on_abg, family = binomial,
    data = subset_data)

Coefficients:
                 Estimate Std. Error z value Pr(>|z|)
(Intercept)     -2.275471   0.005086  -447.4   <2e-16 ***
```

```
hypercap_on_abg  1.259993   0.010700   117.8   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 362580  on 515285  degrees of freedom
Residual deviance: 350435  on 515284  degrees of freedom
AIC: 350439

Number of Fisher Scoring iterations: 5
```

```r
tidy(logit_intubated_abg,
     exponentiate = TRUE,   # turns log-odds → OR
     conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.1027485	0.0050863	-447.3684	0	0.1017279	0.1037765
hypercap_on_abg	3.5253956	0.0106997	117.7601	0	3.4521736	3.6000445

```r
logit_niv_abg <- glm(niv_proc ~ hypercap_on_abg, data = subset_data, family = binomial)
summary(logit_niv_abg)
```

```
Call:
glm(formula = niv_proc ~ hypercap_on_abg, family = binomial,
    data = subset_data)

Coefficients:
                Estimate Std. Error z value Pr(>|z|)
(Intercept)     -2.860418   0.006533 -437.84   <2e-16 ***
hypercap_on_abg  1.201665   0.013093   91.78   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

```
(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 250639  on 515285  degrees of freedom
Residual deviance: 243461  on 515284  degrees of freedom
AIC: 243465

Number of Fisher Scoring iterations: 5
```

```r
tidy(logit_niv_abg,
     exponentiate = TRUE,   # turns log-odds → OR
     conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.0572448	0.0065330	-437.84069	0	0.0565151	0.0579811
hypercap_on_abg	3.3256498	0.0130929	91.77958	0	3.2412752	3.4119744

```r
logit_death_abg <- glm(death_60d ~ hypercap_on_abg, data = subset_data, family = binomial)
summary(logit_death_abg)
```

```
Call:
glm(formula = death_60d ~ hypercap_on_abg, family = binomial,
    data = subset_data)

Coefficients:
                Estimate Std. Error z value Pr(>|z|)
(Intercept)     -2.258743   0.005052 -447.11   <2e-16 ***
hypercap_on_abg  0.756240   0.011903   63.53   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)
```

```
    Null deviance: 344897  on 515285  degrees of freedom
Residual deviance: 341286  on 515284  degrees of freedom
AIC: 341290

Number of Fisher Scoring iterations: 5
```

```r
tidy(logit_death_abg,
     exponentiate = TRUE,   # turns log-odds → OR
     conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.1044817	0.0050519	-447.10674	0	0.1034509	0.105520
hypercap_on_abg	2.1302521	0.0119030	63.53375	0	2.0810535	2.180455

```r
logit_icd_abg <- glm(hypercap_resp_failure ~ hypercap_on_abg, data = subset_data, family = binomial)
summary(logit_icd_abg)
```

```
Call:
glm(formula = hypercap_resp_failure ~ hypercap_on_abg, family = binomial,
    data = subset_data)

Coefficients:
                Estimate Std. Error z value Pr(>|z|)
(Intercept)     -3.355697   0.008192  -409.6   <2e-16 ***
hypercap_on_abg  2.175594   0.012779   170.2   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 223278  on 515285  degrees of freedom
Residual deviance: 197920  on 515284  degrees of freedom
AIC: 197924
```

```
Number of Fisher Scoring iterations: 6
```

```
tidy(logit_icd_abg,
     exponentiate = TRUE,   # turns log-odds → OR
     conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.034885	0.0081920	-409.6314	0	0.034328	0.0354483
hypercap_on_abg	8.807416	0.0127795	170.2414	0	8.589528	9.0307810

Chunk abg-binary-logit-models runtime: 22.09 s

Display the regression coefficients for the binary (hypercapnia yes/no) predictor logistic regressions

```
modelsummary(
  list("Intubated" = logit_intubated_abg,
       "NIV"       = logit_niv_abg,
       "Death"     = logit_death_abg,
       "ICD Hyper" = logit_icd_abg),
  exponentiate = TRUE,
  conf_level   = 0.95,
  estimate     = "{estimate}",
  statistic    = "({conf.low}, {conf.high})",
  coef_omit    = "(Intercept)",
  gof_omit     = ".*",                    # drop all goodness-of-fit rows
  fmt          = 2,                       # 2 decimal places everywhere
  output       = "gt"
) |>
  gt_pdf(title = "Odds Ratios for ABG Hypercapnia (>45 mmHg)'s association with...")
```

```
Profiled confidence intervals may take longer time to compute.
  Use `ci_method="wald"` for faster computation of CIs.
Profiled confidence intervals may take longer time to compute.
```

	Intubated	NIV	Death	ICD Hyper
hypercap_on_abg	3.53 (3.45, 3.60)	3.33 (3.24, 3.41)	2.13 (2.08, 2.18)	8.81 (8.59, 9.03)

```
  Use `ci_method="wald"` for faster computation of CIs.
Profiled confidence intervals may take longer time to compute.
  Use `ci_method="wald"` for faster computation of CIs.
Profiled confidence intervals may take longer time to compute.
  Use `ci_method="wald"` for faster computation of CIs.
```

Chunk abg-binary-or-table runtime: 26.38 s

Unweighted VBG Group

3.0.2 3.2 VBG: Binary hypercapnia models

```r
logit_intubated_vbg <- glm(imv_proc ~ hypercap_on_vbg, data = subset_data, family = binomial)
summary(logit_intubated_vbg)
```

```

Call:
glm(formula = imv_proc ~ hypercap_on_vbg, family = binomial,
    data = subset_data)

Coefficients:
                Estimate Std. Error z value Pr(>|z|)
(Intercept)     -2.134026   0.004735 -450.69   <2e-16 ***
hypercap_on_vbg  0.648004   0.013168   49.21   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 362580  on 515285  degrees of freedom
```

```
Residual deviance: 360405  on 515284  degrees of freedom
AIC: 360409

Number of Fisher Scoring iterations: 4
```

```r
tidy(logit_intubated_vbg,
     exponentiate = TRUE,   # turns log-odds → OR
     conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.1183598	0.0047351	-450.68580	0	0.1172651	0.1194621
hypercap_on_vbg	1.9117219	0.0131682	49.20969	0	1.8629159	1.9616038

```r
logit_niv_vbg <- glm(niv_proc ~ hypercap_on_vbg, data = subset_data, family = binomial)
summary(logit_niv_vbg)
```

```
Call:
glm(formula = niv_proc ~ hypercap_on_vbg, family = binomial,
    data = subset_data)

Coefficients:
                 Estimate Std. Error z value Pr(>|z|)
(Intercept)     -2.735699   0.006091 -449.13   <2e-16 ***
hypercap_on_vbg  0.750555   0.015845   47.37   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 250639  on 515285  degrees of freedom
Residual deviance: 248688  on 515284  degrees of freedom
AIC: 248692

Number of Fisher Scoring iterations: 5
```

```r
tidy(logit_niv_vbg,
     exponentiate = TRUE,   # turns log-odds → OR
     conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.0648486	0.0060911	-449.12691	0	0.0640777	0.0656261
hypercap_on_vbg	2.1181752	0.0158446	47.36965	0	2.0532293	2.1848014

```r
logit_death_vbg <- glm(death_60d ~ hypercap_on_vbg, data = subset_data, family = binomial)
summary(logit_death_vbg)
```

```
Call:
glm(formula = death_60d ~ hypercap_on_vbg, family = binomial,
    data = subset_data)

Coefficients:
                 Estimate Std. Error z value Pr(>|z|)
(Intercept)     -2.197765   0.004856 -452.56   <2e-16 ***
hypercap_on_vbg  0.479895   0.014131   33.96   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 344897  on 515285  degrees of freedom
Residual deviance: 343841  on 515284  degrees of freedom
AIC: 343845

Number of Fisher Scoring iterations: 4
```

```r
tidy(logit_death_vbg,
     exponentiate = TRUE,   # turns log-odds → OR
     conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.1110511	0.0048563	-452.56297	0	0.1099977	0.1121119
hypercap_on_vbg	1.6159045	0.0141315	33.95924	0	1.5716549	1.6611746

```r
logit_icd_vbg <- glm(hypercap_resp_failure ~ hypercap_on_vbg, data = subset_data, family = binomial)
summary(logit_icd_vbg)
```

```
Call:
glm(formula = hypercap_resp_failure ~ hypercap_on_vbg, family = binomial,
    data = subset_data)

Coefficients:
                 Estimate Std. Error z value Pr(>|z|)
(Intercept)     -3.136462   0.007293  -430.1   <2e-16 ***
hypercap_on_vbg  1.831609   0.013731   133.4   <2e-16 ***
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

    Null deviance: 223278  on 515285  degrees of freedom
Residual deviance: 208772  on 515284  degrees of freedom
AIC: 208776

Number of Fisher Scoring iterations: 6
```

```r
tidy(logit_icd_vbg,
     exponentiate = TRUE,   # turns log-odds → OR
      conf.int     = TRUE)   # adds 95 % CI
```

term	estimate	std.error	statistic	p.value	conf.low	conf.high
(Intercept)	0.0434362	0.0072930	-430.0654	0	0.0428184	0.0440602

term	estimate	std.error	statistic	p.value	conf.low	conf.high
hypercap_on_vbg	6.2439262	0.0137314	133.3879	0	6.0779584	6.4140808

Chunk vbg-binary-logit-models runtime: 21.44 s

3.0.3 3.3 Display model coefficients for binary hypercapnia on VBG logistic regression

```
modelsummary(
  list("Intubated" = logit_intubated_vbg,
       "NIV"       = logit_niv_vbg,
       "Death"     = logit_death_vbg,
       "ICD Hyper" = logit_icd_vbg),
  exponentiate = TRUE,
  conf_level   = 0.95,
  estimate     = "{estimate}",
  statistic    = "({conf.low}, {conf.high})",
  coef_omit    = "(Intercept)",
  gof_omit     = ".*",                    # drop all goodness-of-fit rows
  fmt          = 2,                       # 2 decimal places everywhere
  output       = "gt"
) |>
  gt_pdf(title = "Odds ratios for VBG hypercapnia (>45 mmHg) on outcomes")
```

```
Profiled confidence intervals may take longer time to compute.
  Use `ci_method="wald"` for faster computation of CIs.
Profiled confidence intervals may take longer time to compute.
  Use `ci_method="wald"` for faster computation of CIs.
Profiled confidence intervals may take longer time to compute.
  Use `ci_method="wald"` for faster computation of CIs.
Profiled confidence intervals may take longer time to compute.
  Use `ci_method="wald"` for faster computation of CIs.
```

Chunk vbg-binary-or-table runtime: 25.36 s

	Intubated	NIV	Death	ICD Hyper
hypercap_on_vbg	1.91 (1.86, 1.96)	2.12 (2.05, 2.18)	1.62 (1.57, 1.66)	6.24 (6.08, 6.41)

3.1 3) Three-level PCO2 categories (unweighted)

Now doing 3 groups instead of binary (above, normal and below)

```
subset_data <- subset_data %>%
  mutate(
    pco2_cat_abg = case_when(
      !is.na(paco2) & paco2 < 35 ~ "Hypocapnia",
      !is.na(paco2) & paco2 > 45 ~ "Hypercapnia",
      !is.na(paco2)              ~ "Eucapnia"
    ),
    pco2_cat_vbg = case_when(
      !is.na(vbg_co2) & vbg_co2 < 40 ~ "Hypocapnia",
      !is.na(vbg_co2) & vbg_co2 > 50 ~ "Hypercapnia",
      !is.na(vbg_co2)                ~ "Eucapnia"
    )
  ) %>%
  mutate(
    across(c(pco2_cat_abg, pco2_cat_vbg),
           ~factor(.x, levels = c("Eucapnia", "Hypocapnia", "Hypercapnia")))
  )

library(broom)
library(dplyr)

run_logit <- function(data, outcome, exposure, group_name) {
  f <- as.formula(paste(outcome, "~", exposure))
  glm(f, data = data, family = binomial) %>%
    tidy(exponentiate = TRUE, conf.int = TRUE) %>%
    filter(term != "(Intercept)") %>%
    mutate(
      outcome = outcome,
```

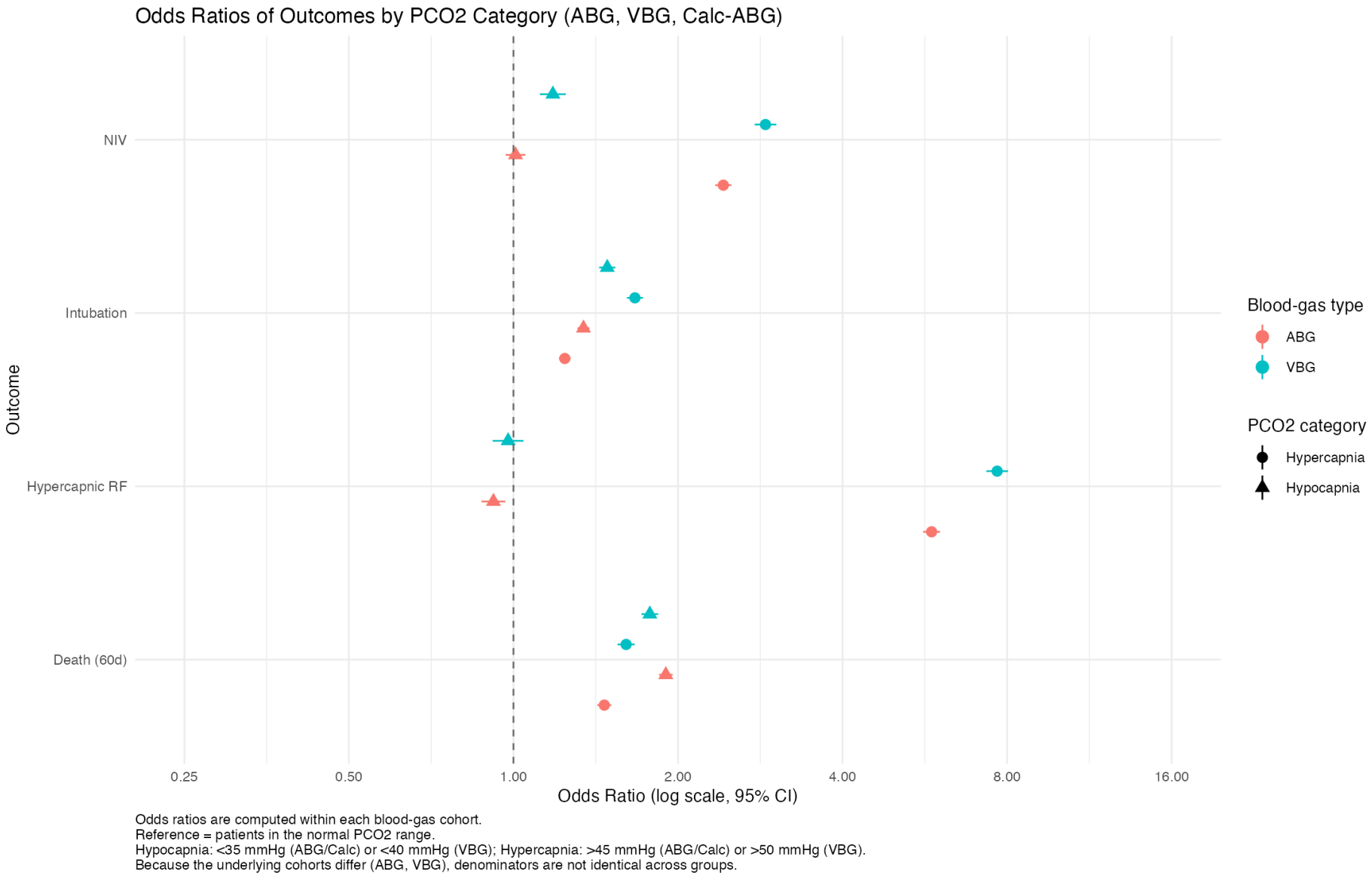
```
      group   = group_name
    )
}

outcomes <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")

results <- bind_rows(
  lapply(outcomes, function(o) run_logit(subset_data, o, "pco2_cat_abg", "ABG")),
  lapply(outcomes, function(o) run_logit(subset_data, o, "pco2_cat_vbg", "VBG"))
)

combined_or_df <- results %>%
  mutate(
    exposure = recode(term,
                      "pco2_cat_abgHypocapnia"   = "Hypocapnia",
                      "pco2_cat_abgHypercapnia"  = "Hypercapnia",
                      "pco2_cat_vbgHypocapnia"   = "Hypocapnia",
                      "pco2_cat_vbgHypercapnia"  = "Hypercapnia"),
    outcome = recode(outcome,
                     imv_proc = "Intubation",
                     niv_proc = "NIV",
                     death_60d = "Death (60d)",
                     hypercap_resp_failure = "Hypercapnic RF")
  ) %>%
  select(outcome, group, exposure, estimate, conf.low, conf.high)
```

Chunk or-data-three-level-unweighted runtime: 22.60 s

```
library(scales)

combined_or_df$group <- factor(
  combined_or_df$group,
  levels = c("ABG", "VBG")
)

ggplot(
```

```
  combined_or_df,
  aes(
    x      = outcome,
    y      = estimate,
    ymin   = conf.low,
    ymax   = conf.high,
    color  = group,
    shape  = exposure
  )
) +
  geom_pointrange(
    position = position_dodge(width = 0.7),
    size     = 0.6
  ) +
  geom_hline(yintercept = 1, linetype = "dashed", colour = "grey40") +
  scale_y_log10(
    breaks = c(0.25, 0.5, 1, 2, 4, 8, 16),
    limits = c(0.25, 16),
    labels = number_format(accuracy = 0.01)
  ) +
  coord_flip() +
  labs(
    title  = "Odds Ratios of Outcomes by PCO2 Category (ABG, VBG, Calc-ABG)",
    x      = "Outcome",
    y      = "Odds Ratio (log scale, 95% CI)",
    color  = "Blood-gas type",
    shape  = "PCO2 category",
    caption = paste(
      "Odds ratios are computed within each blood-gas cohort.",
      "Reference = patients in the normal PCO2 range.",
      "Hypocapnia: <35 mmHg (ABG/Calc) or <40 mmHg (VBG); Hypercapnia: >45 mmHg (ABG/Calc) or >50 mmHg (VBG).",
      "Because the underlying cohorts differ (ABG, VBG), denominators are not identical across groups.",
      sep = "\n"
    )
  ) +
  theme_minimal(base_size = 10) +
```

```
  theme(plot.caption = element_text(hjust = 0))
```



Chunk or-plot-three-level-unweighted runtime: 0.35 s

3.2 4) Restricted cubic spline regressions (unweighted)

```
# ABG spline dataset
subset_data_abg <- subset_data %>%
  select(paco2, imv_proc, niv_proc, death_60d, hypercap_resp_failure) %>%
  filter(!is.na(paco2))

dd_abg <- datadist(subset_data_abg)
options(datadist = "dd_abg")
```

Chunk rcs-abg-data-prep runtime: 0.03 s

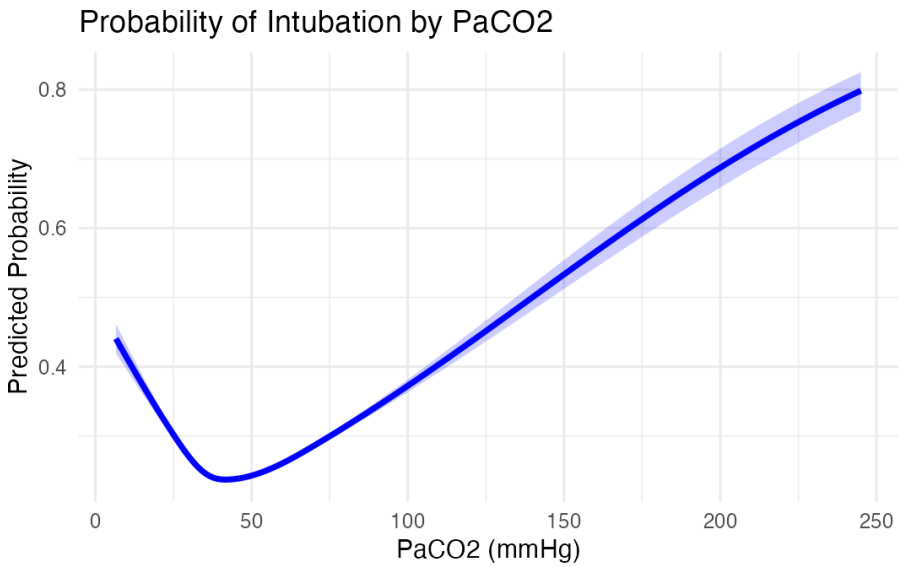
3.2.1 4.1 Unweighted, Restricted Cubic Spline Regression - ABG by PaCO2

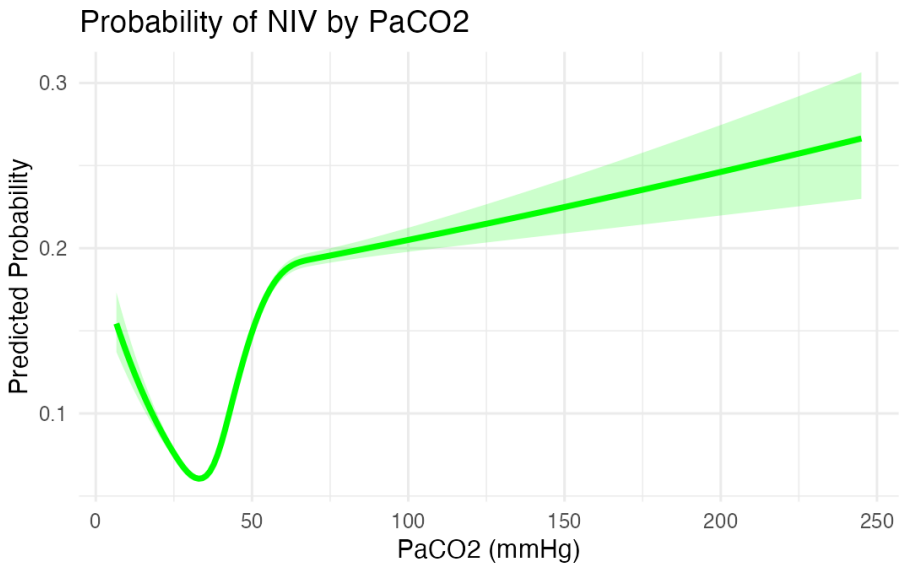
```
fit_imv <- lrm(imv_proc ~ rcs(paco2, 4), data = subset_data_abg)
pred_imv <- as.data.frame(Predict(fit_imv, paco2, fun = plogis))

plot_imv <- ggplot(pred_imv, aes(x = paco2, y = yhat)) +
  geom_line(color = "blue", size = 1.2) +
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "blue", alpha = 0.2) +
labs(title = "Probability of Intubation by PaCO2",
     x = "PaCO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()
```

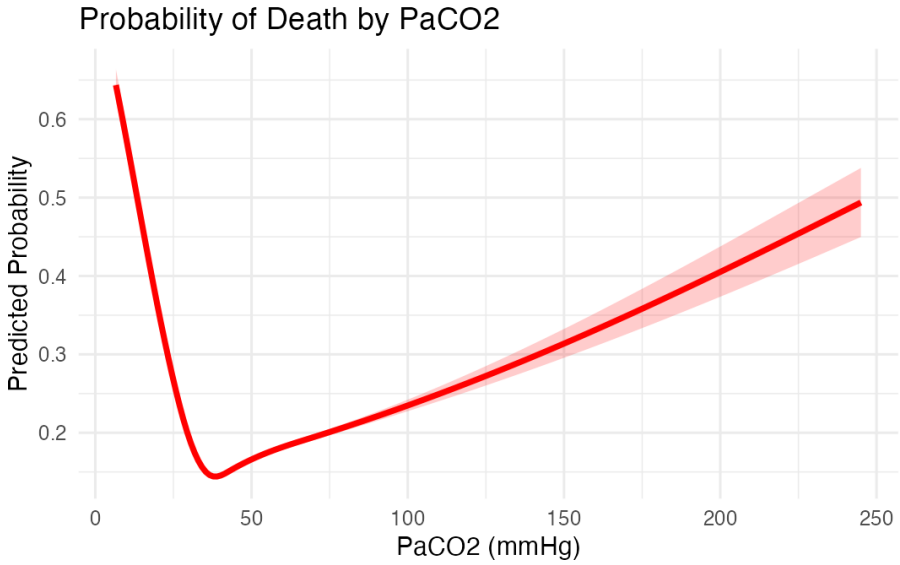
```
Warning: Using `size` aesthetic for lines was deprecated in ggplot2 3.4.0.
i Please use `linewidth` instead.
```

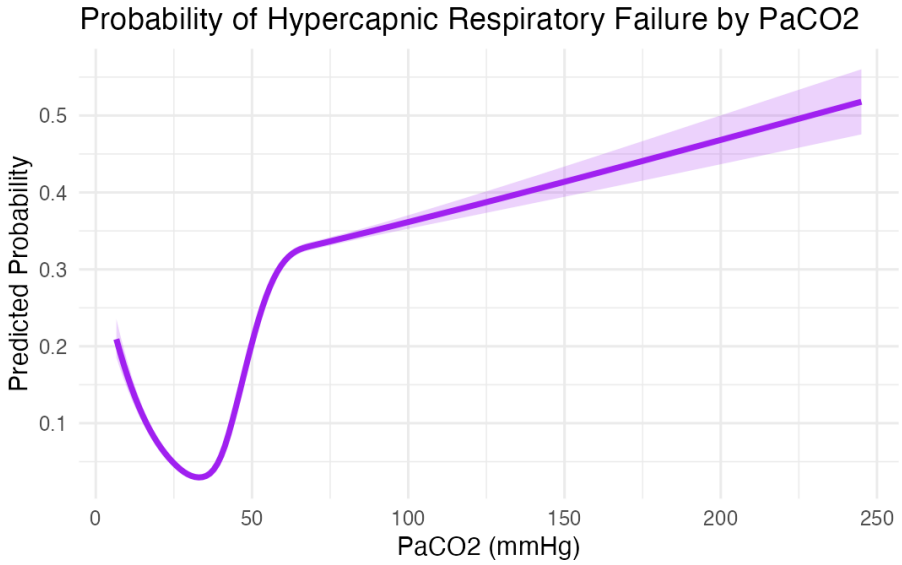
```
fit_niv <- lrm(niv_proc ~ rcs(paco2, 4), data = subset_data_abg)
pred_niv <- as.data.frame(Predict(fit_niv, paco2, fun = plogis))

plot_niv <- ggplot(pred_niv, aes(x = paco2, y = yhat)) +
  geom_line(color = "green", size = 1.2) +
```

```
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "green", alpha = 0.2) +
labs(title = "Probability of NIV by PaCO2",
     x = "PaCO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()

fit_death <- lrm(death_60d ~ rcs(paco2, 4), data = subset_data_abg)
pred_death <- as.data.frame(Predict(fit_death, paco2, fun = plogis))

plot_death <- ggplot(pred_death, aes(x = paco2, y = yhat)) +
  geom_line(color = "red", size = 1.2) +
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "red", alpha = 0.2) +
labs(title = "Probability of Death by PaCO2",
     x = "PaCO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()

fit_hcrf <- lrm(hypercap_resp_failure ~ rcs(paco2, 4), data = subset_data_abg)
pred_hcrf <- as.data.frame(Predict(fit_hcrf, paco2, fun = plogis))

plot_hcrf <- ggplot(pred_hcrf, aes(x = paco2, y = yhat)) +
  geom_line(color = "purple", size = 1.2) +
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "purple", alpha = 0.2) +
labs(title = "Probability of Hypercapnic Respiratory Failure by PaCO2",
     x = "PaCO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()

(plot_imv | plot_niv) / (plot_death | plot_hcrf)
```









Chunk rcs-abg-unweighted-models runtime: 1.68 s

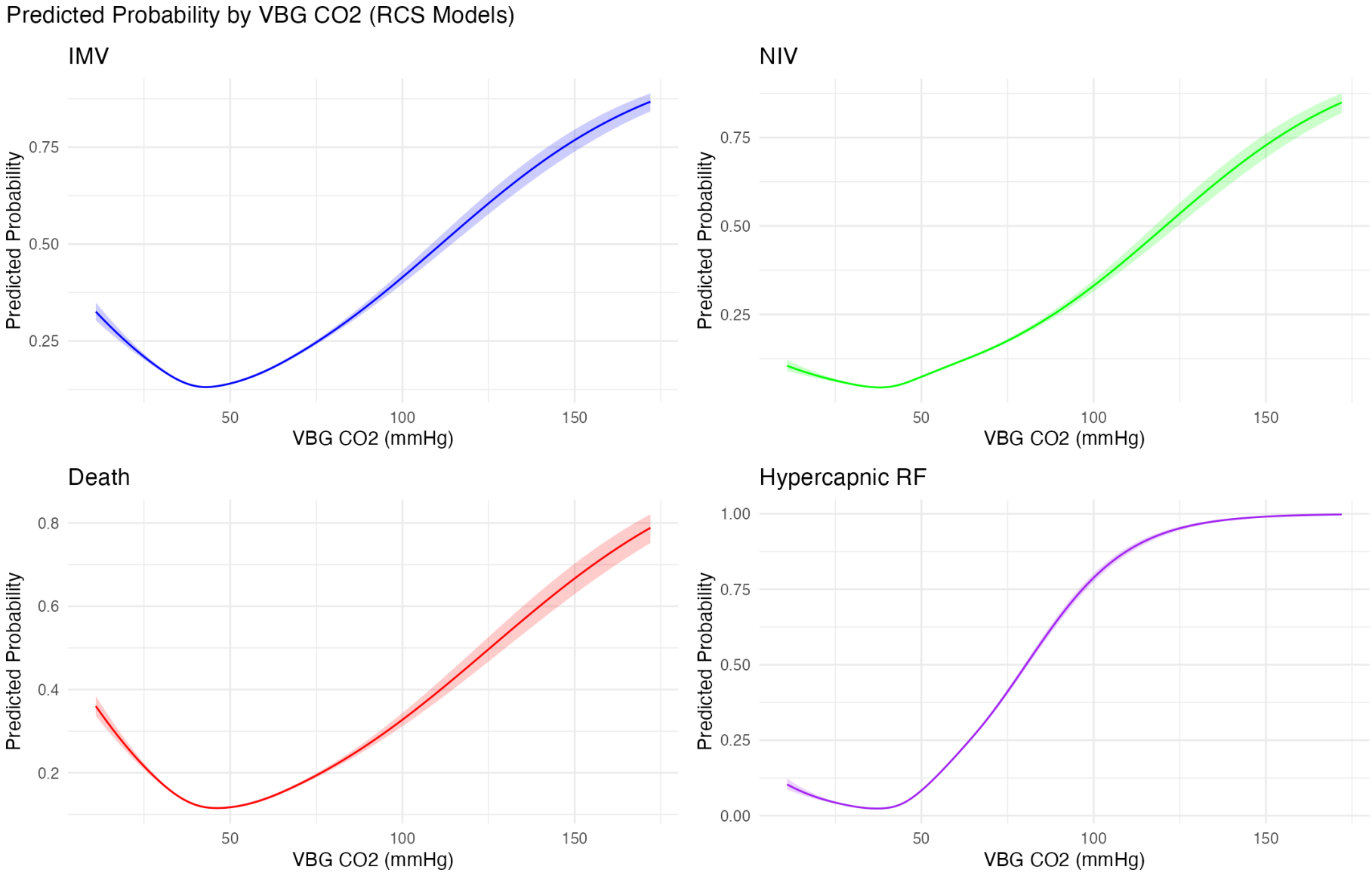
3.2.2 4.2 Unweighted, Restricted Cubic Spline - VBG

```
# --- VBG dataset ---
subset_data_vbg <- subset_data %>%
  dplyr::select(vbg_co2, imv_proc, niv_proc, death_60d, hypercap_resp_failure) %>%
  dplyr::filter(!is.na(vbg_co2) & complete.cases(.))

dd_vbg <- datadist(subset_data_vbg)   # create datadist for VBG
# activate when doing VBG models:
options(datadist = "dd_vbg")
```

Chunk rcs-vbg-data-prep runtime: 0.03 s

```
subset_data_vbg <- subset_data %>%
  select(vbg_co2, imv_proc, niv_proc, death_60d, hypercap_resp_failure) %>%
  filter(!is.na(vbg_co2) & complete.cases(.))

dd <- datadist(subset_data_vbg)
options(datadist = "dd")

fit_imv_vbg <- lrm(imv_proc ~ rcs(vbg_co2, 4), data = subset_data_vbg)
fit_niv_vbg <- lrm(niv_proc ~ rcs(vbg_co2, 4), data = subset_data_vbg)
fit_death_vbg <- lrm(death_60d ~ rcs(vbg_co2, 4), data = subset_data_vbg)
fit_hcrf_vbg <- lrm(hypercap_resp_failure ~ rcs(vbg_co2, 4), data = subset_data_vbg)

pred_imv_vbg <- as.data.frame(Predict(fit_imv_vbg, vbg_co2, fun = plogis))
pred_niv_vbg <- as.data.frame(Predict(fit_niv_vbg, vbg_co2, fun = plogis))
pred_death_vbg <- as.data.frame(Predict(fit_death_vbg, vbg_co2, fun = plogis))
pred_hcrf_vbg <- as.data.frame(Predict(fit_hcrf_vbg, vbg_co2, fun = plogis))

plot_imv_vbg <- ggplot(pred_imv_vbg, aes(x = vbg_co2, y = yhat)) +
  geom_line(color = "blue") +
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "blue", alpha = 0.2) +
  labs(title = "IMV", x = "VBG CO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()
```

```r
plot_niv_vbg <- ggplot(pred_niv_vbg, aes(x = vbg_co2, y = yhat)) +
  geom_line(color = "green") +
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "green", alpha = 0.2) +
  labs(title = "NIV", x = "VBG CO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()

plot_death_vbg <- ggplot(pred_death_vbg, aes(x = vbg_co2, y = yhat)) +
  geom_line(color = "red") +
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "red", alpha = 0.2) +
  labs(title = "Death", x = "VBG CO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()

plot_hcrf_vbg <- ggplot(pred_hcrf_vbg, aes(x = vbg_co2, y = yhat)) +
  geom_line(color = "purple") +
  geom_ribbon(aes(ymin = lower, ymax = upper), fill = "purple", alpha = 0.2) +
  labs(title = "Hypercapnic RF", x = "VBG CO2 (mmHg)", y = "Predicted Probability") +
  theme_minimal()

((plot_imv_vbg | plot_niv_vbg) /
 (plot_death_vbg | plot_hcrf_vbg)) +
 plot_annotation(title = "Predicted Probability by VBG CO2 (RCS Models)")
```



Chunk rcs-vbg-unweighted-models runtime: 1.28 s

4 Inverse Propensity Weighting

IPW done using Gradient Boosting Methods (GBM) - a type of decision-tree based machine learning. "***Random forests and GBM are designed to automatically include relevant interactions for variables included in the model.*** As such, using a GBM to estimate the PS model, can reduce model misspecification, since ***the analyst is not required to identify relevant interactions or nonlinearities.***" from this citation: PMID: 39947224https://pmc.ncbi.nlm.nih.gov/articles/PMC11825193/

Current propensity score uses **age_at_encounter + sex + race_ethnicity** (remember - have to specify to use this as a factor variable) **+ curr_bmi + copd + asthma + osa + chf + acute_nmd + phtn + location (as a factor variable)**

Note: for all these, I suggested new GBM adjustments that accomplish the following:

1. Smaller GBM & stopping rule → faster fit, avoids over-fitting, lighter tails (which lead to extreme weights that are problematic).
2. bal.tab() documents balance; aim is to adjust spec until standard mean difference (SMD) < 0.1.
3. Weight stabilization (divide by mean) mitigates a few huge weights. I also winsorized, which is a way to avoid very extreme weights (ie you set <1st percentile to the 1st percentile value, and >99th percentile to 99th percentile.
4. Uses robust variance estimation (e.g. allows the variances to change by PaCO2) for IP-weighted GLM; works with splines via rcs(). This is a bit nuanced but I think good to change even though it adds complexity
5. Deterministic seed ensures result replication.

4.0.1 5.1 ABG IPW weighting and diagnostics

```
subset_data$encounter_type <- factor(subset_data$encounter_type,
                                     levels = c(2, 3),
                                     labels = c("Emergency", "Inpatient"))
```

Chunk encode-encounter-type runtime: 0.10 s

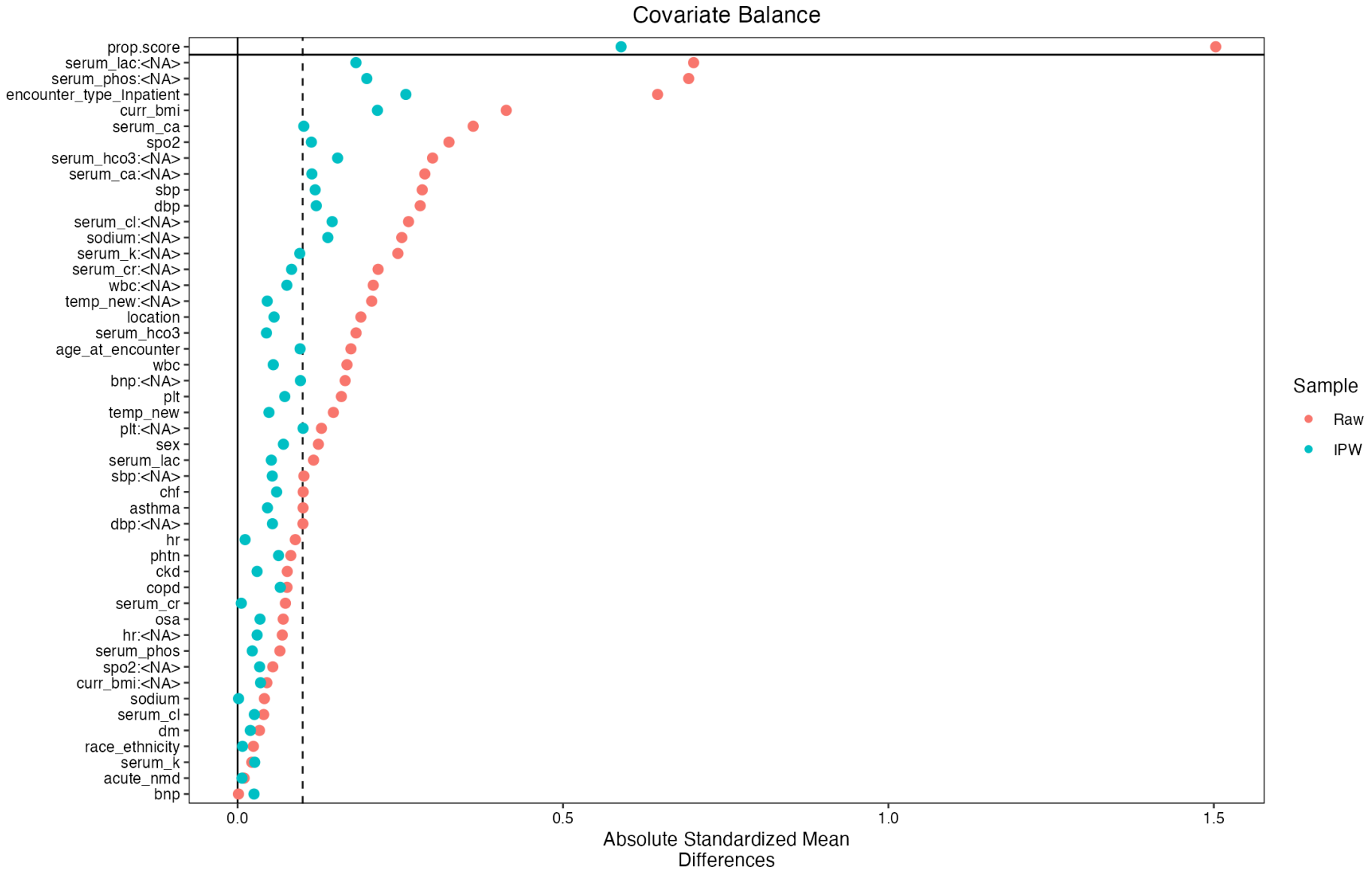
**Removed lactate from weights, decreased n.trees, increased bagging

```r
#   1. fit GBM propensity model, ABG
set.seed(42)

weight_model <- do.call(
  weightit,
  c(
    list(
      formula_abg,
      data        = subset_data,
      method      = "gbm",
      estimand    = "ATE",
      missing    = "ind",
      include.obj = TRUE        # ← REQUIRED for importance/SHAP
    ),
    gbm_params
  )
)
w_abg <- weight_model  # Canonical alias so later code can use `w_abg`

#   2. Winsorise / stabilise weights (two-sided)
w <- weight_model$weights            # original GBM weights
w <- w / mean(w)                     # stabilise
cut <- quantile(w, c(0.01, 0.99), na.rm = TRUE)
w   <- pmin(pmax(w, cut[1]), cut[2]) # two-tail Winsorisation
w <- w / mean(w)                     # re-stabilise so E[w]=1

# overwrite inside the object and attach to data
weight_model$weights <- w
subset_data$w_abg    <- w

#   3. balance diagnostics (only raw vs. IPW)
bal  <- bal.tab(
  weight_model,
  un = TRUE,
  m.threshold = 0.1,
  binary = "std",
```

```
  s.d.denom = "pooled"
)
```

```
Warning: Missing values exist in the covariates. Displayed values omit these
observations.
```

```
love.plot(
  bal,
  stats        = "m",          # standardized mean differences only
  abs          = TRUE,
  var.order    = "unadjusted",
  sample.names = c("Raw", "IPW")
)
```




```
#   4. survey design with the same weights
design <- svydesign(ids = ~1, weights = ~w_abg, data = subset_data)

#   5. outcome models (examples)
```

```r
fit_niv   <- svyglm(niv_proc   ~ has_abg, design = design, family = quasibinomial())
fit_imv   <- svyglm(imv_proc   ~ has_abg, design = design, family = quasibinomial())
fit_death <- svyglm(death_60d       ~ has_abg, design = design, family = quasibinomial())
fit_icd   <- svyglm(hypercap_resp_failure ~ has_abg, design = design, family = quasibinomial())

# quick effect estimates
lapply(list(IMV = fit_imv, NIV = fit_niv, Death = fit_death, ICD = fit_icd), function(m) {
  c(OR  = exp(coef(m)[2]),
    LCL = exp(confint(m)[2,1]),
    UCL = exp(confint(m)[2,2]))
})
```

```
$IMV
OR.has_abg        LCL        UCL
  6.664119   6.497030   6.835505

$NIV
OR.has_abg        LCL        UCL
  1.978913   1.930275   2.028777

$Death
OR.has_abg        LCL        UCL
  2.034938   1.993179   2.077571

$ICD
OR.has_abg        LCL        UCL
  3.367251   3.270841   3.466503
```

Chunk ipw-abg-weighting runtime: 1256.03 s

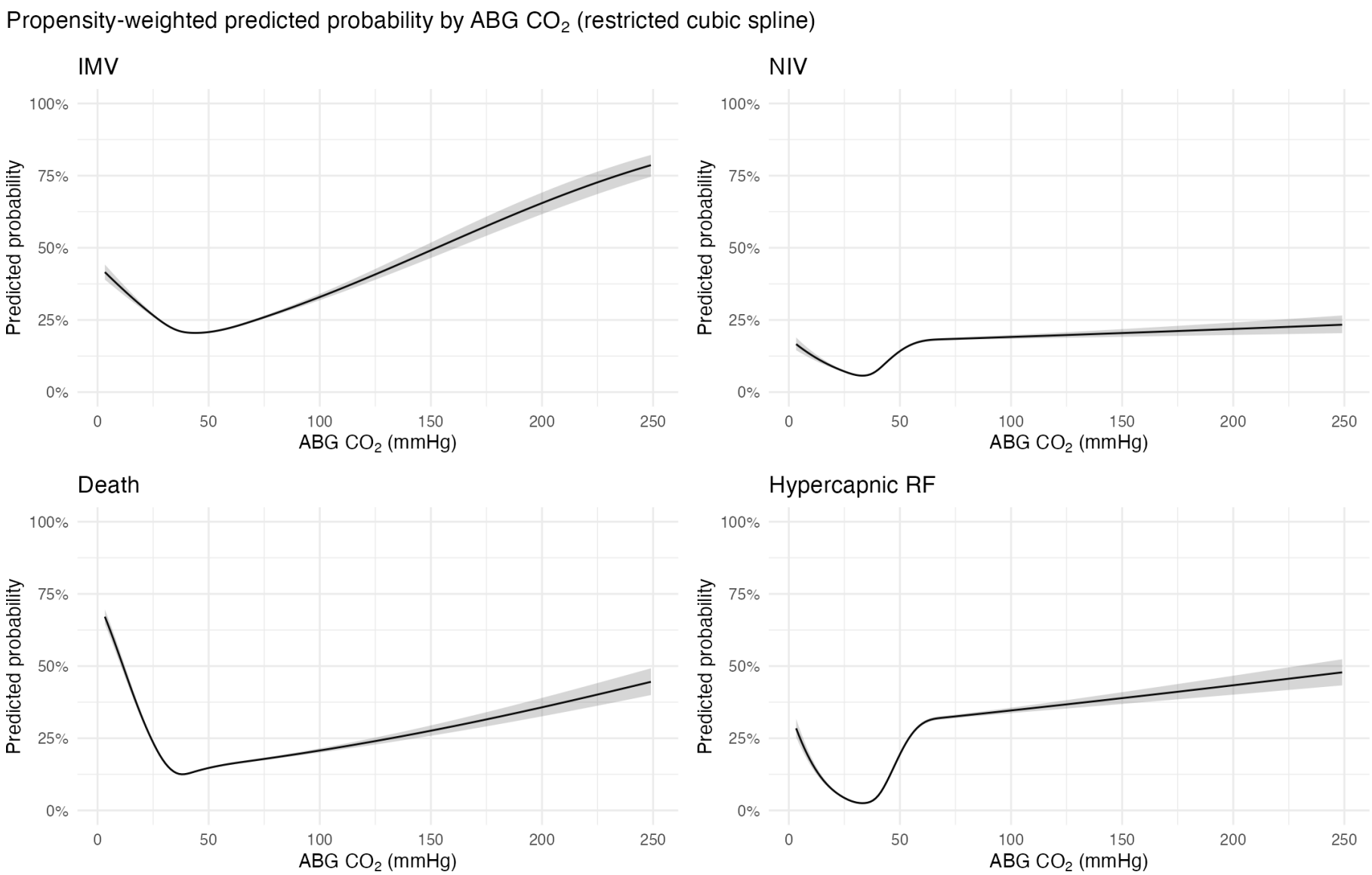
Inverse Propensity-Weighted Logistic Regressions with CO2 predictor represented as a restricted cubic spline.

4.0.2 5.2 ABG IPW spline models

```
# set.seed(42)  # reproducible GBM fit
#
# #   1. inverse-probability weights for receiving an ABG
#
# # done in the last block, so not needed
#

#   2. analysis sample: rows with a measured PaCO2
subset_data_abg <- subset_data %>%
  filter(!is.na(paco2)) %>%                    # implies has_abg == 1
  select(paco2, imv_proc, niv_proc, death_60d,
         hypercap_resp_failure, w_abg) %>%
  filter(complete.cases(.))


#   3. weighted logistic spline models with robust SEs
dd <- datadist(subset_data_abg); options(datadist = "dd")

fitfun <- function(formula)
  svyglm(
    formula,
    design = svydesign(ids = ~1, weights = ~w_abg, data = subset_data_abg),
    family = quasibinomial()
  )

fit_imv_abg   <- fitfun(imv_proc              ~ rcs(paco2, 4))
fit_niv_abg   <- fitfun(niv_proc              ~ rcs(paco2, 4))
fit_death_abg <- fitfun(death_60d                  ~ rcs(paco2, 4))
fit_hcrf_abg  <- fitfun(hypercap_resp_failure ~ rcs(paco2, 4))

#   4. prediction helper
mkpred <- function(fit, data_ref) {
  # 1. Grid of PaCO2 values
```

```
  newd <- data.frame(
    paco2 = seq(min(data_ref$paco2, na.rm = TRUE),
                max(data_ref$paco2, na.rm = TRUE),
                length.out = 200)
  )

  # 2. Design (model) matrix for the new data
  mm <- model.matrix(delete.response(terms(fit)),  # drop outcome
                     data = newd)

  # 3. Linear predictor and its standard error
  eta  <- mm %*% coef(fit)                         #  'x
  vcov <- vcov(fit)                                # robust VCOV from svyglm
  se   <- sqrt(rowSums((mm %*% vcov) * mm))        # √diag(X Σ X )

  # 4. Transform to probability scale
  transform(
    newd,
    yhat  = plogis(eta),
    lower = plogis(eta - 1.96 * se),
    upper = plogis(eta + 1.96 * se)
  )
}

pred_imv_abg   <- mkpred(fit_imv_abg,   subset_data_abg)
pred_niv_abg   <- mkpred(fit_niv_abg,   subset_data_abg)
pred_death_abg <- mkpred(fit_death_abg, subset_data_abg)
pred_hcrf_abg  <- mkpred(fit_hcrf_abg,  subset_data_abg)

#   5. plotting
xlab <- expression(paste("ABG CO"[2], " (mmHg)"))

plt <- function(dat, title)
  ggplot(dat, aes(paco2, yhat)) +
    geom_line() +
    geom_ribbon(aes(ymin = lower, ymax = upper), alpha = 0.2) +
```

```
    scale_y_continuous(limits = c(0, 1), labels = percent_format(accuracy = 1)) +
    labs(title = title, x = xlab, y = "Predicted probability") +
    theme_minimal()

(patchwork::wrap_plots(
    plt(pred_imv_abg,   "IMV"),
    plt(pred_niv_abg,   "NIV"),
    plt(pred_death_abg, "Death"),
    plt(pred_hcrf_abg,  "Hypercapnic RF"),
    ncol = 2
  )
) +
  plot_annotation(
    title = expression(
      paste("Propensity-weighted predicted probability by ABG CO"[2],
            " (restricted cubic spline)")
    )
)
```



Chunk ipw-abg-rcs-models runtime: 4.72 s

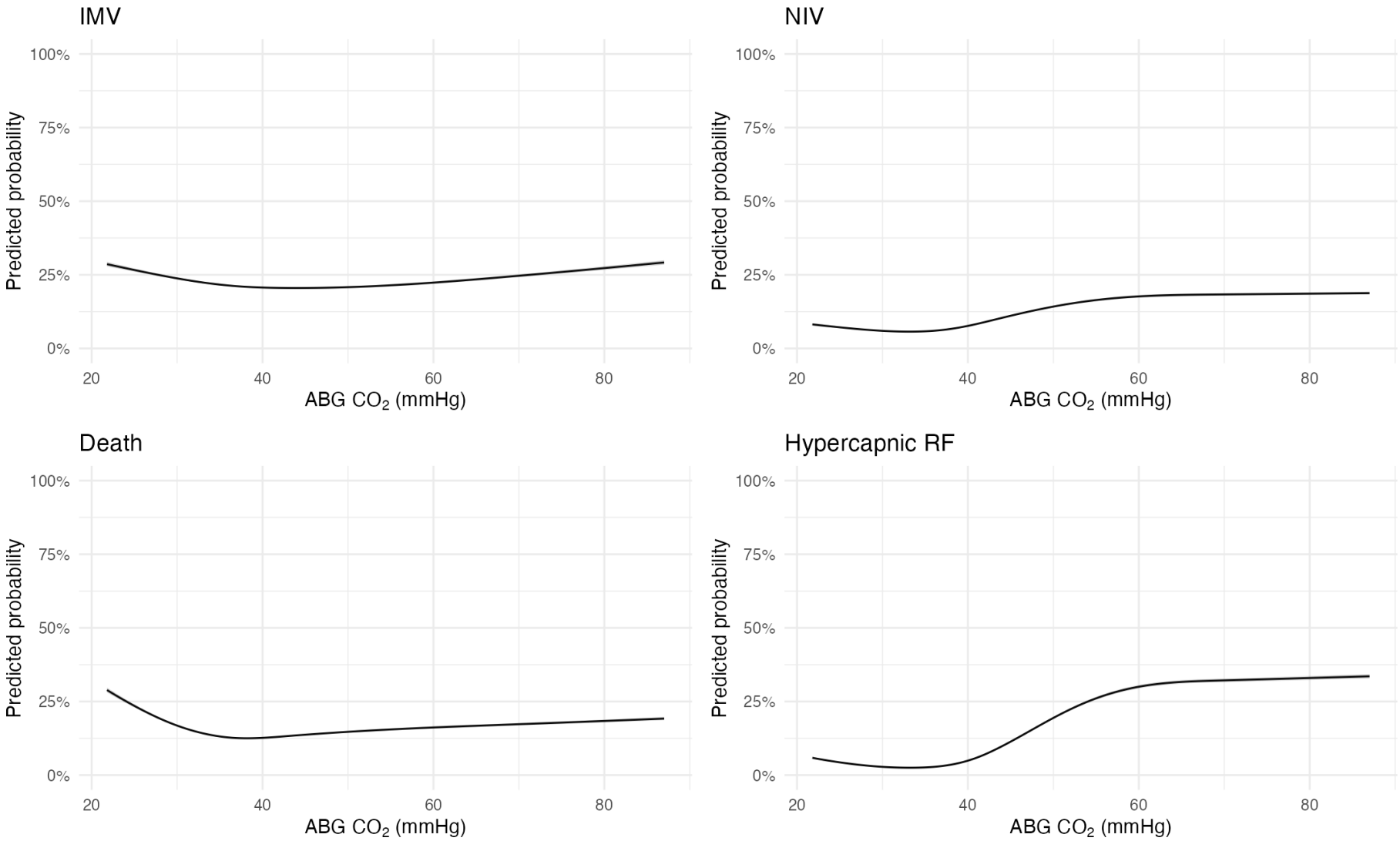
Restricting plots bewtween 0.02 and 0.98

4.0.3 5.3 ABG IPW spline models (2–98th percentile)

```
subset_data_abg <- subset_data %>%
  filter(!is.na(paco2)) %>%                    # implies has_abg == 1
  select(paco2, imv_proc, niv_proc, death_60d,
         hypercap_resp_failure, w_abg) %>%
  filter(complete.cases(.))


#   3. weighted logistic spline models with robust SEs
dd <- datadist(subset_data_abg); options(datadist = "dd")

fitfun <- function(formula)
  svyglm(
    formula,
    design = svydesign(ids = ~1, weights = ~w_abg, data = subset_data_abg),
    family = quasibinomial()
  )

fit_imv_abg   <- fitfun(imv_proc              ~ rcs(paco2, 4))
fit_niv_abg   <- fitfun(niv_proc              ~ rcs(paco2, 4))
fit_death_abg <- fitfun(death_60d                 ~ rcs(paco2, 4))
fit_hcrf_abg  <- fitfun(hypercap_resp_failure ~ rcs(paco2, 4))

#   4. prediction helper
mkpred <- function(fit, data_ref) {
  # 1. Grid of PaCO2 values restricted to 2nd-98th percentile
  q <- quantile(data_ref$paco2, probs = c(0.02, 0.98), na.rm = TRUE)
  newd <- data.frame(
    paco2 = seq(q[1], q[2], length.out = 200)
  )

  # 2. Design (model) matrix for the new data
  mm <- model.matrix(delete.response(terms(fit)), data = newd)
```

```r
  # 3. Linear predictor and its standard error
  eta  <- mm %*% coef(fit)
  vcov <- vcov(fit)
  se   <- sqrt(rowSums((mm %*% vcov) * mm))

  # 4. Transform to probability scale
  transform(
    newd,
    yhat  = plogis(eta),
    lower = plogis(eta - 1.96 * se),
    upper = plogis(eta + 1.96 * se)
  )
}

pred_imv_abg   <- mkpred(fit_imv_abg,   subset_data_abg)
pred_niv_abg   <- mkpred(fit_niv_abg,   subset_data_abg)
pred_death_abg <- mkpred(fit_death_abg, subset_data_abg)
pred_hcrf_abg  <- mkpred(fit_hcrf_abg,  subset_data_abg)

#   5. plotting
xlab <- expression(paste("ABG CO"[2], " (mmHg)"))

plt <- function(dat, title)
  ggplot(dat, aes(paco2, yhat)) +
    geom_line() +
    geom_ribbon(aes(ymin = lower, ymax = upper), alpha = 0.2) +
    scale_y_continuous(limits = c(0, 1), labels = percent_format(accuracy = 1)) +
    labs(title = title, x = xlab, y = "Predicted probability") +
    theme_minimal()

(patchwork::wrap_plots(
    plt(pred_imv_abg,   "IMV"),
    plt(pred_niv_abg,   "NIV"),
    plt(pred_death_abg, "Death"),
    plt(pred_hcrf_abg,  "Hypercapnic RF"),
    ncol = 2
```

```
  )
) +
  plot_annotation(
    title = expression(
      paste("Propensity-weighted predicted probability by ABG CO"[2],
            " (restricted cubic spline)")
    )
)
```



Chunk ipw-abg-rcs-trimmed runtime: 3.45 s

VBG - changed trees and bag fraction

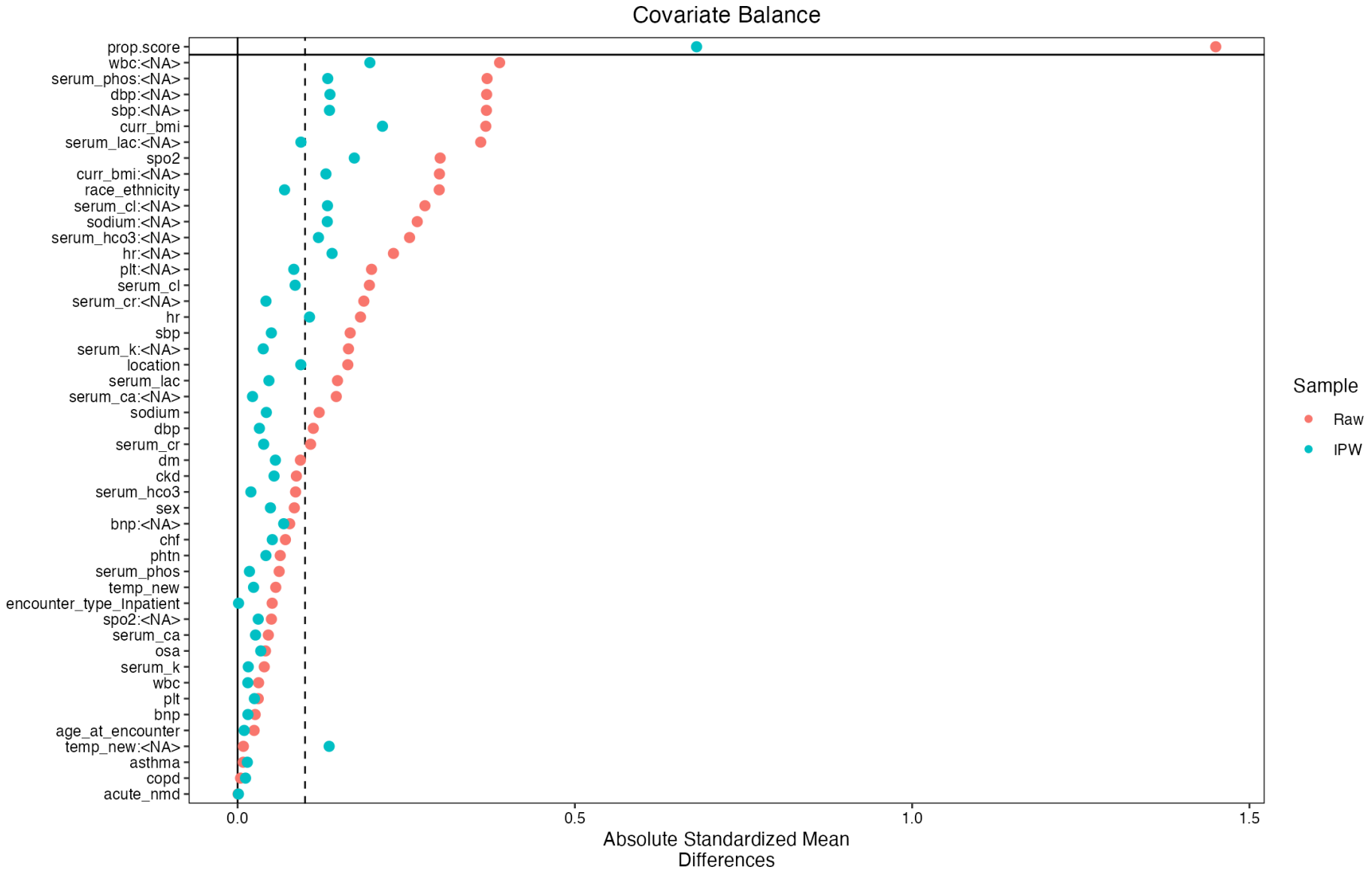
4.0.4 5.4 VBG IPW weighting and spline models

```
#  Inverse-propensity weighting & outcome modelling for **VBG** cohort
#    - mirrored 1-to-1 to the validated ABG workflow

set.seed(42)

# 1. IPW for VBG ---------------------------------------------------------------
set.seed(42)
w_vbg <- do.call(
  weightit,
  c(
    list(
      formula_vbg,
      data        = subset_data,
      method      = "gbm",
      estimand    = "ATE",
      missing     = "ind",
      include.obj = TRUE
    ),
    gbm_params
  )
)

# Stabilise & winsorise weights
w <- w_vbg$weights
w <- w / mean(w)
cut <- quantile(w, c(0.01, 0.99), na.rm = TRUE)
w   <- pmin(pmax(w, cut[1]), cut[2])
w <- w / mean(w)

w_vbg$weights   <- w
subset_data$w_vbg <- w

v_bal <- bal.tab(
```

```
  w_vbg,
  un = TRUE,
  m.threshold = 0.1,
  binary = "std",
  s.d.denom = "pooled"
)
```

```
Warning: Missing values exist in the covariates. Displayed values omit these
observations.
```

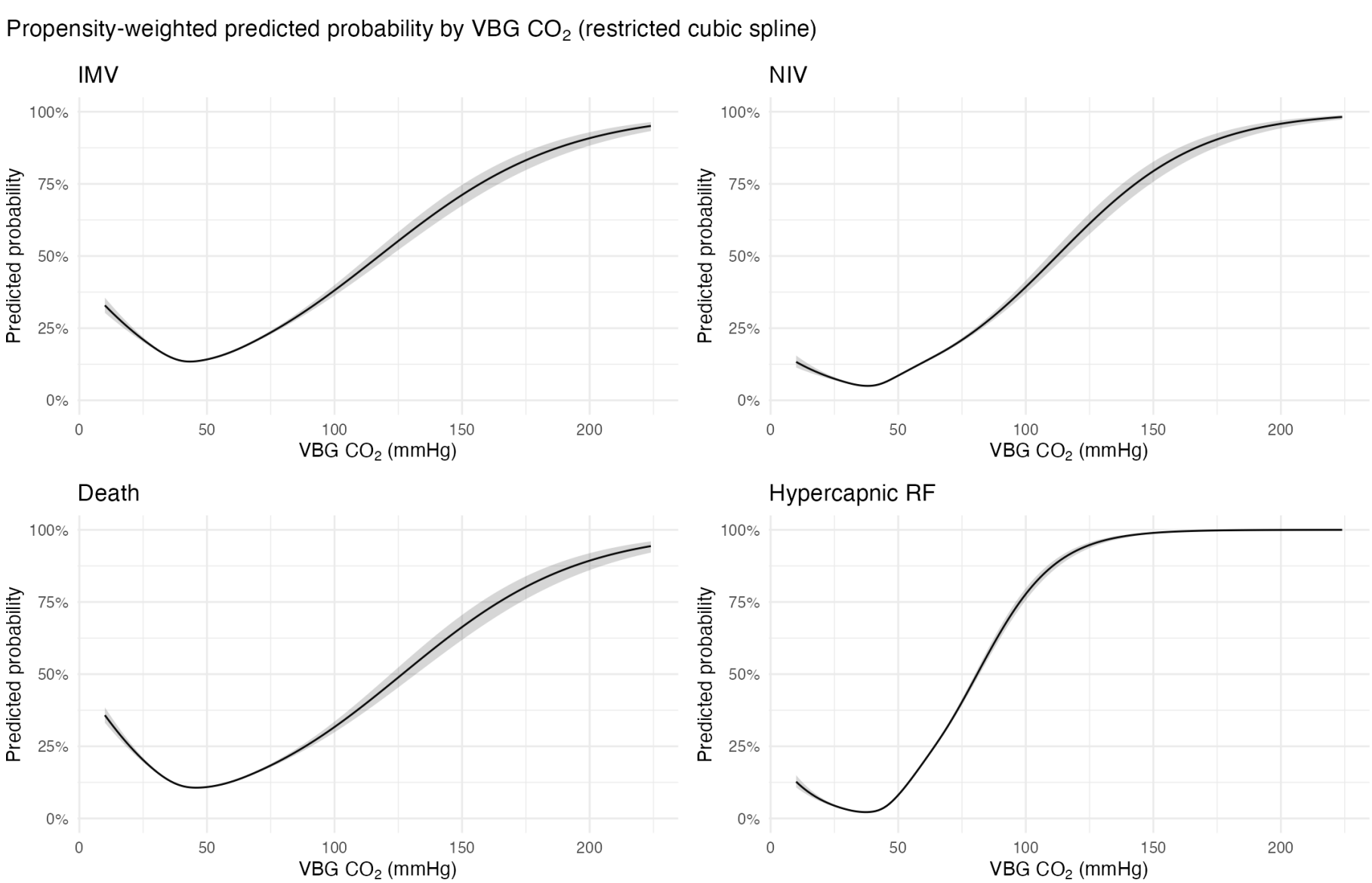
```
love.plot(
  v_bal,
  stats        = "m",          # standardized mean differences only
  abs          = TRUE,
  var.order    = "unadjusted",
  sample.names = c("Raw", "IPW")
)
```




```
# 2. Analysis set (VBG only) ------------------------------------------------
subset_data_vbg <- subset_data %>%
  filter(!is.na(vbg_co2)) %>%
  select(vbg_co2, imv_proc, niv_proc, death_60d,
```

```
         hypercap_resp_failure, w_vbg) %>%
  filter(complete.cases(.))

# 3. Weighted spline models ------------------------------------------------
dd_vbg <- datadist(subset_data_vbg)
options(datadist = "dd_vbg")

fitfun <- function(formula)
  svyglm(
    formula,
    design = svydesign(ids = ~1, weights = ~w_vbg, data = subset_data_vbg),
    family = quasibinomial()
  )

fit_imv_vbg   <- fitfun(imv_proc              ~ rcs(vbg_co2, 4))
fit_niv_vbg   <- fitfun(niv_proc              ~ rcs(vbg_co2, 4))
fit_death_vbg <- fitfun(death_60d             ~ rcs(vbg_co2, 4))
fit_hcrf_vbg  <- fitfun(hypercap_resp_failure ~ rcs(vbg_co2, 4))

# 4. Prediction helper -----------------------------------------------------
mkpred <- function(fit, data_ref) {
  newd <- data.frame(
    vbg_co2 = seq(min(data_ref$vbg_co2, na.rm = TRUE),
                  max(data_ref$vbg_co2, na.rm = TRUE),
                  length.out = 200)
  )
  mm   <- model.matrix(delete.response(terms(fit)), newd)
  eta  <- mm %*% coef(fit)
  vcov <- vcov(fit)
  se   <- sqrt(rowSums((mm %*% vcov) * mm))
  transform(
    newd,
    yhat  = plogis(eta),
    lower = plogis(eta - 1.96 * se),
    upper = plogis(eta + 1.96 * se)
  )
```

```r
}

pred_imv_vbg   <- mkpred(fit_imv_vbg,   subset_data_vbg)
pred_niv_vbg   <- mkpred(fit_niv_vbg,   subset_data_vbg)
pred_death_vbg <- mkpred(fit_death_vbg, subset_data_vbg)
pred_hcrf_vbg  <- mkpred(fit_hcrf_vbg,  subset_data_vbg)

# 5. Plotting (gray scheme) ----------------------------------------------------
xlab <- expression(paste("VBG CO"[2], " (mmHg)"))

plt <- function(dat, title)
  ggplot(dat, aes(vbg_co2, yhat)) +
    geom_line() +
    geom_ribbon(aes(ymin = lower, ymax = upper), alpha = 0.2) +
    scale_y_continuous(limits = c(0, 1), labels = percent_format(accuracy = 1)) +
    labs(title = title, x = xlab, y = "Predicted probability") +
    theme_minimal()

(patchwork::wrap_plots(
    plt(pred_imv_vbg,   "IMV"),
    plt(pred_niv_vbg,   "NIV"),
    plt(pred_death_vbg, "Death"),
    plt(pred_hcrf_vbg,  "Hypercapnic RF"),
    ncol = 2
  )
) +
  plot_annotation(
    title = expression(
      paste("Propensity-weighted predicted probability by VBG CO"[2],
            " (restricted cubic spline)")
    )
)
```



Chunk ipw-vbg-workflow runtime: 2512.90 s

Calculated VBG to ABG / Farkas

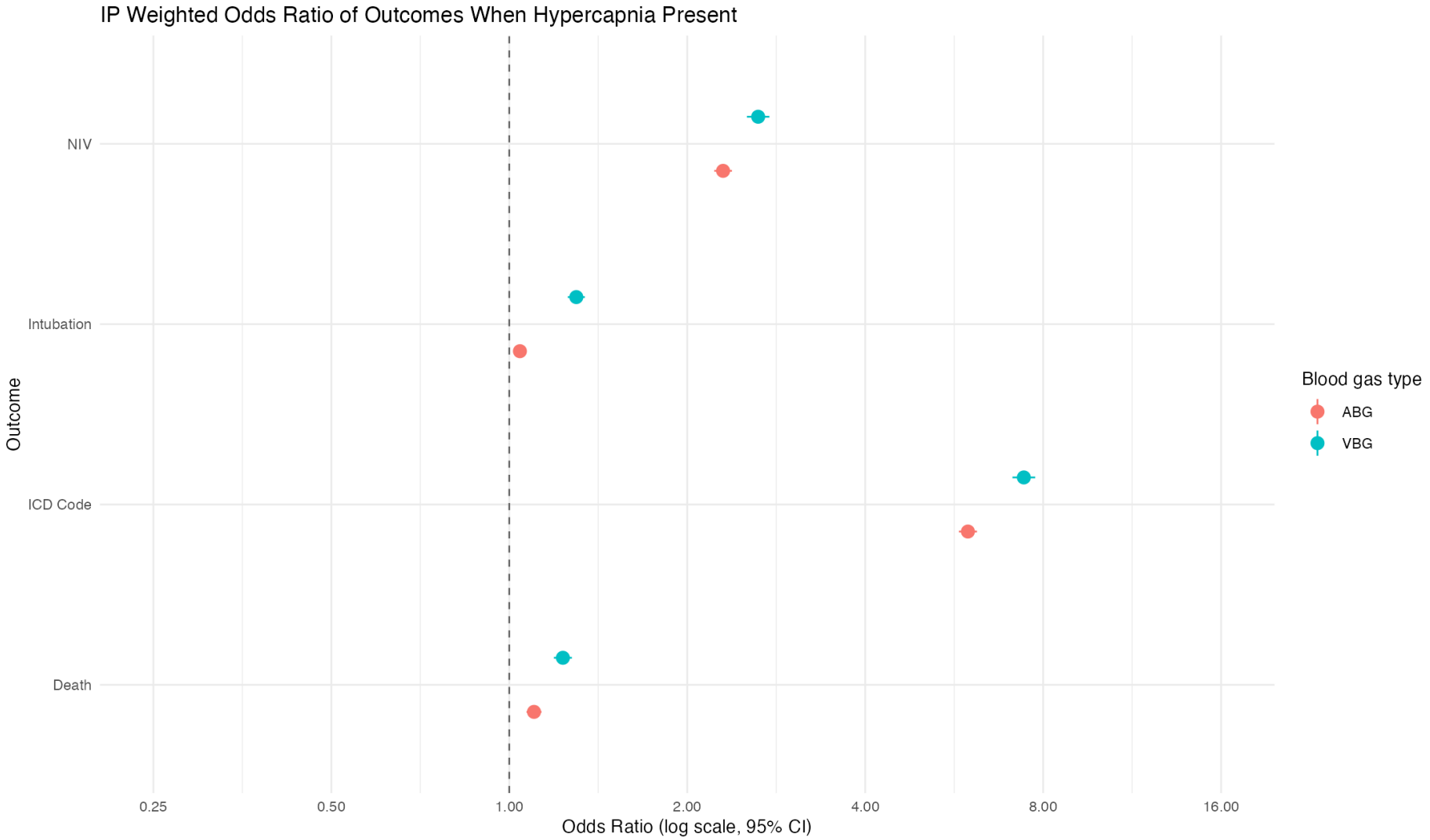
4.1 5) Weighted effect estimates

New weighted binary regression figures.

```
#  IP-weighted odds-ratio plot (ABG, VBG, Calculated-ABG)
#    - exact analogue of the un-weighted figure
#

# weights already attached earlier:
#   • w_abg         - propensity for *ABG*   (column in subset_data)
#   • w_vbg         - propensity for *VBG*   (column in subset_data)
#   •     - same weights, used for calculated ABG CO2

# 1. helper to fit an IP-weighted GLM and return tidy OR ----------------------
tidy_ipw <- function(data, outcome, exposure, weight_var,
                     group_label, outcome_label) {
  des <- svydesign(ids = ~1, weights = as.formula(paste0("~", weight_var)),
                   data = data)
  mod <- svyglm(
    as.formula(paste0(outcome, " ~ ", exposure)),
    design = des,
    family = quasibinomial()
  )

  tidy(mod, exponentiate = TRUE, conf.int = TRUE) %>%
    filter(term == exposure) %>%                # keep the exposure row
    mutate(group = group_label, outcome = outcome_label)
}

# 2. cohort-specific data frames ----------------------------------------------
abg_df   <- subset_data %>% filter(has_abg == 1)
vbg_df   <- subset_data %>% filter(has_vbg == 1)

# 3. fit models & collect estimates -------------------------------------------
ipw_estimates <- bind_rows(
  # ABG
```

```
  tidy_ipw(abg_df,  "imv_proc",              "hypercap_on_abg", "w_abg",      "ABG",          "Intubation"),
  tidy_ipw(abg_df,  "niv_proc",              "hypercap_on_abg", "w_abg",      "ABG",          "NIV"),
  tidy_ipw(abg_df,  "death_60d",                 "hypercap_on_abg", "w_abg",      "ABG",          "Death"),
  tidy_ipw(abg_df,  "hypercap_resp_failure", "hypercap_on_abg", "w_abg",      "ABG",          "ICD Code"),

  # VBG
  tidy_ipw(vbg_df,  "imv_proc",              "hypercap_on_vbg", "w_vbg",      "VBG",          "Intubation"),
  tidy_ipw(vbg_df,  "niv_proc",              "hypercap_on_vbg", "w_vbg",      "VBG",          "NIV"),
  tidy_ipw(vbg_df,  "death_60d",                 "hypercap_on_vbg", "w_vbg",      "VBG",          "Death"),
  tidy_ipw(vbg_df,  "hypercap_resp_failure", "hypercap_on_vbg", "w_vbg",      "VBG",          "ICD Code")
)

# 4. plotting ------------------------------------------------------------------
ipw_estimates$group <- factor(
  ipw_estimates$group,
  levels = c("ABG", "VBG")
)

ggplot(
  ipw_estimates,
  aes(
    x     = outcome,
    y     = estimate,
    ymin  = conf.low,
    ymax  = conf.high,
    color = group
  )
) +
  geom_pointrange(position = position_dodge(width = 0.6), size = 0.6) +
  geom_hline(yintercept = 1, linetype = "dashed", colour = "grey40") +
  scale_y_log10(
    breaks = c(0.25, 0.5, 1, 2, 4, 8, 16),
    limits = c(0.25, 16),
    labels = number_format(accuracy = 0.01)
  ) +
  coord_flip() +
```

```
  labs(
    title  = "IP Weighted Odds Ratio of Outcomes When Hypercapnia Present",
    x      = "Outcome",
    y      = "Odds Ratio (log scale, 95% CI)",
    color  = "Blood gas type",
    caption = paste(
      "Inverse-probability weights adjust for covariates associated with receiving each blood-gas.",
      "Models are fitted within their respective cohorts:",
      "ABG (weights = w_abg), VBG (w_vbg).",
      "Numerator = hypercapnic; denominator = normocapnic within cohort.",
      sep = "\n"
    )
  ) +
  theme_minimal(base_size = 10) +
  theme(plot.caption = element_text(hjust = 0))
```



Chunk ipw-binary-or-plot runtime: 19.05 s

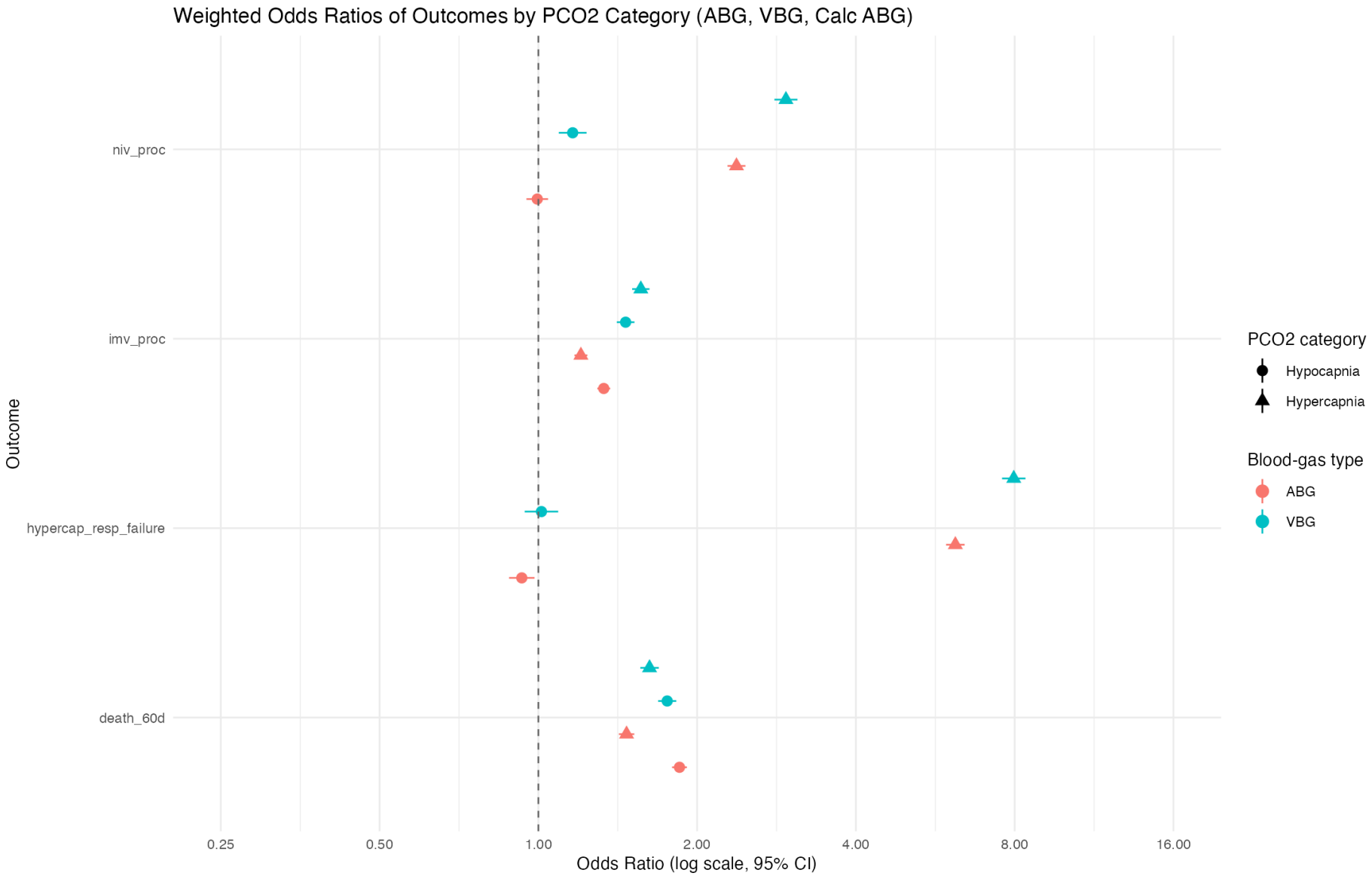
4.1.1 5.5 Three-level PCO2 categories (weighted; ABG, VBG)

Three Groups with Weights

```
library(dplyr)
library(survey)
library(broom)
library(ggplot2)
library(scales)

#   1. Create PCO2 categories
subset_data <- subset_data %>%
  mutate(
    pco2_cat_abg = case_when(
      !is.na(paco2) & paco2 < 35 ~ "Hypocapnia",
      !is.na(paco2) & paco2 >= 35 & paco2 <= 45 ~ "Eucapnia",
      !is.na(paco2) & paco2 > 45 ~ "Hypercapnia",
      TRUE ~ NA_character_
    ),
    pco2_cat_vbg = case_when(
      !is.na(vbg_co2) & vbg_co2 < 40 ~ "Hypocapnia",
      !is.na(vbg_co2) & vbg_co2 >= 40 & vbg_co2 <= 50 ~ "Eucapnia",
      !is.na(vbg_co2) & vbg_co2 > 50 ~ "Hypercapnia",
      TRUE ~ NA_character_
    )
  )

#   2. Function: weighted logistic regression & OR extraction
run_weighted_or <- function(data, outcome, cat_var, weight_var, group_name) {
  dat <- data %>%
    filter(
      !is.na(.data[[cat_var]]),
      !is.na(.data[[outcome]]),
      !is.na(.data[[weight_var]]),
      .data[[weight_var]] > 0
    ) %>%
```

```
    mutate(
      !!cat_var := factor(.data[[cat_var]],
                          levels = c("Eucapnia", "Hypocapnia", "Hypercapnia"))
    ) %>%
    droplevels()

  design <- svydesign(
    ids = ~1,
    weights = as.formula(paste0("~", weight_var)),
    data = dat
  )

  fit <- svyglm(as.formula(paste(outcome, "~", cat_var)),
                design = design, family = quasibinomial())

  tidy(fit, exponentiate = TRUE, conf.int = TRUE) %>%
    filter(term != "(Intercept)") %>%
    mutate(
      group    = group_name,
      outcome  = outcome,
      exposure = gsub(paste0(cat_var), "", term) %>%
                   gsub("`", "", .)
    )
}

#   3. Run across outcomes & cohorts
outcomes <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")

combined_or_df <- bind_rows(
  lapply(outcomes, function(out)
    run_weighted_or(subset_data, out, "pco2_cat_abg",  "w_abg",      "ABG")),
  lapply(outcomes, function(out)
    run_weighted_or(subset_data, out, "pco2_cat_vbg",  "w_vbg",      "VBG"))
)

# Ensure nice ordering
```

```r
combined_or_df$group    <- factor(combined_or_df$group,
                                  levels = c("ABG", "VBG"))
combined_or_df$exposure <- factor(combined_or_df$exposure,
                                  levels = c("Eucapnia", "Hypocapnia", "Hypercapnia"))

#   4. Plot weighted odds ratios
ggplot(
  combined_or_df,
  aes(
    x      = outcome,
    y      = estimate,
    ymin   = conf.low,
    ymax   = conf.high,
    color  = group,
    shape  = exposure
  )
) +
  geom_pointrange(position = position_dodge(width = 0.7), size = 0.6) +
  geom_hline(yintercept = 1, linetype = "dashed", colour = "grey40") +
  scale_y_log10(
    breaks = c(0.25, 0.5, 1, 2, 4, 8, 16),
    limits = c(0.25, 16),
    labels = number_format(accuracy = 0.01)
  ) +
  coord_flip() +
  labs(
    title  = "Weighted Odds Ratios of Outcomes by PCO2 Category (ABG, VBG, Calc ABG)",
    x      = "Outcome",
    y      = "Odds Ratio (log scale, 95% CI)",
    color  = "Blood-gas type",
    shape  = "PCO2 category"
  ) +
  theme_minimal(base_size = 10) +
  theme(plot.caption = element_text(hjust = 0))
```



Chunk ipw-three-level-pco2-all runtime: 30.29 s

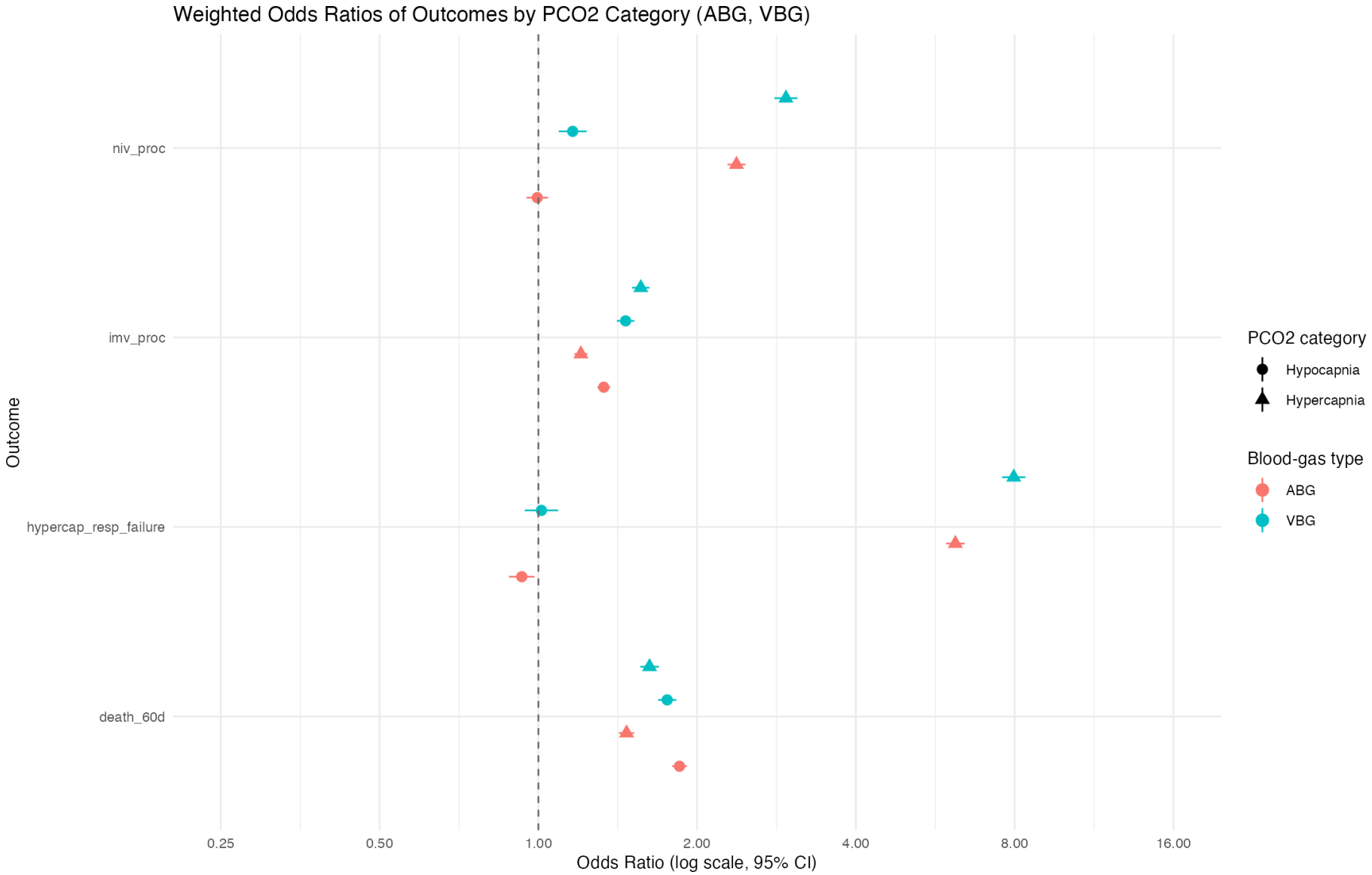
4.1.2 5.6 Three-level PCO2 categories (weighted; ABG vs VBG only)

Three groups with weights: Just ABG and VBG

```
library(dplyr)
library(survey)
library(broom)
library(ggplot2)
library(scales)

#   2. Function: weighted logistic regression & OR extraction
run_weighted_or <- function(data, outcome, cat_var, weight_var, group_name) {
  dat <- data %>%
    filter(
      !is.na(.data[[cat_var]]),
      !is.na(.data[[outcome]]),
      !is.na(.data[[weight_var]]),
      .data[[weight_var]] > 0
    ) %>%
    mutate(
      !!cat_var := factor(.data[[cat_var]],
                          levels = c("Eucapnia", "Hypocapnia", "Hypercapnia"))
    ) %>%
    droplevels()

  design <- svydesign(
    ids = ~1,
    weights = as.formula(paste0("~", weight_var)),
    data = dat
  )

  fit <- svyglm(as.formula(paste(outcome, "~", cat_var)),
                design = design, family = quasibinomial())

  tidy(fit, exponentiate = TRUE, conf.int = TRUE) %>%
    filter(term != "(Intercept)") %>%
```

```
    mutate(
      group    = group_name,
      outcome  = outcome,
      exposure = gsub(paste0(cat_var), "", term) %>%
                   gsub("`", "", .)
    )
}

#   3. Run across outcomes & cohorts
outcomes <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")

combined_or_df <- bind_rows(
  lapply(outcomes, function(out)
    run_weighted_or(subset_data, out, "pco2_cat_abg",  "w_abg",      "ABG")),
  lapply(outcomes, function(out)
    run_weighted_or(subset_data, out, "pco2_cat_vbg",  "w_vbg",      "VBG"))
)

# Ensure nice ordering
combined_or_df$group    <- factor(combined_or_df$group,
                                  levels = c("ABG", "VBG"))
combined_or_df$exposure <- factor(combined_or_df$exposure,
                                  levels = c("Eucapnia", "Hypocapnia", "Hypercapnia"))

#   4. Plot weighted odds ratios
ggplot(
  combined_or_df,
  aes(
    x      = outcome,
    y      = estimate,
    ymin   = conf.low,
    ymax   = conf.high,
    color  = group,
    shape  = exposure
  )
) +
```

```
  geom_pointrange(position = position_dodge(width = 0.7), size = 0.6) +
  geom_hline(yintercept = 1, linetype = "dashed", colour = "grey40") +
  scale_y_log10(
    breaks = c(0.25, 0.5, 1, 2, 4, 8, 16),
    limits = c(0.25, 16),
    labels = number_format(accuracy = 0.01)
  ) +
  coord_flip() +
  labs(
    title  = "Weighted Odds Ratios of Outcomes by PCO2 Category (ABG, VBG)",
    x      = "Outcome",
    y      = "Odds Ratio (log scale, 95% CI)",
    color  = "Blood-gas type",
    shape  = "PCO2 category"
  ) +
  theme_minimal(base_size = 10) +
  theme(plot.caption = element_text(hjust = 0))
```



Chunk ipw-three-level-pco2-abg-vbg runtime: 30.71 s

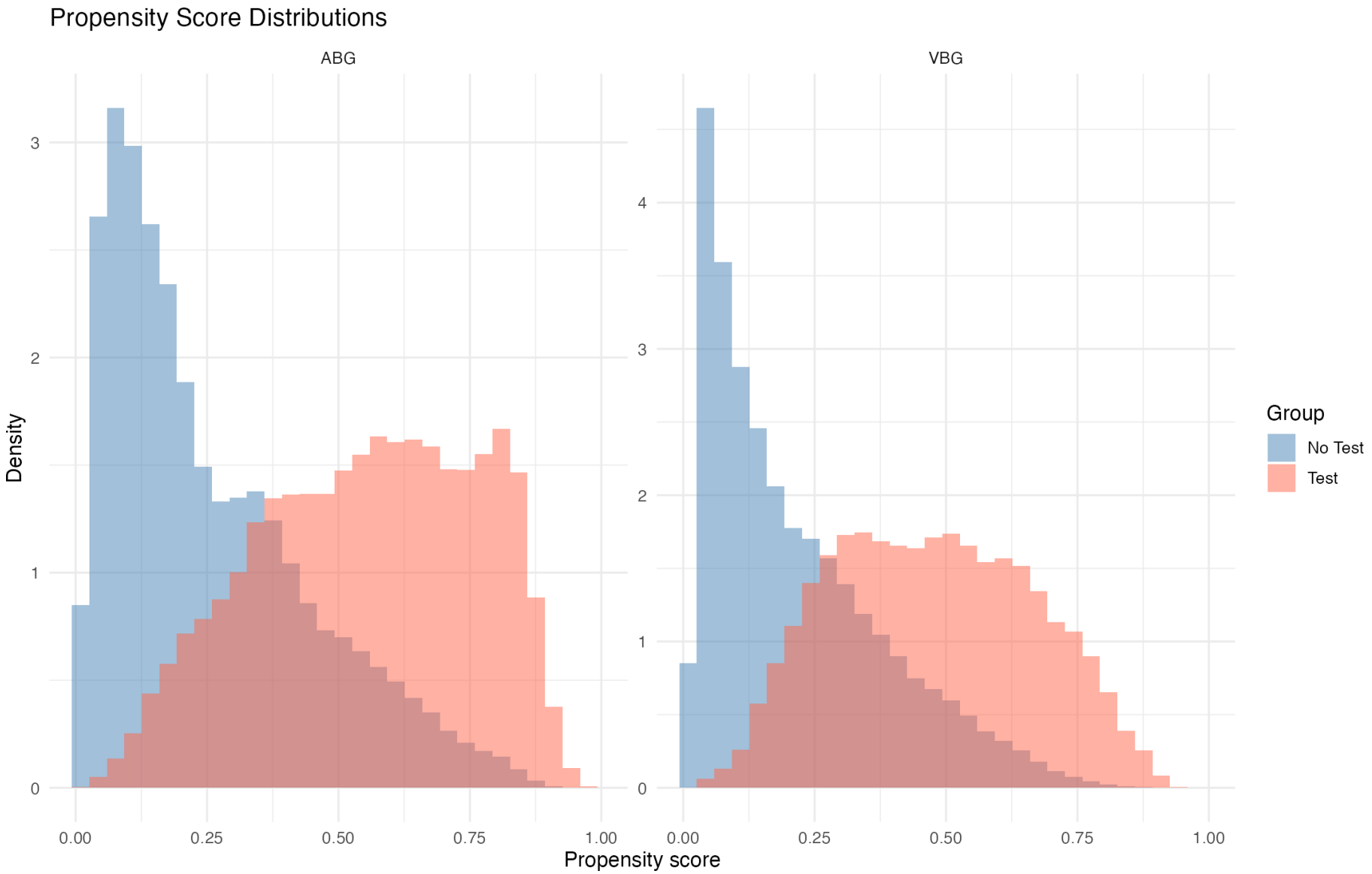
4.2 6) Propensity score diagnostics

Plotting propensity scores

```
# --- Propensity score histograms (ABG / VBG / Calculated-ABG) -----------------
# ABG = arterial blood gas; VBG = venous blood gas

library(dplyr)
library(ggplot2)
library(scales)

# Resolve WeightIt objects regardless of naming used upstream
w_abg_obj <- if (exists("w_abg")) w_abg else if (exists("weight_model")) weight_model else NULL
w_vbg_obj <- if (exists("w_vbg")) w_vbg else NULL

if (is.null(w_abg_obj)) stop("ABG WeightIt object not found. Define `w_abg` or `weight_model` before this block.")
if (!"has_abg" %in% names(subset_data)) stop("`subset_data` must contain `has_abg` for ABG PS plotting.")

# Build list of per-cohort PS data frames conditionally (so missing cohorts don't error)
ps_dfs <- list(
  ABG = data.frame(
    ps        = w_abg_obj$ps,
    treat     = subset_data$has_abg,
    ScoreType = "ABG"
  )
)

if (!is.null(w_vbg_obj) && "has_vbg" %in% names(subset_data)) {
  ps_dfs$VBG <- data.frame(
    ps        = w_vbg_obj$ps,
    treat     = subset_data$has_vbg,
    ScoreType = "VBG"
  )
} else if (is.null(w_vbg_obj)) {
  message("Note: VBG WeightIt object `w_vbg` not found; skipping VBG panel.")
}
```

```r
# Bind, clean, and factorize for plotting
df_ps <- bind_rows(ps_dfs) %>%
  filter(!is.na(ps), !is.na(treat)) %>%
  mutate(
    treat     = factor(treat, levels = c(0, 1), labels = c("No Test", "Test")),
    ScoreType = factor(ScoreType, levels = c("ABG", "VBG"))
  )

# Plot
ggplot(df_ps, aes(x = ps, fill = treat)) +
  geom_histogram(aes(y = ..density..), alpha = 0.5,
                 position = "identity", bins = 30) +
  scale_fill_manual(values = c("No Test" = "steelblue", "Test" = "tomato")) +
  facet_wrap(~ScoreType, scales = "free_y") +
  coord_cartesian(xlim = c(0, 1)) +
  labs(
    title = "Propensity Score Distributions",
    x     = "Propensity score",
    y     = "Density",
    fill  = "Group"
  ) +
  theme_minimal(base_size = 12)
```

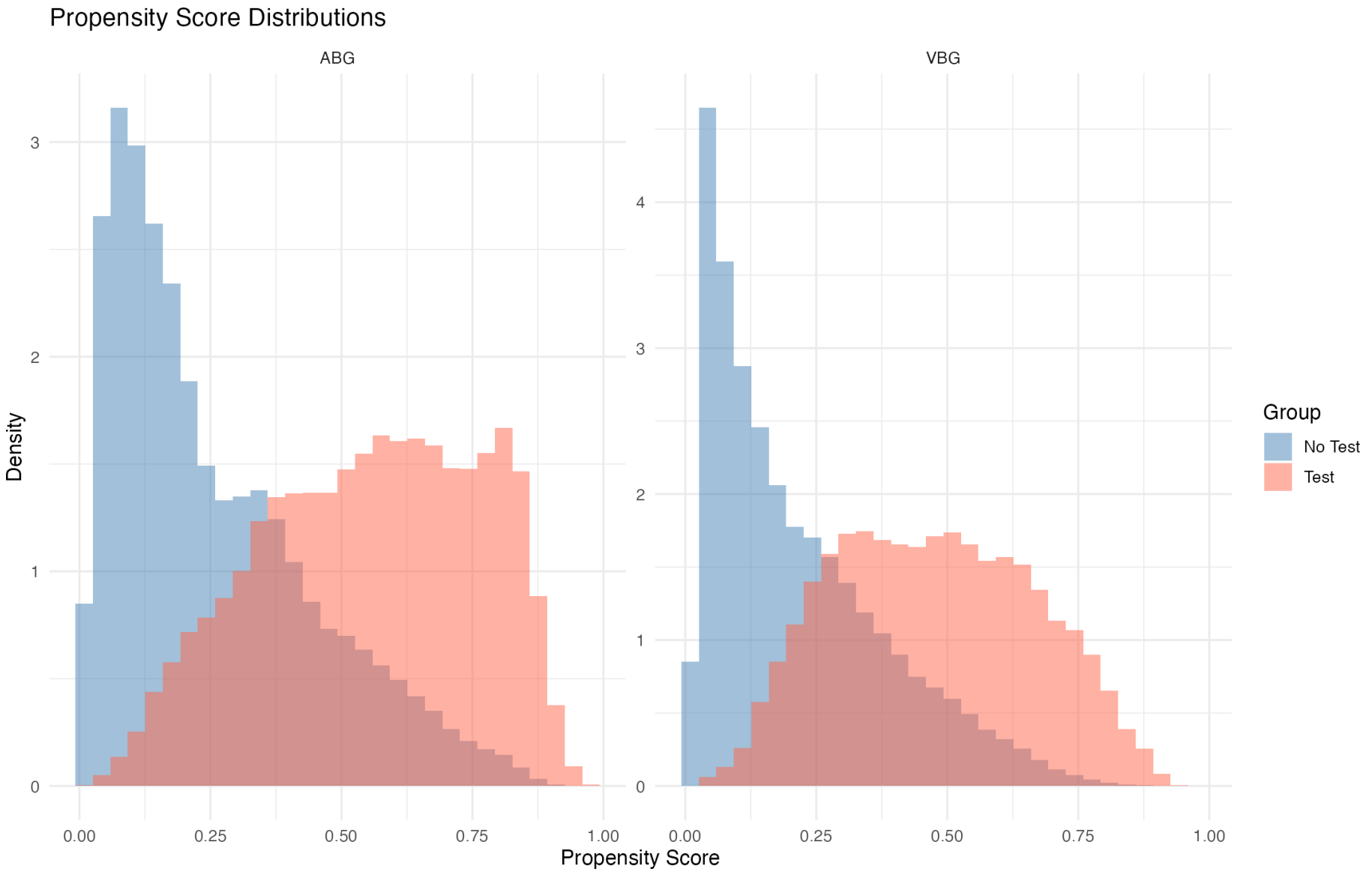
```
Warning: The dot-dot notation (`..density..`) was deprecated in ggplot2 3.4.0.
i Please use `after_stat(density)` instead.
```



Chunk propensity-histograms-conditional runtime: 1.14 s

```
df_ps <- bind_rows(
  data.frame(
```

```
    ps        = w_abg$ps,
    treat     = subset_data$has_abg,
    ScoreType = "ABG"
  ),
  data.frame(
    ps        = w_vbg$ps,
    treat     = subset_data$has_vbg,
    ScoreType = "VBG"
  )
) %>%
  mutate(
    treat     = factor(treat, levels = c(0,1), labels = c("No Test", "Test")),
    ScoreType = factor(ScoreType, levels = c("ABG","VBG"))
  )

ggplot(df_ps, aes(x = ps, fill = treat)) +
  geom_histogram(aes(y = ..density..), alpha = 0.5,
                 position = "identity", bins = 30) +
  scale_fill_manual(values = c("No Test" = "steelblue", "Test" = "tomato")) +
  facet_wrap(~ScoreType, scales = "free_y") +
  labs(
    title = "Propensity Score Distributions",
    x = "Propensity Score",
    y = "Density",
    fill = "Group"
  ) +
  theme_minimal(base_size = 12)
```



Chunk propensity-histograms-all runtime: 0.78 s

5 Multiple Imputation Analysis

added 12/6/2025

5.1 7) Packages and reproducibility

```
# Core MI + diagnostics
library(mice)         # chained equations (MICE)
```

```
Attaching package: 'mice'

The following object is masked from 'package:stats':

    filter

The following objects are masked from 'package:base':

    cbind, rbind
```

```
library(miceadds)     # pooling helpers & utilities
```

```
* miceadds 3.18-36 (2025-09-12 09:54:54)
```

```
library(naniar)       # missingness summaries/plots
```

```
Attaching package: 'naniar'

The following object is masked from 'package:miceadds':

    prop_miss
```

```r
library(visdat)       # quick type/missingness viz
library(skimr)        # data skim for large frames
```

```
Attaching package: 'skimr'
```

```
The following object is masked from 'package:naniar':

    n_complete
```

```r
# Modeling
library(WeightIt)     # GBM propensity with weights
library(gbm)          # underlying GBM engine
library(survey)       # svyglm outcome models
library(cobalt)       # balance diagnostics
library(broom)        # tidy model outputs
library(dplyr)        # data manipulation
library(ggplot2)

# Pooling and MI bookkeeping
library(mitools)      # MIcombine for pooling (generic)
library(parallel)     # basic parallel where helpful

# Parallel + progress setup
library(future)
```

```
Attaching package: 'future'
```

```
The following object is masked from 'package:survival':

    cluster
```

```r
# setup
library(future.apply)
library(progressr)

mi_mids_file    <- results_path("mi_abg_vbg_mids.rds")
mi_w_abg_file   <- results_path("mi_W_abg_list.rds")
mi_w_vbg_file   <- results_path("mi_W_vbg_list.rds")
mi_pooled_file  <- results_path("mi_pooled_results.rds")

workers <- max(1L, future::availableCores() - 1L)
future::plan(multisession, workers = workers)
on.exit(future::plan("sequential"), add = TRUE)

# choose a handler, but DO NOT make it global inside a knitted document
progressr::handlers(progressr::handler_rstudio)   # or handler_txtprogressbar
options(future.rng.onMisuse = "error")            # safer RNG with futures

set.seed(20251206)

# ensure a writable figure dir + stable device on macOS
fs::dir_create(fig_dir, recurse = TRUE)
knitr::opts_chunk$set(fig.path = fig_path, dev = "png", dpi = 144)
options(bitmapType = "cairo")  # prevents device issues on macOS
```

Chunk mi-packages runtime: 2.58 s

5.1.1 Missing data / imputation summary (pre-imputation)

Chunk mi-missing-summary runtime: 0.10 s

5.1.2 7.1 Missingness audit (what, where, how much)

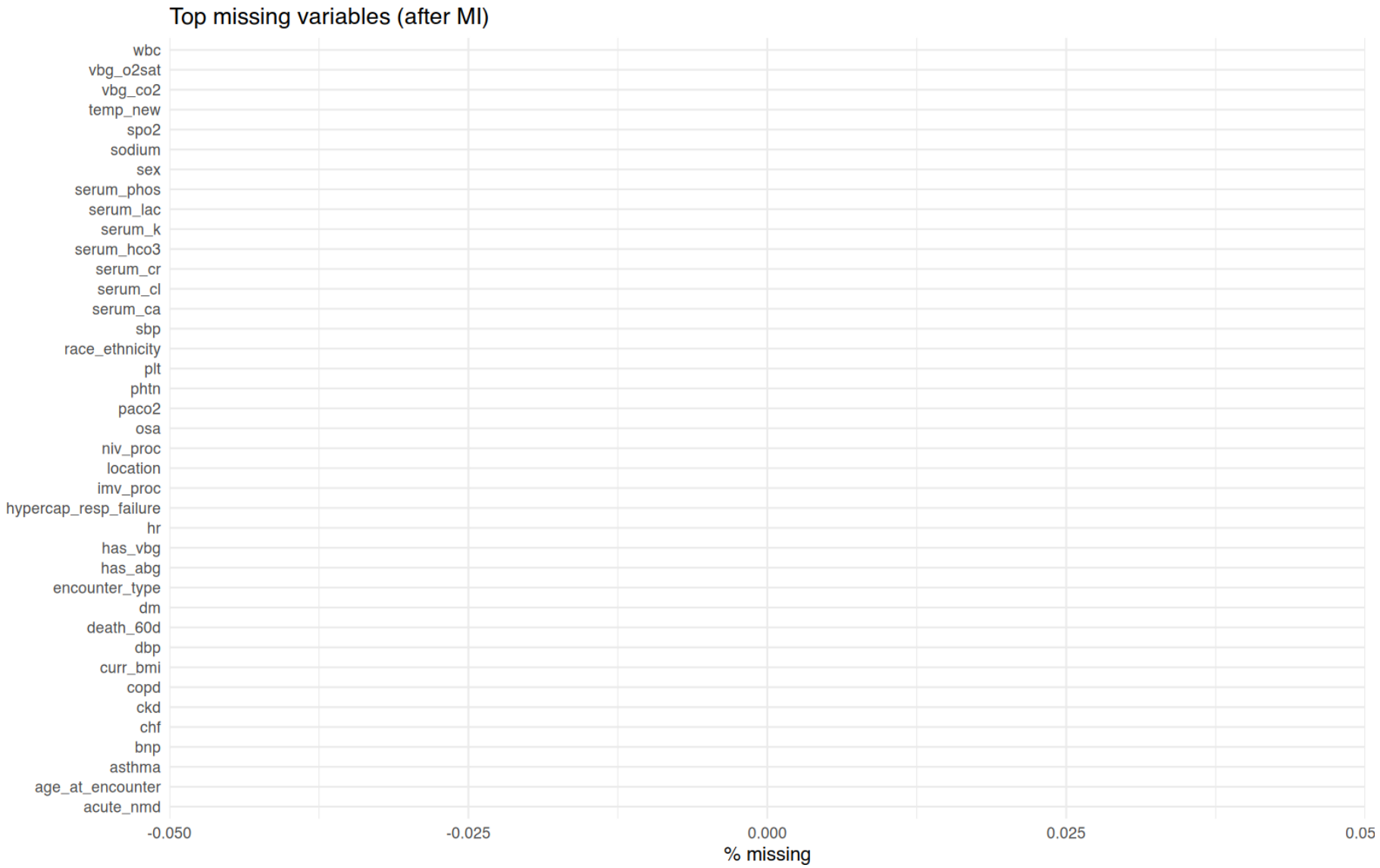
Pre-imputation missingness

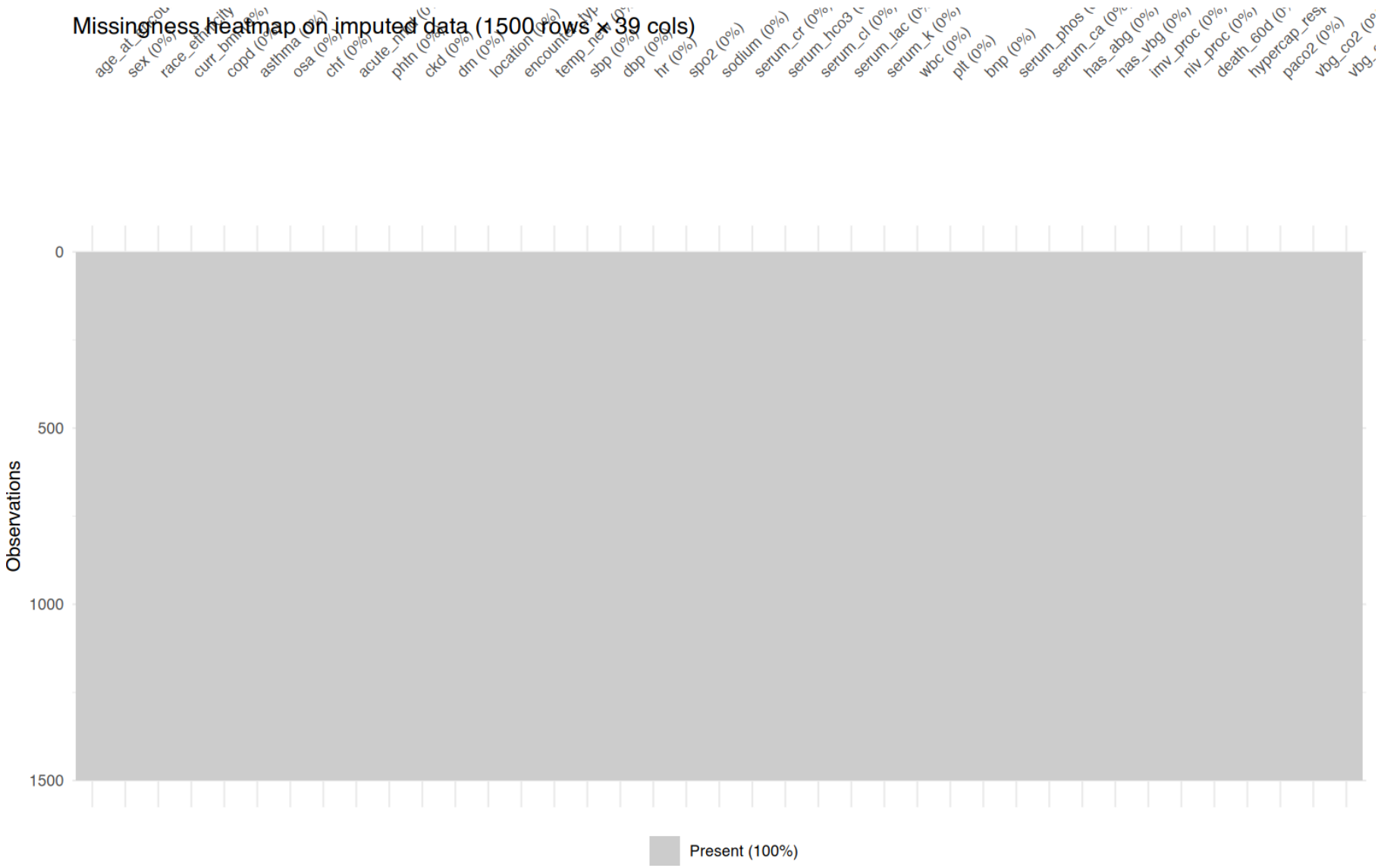
Variable	Missing (n)	Missing (%)
vbg_o2sat	444,799	86.3%
bnp	421,741	81.8%
vbg_co2	365,623	71.0%
spo2	363,720	70.6%
paco2	328,044	63.7%
serum_lac	308,187	59.8%
curr_bmi	293,545	57.0%
serum_phos	273,168	53.0%
temp_new	247,068	47.9%
hr	186,698	36.2%
dbp	154,565	30.0%
sbp	153,161	29.7%
wbc	91,444	17.7%
serum_ca	53,331	10.3%
serum_cr	48,785	9.5%
plt	41,393	8.0%
serum_k	41,266	8.0%
serum_cl	30,694	6.0%
serum_hco3	29,886	5.8%
sodium	27,486	5.3%
age_at_encounter	0	0.0%
sex	0	0.0%
race_ethnicity	0	0.0%
copd	0	0.0%
asthma	0	0.0%
osa	0	0.0%
chf	0	0.0%
acute_nmd	0	0.0%
phtn	0	0.0%
ckd	0	0.0%
dm	0	0.0%
location	0	0.0%
encounter_type	0	0.0%
has_abg	0	0.0%
has_vbg	0	0.0%
imv_proc	0	0.0%

```r
# --- Lean missingness audit (memory-safe) ---------------------------------
library(dplyr)
library(ggplot2)
library(naniar)

# Use imputed data if available (preferred); otherwise skip
imp_obj <- NULL
if (exists("imp")) imp_obj <- imp
if (is.null(imp_obj) && file.exists(mi_mids_file)) {
  imp_obj <- tryCatch(readRDS(mi_mids_file), error = function(e) NULL)
}

if (is.null(imp_obj)) {
  message("MI object not found; skipping imputed missingness visuals.")
} else {
  dat_imp <- mice::complete(imp_obj, action = 1, include = FALSE)

  # 1) Tabular summary on completed data (should be near 0% by design)
  miss_tbl <- naniar::miss_var_summary(dat_imp) %>% arrange(desc(pct_miss))
  print(utils::head(miss_tbl, 40))   # show top 40 in the report

  # 2) Bar plot of top-K (mostly zeros after imputation)
  K <- 40
  top_vars <- miss_tbl$variable[seq_len(min(K, nrow(miss_tbl)))]
  p_top <- ggplot(miss_tbl[miss_tbl$variable %in% top_vars, ],
                  aes(x = reorder(variable, pct_miss), y = pct_miss)) +
    geom_col() +
    coord_flip() +
    labs(title = "Top missing variables (after MI)", x = NULL, y = "% missing") +
    theme_minimal()
  print(p_top)

  # 3) Small heatmap on imputed data (rows/cols sampled)
  M <- 60
  R <- min(1500, nrow(dat_imp))
  cols_heat <- head(top_vars, M)
```

```
  rows_heat <- dplyr::slice_sample(dat_imp, n = R)

  p_heat <- naniar::vis_miss(rows_heat[, cols_heat, drop = FALSE]) +
    labs(title = sprintf("Missingness heatmap on imputed data (%d rows × %d cols)", R, length(cols_heat)))
  print(p_heat)
}
```

```
# A tibble: 39 x 3
   variable         n_miss pct_miss
   <chr>             <int>    <num>
 1 age_at_encounter      0        0
 2 sex                   0        0
 3 race_ethnicity        0        0
 4 curr_bmi              0        0
 5 copd                  0        0
 6 asthma                0        0
 7 osa                   0        0
 8 chf                   0        0
 9 acute_nmd             0        0
10 phtn                  0        0
# i 29 more rows
```


Top missing variables (after MI)
wbc
vbg_o2sat
vbg_co2
temp_new
spo2
sodium
sex
serum_phos
serum_lac
serum_k
serum_hco3
serum_cr
serum_cl
serum_ca
sbp
race_ethnicity
plt
phtn
paco2
osa
niv_proc
location
imv_proc
hypercap_resp_failure
hr
has_vbg
has_abg
encounter_type
dm
death_60d
dbp
curr_bmi
copd
ckd
chf
bnp
asthma
age_at_encounter
acute_nmd
-0.050
-0.025
0.000
0.025
0.05
% missing




```
# 4) Optional, but often heavy: UpSet of co-missingness - skip by default.
# If you really want it, do it for top 6-10 variables only:
# naniar::gg_miss_upset(dat_imp[, head(top_vars, 8), drop = FALSE])
```

Chunk mi-missing-audit runtime: 1.87 s

5.2 8) Pre-imputation data prep (consistent types & predictors)

Why: MI models need coherent types; using exactly the same covariates as the propensity score models avoids model drift.

```
# Ensure intended factor/numeric types for imputation
# --- Inspect current encounter_type ------------------------------------------
cat("encounter_type class:", paste(class(subset_data$encounter_type), collapse = ", "), "\n")
```

```
encounter_type class: factor
```

```
print(utils::head(unique(subset_data$encounter_type), 20))
```

```
[1] Emergency Inpatient
Levels: Emergency Inpatient
```

```
# Keep a raw copy for debugging if mapping fails
encounter_type_raw <- subset_data$encounter_type

# --- Helpers -----------------------------------------------------------------

# Map various encodings to strict 0/1 integer (for sex + 0/1 indicators)
to01 <- function(x) {
  if (is.logical(x)) return(as.integer(x))
  if (is.factor(x))  x <- as.character(x)

  out <- rep(NA_integer_, length(x))
  xs  <- suppressWarnings(as.numeric(x))
  is_num <- !is.na(xs)

  # numeric 0/1
  out[is_num & xs %in% c(0, 1)] <- as.integer(xs[is_num & xs %in% c(0, 1)])
```

```r
  # character encodings (case/space-insensitive)
  if (any(!is_num)) {
    s <- trimws(tolower(as.character(x[!is_num])))
    out[!is_num][s %in% c("0","no","false","female","f")] <- 0L
    out[!is_num][s %in% c("1","yes","true","male","m")]   <- 1L
  }
  out
}

# Robust normalizer for encounter_type:
# - accepts numeric 2/3, digit-strings "2", "3", "2 - ED", etc.
# - accepts common synonyms with word-boundary protection
normalize_encounter_type <- function(x) {
  # to character once
  s_chr <- trimws(tolower(as.character(x)))

  # try to pull numeric code from any digits present
  num_from_text <- suppressWarnings(as.numeric(gsub("[^0-9]+", "", s_chr)))

  lab <- rep(NA_character_, length(s_chr))

  # numeric path
  lab[!is.na(num_from_text) & num_from_text == 2] <- "Emergency"
  lab[!is.na(num_from_text) & num_from_text == 3] <- "Inpatient"

  # synonym path (fill only still-NA)
  is_na <- is.na(lab)

  # Emergency synonyms: "emergency", "emerg", exact "ed", "a&e", "emergency dept"
  is_em <- grepl("\\bemerg(?:ency)?\\b", s_chr) |
           grepl("(^|[^a-z])ed([^a-z]|$)", s_chr) |
           grepl("\\ba&e\\b", s_chr) |
           grepl("\\bemergency\\s+dept\\b", s_chr)

  # Inpatient synonyms: "inpatient", "inpt", "inpat", exact "ip"
  is_ip <- grepl("\\binpatient\\b", s_chr) |
```

```
          grepl("\\binpt\\b",     s_chr) |
          grepl("\\binpat\\b",    s_chr) |
          grepl("(^|[^a-z])ip([^a-z]|$)", s_chr)

  lab[is_na & is_em] <- "Emergency"
  lab[is_na & is_ip] <- "Inpatient"

  factor(lab, levels = c("Emergency", "Inpatient"))
}

# --- Coerce analysis types (including encounter_type) -------------------------
subset_data <- subset_data |>
  mutate(
    sex               = factor(to01(sex), levels = c(0L, 1L), labels = c("Female", "Male")),
    race_ethnicity    = if (is.factor(race_ethnicity)) race_ethnicity else factor(race_ethnicity),
    location          = if (is.factor(location))       location       else factor(location),
    encounter_type    = normalize_encounter_type(encounter_type),
    has_abg           = to01(has_abg),
    has_vbg           = to01(has_vbg),
    hypercap_on_abg   = to01(hypercap_on_abg),
    hypercap_on_vbg   = to01(hypercap_on_vbg)
  )

# immediately drop unused levels and assert exactly two levels in the observed data used by MI
subset_data$encounter_type <- droplevels(subset_data$encounter_type)
stopifnot(nlevels(subset_data$encounter_type) == 2L)

# --- Diagnostics for encounter_type -------------------------------------------
tab_enc <- table(subset_data$encounter_type, useNA = "ifany")
print(tab_enc)
```

```
Emergency Inpatient
   171727    343559
```

```r
if (sum(!is.na(subset_data$encounter_type)) == 0) {
  message("All encounter_type values are NA after normalization. Showing top raw values:")
  s_raw <- trimws(tolower(as.character(encounter_type_raw)))
  print(utils::head(sort(table(s_raw), decreasing = TRUE), 20))
  stop("normalize_encounter_type produced all NA; extend the synonym map to your raw values.")
}

# Must have at least one observed value and (after droplevels) exactly two levels
stopifnot(sum(!is.na(subset_data$encounter_type)) > 0)
stopifnot(nlevels(droplevels(subset_data$encounter_type)) == 2)
```

Chunk mi-prep runtime: 4.54 s

Chunk type-invariants runtime: 0.40 s

5.3 9) Imputation model specification (MICE)

5.3.1 9.1 Predictor matrix & methods. Run MICE (moderate settings for scale)

```r
# --- variables for GBM propensity (kept identical to main analysis) ---
# ---- MICE setup (Option A: include PaCO2 for ABG + keep VBG CO2/O2Sat) ----
library(mice)
library(dplyr)

# --- add analysis targets and CO2 measures explicitly -------------------------
co2_vars <- c("paco2", "vbg_co2", "vbg_o2sat")

mi_vars <- unique(c(
  covars_gbm,
  "has_abg","has_vbg",                                  # treatments (NOT imputed)
  "imv_proc","niv_proc","death_60d","hypercap_resp_failure",  # outcomes (NOT imputed)
  co2_vars
))
```

```r
mi_df <- subset_data[, mi_vars, drop = FALSE]

# Make binary comorbids factors so "logreg" is used (and stays binary)
bin_covars <- c("copd","asthma","osa","chf","acute_nmd","phtn","ckd","dm")
missing_bin <- setdiff(bin_covars, names(mi_df))
stopifnot(length(missing_bin) == 0)
mi_df[bin_covars] <- lapply(mi_df[bin_covars], function(z) {
  if (is.factor(z)) return(droplevels(z))
  zz <- suppressWarnings(as.integer(z))
  factor(zz, levels = c(0L,1L), labels = c("0","1"))
})

# Force CO2 variables to be numeric BEFORE we convert any leftover characters to factor
coerce_num <- function(x) suppressWarnings(as.numeric(as.character(x)))
for (nm in intersect(co2_vars, names(mi_df))) mi_df[[nm]] <- coerce_num(mi_df[[nm]])

# For MICE: convert any remaining characters → factors (after CO2 numeric coercion)
mi_df <- dplyr::mutate(mi_df, across(where(is.character), ~ factor(.x)))

# --- methods & predictor matrix aligned to *mi_df* ----------------------------
meth <- mice::make.method(mi_df)

is_fac      <- vapply(mi_df, is.factor,  logical(1))
is_num      <- vapply(mi_df, is.numeric, logical(1))
is_bin_fac  <- vapply(mi_df, function(x) is.factor(x)  && nlevels(x) == 2, logical(1))
is_multicat <- vapply(mi_df, function(x) is.factor(x)  && nlevels(x) >  2, logical(1))

# robust defaults
meth[is_num]      <- "pmm"      # numerics: predictive mean matching
meth[is_multicat] <- "polyreg"  # unordered multicategory
meth[is_bin_fac]  <- "logreg"   # binary factors: logistic regression

# never impute treatments or outcomes
no_imp <- c("has_abg","has_vbg","imv_proc","niv_proc","death_60d","hypercap_resp_failure")
meth[intersect(names(meth), no_imp)] <- ""
```

```r
# predictor matrix; forbid treatments/outcomes as predictors
pred <- mice::quickpred(mi_df, mincor = 0.05, minpuc = 0.25)
pred[, intersect(colnames(pred), no_imp)] <- 0
pred[intersect(rownames(pred), no_imp), ] <- 0

# MI integrity: treatments/outcomes excluded; binaries use logreg
stopifnot(all(meth[no_imp] == ""))
stopifnot(all(colSums(pred[, intersect(colnames(pred), no_imp), drop = FALSE]) == 0))
stopifnot(all(rowSums(pred[intersect(rownames(pred), no_imp), , drop = FALSE]) == 0))
bin_fac <- names(which(vapply(mi_df, function(x) is.factor(x) && nlevels(x) == 2, logical(1))))
stopifnot(all(meth[bin_fac] == "logreg"))

# integrity checks
stopifnot(
  ncol(pred) == ncol(mi_df),
  nrow(pred) == ncol(mi_df),
  length(meth) == ncol(mi_df),
  identical(names(meth), colnames(mi_df))
)

# --- run MICE ---------------------------------------------------------------
set.seed(20251206)
imp <- mice::mice(
  data            = mi_df,
  m               = 5,
  maxit           = 10,
  predictorMatrix = pred,
  method          = meth,
  printFlag       = TRUE,
  seed            = 20251206
)
```

```
 iter imp variable
  1   1  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
  1   2  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
```

1	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
1	4	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
1	5	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
2	1	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
2	2	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
2	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
2	4	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
2	5	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
3	1	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
3	2	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
3	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
3	4	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
3	5	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
4	1	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
4	2	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
4	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
4	4	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
4	5	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
5	1	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
5	2	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
5	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
5	4	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
5	5	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
6	1	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
6	2	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
6	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
6	4	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
6	5	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
7	1	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
7	2	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
7	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
7	4	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
7	5	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
8	1	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
8	2	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru
8	3	curr_bmi	temp_new	sbp	dbp	hr	spo2	sodium	serum_cr	serum_hco3	serum_cl	serum_lac	serum_k	wbc	plt	bnp	seru

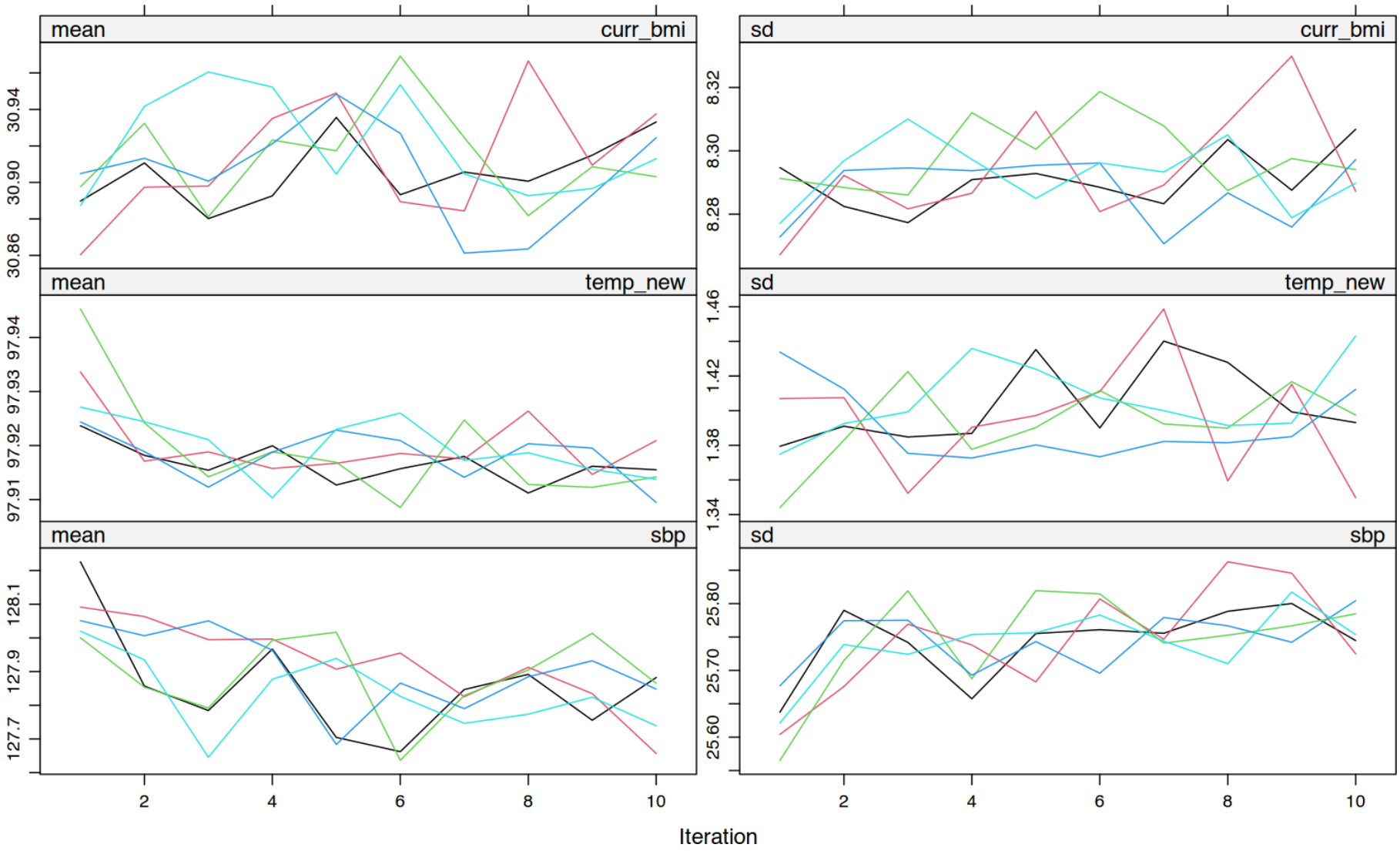
```
  8   4  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
  8   5  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
  9   1  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
  9   2  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
  9   3  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
  9   4  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
  9   5  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
 10   1  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
 10   2  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
 10   3  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
 10   4  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
 10   5  curr_bmi  temp_new  sbp  dbp  hr  spo2  sodium  serum_cr  serum_hco3  serum_cl  serum_lac  serum_k  wbc  plt  bnp  seru
```

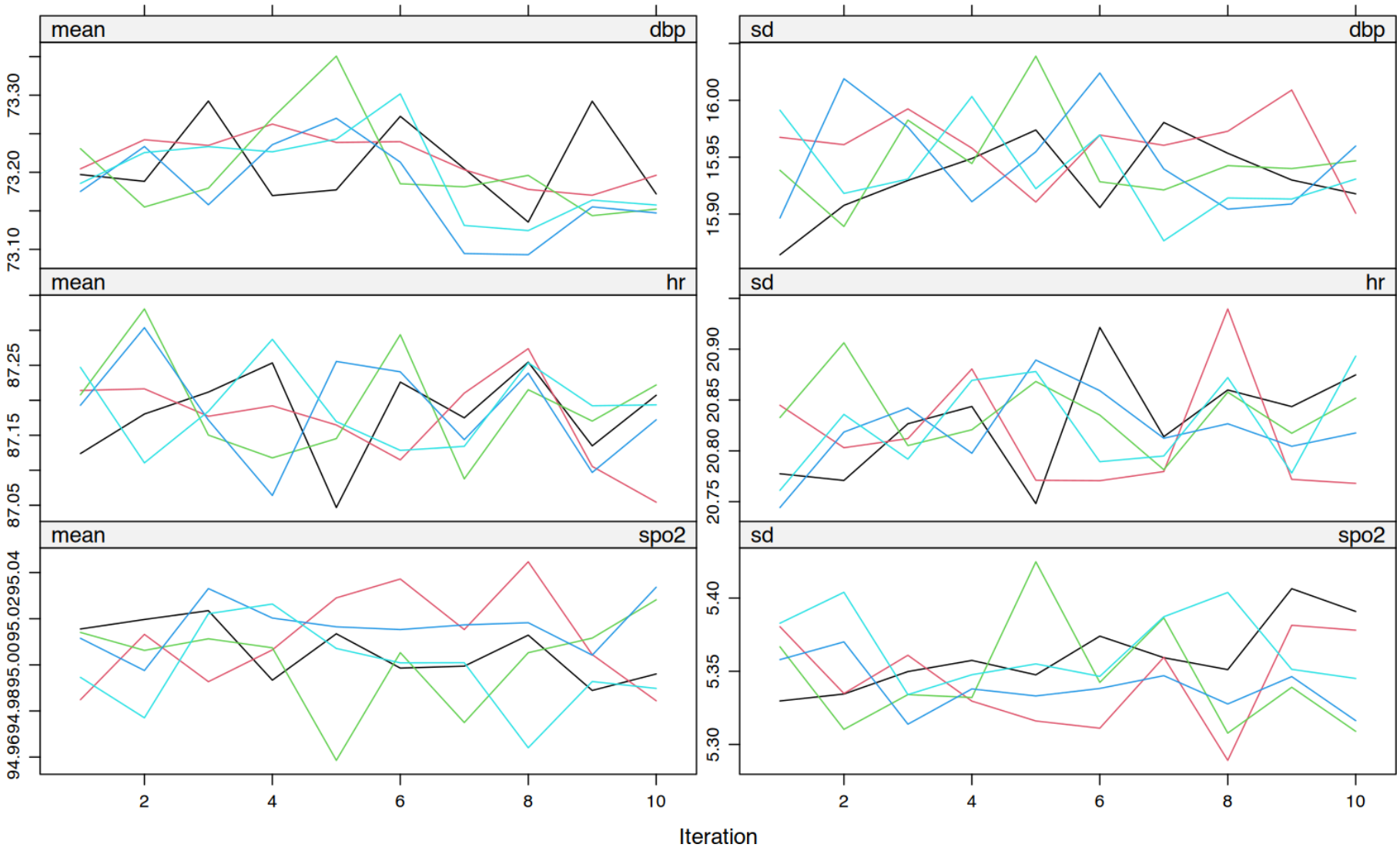
```r
saveRDS(imp, file = mi_mids_file)

# quick sanity: these must exist and be numeric in completed data
dlist <- mice::complete(imp, action = "all")
stopifnot(all(c("paco2","vbg_co2") %in% names(dlist[[1]])))
stopifnot(is.numeric(dlist[[1]]$paco2), is.numeric(dlist[[1]]$vbg_co2))
```

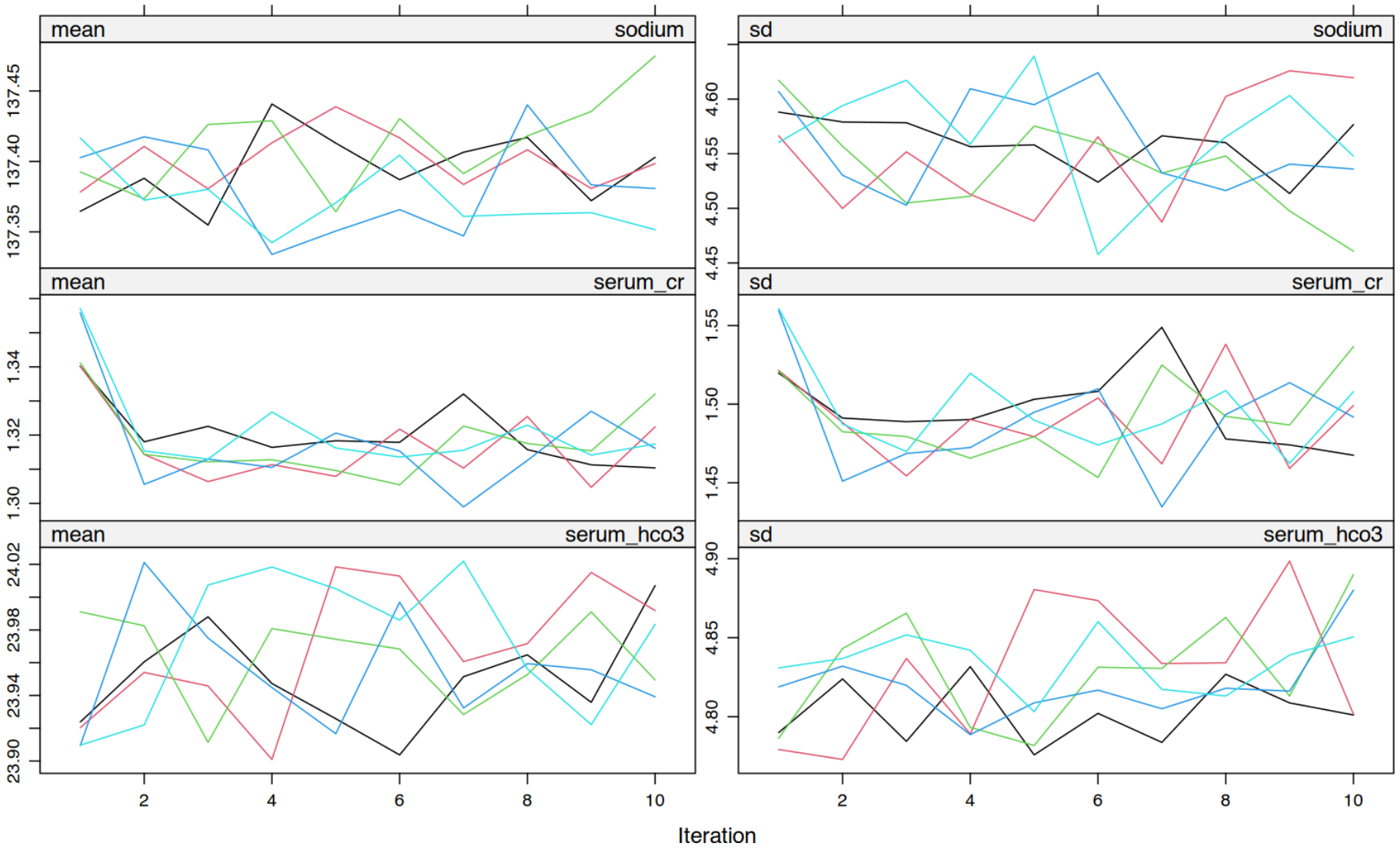
Chunk mi-exec runtime: 2135.97 s

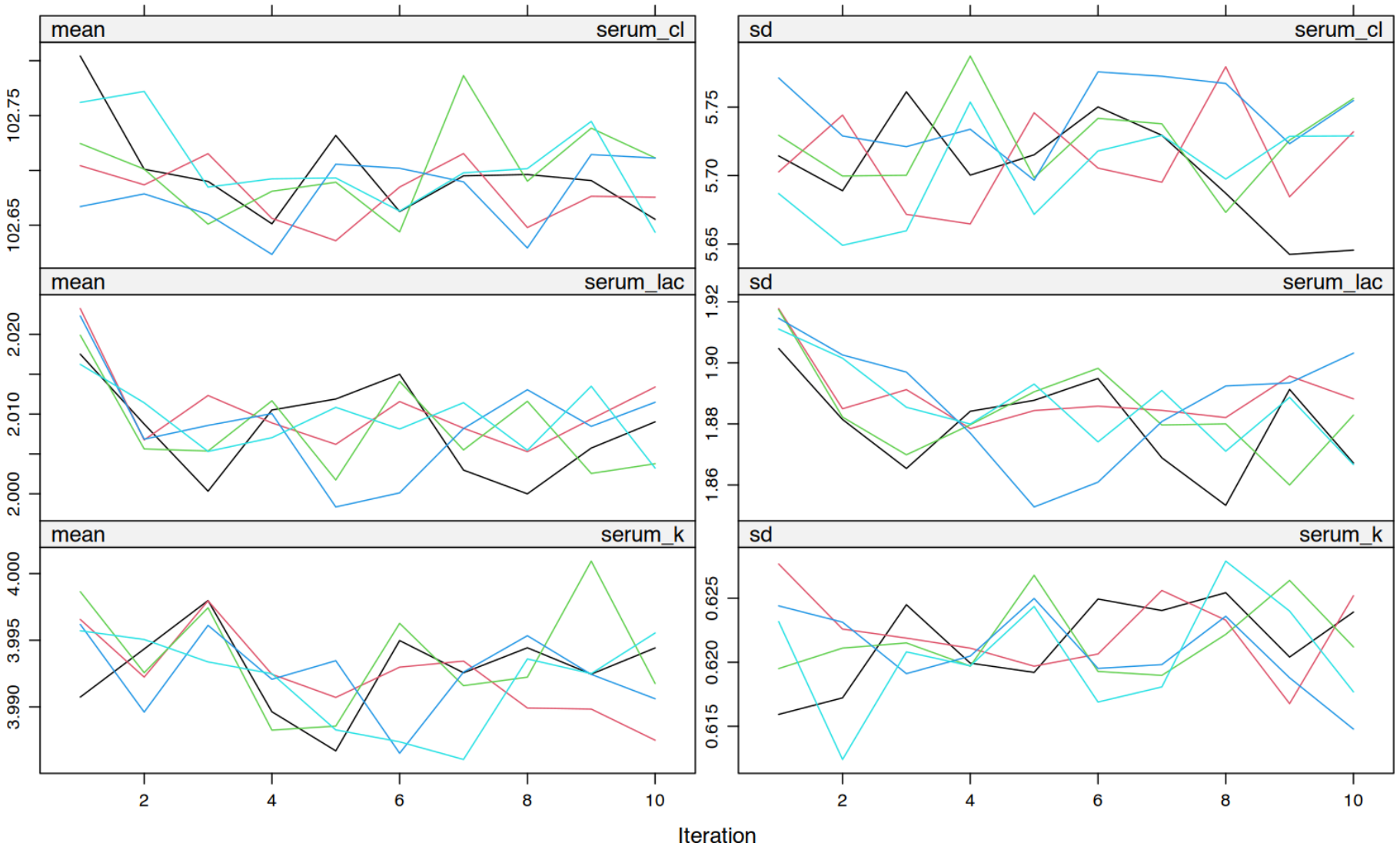
5.3.2 9.2 Convergence & plausibility checks

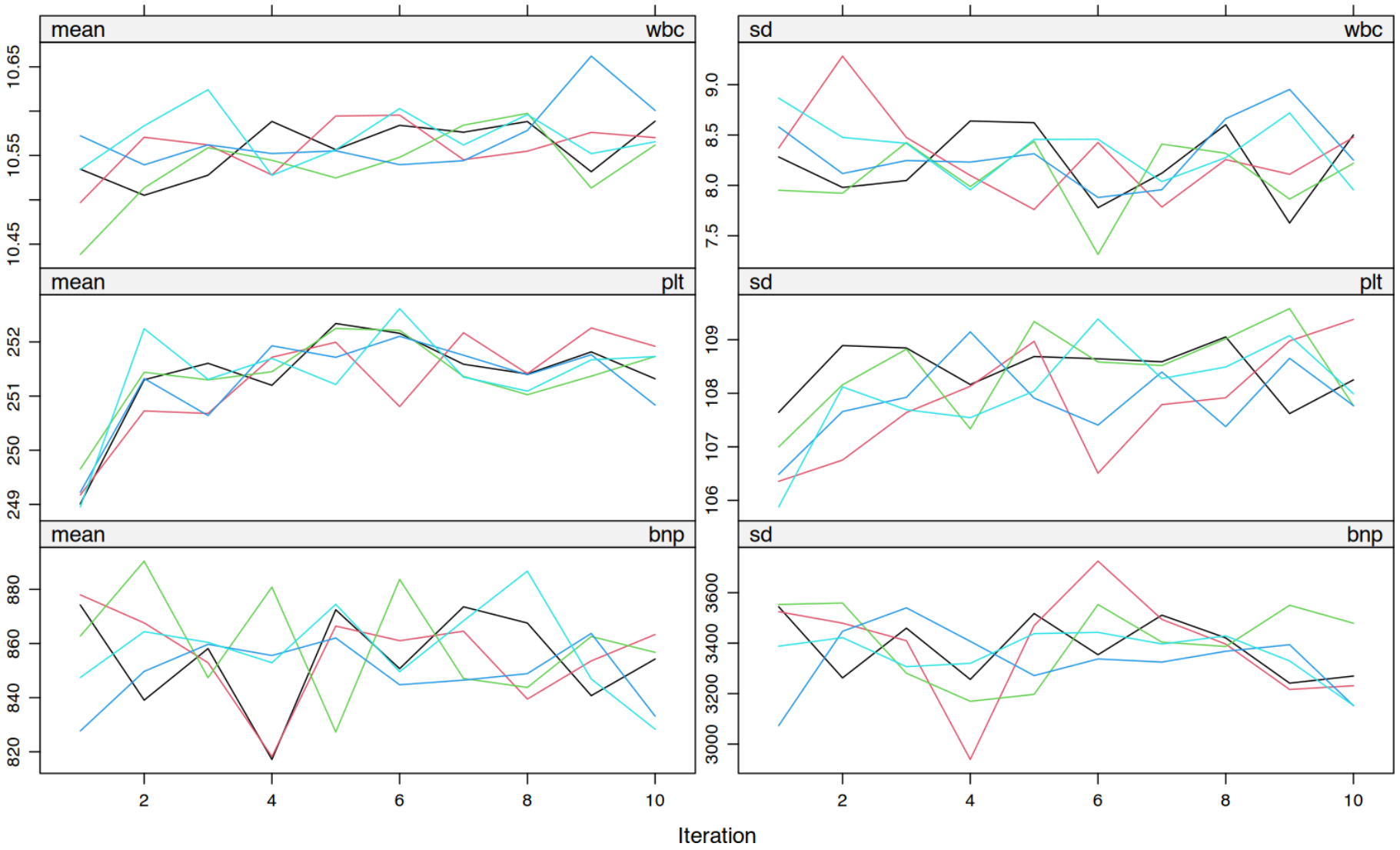
```r
imp <- readRDS(mi_mids_file)

# Throttle diagnostics to avoid memory blow-up
plot(imp)                                          # trace plots (m=5)
```

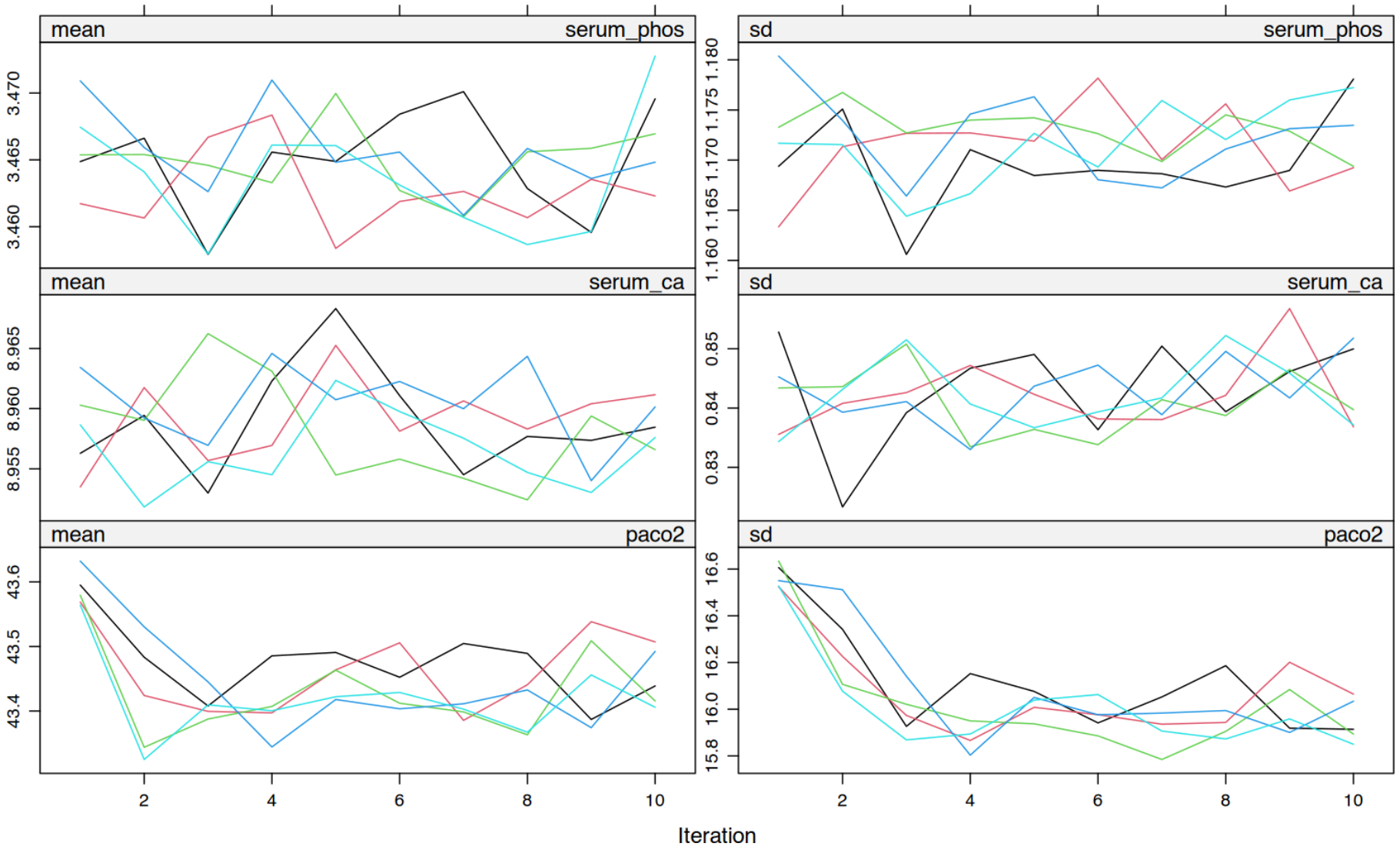

mean
curr_bmi
sd
curr_bmi
mean
temp_new
sd
temp_new
mean
sbp
sd
sbp
30.94
30.90
30.86
8.32
8.30
8.28
97.94
97.93
97.92
97.91
1.46
1.42
1.38
1.34
128.1
127.9
127.7
25.80
25.70
25.60
2
4
6
8
10
Iteration

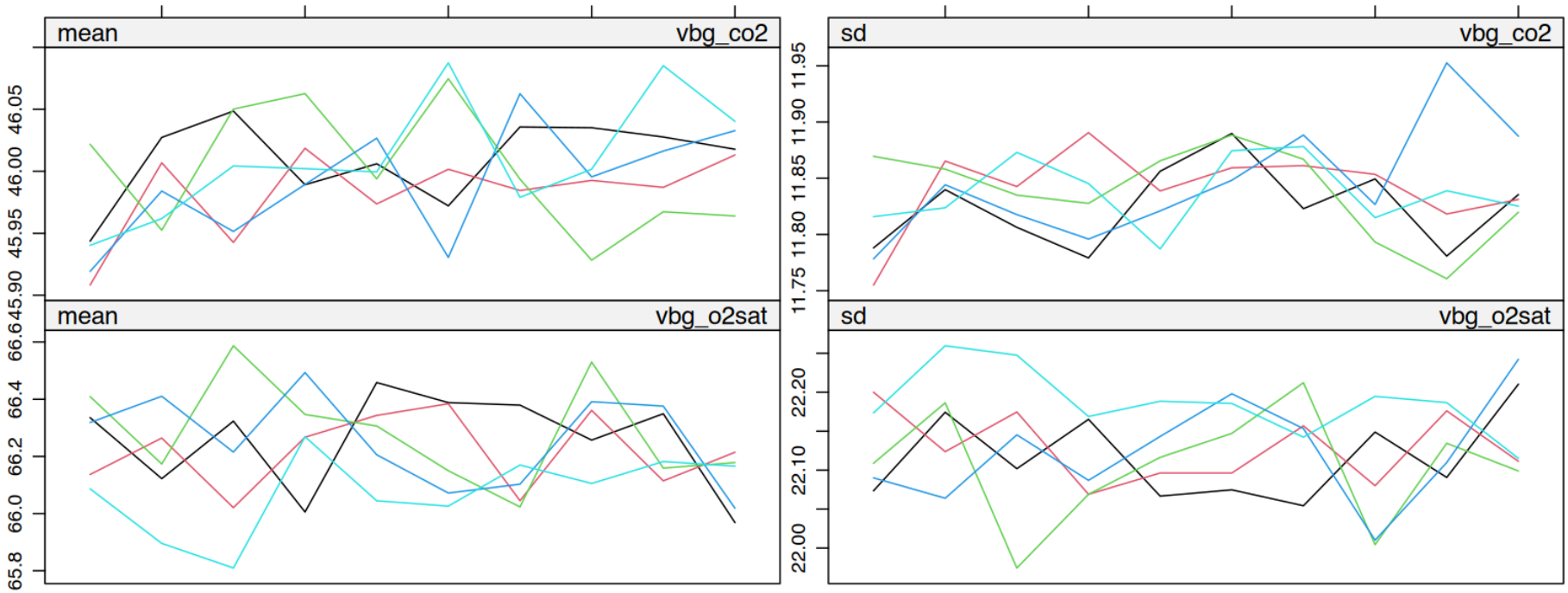

mean
dbp
sd
dbp
mean
hr
sd
hr
mean
spo2
sd
spo2
73.10
73.20
73.30
15.90
15.95
16.00
87.05
87.15
87.25
20.75
20.80
20.85
20.90
94.96
94.98
95.00
95.02
95.04
5.30
5.35
5.40
2
4
6
8
10
Iteration


mean
sodium
sd
sodium
mean
serum_cr
sd
serum_cr
mean
serum_hco3
sd
serum_hco3
137.45
137.40
137.35
4.60
4.55
4.50
4.45
1.34
1.32
1.30
1.55
1.50
1.45
24.02
23.98
23.94
23.90
4.90
4.85
4.80
2
4
6
8
10
Iteration

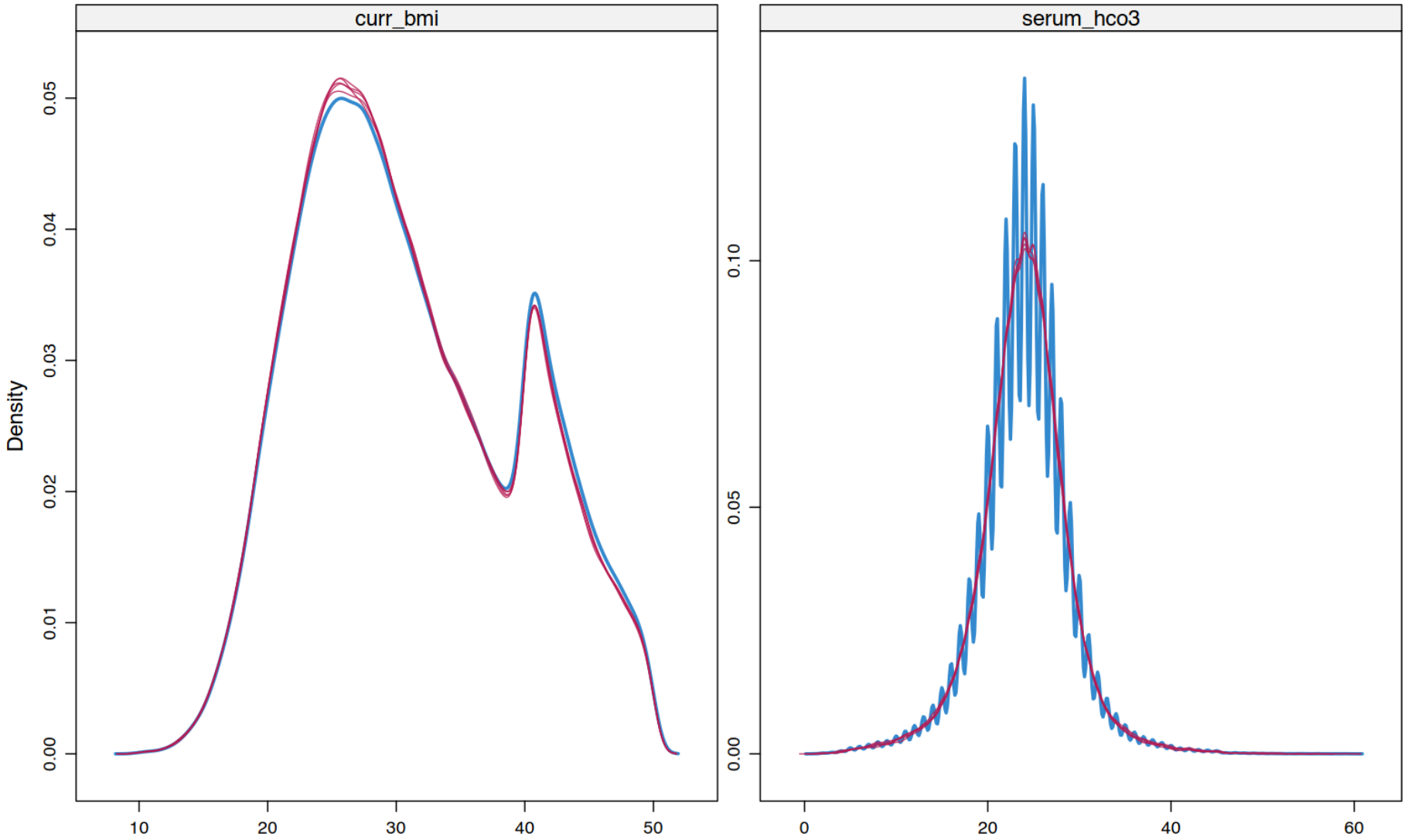

mean
serum_cl
sd
serum_cl
mean
serum_lac
sd
serum_lac
mean
serum_k
sd
serum_k
102.75
102.65
5.75
5.70
5.65
2.020
2.010
2.000
1.92
1.90
1.88
1.86
4.000
3.995
3.990
0.625
0.620
0.615
2
4
6
8
10
Iteration


mean
wbc
sd
wbc
mean
plt
sd
plt
mean
bnp
sd
bnp
10.45
10.55
10.65
249
250
251
252
820
840
860
880
7.5
8.0
8.5
9.0
106
107
108
109
3000
3200
3400
3600
2
4
6
8
10
Iteration

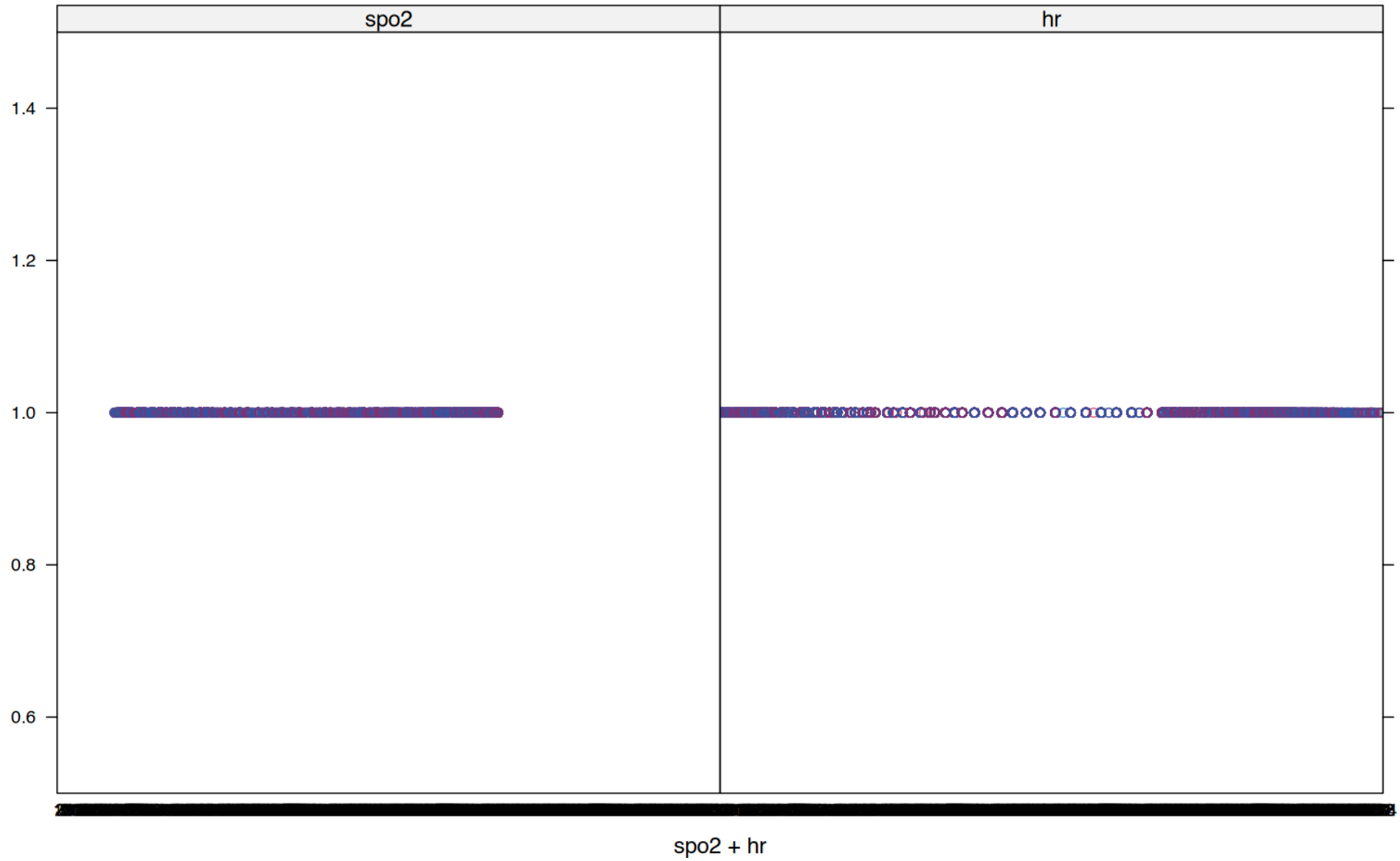

mean
serum_phos
sd
serum_phos
mean
serum_ca
sd
serum_ca
mean
paco2
sd
paco2
3.460
3.465
3.470
1.160
1.165
1.170
1.175
1.180
8.955
8.960
8.965
0.83
0.84
0.85
43.4
43.5
43.6
15.8
16.0
16.2
16.4
16.6
2
4
6
8
10
Iteration




```
densityplot(imp, ~ curr_bmi + serum_hco3)              # imputed vs observed
```




```
stripplot(imp,  ~ spo2 + hr, subset = .imp == 1)      # distribution overlap on first imp only
```




```
md.pattern(complete(imp, "long", include = FALSE))     # pattern after MI (compact)
```

```
 /\     /\
{  `---'  }
```

```
{  O   O  }
==>  V <==  No need for mice. This data set is completely observed.
 \  \|/  /
  `-----'
```

```
        age_at_encounter sex race_ethnicity curr_bmi copd asthma osa chf
2576430                1   1              1        1    1      1   1   1
                       0   0              0        0    0      0   0   0
        acute_nmd phtn ckd dm location encounter_type temp_new sbp dbp hr spo2
2576430         1    1   1  1        1              1        1   1   1  1    1
                0    0   0  0        0              0        0   0   0  0    0
        sodium serum_cr serum_hco3 serum_cl serum_lac serum_k wbc plt bnp
2576430      1        1          1        1         1       1   1   1   1
             0        0          0        0         0       0   0   0   0
        serum_phos serum_ca has_abg has_vbg imv_proc niv_proc death_60d
2576430          1        1       1       1        1        1         1
                 0        0       0       0        0        0         0
        hypercap_resp_failure paco2 vbg_co2 vbg_o2sat .imp .id
2576430                     1     1       1         1    1   1 0
                            0     0       0         0    0   0 0
```

Chunk mi-diagnostics runtime: 140.13 s

5.4 10) Refit propensity models within each imputation

We keep the GBM recipe close to the non-MI run, but with lighter CV (cv.folds = 3) and slightly fewer trees.

5.4.1 10.1 ABG propensity (has_abg)

```r
# Create completed datasets
dlist <- mice::complete(imp, action = "all")

# Fit ABG propensity weights in each imputation
fit_abg_one <- function(d) {
  w <- weightit(
    formula_abg,
    data   = d[, c("has_abg", covars_gbm)],
    method = "gbm",
    estimand    = "ATE",
    include.obj = TRUE,
    n.trees           = gbm_params$n.trees,
    interaction.depth = gbm_params$interaction.depth,
    shrinkage         = gbm_params$shrinkage,
    bag.fraction      = gbm_params$bag.fraction,
    cv.folds          = gbm_params$cv.folds,
    stop.method       = gbm_params$stop.method,
    n.cores           = gbm_params$n.cores
  )
  # stabilise + two-sided Winsorization
  ww <- w$weights; ww <- ww/mean(ww)
  cut <- stats::quantile(ww, c(.01,.99), na.rm = TRUE)
  ww <- pmin(pmax(ww, cut[1]), cut[2]); ww <- ww/mean(ww)
  w$weights <- ww
  w
}

with_progress({
  p <- progressor(along = seq_along(dlist))

  # Avoid hitting future.globals.maxSize with large dlist
  options(future.globals.maxSize = +Inf)
  if (utils::object.size(dlist) > 4e8) future::plan(sequential)

  W_abg_list <- future_lapply(
```

```
    X = seq_along(dlist),
    FUN = function(i) {
      p(sprintf("Fitting ABG on imputation %d", i))
      set.seed(20251206 + i)           # per-imputation seed for reproducibility
      fit_abg_one(dlist[[i]])
    },
    future.seed = TRUE                  # reproducible RNG across workers
  )
})

saveRDS(W_abg_list, mi_w_abg_file)
```

Chunk mi-propensity-abg runtime: 158.14 s

```
         n   min p99.99%   max      ess
[1,] 25724 0.570   3.317 3.317 21042.33
[2,] 25724 0.570   3.313 3.314 21088.17
[3,] 25724 0.569   3.339 3.339 21059.14
[4,] 25724 0.571   3.301 3.301 21054.30
[5,] 25724 0.569   3.361 3.361 21001.74
```

Chunk mi-weight-diagnostics-abg runtime: 0.23 s

5.4.2 10.2 Balance diagnostics across imputations

```
# Vars you intended to use (from your earlier code)
vars0 <- covars_gbm

# Which factors collapse to 1 level AFTER complete-case filtering (per imputation, per arm)?
find_offenders_post_cc <- function(d, treat_var, vars) {
  keep <- c(treat_var, vars)
  dd   <- d[, keep, drop = FALSE]
  dd   <- dd[stats::complete.cases(dd), , drop = FALSE]  # mimic cobalt's CC
```

```r
  if (!nrow(dd)) return(character(0))

  # factor with <2 levels in either arm
  bad <- vapply(vars, function(v) {
    x <- dd[[v]]
    if (!is.factor(x)) return(FALSE)
    by_arm <- tapply(x, dd[[treat_var]], function(z) nlevels(droplevels(z)))
    any(is.na(by_arm)) || any(by_arm < 2)
  }, logical(1))

  names(bad)[bad]
}

off_by_imp <- lapply(dlist, find_offenders_post_cc, treat_var = "has_abg", vars = vars0)
to_drop    <- Reduce(union, off_by_imp)  # union across imputations
message("Offenders (post CC): ", if (length(to_drop)) paste(to_drop, collapse = ", ") else "<none>")
```

```
Offenders (post CC): <none>
```

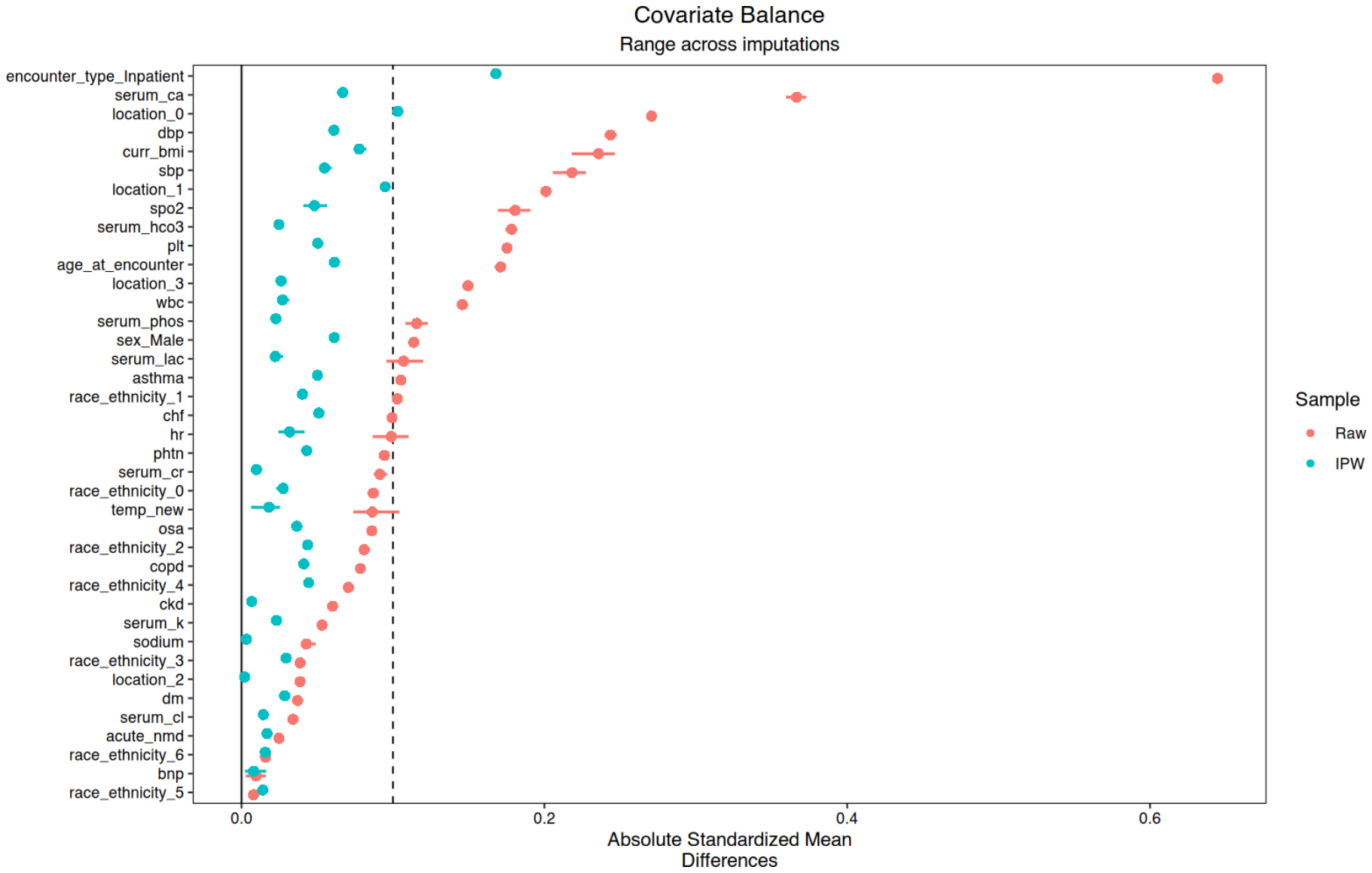
```r
# Keep only variables that never collapse post-CC
vars_keep2 <- setdiff(vars0, to_drop)
stopifnot(length(vars_keep2) > 0)
```

Chunk unnamed-chunk-1 runtime: 0.20 s

```r
# Build a variable set that has  2 levels in *every* imputation (prevents contrasts errors)
vary_ok <- function(z) {
  nz <- z[!is.na(z)]
  if (is.factor(nz)) nlevels(droplevels(nz)) > 1 else dplyr::n_distinct(nz) > 1
}
vars_keep <- Reduce(intersect, lapply(dlist, function(d) {
  keep <- vapply(d[, covars_gbm, drop = FALSE], vary_ok, logical(1))
  names(keep)[keep]
}))
```

```r
# Long data for cobalt with weights and imputation id
make_long_for_cobalt <- function(dlist, W_list, treat_var, covars) {
  stopifnot(length(dlist) == length(W_list))
  do.call(rbind, lapply(seq_along(dlist), function(i) {
    di <- dlist[[i]][, c(treat_var, covars), drop = FALSE]
    di$.imp <- i
    di$.w   <- W_list[[i]]$weights
    di
  }))
}
dlong_abg <- make_long_for_cobalt(dlist, W_abg_list, "has_abg", vars_keep)

# removes empty levels introduced by the per-imputation slicing and prevents spurious contrast errors.
dlong_abg <- droplevels(dlong_abg)

# Final guard: drop any factor that is 1-level in the long frame (should be none after vars_keep)
one_level_factors <- names(Filter(function(x) is.factor(x) && nlevels(droplevels(x)) < 2,
                                  dlong_abg[vars_keep]))
if (length(one_level_factors)) {
  message("Dropping 1-level factors in long data: ", paste(one_level_factors, collapse = ", "))
  vars_keep <- setdiff(vars_keep, one_level_factors)
}

# Balance with imputation identifiers
fml_abg <- reformulate(termlabels = vars_keep, response = "has_abg")
bal_abg <- cobalt::bal.tab(
  fml_abg,
  data        = dlong_abg,
  weights     = dlong_abg$.w,
  imp         = dlong_abg$.imp,      # vector of imputation IDs
  estimand    = "ATE",
  un          = TRUE,
  m.threshold = 0.1,
  binary      = "std",
  s.d.denom   = "pooled"
)
```

```r
# Optional plot
cobalt::love.plot(
  bal_abg,
  var.order    = "unadjusted",
  thresholds   = c(m = .1),
  sample.names = c("Raw", "IPW"),
  abs          = TRUE
)
```



Chunk mi-balance-abg runtime: 3.16 s

5.4.3 10.3 VBG propensity (has_vbg)

```
fit_vbg_one <- function(d) {
  w <- weightit(
    formula_vbg,
    data   = d[, c("has_vbg", covars_gbm)],
    method = "gbm",
    estimand    = "ATE",
    include.obj = TRUE,
    n.trees           = gbm_params$n.trees,
    interaction.depth = gbm_params$interaction.depth,
    shrinkage         = gbm_params$shrinkage,
    bag.fraction      = gbm_params$bag.fraction,
    cv.folds          = gbm_params$cv.folds,
    stop.method       = gbm_params$stop.method,
    n.cores           = gbm_params$n.cores
  )
  ww <- w$weights; ww <- ww/mean(ww); cut <- stats::quantile(ww, c(.01,.99), na.rm=TRUE)
  ww <- pmin(pmax(ww, cut[1]), cut[2]); ww <- ww/mean(ww)
  w$weights <- ww
  w
}

with_progress({
  p <- progressor(along = seq_along(dlist))
  options(future.globals.maxSize = +Inf)
  if (utils::object.size(dlist) > 4e8) future::plan(sequential)

  W_vbg_list <- future_lapply(
    X = seq_along(dlist),
    FUN = function(i) {
      p(sprintf("Fitting VBG on imputation %d", i))
      set.seed(30251206 + i)
      fit_vbg_one(dlist[[i]])
    },
```

```
    future.seed = TRUE
  )
})

saveRDS(W_vbg_list, mi_w_vbg_file)
```

Chunk mi-propensity-vbg runtime: 1365.45 s

```
         n   min p99.99%   max      ess
[1,] 25724 0.576   3.918 3.918 17917.19
[2,] 25724 0.579   3.894 3.894 17922.52
[3,] 25724 0.577   3.933 3.933 17959.65
[4,] 25724 0.580   3.853 3.854 17982.22
[5,] 25724 0.580   3.868 3.868 17957.75
```

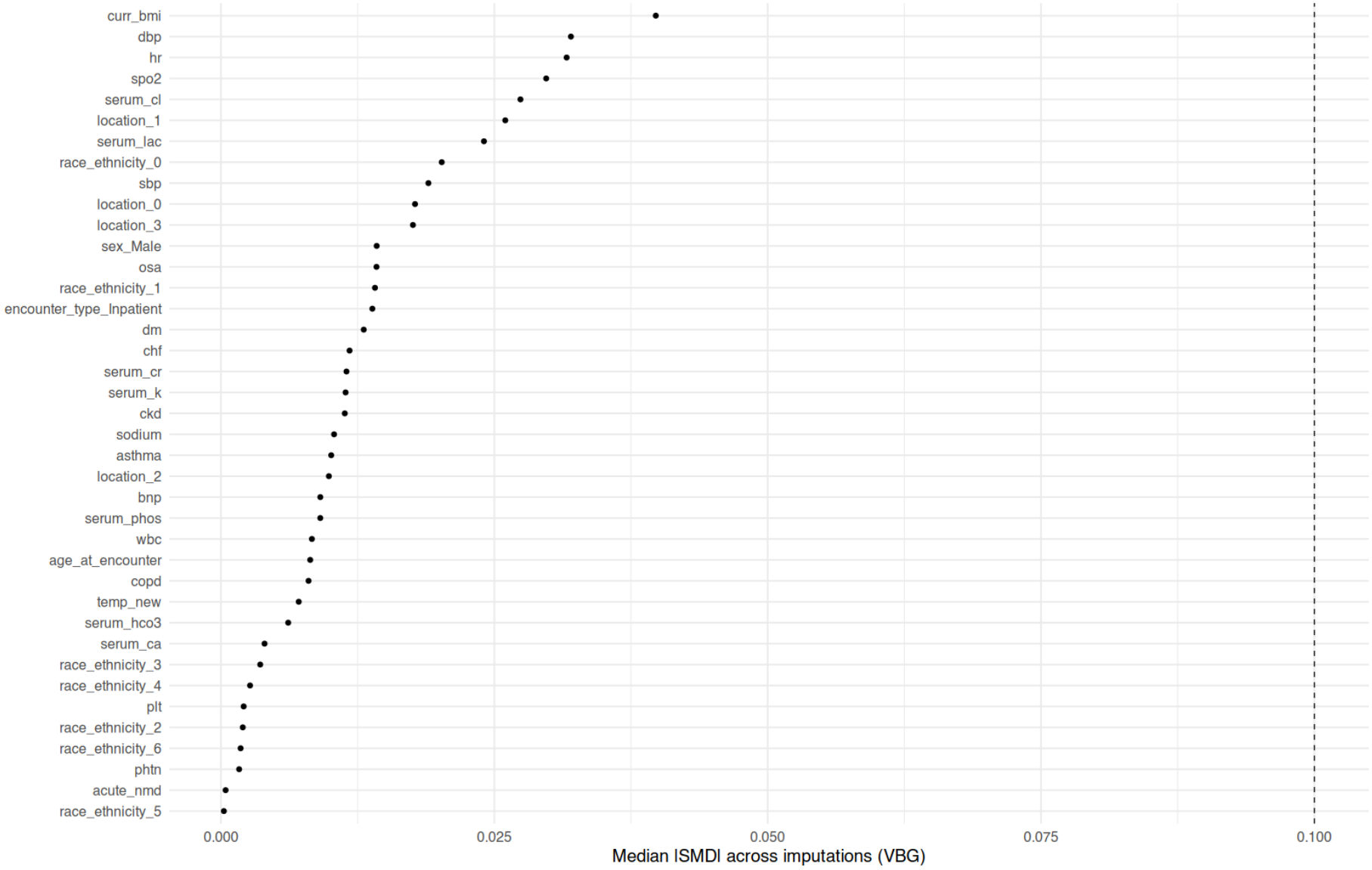
Chunk mi-weight-diagnostics-vbg runtime: 0.02 s

5.4.4 10.4 VBG balance

```
# --- VBG: balance across imputations (fast per-imputation SMD pooling) -------

stopifnot(length(dlist) == length(W_vbg_list))

vary_ok <- function(z) {
  nz <- z[!is.na(z)]
  if (is.factor(nz)) nlevels(droplevels(nz)) > 1 else dplyr::n_distinct(nz) > 1
}

# 1) Keep only covariates that vary ( 2 levels for factors) in every imputation
vars_keep_vbg <- Reduce(intersect, lapply(dlist, function(d) {
  keep <- vapply(d[, covars_gbm, drop = FALSE], vary_ok, logical(1))
  names(keep)[keep]
}))
```

```r
# 2) Build per-imputation lists; align weights and drop non-finite rows
X_list_vbg <- vector("list", length(dlist))
t_list_vbg <- vector("list", length(dlist))
w_list_vbg <- vector("list", length(dlist))
for (i in seq_along(dlist)) {
  di <- dlist[[i]][, vars_keep_vbg, drop = FALSE]
  ids <- rownames(di)
  ti  <- dlist[[i]][["has_vbg"]]
  wi  <- W_vbg_list[[i]]$weights
  if (!is.null(names(wi))) {
    wi <- wi[ids]
  } else if (length(wi) != length(ids)) {
    stop("Length mismatch weights vs data in VBG imp ", i)
  }
  keep <- is.finite(wi)
  if (!all(keep)) {
    di <- di[keep, , drop = FALSE]
    ti <- ti[keep]
    wi <- wi[keep]
  }
  X_list_vbg[[i]] <- di
  t_list_vbg[[i]] <- ti
  w_list_vbg[[i]] <- wi
}

# 3) Per-imputation SMDs (mean diffs only; quick path)
one_imp_bal_vbg <- function(i) {
  b <- cobalt::bal.tab(
    x           = X_list_vbg[[i]],
    treat       = t_list_vbg[[i]],
    weights     = w_list_vbg[[i]],
    stats       = "m",          # mean diffs only
    s.d.denom   = "pooled",
    quick       = TRUE,
    int         = FALSE,
```

```
    disp.v.ratio = FALSE,
    disp.ks      = FALSE,
    un           = TRUE
  )
  S <- as.data.frame(b$Balance)
  setNames(S[["Diff.Adj"]], rownames(S))
}

smd_list_vbg <- lapply(seq_along(dlist), one_imp_bal_vbg)
all_rows_vbg <- Reduce(union, lapply(smd_list_vbg, names))
SMD_mat_vbg  <- do.call(cbind, lapply(smd_list_vbg, function(v) v[match(all_rows_vbg, names(v))]))
smd_abs_vbg  <- abs(SMD_mat_vbg)
smd_pooled_vbg <- data.frame(
  covariate = all_rows_vbg,
  smd_med   = apply(smd_abs_vbg, 1, median, na.rm = TRUE),
  smd_mean  = rowMeans(smd_abs_vbg, na.rm = TRUE),
  smd_max   = apply(smd_abs_vbg, 1, max,    na.rm = TRUE),
  stringsAsFactors = FALSE
)

# Optional quick plot of pooled median |SMD|
ggplot(smd_pooled_vbg, aes(x = reorder(covariate, smd_med), y = smd_med)) +
  geom_hline(yintercept = 0.1, linetype = 2, linewidth = 0.3) +
  geom_point(size = 1) +
  coord_flip() +
  labs(x = NULL, y = "Median |SMD| across imputations (VBG)") +
  theme_minimal(base_size = 10)
```




```
message("VBG balance pooled from per-imputation SMDs; Love plot omitted to save memory.")
```

```
VBG balance pooled from per-imputation SMDs; Love plot omitted to save memory.
```

Chunk mi-balance-vbg runtime: 1.90 s

5.5 11) Weighted outcome models within each imputation + pooling

Pool via Rubin's rules using mitools::MIcombine. Extract the coefficient and its variance for the treatment effect from each imputation.

5.5.1 11.1 Helper: fit + extract log-OR and SE from svyglm

```
# --- Robust coefficient extraction from svyglm (handles factor-coded terms) ---
coef_var_from_svy <- function(fit, treat_name) {
  cn <- names(coef(fit))
  idx <- match(treat_name, cn)
  if (is.na(idx)) {
    # handle factor encodings like has_abg1, has_abgYes, etc.
    pat <- paste0("^", gsub("([\\W])", "\\\\$1", treat_name), "(1|Yes|TRUE|Male)?$")
    idx <- grep(pat, cn, perl = TRUE)[1]
  }
  if (is.na(idx)) stop("Treatment coefficient '", treat_name, "' not found in model.")
  b <- unname(coef(fit)[idx])
  V <- unname(vcov(fit)[idx, idx, drop = TRUE])
  if (!is.finite(b) || !is.finite(V)) stop("Non-finite estimate/variance.")
  list(b = b, V = V)
}

# --- Fit one weighted GLM on one completed dataset and extract log-OR + var ---
fit_and_extract <- function(data, weights, formula, treat_name) {
  stopifnot(length(weights) == nrow(data))
  yname <- all.vars(formula)[1L]

  # keep only rows with finite weights and non-missing outcome/treatment
  data$w <- as.numeric(weights)
  keep <- is.finite(data$w) & !is.na(data[[treat_name]]) & !is.na(data[[yname]])
  data <- data[keep, , drop = FALSE]
  if (nrow(data) == 0L) stop("No rows with finite weights/outcome/treatment.")
```

```r
  # basic guards: variation in outcome and treatment (after filtering)
  if (dplyr::n_distinct(data[[yname]])   < 2L) stop("Outcome '", yname, "' has one level.")
  if (dplyr::n_distinct(data[[treat_name]]) < 2L) stop("Treatment '", treat_name, "' has one level.")

  # design + fit
  des <- survey::svydesign(ids = ~1, weights = ~w, data = data)
  fit <- survey::svyglm(formula, design = des, family = quasibinomial())
  cv  <- coef_var_from_svy(fit, treat_name)
  list(coef = cv$b, vcov = cv$V)
}

# --- Pool across imputations; tolerate failures; report how many used ----------
pool_logOR <- function(est_list, term) {
  ok <- vapply(est_list, function(x) is.list(x) && is.finite(x$coef) && is.finite(x$vcov), logical(1))
  est_list <- est_list[ok]
  m_ok  <- length(est_list); m_tot <- length(ok)
  if (m_ok == 0L) {
    return(data.frame(term = term, logOR = NA_real_, SE = NA_real_, OR = NA_real_,
                      LCL = NA_real_, UCL = NA_real_, m_used = 0L, m_total = m_tot))
  }
  results   <- lapply(est_list, function(x) setNames(c(x$coef), term))
  variances <- lapply(est_list, function(x) { M <- matrix(x$vcov, 1, 1); dimnames(M) <- list(term, term); M })
  pooled <- mitools::MIcombine(results = results, variances = variances)
  est <- as.numeric(coef(pooled))
  se  <- sqrt(diag(pooled$variance))
  data.frame(term = term, logOR = est, SE = se, OR = exp(est),
             LCL = exp(est - 1.96 * se), UCL = exp(est + 1.96 * se),
             m_used = m_ok, m_total = m_tot, row.names = NULL)
}
```

Chunk mi-pool-helpers runtime: 0.00 s

5.5.2 11.2 ABG: outcomes = IMV, NIV, Death(60d), Hypercapnic RF

```
# Parallel ABG outcome fits and pooling across imputations
library(future.apply)
library(progressr)

# Inputs assumed present: imp, W_abg_list
stopifnot(exists("imp"), exists("W_abg_list"))
dlist <- mice::complete(imp, action = "all")
stopifnot(length(W_abg_list) == length(dlist))

outcomes_abg <- list(
  imv_proc = imv_proc ~ has_abg,
  niv_proc = niv_proc ~ has_abg,
  death    = death_60d ~ has_abg,
  hcrf     = hypercap_resp_failure ~ has_abg
)

old_plan <- future::plan()
workers  <- max(1L, as.integer(future::availableCores() - 1L))
future::plan(multisession, workers = workers)
on.exit(future::plan(old_plan), add = TRUE)

abg_results <- NULL
progressr::with_progress({
  p <- progressr::progressor(steps = length(outcomes_abg) * length(dlist))
  abg_results <- lapply(names(outcomes_abg), function(nm) {
    fml <- outcomes_abg[[nm]]
    ests <- future.apply::future_lapply(
      X = seq_along(dlist),
      FUN = function(i) {
        p(sprintf("ABG: %s (imp %d)", nm, i))
        tryCatch(
          fit_and_extract(dlist[[i]], W_abg_list[[i]]$weights, fml, "has_abg"),
          error = function(e) NULL
```

```
        )
      },
      future.seed = TRUE
    )
    out <- pool_logOR(ests, term = "has_abg")
    out$outcome <- nm
    out
  })
})
abg_results <- dplyr::bind_rows(abg_results)[, c("outcome","term","logOR","SE","OR","LCL","UCL","m_used","m_total")]
abg_results
```

outcome	term	logOR	SE	OR	LCL	UCL	m_used	m_total
imv_proc	has_abg	NA	NA	NA	NA	NA	0	5
niv_proc	has_abg	NA	NA	NA	NA	NA	0	5
death	has_abg	NA	NA	NA	NA	NA	0	5
hcrf	has_abg	NA	NA	NA	NA	NA	0	5

Chunk mi-abg-outcomes runtime: 2.60 s

5.5.3 11.3 Repeat for VBG

```
# --- VBG outcomes ------------------------------------------------------------
# Parallel VBG outcome fits and pooling across imputations
library(future.apply)
library(progressr)

# Inputs assumed present: imp, W_vbg_list
stopifnot(exists("imp"), exists("W_vbg_list"))
dlist <- mice::complete(imp, action = "all")
stopifnot(length(W_vbg_list) == length(dlist))
```

```r
outcomes_vbg <- list(
  imv_proc = imv_proc ~ has_vbg,
  niv_proc = niv_proc ~ has_vbg,
  death    = death_60d ~ has_vbg,
  hcrf     = hypercap_resp_failure ~ has_vbg
)

old_plan <- future::plan()
workers  <- max(1L, as.integer(future::availableCores() - 1L))
future::plan(multisession, workers = workers)
on.exit(future::plan(old_plan), add = TRUE)

vbg_results <- NULL
progressr::with_progress({
  p <- progressr::progressor(steps = length(outcomes_vbg) * length(dlist))
  vbg_results <- lapply(names(outcomes_vbg), function(nm) {
    fml <- outcomes_vbg[[nm]]
    ests <- future.apply::future_lapply(
      X = seq_along(dlist),
      FUN = function(i) {
        p(sprintf("VBG: %s (imp %d)", nm, i))
        tryCatch(
          fit_and_extract(dlist[[i]], W_vbg_list[[i]]$weights, fml, "has_vbg"),
          error = function(e) NULL
        )
      },
      future.seed = TRUE
    )
    out <- pool_logOR(ests, term = "has_vbg")
    out$outcome <- nm
    out
  })
})
vbg_results <- dplyr::bind_rows(vbg_results)[, c("outcome","term","logOR","SE","OR","LCL","UCL","m_used","m_total")]
vbg_results
```

outcome	term	logOR	SE	OR	LCL	UCL	m_used	m_total
imv_proc	has_vbg	NA	NA	NA	NA	NA	0	5
niv_proc	has_vbg	NA	NA	NA	NA	NA	0	5
death	has_vbg	NA	NA	NA	NA	NA	0	5
hcrf	has_vbg	NA	NA	NA	NA	NA	0	5

Chunk mi-vbg-outcomes runtime: 2.29 s

5.6 12) Explainability on one representative imputation

To manage runtime, compute SHAP/PDP/ALE on the first imputed dataset and its fitted GBM(s).

Chunk shap-axis-labels runtime: 0.00 s

```
# --- Fast SHAP for WeightIt GBM fits (works with MI) -------------------------

library(fastshap)
```

```
Attaching package: 'fastshap'
```

```
The following object is masked from 'package:dplyr':

    explain
```

```
library(shapviz)
# --- Robust SHAP backend for WeightIt GBM fits -------------------------------
# Works whether gbm$var.names are raw feature names (factors ok) or one-hot names
# like "sexFemale", "race_ethnicity3", "encounter_typeInpatient", etc.

# Map of factor levels observed at training time (for raw-factor path)
.train_levels <- function(df) {
  f <- vapply(df, is.factor, logical(1))
```

```
  lapply(df[f], levels)
}

# Align factors in 'df' to a stored levels map (keeps order, avoids new/ambiguous levels)
.align_to_levels <- function(df, levels_map) {
  out <- as.data.frame(df, stringsAsFactors = FALSE)
  for (nm in intersect(names(levels_map), names(out))) {
    out[[nm]] <- factor(as.character(out[[nm]]), levels = levels_map[[nm]])
  }
  out
}

# Build a design with columns EXACTLY equal to 'varnames' by deriving indicators
# from the raw covariate frame 'X_raw'. This covers one-hot names like "sexMale",
# "race_ethnicity2", "encounter_typeInpatient", etc.
.design_from_varnames <- function(X_raw, varnames) {
  X_raw <- as.data.frame(X_raw, stringsAsFactors = FALSE)

  # normalize odd classes; turn characters into factors (stable level strings)
  for (nm in names(X_raw)) {
    if (inherits(X_raw[[nm]], "haven_labelled")) X_raw[[nm]] <- as.character(X_raw[[nm]])
  }
  X_raw[] <- lapply(X_raw, function(z) if (is.character(z)) factor(z) else z)

  cn    <- colnames(X_raw)
  cn_s  <- make.names(cn)
  vn    <- varnames
  vn_s  <- make.names(vn)

  out <- matrix(NA_real_, nrow = nrow(X_raw), ncol = length(vn))
  colnames(out) <- vn

  for (i in seq_along(vn)) {
    v   <- vn[i]
    v_s <- vn_s[i]
```

```
    # Case 1: exact column present
    if (v %in% cn) {
      z <- X_raw[[v]]
      out[, i] <- if (is.factor(z)) as.numeric(z) else as.numeric(z)
      next
    }

    # Case 2: derive dummy = 1{ base == level } from a base column prefix
    # Find the longest raw name that is a prefix of v (sanitized comparison)
    cand <- which(startsWith(v_s, cn_s))
    if (length(cand)) {
      j <- cand[which.max(nchar(cn_s[cand]))]
      base <- cn[j]
      # level is the suffix of v after the base name (unsanitized; preserves case)
      lev  <- sub(paste0("^", base), "", v)
      x    <- X_raw[[base]]

      # Compare as strings to match labels like "Female", "Inpatient", "0","1",...
      x_chr <- if (is.factor(x)) as.character(x) else as.character(x)
      out[, i] <- as.numeric(x_chr == lev)
      out[is.na(x_chr), i] <- NA_real_
      next
    }

    stop("Cannot construct design column for '", v, "'. ",
         "No matching base variable found in raw covariates.")
  }

  as.data.frame(out, check.names = FALSE)
}

# Unified backend:
#  - If gbm$var.names are raw feature names, pass factors directly (aligning levels).
#  - Otherwise, build a one-hot design with those exact column names and predict on it.
make_shap_backend_any <- function(W) {
  gbm_fit <- if (!is.null(W$obj)) W$obj else if (!is.null(W$info$obj)) W$info$obj else W$info$model.obj
```

```r
stopifnot(inherits(gbm_fit, "gbm"))
best_tree <- if (!is.null(W$info$best.tree)) W$info$best.tree else gbm_fit$n.trees

X_raw <- as.data.frame(W$covs, stringsAsFactors = FALSE)
# tidy odd classes; keep factors where they already are
for (nm in names(X_raw)) {
  if (inherits(X_raw[[nm]], "haven_labelled")) X_raw[[nm]] <- as.character(X_raw[[nm]])
}
X_raw[] <- lapply(X_raw, function(z) if (is.character(z)) factor(z) else z)
X_raw[] <- lapply(X_raw, function(z) if (is.factor(z)) droplevels(z) else z)

vn <- gbm_fit$var.names
levels_map <- .train_levels(X_raw)

# Path A: raw-factor training (names line up directly)
if (all(vn %in% colnames(X_raw))) {
  X_use <- .align_to_levels(X_raw[, vn, drop = FALSE], levels_map)
  pred  <- function(object, newdata) {
    nd <- .align_to_levels(newdata, levels_map)
    predict(object, newdata = nd, n.trees = best_tree, type = "link")
  }
  return(list(gbm = gbm_fit, X = X_use, pred = pred, best_tree = best_tree))
}

# Path B: dummy-coded training (var.names are one-hot)
X_use <- .design_from_varnames(X_raw, vn)
pred  <- function(object, newdata) {
  # If caller already supplies the dummy design, use it; else derive it
  if (all(vn %in% colnames(newdata))) {
    nd <- as.data.frame(newdata)[, vn, drop = FALSE]
  } else {
    nd <- .design_from_varnames(newdata, vn)
  }
  predict(object, newdata = nd, n.trees = best_tree, type = "link")
}
```

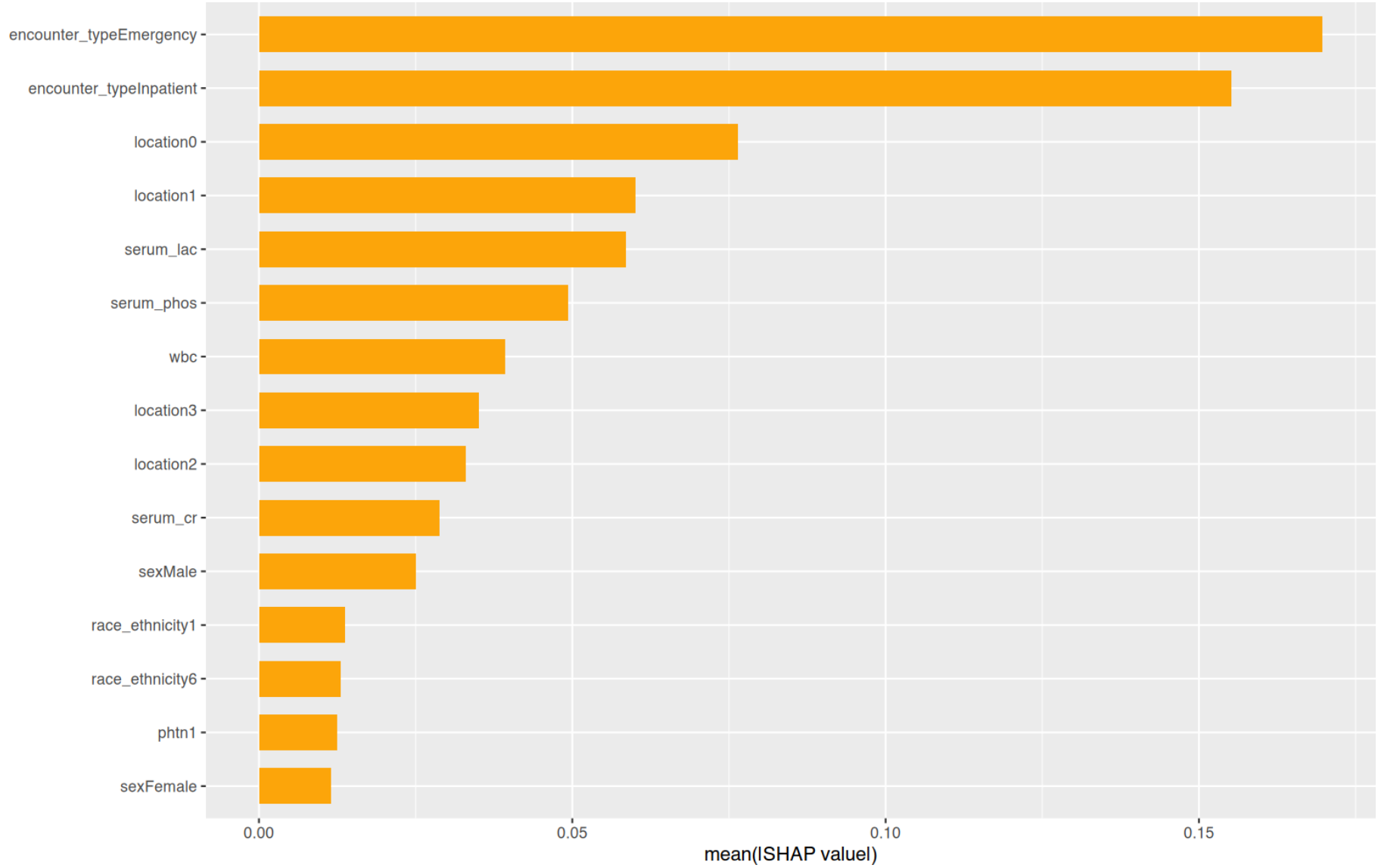
```
  list(gbm = gbm_fit, X = X_use, pred = pred, best_tree = best_tree)
}
```

Chunk unnamed-chunk-2 runtime: 0.04 s

```
# Choose one completed dataset's fit
# Device safety (once per doc)
fs::dir_create(fig_dir, recurse = TRUE)
knitr::opts_chunk$set(fig.path = fig_path, dev = "ragg_png", dpi = 200)

# SHAP throttle knobs (single imputation, subsample rows, fewer sims)
shap_cfg <- list(
  frac_rows = 0.15,
  nsim      = 8,
  top_k     = 20,
  seed      = 123
)

# --- ABG explainability on imputation 1 ----------------------------------
stopifnot(exists("W_abg_list"), length(W_abg_list) >= 1)
W1_abg <- W_abg_list[[1]]
bk_abg <- make_shap_backend_any(W1_abg)

# Equivalence: wrapper vs direct gbm predict on the same design matrix
bk <- make_shap_backend_any(W_abg_list[[1]])
p_wrap <- bk$pred(bk$gbm, bk$X)
p_direct <- predict(
  bk$gbm,
  newdata = bk$X[, bk$gbm$var.names, drop = FALSE],
  n.trees = bk$best_tree,
  type    = "link"
)
stopifnot(mean(abs(p_wrap - p_direct), na.rm = TRUE) < 1e-8)

# Subsample rows for SHAP speed
set.seed(shap_cfg$seed)
```

```r
ix_abg <- sample.int(nrow(bk_abg$X), max(50L, floor(shap_cfg$frac_rows * nrow(bk_abg$X))))
X_abg  <- bk_abg$X[ix_abg, , drop = FALSE]

# Fast SHAP on link (logit) scale
S_abg <- fastshap::explain(
  object       = bk_abg$gbm,
  X            = X_abg,
  pred_wrapper = bk_abg$pred,
  nsim         = shap_cfg$nsim,
  adjust       = FALSE
)

# shapviz object (X can be data.frame or matrix; keep column names)
sv_abg <- shapviz::shapviz(as.matrix(S_abg), X = as.matrix(X_abg))

# Bar importance (top K)
ord_abg   <- order(colMeans(abs(S_abg), na.rm = TRUE), decreasing = TRUE)
topK_abg  <- colnames(S_abg)[ord_abg[1:min(shap_cfg$top_k, ncol(S_abg))]]
p_bar_abg <- shapviz::sv_importance(sv_abg, kind = "bar", v = topK_abg)
p_bar_abg
```

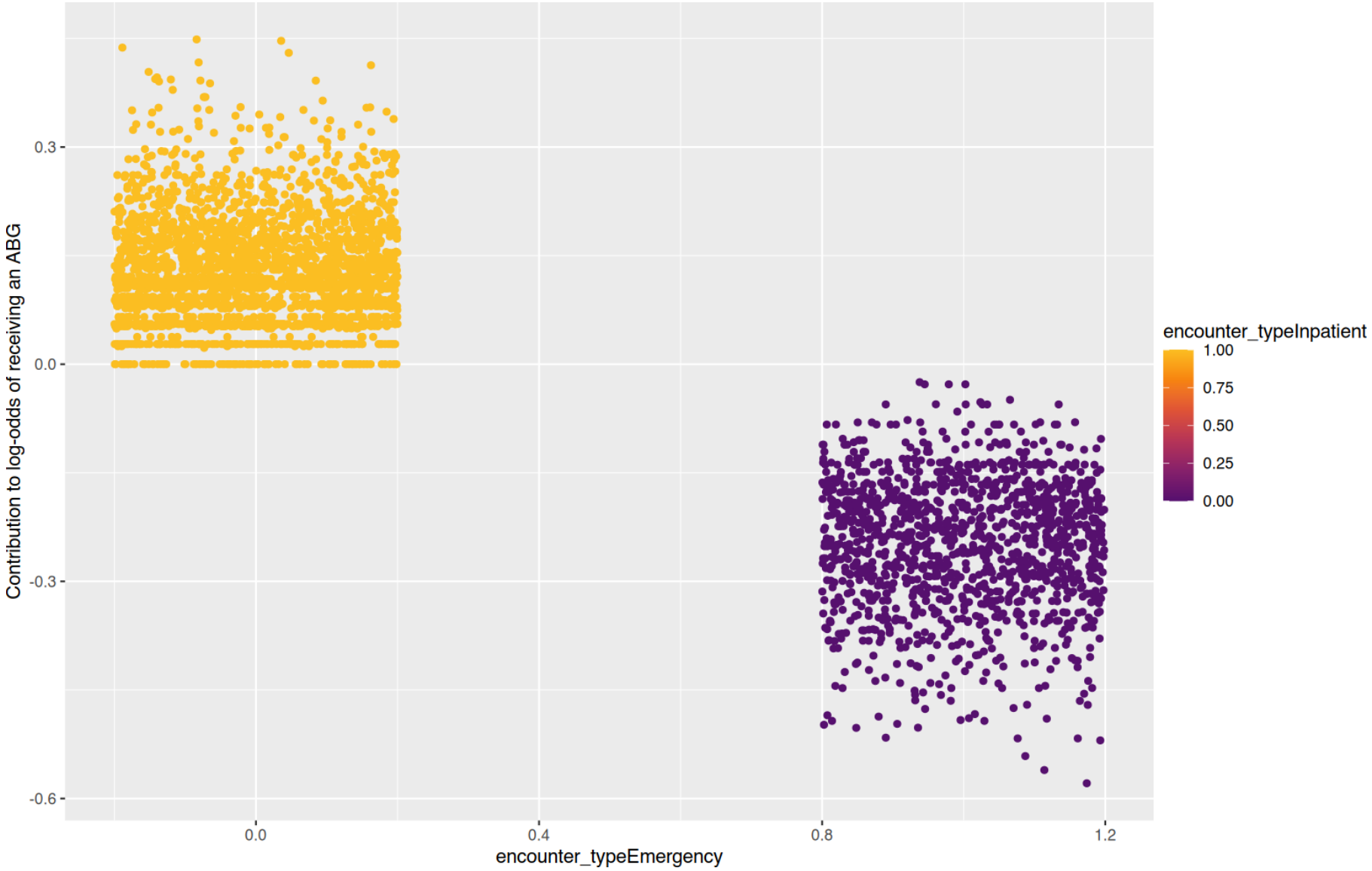
```
Warning: `label` cannot be a <ggplot2::element_blank> object.
```




```
# Dependence: top feature colored by second (add smoother explicitly)
pri_abg <- topK_abg[1]
aux_abg <- topK_abg[2]
# dependence: replace loess with GAM to avoid near-singularity
```

```r
p_dep_abg <- shapviz::sv_dependence(sv_abg, v = pri_abg, color_var = aux_abg) +
  ggplot2::geom_smooth(method = "gam", formula = y ~ s(x, bs = "cs", k = 4),
                       se = FALSE, linewidth = 0.5) +
  ggplot2::labs(y = shap_y_abg, x = pri_abg)

# for importance: don't set label = element_blank() on shapviz's plot; let it draw defaults
# if you see "aesthetics dropped: colour", avoid mapping `colour` in a stat
p_dep_abg
```

```
Warning: Failed to fit group -1.
Caused by error in `smooth.construct.cr.smooth.spec()`:
! x has insufficient unique values to support 4 knots: reduce k.
```

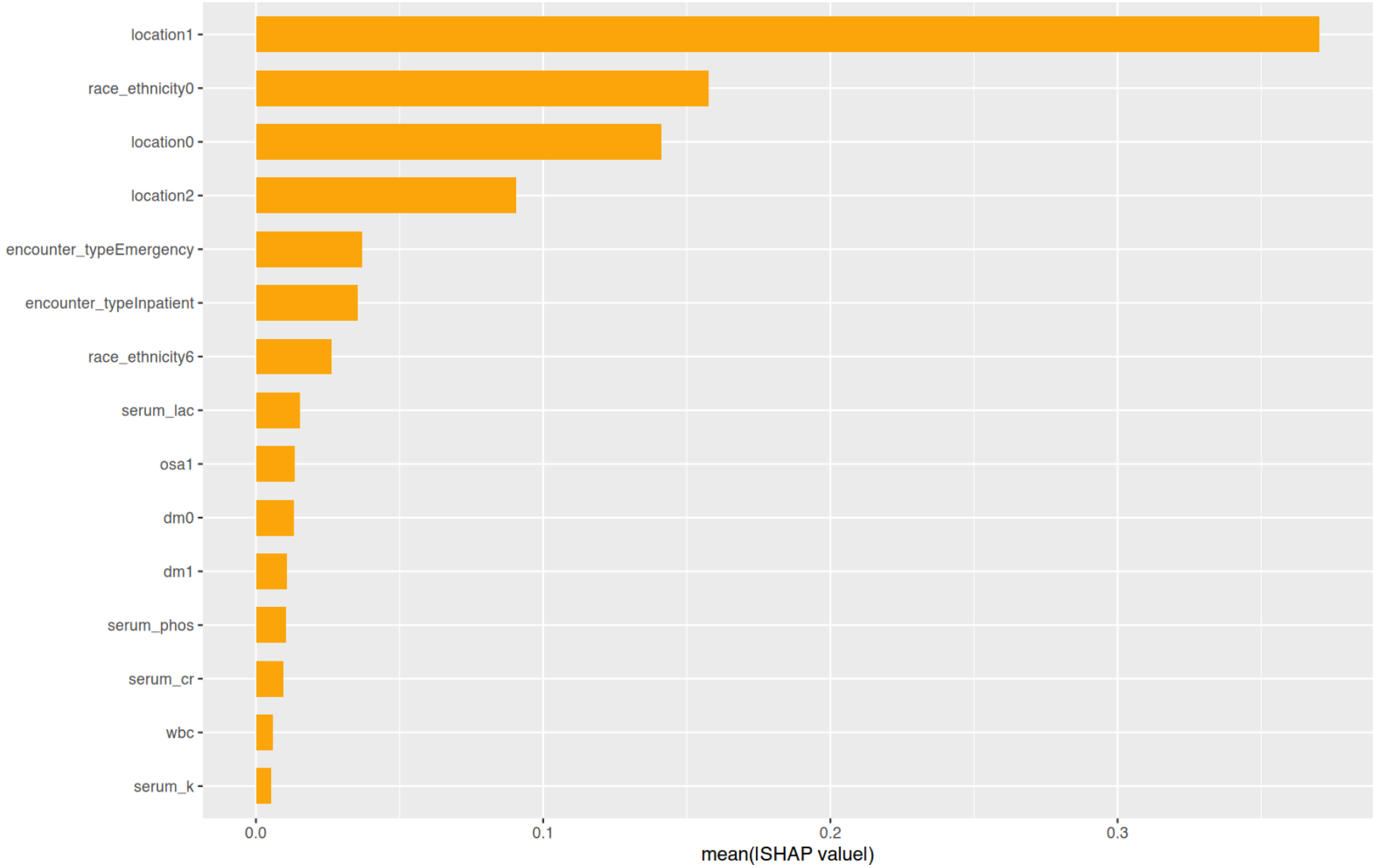


Chunk shap-abg-vbg runtime: 46.96 s

```
# Repeat for VBG
```

```r
# --- VBG explainability on imputation 1 ------------------------------------
stopifnot(exists("W_vbg_list"), length(W_vbg_list) >= 1)
W1_vbg <- W_vbg_list[[1]]

bk_vbg <- make_shap_backend_any(W1_vbg)

set.seed(shap_cfg$seed)
ix_vbg <- sample.int(nrow(bk_vbg$X), max(50L, floor(shap_cfg$frac_rows * nrow(bk_vbg$X))))
X_vbg  <- bk_vbg$X[ix_vbg, , drop = FALSE]

S_vbg <- fastshap::explain(
  object       = bk_vbg$gbm,
  X            = X_vbg,
  pred_wrapper = bk_vbg$pred,
  nsim         = shap_cfg$nsim,
  adjust       = FALSE
)

sv_vbg <- shapviz::shapviz(as.matrix(S_vbg), X = as.matrix(X_vbg))

ord_vbg   <- order(colMeans(abs(S_vbg), na.rm = TRUE), decreasing = TRUE)
topK_vbg  <- colnames(S_vbg)[ord_vbg[1:min(shap_cfg$top_k, ncol(S_vbg))]]
p_bar_vbg <- shapviz::sv_importance(sv_vbg, kind = "bar", v = topK_vbg)
p_bar_vbg
```

```
Warning: `label` cannot be a <ggplot2::element_blank> object.
```




```
pri_vbg <- topK_vbg[1]
aux_vbg <- topK_vbg[2]
p_dep_vbg <- shapviz::sv_dependence(sv_vbg, v = pri_vbg, color_var = aux_vbg) +
  ggplot2::geom_smooth(se = FALSE, linewidth = 0.5, method = "loess", formula = y ~ x) +
```

```
  ggplot2::labs(y = shap_y_vbg, x = pri_vbg)
p_dep_vbg
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: at -0.005
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: radius 2.5e-05
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: all data on boundary of neighborhood. make span bigger
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: pseudoinverse used at -0.005
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: neighborhood radius 0.005
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: reciprocal condition number 1
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: There are other near singularities as well. 1.01
```

```
Warning in simpleLoess(y, x, w, span, degree = degree, parametric = parametric,
: zero-width neighborhood. make span bigger
```

```
Warning: Failed to fit group -1.
Caused by error in `predLoess()`:
! NA/NaN/Inf in foreign function call (arg 5)
```

Chunk unnamed-chunk-3 runtime: 50.88 s

5.7 13) Imputed, weighted, three-level PCO2 (ABG & VBG)

```
# --- helpers ------------------------------------------------------------
library(splines)
library(mitools)
library(survey)
library(dplyr)

# Pool (Rubin) any subset of coefficients across imputed fits (glm/svyglm)
pool_terms <- function(fits, term_prefix = NULL, term_pattern = NULL) {
  fits <- Filter(Negate(is.null), fits)
  if (!length(fits)) return(
    data.frame(term = character(), logOR = numeric(), SE = numeric(),
               OR = numeric(), LCL = numeric(), UCL = numeric())
  )

  coef_names <- lapply(fits, function(f) names(stats::coef(f)))
  common <- Reduce(intersect, coef_names)
  if (!is.null(term_prefix))  common <- common[startsWith(common, term_prefix)]
  if (!is.null(term_pattern)) common <- common[grepl(term_pattern, common)]
  if (!length(common)) return(
    data.frame(term = character(), logOR = numeric(), SE = numeric(),
               OR = numeric(), LCL = numeric(), UCL = numeric())
  )

  rows <- lapply(common, function(tt) {
    results <- lapply(fits, function(f) setNames(c(stats::coef(f)[tt]), tt))
    variances <- lapply(fits, function(f) {
      v <- stats::vcov(f)[tt, tt, drop = TRUE]
      m <- matrix(v, 1, 1); dimnames(m) <- list(tt, tt); m
    })
    pooled <- mitools::MIcombine(results = results, variances = variances)
    est <- as.numeric(coef(pooled))
    se  <- sqrt(diag(pooled$variance))
    data.frame(term = tt,
```

```
                logOR = est, SE = se,
                OR  = exp(est),
                LCL = exp(est - 1.96*se),
                UCL = exp(est + 1.96*se),
                row.names = NULL)
  })
  dplyr::bind_rows(rows)
}

# 3-level CO2 category maker; can use fixed clinical cutpoints or data-driven
# --- CO2 category helper (3-level) ------------------------------------------
make_co2_cat <- function(x,
                         fixed_breaks = NULL,
                         labels = c("Hypocapnia", "Eucapnia", "Hypercapnia"),
                         normal = NULL) {
  x <- suppressWarnings(as.numeric(x))
  x_ok <- x[is.finite(x)]
  if (length(x_ok) < 10) {
    return(factor(rep(NA_character_, length(x)), levels = labels))
  }

  brks <- NULL
  # priority: explicit breaks → "normal" window → quantile fallback
  if (!is.null(fixed_breaks)) {
    brks <- fixed_breaks
  } else if (!is.null(normal)) {
    n <- sort(unique(as.numeric(normal)))
    if (length(n) >= 2 && all(is.finite(n)) && (n[2] > n[1])) {
      brks <- c(-Inf, n[1], n[2], Inf)
    }
  }
  if (is.null(brks)) {
    brks <- stats::quantile(x_ok, probs = c(0, 1 / 3, 2 / 3, 1), na.rm = TRUE)
  }

  brks <- unique(brks)
```

```r
  if (length(brks) < 4 || any(diff(brks) <= 0)) {
    return(factor(rep(NA_character_, length(x)), levels = labels))
  }
  cut(x, breaks = brks, include.lowest = TRUE, labels = labels, right = TRUE)
}

# defaults (safe if you didn't predefine)
use_fixed_abg   <- if (exists("use_fixed_abg")) isTRUE(use_fixed_abg) else FALSE
co2_breaks_abg  <- if (exists("co2_breaks_abg")) co2_breaks_abg else NULL
co2_labels_abg  <- if (exists("co2_labels_abg")) co2_labels_abg else c("Hypocapnia","Eucapnia","Hypercapnia")
ref_label_abg   <- if (exists("ref_label_abg")) ref_label_abg else "Eucapnia"

# (Optional) explicit clinical cutpoints - override by setting use_fixed_* = TRUE
use_fixed_abg <- TRUE
co2_breaks_abg   <- c(-Inf, 35, 45, Inf)
co2_labels_abg   <- c("Hypocapnia", "Eucapnia", "Hypercapnia")
ref_label_abg    <- "Eucapnia"

use_fixed_vbg <- TRUE
co2_breaks_vbg   <- c(-Inf, 40, 50, Inf)
co2_labels_vbg   <- c("Hypocapnia", "Eucapnia", "Hypercapnia")
ref_label_vbg    <- "Eucapnia"

# Fixed spline knots & boundary knots (shared across imputations)
# Use 2-98th percentile boundaries; 2 internal knots (  df=4 total)
make_knots <- function(x) {
  x <- x[is.finite(x)]
  B <- stats::quantile(x, probs = c(0.02, 0.98), na.rm = TRUE)
  K <- stats::quantile(x[x >= B[1] & x <= B[2]], probs = c(1/3, 2/3), na.rm = TRUE)
  list(boundary = unname(B), knots = unname(K))
}
```

Chunk mi_pco2_threelevel runtime: 0.01 s

Chunk mi-co2-cat-checks runtime: 0.63 s

Chunk pool-spline-helpers runtime: 0.00 s

5.8 14) MI + IPW three-level PCO2 (ABG & VBG)

5.8.1 14.1 ABG: MI + IPW, three-level PCO2 outcomes

```
# --- ABG: outcome ~ CO2 category, IPW by W_abg_list --------------------------
# Assumes: dlist, W_abg_list, make_co2_cat(), use_fixed_abg, co2_breaks_abg,
#          co2_labels_abg, ref_label_abg are defined.

fit_abg_cat <- function(outcome_var) {
  fits <- vector("list", length(dlist))
  for (i in seq_along(dlist)) {
    d <- dlist[[i]]
    if (!("paco2" %in% names(d))) { fits[[i]] <- NULL; next }
    d$paco2 <- suppressWarnings(as.numeric(d$paco2))

    g <- with(d, has_abg == 1 & is.finite(paco2))
    if (!any(g)) { fits[[i]] <- NULL; next }

    d2 <- d[g, , drop = FALSE]
    w <- W_abg_list[[i]]$weights[g]
    w[!is.finite(w)] <- NA_real_
    d2$co2_cat <- make_co2_cat(
      d2$paco2,
      fixed_breaks = if (isTRUE(use_fixed_abg)) co2_breaks_abg else NULL,
      labels       = co2_labels_abg,
      normal       = if (exists("co2_breaks_abg", inherits = TRUE)) co2_breaks_abg else c(35, 45)
    )
    d2$co2_cat <- base::droplevels(d2$co2_cat)
    d2$co2_cat <- stats::relevel(d2$co2_cat, ref = ref_label_abg)
    if (nlevels(d2$co2_cat) < 2) { fits[[i]] <- NULL; next }

    ok <- is.finite(w)
    if (!all(ok)) {
      d2 <- d2[ok, , drop = FALSE]
      w  <- w[ok]
```

```
      if (nrow(d2) == 0L) { fits[[i]] <- NULL; next }
    }

    des <- survey::svydesign(ids = ~1, weights = ~w, data = d2)
    fml <- stats::as.formula(sprintf("%s ~ co2_cat", outcome_var))
    fits[[i]] <- survey::svyglm(fml, design = des, family = quasibinomial())
  }
  pool_terms(fits, term_prefix = "co2_cat")
}

abg_cat_results <- dplyr::bind_rows(
  dplyr::mutate(fit_abg_cat("imv_proc"),              outcome = "IMV"),
  dplyr::mutate(fit_abg_cat("niv_proc"),              outcome = "NIV"),
  dplyr::mutate(fit_abg_cat("death_60d"),             outcome = "Death60d"),
  dplyr::mutate(fit_abg_cat("hypercap_resp_failure"), outcome = "HCRF")
) |>
  dplyr::relocate(outcome)
```

Chunk unnamed-chunk-4 runtime: 2.25 s

5.8.2 14.2 VBG: MI + IPW, three-level PCO2 outcomes

```
# Assumes: dlist, W_vbg_list, make_co2_cat(), use_fixed_vbg, co2_breaks_vbg,
#          co2_labels_vbg, ref_label_vbg are defined.

fit_vbg_cat <- function(outcome_var) {
  fits <- vector("list", length(dlist))
  for (i in seq_along(dlist)) {
    d <- dlist[[i]]
    if (!("vbg_co2" %in% names(d))) { fits[[i]] <- NULL; next }
    d$vbg_co2 <- suppressWarnings(as.numeric(d$vbg_co2))

    g <- with(d, has_vbg == 1 & is.finite(vbg_co2))
    if (!any(g)) { fits[[i]] <- NULL; next }
```

```
    d2 <- d[g, , drop = FALSE]
    w <- W_vbg_list[[i]]$weights[g]
    w[!is.finite(w)] <- NA_real_
    d2$co2_cat <- make_co2_cat(
      d2$vbg_co2,
      fixed_breaks = if (isTRUE(use_fixed_vbg)) co2_breaks_vbg else NULL,
      labels       = co2_labels_vbg,
      normal       = if (exists("co2_breaks_vbg", inherits = TRUE)) co2_breaks_vbg else c(40, 50)
    )
    d2$co2_cat <- base::droplevels(d2$co2_cat)
    d2$co2_cat <- stats::relevel(d2$co2_cat, ref = ref_label_vbg)
    if (nlevels(d2$co2_cat) < 2) { fits[[i]] <- NULL; next }

    ok <- is.finite(w)
    if (!all(ok)) {
      d2 <- d2[ok, , drop = FALSE]
      w  <- w[ok]
      if (nrow(d2) == 0L) { fits[[i]] <- NULL; next }
    }

    des <- survey::svydesign(ids = ~1, weights = ~w, data = d2)
    fml <- stats::as.formula(sprintf("%s ~ co2_cat", outcome_var))
    fits[[i]] <- survey::svyglm(fml, design = des, family = quasibinomial())
  }
  pool_terms(fits, term_prefix = "co2_cat")
}

vbg_cat_results <- dplyr::bind_rows(
  dplyr::mutate(fit_vbg_cat("imv_proc"),              outcome = "IMV"),
  dplyr::mutate(fit_vbg_cat("niv_proc"),              outcome = "NIV"),
  dplyr::mutate(fit_vbg_cat("death_60d"),             outcome = "Death60d"),
  dplyr::mutate(fit_vbg_cat("hypercap_resp_failure"), outcome = "HCRF")
) |>
  dplyr::relocate(outcome)
```

Table 3. MI-pooled IPW associations between CO category and outcomes

Cohort	Outcome	Low vs normal OR (95% CI)	High vs normal OR (95% CI)
ABG	IMV	1.20 (1.07, 1.36)	1.16 (1.03, 1.32)
ABG	NIV	0.96 (0.78, 1.18)	2.11 (1.76, 2.52)
ABG	Death (60d)	1.73 (1.50, 1.99)	1.45 (1.25, 1.67)
ABG	Hypercapnic RF	0.80 (0.62, 1.03)	5.39 (4.47, 6.49)
VBG	IMV	1.28 (1.08, 1.52)	1.60 (1.35, 1.90)
VBG	NIV	1.32 (0.99, 1.75)	3.31 (2.59, 4.23)
VBG	Death (60d)	1.98 (1.66, 2.35)	1.69 (1.40, 2.03)
VBG	Hypercapnic RF	1.10 (0.80, 1.50)	8.69 (6.80, 11.09)

Weighted survey GLMs; weights = MI-specific GBM IPW; m = 5 imputations (seed 20251206); reference = Eucapnia.

Chunk unnamed-chunk-5 runtime: 1.84 s

5.8.3 14.3 Table 3: MI-pooled IPW associations (3-level CO)

Chunk table3-ipw-mi-co2 runtime: 0.02 s

```
# After re-running MICE:
dlist <- mice::complete(imp, action = "all")

# 1) must exist and be numeric
stopifnot(all(c("paco2","vbg_co2") %in% names(dlist[[1]])))
stopifnot(is.numeric(dlist[[1]]$paco2), is.numeric(dlist[[1]]$vbg_co2))

# 2) confirm at least two PaCO2 levels among those with ABG in each imputation
table(vapply(dlist, function(d) dplyr::n_distinct(d$paco2[d$has_abg == 1 & is.finite(d$paco2)]), integer(1)) > 1)
```

```
TRUE
   5
```

```r
# 3) smoke test the ABG category fit on the first imputation
tmp <- fit_abg_cat("imv_proc"); print(tmp)
```

```
                term     logOR         SE       OR      LCL      UCL
1  co2_catHypocapnia 0.1859308 0.06190929 1.204339 1.066720 1.359712
2 co2_catHypercapnia 0.1503258 0.06304274 1.162213 1.027123 1.315070
```

Chunk unnamed-chunk-6 runtime: 2.00 s

5.8.4 14.3 Visualization: pooled three-level ORs

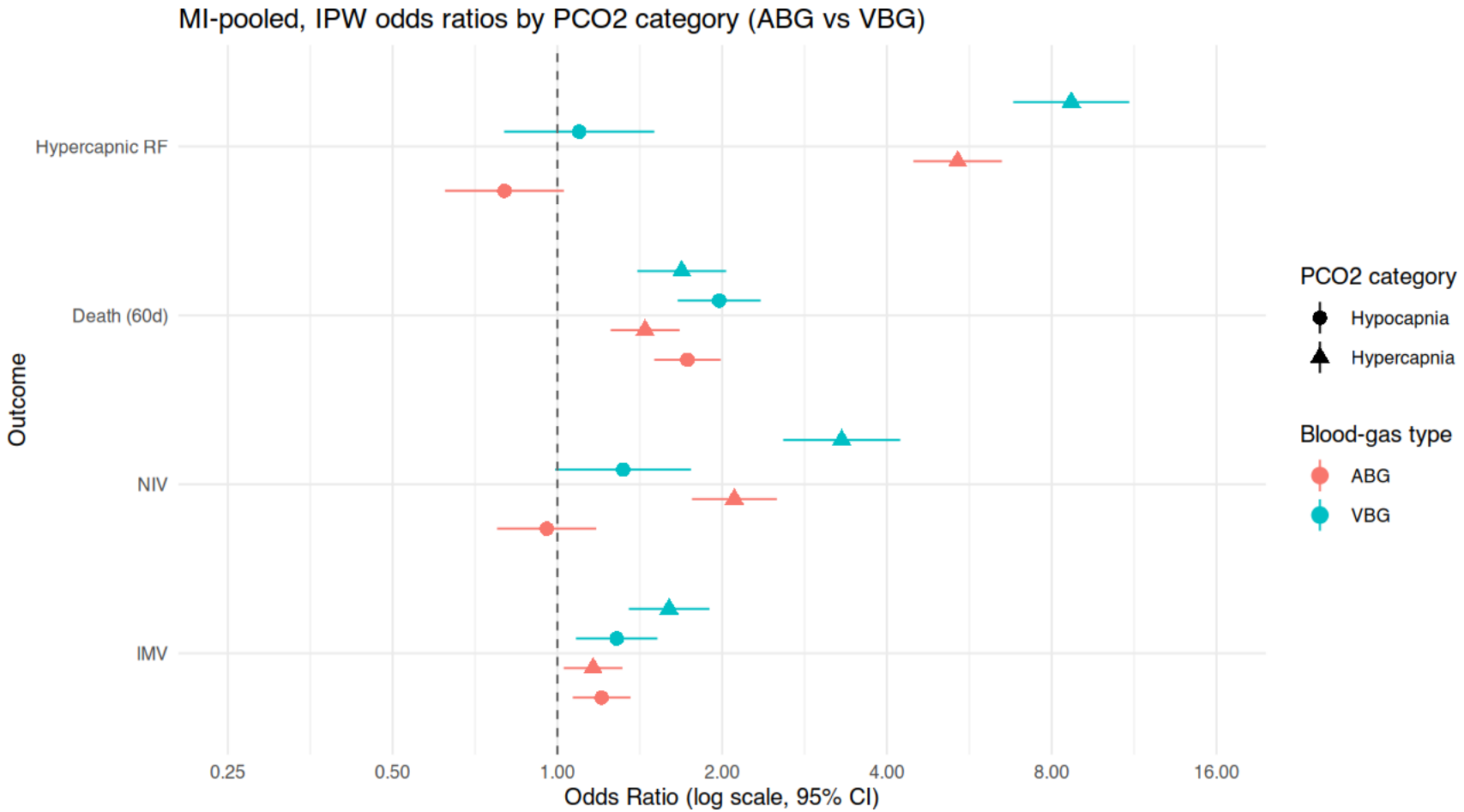
```r
library(dplyr)
library(survey)
library(ggplot2)
library(scales)
library(purrr)
library(mitools)

# --- Pre-flight ------------------------------------------------------------
if (!exists("dlist")) dlist <- mice::complete(imp, action = "all")
stopifnot(length(W_abg_list) == length(dlist),
          length(W_vbg_list) == length(dlist))

# --- Pooling helper for term-level log-ORs across imputations --------------
pool_terms <- function(fits, term_prefix) {
  fits <- Filter(Negate(is.null), fits)
  if (length(fits) == 0L) {
    return(tibble::tibble(term=character(), logOR=numeric(), SE=numeric(),
                          OR=numeric(), LCL=numeric(), UCL=numeric()))
  }
  terms_list <- lapply(fits, function(f) names(stats::coef(f)))
  common     <- Reduce(intersect, terms_list)
  keep_terms <- grep(paste0("^", term_prefix), common, value = TRUE)
```

```r
  if (!length(keep_terms)) {
    return(tibble::tibble(term=character(), logOR=numeric(), SE=numeric(),
                          OR=numeric(), LCL=numeric(), UCL=numeric()))
  }

  purrr::map_dfr(keep_terms, function(term) {
    res <- lapply(fits, function(f) setNames(c(stats::coef(f)[term]), term))
    vars <- lapply(fits, function(f) {
      V <- stats::vcov(f)
      m <- matrix(V[term, term], 1, 1); dimnames(m) <- list(term, term); m
    })
    pooled <- mitools::MIcombine(results = res, variances = vars)
    est <- as.numeric(stats::coef(pooled))
    se  <- sqrt(diag(pooled$variance))
    tibble::tibble(
      term  = term,
      logOR = est,
      SE    = se,
      OR    = exp(est),
      LCL   = exp(est - 1.96 * se),
      UCL   = exp(est + 1.96 * se)
    )
  })
}

# --- Per-group runner over imputations (ABG/VBG) -------------------------------
fit_cat_group <- function(group = c("ABG", "VBG"), outcome) {
  group <- match.arg(group)
  fits <- vector("list", length(dlist))

  for (i in seq_along(dlist)) {
    d <- dlist[[i]]

    if (group == "ABG") {
      if (!("paco2" %in% names(d))) { fits[[i]] <- NULL; next }
      d$paco2 <- suppressWarnings(as.numeric(d$paco2))
```

```
    g <- with(d, has_abg == 1 & is.finite(paco2))
    if (!any(g)) { fits[[i]] <- NULL; next }
    d2 <- d[g, , drop = FALSE]
    d2$co2_cat <- make_co2_cat(
      d2$paco2,
      fixed_breaks = if (exists("use_fixed_abg", inherits = TRUE) && isTRUE(use_fixed_abg)) co2_breaks_abg else NULL,
      labels       = if (exists("co2_labels_abg", inherits = TRUE)) co2_labels_abg else c("Eucapnia","Hypocapnia","Hypercapnia
      normal       = if (exists("co2_breaks_abg", inherits = TRUE)) co2_breaks_abg else c(35, 45)
    )
    w <- W_abg_list[[i]]$weights[g]
    w[!is.finite(w)] <- NA_real_

  } else {
    if (!("vbg_co2" %in% names(d))) { fits[[i]] <- NULL; next }
    d$vbg_co2 <- suppressWarnings(as.numeric(d$vbg_co2))
    g <- with(d, has_vbg == 1 & is.finite(vbg_co2))
    if (!any(g)) { fits[[i]] <- NULL; next }
    d2 <- d[g, , drop = FALSE]
    d2$co2_cat <- make_co2_cat(
      d2$vbg_co2,
      fixed_breaks = if (exists("use_fixed_vbg", inherits = TRUE) && isTRUE(use_fixed_vbg)) co2_breaks_vbg else NULL,
      labels       = if (exists("co2_labels_vbg", inherits = TRUE)) co2_labels_vbg else c("Eucapnia","Hypocapnia","Hypercapnia
      normal       = if (exists("co2_breaks_vbg", inherits = TRUE)) co2_breaks_vbg else c(40, 50)
    )
    w <- W_vbg_list[[i]]$weights[g]
    w[!is.finite(w)] <- NA_real_
  }

  ref_lab <- if (group == "ABG") {
    if (exists("ref_label_abg", inherits = TRUE)) ref_label_abg else levels(d2$co2_cat)[1]
  } else {
    if (exists("ref_label_vbg", inherits = TRUE)) ref_label_vbg else levels(d2$co2_cat)[1]
  }
  if (!ref_lab %in% levels(d2$co2_cat)) ref_lab <- levels(d2$co2_cat)[1]
  d2$co2_cat <- stats::relevel(base::droplevels(d2$co2_cat), ref = ref_lab)
  if (nlevels(d2$co2_cat) < 2) { fits[[i]] <- NULL; next }
```

```
    okw <- is.finite(w)
    if (!all(okw)) {
      d2 <- d2[okw, , drop = FALSE]
      w  <- w[okw]
      if (nrow(d2) == 0L) { fits[[i]] <- NULL; next }
    }

    d2$w <- w
    des  <- survey::svydesign(ids = ~1, weights = ~w, data = d2)
    fml  <- stats::as.formula(paste0(outcome, " ~ co2_cat"))
    fit  <- try(survey::svyglm(fml, design = des, family = quasibinomial()), silent = TRUE)
    fits[[i]] <- if (!inherits(fit, "try-error")) fit else NULL
  }

  out <- pool_terms(fits, term_prefix = "co2_cat")
  out
}

# --- Run & plot ------------------------------------------------------------
outs <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")

abg_df <- purrr::map_dfr(outs, ~ dplyr::mutate(fit_cat_group("ABG", .x),
                                               outcome = .x, group = "ABG"))
vbg_df <- purrr::map_dfr(outs, ~ dplyr::mutate(fit_cat_group("VBG", .x),
                                               outcome = .x, group = "VBG"))
combined <- dplyr::bind_rows(abg_df, vbg_df)

# decode "co2_cat<level>" → exposure
combined <- combined |>
  dplyr::mutate(exposure = gsub("^co2_cat", "", term),
                exposure = factor(exposure, levels = c("Eucapnia","Hypocapnia","Hypercapnia")),
                outcome  = factor(outcome,
                                  levels = c("imv_proc","niv_proc","death_60d","hypercap_resp_failure"),
                                  labels = c("IMV","NIV","Death (60d)","Hypercapnic RF")),
                group    = factor(group, levels = c("ABG","VBG")))
```

```r
ggplot(
  combined,
  aes(x = outcome, y = OR, ymin = LCL, ymax = UCL, color = group, shape = exposure)
) +
  geom_pointrange(position = position_dodge(width = 0.7), size = 0.6) +
  geom_hline(yintercept = 1, linetype = "dashed", colour = "grey40") +
  scale_y_log10(
    breaks = c(0.25, 0.5, 1, 2, 4, 8, 16),
    limits = c(0.25, 16),
    labels = scales::number_format(accuracy = 0.01)
  ) +
  coord_flip() +
  labs(
    title = "MI-pooled, IPW odds ratios by PCO2 category (ABG vs VBG)",
    x = "Outcome",
    y = "Odds Ratio (log scale, 95% CI)",
    color = "Blood-gas type",
    shape = "PCO2 category"
  ) +
  theme_minimal(base_size = 10)
```



Chunk ipw-three-level-pco2-mi-abg-vbg runtime: 4.38 s

5.9 15) Imputed, weighted spline PCO2 (ABG & VBG)

5.9.1 15.1 ABG, imputed, weighted, spline outcome

```
# Use pooled per-group helpers defined above (fit_cat_group + pool_terms)
outs <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")
```

```
abg_cat_results <- purrr::map_dfr(outs, ~ dplyr::mutate(fit_cat_group("ABG", .x),
                                                        outcome = .x, group = "ABG")) |>
  dplyr::relocate(outcome)
abg_cat_results
```

outcome	term	logOR	SE	OR	LCL	UCL	group
imv_proc	co2_catHypocapnia	0.1859308	0.0619093	1.2043389	1.0667201	1.359712	ABG
imv_proc	co2_catHypercapnia	0.1503258	0.0630427	1.1622129	1.0271234	1.315070	ABG
niv_proc	co2_catHypocapnia	-0.0453203	0.1063031	0.9556914	0.7759444	1.177077	ABG
niv_proc	co2_catHypercapnia	0.7444482	0.0911737	2.1052793	1.7607639	2.517203	ABG
death_60d	co2_catHypocapnia	0.5469969	0.0713110	1.7280557	1.5026456	1.987279	ABG
death_60d	co2_catHypercapnia	0.3689829	0.0740196	1.4462629	1.2509515	1.672068	ABG
hypercap_resp_failure	co2_catHypocapnia	-0.2228352	0.1276323	0.8002467	0.6231334	1.027701	ABG
hypercap_resp_failure	co2_catHypercapnia	1.6837993	0.0949891	5.3859800	4.4710384	6.488153	ABG

Chunk unnamed-chunk-7 runtime: 2.34 s

5.9.2 15.2 VBG, imputed, weighted, spline outcome

```
outs <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")

vbg_cat_results <- purrr::map_dfr(outs, ~ dplyr::mutate(fit_cat_group("VBG", .x),
                                                        outcome = .x, group = "VBG")) |>
  dplyr::relocate(outcome)
vbg_cat_results
```

outcome	term	logOR	SE	OR	LCL	UCL	group
imv_proc	co2_catHypocapnia	0.2492526	0.0874820	1.283066	1.0808934	1.523054	VBG
imv_proc	co2_catHypercapnia	0.4700157	0.0864254	1.600019	1.3506985	1.895361	VBG
niv_proc	co2_catHypocapnia	0.2763088	0.1457549	1.318255	0.9906728	1.754157	VBG

outcome	term	logOR	SE	OR	LCL	UCL	group
niv_proc	co2_catHypercapnia	1.1960343	0.1255208	3.306976	2.5857444	4.229379	VBG
death_60d	co2_catHypocapnia	0.6805852	0.0890481	1.975033	1.6587279	2.351655	VBG
death_60d	co2_catHypercapnia	0.5228706	0.0954237	1.686863	1.3991152	2.033790	VBG
hypercap_resp_failure	co2_catHypocapnia	0.0916031	0.1611522	1.095930	0.7991112	1.502997	VBG
hypercap_resp_failure	co2_catHypercapnia	2.1616314	0.1244954	8.685295	6.8047465	11.085550	VBG

Chunk unnamed-chunk-8 runtime: 1.84 s

5.9.3 15.3 Visualization

```
library(dplyr)
library(ggplot2)
library(patchwork)
library(splines)
library(survey)
library(purrr)

if (!exists("dlist")) dlist <- mice::complete(imp, action = "all")
stopifnot(length(W_abg_list) == length(dlist),
          length(W_vbg_list) == length(dlist))

# CO2 support sanity: ensure trimmed ranges exist for both groups
rng_abg <- quantile(
  unlist(lapply(dlist, function(d) as.numeric(d$paco2[d$has_abg == 1]))),
  c(.02, .98), na.rm = TRUE
)
rng_vbg <- quantile(
  unlist(lapply(dlist, function(d) as.numeric(d$vbg_co2[d$has_vbg == 1]))),
  c(.02, .98), na.rm = TRUE
)
stopifnot(rng_abg[1] < rng_abg[2], rng_vbg[1] < rng_vbg[2])
```

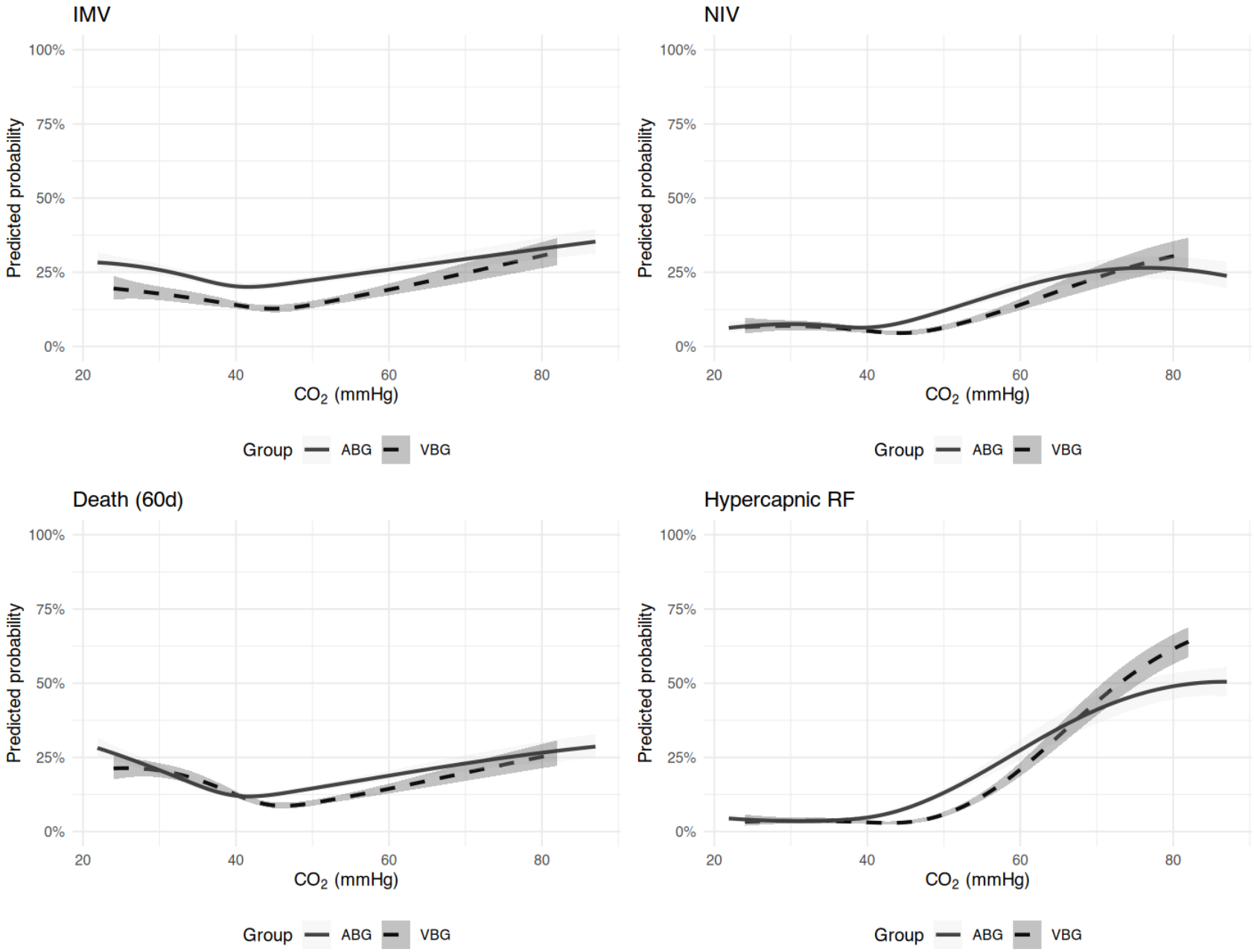
```r
# Predict link for svyglm; fallback to X  and delta method if predict() returns a vector
predict_link_svyglm <- function(fit, newdata) {
  pr <- try(stats::predict(fit, newdata = newdata, type = "link", se.fit = TRUE), silent = TRUE)
  if (!inherits(pr, "try-error") && is.list(pr) && !is.null(pr$fit)) {
    return(list(fit = as.numeric(pr$fit), se.fit = as.numeric(pr$se.fit)))
  }
  # manual:   = X ; Var( ) = X V X^T
  X <- stats::model.matrix(stats::delete.response(stats::terms(fit)), newdata)
  beta <- stats::coef(fit)
  eta  <- drop(X %*% beta)
  V    <- stats::vcov(fit)
  se   <- sqrt(rowSums((X %*% V) * X))
  list(fit = eta, se.fit = se)
}

# Pool predicted curves on the link scale, then transform with logistic
pool_rcs_curve <- function(group = c("ABG","VBG"), outcome,
                           df = 4, grid_n = 220, trim = c(0.02, 0.98)) {
  group <- match.arg(group)

  # global trimmed range for this group
  co2_all <- unlist(lapply(seq_along(dlist), function(i) {
    d <- dlist[[i]]
    if (group == "ABG") as.numeric(d$paco2[d$has_abg == 1])
    else as.numeric(d$vbg_co2[d$has_vbg == 1])
  }), use.names = FALSE)
  co2_all <- co2_all[is.finite(co2_all)]
  stopifnot(length(co2_all) > 0)
  rng  <- as.numeric(stats::quantile(co2_all, probs = trim, na.rm = TRUE))
  if (!is.finite(rng[1]) || !is.finite(rng[2]) || rng[2] <= rng[1]) {
    med <- stats::median(co2_all); rng <- c(med - 1, med + 1)
  }
  xseq <- seq(rng[1], rng[2], length.out = grid_n)

  eta_list <- list()
  var_list <- list()
```

```r
for (i in seq_along(dlist)) {
  d <- dlist[[i]]

  if (group == "ABG") {
    d$paco2 <- suppressWarnings(as.numeric(d$paco2))
    g <- with(d, has_abg == 1 & is.finite(paco2))
    if (!any(g)) next
    d2 <- d[g, , drop = FALSE]
    d2$co2 <- d2$paco2
    w  <- W_abg_list[[i]]$weights[g]
  } else {
    d$vbg_co2 <- suppressWarnings(as.numeric(d$vbg_co2))
    g <- with(d, has_vbg == 1 & is.finite(vbg_co2))
    if (!any(g)) next
    d2 <- d[g, , drop = FALSE]
    d2$co2 <- d2$vbg_co2
    w  <- W_vbg_list[[i]]$weights[g]
  }

  # drop NA/inf weights
  ok <- is.finite(w)
  if (!all(ok)) {
    d2 <- d2[ok, , drop = FALSE]
    w  <- w[ok]
    if (nrow(d2) == 0L) next
  }

  d2$w <- w
  des  <- survey::svydesign(ids = ~1, weights = ~w, data = d2)
  fml  <- stats::as.formula(paste0(outcome, " ~ splines::ns(co2, ", df, ")"))
  fit  <- try(survey::svyglm(fml, design = des, family = quasibinomial()), silent = TRUE)
  if (inherits(fit, "try-error")) next

  newd <- data.frame(co2 = xseq)
  pr   <- predict_link_svyglm(fit, newd)
```

```
    eta_list[[length(eta_list) + 1L]] <- pr$fit
    var_list[[length(var_list) + 1L]] <- pr$se.fit^2
  }

  m <- length(eta_list)
  if (m == 0L) stop("No successful fits to pool for ", group, " / ", outcome)

  ETA <- do.call(cbind, eta_list)   # ngrid × m
  VAR <- do.call(cbind, var_list)   # ngrid × m

  if (m == 1L) {
    etaBar <- as.numeric(ETA)
    Tvar   <- as.numeric(VAR)
  } else {
    etaBar <- rowMeans(ETA)
    Wbar   <- rowMeans(VAR)
    B      <- apply(ETA, 1, stats::var)
    Tvar   <- Wbar + (1 + 1/m) * B
  }
  seBar <- sqrt(pmax(Tvar, 0))

  tibble::tibble(
    co2   = xseq,
    yhat  = plogis(etaBar),
    lower = plogis(etaBar - 1.96 * seBar),
    upper = plogis(etaBar + 1.96 * seBar),
    group = group
  )
}

mk_curves <- function(outcome)
  dplyr::bind_rows(
    pool_rcs_curve("ABG", outcome, df = 4, grid_n = 220, trim = c(0.02, 0.98)),
    pool_rcs_curve("VBG", outcome, df = 4, grid_n = 220, trim = c(0.02, 0.98))
  )
```

```r
cur_imv   <- mk_curves("imv_proc")
cur_niv   <- mk_curves("niv_proc")
cur_death <- mk_curves("death_60d")
cur_hcrf  <- mk_curves("hypercap_resp_failure")

plt_gray <- function(dat, title) {
  ggplot(dat, aes(x = co2, y = yhat, linetype = group)) +
    geom_line(color = "black", linewidth = 1) +
    geom_ribbon(aes(ymin = lower, ymax = upper, fill = group), alpha = 0.3, color = NA) +
    scale_fill_manual(values = c("ABG" = "gray90", "VBG" = "gray20")) +
    scale_linetype_manual(values = c("ABG" = "solid", "VBG" = "dashed")) +
    scale_y_continuous(limits = c(0, 1),
                       labels = scales::percent_format(accuracy = 1)) +
    labs(title = title,
         x = expression(CO[2]~"(mmHg)"),
         y = "Predicted probability",
         fill = "Group", linetype = "Group") +
    theme_minimal(base_size = 10) +
    theme(legend.position = "bottom")
}

(patchwork::wrap_plots(
   plt_gray(cur_imv,   "IMV"),
   plt_gray(cur_niv,   "NIV"),
   plt_gray(cur_death, "Death (60d)"),
   plt_gray(cur_hcrf,  "Hypercapnic RF"),
   ncol = 2
 ) +
  plot_annotation(
    title = expression(
      paste("MI-pooled, propensity-weighted predicted probability: ABG vs VBG CO"[2],
            " (restricted cubic splines, 2-98% range)")
    )
  ))
```

MI-pooled, propensity-weighted predicted probability: ABG vs VBG CO_2 (restricted cubic splines, 2–98% range)



Chunk ipw-rcs-overlay-mi-abg-vbg runtime: 1.89 s

5.10 16) Save, export, and session info

```
saveRDS(list(abg = abg_results, vbg = vbg_results), mi_pooled_file)
```

Chunk mi-save-exports runtime: 0.00 s

```
sessionInfo()
```

```
R version 4.5.0 (2025-04-11)
Platform: aarch64-apple-darwin20
Running under: macOS 26.1

Matrix products: default
BLAS:   /Library/Frameworks/R.framework/Versions/4.5-arm64/Resources/lib/libRblas.0.dylib
LAPACK: /Library/Frameworks/R.framework/Versions/4.5-arm64/Resources/lib/libRlapack.dylib;  LAPACK version 3.12.1

locale:
[1] en_US.UTF-8/en_US.UTF-8/en_US.UTF-8/C/en_US.UTF-8/en_US.UTF-8

time zone: America/Denver
tzcode source: internal

attached base packages:
 [1] splines   grid      parallel  stats     graphics  grDevices utils
 [8] datasets  methods   base

other attached packages:
 [1] shapviz_0.10.2      fastshap_0.1.1      progressr_0.18.0
 [4] future.apply_1.20.0 future_1.67.0       mitools_2.4
 [7] skimr_2.2.1         visdat_0.6.0        naniar_1.1.0
[10] miceadds_3.18-36    mice_3.18.0         fs_1.6.6
[13] here_1.0.2          sensitivitymw_2.1   lubridate_1.9.4
```

```
[16] tibble_3.3.0        survey_4.4-8        survival_3.8-3
[19] Matrix_1.7-4        rms_8.0-0           Hmisc_5.2-3
[22] patchwork_1.3.2     officer_0.7.0       modelsummary_2.5.0
[25] scales_1.4.0        labelled_2.15.0     haven_2.5.5
[28] gt_1.1.0            ggplot2_4.0.0       gbm_2.2.2
[31] flextable_0.9.10    dplyr_1.1.4         codebookr_0.1.8
[34] cobalt_4.6.1        broom_1.0.11        WeightIt_1.5.0
[37] purrr_1.2.0         gtsummary_2.4.0     kableExtra_1.4.0

loaded via a namespace (and not attached):
  [1] polspline_1.1.25        datawizard_1.2.0        rpart_4.1.24
  [4] lifecycle_1.0.4         Rdpack_2.6.4            rprojroot_2.1.1
  [7] globals_0.18.0          lattice_0.22-7          MASS_7.3-65
 [10] insight_1.4.2           backports_1.5.0         magrittr_2.0.4
 [13] rmarkdown_2.30          yaml_2.3.10             zip_2.3.3
 [16] askpass_1.2.1           DBI_1.2.3               minqa_1.2.8
 [19] RColorBrewer_1.1-3      multcomp_1.4-28         nnet_7.3-20
 [22] TH.data_1.1-4           sandwich_3.1-1          gdtools_0.4.3
 [25] listenv_0.9.1           cards_0.7.0             MatrixModels_0.5-4
 [28] performance_0.15.1      parallelly_1.45.1       svglite_2.2.1
 [31] commonmark_2.0.0        codetools_0.2-20        xml2_1.4.0
 [34] tidyselect_1.2.1        shape_1.4.6.1           farver_2.1.2
 [37] lme4_1.1-38             effectsize_1.0.1        base64enc_0.1-3
 [40] jsonlite_2.0.0          mitml_0.4-5             Formula_1.2-5
 [43] iterators_1.0.14        emmeans_1.11.2-8        systemfonts_1.2.3
 [46] foreach_1.5.2           tools_4.5.0             ragg_1.5.0
 [49] Rcpp_1.1.0              glue_1.8.0              pan_1.9
 [52] gridExtra_2.3           mgcv_1.9-3              xfun_0.53
 [55] chk_0.10.0              withr_3.0.2             fastmap_1.2.0
 [58] boot_1.3-32             SparseM_1.84-2          openssl_2.3.3
 [61] litedown_0.7            digest_0.6.37           timechange_0.3.0
 [64] R6_2.6.1                estimability_1.5.1      textshaping_1.0.3
 [67] colorspace_2.1-2        markdown_2.0            utf8_1.2.6
 [70] tidyr_1.3.1             generics_0.1.4          fontLiberation_0.1.0
 [73] data.table_1.17.8       htmlwidgets_1.6.4       parameters_0.28.2
 [76] pkgconfig_2.0.3         gtable_0.3.6            lmtest_0.9-40
```

```
 [79] S7_0.2.0               htmltools_0.5.8.1      fontBitstreamVera_0.1.1
 [82] reformulas_0.4.2       knitr_1.50             rstudioapi_0.17.1
 [85] uuid_1.2-1             coda_0.19-4.1          checkmate_2.3.3
 [88] nlme_3.1-168           nloptr_2.2.1           repr_1.1.7
 [91] zoo_1.8-14             stringr_1.6.0          foreign_0.8-90
 [94] pillar_1.11.1          vctrs_0.6.5            jomo_2.7-6
 [97] xtable_1.8-4           cluster_2.1.8.1        htmlTable_2.4.3
[100] evaluate_1.0.5         tinytex_0.57           magick_2.9.0
[103] mvtnorm_1.3-3          cli_3.6.5              compiler_4.5.0
[106] rlang_1.1.6            crayon_1.5.3           labeling_0.4.3
[109] forcats_1.0.1          stringi_1.8.7          viridisLite_0.4.2
[112] tables_0.9.31          glmnet_4.1-10          bayestestR_0.17.0
[115] quantreg_6.1           fontquiver_0.2.1       hms_1.1.4
[118] rbibutils_2.4          xgboost_1.7.11.1
```

Chunk mi-session runtime: 0.05 s