

ABG-VBG Analysis

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1 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.

```
# put this in your first R chunk
stopifnot(requireNamespace("kableExtra", quietly = TRUE))
library(kableExtra)
library(gtsummary)
library(purrr)      # functional programming

# globally tighten gtsummary/gt tables (smaller font + tighter padding)
gtsummary::theme_gtsummary_compact()

# keep figures anchored in PDF to reduce heading-only/blank pages
if (knitr::is_latex_output()) {
  knitr::opts_chunk$set(fig.pos = "H")
}

# helper: turn any gtsummary table into a PDF-safe, auto-scaling LaTeX table
to_pdf_table <- function(tbl, font_size = 8, landscape = FALSE,
                           label_col_width = NULL, longtable = FALSE) {
  tbl_ncol <- tryCatch(ncol(gtsummary::as_tibble(tbl)), error = function(e) NA_integer_)
  if (is.finite(tbl_ncol) && tbl_ncol > 6 && font_size > 6) font_size <- 6
  kbl <- gtsummary::as_kable(
    tbl,
    format    = "latex",
    booktabs  = TRUE,
    longtable = longtable
  )

  # optional: set a fixed width for the first (label) column to encourage wrapping
  if (!is.null(label_col_width)) {
    kbl <- kableExtra::column_spec(kbl, 1, width = label_col_width)
  }
}
```

```

latex_opts <- if (longtable) {
  c("repeat_header")
} else {
  c("hold_position", "scale_down")
}
kbl <- kableExtra::kable_styling(
  kbl,
  latex_options = latex_opts,
  font_size      = font_size,
  full_width     = !longtable,
  position       = "center"
)

if (landscape) kbl <- kableExtra::landscape(kbl) # needs pdflscape (enabled above)
mark_float_emitted()
kbl
}

# helper: scale generic data.frames for PDF output
kable_pdf <- function(df, caption = NULL, font_size = 7) {
  kbl <- knitr::kable(df, format = "latex", booktabs = TRUE, caption = caption)
  kbl <- kableExtra::kable_styling(
    kbl,
    latex_options = c("hold_position", "scale_down"),
    font_size      = font_size,
    full_width     = TRUE,
    position       = "center"
  )
  mark_float_emitted()
  kbl
}

# helper: pretty, relative paths for PDF output
pretty_path <- function(p) {
  p_abs <- tryCatch(fs::path_abs(p, start = getwd()), error = function(e) NA_character_)
  res_abs <- tryCatch(fs::path_abs(results_dir, start = getwd()), error = function(e) NA_character_)

```

```

if (!is.na(p_abs) && !is.na(res_abs)) {
  if (fs::path_has_parent(p_abs, res_abs) || identical(p_abs, res_abs)) {
    rel <- fs::path_rel(p_abs, res_abs)
    return(fs::path("Results", rel))
  }
}
out <- tryCatch(fs::path_rel(p, start = getwd()), error = function(e) NA_character_)
if (is.na(out) || out == "." || grepl("^\\\\.\\\\.", out)) {
  return(basename(p))
}
out
}

# helper: strip manual "Table X." prefixes in PDF to avoid double numbering
strip_manual_table_number <- function(caption) {
  if (is.null(caption)) return(caption)
  if (!knitr::is_latex_output()) return(caption)
  cap <- gsub("^\\\\s*(\\*\\\\*)?Table\\\\s+[0-9A-Za-z]+\\\\.\\\\.?\\\\s*:?\\\\s*", "", caption)
  cap
}

# helper: escape LaTeX special chars in plain captions
escape_latex_text <- function(x) {
  if (is.null(x)) return(x)
  if (!knitr::is_latex_output()) return(x)
  gsub("[\\\\\\\\%$&#{}_\\\\^]", "\\\\\\1", x, perl = TRUE)
}

# Float barrier helpers (use 4 modes to control float flushing)
mark_float_emitted <- function() {
  invisible(TRUE)
}
float_barrier <- function(mode = c("soft", "section", "hard", "flush")) {
  if (!knitr::is_latex_output()) return(invisible(NULL))
  mode <- match.arg(mode)
  cmd <- switch(

```

```

    mode,
    soft = "\\FloatBarrier\\nopagebreak",
    section = "\\FloatBarrier\\nopagebreak\\par\\noindent",
    hard = "\\FloatBarrier\\clearpage",
    flush = "\\FloatBarrier\\pagebreak"
)
knitr::asis_output(cmd)
}

# helper: render full tables for PDF (no previews)
render_table_pdf <- function(df, caption, file_stub,
                           wide = FALSE,
                           digits = 2,
                           max_cols = 6,
                           landscape = NULL) {
  stopifnot(is.data.frame(df))
  out_csv <- results_path(paste0(file_stub, ".csv"))
  write_csv_safely(df, out_csv, row_names = FALSE)

  if (is.null(landscape)) landscape <- (wide || ncol(df) > max_cols)
  use_longtable <- nrow(df) > 40
  n_cols <- ncol(df)
  parts <- if (n_cols <= max_cols) list(df) else {
    idx <- split(seq_len(n_cols), ceiling(seq_len(n_cols) / max_cols))
    lapply(idx, function(ii) df[, ii, drop = FALSE])
  }

  build_kbl <- function(df_part, cap) {
    cap <- escape_latex_text(strip_manual_table_number(cap))
    kbl <- knitr::kable(
      df_part,
      format = "latex",
      booktabs = TRUE,
      longtable = use_longtable,
      caption = cap,
      digits = digits
  }
}

```

```

)
tbl <- kableExtra::kable_styling(
  kbl,
  latex_options = if (use_longtable) c("repeat_header") else c("hold_position", "scale_down"),
  font_size      = if (ncol(df_part) > max_cols || wide) 6 else 7,
  full_width     = FALSE,
  position       = "center"
)
if (landscape) kbl <- kableExtra::landscape(kbl)
tbl
}

if (length(parts) == 1L) {
  mark_float_emitted()
  return(build_kbl(parts[[1]], caption))
}

letters_part <- LETTERS[seq_along(parts)]
out <- character(0)
for (i in seq_along(parts)) {
  cap_i <- paste0(caption, " (Part ", letters_part[i], ")")
  out <- c(out, build_kbl(parts[[i]], cap_i))
}
mark_float_emitted()
knitr::asis_output(paste(out, collapse = "\n\n"))
}

render_table_pdf_maybe <- function(df, caption, file_stub,
                                    wide = FALSE,
                                    digits = 2,
                                    max_cols = 6,
                                    landscape = NULL,
                                    show = TRUE) {
  tbl <- render_table_pdf(
    df,
    caption = caption,

```

```

    file_stub = file_stub,
    wide = wide,
    digits = digits,
    max_cols = max_cols,
    landscape = landscape
)
if (isTRUE(show)) {
  return(tbl)
}
invisible(NULL)
}

```

1.0.1 Package Set Up

```

# Consolidated package management -----
required_pkgs <- c(
  "WeightIt", "broom", "cobalt", "codebookr", "dplyr", "flextable", "parallel",
  "gbm", "ggplot2", "gt", "gtsummary", "haven", "labelled", "scales",
  "modelsummary", "officer", "patchwork", "rms", "survey", "tibble", "lubridate",
  "sensitivitymw", "here", "fs", "dagitty", "ggdag", "naniar", "mice", "miceadds",
  "digest"
)

# Fail fast if packages are missing (use renv to install)
missing_pkgs <- setdiff(required_pkgs, rownames(installed.packages()))
if (length(missing_pkgs)) {
  stop(
    "Missing packages: ", paste(missing_pkgs, collapse = ", "),
    ". Install with renv::install(c(...)) and then run renv::snapshot()."
  )
}

# Load (or attach) all required packages
invisible(lapply(required_pkgs, require, character.only = TRUE))

```

```

# Centralize outputs under Results/, with paths relative to project root
qmd_dir <- here::here("Code Drafts")
data_dir_param <- Sys.getenv("ABGVBG_DATA_DIR", unset = params$data_dir)
results_dir_param <- Sys.getenv("ABGVBG_RESULTS_DIR", unset = params$results_dir)
data_dir_name <- fs::path_abs(data_dir_param, start = here::here())
results_dir <- fs::path_abs(results_dir_param, start = here::here())
if (!dir.exists(data_dir_name)) {
  stop("Data directory does not exist: ", data_dir_name)
}
fs::dir_create(results_dir, recurse = TRUE)
fig_dir      <- fs::path(results_dir, "figs")
fig_path     <- paste0(fs::path_rel(fig_dir, start = qmd_dir), "/")
results_path <- function(...) fs::path(results_dir, ...)
fs::dir_create(fig_dir, recurse = TRUE)

knitr::opts_chunk$set(
  fig.path    = fig_path,
  dev         = "raster_png",
  dpi         = 200
)
# on macOS and some setups this prevents device headaches
options(bitmapType = "cairo")

flow_png <- results_path("cohort_flow.png")
flow_pdf <- results_path("cohort_flow.pdf")
if (file.exists(flow_png) || file.exists(flow_pdf)) {
  knitr::include_graphics(if (file.exists(flow_png)) flow_png else flow_pdf)
} else {
  cat("Cohort flow diagram will be generated externally and inserted here in the final manuscript packet.\n")
}

```

Cohort flow diagram will be generated externally and inserted here in the final manuscript packet.

```

stopifnot(!is.null(params$run_mode))
stopifnot(!is.null(params$pilot_frac))
stopifnot(!is.null(params$mi_batch_threshold_pilot))
stopifnot(!is.null(params$mi_batch_threshold_full))
stopifnot(!is.null(params$sample_seed))

RUN_MODE <- match.arg(tolower(params$run_mode), c("pilot", "full"))
PILOT_FRAC <- as.numeric(params$pilot_frac)
stopifnot(is.finite(PILOT_FRAC), PILOT_FRAC > 0, PILOT_FRAC <= 1)
if (RUN_MODE == "full") PILOT_FRAC <- 1
SAMPLE_SEED <- as.integer(params$sample_seed)
stopifnot(is.finite(SAMPLE_SEED))

pilot_frac <- PILOT_FRAC
FULL_RUN <- identical(RUN_MODE, "full")
SHOW_LOW_VALUE_TABLES <- FALSE
MI_BATCH_THRESHOLD <- if (RUN_MODE == "pilot") {
  as.integer(params$mi_batch_threshold_pilot)
} else {
  as.integer(params$mi_batch_threshold_full)
}
stopifnot(is.finite(MI_BATCH_THRESHOLD), MI_BATCH_THRESHOLD > 0)
PLOT_DROP_POLICY <- "warn"
PROB_EPS <- 1e-6
MAX_SHAPE_LEVELS <- 6L
SPLINE_GRID_N <- 200L
OR_XLIM <- c(0.25, 16)
TAIL_NFINITE <- 5L
TAIL_WINDOW_ITERS <- 10L
BAL_XLIM_MAX <- 1.0
MC_ERR_RATIO_THRESH <- 0.10
SHOW_CHUNK_RUNTIME_TEXT <- FALSE
MAX_LEVELS_GBM <- 50L
GBM_MM_EST_BYTES_WARN <- 6e9
MAX_GBM_MM_COLS_WARN <- 200L
MAX_GBM_MM_COLS_STOP <- 400L

```

```

MAX_GBM_FACTOR_LEVELS_WARN <- 30L
MAX_GBM_FACTOR_LEVELS_STOP <- 60L

message(
  "CONFIG: RUN_MODE=", RUN_MODE,
  " | PILOT_FRAC=", PILOT_FRAC,
  " | SAMPLE_SEED=", SAMPLE_SEED
)

diag_run_id <- format(Sys.time(), "%Y%m%d_%H%M%S")
diag_run_ts <- as.character(Sys.time())
run_id <- diag_run_id
run_ts <- diag_run_ts
runtime_run_id <- diag_run_id
options(run_id = run_id, run_ts = run_ts)
runtime_log <- data.frame()
mi_warn_log <- data.frame(
  time = character(), stage = character(), component = character(),
  analysis_variant = character(), model_type = character(),
  group = character(), outcome = character(), imputation = integer(),
  batch = integer(), message = character(), stringsAsFactors = FALSE
)
mi_info_log <- mi_warn_log
mi_outcome_diag <- data.frame()
memory_snapshots <- data.frame()
gbm_preflight_design_dims <- data.frame()
gbm_preflight_warnings <- data.frame()
factor_diag_written <- character()
plot_drop_log_df <- data.frame(
  plot = character(), reason = character(), n_dropped = integer(),
  n_before = integer(), n_after = integer(),
  stage = character(), extra = character(),
  stringsAsFactors = FALSE
)
cleanup_diagnostics_outputs <- function() {

```

```

diag_files <- c(
  "runtime_log.csv", "runtime_summary.csv", "runtime_summary_top15.csv",
  "warnings_log.csv", "mi_warnings_log.csv", "mi_info_log.csv",
  "diagnostics_summary.csv", "diagnostics_missingness.csv",
  "diagnostics_missingness-by-strata.csv",
  "balance_target_imp_summary.csv", "balance_target_by_imp.csv",
  "balance_target_worst_rows.csv", "balance_max_smd_by_imp.csv",
  "balance_worst_terms.csv", "balance_worst10.csv", "balance_table.csv",
  "weight_summary.csv", "ps_overlap_summary.csv",
  "model_fit_diagnostics.csv", "mi_outcome_fit_diagnostics.csv",
  "mi_fit_issue_summary.csv", "mi_m_stability.csv", "mi_maxit_sensitivity.csv",
  "mi_obs_vs_imp_summary.csv", "mi_spline_curve_abg.csv",
  "mi_spline_curve_vbg.csv", "mi_spline_coef_abg.csv",
  "mi_spline_coef_vbg.csv", "diag-ps-shap-stability.csv",
  "mice_smoketest.log", "mice_batches_log.csv", "mice_chain_diagnostics.csv",
  "mice_pred_width_preflight.csv", "mice_logged_events_raw.csv",
  "mice_logged_events_summary.csv", "mice_spec.rds",
  "missingness-by-strata.csv", "missingness-drivers.csv",
  "missingness-pattern.csv", "plot_drop_log.csv",
  "plot_registry.csv",
  "mi_logistic_ps_covariate_types.csv",
  "mi_logistic_ps_abg_list.rds",
  "mi_logistic_ps_vbg_list.rds"
)
diag_patterns <- c(
  "^\$mice_.*\\.(csv|log|rds|txt)$",
  "^\$diagnostics_.*\\(.csv$",
  "^\$runtime_.*\\(.csv$",
  "^\$warnings_.*\\(.csv$",
  "^\$balance_.*\\(.csv$",
  "^\$weight_summary\\(.csv$",
  "^\$ps_overlap_summary\\(.csv$",
  "^\$model_fit_diagnostics\\(.csv$",
  "^\$plot_drop_log\\(.csv$",
  "^\$diag-.*\\(.csv$",
  "^\$mi_logistic_ps_.*\\(.csv|rds)$"
)

```

```

)
files <- list.files(results_dir, full.names = TRUE)
base <- basename(files)
match_files <- base %in% diag_files
if (length(diag_patterns)) {
  match_files <- match_files | grepl(paste(diag_patterns, collapse = "|"), base)
}
to_delete <- files[match_files]
if (length(to_delete)) {
  safe_root <- normalizePath(results_dir, winslash = "/", mustWork = FALSE)
  del_paths <- normalizePath(to_delete, winslash = "/", mustWork = FALSE)
  stopifnot(all(startsWith(del_paths, safe_root)))
}
fs::file_delete(to_delete)

diag_figs <- list.files(fig_dir, full.names = TRUE)
diag_figs <- diag_figs[grepl("(diag-|or-plot|ps-)", basename(diag_figs))]
if (length(diag_figs)) {
  safe_root <- normalizePath(results_dir, winslash = "/", mustWork = FALSE)
  del_paths <- normalizePath(diag_figs, winslash = "/", mustWork = FALSE)
  stopifnot(all(startsWith(del_paths, safe_root)))
}
fs::file_delete(diag_figs)
{
  d <- fs::path(results_dir, "mice_batches")
  if (dir.exists(d)) fs::dir_delete(d)
}
{
  d <- fs::path(results_dir, "diagnostics_audit_snippets")
  if (dir.exists(d)) fs::dir_delete(d)
}
{
  f <- fs::path(results_dir, "mi_partial_mids.rds")
  if (file.exists(f)) fs::file_delete(f)
}
}

```

```

cleanup_diagnostics_outputs()
# Ensure any stale Results artifacts from prior runs are removed
stale_patterns <- c(
  "^missingness_by_strata\\.csv$",
  "^missingness-drivers\\.csv$",
  "^missingness_by_strata_preview\\.csv$",
  "^missingness_drivers_top20\\.csv$",
  "^missingness_top10\\.csv$",
  "^outcome_counts_by_cohort\\.csv$",
  "^weighting_diagnostics_non_mi\\.csv$",
  "^mi_specification\\.csv$",
  "^memory_snapshots\\.csv$",
  "^gbm_preflight_design_dims\\.csv$",
  "^gbm_preflight_factor_levels_.*\\.csv$",
  "^mi_logistic_ps_factor_levels_.*\\.csv$",
  "^mi_logistic_ps_.*\\.(csv|rds)$",
  "^get_imp_usage\\.csv$",
  "^diagnostics_audit\\.md$",
  "^pdf_page_text_stats\\.csv$",
  "^pdf_blank_pages\\.json$",
  "^pdf_hygiene_scan\\.csv$"
)
stale_files <- list.files(results_dir, full.names = TRUE)
stale_base <- basename(stale_files)
stale_files <- stale_files[grepl(paste(stale_patterns, collapse = "|"), stale_base)]
if (length(stale_files)) fs::file_delete(stale_files)

```

1.1 Helper functions for model diagnostics

```

# Diagnostics helper functions for MI/IPW pipeline

assert_no_na_covars <- function(df, covars, context = "") {
  missing <- setdiff(covars, names(df))

```

```

stopifnot(length(missing) == 0)
na_counts <- vapply(df[, covars, drop = FALSE], function(x) sum(is.na(x)), numeric(1))
if (any(na_counts > 0)) {
  msg <- paste0(
    "NA values found in covariates (", context, "): ",
    paste(names(na_counts)[na_counts > 0], na_counts[na_counts > 0], collapse = ", "))
  )
  stop(msg)
}
invisible(TRUE)
}

summarize_logged_events <- function(mids_obj) {
  ev <- mids_obj$loggedEvents
  if (is.null(ev) || nrow(ev) == 0L) {
    return(data.frame(
      variable = character(),
      method = character(),
      event = character(),
      n = integer(),
      pct = numeric(),
      stringsAsFactors = FALSE
    ))
  }
  stopifnot(all(c("dep", "meth", "out") %in% names(ev)))
  tbl <- as.data.frame(table(ev$dep, ev$meth, ev$out), stringsAsFactors = FALSE)
  names(tbl) <- c("variable", "method", "event", "n")
  tbl <-tbl[tbl$n > 0, , drop = FALSE]
  tbl <-tbl[order(-tbl$n), , drop = FALSE]
  tbl$pct <-tbl$n / sum(tbl$n)
  tbl
}

extract_weightit_ps <- function(w) {
  stopifnot(!is.null(w$ps))
  as.numeric(w$ps)
}

```

```

}

ess <- function(w) {
  w <- w[is.finite(w)]
  stopifnot(length(w) > 0)
  sum(w)^2 / sum(w^2)
}

weight_concentration <- function(w, top_p = 0.01) {
  w <- w[is.finite(w)]
  stopifnot(length(w) > 0)
  ord <- sort(w, decreasing = TRUE)
  n_top <- max(1L, floor(length(ord) * top_p))
  sum(ord[seq_len(n_top)]) / sum(ord)
}

weight_summary <- function(w, ps, ps_floor, truncated) {
  w_ok <- w[is.finite(w)]
  stopifnot(length(w_ok) > 0)
  ps_ok <- ps[is.finite(ps)]
  stopifnot(length(ps_ok) > 0)
  out <- data.frame(
    n = length(w_ok),
    mean = mean(w_ok, na.rm = TRUE),
    sd = stats::sd(w_ok, na.rm = TRUE),
    min = min(w_ok, na.rm = TRUE),
    p01 = stats::quantile(w_ok, 0.01, na.rm = TRUE),
    p05 = stats::quantile(w_ok, 0.05, na.rm = TRUE),
    p95 = stats::quantile(w_ok, 0.95, na.rm = TRUE),
    p99 = stats::quantile(w_ok, 0.99, na.rm = TRUE),
    max = max(w_ok, na.rm = TRUE),
    sum_w = sum(w_ok, na.rm = TRUE),
    ess = ess(w_ok),
    top01_weight_share = weight_concentration(w_ok, top_p = 0.01),
    ps_floor = ps_floor,
    trunc_rate = mean(truncated, na.rm = TRUE),
  )
}

```

```

ps_min = min(ps_ok, na.rm = TRUE),
ps_p01 = stats::quantile(ps_ok, 0.01, na.rm = TRUE),
ps_p05 = stats::quantile(ps_ok, 0.05, na.rm = TRUE),
ps_p95 = stats::quantile(ps_ok, 0.95, na.rm = TRUE),
ps_max = max(ps_ok, na.rm = TRUE),
stringsAsFactors = FALSE
)
out
}

compute_ipow_weights <- function(w, treat, ps_floor_quantile = 0.01,
                                  stabilize = TRUE) {
  ps <- extract_weightit_ps(w)
  if (length(ps) != length(treat)) stop("Propensity length mismatch.")
  treat <- as.integer(treat)
  if (!all(treat %in% c(0L, 1L))) stop("Treatment indicator must be 0/1.")

  ps_obs <- ps[treat == 1L & is.finite(ps)]
  if (!length(ps_obs)) stop("No treated observations with finite propensity.")
  ps_floor <- as.numeric(stats::quantile(ps_obs, probs = ps_floor_quantile, na.rm = TRUE))
  if (!is.finite(ps_floor) || ps_floor <= 0) stop("Invalid propensity floor.")

  w_raw <- rep(NA_real_, length(ps))
  w_raw[treat == 1L] <- 1 / ps[treat == 1L]

  cap <- 1 / ps_floor
  truncated <- treat == 1L & is.finite(ps) & ps < ps_floor
  w_trunc <- w_raw
  w_trunc[truncated] <- cap

  if (stabilize) {
    w_trunc <- w_trunc / mean(w_trunc[treat == 1L], na.rm = TRUE)
  }

  list(
    weights    = w_trunc,

```

```

        ps      = ps,
        ps_floor = ps_floor,
        cap     = cap,
        truncated = truncated
    )
}

assert_finite_weights <- function(w, name = "weights") {
  if (any(!is.finite(w))) {
    stop("Non-finite values detected in ", name, ".")
  }
  invisible(TRUE)
}

runtime_logger <- function(step_name, expr, notes = NA_character_) {
  start_time <- Sys.time()
  result <- eval(expr)
  end_time <- Sys.time()
  sec <- as.numeric(difftime(end_time, start_time, units = "secs"))
  row <- data.frame(
    step_name = step_name,
    seconds = sec,
    start_time = as.character(start_time),
    end_time = as.character(end_time),
    notes = notes,
    run_id = runtime_run_id,
    run_mode = RUN_MODE,
    n_subset = subset_n,
    stringsAsFactors = FALSE
  )
  runtime_log <- dplyr::bind_rows(runtime_log, row)
  result
}

make_context <- function(stage, component,
                        analysis_variant = NA_character_,

```

```

        model_type = NA_character_,
        group = NA_character_,
        outcome = NA_character_,
        imputation = NA_integer_,
        batch = NA_integer_) {

list(
  stage = stage,
  component = component,
  analysis_variant = analysis_variant,
  model_type = model_type,
  group = group,
  outcome = outcome,
  imputation = imputation,
  batch = batch
)
}

capture_warnings <- function(expr, context) {
  warn_rows <- list()
  stopifnot(all(c("stage", "component", "analysis_variant", "model_type",
    "group", "outcome", "imputation", "batch") %in% names(context)))
  ctx <- list(
    stage = as.character(context$stage),
    component = as.character(context$component),
    analysis_variant = as.character(context$analysis_variant),
    model_type = as.character(context$model_type),
    group = as.character(context$group),
    outcome = as.character(context$outcome),
    imputation = as.integer(context$imputation),
    batch = as.integer(context$batch)
  )
  val <- withCallingHandlers(
    expr,
    warning = function(w) {
      warn_rows <- append(warn_rows, list(data.frame(
        time = as.character(Sys.time())),

```

```

stage = ctx$stage,
component = ctx$component,
analysis_variant = ctx$analysis_variant,
model_type = ctx$model_type,
group = ctx$group,
outcome = ctx$outcome,
imputation = ctx$imputation,
batch = ctx$batch,
message = conditionMessage(w),
stringsAsFactors = FALSE
)))
invokeRestart("muffleWarning")
}
)
warnings_df <- if (length(warn_rows)) {
  dplyr::bind_rows(warn_rows)
} else {
  data.frame(
    time = character(), stage = character(), component = character(),
    analysis_variant = character(), model_type = character(),
    group = character(), outcome = character(), imputation = integer(),
    batch = integer(), message = character(), stringsAsFactors = FALSE
  )
}
list(value = val, warnings = warnings_df)
}

append_warnings <- function(wlist) {
  stopifnot(is.data.frame(wlist) || is.list(wlist))
  df <- if (is.data.frame(wlist)) wlist else dplyr::bind_rows(wlist)
  stopifnot(is.data.frame(df))
  stopifnot("message" %in% names(df))
  info_rows <- df[grep("Number of logged events", df$message), , drop = FALSE]
  if (nrow(info_rows)) {
    mi_info_log <- dplyr::bind_rows(mi_info_log, info_rows)
  }
}

```

```

df <- df[!grepl("Number of logged events", df$message), , drop = FALSE]
if (nrow(df) == 0L) return(invisible(FALSE))
mi_warn_log <- dplyr::bind_rows(mi_warn_log, df)
invisible(TRUE)
}

collect_warnings_from_list <- function(xlist) {
  warn_list <- lapply(xlist, function(x) {
    if (is.list(x) && !is.null(x$warnings)) x$warnings else NULL
  })
  warn_list <- warn_list[!vapply(warn_list, is.null, logical(1))]
  append_warnings(warn_list)
  invisible(TRUE)
}

append_outcome_diag <- function(df) {
  stopifnot(is.data.frame(df))
  if (nrow(df) == 0L) return(invisible(FALSE))
  mi_outcome_diag <- dplyr::bind_rows(mi_outcome_diag, df)
  invisible(TRUE)
}

summarize_warnings_log <- function(path = results_path("warnings_log.csv")) {
  warn_df <- read.csv(path, stringsAsFactors = FALSE)
  if (nrow(warn_df) == 0L) return(data.frame())
  warn_df |>
    dplyr::count(stage, component, analysis_variant, model_type, message, sort = TRUE)
}

write_csv_safely <- function(df, path, row_names = FALSE, required_cols = NULL) {
  run_id <- diag_run_id
  run_ts <- diag_run_ts
  stopifnot(!is.null(df))
  df <- as.data.frame(df)
  # Normalize pillar/vctrs numeric classes to base numeric for CSV export
  df <- dplyr::mutate(

```

```

df,
dplyr::across(
  where(~ inherits(.x, "pillar_num")),
  ~ suppressWarnings(as.numeric(.x))
)
)
if (!is.null(required_cols)) {
  missing <- setdiff(required_cols, names(df))
  stopifnot(length(missing) == 0)
}
if (nrow(df) == 0L) {
  if (!("empty" %in% names(df))) df$empty <- logical(0)
}
df$run_id <- rep(run_id, nrow(df))
df$run_ts <- rep(run_ts, nrow(df))
utils::write.csv(df, path, row.names = row_names)
invisible(TRUE)
}

write_diag_lines <- function(lines, path) {
  run_id <- diag_run_id
  run_ts <- diag_run_ts
  header <- paste0("run_id: ", run_id, " run_ts: ", run_ts)
  writeLines(c(header, lines), con = path)
  invisible(TRUE)
}

droplevels_all <- function(df, vars = NULL) {
  if (is.null(vars)) {
    vars <- names(df)[vapply(df, is.factor, logical(1))]
  } else {
    vars <- intersect(vars, names(df))
    vars <- vars[vapply(df[, vars], is.factor, logical(1))]
  }
  for (nm in vars) df[[nm]] <- droplevels(df[[nm]])
  df
}

```

```

}

append_mem_snapshot <- function(stage_id, context_id = NA_character_, when = "pre") {
  g <- gc()
  cn <- colnames(g)
  used_col <- if ("used" %in% cn) "used" else cn[grep("used", cn)][1]
  trig_col <- if ("gc trigger" %in% cn) "gc trigger" else cn[grep("trigger", cn)][1]
  max_col <- if ("max used" %in% cn) "max used" else cn[grep("max", cn)][1]
  n_used <- as.numeric(g["Ncells", used_col])
  v_used <- as.numeric(g["Vcells", used_col])
  v_trig <- as.numeric(g["Vcells", trig_col])
  v_max <- as.numeric(g["Vcells", max_col])
  mem_max <- tryCatch(mem.maxVSize(), error = function(e) NA_real_)
  row <- data.frame(
    run_id = diag_run_id,
    run_ts = diag_run_ts,
    stage_id = stage_id,
    context_id = context_id,
    when = when,
    time = as.character(Sys.time()),
    Ncells_used = n_used,
    Vcells_used = v_used,
    Vcells_gc_trigger = v_trig,
    Vcells_max_used = v_max,
    mem_max_vszie = mem_max,
    stringsAsFactors = FALSE
  )
  memory_snapshots <- dplyr::bind_rows(memory_snapshots, row)
  invisible(TRUE)
}

write_factor_levels_diag <- function(df, vars, context_id, file_prefix = "gbm_preflight_factor_levels") {
  key <- paste0(file_prefix, "::", context_id)
  if (key %in% factor_diag_written) {
    return(invisible(FALSE))
  }
}

```

```

vars <- intersect(vars, names(df))
if (!length(vars)) {
  return(invisible(FALSE))
}
diag <- lapply(vars, function(v) {
  x <- df[[v]]
  if (!is.factor(x)) return(NULL)
  tab <- table(x, useNA = "ifany")
  n_unused <- sum(tab == 0)
  top <- utils::head(sort(tab, decreasing = TRUE), 5)
  data.frame(
    variable = v,
    class = class(x)[1],
    nlevels = nlevels(x),
    n_unused_levels = n_unused,
    top_levels = paste(names(top), as.integer(top), sep = "=", collapse = "; "),
    n_missing = sum(is.na(x)),
    context_id = context_id,
    stringsAsFactors = FALSE
  )
})
diag <- dplyr::bind_rows(diag)
if (nrow(diag) == 0L) return(invisible(FALSE))
out_path <- results_path(paste0(file_prefix, "_", context_id, ".csv"))
write_csv_safely(diag, out_path, row_names = FALSE)
factor_diag_written <- c(factor_diag_written, key)
invisible(TRUE)
}

log_design_dims <- function(df, covars, context_id, sample_n = 5000L) {
  covars <- intersect(covars, names(df))
  if (!length(covars)) return(invisible(FALSE))
  n_full <- nrow(df)
  n_samp <- min(sample_n, n_full)
  set.seed(20251206)
  idx <- sample.int(n_full, n_samp)
}

```

```

df_s <- df[idx, covars, drop = FALSE]
fml <- stats::as.formula(paste("~", paste(covars, collapse = " + ")))
mm <- stats::model.matrix(fml, data = df_s)
n_factor <- sum(vapply(df_s, is.factor, logical(1)))
max_nlevels <- if (n_factor > 0) max(vapply(df_s[vapply(df_s, is.factor, logical(1))], nlevels, integer(1))) else 0L
row <- data.frame(
  run_id = diag_run_id,
  run_ts = diag_run_ts,
  context_id = context_id,
  nrow_full = n_full,
  nrow_sample = n_samp,
  ncol_model_matrix = ncol(mm),
  n_factor_vars = n_factor,
  max_nlevels_factor = max_nlevels,
  stringsAsFactors = FALSE
)
gbm_preflight_design_dims <- dplyr::bind_rows(gbm_preflight_design_dims, row)
invisible(TRUE)
}

gbm_preflight <- function(df, covars, context_id, sample_n = 50000L) {
  df <- droplevels_all(df)
  write_factor_levels_diag(df, covars, context_id, file_prefix = "gbm_preflight_factor_levels")
  covars <- intersect(covars, names(df))
  if (!length(covars)) return(invisible(FALSE))
  n_full <- nrow(df)
  n_samp <- min(sample_n, n_full)
  set.seed(20251206)
  idx <- sample.int(n_full, n_samp)
  df_s <- df[idx, covars, drop = FALSE]
  fml <- stats::as.formula(paste("~", paste(covars, collapse = " + ")))
  mm <- stats::model.matrix(fml, data = df_s)
  n_factor <- sum(vapply(df_s, is.factor, logical(1)))
  max_nlevels <- if (n_factor > 0) {
    max(vapply(df_s[vapply(df_s, is.factor, logical(1))], nlevels, integer(1)))
  } else 0L
}

```

```

est_bytes <- n_full * ncol(mm) * 8
row <- data.frame(
  run_id = diag_run_id,
  run_ts = diag_run_ts,
  context_id = context_id,
  nrow_full = n_full,
  nrow_sample = n_samp,
  ncol_model_matrix = ncol(mm),
  n_factor_vars = n_factor,
  max_nlevels_factor = max_nlevels,
  est_bytes = est_bytes,
  est_gb = est_bytes / 1024^3,
  stringsAsFactors = FALSE
)
gbm_preflight_design_dims <- dplyr::bind_rows(gbm_preflight_design_dims, row)
warn_msgs <- character()
if (is.finite(est_bytes) && est_bytes > GBM_MM_EST_BYTES_WARN) {
  warn_msgs <- c(warn_msgs, paste0("est_dense_mm_gb>", round(GBM_MM_EST_BYTES_WARN / 1024^3, 2)))
}
if (ncol(mm) > MAX_GBM_MM_COLS_WARN) {
  warn_msgs <- c(warn_msgs, paste0("mm_cols_warn>", MAX_GBM_MM_COLS_WARN))
}
if (max_nlevels > MAX_GBM_FACTOR_LEVELS_WARN) {
  warn_msgs <- c(warn_msgs, paste0("factor_levels_warn>", MAX_GBM_FACTOR_LEVELS_WARN))
}
if (length(warn_msgs)) {
  gbm_preflight_warnings <- dplyr::bind_rows(
    gbm_preflight_warnings,
    data.frame(
      run_id = diag_run_id,
      run_ts = diag_run_ts,
      context_id = context_id,
      nrow_full = n_full,
      ncol_model_matrix = ncol(mm),
      max_nlevels_factor = max_nlevels,
      est_gb = est_bytes / 1024^3,

```

```

        warning = paste(warn_msgs, collapse = ";"),
        stringsAsFactors = FALSE
    )
}
if (ncol(mm) > MAX_GBM_MM_COLS_STOP || max_nlevels > MAX_GBM_FACTOR_LEVELS_STOP) {
  stop(
    "GBM preflight stop: context=", context_id,
    "; ncol_model_matrix=", ncol(mm),
    "; max_nlevels_factor=", max_nlevels,
    ". Consider collapsing factor levels or removing high-cardinality predictors."
  )
}
invisible(TRUE)
}

print_head <- function(df, n = 10, title = NULL) {
  if (!is.null(title)) message(title)
  if (is.null(df) || nrow(df) == 0L) {
    message("No rows to display.")
    return(invisible(FALSE))
  }
  print(utils::head(df, n))
  invisible(TRUE)
}

assert_is_df <- function(x, context = "") {
  if (is.null(x)) {
    stop(context, ": object is NULL")
  }
  if (!inherits(x, "data.frame")) {
    stop(context, ": expected data.frame/tibble; got class=",
        paste(class(x), collapse = ", "), " typeof=", typeof(x))
  }
  invisible(TRUE)
}

```

```

assert_has_cols <- function(df, cols, context = "") {
  missing <- setdiff(cols, names(df))
  if (length(missing)) {
    stop(context, ": missing required columns: ", paste(missing, collapse = ", "))
  }
  invisible(TRUE)
}

safe_nrow <- function(df, context = "") {
  assert_is_df(df, context)
  nr <- nrow(df)
  if (!is.numeric(nr) || length(nr) != 1L || is.na(nr)) {
    stop(context, ": nrow(df) returned invalid value: ",
        paste0(capture.output(str(nr)), collapse = " "))
  }
  as.integer(nr)
}

plot_drop_log <- function() {
  plot_drop_log_df
}

log_plot_drop <- function(plot_name, reason, n_dropped,
                           n_before = NA_integer_, n_after = NA_integer_,
                           stage = NA_character_, extra = NA_character_) {
  plot_drop_log_df <- dplyr::bind_rows(
    plot_drop_log(),
    data.frame(plot = plot_name, reason = reason, n_dropped = n_dropped,
               n_before = n_before, n_after = n_after,
               stage = stage, extra = extra,
               stringsAsFactors = FALSE)
  )
  if (identical(PLOT_DROP_POLICY, "stop")) {
    stop("Plot data dropped in ", plot_name, ":", reason)
  } else {

```

```

    warning("Plot data dropped in ", plot_name, ": ", reason, call. = FALSE)
}

}

fit_with_diagnostics <- function(fit_fun, context, prob_eps = PROB_EPS) {
  stopifnot(all(c("stage", "component", "analysis_variant", "model_type",
                 "group", "outcome", "imputation", "batch") %in% names(context)))
  cap <- capture_warnings(
    tryCatch(fit_fun(), error = function(e) e),
    context = context
  )
  append_warnings(cap$warnings)
  fit <- cap$value
  warn_msgs <- if (is.data.frame(cap$warnings)) cap$warnings$message else character()
  warning_n <- if (is.data.frame(cap$warnings)) nrow(cap$warnings) else 0L
  top_warning <- if (warning_n) warn_msgs[1] else NA_character_

  if (inherits(fit, "error")) {
    diag <- data.frame(
      stage = as.character(context$stage),
      component = as.character(context$component),
      analysis_variant = as.character(context$analysis_variant),
      model_type = as.character(context$model_type),
      group = as.character(context$group),
      outcome = as.character(context$outcome),
      imputation = as.integer(context$imputation),
      n_used = NA_integer_, events = NA_integer_,
      converged = NA, iter = NA_integer_,
      sep_flag = NA, nonconv_flag = NA,
      min_phat = NA_real_, max_phat = NA_real_,
      warning_n = warning_n, top_warning = top_warning,
      error_message = conditionMessage(fit),
      stringsAsFactors = FALSE
    )
    return(list(fit = NULL, diag = diag, warnings = cap$warnings))
  }
}

```

```

phat <- tryCatch(fitted(fit), error = function(e) NA_real_)
min_phat <- if (all(is.na(phat))) NA_real_ else min(phat, na.rm = TRUE)
max_phat <- if (all(is.na(phat))) NA_real_ else max(phat, na.rm = TRUE)
sep_flag <- FALSE
if (is.finite(min_phat) && min_phat < prob_eps) sep_flag <- TRUE
if (is.finite(max_phat) && max_phat > 1 - prob_eps) sep_flag <- TRUE
if (any(grepl("fitted probabilities numerically 0 or 1", warn_msgs, fixed = TRUE))) sep_flag <- TRUE

conv_val <- if (!is.null(fit$converged)) isTRUE(fit$converged) else NA
iter_val <- if (!is.null(fit$iter)) fit$iter else NA_integer_
nonconv_flag <- isFALSE(conv_val) || any(grepl("did not converge", warn_msgs, fixed = TRUE))

mf <- tryCatch(model.frame(fit), error = function(e) NULL)
y <- if (!is.null(mf)) tryCatch(model.response(mf), error = function(e) NULL) else NULL
n_used <- if (!is.null(y)) length(y) else NA_integer_
events <- if (!is.null(y) && is.numeric(y)) sum(y == 1, na.rm = TRUE) else NA_integer_

diag <- data.frame(
  stage = as.character(context$stage),
  component = as.character(context$component),
  analysis_variant = as.character(context$analysis_variant),
  model_type = as.character(context$model_type),
  group = as.character(context$group),
  outcome = as.character(context$outcome),
  imputation = as.integer(context$imputation),
  n_used = n_used, events = events,
  converged = conv_val, iter = iter_val,
  sep_flag = sep_flag, nonconv_flag = nonconv_flag,
  min_phat = min_phat, max_phat = max_phat,
  warning_n = warning_n, top_warning = top_warning,
  error_message = NA_character_,
  stringsAsFactors = FALSE
)
list(fit = fit, diag = diag, warnings = cap$warnings)
}

```

```

pooled_mi_vcov_check <- function(pooled) {
  if (is.null(pooled$variance)) stop("MIcombine object missing variance matrix.")
  V <- pooled$variance
  if (any(!is.finite(V))) stop("Non-finite pooled variance detected.")
  within <- attr(pooled, "within")
  between <- attr(pooled, "between")
  if (!is.null(within) && any(!is.finite(within))) stop("Non-finite within variance.")
  if (!is.null(between) && any(!is.finite(between))) stop("Non-finite between variance.")
  invisible(TRUE)
}

save_diag_plot <- function(p, file, width = 8, height = 6, dpi = 200) {
  ggpplot2::ggsave(filename = file, plot = p, width = width, height = height, dpi = dpi)
  invisible(file)
}

plot_registry_path <- results_path("plot_registry.csv")

read_plot_registry <- function() {
  if (file.exists(plot_registry_path)) {
    utils::read.csv(plot_registry_path, stringsAsFactors = FALSE)
  } else {
    data.frame(
      run_id = character(), run_ts = character(),
      plot_name = character(), fig_path = character(), md5 = character(),
      stringsAsFactors = FALSE
    )
  }
}

write_plot_registry <- function(df) {
  write_csv_safely(df, plot_registry_path, row.names = FALSE)
}

register_plot_file <- function(plot_name, file, run_id = diag_run_id, run_ts = diag_run_ts) {

```

```

md5 <- as.character(tools::md5sum(file))
reg <- read_plot_registry()
dup_name <- nrow(reg) > 0 &&
  any(reg$run_id == run_id & reg$plot_name == plot_name, na.rm = TRUE)
if (dup_name) {
  log_plot_drop(
    plot_name,
    "duplicate_figure",
    n_dropped = 1,
    n_before = NA_integer_,
    n_after = NA_integer_,
    stage = "plot_registry",
    extra = file
  )
  return(FALSE)
}
reg <- dplyr::bind_rows(
  reg,
  data.frame(run_id = run_id, run_ts = run_ts,
             plot_name = plot_name, fig_path = file, md5 = md5,
             stringsAsFactors = FALSE)
)
write_plot_registry(reg)
TRUE
}

print_plot_once <- function(p, plot_name, width = 8, height = 6, dpi = 200) {
  file <- results_path("figs", paste0(plot_name, ".png"))
  save_diag_plot(p, file, width = width, height = height, dpi = dpi)
  if (register_plot_file(plot_name, file)) {
    mark_float_emitted()
    knitr:::include_graphics(file)
  } else {
    invisible(NULL)
  }
}

```

```

compute_or_axis_spec <- function(df_list, lo_col = "conf.low", hi_col = "conf.high",
                                  min_pow = -6, max_pow = 6,
                                  default_limits = c(0.25, 16)) {
  if (inherits(df_list, "data.frame")) df_list <- list(df_list)
  if (!is.list(df_list)) df_list <- list(df_list)
  vals <- unlist(lapply(df_list, function(df) {
    assert_is_df(df, context = "compute_or_axis_spec")
    stopifnot(all(c(lo_col, hi_col) %in% names(df)))
    lo <- df[[lo_col]]
    hi <- df[[hi_col]]
    c(lo, hi)
  }), use.names = FALSE)
  vals <- vals[is.finite(vals) & vals > 0]
  if (!length(vals)) {
    lo_pow <- floor(log2(default_limits[1]))
    hi_pow <- ceiling(log2(default_limits[2]))
  } else {
    lo_pow <- floor(log2(min(vals)))
    hi_pow <- ceiling(log2(max(vals)))
  }
  lo_pow <- max(lo_pow, min_pow)
  hi_pow <- min(hi_pow, max_pow)
  if (lo_pow > hi_pow) hi_pow <- lo_pow
  limits <- 2^c(lo_pow, hi_pow)
  breaks <- 2^(lo_pow:hi_pow)
  list(limits = limits, breaks = breaks)
}

or_axis_scale <- function(spec) {
  list(
    ggplot2::scale_y_log10(
      breaks = spec$breaks,
      labels = scales::number_format(accuracy = 0.01)
    ),
    ggplot2::coord_cartesian(ylim = spec$limits)
}

```

```

    )
}

map_or_exposure <- function(df, plot_name) {
  assert_is_df(df, context = paste0("map_or_exposure(", plot_name, ")"))
  stopifnot(nrow(df) > 0L)
  stopifnot("term" %in% names(df))
  df$term <- gsub("^", "", df$term)
  df$exposure <- dplyr::case_when(
    grepl("^pc02_cat_abg", df$term) ~ gsub("^pc02_cat_abg", "", df$term),
    grepl("^pc02_cat_vbg", df$term) ~ gsub("^pc02_cat_vbg", "", df$term),
    grepl("^co2_cat", df$term)      ~ gsub("^co2_cat", "", df$term),
    TRUE                      ~ NA_character_
  )
  bad <- is.na(df$exposure) | !df$exposure %in% CO2_CAT_CONTRAST_LEVELS
  if (any(bad)) {
    out_path <- results_path("or_term_mapping_failures.csv")
    bad_terms <- data.frame(term = df$term[bad], group = df$group[bad],
                             plot_name = plot_name, stringsAsFactors = FALSE)
    write_csv_safely(bad_terms, out_path, row_names = FALSE)
    stop(paste0("Unmapped OR terms in ", plot_name, ". See ", out_path))
  }
  df$exposure <- factor(df$exposure, levels = CO2_CAT_CONTRAST_LEVELS)
  df
}

build_or_plot_df <- function(df, plot_name, expected_exposure_levels) {
  df <- tibble::as_tibble(df)
  req_cols <- c("outcome", "group", "estimate", "conf.low", "conf.high")
  req_cols <- c(req_cols, "exposure")
  assert_has_cols(df, unique(req_cols), context = paste0("build_or_plot_df(", plot_name, ")"))
  df <- dplyr::mutate(
    df,
    estimate = as.numeric(estimate),
    conf.low = as.numeric(conf.low),
    conf.high = as.numeric(conf.high)
}

```

```

)
if (safe_nrow(df, paste0("build_or_plot_df()", plot_name, "")) == 0L) {
  stop("Empty OR plot data in ", plot_name)
}
drop <- !is.finite(df$estimate) | !is.finite(df$conf.low) | !is.finite(df$conf.high)
if (any(drop)) {
  log_plot_drop(plot_name, "non-finite estimate/conf", sum(drop),
                n_before = nrow(df), n_after = nrow(df) - sum(drop),
                stage = "build_or_plot_df")
  df <- df[!drop, , drop = FALSE]
}
drop_pos <- (df$estimate <= 0) | (df$conf.low <= 0) | (df$conf.high <= 0)
if (any(drop_pos, na.rm = TRUE)) {
  log_plot_drop(plot_name, "non-positive estimate/conf", sum(drop_pos, na.rm = TRUE),
                n_before = nrow(df), n_after = nrow(df) - sum(drop_pos, na.rm = TRUE),
                stage = "build_or_plot_df")
  df <- df[!drop_pos, , drop = FALSE]
}
exp_drop <- is.na(df$exposure) | trimws(as.character(df$exposure)) == ""
if (any(exp_drop)) {
  log_plot_drop(plot_name, "missing exposure level", sum(exp_drop),
                n_before = nrow(df), n_after = nrow(df) - sum(exp_drop),
                stage = "build_or_plot_df")
  df <- df[!exp_drop, , drop = FALSE]
}
df$exposure <- factor(df$exposure, levels = expected_exposure_levels)
bad_exp <- is.na(df$exposure)
if (any(bad_exp)) {
  bad_df <- df[bad_exp, , drop = FALSE]
  bad_path <- results_path(paste0("or_unmapped_terms_", plot_name, ".csv"))
  write_csv_safely(bad_df, bad_path, row_names = FALSE)
  stop(paste0("Unmapped exposure terms in ", plot_name, ". See ", bad_path))
}
missing_levels <- setdiff(expected_exposure_levels, unique(as.character(df$exposure)))
if (length(missing_levels)) {
  stop(paste0("Missing exposure levels in ", plot_name, ":", paste(missing_levels, collapse = ", ")))
}

```

```

}

if (nrow(df) == 0L) {
  msg <- paste0("OR plot data empty after filtering in ", plot_name)
  stop(msg)
}
df
}

plot_or_safe <- function(df, plot_name, axis_spec,
                         color_var = "group", shape_var = "exposure",
                         facet_var = NULL, title = NULL, caption = NULL) {
  df <- tibble::as_tibble(df)
  assert_is_df(df, context = paste0("plot_or_safe(", plot_name, ")"))
  nr <- safe_nrow(df, paste0("plot_or_safe(", plot_name, ")"))
  if (nr == 0L) {
    stop("plot_or_safe(", plot_name, "): no rows to plot.")
  }
  assert_has_cols(df, c("outcome", "group", "exposure", "estimate", "conf.low", "conf.high"),
                  context = paste0("plot_or_safe(", plot_name, ")"))
  if (isTRUE(getOption("ABG_VBG_DEBUG", FALSE))) {
    message("plot_or_safe(", plot_name, "): class=", paste(class(df), collapse = ", "),
            " nrow=", nr, " ncol=", ncol(df))
  }
  stopifnot(color_var %in% names(df))
  stopifnot(shape_var %in% names(df))
  stopifnot(!is.null(axis_spec))
  df[[shape_var]] <- as.factor(df[[shape_var]])
  n_shape <- dplyr::n_distinct(df[[shape_var]])
  if (n_shape > MAX_SHAPE_LEVELS) {
    message("OR plot: too many shape levels (", n_shape, ") in ", plot_name,
           ". Dropping shape and faceting by ", shape_var, ".")
    facet_var <- shape_var
    shape_var <- NULL
  }
  df$.grp <- 1L
}

```

```

if (!is.null(color_var) && !is.null(shape_var)) {
  df$.grp <- interaction(df[[color_var]], df[[shape_var]], drop = TRUE)
} else if (!is.null(color_var)) {
  df$.grp <- df[[color_var]]
} else if (!is.null(shape_var)) {
  df$.grp <- df[[shape_var]]
}

p <- ggplot2::ggplot(df, ggplot2::aes(x = outcome, y = estimate, ymin = conf.low, ymax = conf.high, group = .grp))
if (!is.null(color_var)) {
  p <- p + ggplot2::aes(color = .data[[color_var]])
}
if (!is.null(shape_var)) {
  p <- p + ggplot2::aes(shape = .data[[shape_var]])
}

p <- p +
  ggplot2::geom_pointrange(position = ggplot2::position_dodge(width = 0.7), size = 0.6) +
  ggplot2::geom_hline(yintercept = 1, linetype = "dashed", colour = "grey40") +
  or_axis_scale(axis_spec) +
  ggplot2::labs(
    title = title,
    x = "Outcome",
    y = "Odds Ratio (log scale, 95% CI)",
    color = if (!is.null(color_var)) "Blood-gas type" else NULL,
    shape = if (!is.null(shape_var)) "PC02 category" else NULL,
    caption = caption
  ) +
  ggplot2::theme_minimal(base_size = 9) +
  ggplot2::theme(
    plot.caption = ggplot2::element_text(hjust = 0),
    axis.text.x = ggplot2::element_text(angle = 15, hjust = 1),
    legend.position = "bottom",
    plot.margin = ggplot2::margin(6, 6, 6, 6)
  )
if (!is.null(color_var) || !is.null(shape_var)) {

```

```

    p <- p + ggplot2::guides(
      color = ggplot2::guide_legend(nrow = 2, byrow = TRUE),
      shape = ggplot2::guide_legend(nrow = 1, byrow = TRUE)
    )
  }

  if (!is.null(facet_var)) {
    p <- p + ggplot2::facet_wrap(stats::as.formula(paste("~", facet_var)))
  }
  p
}

```

```

library(dagitty)
library(ggdag)

# Toggle to show diagrams inline in the PDF
show_model_diagrams <- FALSE

model_diagram_dir <- fs::path(results_dir, "figs", "model-diagrams")
fs::dir_create(model_diagram_dir)

.make_safe_name <- function(x) {
  x <- gsub("[^A-Za-z0-9]+", "-", x)
  x <- gsub("(^-|-$)", "", x)
  tolower(x)
}

.extract_model_vars <- function(fml) {
  tt <- stats::terms(fml)
  response <- all.vars(stats::update(fml, . ~ 1))
  response <- if (length(response)) response[1] else NA_character_
  term_labels <- attr(tt, "term.labels")
  preds <- unique(unlist(lapply(term_labels, function(t) {
    all.vars(stats::as.formula(paste("~", t)))
  })))
  preds <- setdiff(preds, response)
}

```

```

    list(response = response, preds = preds)
}

.build_model_dag <- function(fml) {
  vars <- .extract_model_vars(fml)
  if (is.na(vars$response) || length(vars$preds) == 0L) {
    stop("Model diagram: formula has no response or predictors: ", deparse(fml))
  }
  edges <- paste(sprintf("%s -> %s", vars$preds, vars$response), collapse = "\n  ")
  dagitty::dagitty(sprintf("dag { %s }", edges))
}

save_model_diagram <- function(name, fml, width = NULL, height = NULL) {
  dag <- .build_model_dag(fml)

  vars <- .extract_model_vars(fml)
  n_pred <- length(vars$preds)
  n_nodes <- n_pred + 1L

  label_size <- if (n_pred >= 35) 1.4 else if (n_pred >= 25) 1.8 else if (n_pred >= 15) 2.2 else 2.8
  point_size <- if (n_pred >= 25) 2.0 else if (n_pred >= 15) 2.5 else 3.0

  base_width <- if (is.null(width)) 8 else width
  base_height <- if (is.null(height)) 6 else height
  width <- max(base_width, min(24, 0.4 * n_nodes + 4))
  height <- max(base_height, min(16, 0.25 * n_nodes + 4))

  layout <- if (n_pred >= 8) "sugiyama" else "nicely"
  dag_data <- ggdag::tidy_dagitty(dag, layout = layout)$data

  p <- ggplot2::ggplot(
    dag_data,
    ggplot2::aes(x = x, y = y, xend = xend, yend = yend)
  ) +
    ggdag::geom_dag_edges() +
    ggdag::geom_dag_point(size = point_size) +

```

```

ggdag::geom_dag_text_repel(
  ggplot2::aes(label = name),
  size = label_size,
  max.overlaps = Inf
) +
  ggplot2::scale_x_continuous(expand = ggplot2::expansion(mult = 0.15)) +
  ggplot2::scale_y_continuous(expand = ggplot2::expansion(mult = 0.15)) +
  ggplot2::theme_void() +
  ggplot2::labs(title = name) +
  ggplot2::theme(
    plot.title = ggplot2::element_text(size = 10, hjust = 0.5),
    plot.margin = ggplot2::margin(10, 10, 10, 10)
  )

file <- fs::path(model_diagram_dir, paste0(.make_safe_name(name), ".png"))
ggplot2::ggsave(file, p, width = width, height = height, dpi = 200)
if (isTRUE(show_model_diagrams)) print(p)
file
}

model_diagrams <- list()
register_model_diagram <- function(name, fml, width = 8, height = 6) {
  file <- save_model_diagram(name, fml, width = width, height = height)
  model_diagrams[[name]] <- file
  invisible(file)
}

register_model_diagrams <- function(forms, width = 8, height = 6) {
  purrr::iwalk(forms, function(fml, nm) {
    register_model_diagram(nm, fml, width = width, height = height)
  })
}

RUN_SHAP <- FALSE
if (RUN_SHAP) {
  if (!requireNamespace("shapviz", quietly = TRUE) ||

```

```

  packageVersion("shapviz") < "0.2.0" ) {
  stop("Package 'shapviz' (>= 0.2.0) is required. Install with renv::install(\"shapviz\")")
}
if (!requireNamespace("fastshap", quietly = TRUE)) {
  stop("Package 'fastshap' is required. Install with renv::install(\"fastshap\")")
}
}

```

```

# Chunk runtime annotation (printed into PDF) - disabled by default
if (isTRUE(SHOW_CHUNK_RUNTIME_TEXT)) {
  knitr::knit_hooks$set(runtimelog = local({
    starts <- list()
    escape_latex <- function(x) {
      gsub("(\\\\\\\\\\$&{}_\\^~)", "\\\\\\1", x, perl = TRUE)
    }
    function(before, options) {
      if (before) {
        starts[[options$label]] <- proc.time()
      } else {
        st <- starts[[options$label]]
        if (is.null(st)) return(NULL)
        elapsed <- (proc.time() - st)[["elapsed"]]
        lbl <- escape_latex(options$label)
        paste0(
          "\n\n",
          "\\textit{Chunk ", lbl, " runtime: ", sprintf("%.2f", elapsed), " s}",
          "\n\n"
        )
      }
    }
  }))
  knitr::opts_chunk$set(runtimelog = TRUE)
} else {
  knitr::opts_chunk$set(runtimelog = FALSE)
}

```

```

seed_escrow <- data.frame(
  component = c(
    "Multiple imputation (mice)",
    "ABG propensity GBM (non-MI)",
    "VBG propensity GBM (non-MI)",
    "MI PS (glm RCS) seeds (ABG per imputation)",
    "MI PS (glm RCS) seeds (VBG per imputation)"
  ),
  seed = c(
    "20251206",
    "42",
    "42",
    "20251206 + imputation index",
    "30251206 + imputation index"
  ),
  stringsAsFactors = FALSE
)
render_table_pdf(
  seed_escrow,
  caption = "Seed escrow for MI and GBM runs",
  file_stub = "seed_escrow",
  digits = 0
)

```

Table 1: Seed escrow for MI and GBM runs

component	seed
Multiple imputation (mice)	20251206
ABG propensity GBM (non-MI)	42
VBG propensity GBM (non-MI)	42
MI PS (glm RCS) seeds (ABG per imputation)	20251206 + imputation index
MI PS (glm RCS) seeds (VBG per imputation)	30251206 + imputation index

```
DEBUG_SPLINE <- FALSE
```

```

# Make gt tables robust in PDF: full width, caption, small font
gt_pdf <- function(x, title = NULL, subtitle = NULL) {
  out <- x |>
    gt::tab_options(
      table.width          = gt::pct(100),
      table.align           = "left",
      table.font.size       = gt::px(9),
      data_row.padding      = gt::px(1),
      column_labels.font.size = gt::px(9),
      heading.title.font.size = gt::px(10),
      heading.subtitle.font.size = gt::px(9)
    ) |>
    gt::opt_align_table_header(align = "left")
  if (!is.null(title))   out <- out |> gt::tab_caption(title)
  if (!is.null(subtitle)) out <- out |> gt::tab_source_note(subtitle)
  out
}

```

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.

```

append_mem_snapshot("stage1", "start", "pre")

# data_dir_name resolved in setup-packages from params/env
stata_file <- file.path(data_dir_name, "full_db.dta")

stata_data <- read_dta(stata_file)

# Sanitize variable labels for PDF/TOC safety (avoid Unicode subscripts)
sanitize_label_text <- function(x) {
  if (is.null(x)) return(x)
  x <- gsub("\u2080", "0", x, fixed = TRUE)
  x <- gsub("\u2081", "1", x, fixed = TRUE)
  x <- gsub("\u2082", "2", x, fixed = TRUE)
  x <- gsub("\u2083", "3", x, fixed = TRUE)
  x <- gsub("\u2084", "4", x, fixed = TRUE)

```

```

x <- gsub("\u2085", "5", x, fixed = TRUE)
x <- gsub("\u2086", "6", x, fixed = TRUE)
x <- gsub("\u2087", "7", x, fixed = TRUE)
x <- gsub("\u2088", "8", x, fixed = TRUE)
x <- gsub("\u2089", "9", x, fixed = TRUE)
x
}
sanitize_var_labels <- function(df) {
  labs <- labelled::var_label(df)
  labs <- lapply(labs, sanitize_label_text)
  labelled::var_label(df) <- labs
  df
}
stata_data <- sanitize_var_labels(stata_data)

var_labels <- labelled::var_label(stata_data)
value_labels <- lapply(stata_data, function(x) if (is.labelled(x)) val_labels(x))
saveRDS(
  list(var_labels = var_labels, value_labels = value_labels),
  results_path("stata_labels.rds")
)

```

1.1.1 Configuration for the IPW models

```

drop_vars_ultra_missing <- c("bpn", "spo2")
cat_vars <- c("sex", "race_ethnicity", "location", "encounter_type")
numeric_vars <- c(
  "age_at_encounter", "curr_bmi", "temp_new", "sbp", "dbp", "hr",
  "sodium", "serum_cr", "serum_hco3", "serum_cl", "serum_lac", "serum_k",
  "wbc", "plt", "serum_phos", "serum_ca"
)
co2_vars <- c("paco2", "vbg_co2", "vbg_o2sat")

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",
"sodium", "serum_cr", "serum_hco3", "serum_cl", "serum_lac", "serum_k",
"wbc", "plt", "serum_phos", "serum_ca"
)
covars_gbm <- setdiff(covars_gbm, drop_vars_ultra_missing)
covars_ps <- covars_gbm

# Core adjustment set for conditional prognostic models
adj_core <- c("age_at_encounter", "sex", "race_ethnicity", "location", "encounter_type")

gbm_params <- list(
  n.trees          = 800,
  interaction.depth = 3,
  shrinkage        = 0.01,
  bag.fraction     = 0.8,
  n.minobsinnode  = 10,
  cv.folds         = 0,
  stop.method      = "smd.max",
  n.cores          = 1L
)
stopifnot(gbm_params$stop.method == "smd.max")
SPLINE_BASIS <- "ns"
SPLINE_DF <- 4L
stopifnot(SPLINE_BASIS %in% c("ns", "rcs"))
get_gbm_cores <- function() {
  n_rows <- nrow(subset_data)
  if (is.finite(n_rows) && n_rows > 200000L) return(1L)
  gbm_params$n.cores
}
ps_trunc_quantile <- 0.01
stopifnot(ps_trunc_quantile > 0, ps_trunc_quantile < 0.5)

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

```

```

# Model diagrams: propensity models (GBM PS)
register_model_diagram("PS model: ABG test (GBM)", formula_abg, width = 10, height = 7)
register_model_diagram("PS model: VBG test (GBM)", formula_vbg, width = 10, height = 7)

# TODO: consider stop.method = "es.mean" (ATS version) if smd.max remains unstable on full N.

```

```

subset_data <- stata_data
if (PILOT_FRAC < 1) {
  set.seed(SAMPLE_SEED)
  subset_data <- dplyr::sample_frac(stata_data, size = PILOT_FRAC)
}
message("DATA: full_n=", nrow(stata_data), " | subset_n=", nrow(subset_data))
if (RUN_MODE == "full" && PILOT_FRAC < 1) {
  stop("RUN_MODE='full' but PILOT_FRAC < 1. Set pilot_frac=1 or run_mode='pilot'.")
}
run_rowcounts <- data.frame(
  run_id = diag_run_id,
  run_ts = diag_run_ts,
  run_mode = RUN_MODE,
  pilot_frac = PILOT_FRAC,
  full_n = nrow(stata_data),
  subset_n = nrow(subset_data),
  stringsAsFactors = FALSE
)
write_csv_safely(run_rowcounts, results_path("run_rowcounts.csv"), row_names = FALSE)

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

```

```

# Normalize once early and reuse everywhere

# Keep raw copy for missingness reporting
subset_data_raw <- subset_data
encounter_type_raw <- subset_data_raw$encounter_type

```

```

to01 <- function(x) {
  if (inherits(x, "haven_labelled")) x <- unclass(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)
  out[is_num & xs %in% c(0, 1)] <- as.integer(xs[is_num & xs %in% c(0, 1)])
  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
}

normalize_encounter_type <- function(x) {
  s_chr <- trimws(tolower(as.character(x)))
  num_from_text <- suppressWarnings(as.numeric(gsub("[^0-9]+", "", s_chr)))
  lab <- rep(NA_character_, length(s_chr))
  lab[!is.na(num_from_text) & num_from_text == 2] <- "Emergency"
  lab[!is.na(num_from_text) & num_from_text == 3] <- "Inpatient"
  is_na <- is.na(lab)
  is_em <- grepl("\\bemerg(?:ency)?\\b", s_chr) |
    grepl("(^|[^a-z])ed([a-z]|$)", s_chr) |
    grepl("\\ba&e\\b", s_chr) |
    grepl("\\bemergency\\s+dept\\b", s_chr)
  is_ip <- grepl("\\binpatient\\b", s_chr) |
    grepl("\\binpt\\b", s_chr) |
    grepl("\\binpat\\b", s_chr) |
    grepl("(^|[^a-z])ip([a-z]|$)", s_chr)
  lab[is_na & is_em] <- "Emergency"
  lab[is_na & is_ip] <- "Inpatient"
  factor(lab, levels = c("Emergency", "Inpatient"))
}

```

```

coerce_num <- function(x) {
  if (inherits(x, "haven_labelled")) x <- unclass(x)
  if (is.factor(x)) x <- as.character(x)
  if (is.character(x)) x <- gsub("[^0-9.+-]", "", x)
  suppressWarnings(as.numeric(x))
}

levels_ref <- list(
  sex = c("Female", "Male"),
  race_ethnicity = levels(factor(stata_data$race_ethnicity)),
  location = levels(factor(stata_data$location)),
  encounter_type = levels(normalize_encounter_type(stata_data$encounter_type))
)

normalize_types <- function(df, levels_ref = NULL) {
  df <- df[, setdiff(names(df), drop_vars_ultra_missing), drop = FALSE]

  num_vars <- intersect(c(numeric_vars, co2_vars), names(df))
  for (nm in num_vars) df[[nm]] <- coerce_num(df[[nm]])

  stopifnot("sex" %in% names(df))
  df$sex <- factor(to01(df$sex), levels = c(0L, 1L), labels = c("Female", "Male"))

  stopifnot("encounter_type" %in% names(df))
  df$encounter_type <- normalize_encounter_type(df$encounter_type)

  for (nm in setdiff(cat_vars, c("sex", "encounter_type"))) {
    stopifnot(nm %in% names(df))
    if (!is.null(levels_ref) && !is.null(levels_ref[[nm]])) {
      df[[nm]] <- factor(df[[nm]], levels = levels_ref[[nm]])
    } else {
      df[[nm]] <- factor(df[[nm]])
    }
  }

  stopifnot(all(c("has_abg", "has_vbg") %in% names(df)))
}

```

```

df$has_abg <- to01(df$has_abg)
df$has_vbg <- to01(df$has_vbg)

df
}

subset_data <- normalize_types(subset_data_raw, levels_ref)
subset_data <- droplevels_all(subset_data)
subset_data$encounter_type <- droplevels(subset_data$encounter_type)
stopifnot(nlevels(subset_data$encounter_type) == 2L)
subset_n <- nrow(subset_data)

# Factor-level diagnostic (CSV + short summary)
factor_diag <- lapply(names(subset_data), function(v) {
  x <- subset_data[[v]]
  data.frame(
    variable = v,
    class = class(x)[1],
    nlevels = if (is.factor(x)) nlevels(x) else NA_integer_,
    n_missing = sum(is.na(x)),
    stringsAsFactors = FALSE
  )
})
factor_diag <- dplyr::bind_rows(factor_diag)
write_csv_safely(factor_diag, results_path("factor_levels_diagnostic.csv"), row_names = FALSE)
render_table_pdf(
  factor_diag,
  caption = "Factor level diagnostics (all variables)",
  file_stub = "factor_levels_diagnostic",
  digits = 0
)

```

Table 2: Factor level diagnostics (all variables)

variable	class	nlevels	n_missing
encounter_id	character	NA	0

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
rfs	character	NA	0
sex	factor	2	0
race	haven_labelled	NA	0
ethnicity	haven_labelled	NA	0
location	factor	4	0
age_at_encounter	numeric	NA	0
los	numeric	NA	0
curr_bmi	numeric	NA	2934
hr	numeric	NA	1890
curr_height	numeric	NA	1462
vbg_temp	numeric	NA	5175
abg_temp	numeric	NA	5175
vbg_o2sat	numeric	NA	4474
abg_o2sat	numeric	NA	4097
sao2_blood	numeric	NA	4932
value_prev_weight	numeric	NA	4720
value_prev_height	numeric	NA	4488
value_prev_bmi	numeric	NA	4859
value_highest_20198	numeric	NA	3929
value_highest_115576	numeric	NA	4652
value_highest_327718	numeric	NA	4939
vbg_co2	numeric	NA	3730
highest_vbg_co2	numeric	NA	3726
pco2_nos	numeric	NA	4568
highest_pco2_nos	numeric	NA	4568
abg_ph	numeric	NA	3240
vbg_ph	numeric	NA	3638
abg_hco3	numeric	NA	4021
vbg_hco3	numeric	NA	3859
sodium	numeric	NA	261
serum_cr	numeric	NA	481
hgb	numeric	NA	566
serum_hco3	numeric	NA	282
serum_cl	numeric	NA	298
serum_lac	numeric	NA	3125
serum_k	numeric	NA	402
temp_cor_oxygen	numeric	NA	5090
vbg_ph_temp_cor	numeric	NA	5091
vbg_po2	numeric	NA	3878
vbg_lactate	numeric	NA	4993
vbg_hco3_calc	numeric	NA	5050
abg_po2	numeric	NA	3983
abg_po2_temp_cor	numeric	NA	4925
abg_ph_temp_cor	numeric	NA	4933
abg_lactate	numeric	NA	4975

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
ph_blood	numeric	NA	4621
po2_blood	numeric	NA	4670
wbc	numeric	NA	894
plt	numeric	NA	401
bnp_date	character	NA	0
serum_phos_date	character	NA	0
serum_phos	numeric	NA	2732
serum_ca_date	character	NA	0
serum_ca	numeric	NA	515
serum_albumin_date	character	NA	0
serum_albumin	numeric	NA	1859
serum_tprot_date	character	NA	0
serum_tprot	numeric	NA	1961
has_j9612	numeric	NA	0
has_j9622	numeric	NA	0
has_j9602	numeric	NA	0
has_j9692	numeric	NA	0
ohs_code	numeric	NA	0
has_j9600	numeric	NA	0
principal_diagnosis_indicator	character	NA	0
admitting_diagnosis	character	NA	0
reason_for_visit	character	NA	0
has_j9601	numeric	NA	0
has_j961	numeric	NA	0
has_j9610	numeric	NA	0
has_j9611	numeric	NA	0
has_j962	numeric	NA	0
has_j9620	numeric	NA	0
has_j9621	numeric	NA	0
has_j9690	numeric	NA	0
has_j9691	numeric	NA	0
other_abn_of_br	haven_labelled	NA	0
cfdo	haven_labelled	NA	0
has_i50_acute	numeric	NA	0
acute_nmd	haven_labelled	NA	0
sepsis_dx	haven_labelled	NA	0
stupor_dx	haven_labelled	NA	0
cog_signs_dx	haven_labelled	NA	0
mal_fat_dx	haven_labelled	NA	0
resp_acid_dx	haven_labelled	NA	0
sleep_hypovent_dx	haven_labelled	NA	0
cchs_dx	haven_labelled	NA	0
other_sleep_hypovent_dx	haven_labelled	NA	0
acidosis_unspec	haven_labelled	NA	0
headache_dx	haven_labelled	NA	0

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
cpap	haven_labelled	NA	0
tte_proc	haven_labelled	NA	0
aero	haven_labelled	NA	0
inh_teaching	haven_labelled	NA	0
cxr1v	haven_labelled	NA	0
cxr2v	haven_labelled	NA	0
ctcnoncon	haven_labelled	NA	0
ctccon	haven_labelled	NA	0
cc_time	haven_labelled	NA	0
meas_venous_o2_proc	haven_labelled	NA	0
meas_arterial_gas_proc	haven_labelled	NA	0
blood_cx_proc	haven_labelled	NA	0
art_punct_proc	haven_labelled	NA	0
ctabdpelv	haven_labelled	NA	0
osa	haven_labelled	NA	0
asthma	haven_labelled	NA	0
copd	haven_labelled	NA	0
chf	haven_labelled	NA	0
stroke	haven_labelled	NA	0
ckd	haven_labelled	NA	0
pvd	haven_labelled	NA	0
oud	haven_labelled	NA	0
sedatives	haven_labelled	NA	0
phtn	haven_labelled	NA	0
polycy	haven_labelled	NA	0
po_steroid	haven_labelled	NA	0
narcan	haven_labelled	NA	0
inpt_inh	haven_labelled	NA	0
vasodilators	haven_labelled	NA	0
ip_diuretics	haven_labelled	NA	0
ip_abx	haven_labelled	NA	0
paralytic	haven_labelled	NA	0
op_diuretics	haven_labelled	NA	0
op_opiate	haven_labelled	NA	0
op_mat	haven_labelled	NA	0
op_nrt	haven_labelled	NA	0
copd_med	haven_labelled	NA	0
muscle_relax	haven_labelled	NA	0
pat_enc_hash	character	NA	0
ABG_rfs	numeric	NA	0
is_amb	numeric	NA	0
encounter_date	Date	NA	0
age_by_ten	numeric	NA	0
age_decade	haven_labelled	NA	0
death_date	numeric	NA	4467

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
died	numeric	NA	0
months_death_or_cens	numeric	NA	0
curr_weight	numeric	NA	1624
curr_weight_date	numeric	NA	1624
prev_weight_date	numeric	NA	4720
curr_height_date	numeric	NA	1462
prev_height_date	numeric	NA	4488
curr_bmi_date	numeric	NA	2934
prev_bmi_date	numeric	NA	4858
height	numeric	NA	1459
height_date	numeric	NA	1459
weight	numeric	NA	1620
weight_date	numeric	NA	1620
calc_bmi	numeric	NA	2191
calc_bmi_date	numeric	NA	2191
working_bmi	numeric	NA	2932
working_bmi_date	numeric	NA	2932
bmi	numeric	NA	1777
bmi_date	numeric	NA	1777
bmi_int	numeric	NA	1777
bmi_by_five	numeric	NA	1777
rr	numeric	NA	2845
rr_date	numeric	NA	2838
temp_new	numeric	NA	2501
new_temp_date	numeric	NA	2501
sbp	numeric	NA	1544
sbp_date	numeric	NA	1544
dbp	numeric	NA	1556
dbp_date	numeric	NA	1550
spo2_date	numeric	NA	3665
hr_date	numeric	NA	1889
abg_ph_date	numeric	NA	4054
vbg_ph_date	numeric	NA	3754
abg_hco3_date	numeric	NA	4004
abg_hco3_int	numeric	NA	4021
vbg_hco3_date	numeric	NA	3841
sodium_date	numeric	NA	260
serum_k_date	numeric	NA	402
hgb_date	numeric	NA	426
wbc_date	numeric	NA	759
plt_date	numeric	NA	344
serum_hco3_date	numeric	NA	276
any_bicarb	numeric	NA	230
int_bicarb	numeric	NA	230
hco3_cat	haven_labelled	NA	282

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
serum_cl_date	numeric	NA	292
serum_cr_date	numeric	NA	444
serum_lac_date	numeric	NA	3085
vbg_co2_date	numeric	NA	3723
pco2_nos_date	numeric	NA	4568
highest_vbg_co2_date	numeric	NA	3723
highest_pco2_nos_date	numeric	NA	4568
paco2	numeric	NA	3264
paco2_date_1	numeric	NA	3928
paco2_date_2	numeric	NA	4652
paco2_date_3	numeric	NA	4939
paco2_date	numeric	NA	3259
paco2_int	numeric	NA	3264
highest_paco2	numeric	NA	3260
paco2_date_highest_1	numeric	NA	3928
paco2_date_highest_2	numeric	NA	4652
paco2_date_highest_3	numeric	NA	4939
paco2_date_highest	numeric	NA	3259
temp_cor_oxygen_date	numeric	NA	5060
temp_cor_vbg_ph_date	numeric	NA	5091
vbg_po2_date	numeric	NA	3847
vbg_lactate_date	numeric	NA	4992
vbg_hco3_calc_date	numeric	NA	5049
abg_po2_date	numeric	NA	3982
abg_po2_temp_cor_date	numeric	NA	4925
abg_ph_temp_cor_date	numeric	NA	4933
abg_lactate_date	numeric	NA	4974
ph_blood_date	numeric	NA	4621
po2_blood_date	numeric	NA	4662
vbg_temp_date	numeric	NA	5175
abg_temp_date	numeric	NA	5166
vbg_o2sat_date	numeric	NA	4468
abg_o2sat_date	numeric	NA	3959
sao2_blood_date	numeric	NA	4890
paco2_flag	haven_labelled	NA	3264
highest_paco2_flag	haven_labelled	NA	3260
paco2_52_flag	haven_labelled	NA	3264
vbg_co2_flag	haven_labelled	NA	3730
highest_vbg_co2_flag	haven_labelled	NA	3726
miss_paco2_flag	numeric	NA	0
miss_vbg_co2_flag	numeric	NA	0
miss_vbg_or_abg_co2_flag	numeric	NA	0
hco3_flag	haven_labelled	NA	282
not_paco2_flag	numeric	NA	3264
not_hco3_flag	numeric	NA	282

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
k_cat	haven_labelled	NA	402
acidemia	haven_labelled	NA	2284
abg_sbe	numeric	NA	4062
vbg_sbe	numeric	NA	3867
cw_simple_acute_resp_acid	haven_labelled	NA	4331
paco2_52_comp_flag	haven_labelled	NA	3266
po_steroid_date	numeric	NA	2857
narcan_date	numeric	NA	4148
inpt_inh_date	numeric	NA	2994
vasodilators_date	numeric	NA	5152
ip_diuretics_date	numeric	NA	5112
ip_abx_date	numeric	NA	5065
paralytic_date	numeric	NA	5134
inpt_inh_0	numeric	NA	0
ip_abx_0	numeric	NA	0
ip_diuretics_0	numeric	NA	0
narcan_0	numeric	NA	0
paralytic_0	numeric	NA	0
po_steroid_0	numeric	NA	0
vasodilators_0	numeric	NA	0
op_diuretics_first_date	numeric	NA	3245
op_diuretics_last_date	numeric	NA	3256
op_diuretics_365d	haven_labelled	NA	0
op_opiate_first_date	numeric	NA	1907
op_opiate_last_date	numeric	NA	1917
op_opiate_365d	haven_labelled	NA	0
op_mat_first_date	numeric	NA	4967
op_mat_last_date	numeric	NA	4970
op_mat_365d	haven_labelled	NA	0
op_nrt_first_date	numeric	NA	4588
op_nrt_last_date	numeric	NA	4590
op_nrt_365d	haven_labelled	NA	0
copd_med_first_date	numeric	NA	2608
copd_med_last_date	numeric	NA	2615
copd_med_365d	haven_labelled	NA	0
muscle_relax_first_date	numeric	NA	3983
muscle_relax_last_date	numeric	NA	3989
muscle_relax_365d	haven_labelled	NA	0
tte_proc_first_date	numeric	NA	4527
tte_proc_last_date	numeric	NA	4527
vent_proc	haven_labelled	NA	0
niv_proc	haven_labelled	NA	0
imv_proc	haven_labelled	NA	0
cpap_first_date	numeric	NA	4868
cpap_last_date	numeric	NA	4868

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
niv_proc_first_date	numeric	NA	4841
niv_proc_last_date	numeric	NA	4841
imv_proc_first_date	numeric	NA	4621
imv_proc_last_date	numeric	NA	4621
vent_proc_first_date	numeric	NA	4344
vent_proc_last_date	numeric	NA	4344
aero_first_date	numeric	NA	4506
aero_last_date	numeric	NA	4506
inh_teaching_first_date	numeric	NA	5020
inh_teaching_last_date	numeric	NA	5020
cxr1v_first_date	numeric	NA	3799
cxr1v_last_date	numeric	NA	3799
cxr2v_first_date	numeric	NA	5025
cxr2v_last_date	numeric	NA	5025
ctcnoncon_first_date	numeric	NA	5025
ctcnoncon_last_date	numeric	NA	5025
ctccon_first_date	numeric	NA	4944
ctccon_last_date	numeric	NA	4944
ctabdpelv_first_date	numeric	NA	4870
ctabdpelv_last_date	numeric	NA	4870
meas_venous_o2_proc_first_date	numeric	NA	5109
meas_venous_o2_proc_last_date	numeric	NA	5109
meas_art_gas_proc_first_date	numeric	NA	5130
meas_art_gas_proc_last_date	numeric	NA	5130
blood_cx_proc_first_date	numeric	NA	4493
blood_cx_proc_last_date	numeric	NA	4493
art_punct_proc_first_date	numeric	NA	4892
art_punct_proc_last_date	numeric	NA	4892
cc_time_first_date	numeric	NA	4002
cc_time_last_date	numeric	NA	4002
aero_0	numeric	NA	0
blood_cx_proc_0	numeric	NA	0
cc_time_0	numeric	NA	0
cpap_0	numeric	NA	0
ctabdpelv_0	numeric	NA	0
ctccon_0	numeric	NA	0
ctcnoncon_0	numeric	NA	0
cxr1v_0	numeric	NA	0
cxr2v_0	numeric	NA	0
imv_proc_0	numeric	NA	0
inh_teaching_0	numeric	NA	0
niv_proc_0	numeric	NA	0
tte_proc_0	numeric	NA	0
vent_proc_0	numeric	NA	0
aero_dur	numeric	NA	4506

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
blood_cx_proc_dur	numeric	NA	4493
cpap_dur	numeric	NA	4868
ctabdpelv_dur	numeric	NA	4870
ctccon_dur	numeric	NA	4944
ctcnoncon_dur	numeric	NA	5025
cxr1v_dur	numeric	NA	3799
cxr2v_dur	numeric	NA	5025
inv_proc_dur	numeric	NA	4621
inh_teaching_dur	numeric	NA	5020
niv_proc_dur	numeric	NA	4841
tte_proc_dur	numeric	NA	4527
hypercap_resp_failure	haven_labelled	NA	0
j9612_date	numeric	NA	5139
j9612_pcpl	haven_labelled	NA	5139
j9612_adm	haven_labelled	NA	5139
j9612_vr	haven_labelled	NA	5139
j9622_date	numeric	NA	5064
j9622_pcpl	haven_labelled	NA	5067
j9622_adm	haven_labelled	NA	5064
j9622_vr	haven_labelled	NA	5064
j9602_date	numeric	NA	5007
j9602_pcpl	haven_labelled	NA	5010
j9602_adm	haven_labelled	NA	5007
j9602_vr	haven_labelled	NA	5007
j9692_date	numeric	NA	5153
j9692_pcpl	haven_labelled	NA	5153
j9692_adm	haven_labelled	NA	5153
j9692_vr	haven_labelled	NA	5153
ohs_code_date	numeric	NA	5124
e662_pcpl	haven_labelled	NA	5124
e662_adm	haven_labelled	NA	5124
e662_vr	haven_labelled	NA	5124
hypercap_resp_failure_date	numeric	NA	4873
other_resp_failure	haven_labelled	NA	0
j9600_date	numeric	NA	4995
j9601_date	numeric	NA	4265
j961_date	numeric	NA	5175
j9610_date	numeric	NA	5140
j9611_date	numeric	NA	5047
j962_date	numeric	NA	5175
j9620_date	numeric	NA	5153
j9621_date	numeric	NA	4916
j9690_date	numeric	NA	5050
j9691_date	numeric	NA	5105
other_resp_failure_date	numeric	NA	3864

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
sepsis_dx_date	numeric	NA	4571
stupor_dx_date	numeric	NA	5057
cog_signs_dx_date	numeric	NA	4689
mal_fat_dx_date	numeric	NA	4598
resp_acid_dx_date	numeric	NA	5127
sleep_hypovent_dx_date	numeric	NA	5170
cchs_dx_date	numeric	NA	5175
other_sleep_hypovent_dx_date	numeric	NA	5169
acidosis_unspec_date	numeric	NA	5016
headache_dx_date	numeric	NA	5023
dysp_dx	haven_labelled	NA	0
dysp_dx_date	numeric	NA	4423
symp_obs	haven_labelled	NA	0
symp_obs_date	numeric	NA	5124
abn_br_dx	haven_labelled	NA	0
abn_br_dx_date	numeric	NA	5167
resp_abnormality	haven_labelled	NA	0
r0689_date	numeric	NA	5089
resp_abnormality_date	numeric	NA	5076
other_abn_of_br_date	numeric	NA	5089
fast_br	haven_labelled	NA	0
fast_br_date	numeric	NA	5147
pulm_edema_dx	haven_labelled	NA	0
pulm_edema_dx_date	numeric	NA	5018
pna_dx	haven_labelled	NA	0
pna_dx_date	numeric	NA	4440
acute_chf	numeric	NA	0
acute_old	haven_labelled	NA	0
acute_old_date	numeric	NA	0
resp_dep_compl	haven_labelled	NA	0
resp_dep_compl_date	numeric	NA	5004
acute_nmd_date	numeric	NA	5164
osa_first_date	numeric	NA	4294
osa_last_date	numeric	NA	4296
asthma_first_date	numeric	NA	4491
asthma_last_date	numeric	NA	4491
copd_first_date	numeric	NA	4159
copd_last_date	numeric	NA	4160
chf_first_date	numeric	NA	4122
chf_last_date	numeric	NA	4126
stroke_first_date	numeric	NA	4805
stroke_last_date	numeric	NA	4807
ckd_first_date	numeric	NA	4267
ckd_last_date	numeric	NA	4268
ctd	haven_labelled	NA	0

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
ctd_first_date	numeric	NA	4897
ctd_last_date	numeric	NA	4897
dem	haven_labelled	NA	0
dem_first_date	numeric	NA	4853
dem_last_date	numeric	NA	4853
dm	haven_labelled	NA	0
dm_first_date	numeric	NA	3654
dm_last_date	numeric	NA	3658
pvd_first_date	numeric	NA	4669
pvd_last_date	numeric	NA	4669
oud_first_date	numeric	NA	4892
oud_last_date	numeric	NA	4893
sedatives_first_date	numeric	NA	5124
sedatives_last_date	numeric	NA	5124
cfdo_first_date	numeric	NA	5166
cfdo_last_date	numeric	NA	5166
phtn_first_date	numeric	NA	4739
phtn_last_date	numeric	NA	4739
polocy_first_date	numeric	NA	5112
polocy_last_date	numeric	NA	5112
nmd	haven_labelled	NA	0
nmd_first_date	numeric	NA	4942
nmd_last_date	numeric	NA	4943
nic	haven_labelled	NA	0
nic_first_date	numeric	NA	3951
nic_last_date	numeric	NA	3952
ovs	haven_labelled	NA	0
ats_ohs_flag	numeric	NA	4531
pos_ohs_flag	numeric	NA	0
ats_copd_flag	numeric	NA	4560
guidelines	haven_labelled	NA	4560
OBESITY_rfs	numeric	NA	0
_merge_amb_obes	haven_labelled	NA	5175
PREDISPOSITION_rfs	numeric	NA	0
_merge_amb_predisp	haven_labelled	NA	5175
RESPFAIL_rfs	numeric	NA	0
_merge_amb_respfail	haven_labelled	NA	5175
VBG_rfs	numeric	NA	0
_merge_amb_vbg	haven_labelled	NA	5175
VENTSUPPORT_rfs	numeric	NA	0
_merge_amb_ventsupp	haven_labelled	NA	5175
is_emer	numeric	NA	0
_merge_emer_obes	haven_labelled	NA	4674
_merge_emer_predisp	haven_labelled	NA	3875
_merge_emer_respfail	haven_labelled	NA	3818

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
_merge_emer_vbg	haven_labelled	NA	3480
_merge_emer_ventsupp	haven_labelled	NA	3465
_merge_emer	haven_labelled	NA	3465
is_inp	haven_labelled	NA	1710
_merge_inpat_obes	haven_labelled	NA	3752
_merge_inpat_predisp	haven_labelled	NA	2575
_merge_inpat_respfail	haven_labelled	NA	2264
_merge_inpat_vbg	haven_labelled	NA	1841
_merge_inpat_ventsupp	haven_labelled	NA	1710
_merge_inpat	haven_labelled	NA	0
patient_id	numeric	NA	0
rfsgroup	haven_labelled	NA	0
encounter_type	factor	2	0
first_encounter	haven_labelled	NA	0
has_abg	integer	NA	0
has_vbg	integer	NA	0
max_hco3_or_its_met_alk	numeric	NA	3264
prim_met_alk	numeric	NA	4560
max_hco3_or_its_comb_met_alk	numeric	NA	3264
combo_met_alk	numeric	NA	4560
alkalemia	numeric	NA	2284
paco2_flag_and_alk	numeric	NA	4560
paco2_50_flag	haven_labelled	NA	3264
hypercap_dx_adm_flag	numeric	NA	4873
hypercap_dx_pcpl_flag	numeric	NA	4877
hypercap_dx_vr_flag	numeric	NA	4873
hypercap_on_abg	numeric	NA	0
hypercap_on_vbg	numeric	NA	0
has_both_abg_vbg	haven_labelled	NA	0
has_neither_abg_vbg	haven_labelled	NA	0
vbg_or_abg_co2_flag	haven_labelled	NA	0
dx_hypercap_on_abg	numeric	NA	4873
sugg_hypercap_dx_on_vbg	numeric	NA	4873
dx_hypercap_on_vbg	numeric	NA	4873
vbg_o2sat_calc	numeric	NA	0
abg_o2sat_calc	numeric	NA	0
corr_vbg_co2	numeric	NA	3730
corr_vbg_co2_flag	haven_labelled	NA	3730
corr_hypercap_on_vbg	numeric	NA	0
race_ethnicity	factor	7	0
has_vbg_and_cat	haven_labelled	NA	0
has_bmi_and_cat	haven_labelled	NA	0
has_weight_and_cat	haven_labelled	NA	0
has_height_and_cat	haven_labelled	NA	0
has_hr_and_cat	haven_labelled	NA	0

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
has_sbp_and_cat	haven_labelled	NA	0
has_rr_and_cat	haven_labelled	NA	0
has_temp_and_cat	haven_labelled	NA	0
has_spo2_and_cat	haven_labelled	NA	0
has_cl_and_cat	haven_labelled	NA	0
has_k_and_cat	haven_labelled	NA	0
has_hco3_and_cat	haven_labelled	NA	0
has_lactate_and_cat	haven_labelled	NA	0
has_na_and_cat	haven_labelled	NA	0
has_cr_and_cat	haven_labelled	NA	0
has_hgb_and_cat	haven_labelled	NA	0
has_wbc_and_cat	haven_labelled	NA	0
has_plt_and_cat	haven_labelled	NA	0
has_bnp_and_cat	haven_labelled	NA	0
has_phos_and_cat	haven_labelled	NA	0
has_ca_and_cat	haven_labelled	NA	0
has_alb_and_cat	haven_labelled	NA	0
has_tprot_and_cat	haven_labelled	NA	0
encounter_type_dummy1	numeric	NA	0
encounter_type_dummy2	numeric	NA	0
encounter_type_dummy3	numeric	NA	0
female	haven_labelled	NA	0
male	numeric	NA	0
white_race	numeric	NA	0
black_race	numeric	NA	0
unknown_race	numeric	NA	0
asian_race	numeric	NA	0
nat_am_race	numeric	NA	0
nhpi_race	numeric	NA	0
not_hisp_eth	numeric	NA	0
hisp_eth	numeric	NA	0
unknown_eth	numeric	NA	0
location_dummy1	numeric	NA	0
location_dummy2	numeric	NA	0
location_dummy3	numeric	NA	0
location_dummy4	numeric	NA	0
ps	numeric	NA	0
tx_pr_decile	numeric	NA	0
ps_trunc	numeric	NA	0
sumofweights	numeric	NA	0
ipw	numeric	NA	0
stabilized_weight	numeric	NA	0
approx_ipw_fweight	numeric	NA	0
vbg_ps	numeric	NA	0
vbg_tx_pr_decile	numeric	NA	0

Table 2: Factor level diagnostics (all variables) (*continued*)

variable	class	nlevels	n_missing
vbg_ps_trunc	numeric	NA	0
vbg_sumofweights	numeric	NA	0
vbg_ipw	numeric	NA	0
vbg_stabilized_weight	numeric	NA	0
vbg_approx_ipw_fweight	numeric	NA	0

```

# Factor expansion guard (logs only)
factor_guard <- factor_diag |>
  dplyr::filter(!is.na(nlevels) & nlevels > MAX_LEVELS_GBM)
write_csv_safely(factor_guard, results_path("factor_expansion_guard.csv"), row_names = FALSE)
if (nrow(factor_guard)) {
  warning("GBM factor expansion guard: factors exceeding MAX_LEVELS_GBM detected. See Results/factor_expansion_guard.csv.",
         call. = FALSE)
}

tab_enc <- table(subset_data$encounter_type, useNA = "ifany")
if (sum(!is.na(subset_data$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.")
}

# Reference profile for conditional curves
stopifnot(all(adj_core %in% names(subset_data)))

mode_level <- function(x) {
  if (is.factor(x)) {
    tab <- table(x, useNA = "no")
    if (!length(tab)) return(factor(NA, levels = levels(x)))
    lev <- names(tab)[which.max(tab)]
    return(factor(lev, levels = levels(x)))
  }
  if (is.character(x)) {

```

```

tab <- table(x, useNA = "no")
if (!length(tab)) return(NA_character_)
return(names(tab)[which.max(tab)])
}

stats::median(as.numeric(x), na.rm = TRUE)
}

make_ref_profile <- function(data, adj_vars) {
  out <- lapply(adj_vars, function(v) mode_level(data[[v]]))
  names(out) <- adj_vars
  as.data.frame(out, stringsAsFactors = FALSE)
}

make_co2_grid <- function(co2_var, co2_vals, ref_df) {
  grid <- data.frame(co2_vals)
  names(grid) <- co2_var
  stopifnot(!is.null(ref_df))
  stopifnot(nrow(ref_df) > 0L)
  ref_rep <- ref_df[rep(1L, nrow(grid)), , drop = FALSE]
  grid <- cbind(grid, ref_rep)
  grid
}

make_co2_grid_ref <- function(co2_var, co2_vals, ref_df, co2_ref) {
  grid_vals <- c(co2_vals, co2_ref)
  grid_vals <- grid_vals[is.finite(grid_vals)]
  grid_vals <- sort(unique(as.numeric(grid_vals)))
  if (length(grid_vals) < 2) {
    fallback_center <- NA_real_
    if (is.finite(co2_ref)) {
      fallback_center <- co2_ref
    } else if (length(co2_vals) && is.finite(co2_vals[1])) {
      fallback_center <- co2_vals[1]
    }
    if (is.finite(fallback_center)) {
      grid_vals <- sort(unique(c(fallback_center - 1, fallback_center, fallback_center + 1)))
    }
  }
}

```

```

    grid_vals <- grid_vals[is.finite(grid_vals)]
  }
}

if (length(grid_vals) < 2) stop("CO2 grid is too small for ", co2_var, ".")
grid <- make_co2_grid(co2_var, grid_vals, ref_df)
ref_val <- if (is.finite(co2_ref)) co2_ref else stats::median(grid[[co2_var]], na.rm = TRUE)
ref_idx <- match(ref_val, grid[[co2_var]])
if (is.na(ref_idx)) {
  ref_idx <- which.min(abs(grid[[co2_var]] - ref_val))
}
if (any(diff(grid[[co2_var]]) <= 0)) {
  stop("CO2 grid is not strictly increasing for ", co2_var, ".")
}
list(grid = grid, ref_idx = ref_idx, co2_ref = grid[[co2_var]][ref_idx])
}

predict_or_curve_from_fit <- function(fit, grid_df, ref_idx, co2_var) {
  # Build a model matrix consistent with the fitted model (handles factor levels)
  tt <- stats::delete.response(stats::terms(fit))
  xlev <- stats:::getXlevels(tt, stats::model.frame(fit))
  mf_new <- stats::model.frame(tt, grid_df, na.action = stats::na.pass, xlev = xlev)
  mm <- stats::model.matrix(tt, mf_new)
  beta <- stats::coef(fit)
  V <- stats::vcov(fit)

  # Align model matrix columns to coefficient names (fill missing with 0, drop extras)
  bn <- names(beta)
  if (is.null(bn) || any(!nzchar(bn))) {
    if (length(beta) == ncol(mm)) {
      bn <- colnames(mm)
      names(beta) <- bn
    } else {
      stop("predict_or_curve_from_fit: coefficient names missing and dimensions do not match.")
    }
  }
  if (!all(bn %in% colnames(mm))) {

```

```

missing_cols <- setdiff(bn, colnames(mm))
if (length(missing_cols)) {
  mm <- cbind(mm, matrix(0, nrow = nrow(mm), ncol = length(missing_cols),
                        dimnames = list(NULL, missing_cols)))
}
}

mm <- mm[, bn, drop = FALSE]
stopifnot(ncol(mm) == length(beta))

eta <- as.numeric(mm %*% beta)
mmV <- mm %*% V
var_eta <- rowSums(mmV * mm)

mm_ref <- mm[ref_idx, , drop = FALSE]
eta_ref <- eta[ref_idx]
var_ref <- as.numeric(mm_ref %*% V %*% t(mm_ref))
cov_ref <- as.numeric(mmV %*% t(mm_ref))

logOR <- eta - eta_ref
var_logOR <- var_eta + var_ref - 2 * cov_ref
var_logOR <- pmax(var_logOR, 0)
logOR[ref_idx] <- 0
var_logOR[ref_idx] <- 0
se <- sqrt(var_logOR)

data.frame(
  grid_df,
  logOR = logOR,
  SE_logOR = se,
  var_logOR = var_logOR,
  OR = exp(logOR),
  LCL = exp(logOR - 1.96 * se),
  UCL = exp(logOR + 1.96 * se),
  co2_ref = grid_df[[co2_var]][ref_idx],
  ref_idx = ref_idx,
  row.names = NULL
)

```

```

    )
}

x_ref_abg <- make_ref_profile(
  subset_data |> dplyr::filter(has_abg == 1, !is.na(paco2)),
  adj_core
)
x_ref_vbg <- make_ref_profile(
  subset_data |> dplyr::filter(has_vbg == 1, !is.na(vbg_co2)),
  adj_core
)

```

```

run_meta <- tibble::tibble(
  run_id      = diag_run_id,
  run_mode    = RUN_MODE,
  pilot_frac = PILOT_FRAC,
  mi_batch_threshold = MI_BATCH_THRESHOLD,
  full_n      = nrow(stata_data),
  subset_n    = nrow(subset_data)
)
render_table_pdf(run_meta,
                 "Run metadata (pilot vs full)",
                 "run_metadata",
                 digits = 0)

```

Table 3: Run metadata (pilot vs full)

run_id	run_mode	pilot_frac	mi_batch_threshold	full_n	subset_n
20260205_144255	pilot	0	5000	833476	5175

```

# Write run config JSON for portability
json_escape <- function(x) gsub("\"", "\\\"", x)
run_cfg <- list(
  run_id = diag_run_id,
  run_mode = RUN_MODE,

```

```

pilot_frac = PILOT_FRAC,
mi_batch_threshold = MI_BATCH_THRESHOLD,
data_dir = data_dir_name,
results_dir = results_dir,
full_n = nrow(stata_data),
subset_n = nrow(subset_data)
)
json_lines <- c(
  "{",
  paste0("  \"run_id\": \"", json_escape(run_cfg$run_id), "\","),
  paste0("  \"run_mode\": \"", json_escape(run_cfg$run_mode), "\","),
  paste0("  \"pilot_frac\": ", run_cfg$pilot_frac, ","),
  paste0("  \"mi_batch_threshold\": ", run_cfg$mi_batch_threshold, ","),
  paste0("  \"data_dir\": \"", json_escape(run_cfg$data_dir), "\","),
  paste0("  \"results_dir\": \"", json_escape(run_cfg$results_dir), "\","),
  paste0("  \"full_n\": ", run_cfg$full_n, ","),
  paste0("  \"subset_n\": ", run_cfg$subset_n),
  "}"
)
writeLines(json_lines, results_path("run_config.json"))

```

Codebook exported to Results/codebookr.docx.

```

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)

```

1.1.2 Outcome Variable Creation

```
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"),

    ## 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)
)

```

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

```

0      1
4641  534

```

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

```

0      1
0.8968116 0.1031884

```

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

Min.	1st Qu.	Median	Mean	3rd Qu.	Max.
0.0000	0.0000	0.0000	0.1032	0.0000	1.0000

1.2 2) Baseline tables

```

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

# helper: label binary 0/1 → "No"/"Yes"
bin_lab <- function(x) {
  y <- to01(x)
  if (all(is.na(y))) {
    return(factor(y, levels = c(0, 1), labels = c("No", "Yes")))
  }
  factor(y, levels = c(0, 1), labels = c("No", "Yes"))
}

# helper: preserve labeled factors if already present; otherwise map numeric codes
label_from_codes <- function(x, codes, labels) {
  if (is.factor(x)) {
    lev <- levels(x)
    if (all(lev %in% labels)) {
      return(factor(x, levels = labels))
    }
    lev_num <- suppressWarnings(as.numeric(lev))
    if (all(!is.na(lev_num)) && all(lev_num %in% codes)) {
      return(factor(as.numeric(as.character(x)), levels = codes, labels = labels))
    }
    return(x)
  }
  x_num <- suppressWarnings(as.numeric(as.character(x)))
  if (all(is.na(x_num))) return(factor(x, levels = labels))
  if (all(x_num %in% codes, na.rm = TRUE)) {
    return(factor(x_num, levels = codes, labels = labels))
  }
  factor(x)
}

subset_data <- subset_data %>%
  mutate(

```

```

## ensure 0/1 numerics (avoids factor-level coercion)
across(c(has_abg, has_vbg),
       ~ to01(.)),

## derive ABG / VBG status groups (binary test status only)
abg_group = case_when(
  has_abg == 0 ~ "No ABG",
  has_abg == 1 ~ "ABG",
  TRUE          ~ "Missing"
),
vbg_group = case_when(
  has_vbg == 0 ~ "No VBG",
  has_vbg == 1 ~ "VBG",
  TRUE          ~ "Missing"
),

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

## labelled covariates (robust to factor or numeric codes)
sex_label = label_from_codes(sex, c(0, 1), c("Female", "Male")),
race_ethnicity_label = label_from_codes(
  race_ethnicity,
  0:6,
  c("White", "Black or African American", "Hispanic",
    "Asian", "American Indian", "Pacific Islander", "Unknown")
),
location_label = label_from_codes(
  location,

```

```

  0:3,
  c("South", "Northeast", "Midwest", "West")
),
encounter_type_label = label_from_codes(
  encounter_type,
  c(2, 3),
  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"
)
vars_baseline <- setdiff(vars, c("vbg_co2", "paco2"))
vars_abg <- c(vars_baseline, "paco2")
vars_vbg <- c(vars_baseline, "vbg_co2")

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

  df <- data %>%
    filter(!is.na (!!group_sym),                      # drop explicit NA
           !!group_sym != "Missing") %>%            # drop "Missing" cohort
    mutate (!!group_sym := droplevels (!!group_sym)) %>% # only drop group levels
}

```

```

select(all_of(c(group_var, vars_baseline)))

empty_fac <- names(which(vapply(df, function(z) is.factor(z) && length(levels(z)) == 0L, logical(1))))
if (length(empty_fac) > 0) {
  warning("0-level factor columns detected: ", paste(empty_fac, collapse = ", "),
  ". Converting to character to prevent gtsummary failure.", call. = FALSE)
  df[empty_fac] <- lapply(df[empty_fac], as.character)
}

df %>%
  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(strip_manual_table_number(caption))
}

if (sum(!is.na(subset_data$sex_label)) == 0L || length(levels(subset_data$sex_label)) == 0L) {
  warning("sex_label is all NA or has zero levels; check sex normalization/mapping.", call. = FALSE)
  stopifnot("sex" %in% names(subset_data))
}

# 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")

tbl1a_pdf <- to_pdf_table(table1A, font_size = 7, landscape = FALSE, label_col_width = "2.0in",
                           longtable = TRUE)
tbl1b_pdf <- to_pdf_table(table1B, font_size = 7, landscape = FALSE, label_col_width = "2.0in",

```

```

longtable = TRUE)
tbl1a_pdf

```

Table 4: ABG cohorts

Variable	**No ABG** N = 3,264	**ABG** N = 1,911
age_at_encounter	58.4 ± 17.7; 0.0/3,264.0 missing (0.0%)	61.3 ± 17.2; 0.0/1,911.0 missing (0.0%)
curr_bmi	32.6 ± 8.9; 1,821.0/3,264.0 missing (55.8%)	28.8 ± 7.0; 1,113.0/1,911.0 missing (58.2%)
sex_label		
Female	1,737 (53%)	854 (45%)
Male	1,527 (47%)	1,057 (55%)
race_ethnicity_label		
White	2,009 (62%)	1,271 (67%)
Black or African American	601 (18%)	283 (15%)
Hispanic	250 (7.7%)	84 (4.4%)
Asian	46 (1.4%)	37 (1.9%)
American Indian	11 (0.3%)	25 (1.3%)
Pacific Islander	8 (0.2%)	2 (0.1%)
Unknown	339 (10%)	209 (11%)
location_label		
South	1,374 (42%)	1,057 (55%)
Northeast	921 (28%)	379 (20%)
Midwest	246 (7.5%)	160 (8.4%)
West	723 (22%)	315 (16%)
osa_label	576 (18%)	303 (16%)
asthma_label	464 (14%)	220 (12%)
copd_label	579 (18%)	434 (23%)
chf_label	587 (18%)	457 (24%)
nmd_label	130 (4.0%)	103 (5.4%)
phtn_label	239 (7.3%)	195 (10%)
ckd_label	519 (16%)	385 (20%)
diabetes_label	954 (29%)	559 (29%)
encounter_type_label		
Emergency	1,427 (44%)	283 (15%)
Inpatient	1,837 (56%)	1,628 (85%)

tbl1b_pdf

Table 5: VBG cohorts

Variable	**No VBG** N = 3,730	**VBG** N = 1,445
age_at_encounter	59.6 ± 17.6; 0.0/3,730.0 missing (0.0%)	59.0 ± 17.7; 0.0/1,445.0 missing (0.0%)
curr_bmi	31.9 ± 8.6; 1,939.0/3,730.0 missing (52.0%)	28.9 ± 7.5; 995.0/1,445.0 missing (68.9%)

Table 5: VBG cohorts (*continued*)

Variable	**No VBG** N = 3,730	**VBG** N = 1,445
sex_label		
Female	1,921 (52%)	670 (46%)
Male	1,809 (48%)	775 (54%)
race_ethnicity_label		
White	2,513 (67%)	767 (53%)
Black or African American	616 (17%)	268 (19%)
Hispanic	221 (5.9%)	113 (7.8%)
Asian	54 (1.4%)	29 (2.0%)
American Indian	13 (0.3%)	23 (1.6%)
Pacific Islander	8 (0.2%)	2 (0.1%)
Unknown	305 (8.2%)	243 (17%)
location_label		
South	1,987 (53%)	444 (31%)
Northeast	703 (19%)	597 (41%)
Midwest	264 (7.1%)	142 (9.8%)
West	776 (21%)	262 (18%)
osa_label	648 (17%)	231 (16%)
asthma_label	513 (14%)	171 (12%)
copd_label	731 (20%)	282 (20%)
clf_label	741 (20%)	303 (21%)
nmd_label	175 (4.7%)	58 (4.0%)
phtn_label	295 (7.9%)	139 (9.6%)
ckd_label	628 (17%)	276 (19%)
diabetes_label	1,034 (28%)	479 (33%)
encounter_type_label		
Emergency	1,247 (33%)	463 (32%)
Inpatient	2,483 (67%)	982 (68%)

```

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"))

```

```

# 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_baseline), 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 with "Everyone" column first
tbl1_vbg <- subset_data %>%
  select(all_of(vars_baseline), 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"
  )

```

```

missing = "no"
) %>%
gtsummary::add_overall(last = FALSE, col_label = "Everyone") %>%
gtsummary::modify_header(label = "**Variable**")

tbl1_abg <- tbl1_abg %>%
  modify_caption(strip_manual_table_number("**Table 1A. Baseline summary: Everyone and ABG status**"))
tbl1_vbg <- tbl1_vbg %>%
  modify_caption(strip_manual_table_number("**Table 1B. Baseline summary: Everyone and VBG status**"))

# merged table for Word export (Table 1: Everyone + ABG/VBG status)
tbl1 <- gtsummary::tbl_merge(
  list(tbl1_abg, tbl1_vbg),
  tab_spanner = c("**ABG status**", "**VBG status**")
)

tbl1_abg_pdf <- to_pdf_table(tbl1_abg, font_size = 7, landscape = FALSE, label_col_width = "2.0in",
                               longtable = TRUE)
tbl1_vbg_pdf <- to_pdf_table(tbl1_vbg, font_size = 7, landscape = FALSE, label_col_width = "2.0in",
                               longtable = TRUE)
tbl1_abg_pdf

```

Table 6: Baseline summary: Everyone and ABG status**

Variable	Everyone	**Did not get ABG** N = 3,264	**Did get ABC** N = 1,911
age_at_encounter	59.5 ± 17.6; 0.0/5,175.0 missing (0.0%)	58.4 ± 17.7; 0.0/3,264.0 missing (0.0%)	61.3 ± 17.2; 0.0/1,911.0 missing (0.0%)
curr_bmi	31.3 ± 8.5; 2,934.0/5,175.0 missing (56.7%)	32.6 ± 8.9; 1,821.0/3,264.0 missing (55.8%)	28.8 ± 7.0; 1,113.0/1,911.0 missing (58.2%)
sex_label			
Female	2,591 (50%)	1,737 (53%)	854 (45%)
Male	2,584 (50%)	1,527 (47%)	1,057 (55%)
race_ethnicity_label			
White	3,280 (63%)	2,009 (62%)	1,271 (67%)
Black or African American	884 (17%)	601 (18%)	283 (15%)
Hispanic	334 (6.5%)	250 (7.7%)	84 (4.4%)
Asian	83 (1.6%)	46 (1.4%)	37 (1.9%)
American Indian	36 (0.7%)	11 (0.3%)	25 (1.3%)
Pacific Islander	10 (0.2%)	8 (0.2%)	2 (0.1%)
Unknown	548 (11%)	339 (10%)	209 (11%)
location_label			
South	2,431 (47%)	1,374 (42%)	1,057 (55%)

Table 6: Baseline summary: Everyone and ABG status** (*continued*)

Variable	Everyone	**Did not get ABG** N = 3,264	**Did get ABG** N = 1,911
Northeast	1,300 (25%)	921 (28%)	379 (20%)
Midwest	406 (7.8%)	246 (7.5%)	160 (8.4%)
West	1,038 (20%)	723 (22%)	315 (16%)
osa_label	879 (17%)	576 (18%)	303 (16%)
asthma_label	684 (13%)	464 (14%)	220 (12%)
copd_label	1,013 (20%)	579 (18%)	434 (23%)
chf_label	1,044 (20%)	587 (18%)	457 (24%)
nmd_label	233 (4.5%)	130 (4.0%)	103 (5.4%)
phtn_label	434 (8.4%)	239 (7.3%)	195 (10%)
ckd_label	904 (17%)	519 (16%)	385 (20%)
diabetes_label	1,513 (29%)	954 (29%)	559 (29%)
encounter_type_label			
Emergency	1,710 (33%)	1,427 (44%)	283 (15%)
Inpatient	3,465 (67%)	1,837 (56%)	1,628 (85%)

tbl1_vbg_pdf

Table 7: Baseline summary: Everyone and VBG status**

Variable	Everyone	**Did not get VBG** N = 3,730	**Did get VBG** N = 1,445
age_at_encounter	59.5 ± 17.6; 0.0/5,175.0 missing (0.0%)	59.6 ± 17.6; 0.0/3,730.0 missing (0.0%)	59.0 ± 17.7; 0.0/1,445.0 missing (0.0%)
curr_bmi	31.3 ± 8.5; 2,934.0/5,175.0 missing (56.7%)	31.9 ± 8.6; 1,939.0/3,730.0 missing (52.0%)	28.9 ± 7.5; 995.0/1,445.0 missing (68.9%)
sex_label			
Female	2,591 (50%)	1,921 (52%)	670 (46%)
Male	2,584 (50%)	1,809 (48%)	775 (54%)
race_ethnicity_label			
White	3,280 (63%)	2,513 (67%)	767 (53%)
Black or African American	884 (17%)	616 (17%)	268 (19%)
Hispanic	334 (6.5%)	221 (5.9%)	113 (7.8%)
Asian	83 (1.6%)	54 (1.4%)	29 (2.0%)
American Indian	36 (0.7%)	13 (0.3%)	23 (1.6%)
Pacific Islander	10 (0.2%)	8 (0.2%)	2 (0.1%)
Unknown	548 (11%)	305 (8.2%)	243 (17%)
location_label			
South	2,431 (47%)	1,987 (53%)	444 (31%)
Northeast	1,300 (25%)	703 (19%)	597 (41%)
Midwest	406 (7.8%)	264 (7.1%)	142 (9.8%)
West	1,038 (20%)	776 (21%)	262 (18%)
osa_label	879 (17%)	648 (17%)	231 (16%)
asthma_label	684 (13%)	513 (14%)	171 (12%)
copd_label	1,013 (20%)	731 (20%)	282 (20%)
chf_label	1,044 (20%)	741 (20%)	303 (21%)

Table 7: Baseline summary: Everyone and VBG status** (*continued*)

Variable	Everyone	**Did not get VBG** N = 3,730	**Did get VBG** N = 1,445
nmd_label	233 (4.5%)	175 (4.7%)	58 (4.0%)
phtn_label	434 (8.4%)	295 (7.9%)	139 (9.6%)
ckd_label	904 (17%)	628 (17%)	276 (19%)
diabetes_label	1,513 (29%)	1,034 (28%)	479 (33%)
encounter_type_label			
Emergency	1,710 (33%)	1,247 (33%)	463 (32%)
Inpatient	3,465 (67%)	2,483 (67%)	982 (68%)

```

ABG_CO2_VAR <- "paco2"
VBG_CO2_VAR <- "vbg_co2"
ABG_CO2_LOW <- 35
ABG_CO2_HIGH <- 45
VBG_CO2_LOW <- 40
VBG_CO2_HIGH <- 50
CO2_SPEC <- list(
  ABG = list(var = ABG_CO2_VAR, normal_lo = ABG_CO2_LOW, normal_hi = ABG_CO2_HIGH),
  VBG = list(var = VBG_CO2_VAR, normal_lo = VBG_CO2_LOW, normal_hi = VBG_CO2_HIGH)
)
CO2_SPEC$ABG$ref <- (CO2_SPEC$ABG$normal_lo + CO2_SPEC$ABG$normal_hi) / 2
CO2_SPEC$VBG$ref <- (CO2_SPEC$VBG$normal_lo + CO2_SPEC$VBG$normal_hi) / 2
# Reference values for spline OR curves (midpoint of normal range)
ABG_CO2_REF <- CO2_SPEC$ABG$ref
VBG_CO2_REF <- CO2_SPEC$VBG$ref
CO2_CAT_LEVELS <- c("Normal", "Low", "High")
CO2_CAT_CONTRAST_LEVELS <- setdiff(CO2_CAT_LEVELS, "Normal")

make_co2_cat3 <- function(x, low_cut, high_cut) {
  x <- suppressWarnings(as.numeric(x))
  out <- dplyr::case_when(
    is.na(x) ~ NA_character_,
    x < low_cut ~ "Low",
    x > high_cut ~ "High",
    TRUE ~ "Normal"
)
    
```

```

    factor(out, levels = CO2_CAT_LEVELS)
}

subset_data <- subset_data %>%
  mutate(
    pco2_cat_abg = make_co2_cat3(.data[[ABG_CO2_VAR]], ABG_CO2_LOW, ABG_CO2_HIGH),
    pco2_cat_vbg = make_co2_cat3(.data[[V ро_2_VAR]], VBG_CO2_LOW, VBG_CO2_HIGH)
  )

stopifnot("Normal" %in% levels(subset_data$pco2_cat_abg),
          "Normal" %in% levels(subset_data$pco2_cat_vbg))

warn_low_counts <- function(cat, label) {
  tab <- table(cat, useNA = "no")
  if (length(tab) && any(tab < 10)) {
    warning(label, ": low counts in CO2 categories: ",
            paste(names(tab), tab, collapse = ", "), call. = FALSE)
  }
}
warn_low_counts(subset_data$pco2_cat_abg[subset_data$has_abg == 1 & !is.na(subset_data$paco2)],
                "ABG")
warn_low_counts(subset_data$pco2_cat_vbg[subset_data$has_vbg == 1 & !is.na(subset_data$vbg_co2)],
                "VBG")

```

```

# Fail-fast if any binary CO2 indicator references remain in this QMD
qmd_path <- knitr::current_input()
stopifnot(!is.null(qmd_path), file.exists(qmd_path))
txt <- readLines(qmd_path, warn = FALSE)
pat_var <- paste0("hypercap", "_on_")
pat_txt <- paste0("binary", " hypercapnia")
if (any(grepl(pat_var, txt))) {
  stop("Binary CO2 indicator variable references remain in the QMD.")
}
if (any(grepl(pat_txt, txt, ignore.case = TRUE))) {
  stop("Binary CO2 indicator text remains in the QMD.")
}
```

```

# ABG cohort (has_abg == 1)
tbl2_abg <- subset_data %>%
  filter(has_abg == 1) %>%
  select(all_of(vars_abg), pco2_cat_abg) %>%
  gtsummary::tbl_summary(
    by = pco2_cat_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 = "***Normal***",
    stat_2 = "***Low***",
    stat_3 = "***High***"
  )

# VBG cohort (has_vbg == 1)
tbl2_vbg <- subset_data %>%
  filter(has_vbg == 1) %>%
  select(all_of(vars_vbg), pco2_cat_vbg) %>%
  gtsummary::tbl_summary(
    by = pco2_cat_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 = "##Normal**",
stat_2 = "##Low**",
stat_3 = "##High**"
)

tbl2 <- gtsummary::tbl_merge(
  tbls = list(tbl2_abg, tbl2_vbg),
  tab_spanner = c("##ABG (PaCO2)**", "##VBG (PvCO2)**")
) %>%
  gtsummary::modify_caption(strip_manual_table_number("##Table 2. Baseline summary by CO2 category within ABG and VBG cohorts##"))

tbl2_pdf <- to_pdf_table(tbl2, font_size = 7, landscape = FALSE, label_col_width = "2.0in",
                           longtable = TRUE)
tbl2_pdf

```

Table 8: Baseline summary by CO2 category within ABG and VBG cohorts**

##Variable##	##Normal##	##Low##	##High##	##Normal##
age_at_encounter	61.9 ± 16.8; 0.0/825.0 missing (0.0%)	59.6 ± 18.4; 0.0/521.0 missing (0.0%)	61.9 ± 16.5; 0.0/565.0 missing (0.0%)	57.2 ± 18.3; 0.0/647.0 missing (0.0%)
curr_bmi	28.5 ± 6.8; 457.0/825.0 missing (55.4%)	28.1 ± 6.5; 318.0/521.0 missing (61.0%)	29.9 ± 7.7; 338.0/565.0 missing (59.8%)	29.7 ± 7.6; 465.0/647.0 missing (71.9%)
sex_label				27.7
Female	372 (45%)	225 (43%)	257 (45%)	323 (50%)
Male	453 (55%)	296 (57%)	308 (55%)	324 (50%)
race_ethnicity_label				
White	556 (67%)	330 (63%)	385 (68%)	325 (50%)
Black or African American	115 (14%)	82 (16%)	86 (15%)	115 (18%)
Hispanic	36 (4.4%)	29 (5.6%)	19 (3.4%)	59 (9.1%)
Asian	12 (1.5%)	14 (2.7%)	11 (1.9%)	16 (2.5%)
American Indian	15 (1.8%)	8 (1.5%)	2 (0.4%)	9 (1.4%)
Pacific Islander	2 (0.2%)	0 (0%)	0 (0%)	1 (0.2%)
Unknown	89 (11%)	58 (11%)	62 (11%)	122 (19%)
location_label				
South	467 (57%)	284 (55%)	306 (54%)	205 (32%)
Northeast	148 (18%)	84 (16%)	147 (26%)	273 (42%)
Midwest	69 (8.4%)	47 (9.0%)	44 (7.8%)	61 (9.4%)
West	141 (17%)	106 (20%)	68 (12%)	108 (17%)
osa_label	116 (14%)	53 (10%)	134 (24%)	95 (15%)
asthma_label	84 (10%)	58 (11%)	78 (14%)	66 (10%)
copd_label	154 (19%)	83 (16%)	197 (35%)	89 (14%)
chf_label	175 (21%)	115 (22%)	167 (30%)	110 (17%)
nmd_label	48 (5.8%)	25 (4.8%)	30 (5.3%)	19 (2.9%)
phtn_label	82 (9.9%)	45 (8.6%)	68 (12%)	47 (7.3%)
ckd_label	157 (19%)	112 (21%)	116 (21%)	103 (16%)

Table 8: Baseline summary by CO2 category within ABG and VBG cohorts** (*continued*)

Variable	**Normal**	**Low**	**High**	**Normal**
diabetes_label	243 (29%)	145 (28%)	171 (30%)	194 (30%)
encounter_type_label				
Emergency	127 (15%)	65 (12%)	91 (16%)	240 (37%)
Inpatient	698 (85%)	456 (88%)	474 (84%)	407 (63%)
paco2	39.8 ± 3.0; 0.0/825.0 missing (0.0%)	29.6 ± 4.5; 0.0/521.0 missing (0.0%)	59.1 ± 19.3; 0.0/565.0 missing (0.0%)	
vbg_co2				44.5 ± 3.0; 0.0/647.0 missing (0.0%)
				33

Table 9: Table 2a. Crude outcomes by CO2 category

Cohort	Outcome	Normal	Low	High
ABG	IMV	174/825 (21.1%)	145/521 (27.8%)	144/565 (25.5%)
ABG	NIV	60/825 (7.3%)	38/521 (7.3%)	85/565 (15.0%)
ABG	Death (60d)	110/825 (13.3%)	103/521 (19.8%)	109/565 (19.3%)
ABG	Hypercapnic RF	33/825 (4.0%)	28/521 (5.4%)	145/565 (25.7%)
VBG	IMV	72/647 (11.1%)	63/402 (15.7%)	73/396 (18.4%)
VBG	NIV	31/647 (4.8%)	23/402 (5.7%)	46/396 (11.6%)
VBG	Death (60d)	69/647 (10.7%)	68/402 (16.9%)	63/396 (15.9%)
VBG	Hypercapnic RF	26/647 (4.0%)	16/402 (4.0%)	91/396 (23.0%)

```

library(gtsummary)
library(flextable)
library(officer)

# gtsummary objects (example: tbl1, tbl2)
ft1 <- as_flex_table(tbl1)
ft2 <- as_flex_table(tbl2)

doc1 <- read_docx() %>%
  body_add_par("Table 1. Baseline summary: Everyone, ABG status, and VBG status",
               style = "heading 1") %>%
  body_add_flextable(ft1)
print(doc1, target = results_path("Table1.docx"))

doc2 <- read_docx() %>%
  body_add_par("Table 2. Baseline summary by CO2 category within ABG and VBG cohorts",

```

```

      style = "heading 1") %>%
body_add_flextable(ft2)
print(doc2, target = results_path("Table2.docx"))

```

1.3 3) Three-level PCO2 categories (unweighted)

Three groups using low/normal/high CO2 categories

```

stopifnot(all(c("pco2_cat_abg", "pco2_cat_vbg") %in% names(subset_data)))

library(broom)
library(tidyr)
library(dplyr)

run_logit <- function(data, outcome, exposure, group_name, adj_vars = NULL, model_type = "Crude") {
  f <- if (length(adj_vars)) {
    reformulate(c(exposure, adj_vars), response = outcome)
  } else {
    as.formula(paste(outcome, "~", exposure))
  }
  fit_res <- fit_with_diagnostics(
    function() glm(f, data = data, family = binomial, control = glm.control(maxit = 50)),
    context = make_context(
      stage = "outcome",
      component = "cat3",
      analysis_variant = "unweighted",
      model_type = "cat3",
      group = group_name,
      outcome = outcome,
      imputation = NA_integer_,
      batch = NA_integer_
    )
  )
  append_outcome_diag(fit_res$diag)
  if (is.null(fit_res$fit)) {

```

```

stop("run_logit: model fit failed for outcome=", outcome,
     " exposure=", exposure, " group=", group_name)
}
tidy(fit_res$fit, exponentiate = TRUE, conf.int = TRUE) %>%
  filter(term != "(Intercept)", startsWith(term, exposure)) %>%
  mutate(
    outcome = outcome,
    group = group_name,
    model = model_type
  )
}

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

unw_three_level_forms <- list(
  "ABG 3-level: IMV ~ CO2 category + X"      = reformulate(c("pco2_cat_abg", adj_core), response = "imv_proc"),
  "ABG 3-level: NIV ~ CO2 category + X"        = reformulate(c("pco2_cat_abg", adj_core), response = "niv_proc"),
  "ABG 3-level: Death60d ~ CO2 category + X"   = reformulate(c("pco2_cat_abg", adj_core), response = "death_60d"),
  "ABG 3-level: HCRF ~ CO2 category + X"       = reformulate(c("pco2_cat_abg", adj_core), response = "hypercap_resp_failure"),
  "V рG 3-level: IMV ~ CO2 category + X"        = reformulate(c("pco2_cat_vbg", adj_core), response = "imv_proc"),
  "V рG 3-level: NIV ~ CO2 category + X"        = reformulate(c("pco2_cat_vbg", adj_core), response = "niv_proc"),
  "V рG 3-level: Death60d ~ CO2 category + X"   = reformulate(c("pco2_cat_vbg", adj_core), response = "death_60d"),
  "V рG 3-level: HCRF ~ CO2 category + X"       = reformulate(c("pco2_cat_vbg", adj_core), response = "hypercap_resp_failure")
)
register_model_diagrams(unw_three_level_forms)

unw_results_crude <- bind_rows(
  lapply(outcomes_unw, function(o) run_logit(subset_data, o, "pco2_cat_abg", "ABG")),
  lapply(outcomes_unw, function(o) run_logit(subset_data, o, "pco2_cat_vbg", "V рG"))
)
unw_results_adj <- bind_rows(
  lapply(outcomes_unw, function(o) run_logit(subset_data, o, "pco2_cat_abg", "ABG", adj_core, "Adjusted")),
  lapply(outcomes_unw, function(o) run_logit(subset_data, o, "pco2_cat_vbg", "V рG", adj_core, "Adjusted"))
)
unw_threel level_results <- unw_results_adj %>%

```

```

mutate(method = "Unweighted adjusted")

unw_combined_or_df <- unw_results_adj %>%
  mutate(
    outcome = recode(outcome,
                      imv_proc = "Intubation",
                      niv_proc = "NIV",
                      death_60d = "Death (60d)",
                      hypercap_resp_failure = "Hypercapnic RF")
  )
unw_combined_or_df <- map_or_exposure(unw_combined_or_df, "or-plot-three-level-unweighted") |>
  select(outcome, group, exposure, estimate, conf.low, conf.high)

```

```

library(scales)

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

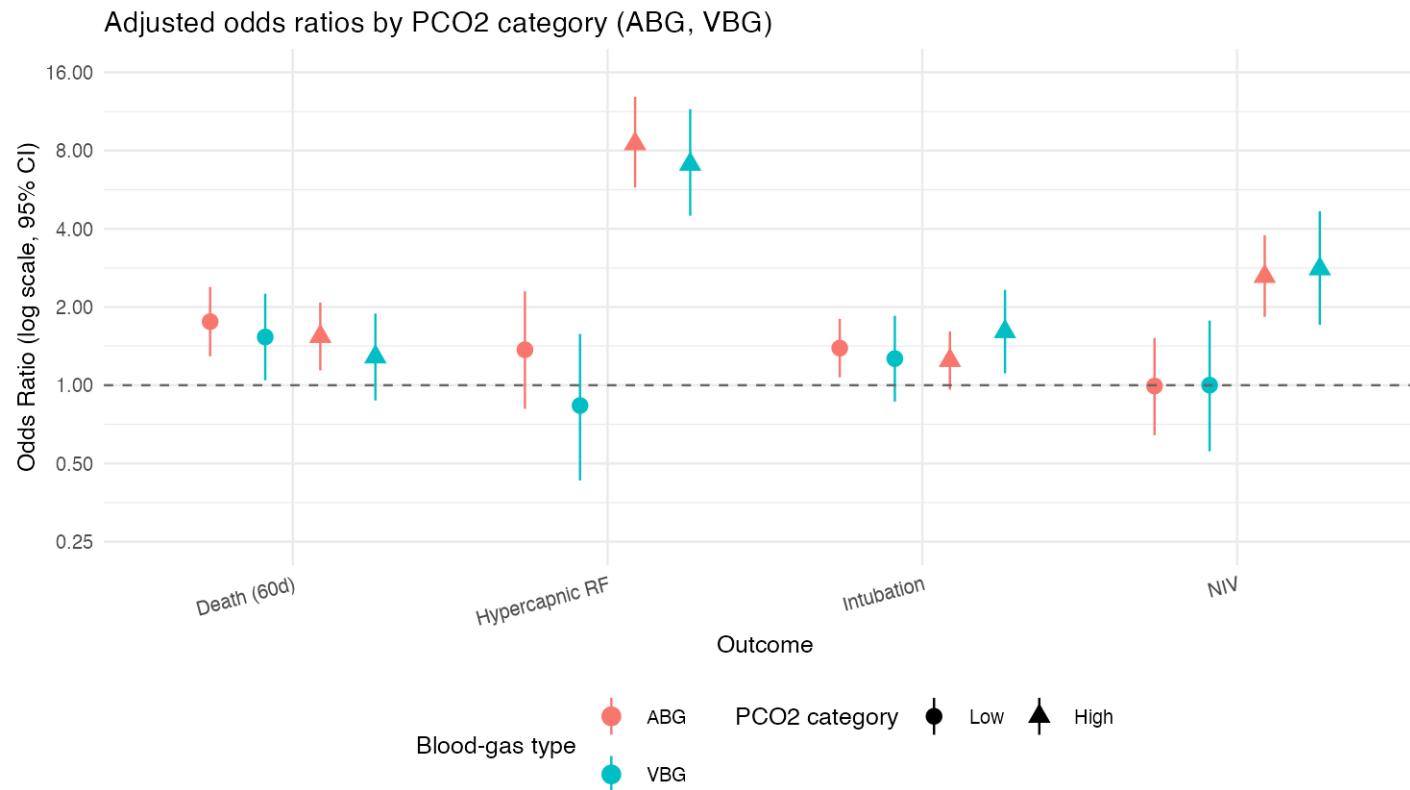
unw_plot_df <- build_or_plot_df(unw_combined_or_df, "or-plot-three-level-unweighted",
                                 expected_exposure_levels = CO2_CAT_CONTRAST_LEVELS)
stopifnot(is.data.frame(unw_plot_df))
unw_axis_spec <- compute_or_axis_spec(unw_plot_df, lo_col = "conf.low", hi_col = "conf.high",
                                       default_limits = OR_XLIM)
unw_p_or <- plot_or_safe(
  unw_plot_df,
  plot_name = "or-plot-three-level-unweighted",
  axis_spec = unw_axis_spec,
  title = "Adjusted odds ratios by PCO2 category (ABG, VBG)",
  caption = paste(
    "Adjusted for age, sex, race/ethnicity, location, and encounter type.",
    "Reference = patients in the normal PCO2 range.",
    "Low: <35 mmHg (ABG) or <40 mmHg (VBG); High: >45 mmHg (ABG) or >50 mmHg (VBG).",
    "Because the underlying cohorts differ (ABG, VBG), denominators are not identical across groups.",
    sep = "\n"
)

```

```

)
print_plot_once(unw_p_or, "or-plot-three-level-unweighted", width = 7.5, height = 4.8)

```



1.4 4) Restricted cubic spline regressions (unweighted)

Spline curves are shown as odds ratios relative to CO₂_ref (midpoint of the normal range), holding covariates at the reference profile.

```
# ABG spline dataset
subset_data_abg <- subset_data %>%
  filter(has_abg == 1, !is.na(paco2)) %>%
  select(paco2, imv_proc, niv_proc, death_60d, hypercap_resp_failure, all_of(adj_core)) %>%
  filter(complete.cases(.))
```

1.4.1 4.1 Unweighted, Restricted Cubic Spline Regression - ABG by PaCO2

```
make_spline_fml <- function(outcome, co2_var, adj_vars) {
  spline_term <- if (SPLINE_BASIS == "rcs") {
    sprintf("rms::rcs(%s, %d)", co2_var, SPLINE_DF)
  } else {
    sprintf("splines::ns(%s, %d)", co2_var, SPLINE_DF)
  }
  stats::as.formula(
    paste0(outcome, " ~ ", spline_term,
           if (length(adj_vars)) paste0(" + ", paste(adj_vars, collapse = " + ")) else ""))
}
}

#| code-block-title: "Unweighted ABG spline models (adjusted)"
abg_spline_forms <- list(
  "ABG spline (adjusted): IMV ~ CO2 spline + X"      = make_spline_fml("imv_proc", "paco2", adj_core),
  "ABG spline (adjusted): NIV ~ CO2 spline + X"      = make_spline_fml("niv_proc", "paco2", adj_core),
  "ABG spline (adjusted): Death60d ~ CO2 spline + X" = make_spline_fml("death_60d", "paco2", adj_core),
  "ABG spline (adjusted): HCRF ~ CO2 spline + X"     = make_spline_fml("hypercap_resp_failure", "paco2", adj_core)
)
register_model_diagrams(abg_spline_forms)

co2_seq_abg <- stats::quantile(subset_data_abg$paco2, probs = c(0.02, 0.98), na.rm = TRUE)
grid_abg_info_unw <- make_co2_grid_ref(
  "paco2",
  seq(co2_seq_abg[1], co2_seq_abg[2], length.out = SPLINE_GRID_N),
  x_ref_abg,
```

```

    ABG_CO2_REF
)
grid_abg_unw <- grid_abg_info_unw$grid
ref_idx_abg_unw <- grid_abg_info_unw$ref_idx
co2_ref_abg_unw <- grid_abg_info_unw$co2_ref

fit_spline_glm <- function(outcome, co2_var, data, group_label) {
  fit_res <- fit_with_diagnostics(
    function() glm(make_spline_fml(outcome, co2_var, adj_core),
                  data = data, family = binomial,
                  control = glm.control(maxit = 50)),
    context = make_context(
      stage = "outcome",
      component = "spline",
      analysis_variant = "unweighted",
      model_type = "spline",
      group = group_label,
      outcome = outcome,
      imputation = NA_integer_,
      batch = NA_integer_
    )
  )
  append_outcome_diag(fit_res$diag)
  fit_res$fit
}

fit_imv <- fit_spline_glm("imv_proc", "paco2", subset_data_abg, "ABG")
fit_niv <- fit_spline_glm("niv_proc", "paco2", subset_data_abg, "ABG")
fit_death <- fit_spline_glm("death_60d", "paco2", subset_data_abg, "ABG")
fit_hcrcf <- fit_spline_glm("hypercap_resp_failure", "paco2", subset_data_abg, "ABG")
if (any(vapply(list(fit_imv, fit_niv, fit_death, fit_hcrcf), is.null, logical(1)))) {
  stop("Unweighted ABG spline fits failed; see model_fit_diagnostics.csv.")
}

pred_imv <- predict_or_curve_from_fit(fit_imv, grid_abg_unw, ref_idx_abg_unw, "paco2")
pred_niv <- predict_or_curve_from_fit(fit_niv, grid_abg_unw, ref_idx_abg_unw, "paco2")

```

```

pred_death <- predict_or_curve_from_fit(fit_death, grid_abg_unw, ref_idx_abg_unw, "paco2")
pred_hcrf <- predict_or_curve_from_fit(fit_hcrf, grid_abg_unw, ref_idx_abg_unw, "paco2")
## Plotting deferred until VBG curves are computed so axes can be shared.

```

1.4.2 4.2 Unweighted, Restricted Cubic Spline - VBG

```

# --- VBG dataset ---
subset_data_vbg <- subset_data %>%
  dplyr::filter(has_vbg == 1, !is.na(vbg_co2)) %>%
  dplyr::select(vbg_co2, imv_proc, niv_proc, death_60d, hypercap_resp_failure, all_of(adj_core)) %>%
  dplyr::filter(complete.cases(.))

vbg_spline_forms <- list(
  "VBG spline (adjusted): IMV ~ CO2 spline + X"      = make_spline_fml("imv_proc", "vbg_co2", adj_core),
  "VBG spline (adjusted): NIV ~ CO2 spline + X"      = make_spline_fml("niv_proc", "vbg_co2", adj_core),
  "VBG spline (adjusted): Death60d ~ CO2 spline + X" = make_spline_fml("death_60d", "vbg_co2", adj_core),
  "VBG spline (adjusted): HCRF ~ CO2 spline + X"     = make_spline_fml("hypercap_resp_failure", "vbg_co2", adj_core)
)
register_model_diagrams(vbg_spline_forms)

co2_seq_vbg <- stats::quantile(subset_data_vbg$vbg_co2, probs = c(0.02, 0.98), na.rm = TRUE)
grid_vbg_info_unw <- make_co2_grid_ref(
  "vbg_co2",
  seq(co2_seq_vbg[1], co2_seq_vbg[2], length.out = SPLINE_GRID_N),
  x_ref_vbg,
  VBG_CO2_REF
)
grid_vbg_unw <- grid_vbg_info_unw$grid
ref_idx_vbg_unw <- grid_vbg_info_unw$ref_idx
co2_ref_vbg_unw <- grid_vbg_info_unw$co2_ref

fit_imv_vbg <- fit_spline_glm("imv_proc", "vbg_co2", subset_data_vbg, "VBG")
fit_niv_vbg <- fit_spline_glm("niv_proc", "vbg_co2", subset_data_vbg, "VBG")
fit_death_vbg <- fit_spline_glm("death_60d", "vbg_co2", subset_data_vbg, "VBG")

```

```

fit_hcrf_vbg <- fit_spline_glm("hypercap_resp_failure", "vbg_co2", subset_data_vbg, "VBG")
if (any(vapply(list(fit_imv_vbg, fit_niv_vbg, fit_death_vbg, fit_hcrf_vbg), is.null, logical(1)))) {
  stop("Unweighted VBG spline fits failed; see model_fit_diagnostics.csv.")
}

pred_imv_vbg <- predict_or_curve_from_fit(fit_imv_vbg, grid_vbg_unw, ref_idx_vbg_unw, "vbg_co2")
pred_niv_vbg <- predict_or_curve_from_fit(fit_niv_vbg, grid_vbg_unw, ref_idx_vbg_unw, "vbg_co2")
pred_death_vbg <- predict_or_curve_from_fit(fit_death_vbg, grid_vbg_unw, ref_idx_vbg_unw, "vbg_co2")
pred_hcrf_vbg <- predict_or_curve_from_fit(fit_hcrf_vbg, grid_vbg_unw, ref_idx_vbg_unw, "vbg_co2")
axis_unw_common <- compute_or_axis_spec(
  list(pred_imv, pred_niv, pred_death, pred_hcrf,
    pred_imv_vbg, pred_niv_vbg, pred_death_vbg, pred_hcrf_vbg),
  lo_col = "LCL", hi_col = "UCL"
)

plot_imv <- ggplot(pred_imv, aes(x = paco2, y = OR)) +
  geom_line(color = "blue", linewidth = 1.2) +
  geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "blue", alpha = 0.2) +
  geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
  or_axis_scale(axis_unw_common) +
  labs(title = "Intubation (adjusted)", x = "PaCO2 (mmHg)",
    y = paste0("Odds ratio (ref PaCO2 = ", co2_ref_abg_unw, "; log scale)")) +
  theme_minimal()

plot_niv <- ggplot(pred_niv, aes(x = paco2, y = OR)) +
  geom_line(color = "green", linewidth = 1.2) +
  geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "green", alpha = 0.2) +
  geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
  or_axis_scale(axis_unw_common) +
  labs(title = "NIV (adjusted)", x = "PaCO2 (mmHg)",
    y = paste0("Odds ratio (ref PaCO2 = ", co2_ref_abg_unw, "; log scale)")) +
  theme_minimal()

plot_death <- ggplot(pred_death, aes(x = paco2, y = OR)) +
  geom_line(color = "red", linewidth = 1.2) +
  geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "red", alpha = 0.2) +

```

```

geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
or_axis_scale(axis_unw_common) +
labs(title = "Death (60d, adjusted)", x = "PaCO2 (mmHg)",
y = paste0("Odds ratio (ref PaCO2 = ", co2_ref_abg_unw, "; log scale)")) +
theme_minimal()

plot_hcrcf <- ggplot(pred_hcrcf, aes(x = paco2, y = OR)) +
geom_line(color = "purple", linewidth = 1.2) +
geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "purple", alpha = 0.2) +
geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
or_axis_scale(axis_unw_common) +
labs(title = "Hypercapnic RF (adjusted)", x = "PaCO2 (mmHg)",
y = paste0("Odds ratio (ref PaCO2 = ", co2_ref_abg_unw, "; log scale)")) +
theme_minimal()

plot_imv_vbg <- ggplot(pred_imv_vbg, aes(x = vbg_co2, y = OR)) +
geom_line(color = "blue") +
geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "blue", alpha = 0.2) +
geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
or_axis_scale(axis_unw_common) +
labs(title = "IMV (adjusted)", x = "VBG CO2 (mmHg)",
y = paste0("Odds ratio (ref VBG CO2 = ", co2_ref_vbg_unw, "; log scale)")) +
theme_minimal()

plot_niv_vbg <- ggplot(pred_niv_vbg, aes(x = vbg_co2, y = OR)) +
geom_line(color = "green") +
geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "green", alpha = 0.2) +
geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
or_axis_scale(axis_unw_common) +
labs(title = "NIV (adjusted)", x = "VBG CO2 (mmHg)",
y = paste0("Odds ratio (ref VBG CO2 = ", co2_ref_vbg_unw, "; log scale)")) +
theme_minimal()

plot_death_vbg <- ggplot(pred_death_vbg, aes(x = vbg_co2, y = OR)) +
geom_line(color = "red") +
geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "red", alpha = 0.2) +

```

```

geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
or_axis_scale(axis_unw_common) +
labs(title = "Death (60d, adjusted)", x = "VBG CO2 (mmHg)",
y = paste0("Odds ratio (ref VBG CO2 = ", co2_ref_vbg_unw, "; log scale)")) +
theme_minimal()

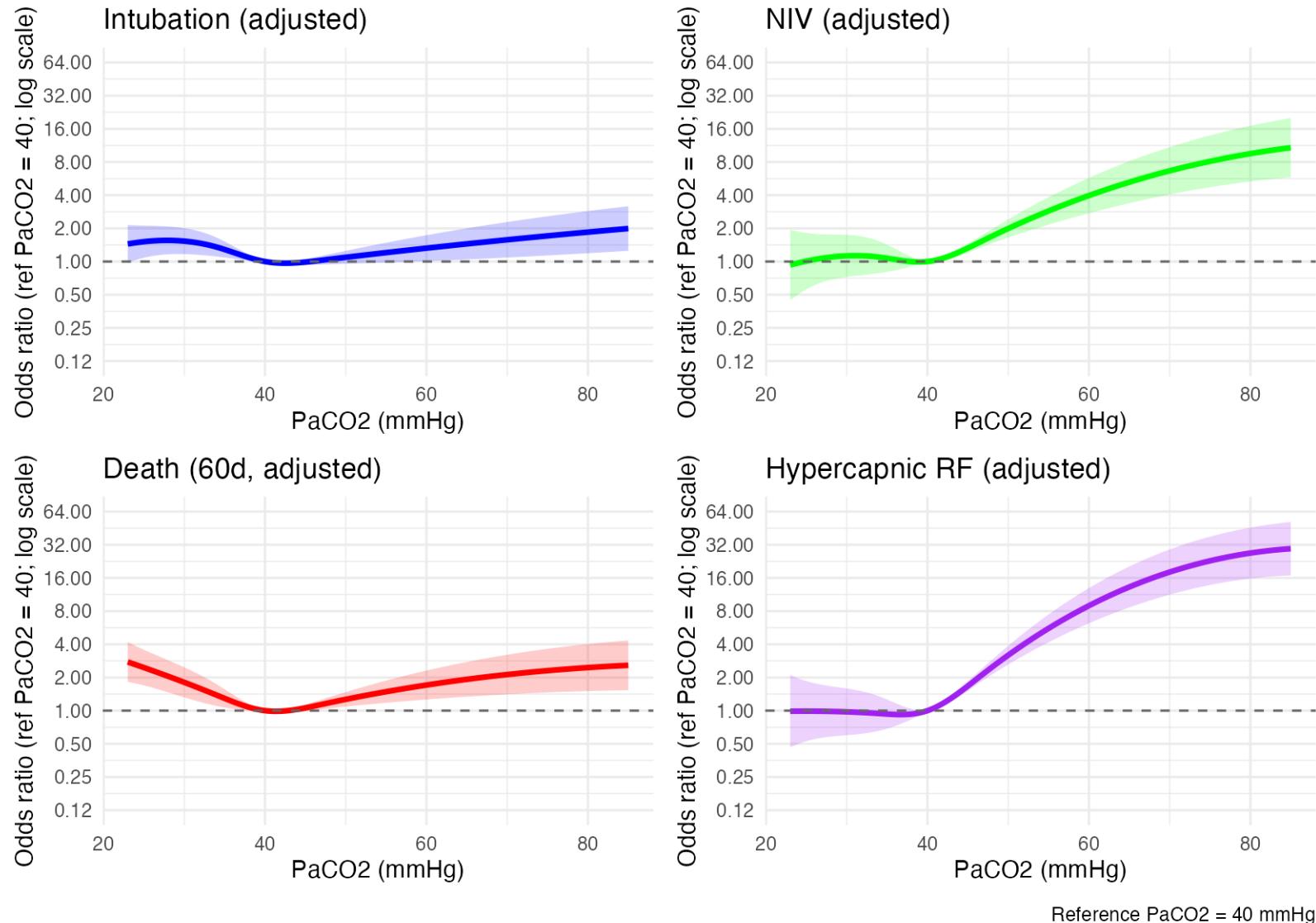
plot_hcrcf_vbg <- ggplot(pred_hcrcf_vbg, aes(x = vbg_co2, y = OR)) +
geom_line(color = "purple") +
geom_ribbon(aes(ymin = LCL, ymax = UCL), fill = "purple", alpha = 0.2) +
geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
or_axis_scale(axis_unw_common) +
labs(title = "Hypercapnic RF (adjusted)", x = "VBG CO2 (mmHg)",
y = paste0("Odds ratio (ref VBG CO2 = ", co2_ref_vbg_unw, "; log scale)")) +
theme_minimal()

unw_abg_panel <- (plot_imv | plot_niv) / (plot_death | plot_hcrcf) +
plot_annotation(caption = paste0("Reference PaCO2 = ", co2_ref_abg_unw, " mmHg"))

unw_vbg_panel <- ((plot_imv_vbg | plot_niv_vbg) /
(plot_death_vbg | plot_hcrcf_vbg)) +
plot_annotation(
  title = paste0("Adjusted odds ratios by VBG CO2 (ref = ", co2_ref_vbg_unw, ")"),
  caption = paste0("Reference VBG CO2 = ", co2_ref_vbg_unw, " mmHg")
)

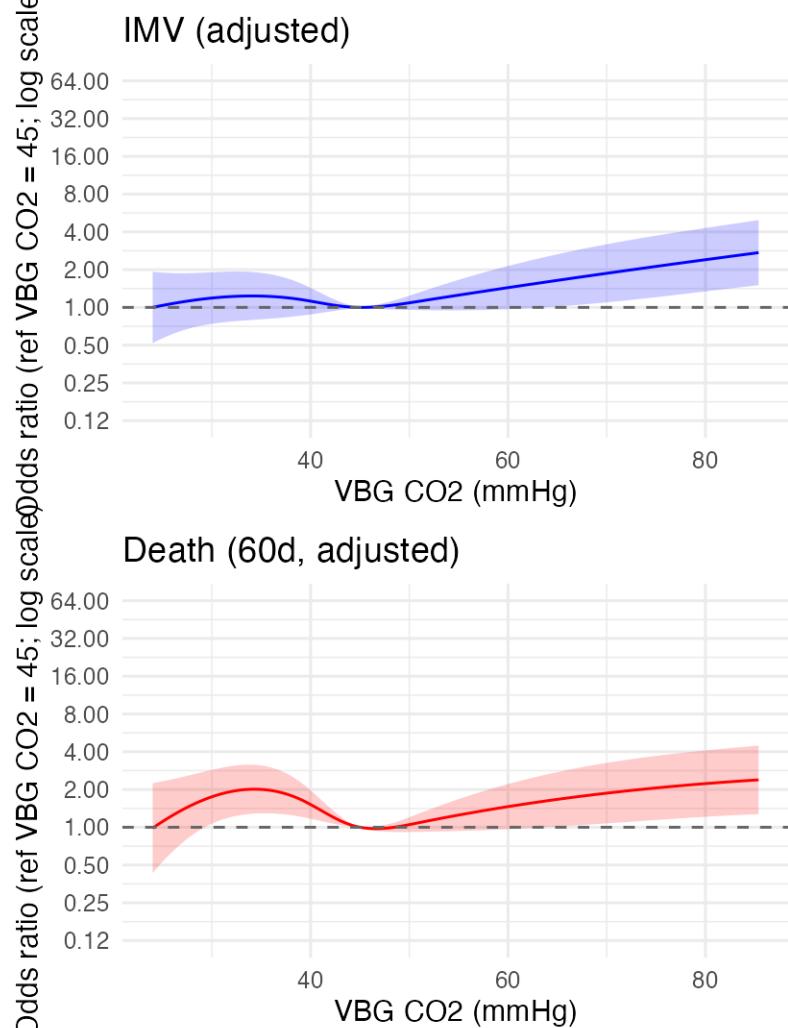
print_plot_once(unw_abg_panel, "spline-unweighted-abg", width = 8.5, height = 6)

```

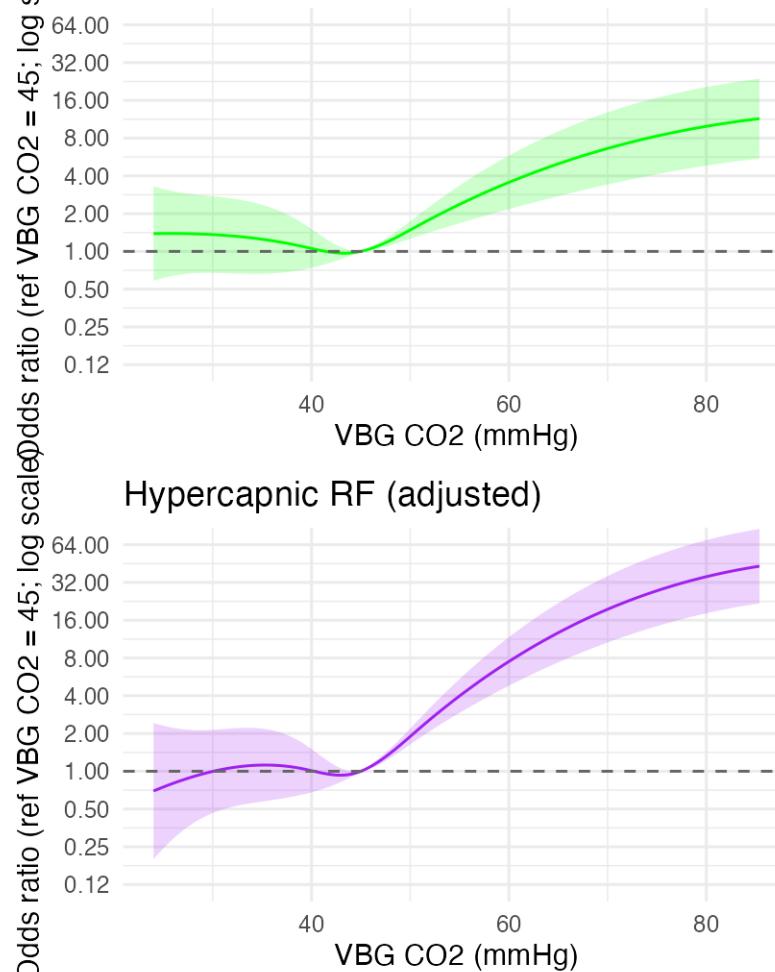


```
print_plot_once(unw_vbg_panel, "spline-unweighted-vbg", width = 8.5, height = 6)
```

Adjusted odds ratios by VBG CO₂ (ref = 45)



NIV (adjusted)



Reference VBG CO₂ = 45 mmHg

2 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: [39947224](#). PMCID: [PMC11825193](#).

Current propensity score uses `covars_gbm` (demographics, comorbidities, encounter type, vitals, labs) as defined above; in this block only `encounter_type` is explicitly factored before weighting.

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

1. Smaller GBM & balance-based stopping (`stop.method = “smd.max”`) → faster fit, avoids over-fitting, lighter tails (which lead to extreme weights that are problematic).
2. Target balance compares weighted treated cohort to the full sample; aim for $|SMD| < 0.1$.
3. Weight stabilization (divide by mean) mitigates a few huge weights. We use one-sided truncation at very small propensities (caps large weights only).
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.

2.0.1 5.1 ABG IPW weighting and diagnostics

```
# Already normalized globally; just drop unused levels
subset_data$encounter_type <- droplevels(subset_data$encounter_type)
```

GBM tuning is shared across ABG and VBG via `gbm_params` to keep symmetry; update there if needed.

```
#   1. fit GBM propensity model, ABG
set.seed(42)
gbm_df_abg <- subset_data[, c("has_abg", "has_vbg", covars_gbm), drop = FALSE]
gbm_df_abg <- normalize_types(gbm_df_abg, levels_ref)
gbm_df_abg <- droplevels_all(gbm_df_abg)
```

```

gbm_preflight(gbm_df_abg, covars_gbm, "unimp_abg")
append_mem_snapshot("gbm_unimp", "unimp_abg", "pre")

weight_model <- do.call(
  weightit,
  c(
    list(
      formula_abg,
      data      = gbm_df_abg,
      method    = "gbm",
      estimand  = "ATE",
      missing   = "ind",
      include.obj = FALSE
    ),
    gbm_params
  )
)
append_mem_snapshot("gbm_unimp", "unimp_abg", "post")

# 2. One-sided IPSW (ABG observed only) + truncation of small propensities
ipow_abg <- compute_ipow_weights(
  weight_model,
  treat = gbm_df_abg$has_abg,
  ps_floor_quantile = ps_trunc_quantile,
  stabilize = TRUE
)
w_abg <- ipow_abg$weights
ps_floor_abg <- ipow_abg$ps_floor
subset_data$trunc_abg <- ipow_abg$truncated
subset_data$ps_abg <- ipow_abg$ps
subset_data$w_abg <- w_abg
assert_finite_weights(w_abg[subset_data$has_abg == 1], "w_abg")
rm(weight_model, gbm_df_abg)
invisible(gc())

# Balance diagnostics and treated-only outcome models are handled later.

```

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

These are covariate-adjusted outcome models ($\text{outcome} \sim \text{spline}(\text{CO2}) + \text{X}$), fit separately for ABG and VBG cohorts using `survey::svyglm` with robust (design-based) SEs. Spline curves are shown as odds ratios relative to `CO2_ref` (midpoint of the normal range).

2.0.2 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
#
#
# Model diagrams: IPW ABG spline models
ipw_abg_rcs_forms <- list(
  "ABG IPW spline (adjusted): IMV ~ CO2 spline + X"      = make_spline_fml("imv_proc", "paco2", adj_core),
  "ABG IPW spline (adjusted): NIV ~ CO2 spline + X"      = make_spline_fml("niv_proc", "paco2", adj_core),
  "ABG IPW spline (adjusted): Death60d ~ CO2 spline + X" = make_spline_fml("death_60d", "paco2", adj_core),
  "ABG IPW spline (adjusted): HCRF ~ CO2 spline + X"     = make_spline_fml("hypercap_resp_failure", "paco2", adj_core)
)
register_model_diagrams(ipw_abg_rcs_forms)

# 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, all_of(adj_core)) %>%
  filter(complete.cases(.))

#
# 3. weighted logistic spline models with robust SEs
fitfun <- function(formula, outcome) {
  fit_res <- fit_with_diagnostics(
    function() svyglm(
```

```

formula,
design = svydesign(ids = ~1, weights = ~w_abg, data = subset_data_abg),
family = quasibinomial(),
control = glm.control(maxit = 50)
),
context = make_context(
  stage = "outcome",
  component = "spline",
  analysis_variant = "ipw",
  model_type = "spline",
  group = "ABG",
  outcome = outcome,
  imputation = NA_integer_,
  batch = NA_integer_
)
)
append_outcome_diag(fit_res$diag)
fit_res$fit
}

fit_imv_abg  <- fitfun(make_spline_fml("imv_proc", "paco2", adj_core), "imv_proc")
fit_niv_abg  <- fitfun(make_spline_fml("niv_proc", "paco2", adj_core), "niv_proc")
fit_death_abg <- fitfun(make_spline_fml("death_60d", "paco2", adj_core), "death_60d")
fit_hcrcf_abg <- fitfun(make_spline_fml("hypercap_resp_failure", "paco2", adj_core),
                           "hypercap_resp_failure")
if (any(vapply(list(fit_imv_abg, fit_niv_abg, fit_death_abg, fit_hcrcf_abg), is.null, logical(1)))) {
  stop("IPW ABG spline fits failed; see model_fit_diagnostics.csv.")
}

# 4. prediction helper
mkpred <- function(fit, data_ref, co2_var, ref_df, co2_ref) {
  co2_seq <- stats::quantile(data_ref[[co2_var]], probs = c(0.02, 0.98), na.rm = TRUE)
  grid_info <- make_co2_grid_ref(
    co2_var,
    seq(co2_seq[1], co2_seq[2], length.out = SPLINE_GRID_N),
    ref_df,

```

```

    co2_ref
  )
  predict_or_curve_from_fit(fit, grid_info$grid, grid_info$ref_idx, co2_var)
}

pred_imv_abg  <- mkpred(fit_imv_abg, subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)
pred_niv_abg  <- mkpred(fit_niv_abg, subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)
pred_death_abg <- mkpred(fit_death_abg, subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)
pred_hcrf_abg <- mkpred(fit_hcrf_abg, subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)
axis_abg_ipw_trim <- compute_or_axis_spec(
  list(pred_imv_abg, pred_niv_abg, pred_death_abg, pred_hcrf_abg),
  lo_col = "LCL", hi_col = "UCL"
)
# 5. plotting
# Plotting deferred until VBG curves are computed so axes can be shared.

```

Restricting plots bewtween 0.02 and 0.98

2.0.3 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, all_of(adj_core)) %>%
  filter(complete.cases(.))

fitfun <- function(formula, outcome) {
  fit_res <- fit_with_diagnostics(
    function() svyglm(
      formula,
      design = svydesign(ids = ~1, weights = ~w_abg, data = subset_data_abg),
      family = quasibinomial(),
      control = glm.control(maxit = 50)
    ),

```

```

context = make_context(
  stage = "outcome",
  component = "spline",
  analysis_variant = "ipw",
  model_type = "spline",
  group = "ABG",
  outcome = outcome,
  imputation = NA_integer_,
  batch = NA_integer_
)
)
append_outcome_diag(fit_res$diag)
fit_res$fit
}

fit_imv_abg <- fitfun(make_spline_fml("imv_proc", "paco2", adj_core), "imv_proc")
fit_niv_abg <- fitfun(make_spline_fml("niv_proc", "paco2", adj_core), "niv_proc")
fit_death_abg <- fitfun(make_spline_fml("death_60d", "paco2", adj_core), "death_60d")
fit_hcrcf_abg <- fitfun(make_spline_fml("hypercap_resp_failure", "paco2", adj_core),
                           "hypercap_resp_failure")
if (any(vapply(list(fit_imv_abg, fit_niv_abg, fit_death_abg, fit_hcrcf_abg), is.null, logical(1)))) {
  stop("IPW ABG spline fits (trimmed) failed; see model_fit_diagnostics.csv.")
}

# 4. prediction helper
mkpred <- function(fit, data_ref, co2_var, ref_df, co2_ref) {
  q <- stats::quantile(data_ref[[co2_var]], probs = c(0.02, 0.98), na.rm = TRUE)
  grid_info <- make_co2_grid_ref(
    co2_var,
    seq(q[1], q[2], length.out = SPLINE_GRID_N),
    ref_df,
    co2_ref
  )
  predict_or_curve_from_fit(fit, grid_info$grid, grid_info$ref_idx, co2_var)
}

```

```

pred_imv_abg   <- mkpred(fit_imv_abg,   subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)
pred_niv_abg   <- mkpred(fit_niv_abg,   subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)
pred_death_abg <- mkpred(fit_death_abg, subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)
pred_hcrcf_abg <- mkpred(fit_hcrcf_abg, subset_data_abg, "paco2", x_ref_abg, ABG_CO2_REF)

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

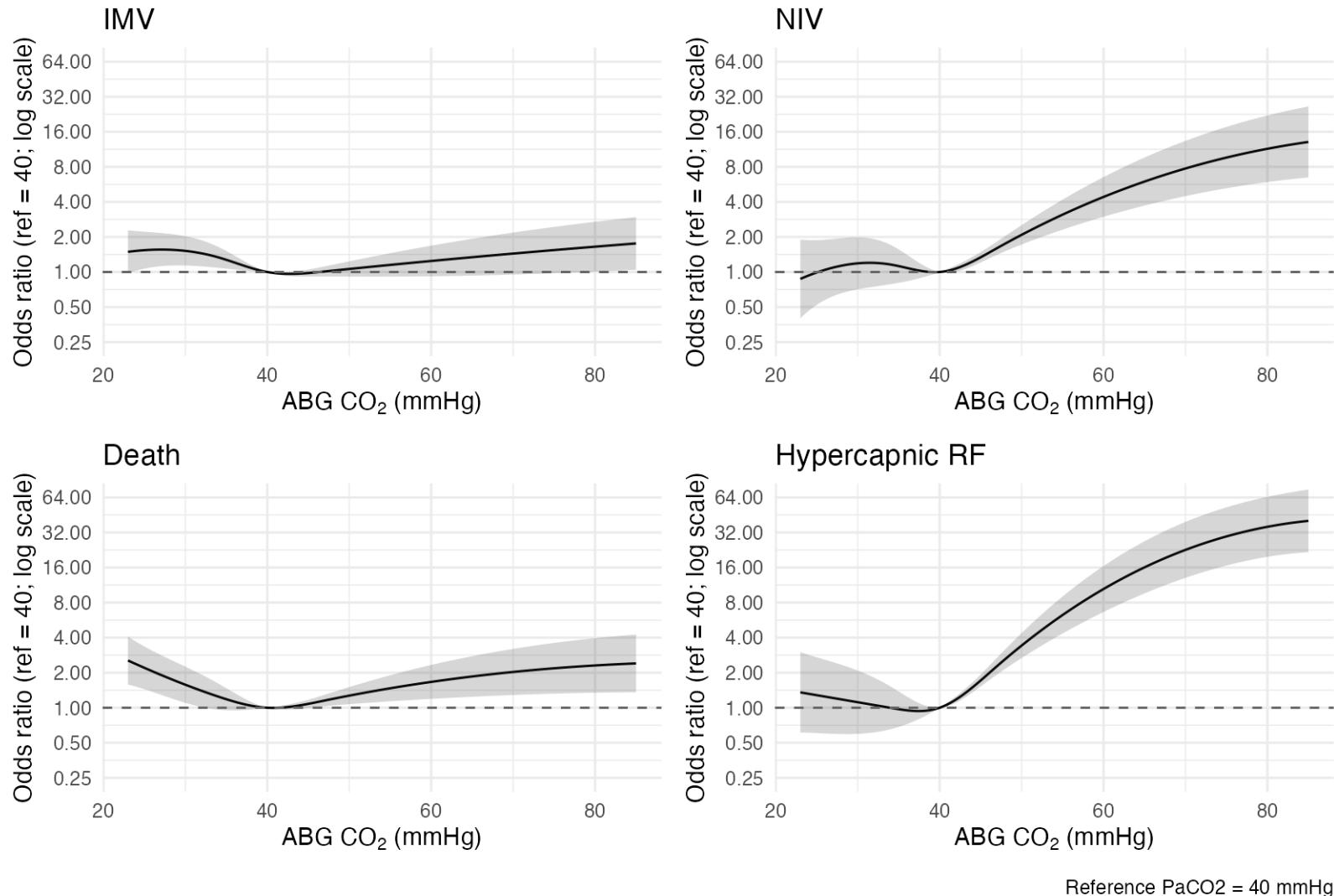
plt <- function(dat, title)
  ggplot(dat, aes(paco2, OR)) +
    geom_line() +
    geom_ribbon(aes(ymin = LCL, ymax = UCL), alpha = 0.2) +
    geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
    or_axis_scale(axis_abg_ipw_trim) +
    labs(title = title, x = xlab,
         y = paste0("Odds ratio (ref = ", ABG_CO2_REF, "; log scale)")) +
    theme_minimal()

ipw_abg_panel <- (patchwork::wrap_plots(
  plt(pred_imv_abg,    "IMV"),
  plt(pred_niv_abg,    "NIV"),
  plt(pred_death_abg,  "Death"),
  plt(pred_hcrcf_abg,  "Hypercapnic RF"),
  ncol = 2
)) +
  plot_annotation(
    title = paste0("Propensity-weighted adjusted odds ratios by ABG CO2 (ref = ",
                  ABG_CO2_REF, "; conditional on X; 2-98% range)"),
    caption = paste0("Reference PaCO2 = ", ABG_CO2_REF, " mmHg")
  )

print_plot_once(ipw_abg_panel, "spline-ipw-abg-trimmed", width = 8.5, height = 6)

```

Propensity-weighted adjusted odds ratios by ABG CO₂ (ref = 40; conditional on X; 2–98% range)



VBG uses the same GBM tuning as ABG (shared `gbm_params`).

2.0.4 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)
gbm_df_vbg <- subset_data[, c("has_abg", "has_vbg", covars_gbm), drop = FALSE]
gbm_df_vbg <- normalize_types(gbm_df_vbg, levels_ref)
gbm_df_vbg <- droplevels_all(gbm_df_vbg)
gbm_preflight(gbm_df_vbg, covars_gbm, "unimp_vbg")
append_mem_snapshot("gbm_unimp", "unimp_vbg", "pre")
w_vbg <- do.call(
  weightit,
  c(
    list(
      formula_vbg,
      data      = gbm_df_vbg,
      method    = "gbm",
      estimand  = "ATE",
      missing   = "ind",
      include.obj = FALSE
    ),
    gbm_params
  )
)
append_mem_snapshot("gbm_unimp", "unimp_vbg", "post")

# One-sided IPSW (VBG observed only) + truncation of small propensities
ipow_vbg <- compute_ipow_weights(
  w_vbg,
  treat = gbm_df_vbg$has_vbg,
  ps_floor_quantile = ps_trunc_quantile,
```

```

    stabilize = TRUE
)
w_vbg_ipow <- ipow_vbg$weights
ps_floor_vbg <- ipow_vbg$ps_floor
subset_data$trunc_vbg <- ipow_vbg$truncated
subset_data$ps_vbg <- ipow_vbg$ps
subset_data$w_vbg <- w_vbg_ipow
assert_finite_weights(w_vbg_ipow[subset_data$has_vbg == 1], "w_vbg")
rm(w_vbg, gbm_df_vbg)
invisible(gc())

# Balance diagnostics are handled later.

# 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, all_of(adj_core)) %>%
  filter(complete.cases(.))

fitfun <- function(formula, outcome) {
  fit_res <- fit_with_diagnostics(
    function() svyglm(
      formula,
      design = svydesign(ids = ~1, weights = ~w_vbg, data = subset_data_vbg),
      family = quasibinomial(),
      control = glm.control(maxit = 50)
    ),
    context = make_context(
      stage = "outcome",
      component = "spline",
      analysis_variant = "ipw",
      model_type = "spline",
      group = "VBG",
      outcome = outcome,
      imputation = NA_integer_
    )
  )
}
```

```

    batch = NA_integer_
  )
)
append_outcome_diag(fit_res$diag)
fit_res$fit
}

# Model diagrams: IPW VBG spline models
ipw_vbg_rcs_forms <- list(
  "VBG IPW spline (adjusted): IMV ~ CO2 spline + X"      = make_spline_fml("imv_proc", "vbg_co2", adj_core),
  "VBG IPW spline (adjusted): NIV ~ CO2 spline + X"      = make_spline_fml("niv_proc", "vbg_co2", adj_core),
  "VBG IPW spline (adjusted): Death60d ~ CO2 spline + X" = make_spline_fml("death_60d", "vbg_co2", adj_core),
  "VBG IPW spline (adjusted): HCRF ~ CO2 spline + X"      = make_spline_fml("hypercap_resp_failure", "vbg_co2", adj_core)
)
register_model_diagrams(ipw_vbg_rcs_forms)

fit_imv_vbg   <- fitfun(make_spline_fml("imv_proc", "vbg_co2", adj_core), "imv_proc")
fit_niv_vbg   <- fitfun(make_spline_fml("niv_proc", "vbg_co2", adj_core), "niv_proc")
fit_death_vbg <- fitfun(make_spline_fml("death_60d", "vbg_co2", adj_core), "death_60d")
fit_hcrf_vbg  <- fitfun(make_spline_fml("hypercap_resp_failure", "vbg_co2", adj_core),
                           "hypercap_resp_failure")
if (any(vapply(list(fit_imv_vbg, fit_niv_vbg, fit_death_vbg, fit_hcrf_vbg), is.null, logical(1)))) {
  stop("IPW VBG spline fits failed; see model_fit_diagnostics.csv.")
}

# 4. Prediction helper -----
mkpred <- function(fit, data_ref, co2_var, ref_df, co2_ref) {
  co2_seq <- stats::quantile(data_ref[[co2_var]], probs = c(0.02, 0.98), na.rm = TRUE)
  grid_info <- make_co2_grid_ref(
    co2_var,
    seq(co2_seq[1], co2_seq[2], length.out = SPLINE_GRID_N),
    ref_df,
    co2_ref
  )
  predict_or_curve_from_fit(fit, grid_info$grid, grid_info$ref_idx, co2_var)
}

```

```

pred_imv_vbg   <- mkpred(fit_imv_vbg,   subset_data_vbg, "vbg_co2", x_ref_vbg, VBG_CO2_REF)
pred_niv_vbg   <- mkpred(fit_niv_vbg,   subset_data_vbg, "vbg_co2", x_ref_vbg, VBG_CO2_REF)
pred_death_vbg <- mkpred(fit_death_vbg, subset_data_vbg, "vbg_co2", x_ref_vbg, VBG_CO2_REF)
pred_hcrf_vbg  <- mkpred(fit_hcrf_vbg,  subset_data_vbg, "vbg_co2", x_ref_vbg, VBG_CO2_REF)
axis_ipw_common <- compute_or_axis_spec(
  list(pred_imv_abg, pred_niv_abg, pred_death_abg, pred_hcrf_abg,
       pred_imv_vbg, pred_niv_vbg, pred_death_vbg, pred_hcrf_vbg),
  lo_col = "LCL", hi_col = "UCL"
)

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

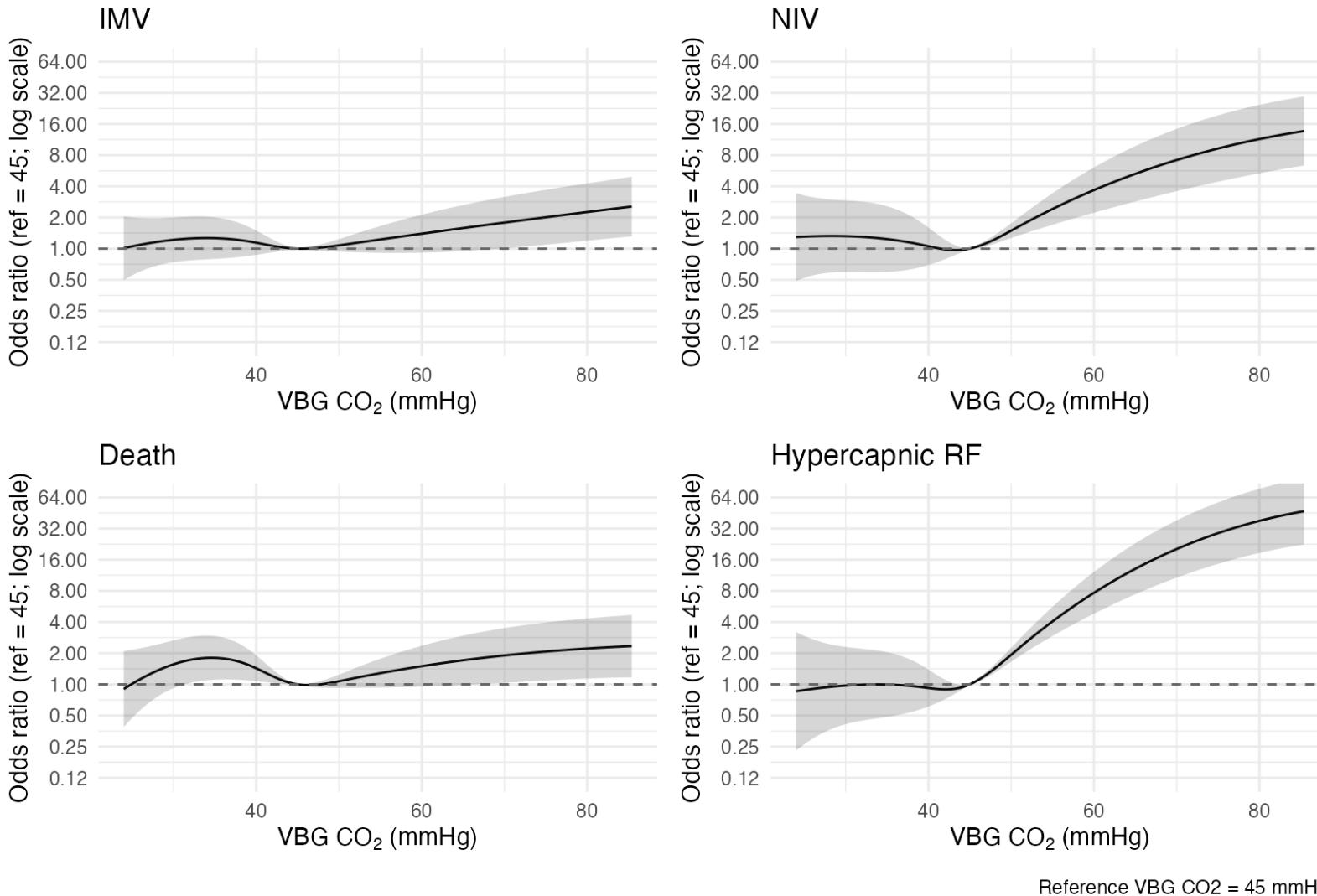
plt <- function(dat, title)
  ggplot(dat, aes(vbg_co2, OR)) +
    geom_line() +
    geom_ribbon(aes(ymin = LCL, ymax = UCL), alpha = 0.2) +
    geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
    or_axis_scale(axis_ipw_common) +
    labs(title = title, x = xlab,
         y = paste0("Odds ratio (ref = ", VBG_CO2_REF, "; log scale)")) +
    theme_minimal()

ipw_vbg_panel <- (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 = paste0("Propensity-weighted adjusted odds ratios by VBG CO2 (ref = ",
                  VBG_CO2_REF, "; conditional on X)"),
    caption = paste0("Reference VBG CO2 = ", VBG_CO2_REF, " mmHg")
)

```

```
print_plot_once(ipw_vbg_panel, "spline-ipw-vbg", width = 8.5, height = 6)
```

Propensity-weighted adjusted odds ratios by VBG CO₂ (ref = 45; conditional on X)



```

# ABG plots with the same axis (shared with VBG)
xlab_abg <- expression(paste("ABG CO"[2], " (mmHg)"))

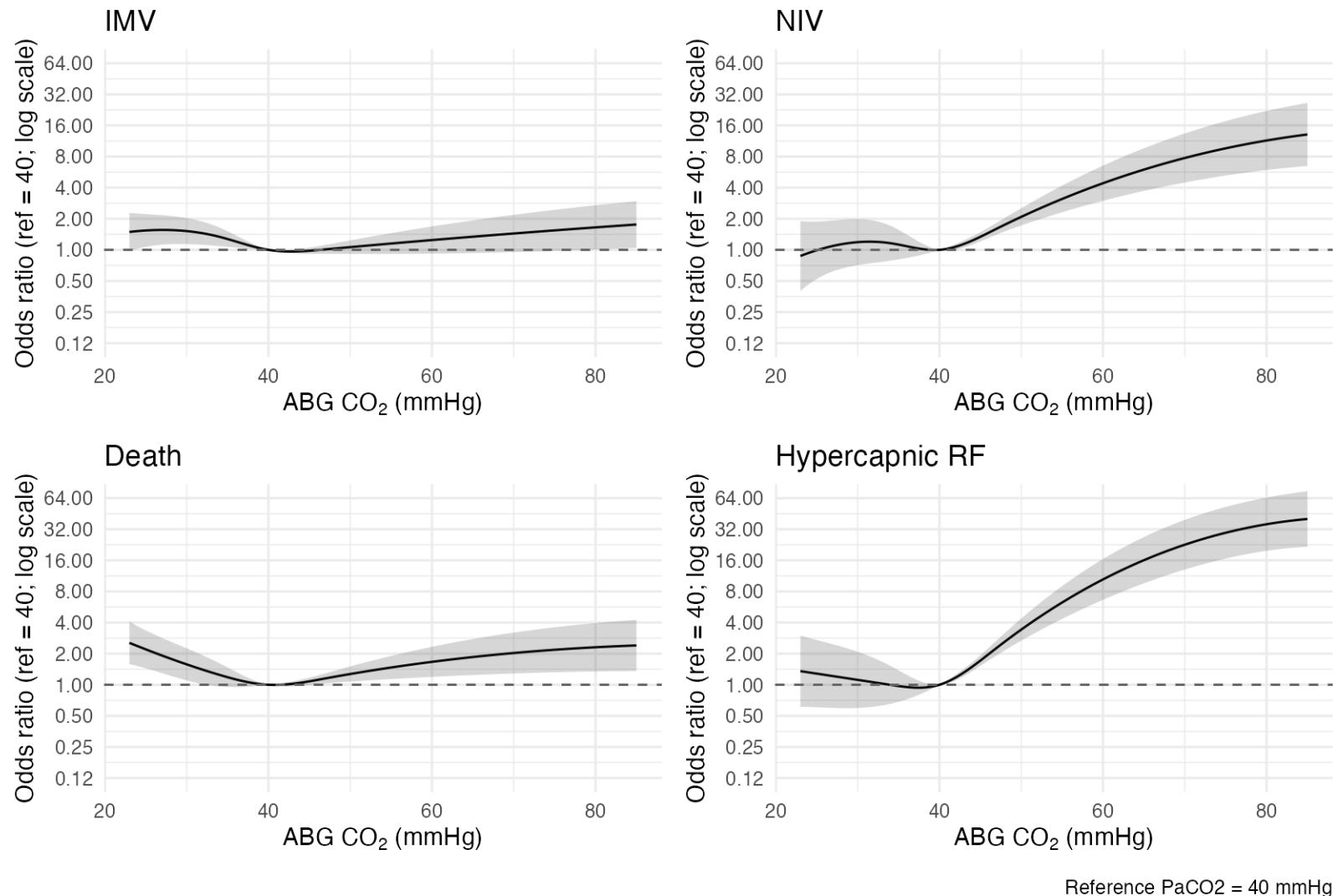
plt_abg <- function(dat, title)
  ggplot(dat, aes(paco2, OR)) +
    geom_line() +
    geom_ribbon(aes(ymin = LCL, ymax = UCL), alpha = 0.2) +
    geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
    or_axis_scale(axis_ipw_common) +
    labs(title = title, x = xlab_abg,
         y = paste0("Odds ratio (ref = ", ABG_CO2_REF, "; log scale)")) +
    theme_minimal()

ipw_abg_shared_panel <- (patchwork::wrap_plots(
  plt_abg(pred_imv_abg,    "IMV"),
  plt_abg(pred_niv_abg,    "NIV"),
  plt_abg(pred_death_abg, "Death"),
  plt_abg(pred_hcrf_abg,   "Hypercapnic RF"),
  ncol = 2
)) +
  plot_annotation(
    title = paste0("Propensity-weighted adjusted odds ratios by ABG CO2 (ref = ",
                  ABG_CO2_REF, "; conditional on X)"),
    caption = paste0("Reference PaCO2 = ", ABG_CO2_REF, " mmHg")
  )

print_plot_once(ipw_abg_shared_panel, "spline-ipw-abg-shared", width = 8.5, height = 6)

```

Propensity-weighted adjusted odds ratios by ABG CO₂ (ref = 40; conditional on X)



2.0.5 5.5 Three-level PCO₂ categories (weighted; ABG, VBG)

Three groups with weights and covariate adjustment

```

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

# 1. Ensure PCO2 categories are present
stopifnot(all(c("pc02_cat_abg", "pc02_cat_vbg") %in% names(subset_data)))

# 2. Function: weighted logistic regression & OR extraction
run_weighted_or <- function(data, outcome, cat_var, weight_var, group_name,
                           treat_var, adj_vars) {
  stopifnot(!is.null(treat_var))
  stopifnot(!is.null(adj_vars))
  dat <- data %>%
    filter(
      .data[[treat_var]] == 1,
      !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 = CO2_CAT_LEVELS)
    ) %>%
    droplevels()

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

  rhs_terms <- c(cat_var, adj_vars)
  fml <- stats::reformulate(rhs_terms, response = outcome)
}

```

```

fit_res <- fit_with_diagnostics(
  function() svyglm(fml, design = design, family = quasibinomial(),
    control = glm.control(maxit = 50)),
  context = make_context(
    stage = "outcome",
    component = "cat3",
    analysis_variant = "ipw",
    model_type = "cat3",
    group = group_name,
    outcome = outcome,
    imputation = NA_integer_,
    batch = NA_integer_
  )
)
append_outcome_diag(fit_res$diag)
if (is.null(fit_res$fit)) {
  stop("run_weighted_or: model fit failed for outcome=", outcome,
    " cat_var=", cat_var, " group=", group_name)
}

tidy(fit_res$fit, exponentiate = TRUE, conf.int = TRUE) %>%
  filter(term != "(Intercept)", startsWith(term, cat_var)) %>%
  mutate(
    group    = group_name,
    outcome   = outcome
  )
}

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

ipw_three_level_forms <- list(
  "ABG IPW 3-level: IMV ~ CO2 category + X"      = reformulate(c("pc02_cat_abg", adj_core), response = "imv_proc"),
  "ABG IPW 3-level: NIV ~ CO2 category + X"      = reformulate(c("pc02_cat_abg", adj_core), response = "niv_proc"),
  "ABG IPW 3-level: Death60d ~ CO2 category + X" = reformulate(c("pc02_cat_abg", adj_core), response = "death_60d"),
  "ABG IPW 3-level: HCRF ~ CO2 category + X"     = reformulate(c("pc02_cat_abg", adj_core), response = "hypercap_resp_failure"),
)

```

```

"VBG IPW 3-level: IMV ~ CO2 category + X"      = reformulate(c("pco2_cat_vbg", adj_core), response = "imv_proc"),
"VBG IPW 3-level: NIV ~ CO2 category + X"      = reformulate(c("pco2_cat_vbg", adj_core), response = "niv_proc"),
"VBG IPW 3-level: Death60d ~ CO2 category + X" = reformulate(c("pco2_cat_vbg", adj_core), response = "death_60d"),
"VBG IPW 3-level: HCRF ~ CO2 category + X"      = reformulate(c("pco2_cat_vbg", adj_core), response = "hypercap_resp_failure")
)
register_model_diagrams(ipw_three_level_forms)

ipw_combined_or_df <- bind_rows(
  lapply(outcomes_ipw, function(out)
    run_weighted_or(subset_data, out, "pco2_cat_abg", "w_abg",       "ABG",
                     treat_var = "has_abg", adj_vars = adj_core)),
  lapply(outcomes_ipw, function(out)
    run_weighted_or(subset_data, out, "pco2_cat_vbg", "w_vbg",       "VBG",
                     treat_var = "has_vbg", adj_vars = adj_core))
)
ipw_threellevel_results <- ipw_combined_or_df %>%
  mutate(method = "IPW adjusted")

ipw_combined_or_df <- map_or_exposure(ipw_combined_or_df, "or-plot-three-level-weighted")
ipw_combined_or_df$group <- factor(ipw_combined_or_df$group, levels = c("ABG", "VBG"))

# 4. Plot weighted odds ratios
ipw_plot_df <- build_or_plot_df(ipw_combined_or_df, "or-plot-three-level-weighted",
                                  expected_exposure_levels = CO2_CAT_CONTRAST_LEVELS)
ipw_axis_spec <- compute_or_axis_spec(ipw_plot_df, lo_col = "conf.low", hi_col = "conf.high",
                                       default_limits = OR_XLIM)
ipw_p_or <- plot_or_safe(
  ipw_plot_df,
  plot_name = "or-plot-three-level-weighted",
  axis_spec = ipw_axis_spec,
  title   = "Adjusted weighted odds ratios by PCO2 category (ABG, VBG)"
)
print_plot_once(ipw_p_or, "or-plot-three-level-weighted", width = 7.5, height = 4.8)

```



2.1 6) Propensity score diagnostics

Plotting propensity scores

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

library(dplyr)
library(ggplot2)
```

```

library(scales)

stopifnot("has_abg" %in% names(subset_data))
stopifnot("has_vbg" %in% names(subset_data))
stopifnot(all(c("ps_abg", "ps_vbg") %in% names(subset_data)))

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

# Bind, clean, and factorize for plotting
df_ps_cond <- bind_rows(ps_dfs_cond) %>%
  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
p_ps_cond <- ggplot(df_ps_cond, aes(x = ps, fill = treat)) +
  geom_histogram(aes(y = after_stat(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(

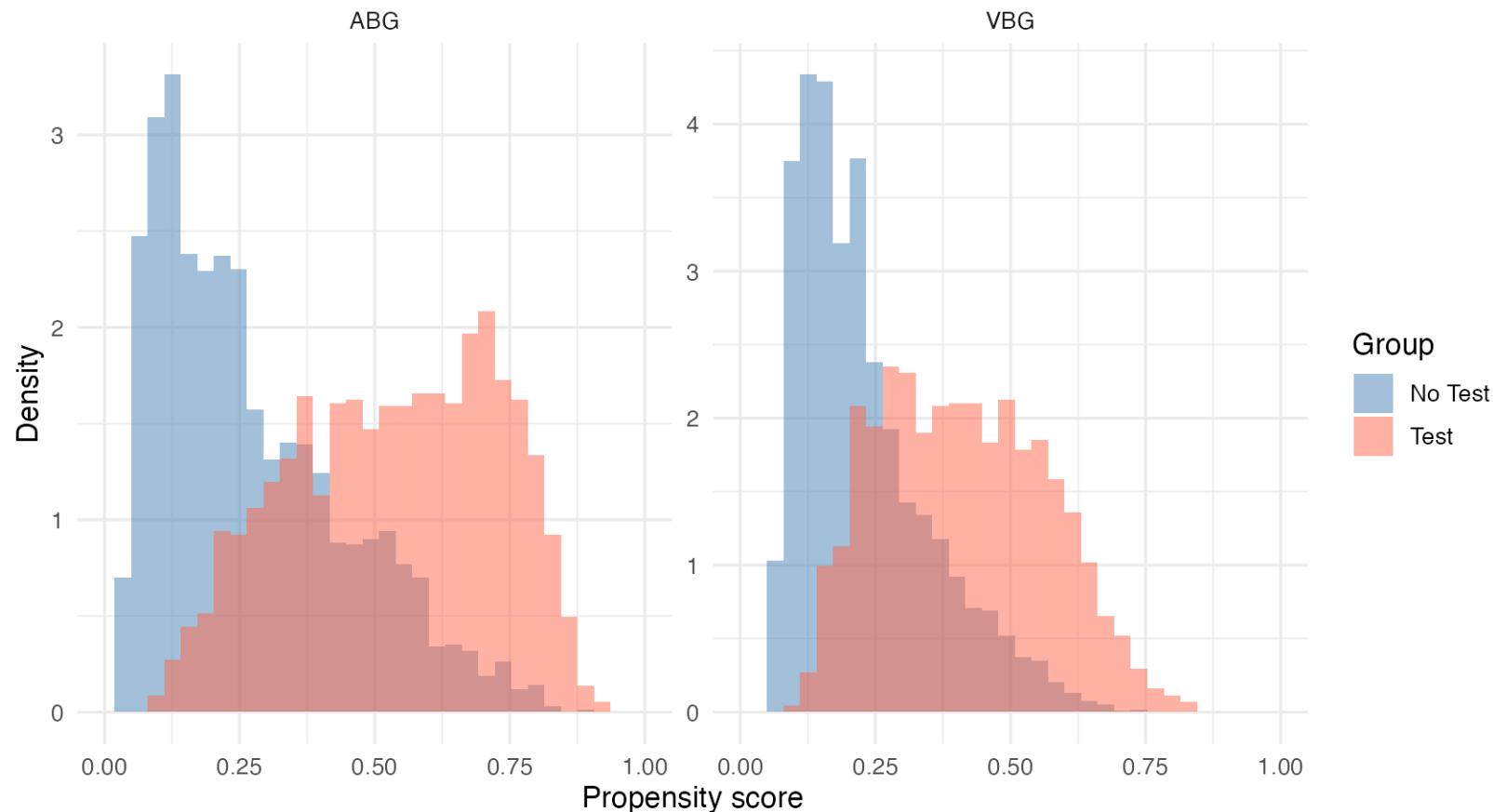
```

```

title = "Propensity Score Distributions",
x      = "Propensity score",
y      = "Density",
fill   = "Group"
) +
theme_minimal(base_size = 12)
print_plot_once(p_ps_cond, "propensity-histograms-conditional", width = 8.5, height = 5)

```

Propensity Score Distributions



```

stopifnot(all(c("ps_abg", "ps_vbg") %in% names(subset_data)))

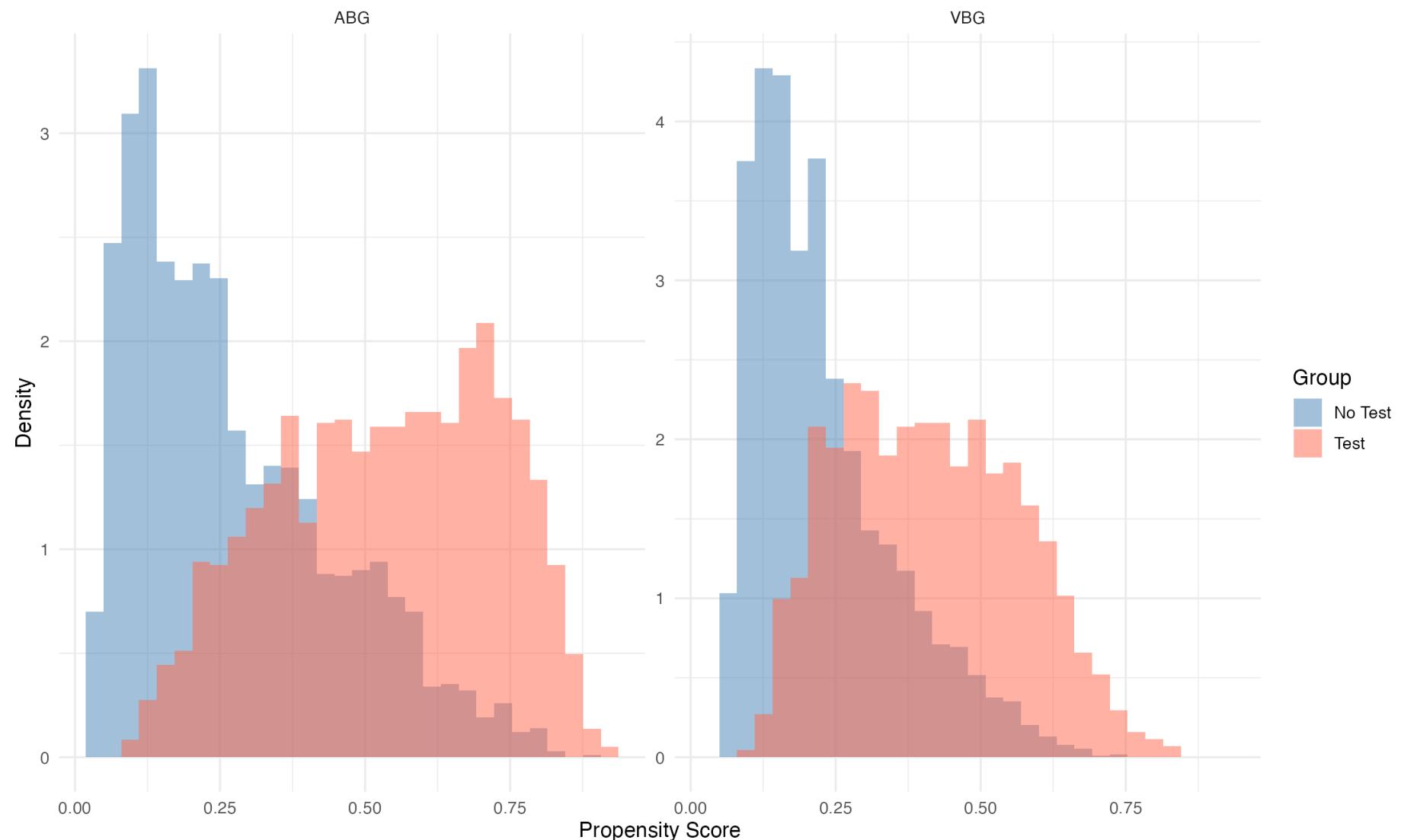
ps_dfs_all <- list(
  ABG = data.frame(
    ps      = subset_data$ps_abg,
    treat   = subset_data$has_abg,
    ScoreType = "ABG"
  ),
  VBG = data.frame(
    ps      = subset_data$ps_vbg,
    treat   = subset_data$has_vbg,
    ScoreType = "VBG"
  )
)

df_ps_all <- bind_rows(ps_dfs_all) %>%
  mutate(
    treat     = factor(treat, levels = c(0,1), labels = c("No Test", "Test")),
    ScoreType = factor(ScoreType, levels = c("ABG", "VBG"))
  )

ggplot(df_ps_all, aes(x = ps, fill = treat)) +
  geom_histogram(aes(y = after_stat(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)

```

Propensity Score Distributions



```
append_mem_snapshot("stage2", "end", "post")
stage2_rm <- c(
  "ipow_abg", "ipow_vbg", "w_abg", "w_vbg_ipow",
```

```

"subset_data_abg", "subset_data_vbg",
"fit_imv_abg", "fit_niv_abg", "fit_death_abg", "fit_hcrf_abg",
"pred_imv_abg", "pred_niv_abg", "pred_death_abg", "pred_hcrf_abg",
"fit_imv_vbg", "fit_niv_vbg", "fit_death_vbg", "fit_hcrf_vbg",
"pred_imv_vbg", "pred_niv_vbg", "pred_death_vbg", "pred_hcrf_vbg",
"plt", "mkpred",
"ipw_combined_or_df", "ipw_plot_df", "ipw_p_or", "ipw_axis_spec", "outcomes_ipw",
"df_ps_cond", "ps_dfs_cond", "p_ps_cond",
"df_ps_all", "ps_dfs_all"
)
missing_stage2 <- setdiff(stage2_rm, ls())
stopifnot(length(missing_stage2) == 0)
rm(list = stage2_rm)
invisible(gc())
append_mem_snapshot("stage2", "cleanup", "post")

```

3 Multiple Imputation Analysis

added 12/6/2025

```

# Core MI + diagnostics
library(mice)          # chained equations (MICE)
library(miceadds)       # pooling helpers & utilities
library(naniar)         # missingness summaries/plots
library(visdat)         # quick type/missingness viz
library(skimr)          # data skim for large frames

# 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(mitoools)      # MIcombine for pooling (generic)
library(parallel)       # basic parallel where helpful

# Parallel + progress setup
library(future)

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

mi_mids_file    <- results_path("mi_abg_vbg_mids.rds")
mi_logistic_ps_abg_file   <- results_path("mi_logistic_ps_abg_list.rds")
mi_logistic_ps_vbg_file   <- results_path("mi_logistic_ps_vbg_list.rds")
mi_pooled_file   <- results_path("mi_pooled_results.rds")

# Use sequential futures to avoid PSOCK cluster startup failures during render
future::plan(sequential)

# 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

M_IMP    <- 80
MAXIT_MI <- 20
MI_SEED   <- 20251206
DEBUG_SPLINE <- FALSE

```

```

M_IMP_TARGET <- 80
M_IMP_MIN <- 20
M_IMP_STEP <- 10
MCERR_RATIO_TARGET <- 0.10
ALLOW_M_IMP_EARLY_STOP <- FALSE

# MI propensity model (MI-only)
MI_PS_METHOD      <- "glm_rcs4"
MI_PS_SPLINE_K    <- 4L
MI_GLM_MAXIT      <- 25L

MINCOR_QUICKPRED <- 0.05
MINPUC_QUICKPRED <- 0.25
MAX_PRED_PER_VAR <- 40L
MAX_MM_COLS <- 300L
MAX_LEVELS_PRED <- 100L
COR_SAMPLE_N <- 50000L
MI_MAX_BYTES <- 8e9

MI_RAM_GB <- 16L
MI_BATCH_START <- ifelse(MI_RAM_GB <= 16, 2L, 5L)
MI_BATCH_MIN <- 1L
MI_BATCH_SEED_STRIDE <- 100000L
MI_GC_EVERY_BATCH <- TRUE
MI_PREEMPTIVE_BATCH_REDUCE <- TRUE
MI_VCELLS_FRAC_THRESHOLD <- 0.80
MI_SMOKE_TEST <- TRUE
MI_DEBUG_PRINTFLAG <- FALSE
MI_MEMORY_HYGIENE <- TRUE
FORCE_MI_BATCHED <- FALSE

stopifnot(exists("RUN_MODE"), exists("FULL_RUN"))

M_IMP <- M_IMP_TARGET
M_IMP_MIN <- max(M_IMP_MIN, 50L)
if (isTRUE(DEBUG_SPLINE)) {

```

```

    stop("DEBUG_SPLINE must be FALSE; pilot and full runs must use the same model workflow.")
}
stopifnot(M_IMP >= M_IMP_MIN, M_IMP <= 100)
stopifnot(MI_PS_METHOD %in% c("glm_rcs4"))

# Key covariates + outcomes used in MI (plus report-only BNP/Spo2)
extra_miss_vars <- intersect(c("bpn", "spo2"), names(subset_data_raw))
miss_vars <- unique(c(
  covars_ps,
  extra_miss_vars,
  "paco2", "vbg_co2", "vbg_o2sat",
  "has_abg", "has_vbg",
  "imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure"
))
miss_vars <- intersect(miss_vars, names(subset_data_raw))

miss_tbl <- subset_data_raw |>
  dplyr::select(dplyr::all_of(miss_vars)) |>
  dplyr::summarise(dplyr::across(dplyr::everything(), ~ sum(is.na(.)))) |>
  tidyr::pivot_longer(dplyr::everything(), names_to = "variable", values_to = "n_missing") |>
  dplyr::mutate(
    total_n      = nrow(subset_data_raw),
    pct_missing = 100 * n_missing / total_n
  ) |>
  dplyr::arrange(dplyr::desc(pct_missing))

miss_tbl_disp <- miss_tbl |>
  dplyr::mutate(
    n_missing    = scales::comma(n_missing),
    pct_missing = sprintf("%.1f%%", pct_missing)
  ) |>
  dplyr::select(variable, n_missing, pct_missing)

gt::gt(miss_tbl_disp) |>
  gt::tab_header(title = "Pre-imputation missingness") |>
  gt::cols_label(

```

```

variable      = "Variable",
n_missing    = "Missing (n)",
pct_missing  = "Missing (%)"
) |>
gt::tab_source_note(
  paste0(
    "n = ", nrow(subset_data_raw),
    "; MI plan: m = ", M_IMP, " imputations (seed ", MI_SEED,
    "); methods: logreg (binary), polyreg (categorical), pmm (numeric).",
    if (length(extra_miss_vars)) " BNP and Sp02 are reported here but excluded from MI/weighting models." else ""
  )
)

```

```

# MI propensity model helpers (glm with RCS on continuous covariates)
ps_is_continuous <- function(v, df) {
  x <- df[[v]]
  if (!is.numeric(x)) return(FALSE)
  x <- x[is.finite(x)]
  if (length(x) < 10) return(FALSE)
  if (length(unique(x)) < 10) return(FALSE)
  TRUE
}

build_mi_ps_formula <- function(treat, covars, df, k = 4L, basis = "rcs") {
  cont <- covars[vapply(covars, ps_is_continuous, logical(1), df = df)]
  catv <- setdiff(covars, cont)
  term_cont <- character()
  if (length(cont)) {
    term_cont <- if (basis == "rcs") {
      paste0("rms::rcs(`", cont, "`", ", k, `")")
    } else {
      paste0("splines::ns(`", cont, "`", ", k, `")")
    }
  }
  term_cat <- if (length(catv)) paste0("`", catv, "`") else character()

```

Pre-imputation missingness

Variable	Missing (n)	Missing (%)
vbg_o2sat	4,474	86.5%
bnp	4,221	81.6%
vbg_co2	3,730	72.1%
spo2	3,676	71.0%
paco2	3,264	63.1%
serum_lac	3,125	60.4%
curr_bmi	2,934	56.7%
serum_phos	2,732	52.8%
temp_new	2,501	48.3%
hr	1,890	36.5%
dbp	1,556	30.1%
sbp	1,544	29.8%
wbc	894	17.3%
serum_ca	515	10.0%
serum_cr	481	9.3%
serum_k	402	7.8%
plt	401	7.7%
serum_cl	298	5.8%
serum_hco3	282	5.4%
sodium	261	5.0%
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%
	124	0.0%

```

rhs <- c(term_cont, term_cat)
if (!length(rhs)) stop("No covariates available for MI PS model.")
stats::as.formula(paste0(``, treat, `` ~ ``, paste(rhs, collapse = " + ")))
}

fit_mi_ps_glm <- function(df, treat, covars, k = 4L, maxit = 25L, context = NULL) {
  stopifnot(all(c(treat, covars) %in% names(df)))
  df <- droplevels_all(df)
  basis <- if (requireNamespace("rms", quietly = TRUE)) "rcs" else "ns"
  if (is.null(context)) {
    context <- make_context(
      stage = "MI", component = "mi_ps_glm",
      analysis_variant = "weighted_imputed",
      model_type = "ps",
      group = NA_character_,
      outcome = NA_character_,
      imputation = NA_integer_,
      batch = NA_integer_
    )
  }

  fit_once <- function(basis_type) {
    if (basis_type == "rcs") {
      dd <- rms::datadist(df)
      old_opt <- options(datadist = ".__dd_ps__")
      assign(".__dd_ps__", dd, envir = .GlobalEnv)
      on.exit({
        options(old_opt)
        rm(list = ".__dd_ps__", envir = .GlobalEnv)
      }, add = TRUE)
    }
    form <- build_mi_ps_formula(treat, covars, df, k = k, basis = basis_type)
    cap <- capture_warnings(
      tryCatch(
        stats::glm(form, data = df, family = stats::binomial(),
                  control = stats::glm.control(maxit = maxit),

```

```

        model = FALSE, x = FALSE, y = FALSE),
    error = function(e) e
  ),
  context = context
)
append_warnings(cap$warnings)
list(fit = cap$value, formula = form, basis = basis_type)
}

res <- fit_once(basis)
if (inherits(res$fit, "error") && basis == "rcs") {
  res <- fit_once("ns")
}
if (inherits(res$fit, "error")) {
  return(list(error = conditionMessage(res$fit), method = paste0("glm_", res$basis)))
}

ps <- as.numeric(res$fit$fitted.values)
ps <- pmin(pmax(ps, 1e-8), 1 - 1e-8)
list(
  ps = ps,
  fit_ok = TRUE,
  converged = if (!is.null(res$fit$converged)) isTRUE(res$fit$converged) else NA,
  formula = as.character(res$formula),
  n = nrow(df),
  p = length(res$fit$coefficients),
  method = paste0("glm_", res$basis)
)
}

```

3.0.1 7.2 Missingness structure and drivers

```

library(dplyr)
library(tidyr)

```

```

library(rlang)

# Use raw data for missingness rates; normalized data for model-based drivers
miss_data <- subset_data_raw
model_data <- subset_data

# Focus on key variables (same as MI set) for consistency
extra_miss_vars <- intersect(c("bnp", "spo2"), names(miss_data))
miss_vars <- unique(c(
  covars_ps,
  extra_miss_vars,
  "paco2", "vbg_co2", "vbg_o2sat",
  "has_abg", "has_vbg",
  "imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure"
))
miss_vars <- intersect(miss_vars, names(miss_data))
stopifnot(length(miss_vars) > 0)

# Strata to compare missingness across
strata_vars <- c("has_abg", "has_vbg",
                 "imv_proc", "death_60d", "encounter_type", "location")
strata_vars <- intersect(strata_vars, names(miss_data))

# Overall missingness %
miss_overall <- miss_data |>
  summarise(across(all_of(miss_vars), ~ mean(is.na(.)) * 100)) |>
  pivot_longer(everything(), names_to = "variable", values_to = "pct_missing_overall")

# Missingness % on model_data (used for driver models)
miss_overall_model <- model_data |>
  summarise(across(all_of(intersect(miss_vars, names(model_data)))), ~ mean(is.na(.)) * 100)) |>
  pivot_longer(everything(), names_to = "variable", values_to = "pct_missing_overall_model")

# Missingness by strata (percent within each level)
miss_by_strata <- purrr::map_dfr(strata_vars, function(sv) {
  # drop the current grouping variable from targets

```

```

vars_here <- setdiff(intersect(miss_vars, names(miss_data)), sv)
stopifnot(length(vars_here) > 0L)
stopifnot(sv %in% names(miss_data))

miss_data |>
  group_by(.data[[sv]]) |>
  summarise(across(all_of(vars_here), ~ mean(is.na(.)) * 100), .groups = "drop") |>
  pivot_longer(-all_of(sv), names_to = "variable", values_to = "pct_missing") |>
  rename(level = !!sym(sv)) |>
  mutate(
    stratum = sv,
    level   = as.character(level)
  )
}

# Combine overall + strata (save full table; display full table in PDF)
miss_panel_full <- miss_by_strata |>
  left_join(miss_overall, by = "variable") |>
  arrange(desc(pct_missing_overall), stratum, level)

miss_panel_file <- results_path("missingness-by-strata.csv")
write_csv_safely(miss_panel_full, miss_panel_file, row_names = FALSE)

render_table_pdf_maybe(
  miss_panel_full,
  caption = "Missingness by key strata (pre-imputation).",
  file_stub = "missingness_by_strata",
  digits = 1,
  show = SHOW_LOW_VALUE_TABLES
)

```

```

# --- Drivers of missingness (logit I(NA) on observed covariates) -----
# Candidate predictors (observed covariates only)
driver_covars <- intersect(
  c("age_at_encounter", "sex", "encounter_type", "location", "curr_bmi",

```

```

  "has_abg", "has_vbg", "imv_proc", "death_60d"),
  names(model_data)
)

# Fit models for variables with any missingness
vars_to_model <- miss_overall_model |>
  filter(pct_missing_overall_model > 0) |>
  pull(variable)
vars_to_model <- intersect(vars_to_model, names(model_data))

skip_log <- list()

model_results <- purrr::map_dfr(vars_to_model, function(v) {
  df <- model_data |>
    select(all_of(c(v, driver_covars))) |>
    mutate(miss = as.integer(is.na(.data[[v]])))

  # use only rows with observed predictors and varying miss indicator
  df <- df[stats::complete.cases(df[driver_covars]), , drop = FALSE]
  if (nrow(df) == 0L) {
    skip_log[[length(skip_log) + 1L]] <- data.frame(
      variable = v,
      reason = "no_complete_cases",
      stringsAsFactors = FALSE
    )
    return(tibble::tibble())
  }
  if (dplyr::n_distinct(df$miss) < 2L) {
    skip_log[[length(skip_log) + 1L]] <- data.frame(
      variable = v,
      reason = "miss_indicator_constant",
      stringsAsFactors = FALSE
    )
    return(tibble::tibble())
  }
})

```

```

fml <- as.formula(paste0("miss ~ ", paste(driver_covars, collapse = " + ")))
if (length(driver_covars) > 0L) {
  diag_outcome <- paste0("missing_", make.names(v))
  diag_terms <- paste0(~, driver_covars, ~, collapse = " + ")
  diag_fml <- stats::as.formula(paste0(diag_outcome, " ~ ", diag_terms))
  register_model_diagram(paste("Missingness model:", v), diag_fml, width = 10, height = 6)
}
fit <- tryCatch(
  suppressWarnings(glm(fml, data = df, family = binomial())),
  error = function(e) e
)
if (inherits(fit, "error")) {
  stop("Missingness driver: glm failed for variable ", v)
}

broom::tidy(fit, conf.int = FALSE, exponentiate = FALSE) |>
  filter(term != "(Intercept)") |>
  mutate(
    OR = exp(estimate),
    LCL = exp(estimate - 1.96 * std.error),
    UCL = exp(estimate + 1.96 * std.error)
  ) |>
  transmute(
    variable = v,
    term,
    OR,
    LCL,
    UCL,
    p.value
  )
}

skip_tbl <- dplyr::bind_rows(skip_log)
write_csv_safely(skip_tbl, results_path("missingness_driver_skips.csv"), row_names = FALSE)

if (nrow(model_results) > 0) {

```

```

model_results_file <- results_path("missingness-drivers.csv")
model_results_out <- model_results |>
  dplyr::mutate(run_id = diag_run_id)
write_csv_safely(model_results_out, model_results_file, row_names = FALSE)

model_results_disp <- model_results_out |>
  dplyr::select(-run_id) |>
  arrange(p.value) |>
  mutate(
    OR = round(OR, 2),
    LCL = round(LCL, 2),
    UCL = round(UCL, 2),
    p.value = signif(p.value, 3)
  )

render_table_pdf_maybe(
  model_results_disp,
  caption = "Predictors of missingness (logit OR).",
  file_stub = "missingness-drivers",
  digits = 2,
  show = SHOW_LOW_VALUE_TABLES
)
} else {
  model_results_stub <- data.frame(
    variable = character(),
    term = character(),
    OR = numeric(),
    LCL = numeric(),
    UCL = numeric(),
    p.value = numeric(),
    stringsAsFactors = FALSE
  )
  write_csv_safely(model_results_stub, results_path("missingness-drivers.csv"), row_names = FALSE)
  message("No modelable missingness signals (all complete or no variation).")
}

```

3.0.2 7.3 Monte Carlo error check after MI

3.1 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.

```
# Types are normalized in the schema-normalize block.
```

3.2 9) Imputation model specification (MICE)

3.2.1 9.1 Predictor matrix & methods. Run MICE (moderate settings for scale)

```
# --- variables for propensity score model (kept identical to main analysis) ---
# ----- MICE setup: include PaCO2/VBG CO2 as predictors but do not impute -----
library(mice)
library(dplyr)

# --- add analysis targets and CO2 measures explicitly -----
mi_vars <- setdiff(unique(c(
  covars_ps,
  "has_abg", "has_vbg",                                # treatments (NOT imputed)
  "imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure",  # outcomes (NOT imputed)
  co2_vars
)), drop_vars_ultra_missing)

mi_df <- subset_data[, mi_vars, drop = FALSE]
mi_df <- normalize_types(mi_df, levels_ref)

mi_df_size <- utils::object.size(mi_df)
message("MI data size (bytes): ", format(mi_df_size, units = "auto"))

# Rough memory preflight based on total missing cells (imputed values only).
miss_counts <- vapply(mi_df, function(x) sum(is.na(x)), numeric(1))
miss_total <- sum(miss_counts)
```

```

if (is.finite(miss_total) && miss_total > 0) {
  est_bytes <- miss_total * M_IMP * 8
  message("MI imputation storage estimate: ", format(structure(est_bytes, class = "object_size"), units = "auto"))
  if (est_bytes > MI_MAX_BYTES) {
    m_max <- floor(MI_MAX_BYTES / (miss_total * 8))
    m_target <- max(50L, m_max)
    if (m_target < 50L) {
      stop("Estimated MI storage exceeds memory (m=", M_IMP,
           ", estimated=", format(structure(est_bytes, class = "object_size"), units = "auto"),
           "). Reduce missingness or MI scope, or increase available memory.")
    }
    if (m_target < M_IMP) {
      message("Reducing M_IMP from ", M_IMP, " to ", m_target,
              " to stay within MI_MAX_BYTES.")
      M_IMP <- m_target
    }
  }
}

# Make binary comorbid 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"))
})

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

# Guardrail: high-cardinality factors can blow up MICE model matrices.
# Exclude them from predictorMatrix and (if missing) make "Missing" explicit.
high_card <- names(which(vapply(mi_df, function(x) is.factor(x) && nlevels(x) > MAX_LEVELS_PRED, logical(1))))
if (length(high_card)) {

```

```

message("MICE: high-cardinality factors detected (nlevels > ", MAX_LEVELS_PRED, "): ",
       paste(high_card, collapse = ", "))
for (v in high_card) {
  if (any(is.na(mi_df[[v]]))) {
    lv <- levels(mi_df[[v]])
    tmp <- as.character(mi_df[[v]])
    tmp[is.na(tmp)] <- "Missing"
    mi_df[[v]] <- factor(tmp, levels = unique(c(lv, "Missing")))
    if (!is.null(levels_ref) && !is.null(levels_ref[[v]])) &&
      !"Missing" %in% levels_ref[[v]]) {
      levels_ref[[v]] <- c(levels_ref[[v]], "Missing")
    }
  }
}

# --- 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, outcomes, or CO2 exposures
no_imp <- c("has_abg", "has_vbg", "imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure",
           "paco2", "vbg_co2")
if (length(high_card)) no_imp <- unique(c(no_imp, high_card))
meth[intersect(names(meth), no_imp)] <- ""

# predictor matrix; force has_abg/has_vbg as predictors, but do not impute no_imp

```

```

pred <- mice:::quickpred(mi_df, mincor = MINCOR_QUICKPRED, minpuc = MINPUC_QUICKPRED)
for (nm in intersect(c("has_abg", "has_vbg"), colnames(pred))) {
  pred[, nm] <- 1
}
pred[intersect(rownames(pred), no_imp), ] <- 0

if (length(high_card)) {
  pred[, intersect(high_card, colnames(pred))] <- 0
  pred[intersect(high_card, rownames(pred)), ] <- 0
}

# Ensure dropped covariates do not appear as predictors
drop_covars <- intersect(drop_vars_ultra_missing, colnames(pred))
if (length(drop_covars)) {
  pred[, drop_covars] <- 0
}

# Non-imputed variables with missingness should NOT be predictors
no_imp_with_missing <- intersect(no_imp, names(mi_df))
no_imp_with_missing <- no_imp_with_missing[
  vapply(mi_df[no_imp_with_missing], function(x) any(is.na(x)), logical(1))
]
no_imp_with_missing <- setdiff(no_imp_with_missing, c("has_abg", "has_vbg"))

pred_cols_check <- intersect(c("paco2", "vbg_co2"), colnames(pred))
if (length(pred_cols_check)) {
  message(
    "MICE: predictor column sums (pre-exclude) for ",
    paste(pred_cols_check, collapse = ", "),
    ":",
    paste(colSums(pred[, pred_cols_check, drop = FALSE]), collapse = ", ")
  )
}
if (length(no_imp_with_missing)) {
  pred[, intersect(no_imp_with_missing, colnames(pred))] <- 0
  message("MICE: excluded non-imputed missing predictors: ",
}

```

```

        paste(no_imp_with_missing, collapse = " ", ""))
}

if (length(pred_cols_check)) {
  message(
    "MICE: predictor column sums (post-exclude) for ",
    paste(pred_cols_check, collapse = " ", ""),
    ": ",
    paste(colSums(pred[, pred_cols_check, drop = FALSE]), collapse = " ", "")
  )
}

# Ensure key covariates with missingness have predictors (avoid zero-row pred)
core_preds <- intersect(
  c("age_at_encounter", "sex", "race_ethnicity", "location", "encounter_type",
    "has_abg", "has_vbg", "imv_proc", "niv_proc", "death_60d",
    "hypercap_resp_failure", "paco2", "vbg_co2"),
  colnames(pred)
)
core_preds <- setdiff(core_preds, no_imp_with_missing)
vars_need_pred <- intersect(covars_ps, rownames(pred))
vars_need_pred <- setdiff(vars_need_pred, no_imp)
vars_need_pred <- vars_need_pred[vapply(mi_df[vars_need_pred], function(x) any(is.na(x)), logical(1))]
zero_pred <- vars_need_pred[rowSums(pred[vars_need_pred, , drop = FALSE] != 0, na.rm = TRUE) == 0]
if (length(zero_pred)) {
  message("MICE predictor rows empty for: ", paste(zero_pred, collapse = " ", ),
         ". Adding core predictors.")
  pred[zero_pred, core_preds] <- 1
}
pred[intersect(rownames(pred), no_imp), ] <- 0
pred[c(zero_pred), c(zero_pred)] <- 0

# --- Preflight and cap predictor rows to avoid huge model matrices -------

n_mm_cols <- function(pred_row, df) {
  preds <- names(which(pred_row != 0))
  cols <- 1L
}

```

```

for (p in preds) {
  x <- df[[p]]
  if (is.factor(x)) {
    lv <- nlevels(x)
    cols <- cols + max(1L, lv - 1L)
  } else {
    cols <- cols + 1L
  }
}
cols
}

pred_width_preflight <- function(pred, df, meth) {
  vars <- names(meth)[meth != ""]
  vars <- vars[vapply(df[vars], function(x) any(is.na(x)), logical(1))]
  rows <- lapply(vars, function(v) {
    pred_row <- pred[v, ]
    n_pred <- sum(pred_row != 0, na.rm = TRUE)
    mm_cols <- n_mm_cols(pred_row, df)
    x <- df[[v]]
    nlevels_v <- if (is.factor(x)) nlevels(x) else NA_integer_
    miss_n <- sum(is.na(x))
    data.frame(
      variable = v,
      method = meth[[v]],
      n_pred = n_pred,
      mm_cols = mm_cols,
      nlevels_v = nlevels_v,
      miss_n = miss_n,
      stringsAsFactors = FALSE
    )
  })
  if (!length(rows)) {
    return(data.frame(variable = character(), method = character(), n_pred = integer(),
                     mm_cols = integer(), nlevels_v = integer(), miss_n = integer()))
  }
}

```

```

    dplyr::bind_rows(rows)
}

preflight_pre <- pred_width_preflight(pred, mi_df, meth) |>
  dplyr::mutate(stage = "pre")

core_preds <- intersect(
  c("age_at_encounter", "sex", "race_ethnicity", "location", "encounter_type",
    "has_abg", "has_vbg", "imv_proc", "niv_proc", "death_60d",
    "hypercap_resp_failure", "paco2", "vbg_co2"),
  colnames(pred))
)
core_preds <- setdiff(core_preds, no_imp_with_missing)

set.seed(MI_SEED + 100)
idx <- sample.int(nrow(mi_df), min(COR_SAMPLE_N, nrow(mi_df)))

vars_cap <- names(meth)[meth != ""]
vars_cap <- vars_cap[vapply(mi_df[vars_cap], function(x) any(is.na(x))), logical(1)]]

pred_nlevels <- function(x) {
  if (is.factor(x)) nlevels(x) else 1L
}

for (v in vars_cap) {
  cand <- names(which(pred[, ] != 0))
  if (!length(cand)) next
  keep <- intersect(core_preds, cand)
  rem  <- setdiff(cand, keep)

  if (length(rem)) {
    y_raw <- mi_df[[v]][idx]
    y <- if (is.factor(y_raw)) as.integer(y_raw) else suppressWarnings(as.numeric(y_raw))
    scores <- vapply(rem, function(r) {
      x_raw <- mi_df[[r]][idx]
      x <- if (is.factor(x_raw)) as.integer(x_raw) else suppressWarnings(as.numeric(x_raw))
    })
  }
}

```

```

    suppressWarnings(abs(stats::cor(y, x, use = "pairwise.complete.obs")))
}, numeric(1))
ord <- order(is.na(scores), -scores)
rem_keep <- rem[ord]
rem_keep <- rem_keep[seq_len(min(length(rem_keep), max(0L, MAX_PRED_PER_VAR - length(keep))))]
} else {
  rem_keep <- character()
}

keep_all <- unique(c(keep, rem_keep))
pred[v, ] <- 0
pred[v, keep_all] <- 1
pred[v, v] <- 0

mm_cols <- n_mm_cols(pred[v, ], mi_df)
if (mm_cols > MAX_MM_COLS) {
  drop_pool <- setdiff(keep_all, keep)
  if (!length(drop_pool)) drop_pool <- keep
  drop_order <- drop_pool[order(vapply(drop_pool, function(p) pred_nlevels(mi_df[[p]]), integer(1)),
                                 decreasing = TRUE)]
  for (p in drop_order) {
    if (p %in% keep && length(keep) == 1) break
    pred[v, p] <- 0
    mm_cols <- n_mm_cols(pred[v, ], mi_df)
    if (mm_cols <= MAX_MM_COLS) break
  }
}
}

preflight_post <- pred_width_preflight(pred, mi_df, meth) |>
  dplyr::mutate(stage = "post")
preflight_all <- dplyr::bind_rows(preflight_pre, preflight_post)
write_csv_safely(preflight_all, results_path("mice_pred_width_preflight.csv"), row_names = FALSE)

# MI integrity: treatments/outcomes excluded; binaries use logreg
stopifnot(all(meth[no_imp] == ""))

```

```

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))))
bin_fac <- setdiff(bin_fac, no_imp)
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 -----
mi_df_run <- mi_df
M_IMP_RUN <- M_IMP
MAXIT_RUN <- MAXIT_MI
FORCE_MI_BATCHED <- nrow(mi_df_run) > MI_BATCH_THRESHOLD

if (!requireNamespace("digest", quietly = TRUE)) {
  stop("Package 'digest' is required for MI checkpoint signatures.")
}

make_mi_signature <- function(df) {
  classes <- vapply(df, function(x) class(x)[1], character(1))
  na_counts <- vapply(df, function(x) sum(is.na(x)), integer(1))
  nlevels <- vapply(df, function(x) if (is.factor(x)) nlevels(x) else NA_integer_, integer(1))
  lvl_hash <- vapply(df, function(x) {
    if (!is.factor(x)) return(NA_character_)
    digest::digest(levels(x), algo = "xxhash64")
  }, character(1))
  col_sig <- data.frame(
    name = names(df),
    class = classes,
    na = na_counts,
    nlevels = nlevels,

```

```

    lvl_hash = lvl_hash,
    stringsAsFactors = FALSE
)
hash <- digest::digest(
  list(dim = dim(df), col_sig = col_sig),
  algo = "xxhash64"
)
list(
  hash = hash,
  nrow = nrow(df),
  ncol = ncol(df),
  run_mode = RUN_MODE,
  pilot_frac = PILOT_FRAC,
  mi_pilot_mode = RUN_MODE,
  sample_seed = SAMPLE_SEED,
  mi_seed = MI_SEED,
  col_sig = col_sig
)
}

mi_smoke_log_path <- results_path("mice_smoketest.log")
write_smoke_log <- function(lines) {
  write_diag_lines(lines, mi_smoke_log_path)
}

mem_max <- tryCatch(mem.maxVSize(), error = function(e) NA_real_)
mem_env <- Sys.getenv("R_MAX_VSIZE", unset = NA_character_)
gc_pre <- utils::capture.output(gc())
write_smoke_log(c(
  paste0("MI smoke test log: ", Sys.time()),
  paste0("mem.maxVSize: ", ifelse(is.na(mem_max), "NA", format(mem_max, scientific = FALSE))),
  paste0("R_MAX_VSIZE env: ", ifelse(nchar(mem_env), mem_env, "NA")),
  paste0("mi_df size: ", format(utils::object.size(mi_df), units = "auto")),
  paste0("mi_df_run size: ", format(utils::object.size(mi_df_run), units = "auto")),
  "gc() pre:",
  gc_pre
)

```

```

))
if (RUN_MODE == "full" && is.finite(mem_max) && mem_max < 2.2e10) {
  message("Full run on ~16GB memory: consider running MI/weights on a >32GB machine for speed.")
}

subset_data_saved <- FALSE
subset_data_path <- results_path("subset_data_pre_mi.rds")
if (MI_MEMORY_HYGIENE) {
  saveRDS(subset_data, subset_data_path)
  rm(subset_data)
  subset_data_saved <- TRUE
  invisible(gc())
}

run_mice_call <- function(m_val, maxit, seed_val, print_flag = FALSE) {
  mice::mice(
    data          = mi_df_run,
    m            = m_val,
    maxit        = maxit,
    predictorMatrix = pred,
    method       = meth,
    printFlag     = print_flag,
    seed         = seed_val
  )
}

if (MI_SMOKE_TEST) {
  smoke_con <- file(mi_smoke_log_path, open = "at")
  sink(smoke_con, type = "output")

  cap_smoke <- capture_warnings(
    tryCatch(
      run_mice_call(m_val = 1L, maxit = 1L, seed_val = MI_SEED, print_flag = TRUE),
      error = function(e) e
    ),
    context = make_context(

```

```

stage = "MI",
component = "mice_smoketest",
analysis_variant = "mi",
model_type = "mice",
group = NA_character_,
outcome = NA_character_,
imputation = NA_integer_,
batch = NA_integer_
)
)
append_warnings(cap_smoke$warnings)
sink(type = "output")
close(smoke_con)

if (inherits(cap_smoke$value, "error")) {
  smoke_msg <- conditionMessage(cap_smoke$value)
  message("MICE smoke test failed: ", smoke_msg)
  write_smoke_log(c(
    "Smoke test failed.",
    paste0("Error: ", smoke_msg)
  ))
  if (grepl("vector memory limit", smoke_msg, fixed = TRUE)) {
    MI_DEBUG_PRINTFLAG <- TRUE
  }
  if (subset_data_saved) {
    subset_data <- readRDS(subset_data_path)
  }
  if (MI_DEBUG_PRINTFLAG) {
    debug_path <- results_path("mice_debug_print.txt")
    dbg_con <- file(debug_path, open = "wt")
    sink(dbg_con, type = "output")
    message("Debug MI: running m=1, maxit=1 with printFlag=TRUE.")
    tryCatch(
      run_mice_call(m_val = 1L, maxit = 1L, seed_val = MI_SEED, print_flag = TRUE),
      error = function(e) e
    )
  }
}

```

```

    sink(type = "output")
    close(dbg_con)
}
stop("MICE smoke test failed; see ", mi_smoke_log_path, " and Results/mice_debug_print.txt.")
} else {
  message("MICE smoke test succeeded (m=1, maxit=1).")
}
}

get_vcells_stats <- function() {
  g <- gc()
  cn <- colnames(g)
  mb_cols <- cn[grep("\\\\(Mb\\\\)", cn)]
  used_mb_col <- if (length(mb_cols)) mb_cols[1] else NA_character_
  limit_col <- cn[grep("limit", cn, ignore.case = TRUE)]
  limit_col <- if (length(limit_col)) limit_col[1] else NA_character_
  trig_col <- cn[grep("trigger", cn, ignore.case = TRUE)]
  trig_col <- if (length(trig_col)) trig_col[1] else NA_character_
  max_col <- cn[grep("max", cn, ignore.case = TRUE)]
  max_col <- if (length(max_col)) max_col[1] else NA_character_

  used_mb <- if (!is.na(used_mb_col)) as.numeric(g["Vcells", used_mb_col]) else NA_real_
  limit_mb <- if (!is.na(limit_col)) as.numeric(g["Vcells", limit_col]) else NA_real_
  trig_mb <- if (!is.na(trig_col)) as.numeric(g["Vcells", trig_col]) else NA_real_
  max_mb <- if (!is.na(max_col)) as.numeric(g["Vcells", max_col]) else NA_real_

  if (!is.finite(limit_mb) || limit_mb <= 0) {
    mem_lim <- tryCatch(mem.maxVSize(), error = function(e) NA_real_)
    if (is.finite(mem_lim) && mem_lim > 0) {
      limit_mb <- if (mem_lim < 1e8) mem_lim else mem_lim / 1024^2
    }
  }

  data.frame(
    gc_vcells_used_mb = used_mb,
    gc_vcells_limit_mb = limit_mb,

```

```

    gc_vcells_frac = ifelse(is.finite(limit_mb) && limit_mb > 0, used_mb / limit_mb, NA_real_),
    gc_vcells_trigger_mb = trig_mb,
    gc_vcells_max_used_mb = max_mb,
    stringsAsFactors = FALSE
)
}

set.seed(MI_SEED)
run_mice_single <- function(m_val) {
  runtime_logger(
    "mice_imputation",
    run_mice_call(m_val = m_val, maxit = MAXIT_RUN, seed_val = MI_SEED, print_flag = FALSE),
    notes = paste0("m=", m_val, "; maxit=", MAXIT_RUN)
  )
}

mc_progress <- list()
sentinel_specs <- list(
  list(name = "abg_imv", outcome = "imv_proc", treat = "has_abg", co2_var = "paco2",
       low = ABG_CO2_LOW, high = ABG_CO2_HIGH),
  list(name = "vbg_imv", outcome = "imv_proc", treat = "has_vbg", co2_var = "vbg_co2",
       low = VBG_CO2_LOW, high = VBG_CO2_HIGH)
)

mcerr_ratio_for_spec <- function(imp_obj, spec) {
  fits <- lapply(seq_len(imp_obj$m), function(i) {
    d <- mice::complete(imp_obj, action = i)
    d <- d[, c(spec$outcome, spec$treat, spec$co2_var), drop = FALSE]
    d <- d[d[[spec$treat]] == 1 & is.finite(d[[spec$co2_var]]), , drop = FALSE]
    if (nrow(d) == 0L) return(NULL)
    d$co2_cat <- make_co2_cat3(d[[spec$co2_var]], spec$low, spec$high)
    d$co2_cat <- stats::relevel(base::droplevels(d$co2_cat), ref = "Normal")
    if (dplyr::n_distinct(d[[spec$outcome]]) < 2L) return(NULL)
    fit <- tryCatch(
      stats::glm(stats::reformulate("co2_cat", response = spec$outcome),
                 data = d, family = binomial(), x = FALSE, y = FALSE, model = FALSE),

```

```

    error = function(e) NULL
  )
  if (is.null(fit)) return(NULL)
  list(coef = stats::coef(fit), vcov = stats::vcov(fit))
})
fits <- fits[!vapply(fits, is.null, logical(1))]
if (length(fits) < 2L) return(NA_real_)
results <- lapply(fits, `[[`, "coef")
variances <- lapply(fits, `[[`, "vcov")
pooled <- mitools::MIcombine(results = results, variances = variances)
est <- as.numeric(stats::coef(pooled))
names(est) <- names(stats::coef(pooled))
se <- sqrt(diag(pooled$variance))
names(se) <- names(stats::coef(pooled))
coef_mat <- do.call(cbind, lapply(results, function(v) v[names(est)]))
B <- apply(coef_mat, 1, stats::var, na.rm = TRUE)
mcerr <- sqrt(B / length(results))
ratio <- mcerr / se
idx <- grep("co2_cat", names(ratio))
if (!any(idx)) return(max(ratio, na.rm = TRUE))
max(ratio[idx], na.rm = TRUE)
}

run_mice_batched <- function(m_total, m_batch_start, maxit, base_seed) {
  imp_acc <- NULL
  m_done <- 0L
  batch_attempt_idx <- 0L
  m_batch <- m_batch_start
  batch_log <- list()
  logged_events_acc <- list()

  while (m_done < m_total) {
    if (MI_GC_EVERY_BATCH) invisible(gc())
    mem_stats <- get_vcells_stats()
    if (MI_PREEMPTIVE_BATCH_REDUCE &&
        is.finite(mem_stats$gc_vcells_frac) &&

```

```

mem_stats$gc_vcells_frac > MI_VCELLS_FRAC_THRESHOLD &&
  m_batch > MI_BATCH_MIN) {
  m_batch <- max(MI_BATCH_MIN, floor(m_batch / 2))
  message("Preemptively reducing MI batch size to ", m_batch,
         " (Vcells pressure: ", round(mem_stats$gc_vcells_frac, 2), ".")
}

m_b <- min(m_batch, m_total - m_done)
batch_attempt_idx <- batch_attempt_idx + 1L
seed_b <- base_seed + batch_attempt_idx * MI_BATCH_SEED_STRIDE
message("MICE batch ", batch_attempt_idx, " (m=", m_b, ", seed=", seed_b, ")")

t0 <- Sys.time()
mem_pre <- get_vcells_stats()
cap <- capture_warnings(
  tryCatch(
    runtime_logger(
      paste0("mice_batch_", batch_attempt_idx),
      mice::mice(
        data = mi_df_run,
        m = m_b,
        maxit = maxit,
        predictorMatrix = pred,
        method = meth,
        printFlag = FALSE,
        seed = seed_b
      ),
      notes = paste0("batch=", batch_attempt_idx, "; m=", m_b, "; maxit=", maxit)
    ),
    error = function(e)
  ),
  context = make_context(
    stage = "MI",
    component = "mice_batch",
    analysis_variant = "mi",
    model_type = "mice",

```

```

group = NA_character_,
outcome = NA_character_,
imputation = NA_integer_,
batch = batch_attempt_idx
)
)
append_warnings(cap$warnings)

imp_b <- cap$value
if (inherits(imp_b, "error")) {
  err_msg <- conditionMessage(imp_b)
  message("MICE batch ", batch_attempt_idx, " failed: ", err_msg)
  mem_stats <- get_vcells_stats()
  batch_log[[batch_attempt_idx]] <- data.frame(
    batch = batch_attempt_idx,
    m_batch = m_b,
    seed = seed_b,
    ok = FALSE,
    error_message = err_msg,
    seconds = as.numeric(difftime(Sys.time(), t0, units = "secs")),
    gc_vcells_used_mb_pre = mem_pre$gc_vcells_used_mb,
    gc_vcells_limit_mb_pre = mem_pre$gc_vcells_limit_mb,
    gc_vcells_frac_pre = mem_pre$gc_vcells_frac,
    gc_vcells_used_mb_post = mem_stats$gc_vcells_used_mb,
    gc_vcells_limit_mb_post = mem_stats$gc_vcells_limit_mb,
    gc_vcells_frac_post = mem_stats$gc_vcells_frac,
    stringsAsFactors = FALSE
  )
  if (grepl("vector memory limit", err_msg, fixed = TRUE) && m_batch > MI_BATCH_MIN) {
    m_batch <- max(MI_BATCH_MIN, floor(m_batch / 2))
    message("Reducing MI batch size to ", m_batch, " and retrying.")
    invisible(gc())
    next
  }
  write_csv_safely(dplyr::bind_rows(batch_log), results_path("mice_batches_log.csv"), row_names = FALSE)
  stop("MICE batch ", batch_attempt_idx, " failed; see log: ", results_path("mice_batches_log.csv"))
}

```

```

}

if (is.null(imp_acc)) {
  imp_acc <- imp_b
} else {
  imp_acc <- mice::bind(imp_acc, imp_b)
}

le_b <- imp_b$loggedEvents
le_b <- if (is.null(le_b)) data.frame() else as.data.frame(le_b)
if (NROW(le_b) > 0) {
  le_b <- le_b |>
    dplyr::mutate(
      batch = batch_attempt_idx,
      seed = seed_b,
      m_global_start = m_done + 1L
    )
  logged_events_acc[[length(logged_events_acc) + 1L]] <- le_b
}

m_done <- imp_acc$m
mem_stats <- get_vcells_stats()
batch_log[[batch_attempt_idx]] <- data.frame(
  batch = batch_attempt_idx,
  m_batch = m_b,
  seed = seed_b,
  ok = TRUE,
  error_message = NA_character_,
  seconds = as.numeric(difftime(Sys.time(), t0, units = "secs")),
  gc_vcells_used_mb_pre = mem_pre$gc_vcells_used_mb,
  gc_vcells_limit_mb_pre = mem_pre$gc_vcells_limit_mb,
  gc_vcells_frac_pre = mem_pre$gc_vcells_frac,
  gc_vcells_used_mb_post = mem_stats$gc_vcells_used_mb,
  gc_vcells_limit_mb_post = mem_stats$gc_vcells_limit_mb,
  gc_vcells_frac_post = mem_stats$gc_vcells_frac,
  stringsAsFactors = FALSE

```

```

)
rm(imp_b)
if (MI_GC_EVERY_BATCH) invisible(gc())

if (ALLOW_M_IMP_EARLY_STOP &&
    m_done >= M_IMP_MIN &&
    (m_done %% M_IMP_STEP == 0 || m_done == m_total)) {
  ratios <- vapply(sentinel_specs, function(s) mcerr_ratio_for_spec(imp_acc, s), numeric(1))
  mc_progress[[length(mc_progress) + 1L]] <- data.frame(
    m = m_done,
    abg_ratio = ratios[["abg_imv"]],
    vbg_ratio = ratios[["vbg_imv"]],
    max_ratio = max(ratios, na.rm = TRUE),
    stringsAsFactors = FALSE
  )
  write_csv_safely(dplyr::bind_rows(mc_progress),
                  results_path("mi_mcerr_progress.csv"),
                  row_names = FALSE)
  if (all(is.finite(ratios)) && max(ratios, na.rm = TRUE) <= MCERR_RATIO_TARGET) {
    message("MC error criterion met at m=", m_done,
           " (max MCerr/SE=", round(max(ratios, na.rm = TRUE), 3), "). Stopping early.")
    break
  }
}

write_csv_safely(dplyr::bind_rows(batch_log), results_path("mice_batches_log.csv"), row_names = FALSE)
log_events_raw_batched <- dplyr::bind_rows(logged_events_acc)
attr(imp_acc, "logged_events_batched") <- log_events_raw_batched
imp_acc
}

imp <- NULL
use_batched <- isTRUE(FORCE_MI_BATCHED)
if (!use_batched) {

```

```

cap_mice <- capture_warnings(
  tryCatch(run_mice_single(M_IMP_RUN), error = function(e) e),
  context = make_context(
    stage = "MI",
    component = "mice",
    analysis_variant = "mi",
    model_type = "mice",
    group = NA_character_,
    outcome = NA_character_,
    imputation = NA_integer_,
    batch = NA_integer_
  )
)
append_warnings(cap_mice$warnings)
imp <- cap_mice$value
if (inherits(imp, "error") && grepl("vector memory limit", conditionMessage(imp), fixed = TRUE)) {
  message("MICE memory limit hit; switching to batched mode.")
  use_batched <- TRUE
}
if (use_batched) {
  message("MICE: running in batches (start=", MI_BATCH_START, ").")
  imp <- run_mice_batched(M_IMP_RUN, MI_BATCH_START, MAXIT_RUN, MI_SEED)
} else {
  write_csv_safely(data.frame(), results_path("mice_batches_log.csv"), row_names = FALSE)
}
if (inherits(imp, "error")) stop(imp)
stopifnot(inherits(imp, "mids"))
if (ALLOW_M_IMP_EARLY_STOP && imp$m < M_IMP_RUN) {
  message("Early stop: stopping at m=", imp$m, " (target ", M_IMP_RUN, ").")
  M_IMP_RUN <- imp$m
} else {
  stopifnot(imp$m == M_IMP_RUN)
}
if (M_IMP != M_IMP_RUN) M_IMP <- M_IMP_RUN
if (MAXIT_MI != MAXIT_RUN) MAXIT_MI <- MAXIT_RUN

```

```

write_csv_safely(dplyr::bind_rows(mc_progress), results_path("mi_mcerr_progress.csv"), row_names = FALSE)
saveRDS(imp, file = mi_mids_file)

# Save MICE spec for reproducibility
saveRDS(
  list(method = imp$method, predictorMatrix = imp$predictorMatrix),
  results_path("mice_spec.rds")
)
if (use_batched) {
  message("Multiple imputation was run in batches and combined via mice::ibind() .")
}
if (subset_data_saved) {
  subset_data <- readRDS(subset_data_path)
}

# Logged events: raw + summary (by dep/out/meth)
log_events_raw <- as.data.frame(imp$loggedEvents)
log_events_batched <- as.data.frame(attr(imp, "logged_events_batched"))
log_events_raw <- dplyr::bind_rows(log_events_raw, log_events_batched)

if (nrow(log_events_raw)) {
  write_csv_safely(log_events_raw, results_path("mice_logged_events_raw.csv"), row_names = FALSE,
                  required_cols = c("dep", "out", "meth"))
  log_events_summary <- log_events_raw |>
    dplyr::count(dep, out, meth, name = "n") |>
    dplyr::mutate(variable = dep) |>
    dplyr::arrange(dplyr::desc(n)) |>
    dplyr::mutate(pct = n / sum(n))
  write_csv_safely(log_events_summary, results_path("mice_logged_events_summary.csv"), row_names = FALSE,
                  required_cols = c("variable", "n", "pct"))
} else {
  log_events_raw_empty <- data.frame(
    dep = character(), out = character(), meth = character(),
    stringsAsFactors = FALSE
)
  log_events_summary_empty <- data.frame(

```

```

variable = character(), n = integer(), pct = numeric(),
stringsAsFactors = FALSE
)
write_csv_safely(log_events_raw_empty, results_path("mice_logged_events_raw.csv"), row_names = FALSE,
                 required_cols = c("dep", "out", "meth"))
write_csv_safely(log_events_summary_empty, results_path("mice_logged_events_summary.csv"), row_names = FALSE,
                 required_cols = c("variable", "n", "pct"))
log_events_summary <- log_events_summary_empty
}
if (nrow(mi_info_log)) {
  warns_events <- mi_info_log |>
    dplyr::filter(stage == "MI", component %in% c("mice", "mice_batch"))
  if (nrow(warns_events) && nrow(log_events_raw) == 0L) {
    warning("Mismatch: main MI run reported logged events but loggedEvents table is empty; ",
            "check batch capture and loggedEvents exports.", call. = FALSE)
  }
}

# Chain diagnostics (lightweight; no complete("long"))
chain_diag <- data.frame()
chain_diag_stats <- list(
  n_imputed_vars = 0L,
  n_with_chainMean = 0L,
  n_with_drift_tail = 0L,
  drift_tail_na_frac = NA_real_,
  tail_window_na_mean = NA_real_
)
stopifnot(!is.null(imp$method))
impute_vars <- names(imp$method)[imp$method != ""]
impute_vars <- intersect(impute_vars, names(imp$data))
if (length(impute_vars)) {
  impute_vars <- impute_vars[vapply(imp$data[impute_vars], function(x) any(is.na(x)), logical(1))]
}
stopifnot(!is.null(imp$chainMean))
{
  cm <- imp$chainMean
}

```

```

dims <- dim(cm)
dn <- dimnames(cm)
iter_candidates <- unique(c(imp$iteration, MAXIT_MI, MAXIT_MI + 1L))
iter_candidates <- iter_candidates[is.finite(iter_candidates) & iter_candidates > 0]
imp_m <- imp$m

extract_chain_mean <- function(cm_obj, dims_obj, dn_obj, imp_m_val, iter_cand) {
  mean_chain <- NULL
  var_names <- NULL
  iter_dim <- NA_integer_
  var_dim <- NA_integer_
  m_dim <- NA_integer_
  if (!is.null(dims_obj) && length(dims_obj) == 2) {
    iter_dim <- which(dims_obj %in% iter_cand)[1]
    if (length(iter_dim) == 0) iter_dim <- 1L
    var_dim <- setdiff(seq_along(dims_obj), iter_dim)[1]
    mean_chain <- cm_obj
    if (iter_dim == 2L) mean_chain <- t(mean_chain)
  } else if (!is.null(dims_obj) && length(dims_obj) == 3) {
    m_dim <- which(dims_obj == imp_m_val)
    if (length(m_dim)) {
      m_dim <- m_dim[1]
    } else {
      m_dim <- 3L
    }
    iter_dim <- setdiff(which(dims_obj %in% iter_cand), m_dim)[1]
    if (length(iter_dim) == 0) iter_dim <- setdiff(1:3, c(m_dim, NA_integer_))[1]
    var_dim <- setdiff(1:3, c(iter_dim, m_dim))[1]
    if (all(is.finite(c(iter_dim, var_dim, m_dim)))) {
      cm_std <- aperm(cm_obj, c(iter_dim, var_dim, m_dim))
      mean_chain <- apply(cm_std, c(1, 2), mean, na.rm = TRUE)
      if (!is.null(dimnames(cm_std))) {
        if (!is.null(dimnames(cm_std)[[2]])) {
          var_names <- dimnames(cm_std)[[2]]
        }
        if (!is.null(dimnames(cm_std)[[1]])) {

```

```

        rownames(mean_chain) <- dimnames(cm_std)[[1]]
    }
}
}
}

if (is.null(mean_chain)) {
  return(list(mean_chain = NULL, var_names = NULL, iter_dim = iter_dim, var_dim = var_dim, m_dim = m_dim))
}

if (is.null(var_names) && !is.null(dn_obj) && length(dn_obj) >= var_dim) {
  var_names <- dn_obj[[var_dim]]
}

if (is.null(var_names)) {
  var_names <- colnames(mean_chain)
}

list(mean_chain = mean_chain, var_names = var_names, iter_dim = iter_dim, var_dim = var_dim, m_dim = m_dim)
}

res_chain <- extract_chain_mean(cm, dims, dn, imp_m, iter_candidates)
mean_chain <- res_chain$mean_chain
var_names <- res_chain$var_names
if (is.null(mean_chain)) {
  stop("Chain diagnostics: unable to construct mean_chain from imp$chainMean.")
}

{
  iter_idx <- seq_len(nrow(mean_chain))
  numeric_names <- !is.null(var_names) && all(grepl("^\\d+$", var_names))
  if (is.null(var_names) || numeric_names) {
    if (length(impute_vars) && length(impute_vars) == ncol(mean_chain)) {
      var_names <- impute_vars
      numeric_names <- FALSE
    }
  }
  if (is.null(var_names)) {
    stop("Chain diagnostics: variable names missing and could not be matched to imp$method.")
  }
}

```

```

colnames(mean_chain) <- var_names

if (numeric_names) {
  warn_df <- data.frame(
    time = as.character(Sys.time()),
    stage = "MI",
    component = "chain_diagnostics",
    analysis_variant = NA_character_,
    model_type = NA_character_,
    group = NA_character_,
    outcome = NA_character_,
    imputation = NA_integer_,
    batch = NA_integer_,
    message = "Chain diagnostics variable name mapping failed; using numeric/fallback names.",
    stringsAsFactors = FALSE
  )
  append_warnings(warn_df)
}

vars_imputed <- impute_vars
chain_diag_stats$n_imputed_vars <- length(vars_imputed)
keep_vars <- intersect(vars_imputed, var_names)
missing_in_chain <- setdiff(vars_imputed, var_names)
if (length(missing_in_chain)) {
  missing_df <- data.frame(
    variable = missing_in_chain,
    stringsAsFactors = FALSE
  )
  write_csv_safely(missing_df, results_path("mice_chain_diagnostics_missing_vars.csv"), row.names = FALSE)
}
if (length(vars_imputed) && length(keep_vars) == 0L) {
  warn_df <- data.frame(
    time = as.character(Sys.time()),
    stage = "MI",
    component = "chain_diagnostics",
    analysis_variant = NA_character_,
    stringsAsFactors = FALSE
  )
  append_warnings(warn_df)
}

```

```

model_type = NA_character_,
group = NA_character_,
outcome = NA_character_,
imputation = NA_integer_,
batch = NA_integer_,
message = "Chain diagnostics: no imputed variables matched chainMean names; skipping drift metrics.",
stringsAsFactors = FALSE
)
append_warnings(warn_df)
mean_chain <- mean_chain[, 0, drop = FALSE]
var_names <- character()
} else if (length(keep_vars)) {
  mean_chain <- mean_chain[, keep_vars, drop = FALSE]
  var_names <- keep_vars
}

safe_sd <- function(x) if (sum(is.finite(x)) < 2) NA_real_ else stats::sd(x, na.rm = TRUE)
safe_maxdiff <- function(x) {
  x <- x[is.finite(x)]
  if (length(x) < 2) return(NA_real_)
  max(abs(diff(x)))
}
safe_slope <- function(x, iter) {
  ok <- is.finite(x)
  if (sum(ok) < 2) return(NA_real_)
  coef(stats::lm(x[ok] ~ iter[ok]))[2]
}
tail_finite <- function(x, k) tail(x[is.finite(x)], k)
safe_maxdiff_tail <- function(x, k) {
  xf <- tail_finite(x, k)
  if (length(xf) < 2) return(NA_real_)
  max(abs(diff(xf)))
}

n_vars <- ncol(mean_chain)
n_finite <- integer(n_vars)

```

```

drift_all <- numeric(n_vars)
drift_tail <- numeric(n_vars)
tail_n_finite <- integer(n_vars)
tail_window_na_frac <- numeric(n_vars)
slope <- numeric(n_vars)
sd_chain <- numeric(n_vars)
overall_reason <- character(n_vars)
tail_reason <- character(n_vars)
flag_reason <- character(n_vars)
flag <- logical(n_vars)
diagnostic_available <- logical(n_vars)
sd_obs <- rep(NA_real_, n_vars)

chain_src_df <- mi_df_run
stopifnot(is.data.frame(chain_src_df))
sd_obs <- vapply(var_names, function(v) {
  stopifnot(v %in% names(chain_src_df))
  x <- chain_src_df[[v]]
  if (inherits(x, "haven_labelled")) x <- suppressWarnings(as.numeric(x))
  if (!is.numeric(x)) return(NA_real_)
  safe_sd(x)
}, numeric(1))

for (j in seq_len(n_vars)) {
  x <- mean_chain[, j]
  n_finite[j] <- sum(is.finite(x))
  drift_all[j] <- safe_maxdiff(x)
  slope[j] <- safe_slope(x, iter_idx)
  sd_chain[j] <- safe_sd(x)
  tail_vals <- tail_finite(x, TAIL_NFINITE)
  tail_n_finite[j] <- length(tail_vals)
  drift_tail[j] <- safe_maxdiff_tail(x, TAIL_NFINITE)
  tail_window <- tail(x, min(TAIL_WINDOW_ITERS, length(x)))
  tail_window_na_frac[j] <- mean(!is.finite(tail_window))
  overall_reason[j] <- if (n_finite[j] >= 2) "ok" else "insufficient_finite_overall"
  tail_reason[j] <- if (tail_n_finite[j] >= 2) "ok" else "insufficient_finite_tail"
}

```

```

}

drift_all_scaled <- drift_all / sd_obs
drift_tail_scaled <- drift_tail / sd_obs
slope_scaled <- slope / sd_obs

for (j in seq_len(n_vars)) {
  if (!is.finite(sd_obs[j]) || sd_obs[j] <= 0) {
    flag[j] <- NA
    flag_reason[j] <- "missing_scale"
    diagnostic_available[j] <- FALSE
    next
  }
  if (tail_n_finite[j] < 2) {
    flag[j] <- NA
    flag_reason[j] <- "tail_insufficient"
    diagnostic_available[j] <- FALSE
    next
  }
  if (!is.finite(drift_tail_scaled[j]) || !is.finite(slope_scaled[j])) {
    flag[j] <- NA
    flag_reason[j] <- "insufficient_data"
    diagnostic_available[j] <- FALSE
    next
  }
  flag_tail <- drift_tail_scaled[j] > 0.01
  flag_slope <- abs(slope_scaled[j]) > 0.001
  flag[j] <- flag_tail | flag_slope
  flag_reason[j] <- if (flag_tail & flag_slope) {
    "both"
  } else if (flag_tail) {
    "tail_drift"
  } else if (flag_slope) {
    "slope"
  } else {
    "none"
  }
}

```

```

    }
    diagnostic_available[j] <- TRUE
}

chain_diag <- data.frame(
  variable = var_names,
  method = imp$method[var_names],
  n_finite = n_finite,
  drift_all = drift_all,
  drift_tail = drift_tail,
  drift_all_scaled = drift_all_scaled,
  drift_tail_scaled = drift_tail_scaled,
  tail_n_finite = tail_n_finite,
  tail_window_na_frac = tail_window_na_frac,
  slope = slope,
  slope_scaled = slope_scaled,
  sd_chain = sd_chain,
  sd_obs = sd_obs,
  overall_reason = overall_reason,
  tail_reason = tail_reason,
  flag_reason = flag_reason,
  diagnostic_available = diagnostic_available,
  flag = flag,
  stringsAsFactors = FALSE
)

chain_diag_stats$n_with_chainMean <- nrow(chain_diag)
chain_diag_stats$n_with_drift_tail <- sum(is.finite(chain_diag$drift_tail))
if (chain_diag_stats$n_with_chainMean > 0) {
  chain_diag_stats$drift_tail_na_frac <- 1 - (chain_diag_stats$n_with_drift_tail /
                                                chain_diag_stats$n_with_chainMean)
  chain_diag_stats$tail_window_na_mean <- mean(chain_diag$tail_window_na_frac, na.rm = TRUE)
}
write_csv_safely(chain_diag, results_path("mice_chain_diagnostics.csv"), row.names = FALSE)
if (any(isTRUE(chain_diag$flag), na.rm = TRUE)) {
  frac_flag <- mean(chain_diag$flag, na.rm = TRUE)
}

```

```

        if (is.finite(frac_flag) && frac_flag < 0.05) {
            message("Chain diagnostics: low drift flags (", round(frac_flag * 100, 1),
                    "%). MAXIT_MI may be reduced safely (consider 10 or 5).")
        }
    }
}

# quick sanity: these must exist and be numeric in completed data
imp_n <- imp$m
get_imp_stats <- list(count = 0L, seconds = 0)
get_imp <- function(i, imp_obj = imp) {
    t0 <- Sys.time()
    d <- normalize_types(mice::complete(imp_obj, action = i), levels_ref)
    get_imp_stats$count <-> get_imp_stats$count + 1L
    get_imp_stats$seconds <-> get_imp_stats$seconds +
        as.numeric(difftime(Sys.time(), t0, units = "secs"))
    d
}
d1 <- get_imp(1)
stopifnot(all(c("paco2", "vbg_co2") %in% names(d1)))
stopifnot(is.numeric(d1$paco2), is.numeric(d1$vbg_co2))

# post-MICE sanity: no remaining NA in covars_ps
covars_check <- intersect(covars_ps, names(d1))
na_counts <- vapply(d1[, covars_check, drop = FALSE], function(x) sum(is.na(x)), numeric(1))
na_counts <- na_counts[na_counts > 0]
if (length(na_counts)) {
    message("Post-MICE NA counts (covars_ps): ",
           paste(names(na_counts), na_counts, collapse = ", "))
    ev_sum <- summarize_logged_events(imp)
    if (nrow(ev_sum)) {
        ev_sub <- ev_sum[ev_sum$variable %in% names(na_counts), , drop = FALSE]
        if (nrow(ev_sub)) {
            print(utils::head(ev_sub, 10))
        } else {

```

```

    message("No loggedEvents entries for covars_ps with NA.")
}
} else {
  message("No loggedEvents recorded.")
}
stop("Post-MICE check failed: remaining NA in covars_ps. See loggedEvents summary above.")
}

```

```

stopifnot(exists("imp"))

# Representative logistic model (unweighted) to assess Monte Carlo error
mc_diag_fml <- imv_proc ~ has_abg + age_at_encounter + curr_bmi + sex + encounter_type
register_model_diagram("MI MC error: IMV ~ ABG + covariates", mc_diag_fml, width = 10, height = 6)
cap_mc <- capture_warnings(
  tryCatch(
    with(
      imp,
      glm(imv_proc ~ has_abg + age_at_encounter + curr_bmi + sex + encounter_type,
           family = binomial(), x = FALSE, y = FALSE, model = FALSE)
    ),
    error = function(e) e
  ),
  context = make_context(
    stage = "diagnostics",
    component = "mi_mcerror_glm",
    analysis_variant = "mi",
    model_type = "glm",
    group = NA_character_,
    outcome = "imv_proc",
    imputation = NA_integer_,
    batch = NA_integer_
  )
)
append_warnings(cap_mc$warnings)
mc_fit <- cap_mc$value

```

```

use_compact <- inherits(mc_fit, "error")
if (use_compact) {
  message("MC error: fallback to compact per-imputation fits (", conditionMessage(mc_fit), ".)")
}

mc_pool <- NULL
mc_sum <- NULL
mc_results <- NULL
mc_variances <- NULL
if (!use_compact) {
  mc_pool <- pool(mc_fit)
  mc_sum <- summary(mc_pool, conf.int = TRUE)
}

compute_mc_error <- function(mc_pool, mc_fit, m) {
  stopifnot(!is.null(mc_fit$analyses), length(mc_fit$analyses) >= 2)
  coefs <- lapply(mc_fit$analyses, coef)
  common_terms <- Reduce(intersect, lapply(coefs, names))
  stopifnot(length(common_terms) > 0)
  Q <- do.call(cbind, lapply(coefs, function(v) v[common_terms]))
  B <- apply(Q, 1, stats::var, na.rm = TRUE)
  out <- sqrt(B / ncol(Q))
  names(out) <- common_terms
  out
}

compute_mc_error_from_results <- function(results_list) {
  coefs <- results_list
  common_terms <- Reduce(intersect, lapply(coefs, names))
  if (!length(common_terms)) return(NA_real_)
  Q <- do.call(cbind, lapply(coefs, function(v) v[common_terms]))
  B <- apply(Q, 1, stats::var, na.rm = TRUE)
  out <- sqrt(B / ncol(Q))
  names(out) <- common_terms
  out
}

```

```

if (use_compact) {
  mc_terms <- all.vars(mc_diag_fml)
  mc_fit_list <- lapply(seq_len(imp$m), function(i) {
    d <- mice:::complete(imp, action = i)
    d <- d[, mc_terms, drop = FALSE]
    cap_i <- capture_warnings(
      tryCatch(
        glm(mc_diag_fml, data = d, family = binomial(), x = FALSE, y = FALSE, model = FALSE),
        error = function(e) e
      ),
      context = make_context(
        stage = "diagnostics",
        component = "mi_mcerror_glm",
        analysis_variant = "mi",
        model_type = "glm",
        group = NA_character_,
        outcome = "imv_proc",
        imputation = i,
        batch = NA_integer_
      )
    )
    append_warnings(cap_i$warnings)
    fit_i <- cap_i$value
    if (inherits(fit_i, "error")) return(list(error = conditionMessage(fit_i)))
    list(coef = coef(fit_i), vcov = vcov(fit_i))
  ))
}

ok <- vapply(mc_fit_list, function(x) is.list(x) && is.null(x$error), logical(1))
mc_fit_list <- mc_fit_list[ok]
if (!length(mc_fit_list)) stop("MC error fallback failed: no successful fits.")

mc_results <- lapply(mc_fit_list, function(x) x$coef)
mc_variances <- lapply(mc_fit_list, function(x) x$vcov)

mc_pool <- mitools::MIcombine(results = mc_results, variances = mc_variances)

```

```

est <- as.numeric(coef(mc_pool))
se  <- sqrt(diag(mc_pool$variance))
mc_sum <- data.frame(
  term = names(coef(mc_pool)),
  estimate = est,
  std.error = se,
  conf.low = est - 1.96 * se,
  conf.high = est + 1.96 * se,
  stringsAsFactors = FALSE
)
}

m_mc <- if (!use_compact && !is.null(mc_fit$analyses)) length(mc_fit$analyses) else imp$m
mc_err_vec <- if (!use_compact) {
  compute_mc_error(mc_pool, mc_fit, m_mc)
} else {
  compute_mc_error_from_results(mc_results)
}

if (is.null(names(mc_err_vec)) || all(names(mc_err_vec) == "")) {
  names(mc_err_vec) <- mc_sum$term[seq_len(min(length(mc_err_vec), nrow(mc_sum)))]
}
mc_err_aligned <- mc_err_vec[mc_sum$term]
if (all(is.na(mc_err_aligned))) {
  message("MC error not computed (all NA). mice version: ", as.character(packageVersion("mice")))
  if (!is.null(mc_pool$pooled)) {
    message("mc_pool$pooled columns: ", paste(names(mc_pool$pooled), collapse = ", "))
  }
}

stopifnot(all(c("conf.low", "conf.high") %in% names(mc_sum)))

mc_tab <- mc_sum |>
  mutate(
    mc_error = mc_err_aligned,
    mc_err_over_se = mc_error / std.error

```

Monte Carlo error vs SE (diagnostic only)

Term	Estimate	SE	MC error	MC error / SE	2.5%	97.5%
(Intercept)	-3.948	0.410	0.027	0.067	-4.753766048	-3.143213659
has_abg	2.133	0.123	0.002	0.013	1.892069856	2.374000259
age_at_encounter	-0.003	0.003	0.000	0.012	-0.008447498	0.002916156
curr_bmi	-0.012	0.010	0.001	0.081	-0.031285028	0.006983105
sexMale	0.241	0.099	0.001	0.011	0.047718257	0.434390921
encounter_typeInpatient	1.184	0.165	0.001	0.006	0.859343534	1.508064673

```
) |>
select(term, estimate, std.error, mc_error, mc_err_over_se, conf.low, conf.high)

mc_model_desc <- "Diagnostic model: imv_proc ~ has_abg + age_at_encounter + curr_bmi + sex + encounter_type (unweighted)."
knitr::asis_output(paste0("**MC error diagnostic model:** ", mc_model_desc, "\n"))
```

MC error diagnostic model: Diagnostic model: imv_proc ~ has_abg + age_at_encounter + curr_bmi + sex + encounter_type (unweighted).

```
gt::gt(mc_tab) |>
  gt::tab_header(title = "Monte Carlo error vs SE (diagnostic only)") |>
  gt::cols_label(
    term      = "Term",
    estimate  = "Estimate",
    std.error = "SE",
    mc_error  = "MC error",
    mc_err_over_se = "MC error / SE",
    conf.low   = "2.5%",
    conf.high  = "97.5%"
  ) |>
  gt::fmt_number(columns = c(estimate, std.error, mc_error, mc_err_over_se), decimals = 3) |>
  gt::fmt_missing(columns = gt::everything(), missing_text = "-")
```

```

# QC flag for key estimands only (diagnostic, not pass/fail for all coefficients)
mc_key_terms <- intersect(c("has_abg"), mc_tab$term)
if (length(mc_key_terms)) {
  mc_key <- mc_tab |>
    dplyr::filter(term %in% mc_key_terms) |>
    dplyr::mutate(qc_flag = mc_err_over_se > MC_ERR_RATIO_THRESH)
  render_table_pdf_maybe(
    mc_key,
    caption = paste0("MC error QC (key terms only; threshold = ", MC_ERR_RATIO_THRESH, ")"),
    file_stub = "mc_error_qc_key_terms",
    digits = 3,
    show = SHOW_LOW_VALUE_TABLES
  )
  if (any(mc_key$qc_flag, na.rm = TRUE)) {
    knitr::asis_output(
      paste0(
        "**QC note:** MC error/SE exceeds ",
        MC_ERR_RATIO_THRESH,
        " for at least one key term; consider larger m or report as a limitation."
      )
    )
  }
}
}

```

```

stopifnot(exists("imp"))
imp_n <- imp$m
get_imp <- function(i, imp_obj = imp) {
  normalize_types(mice::complete(imp_obj, action = i), levels_ref)
}

# Guard against memory blow-up from complete("long")
N <- nrow(imp$data)
M <- imp$m
long_rows <- (M + 1L) * N
LONG_ROWS_MAX <- 2e6
imp_size <- as.numeric(utils::object.size(imp))

```

```

if (long_rows > LONG_ROWS_MAX || imp_size > 1e9) {
  message("Skipping mice::densityplot/stripplot (mids -> complete('long')) due to size; using memory-safe diagnostics.")
}

get_obs_imp_vectors <- function(imp_obj, var) {
  obs <- imp_obj$data[[var]]
  obs <- obs[!is.na(obs)]
  impv <- imp_obj$imp[[var]]
  stopifnot(!is.null(impv))
  imp_vals <- unlist(impv, use.names = FALSE)
  if (is.numeric(obs)) obs <- obs[is.finite(obs)]
  if (is.numeric(imp_vals)) imp_vals <- imp_vals[is.finite(imp_vals)]
  list(obs = obs, imp = imp_vals)
}

plot_obs_imp <- function(imp_obj, var, fig_dir, n_obs = 50000, n_imp = 50000) {
  vecs <- get_obs_imp_vectors(imp_obj, var)
  obs <- vecs$obs
  imp_vals <- vecs$imp
  stopifnot(length(obs) + length(imp_vals) > 0)

  is_cat <- is.factor(obs) || is.character(obs) ||
    (is.numeric(obs) && length(unique(obs[!is.na(obs)])) <= 5)

  if (!is_cat) {
    set.seed(MI_SEED)
    if (length(obs) > n_obs) obs <- sample(obs, n_obs)
    if (length(imp_vals) > n_imp) imp_vals <- sample(imp_vals, n_imp)

    df <- dplyr::tibble(
      value = c(obs, imp_vals),
      status = c(rep("Observed", length(obs)), rep("Imputed", length(imp_vals)))
    )
    p <- ggplot2::ggplot(df, ggplot2::aes(x = value, color = status, fill = status)) +
      ggplot2::geom_density(alpha = 0.2, na.rm = TRUE) +
      ggplot2::theme_minimal(base_size = 10) +

```

```

ggplot2::labs(title = paste("Observed vs imputed:", var), x = NULL, y = "Density")
out_file <- fs::path(fig_dir, paste0("diag-mi-density-", .make_safe_name(var), ".png"))
ggplot2::ggsave(out_file, p, width = 7, height = 5, dpi = 200)

stat_names <- c("mean", "sd", "p10", "p50", "p90", "n")
obs_stats <- c(
  mean = mean(obs, na.rm = TRUE),
  sd = stats::sd(obs, na.rm = TRUE),
  p10 = stats::quantile(obs, 0.10, na.rm = TRUE),
  p50 = stats::quantile(obs, 0.50, na.rm = TRUE),
  p90 = stats::quantile(obs, 0.90, na.rm = TRUE),
  n = length(obs)
)
imp_stats <- c(
  mean = if (length(imp_vals)) mean(imp_vals, na.rm = TRUE) else NA_real_,
  sd = if (length(imp_vals)) stats::sd(imp_vals, na.rm = TRUE) else NA_real_,
  p10 = if (length(imp_vals)) stats::quantile(imp_vals, 0.10, na.rm = TRUE) else NA_real_,
  p50 = if (length(imp_vals)) stats::quantile(imp_vals, 0.50, na.rm = TRUE) else NA_real_,
  p90 = if (length(imp_vals)) stats::quantile(imp_vals, 0.90, na.rm = TRUE) else NA_real_,
  n = length(imp_vals)
)
return(dplyr::tibble(
  variable = var,
  type = "numeric",
  stat = stat_names,
  observed = unname(obs_stats),
  imputed = unname(imp_stats)
))
}

obs_chr <- as.character(obs)
imp_chr <- as.character(imp_vals)
levels_all <- sort(unique(c(obs_chr, imp_chr)))
prop_obs <- if (length(obs_chr)) {
  as.numeric(table(factor(obs_chr, levels = levels_all))) / length(obs_chr)
} else {

```

```

    rep(0, length(levels_all))
}
prop_imp <- if (length(imp_chr)) {
  as.numeric(table(factor(imp_chr, levels = levels_all))) / length(imp_chr)
} else {
  rep(0, length(levels_all))
}
prop_df <- dplyr::tibble(
  level = levels_all,
  observed = prop_obs,
  imputed = prop_imp
)
miss_plot_df <- tidyr::pivot_longer(prop_df, c(observed, imputed),
                                      names_to = "status", values_to = "prop")
p <- ggplot2::ggplot(miss_plot_df, ggplot2::aes(x = level, y = prop, fill = status)) +
  ggplot2::geom_col(position = "dodge", width = 0.7) +
  ggplot2::theme_minimal(base_size = 10) +
  ggplot2::theme(axis.text.x = ggplot2::element_text(angle = 20, hjust = 1)) +
  ggplot2::labs(title = paste("Observed vs imputed:", var), x = NULL, y = "Proportion")
out_file <- fs::path(fig_dir, paste0("diag-mi-bar-", .make_safe_name(var), ".png"))
ggplot2::ggsave(out_file, p, width = 7, height = 5, dpi = 200)

return(prop_df |>
  tidyr::pivot_longer(c(observed, imputed), names_to = "status", values_to = "prop") |>
  dplyr::mutate(variable = var, type = "categorical", stat = "prop"))
}

# Throttle diagnostics to avoid memory blow-up
trace_vars <- intersect(c("curr_bmi", "serum_hco3", "hr"), names(imp$imp))
if (length(trace_vars)) {
  trace_list <- lapply(trace_vars, function(v) {
    imp_mat <- imp$imp[[v]]
    stopifnot(!is.null(imp_mat))
    means <- colMeans(imp_mat, na.rm = TRUE)
    dplyr::tibble(variable = v, imputation = seq_along(means), mean_imputed = means)
  })
}

```

```

trace_df <- dplyr::bind_rows(trace_list)
if (nrow(trace_df)) {
  p_trace <- ggplot2::ggplot(trace_df, ggplot2::aes(x = imputation, y = mean_imputed)) +
    ggplot2::geom_line() +
    ggplot2::geom_point(size = 0.6) +
    ggplot2::facet_wrap(~variable, scales = "free_y") +
    ggplot2::theme_minimal(base_size = 10) +
    ggplot2::labs(title = "Mean imputed value by imputation", x = "Imputation", y = "Mean")
  print(p_trace)
}

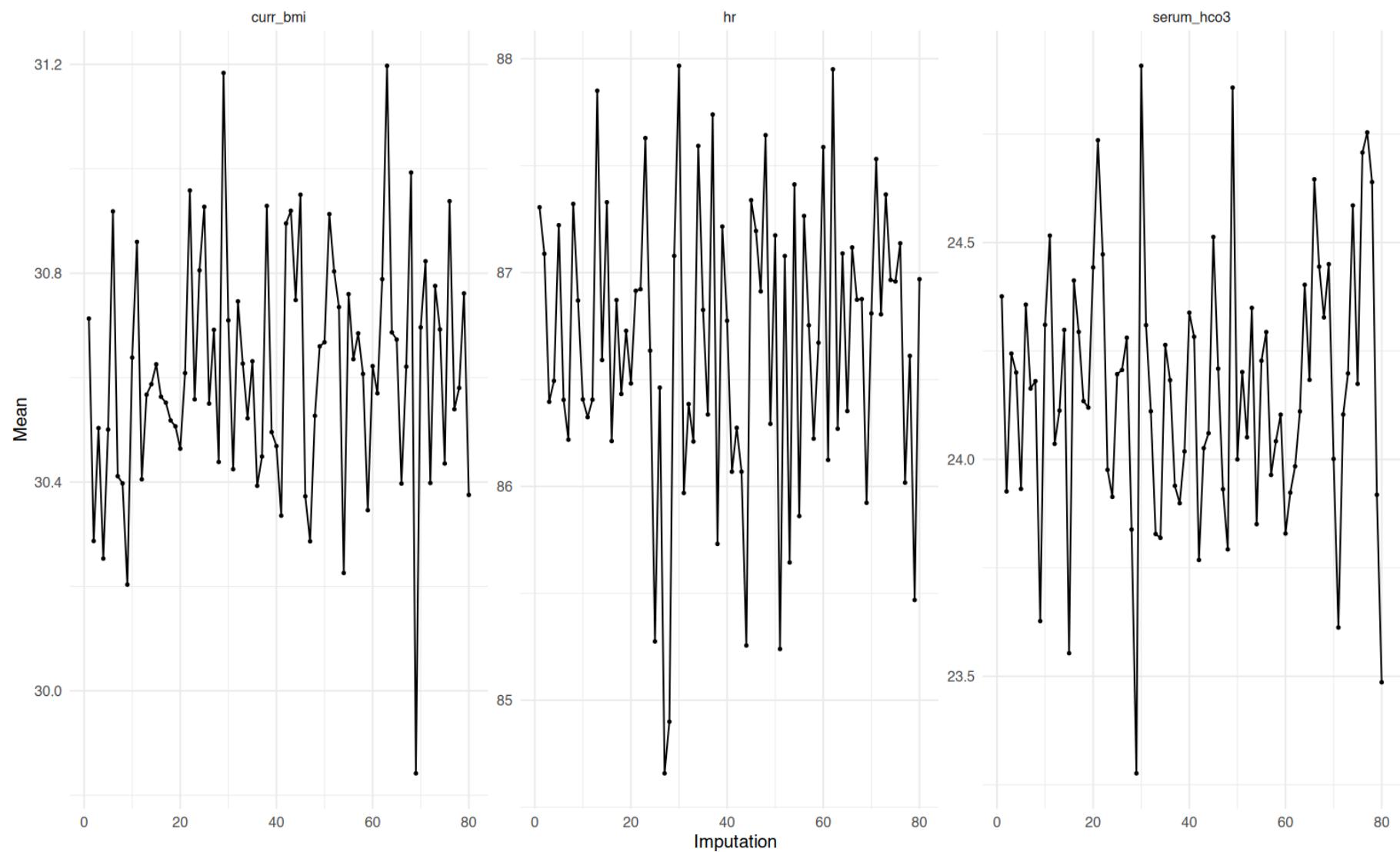
vars_show <- trace_vars[seq_len(min(2, length(trace_vars)))]
dens_list <- lapply(vars_show, function(v) {
  obs <- imp$data[[v]]
  imp1 <- get_imp(1)[[v]]
  obs_vals <- obs[!is.na(obs)]
  imp_vals <- imp1[is.na(obs)]
  if (length(obs_vals) > 5000) obs_vals <- sample(obs_vals, 5000)
  if (length(imp_vals) > 5000) imp_vals <- sample(imp_vals, 5000)
  dplyr::tibble(
    variable = v,
    value = c(obs_vals, imp_vals),
    status = c(rep("Observed", length(obs_vals)),
              rep("Imputed (imp1)", length(imp_vals)))
  )
})
dens_df <- dplyr::bind_rows(dens_list)
p_dens <- ggplot2::ggplot(dens_df, ggplot2::aes(x = value, color = status, fill = status)) +
  ggplot2::geom_density(alpha = 0.2, na.rm = TRUE) +
  ggplot2::facet_wrap(~variable, scales = "free") +
  ggplot2::theme_minimal(base_size = 10) +
  ggplot2::labs(title = "Observed vs imputed distributions (imp1)", x = NULL, y = "Density")
print(p_dens)

p_box <- ggplot2::ggplot(dens_df, ggplot2::aes(x = status, y = value, fill = status)) +
  ggplot2::geom_boxplot(outlier.size = 0.5, na.rm = TRUE) +

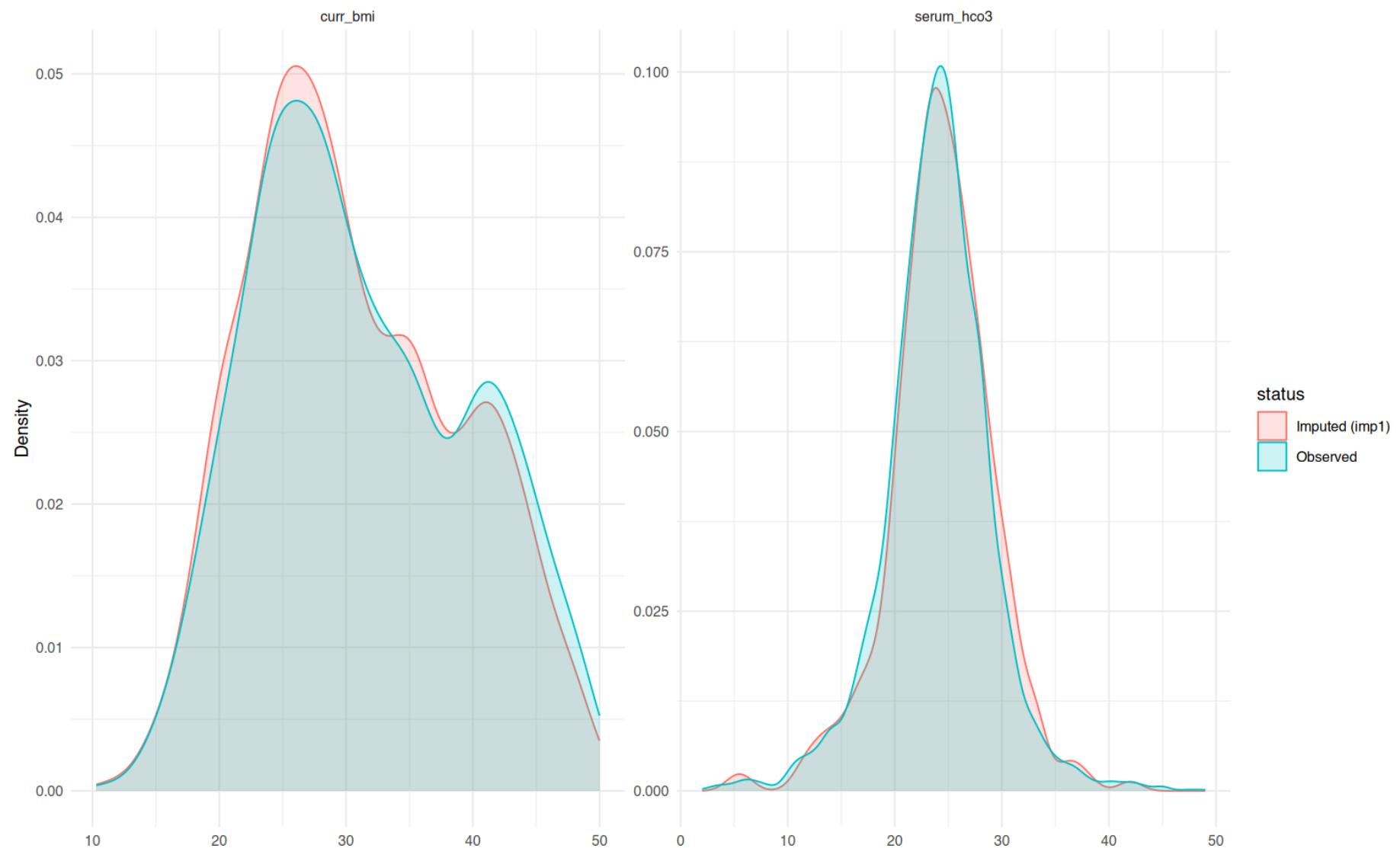
```

```
ggplot2::facet_wrap(~variable, scales = "free") +  
  ggplot2::theme_minimal(base_size = 10) +  
  ggplot2::theme(axis.text.x = ggplot2::element_text(angle = 20, hjust = 1)) +  
  ggplot2::labs(title = "Observed vs imputed (imp1)", x = NULL, y = NULL)  
  print(p_box)  
}
```

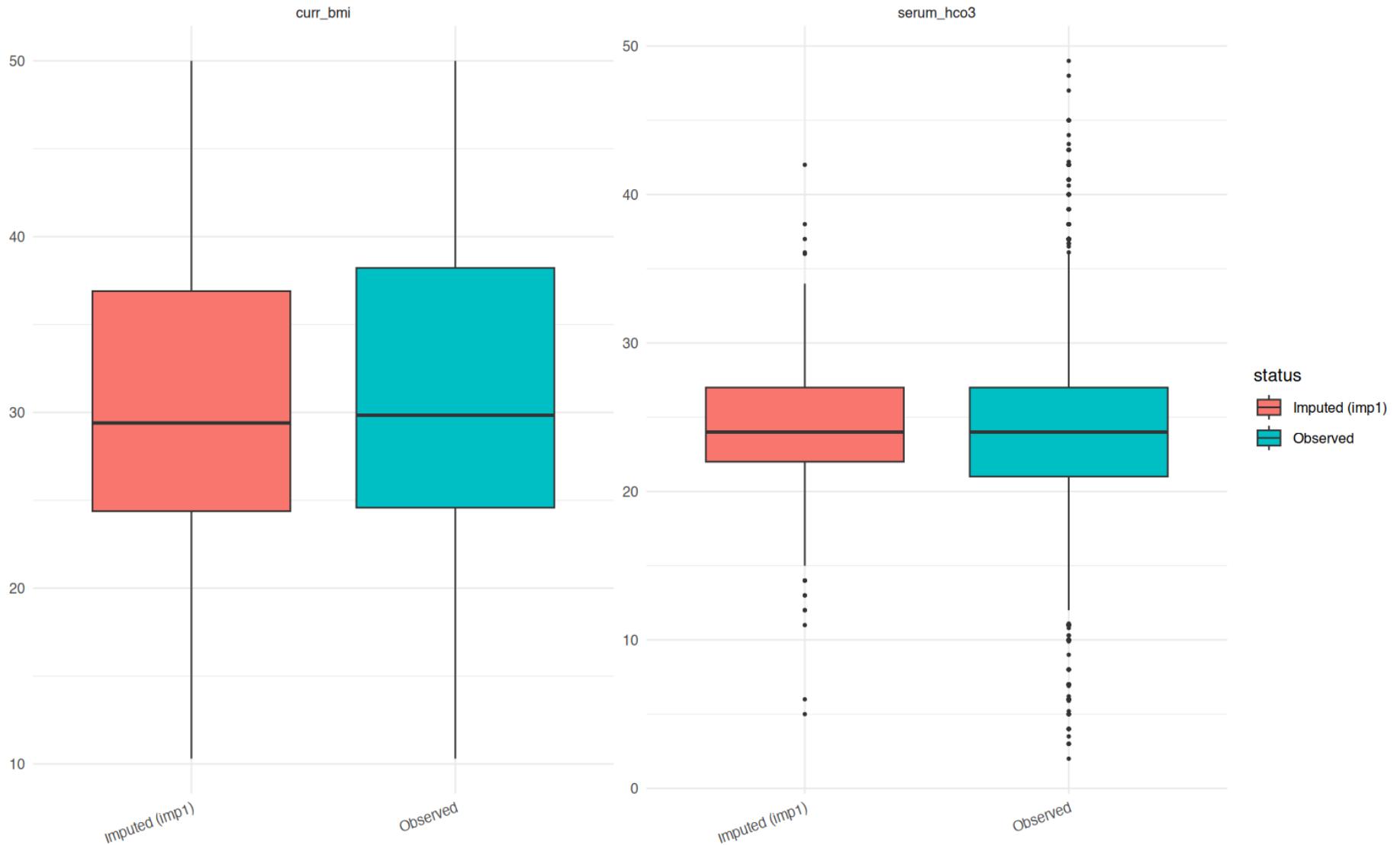
Mean imputed value by imputation



Observed vs imputed distributions (imp1)



Observed vs imputed (imp1)



```
# Observed vs imputed summaries (memory-safe)
diag_vars <- intersect(
  c("age_at_encounter", "curr_bmi", "temp_new", "sbp", "dbp", "hr",
    "sodium", "serum_cr", "serum_hco3", "serum_lac", "wbc", "plt",
```

```

"sex", "race_ethnicity", "location", "encounter_type",
"copd", "asthma", "chf", "dm"),
names(imp$data)
)
diag_vars <- intersect(diag_vars, names(imp$imp))
if (length(diag_vars)) {
  miss_counts <- colSums(is.na(imp$data[diag_vars]))
  diag_vars <- diag_vars[miss_counts > 0]
}

mi_obs_imp_summary <- dplyr::bind_rows(lapply(diag_vars, function(v) {
  out <- plot_obs_imp(imp, v, results_path("figs"))
  invisible(gc())
  out
})))
mi_obs_imp_summary_file <- results_path("mi_obs_vs_imp_summary.csv")
if (nrow(mi_obs_imp_summary)) {
  write_csv_safely(mi_obs_imp_summary, mi_obs_imp_summary_file, row_names = FALSE)
  render_table_pdf_maybe(
    mi_obs_imp_summary,
    caption = "Observed vs imputed summaries",
    file_stub = "mi_obs_vs_imp_summary",
    digits = 3,
    show = SHOW_LOW_VALUE_TABLES
  )
} else {
  mi_obs_imp_stub <- data.frame(
    variable = character(),
    n_obs = numeric(),
    mean_obs = numeric(),
    sd_obs = numeric(),
    mean_imp = numeric(),
    sd_imp = numeric(),
    stringsAsFactors = FALSE
  )
  write_csv_safely(mi_obs_imp_stub, mi_obs_imp_summary_file, row_names = FALSE)
}

```

```

    message("No variables with missingness available for observed vs imputed summaries.")
}

md_pat <- NULL
invisible(utils::capture.output(
  md_pat <- mice::md.pattern(imp$data, plot = FALSE)
))

md_pat_file <- results_path("missingness-pattern.csv")
write_csv_safely(md_pat, md_pat_file, row_names = TRUE)

md_fig_file <- results_path("figs", "missingness-pattern.png")
grDevices::png(md_fig_file, width = 1800, height = 1200, res = 200)
mice::md.pattern(imp$data, plot = TRUE)
grDevices::dev.off()

stopifnot(exists("imp"))
imp_n <- imp$m
get_imp <- function(i, imp_obj = imp) { normalize_types(mice::complete(imp_obj, action = i), levels_ref) }

# Choose a manageable set of incomplete variables
miss_overall <- naniar::miss_var_summary(subset_data) %>% arrange(desc(pct_miss))
vars_incomplete <- miss_overall$variable[miss_overall$n_miss > 0]
per_imp_n <- min(500, nrow(imp$data))
dat_obs <- imp$data %>%
  dplyr::slice_sample(n = min(per_imp_n, nrow(imp$data))) %>%
  dplyr::mutate(.imp = 0L, .imp_label = "Observed")
dat_imp <- purrr::map_dfr(seq_len(imp_n), function(i) {
  di <- get_imp(i)
  di <- dplyr::slice_sample(di, n = min(per_imp_n, nrow(di)))
  di$.imp <- i
  di$.imp_label <- "Imputed"
  di
})
dat_long <- dplyr::bind_rows(dat_obs, dat_imp)
vars_show <- head(intersect(vars_incomplete, names(dat_long)), 6) # limit for plotting & ensure present in imp

```

```

# Density plots by imputation status
if (length(vars_show)) {
  strata_candidates <- intersect(c("has_abg", "has_vbg", "imv_proc", "death_60d"), names(dat_long))
  printed_counts <- FALSE

  for (v in vars_show) {
    if (is.numeric(dat_long[[v]])) {
      df_plot <- dat_long |>
        dplyr::filter(is.finite(.data[[v]]))
      p <- ggplot(df_plot, aes(x = .data[[v]], fill = .imp_label)) +
        geom_density(alpha = 0.4, adjust = 1, na.rm = TRUE) +
        labs(title = paste("Observed vs imputed density:", v), x = v, fill = "Source") +
        theme_minimal()
    } else {
      df_plot <- dat_long |>
        dplyr::filter(!is.na(.data[[v]]))
      p <- ggplot(df_plot, aes(x = .data[[v]], fill = .imp_label)) +
        geom_bar(position = "fill", na.rm = TRUE) +
        labs(title = paste("Observed vs imputed proportions:", v), x = v, y = "Proportion", fill = "Source") +
        theme_minimal() +
        coord_flip()
    }
    print(p)
  }

  # Box/violin plots by strata (numeric vars only)
  if (length(strata_candidates)) {
    pd <- position_dodge(width = 0.8)
    for (sv in strata_candidates) {
      for (v in vars_show) {
        if (!is.numeric(dat_long[[v]])) next
        df_plot <- dat_long |>
          dplyr::filter(!is.na(.data[[sv]]), is.finite(.data[[v]])) |>
          dplyr::mutate(.strata = factor(.data[[sv]]))
        if (nrow(df_plot) == 0L) next
        p <- ggplot(df_plot, aes(x = .strata, y = ..density.., fill = .imp_label))
        p <- p + geom_boxplot(outlier.colour = NA, outlier.size = 0) +
          geom_violin(trim = FALSE, fill = "#F0E68C", alpha = 0.5) +
          scale_y_continuous(breaks = c(0, 0.2, 0.4, 0.6, 0.8, 1))
        p <- p + facet_grid(~v)
        p <- p + theme_minimal()
        print(p)
      }
    }
  }
}

```

```

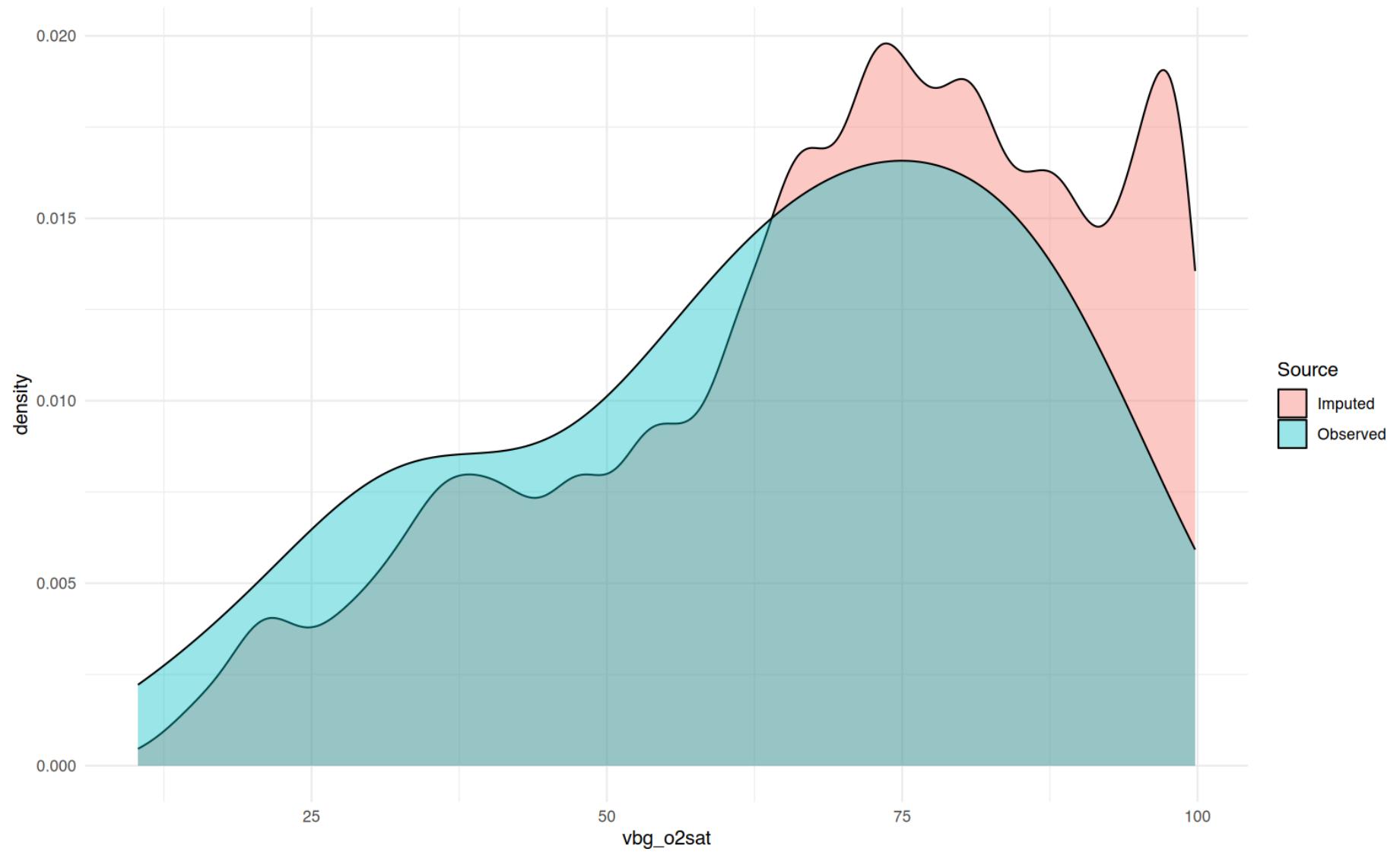
if (!printed_counts) {
  invisible(table(strata = df_plot$strata, source = df_plot$imp_label))
  printed_counts <- TRUE
}

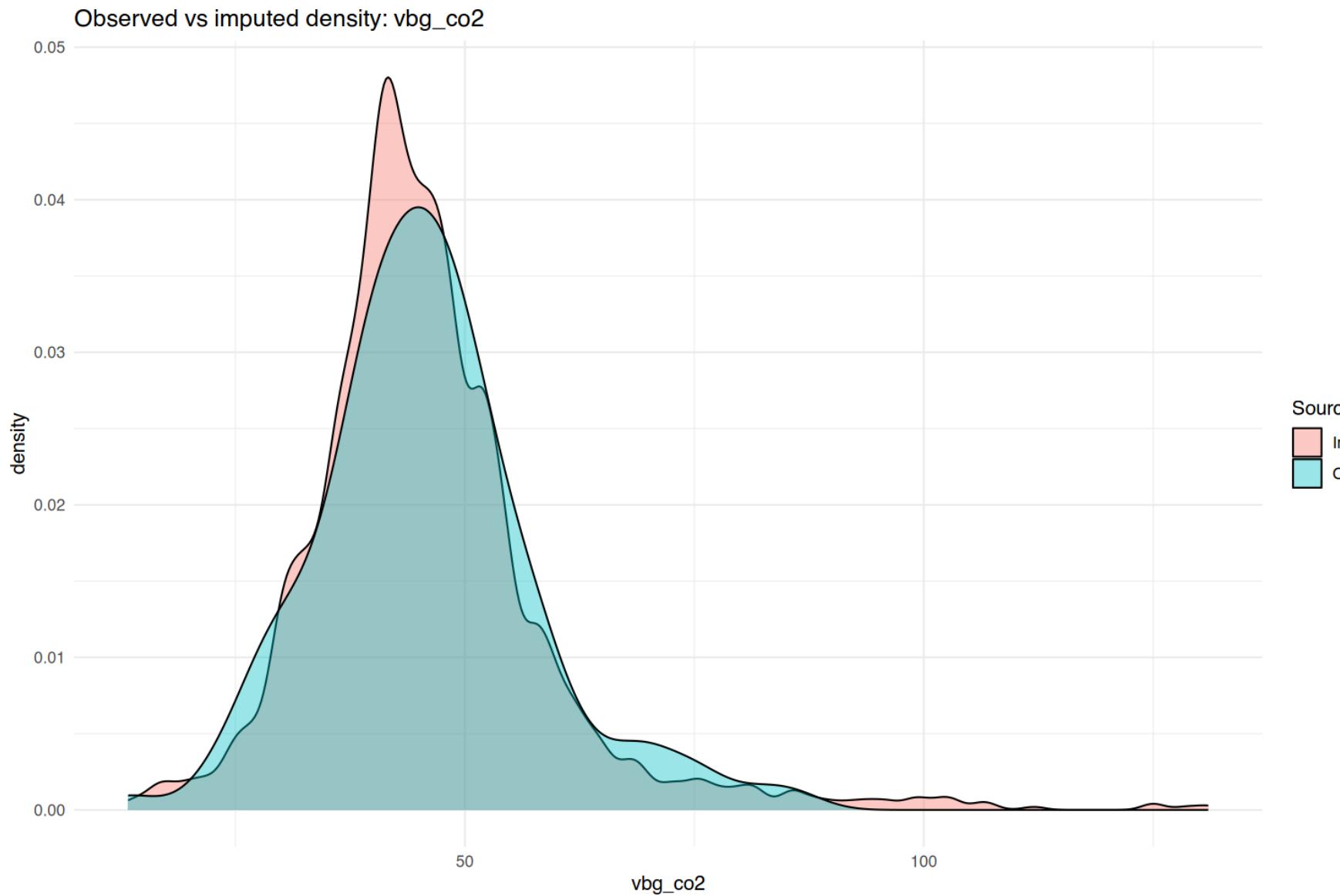
if (all(levels(df_plot$strata) %in% c("0", "1"))) {
  x_scale <- ggplot2::scale_x_discrete(labels = c("0" = "No", "1" = "Yes"))
} else {
  x_scale <- ggplot2::scale_x_discrete(drop = FALSE)
}

p <- ggplot(df_plot, aes(
  x = .strata,
  y = .data[[v]],
  fill = .imp_label,
  group = interaction(.imp_label, .strata)
)) +
  geom_violin(alpha = 0.5, scale = "width", trim = TRUE, position = pd, na.rm = TRUE) +
  geom_boxplot(width = 0.2, outlier.size = 0.6, position = pd, na.rm = TRUE) +
  x_scale +
  labs(title = paste("Observed vs imputed:", v, "by", sv),
       x = sv, y = v, fill = "Source") +
  theme_minimal()
print(p)
out_file <- results_path(
  "figs",
  paste0("diag-mi-obs-imp-by-", .make_safe_name(sv), "-", .make_safe_name(v), ".png")
)
save_diag_plot(p, out_file, width = 7, height = 5)
}
}
}
}

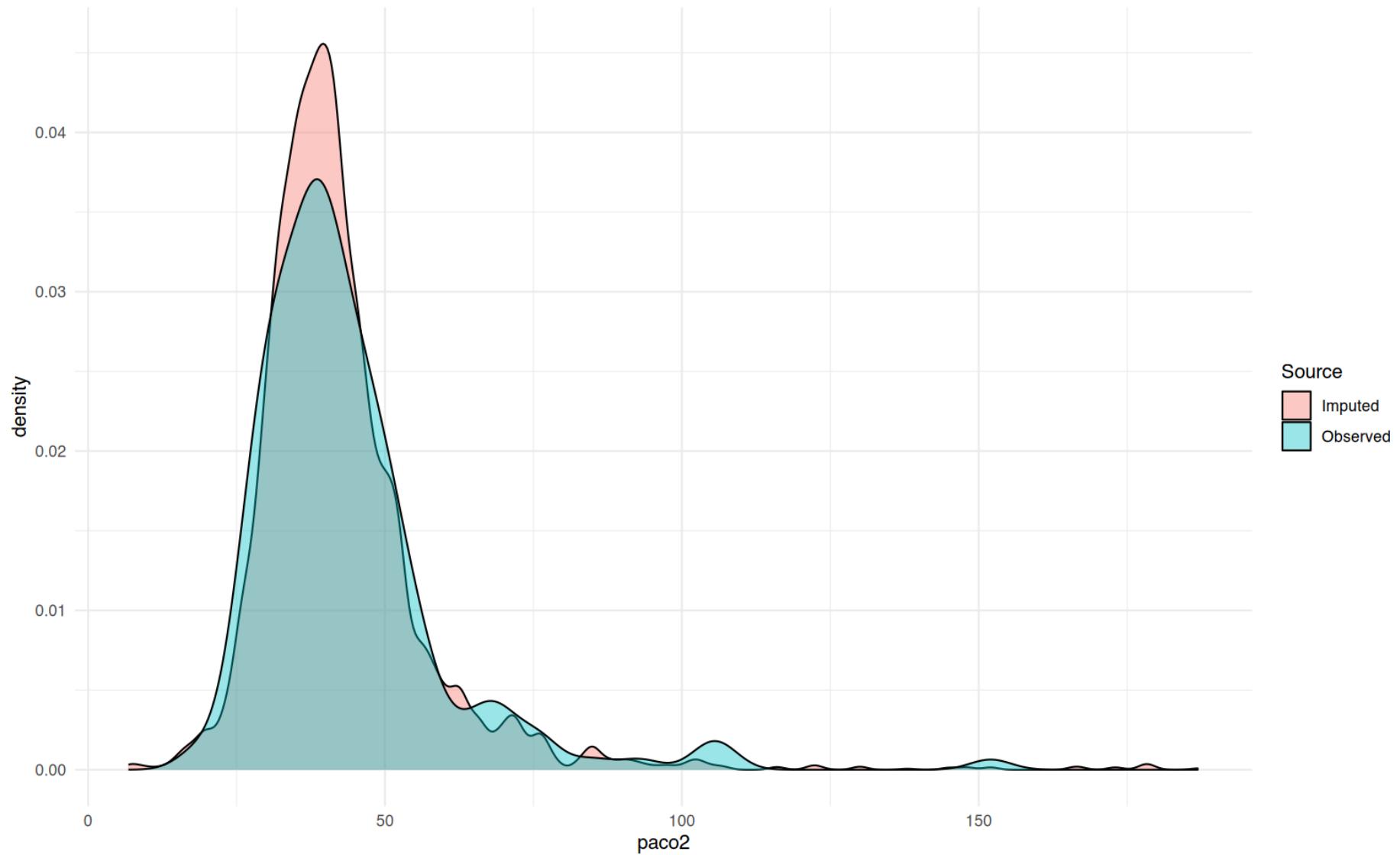
```

Observed vs imputed density: vbg_o2sat

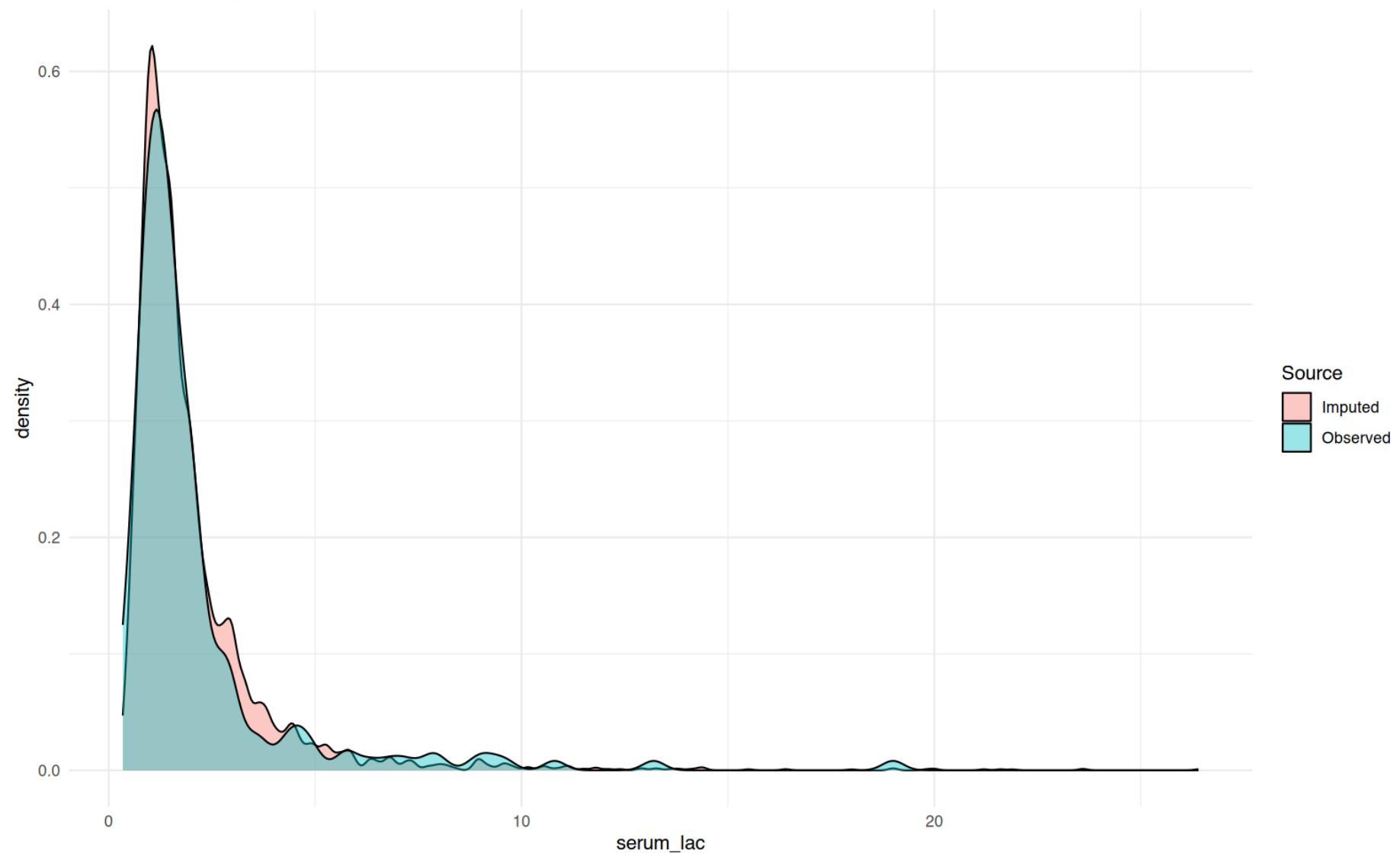




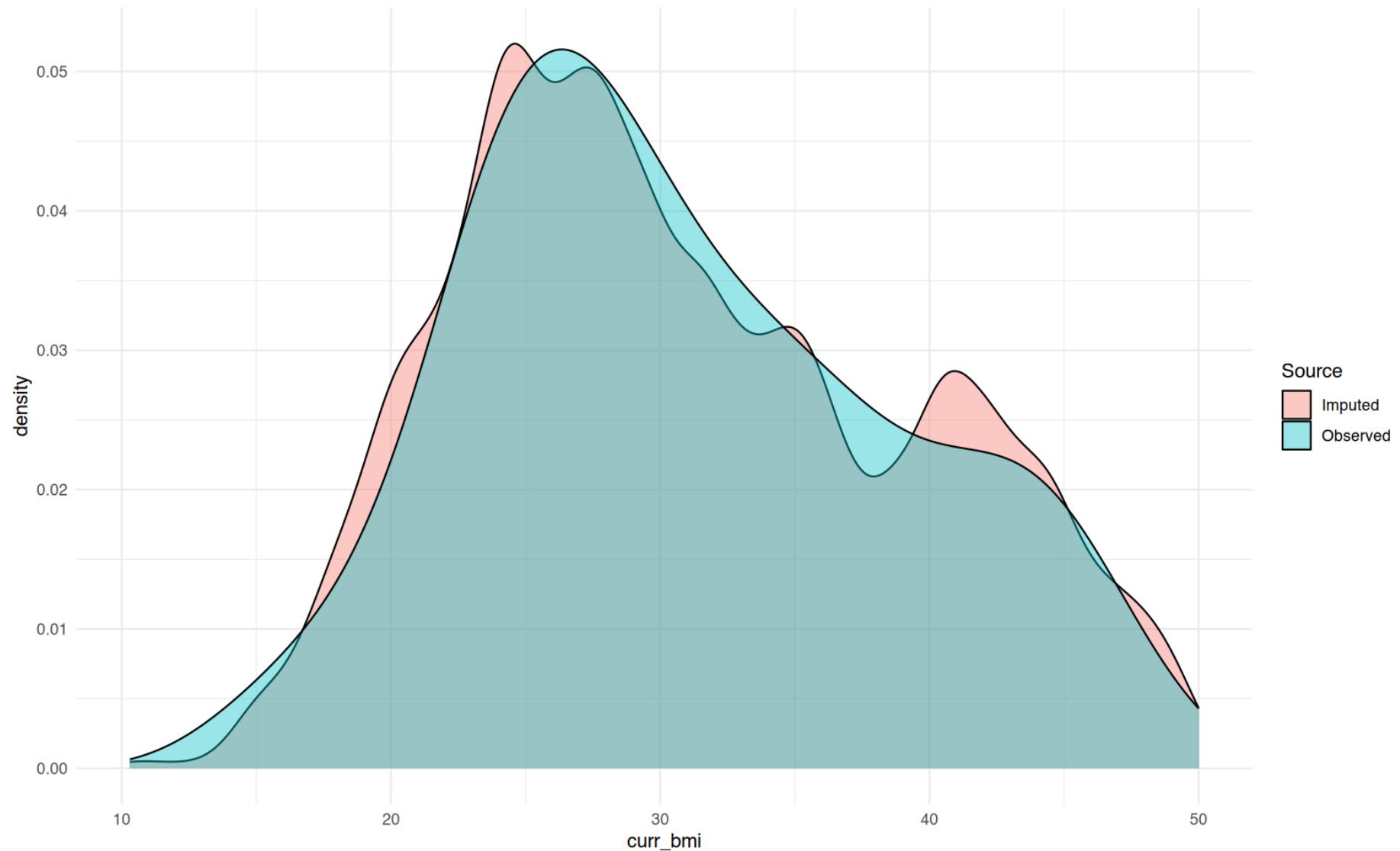
Observed vs imputed density: paco2



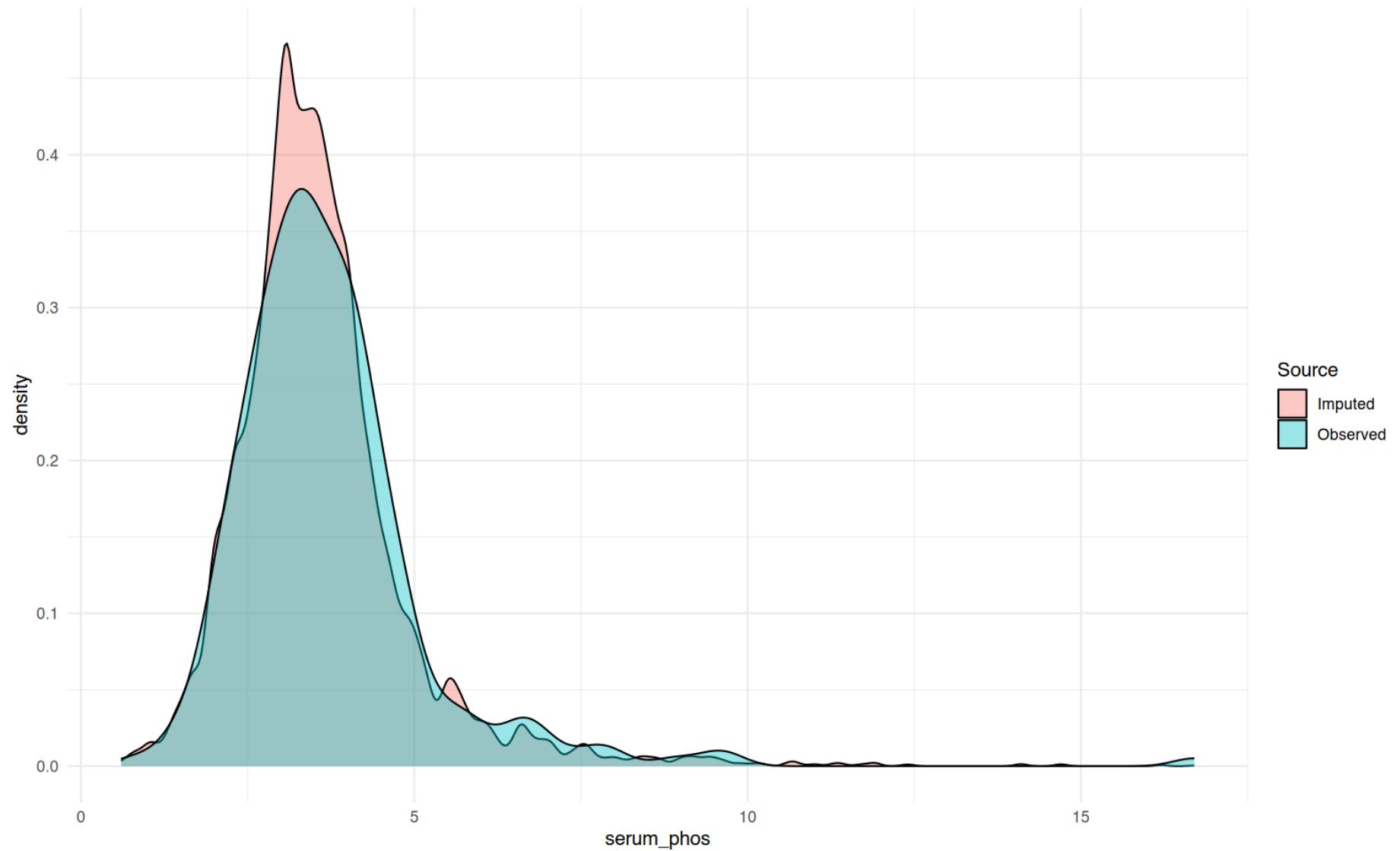
Observed vs imputed density: serum_lac



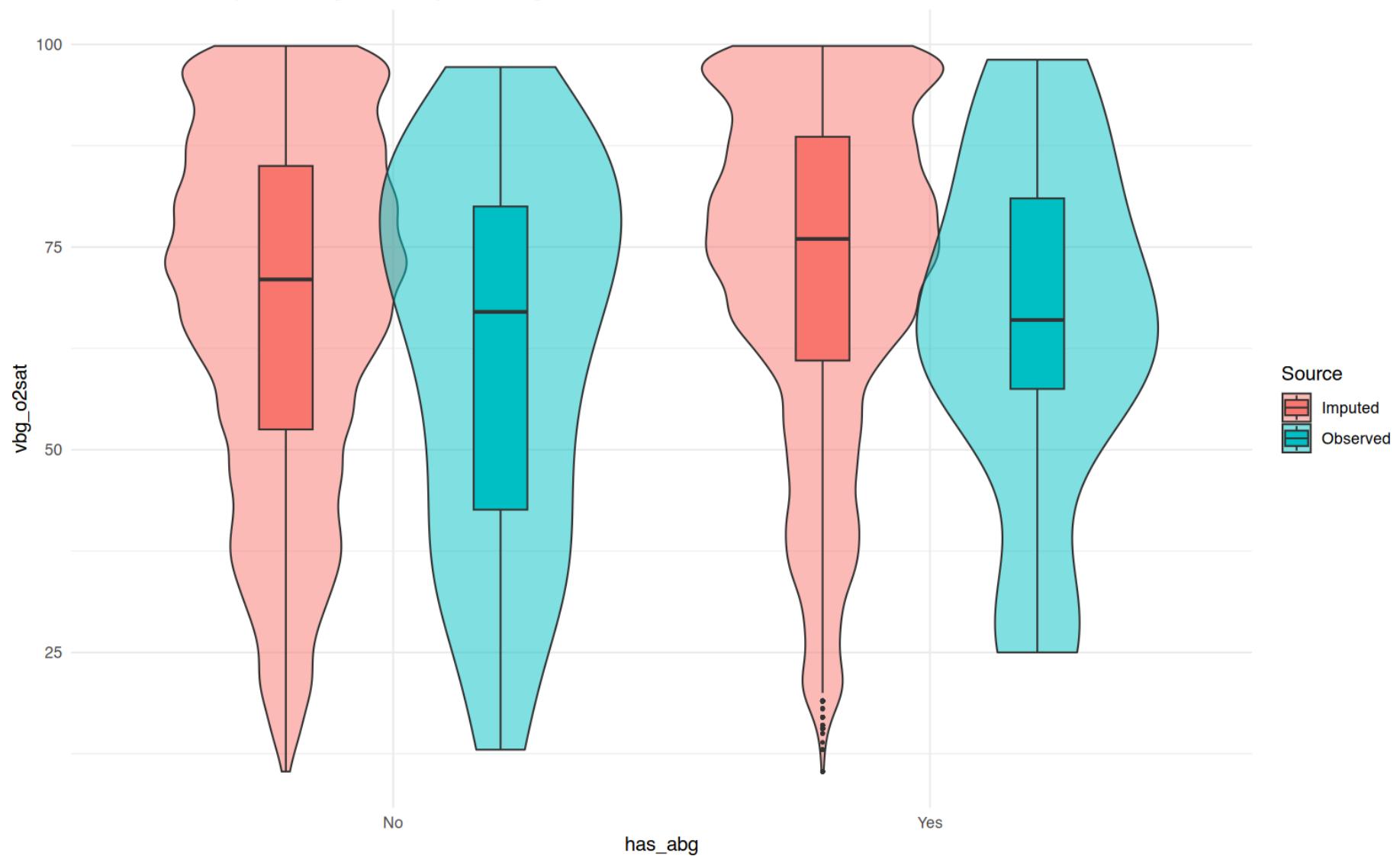
Observed vs imputed density: curr_bmi



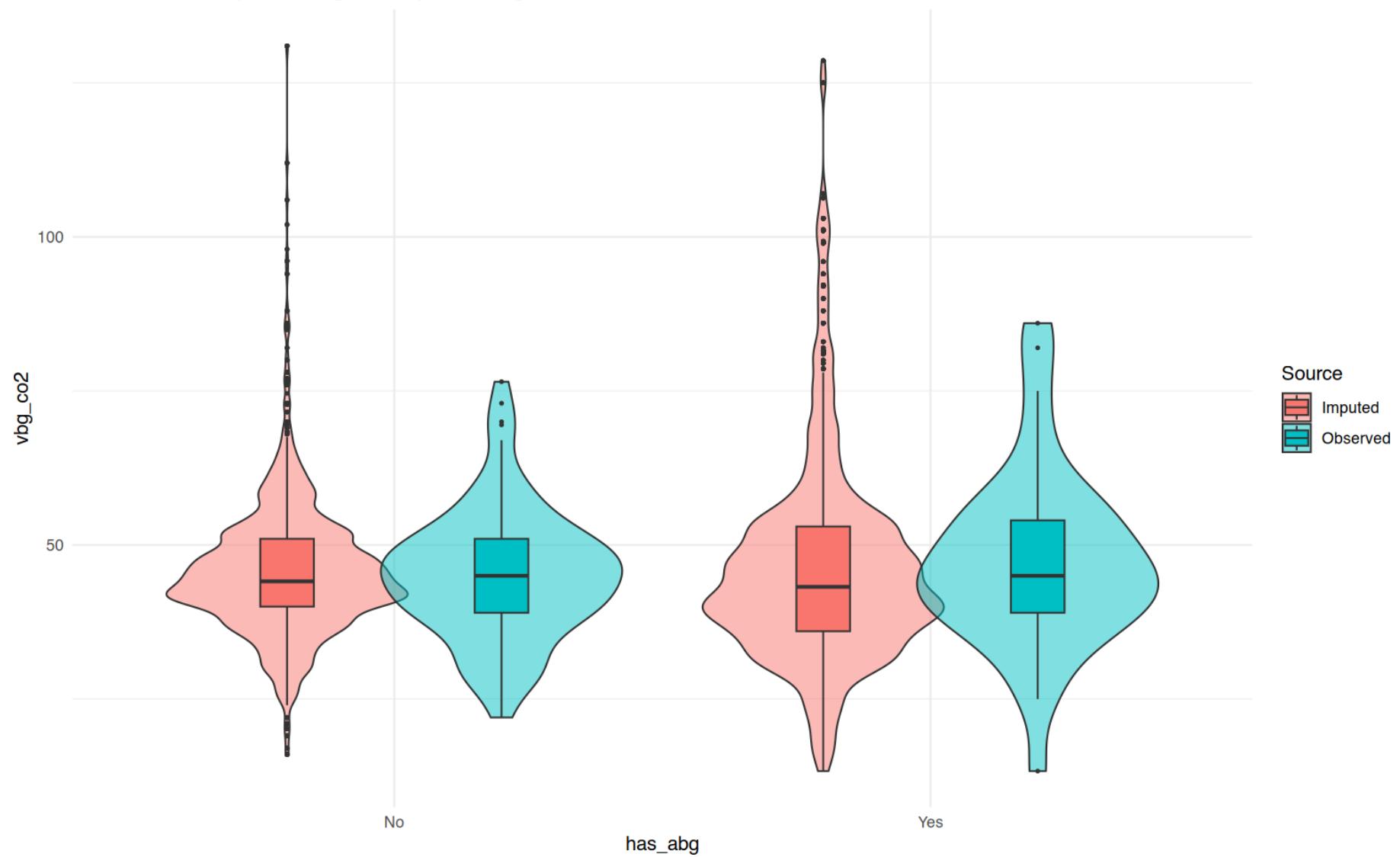
Observed vs imputed density: serum_phos



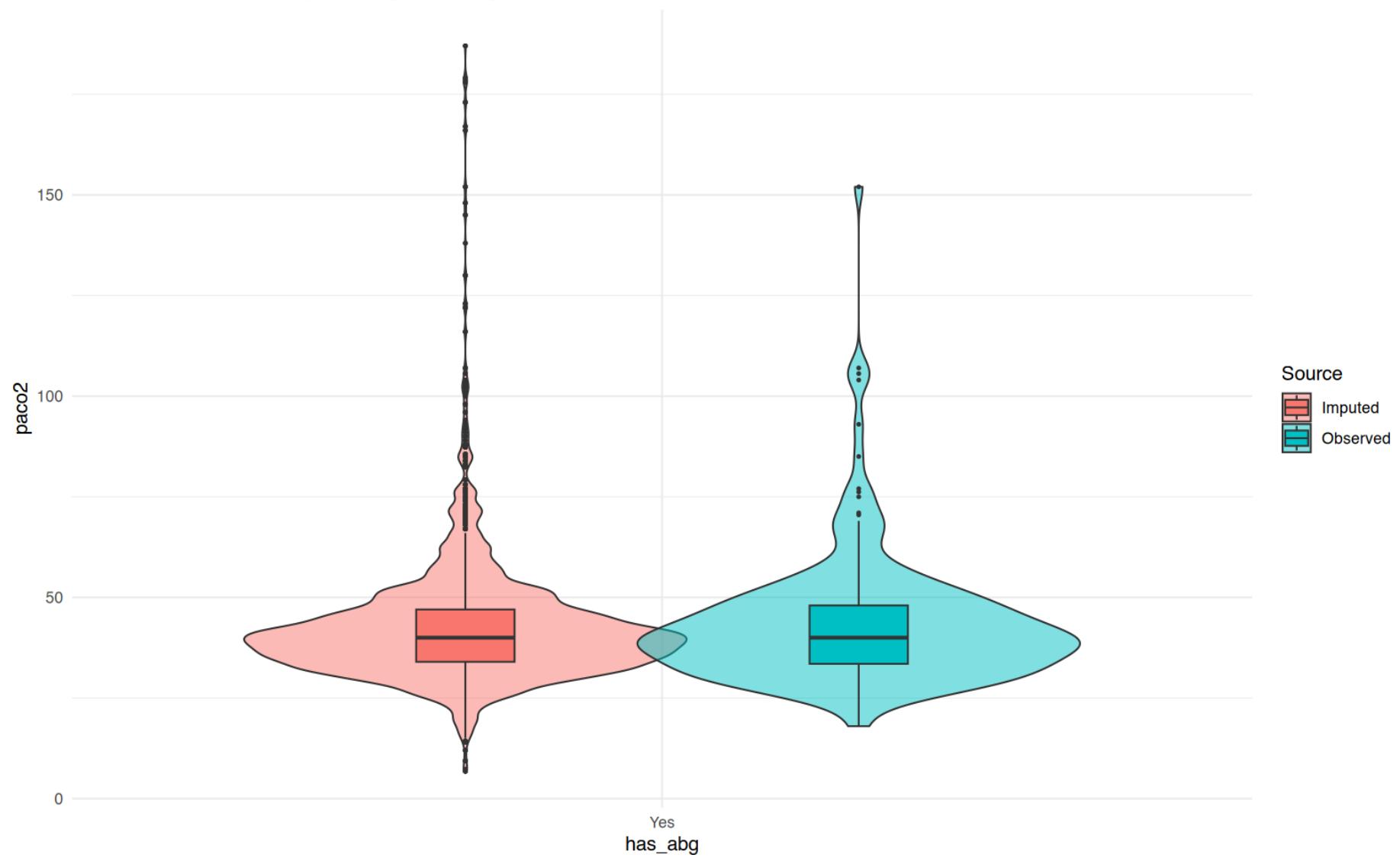
Observed vs imputed: vbg_o2sat by has_abg



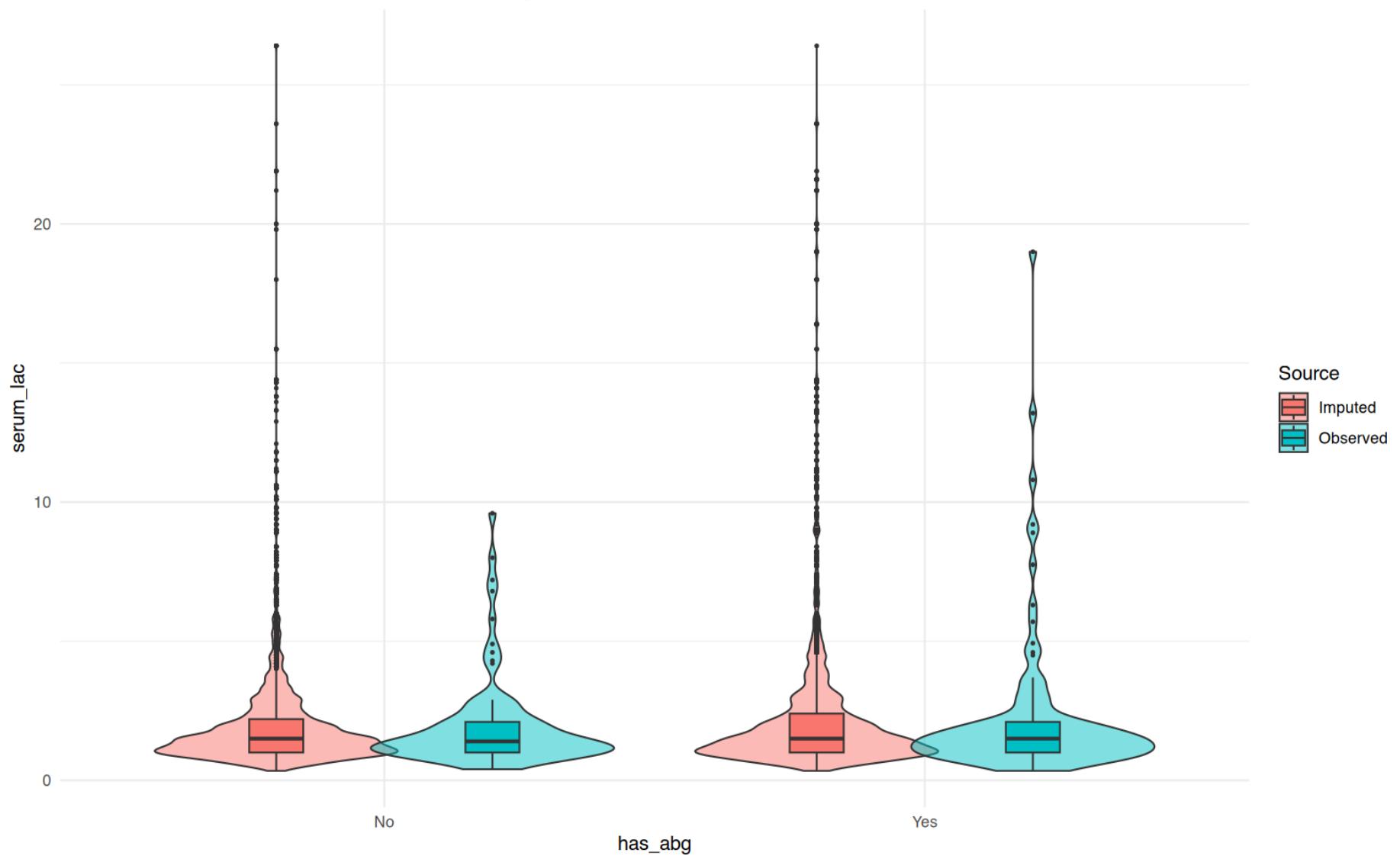
Observed vs imputed: vbg_co2 by has_abg



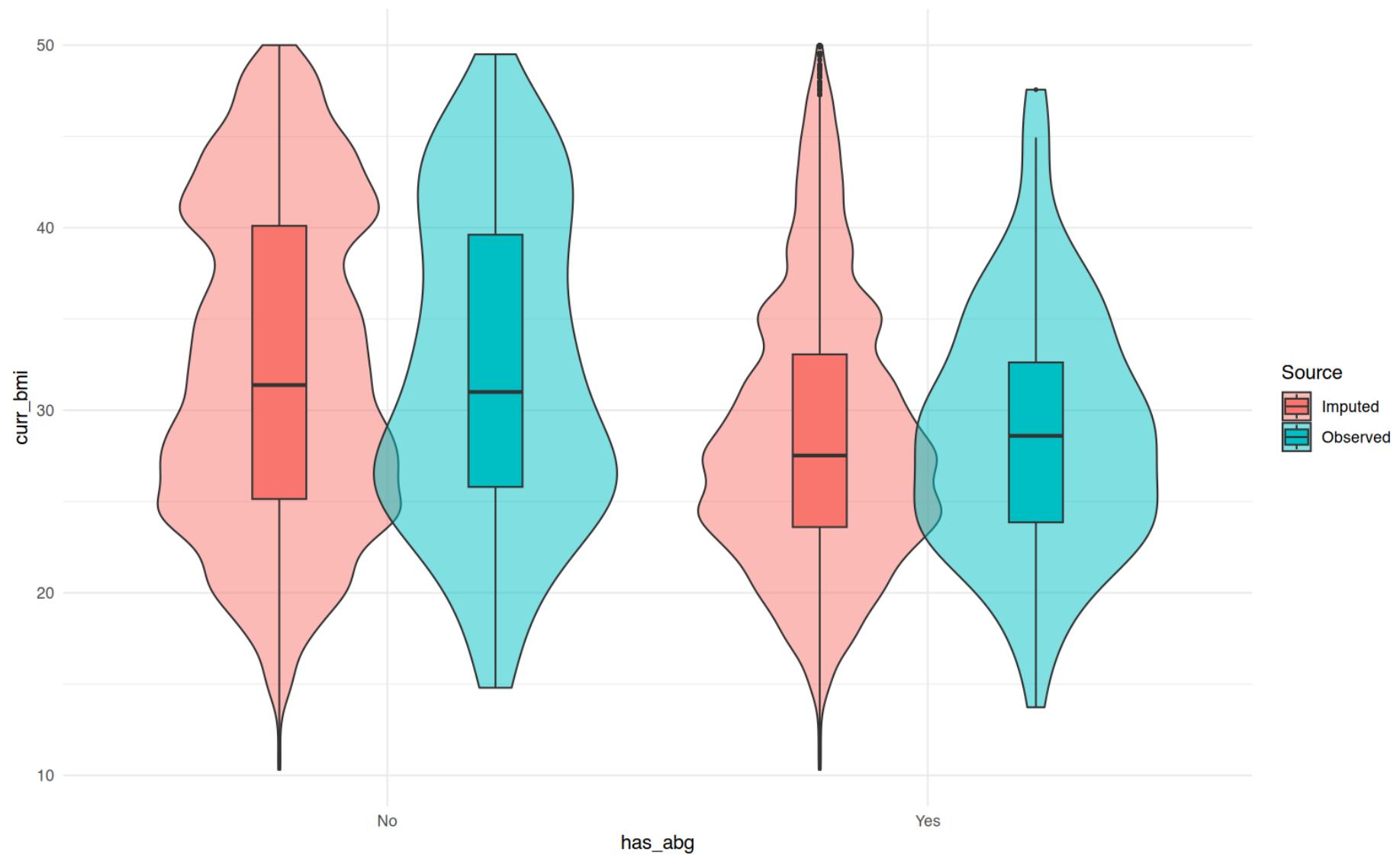
Observed vs imputed: paco2 by has_abg



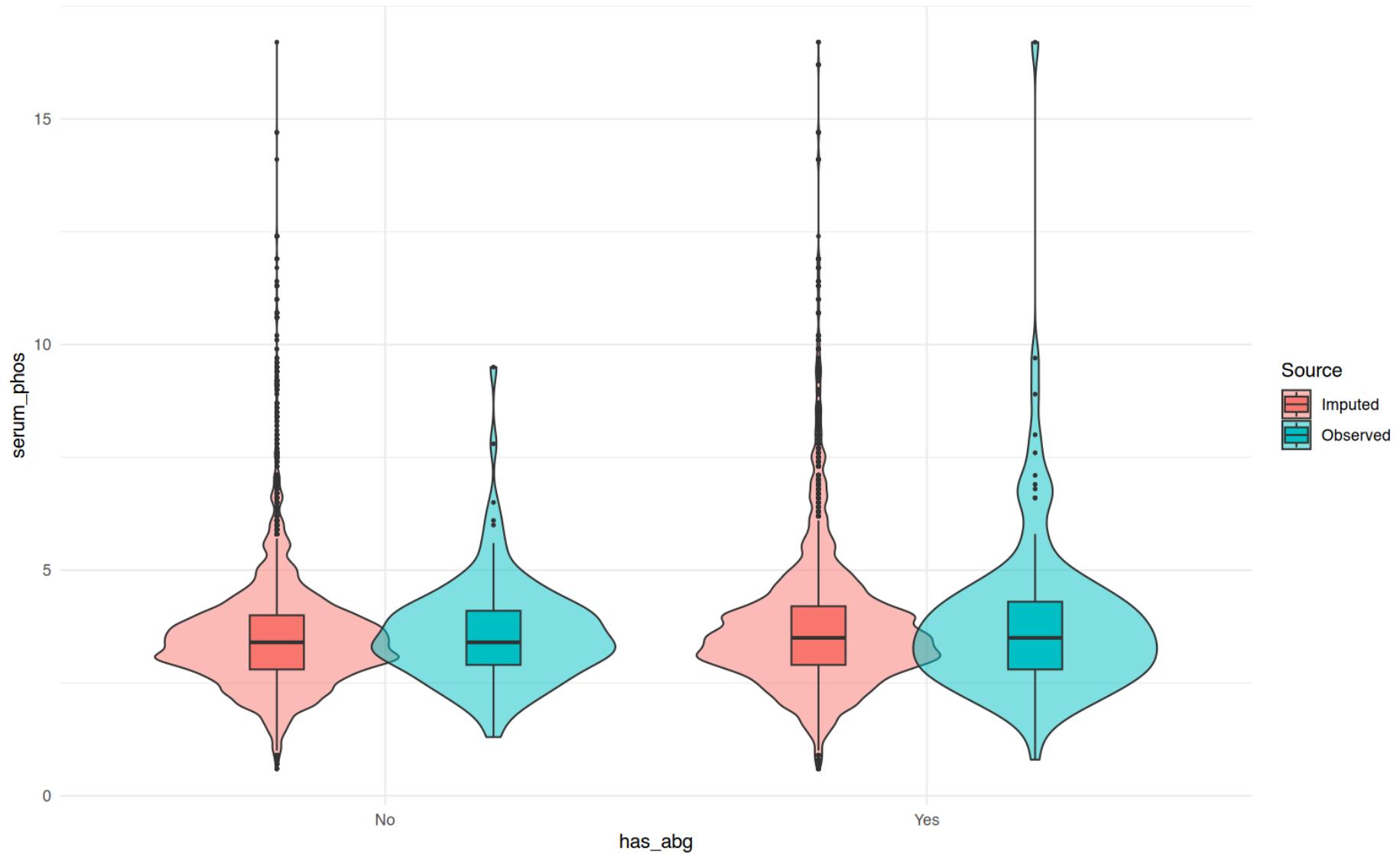
Observed vs imputed: serum_lac by has_abg



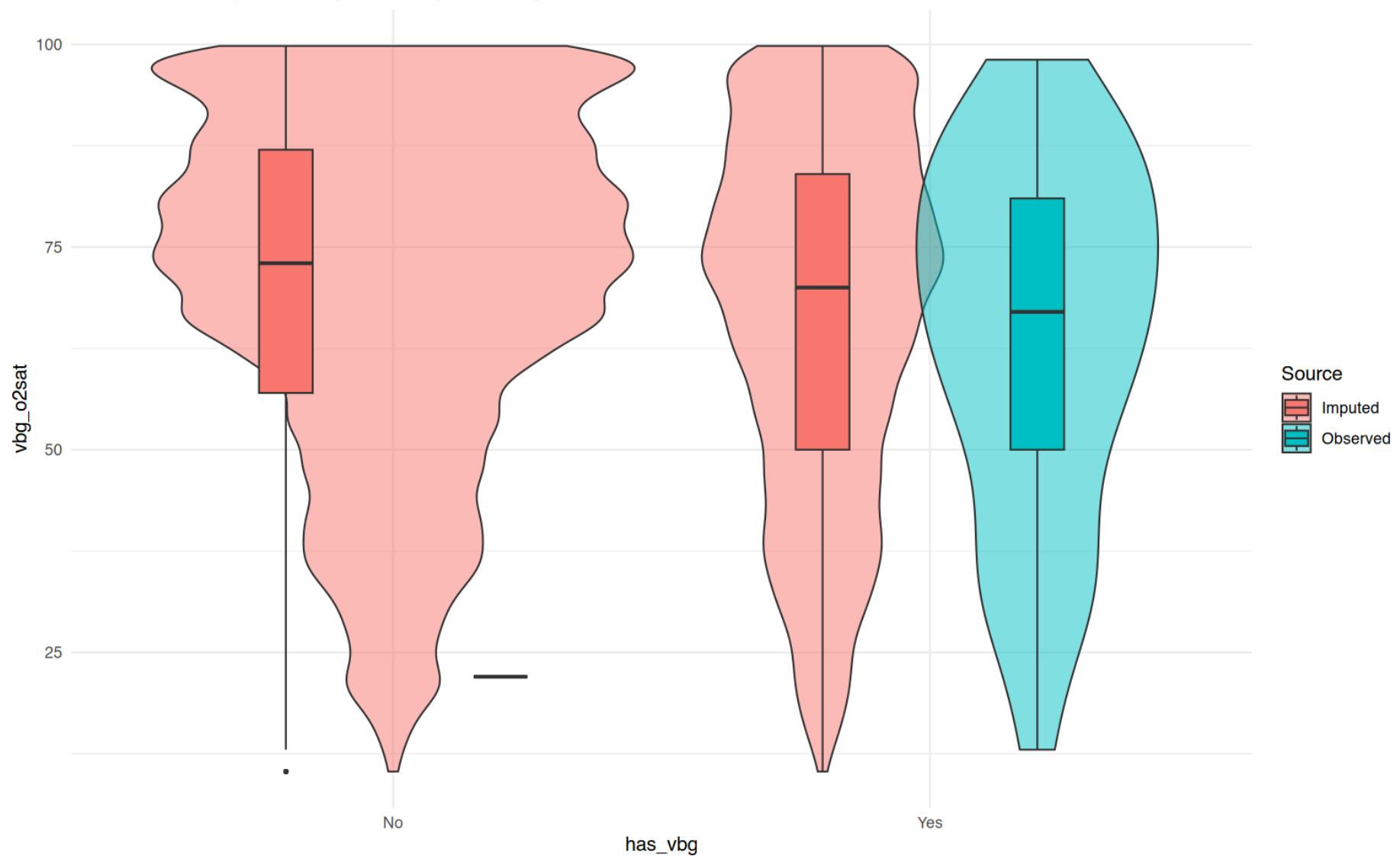
Observed vs imputed: curr_bmi by has_abg



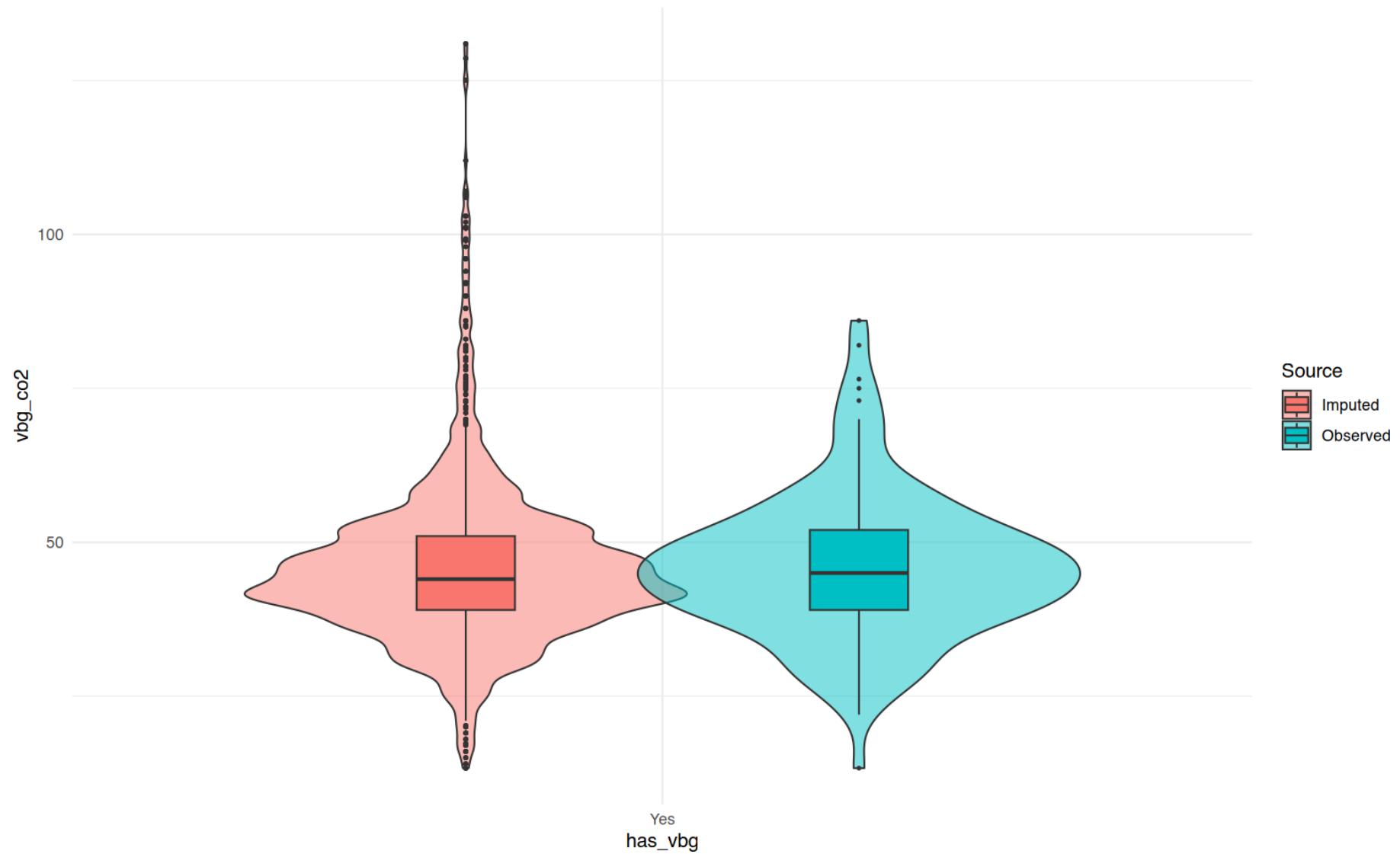
Observed vs imputed: serum_phos by has_abg



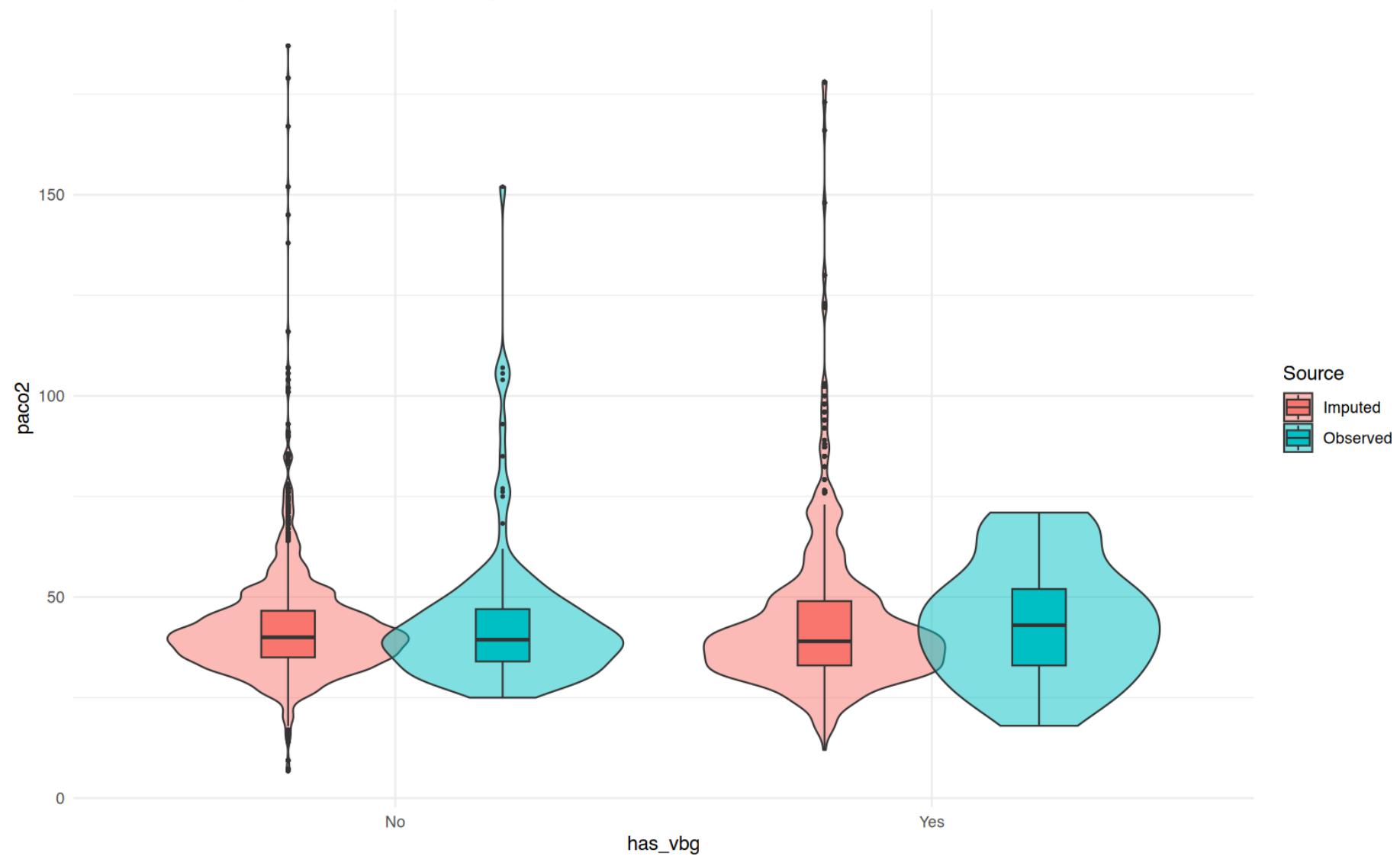
Observed vs imputed: vbg_o2sat by has_vbg



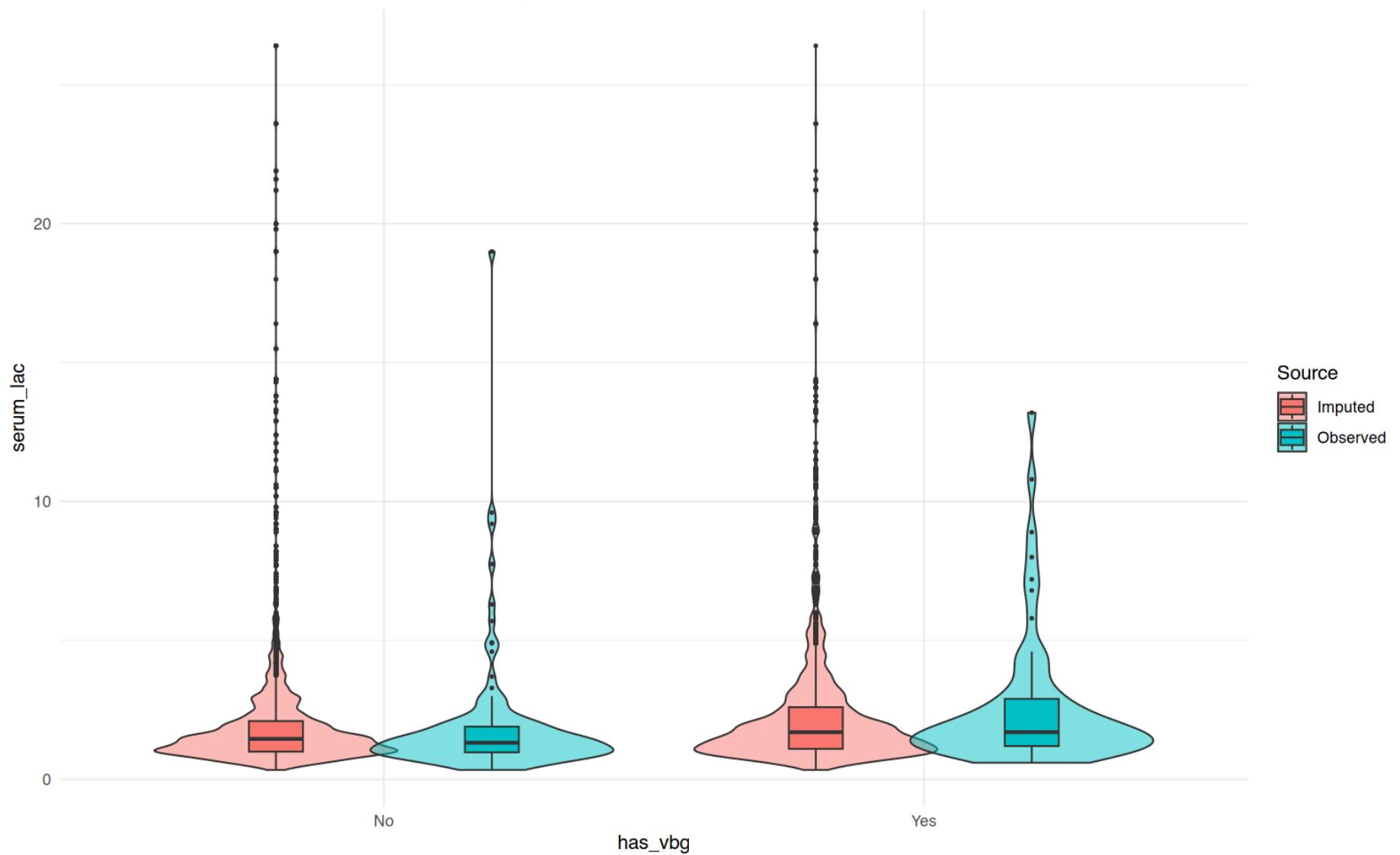
Observed vs imputed: vbg_co2 by has_vbg



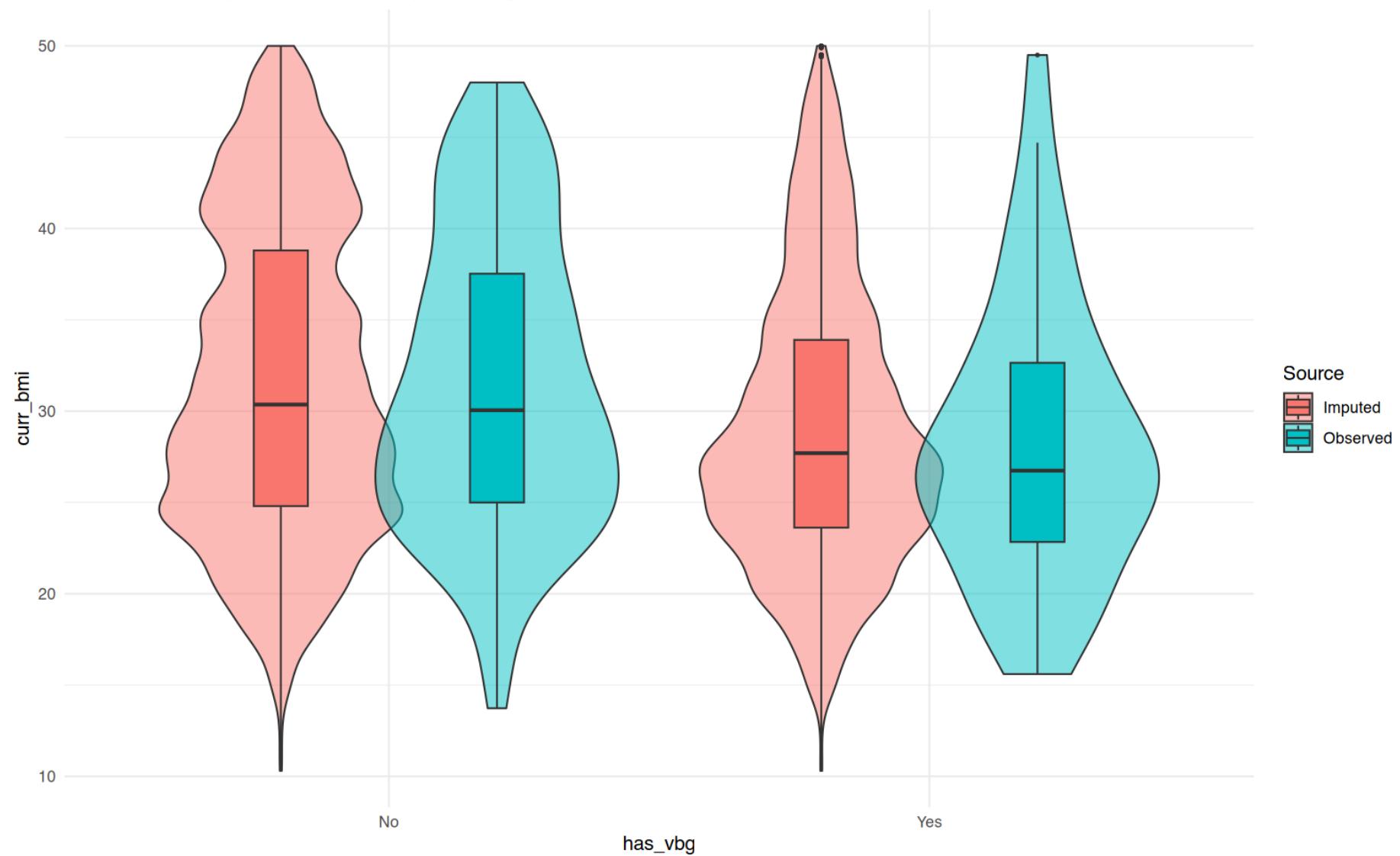
Observed vs imputed: paco2 by has_vbg



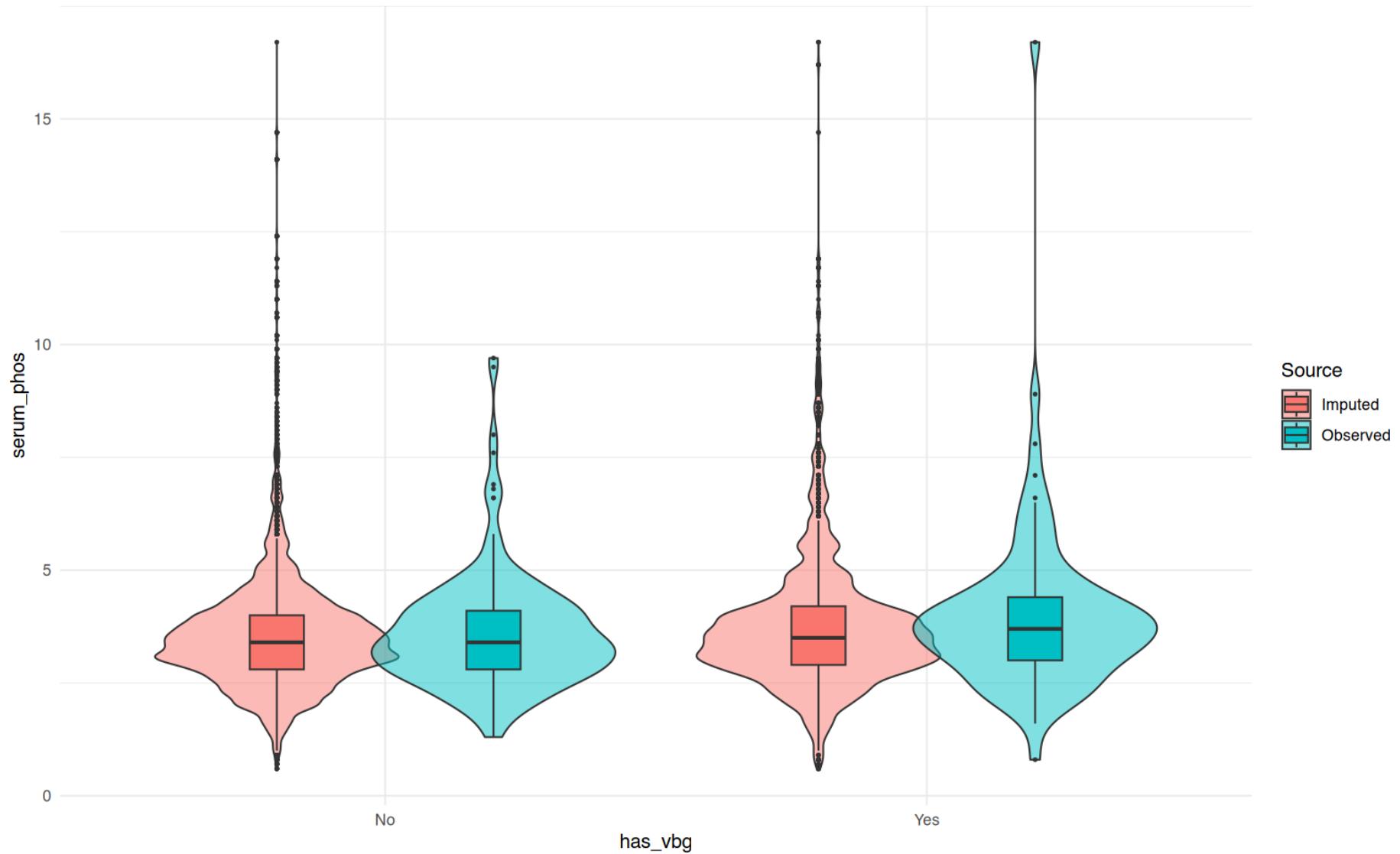
Observed vs imputed: serum_lac by has_vbg



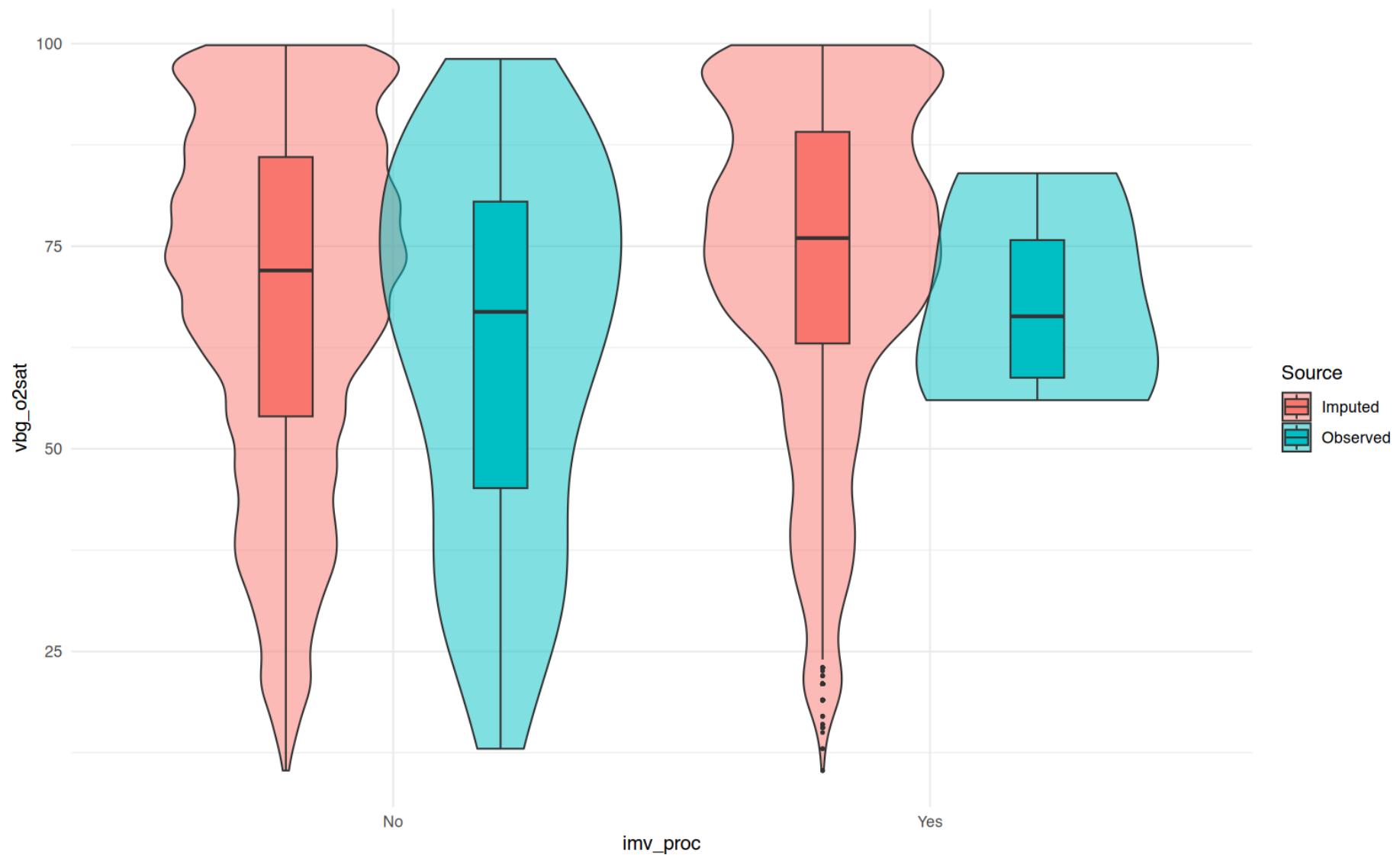
Observed vs imputed: curr_bmi by has_vbg



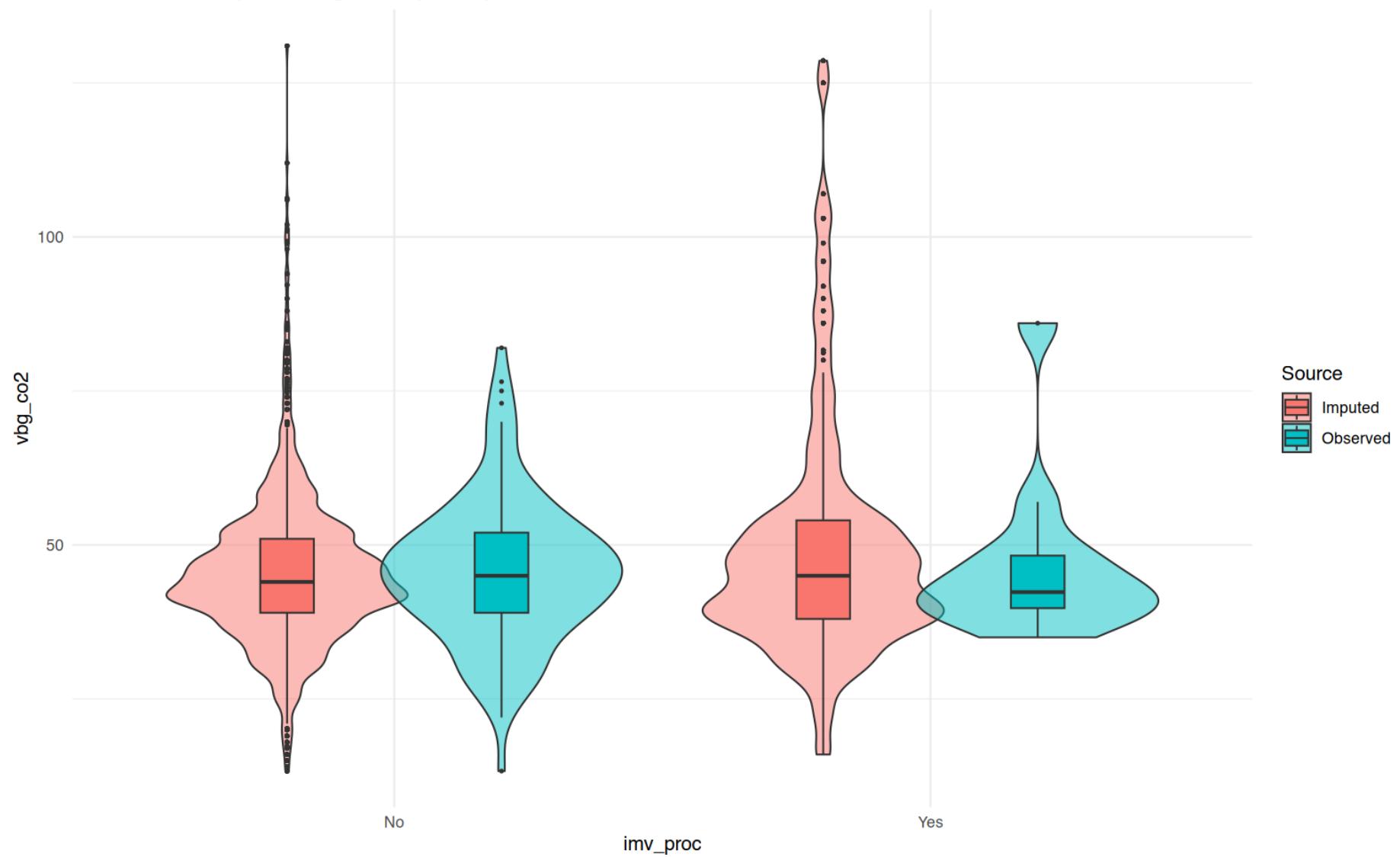
Observed vs imputed: serum_phos by has_vbg



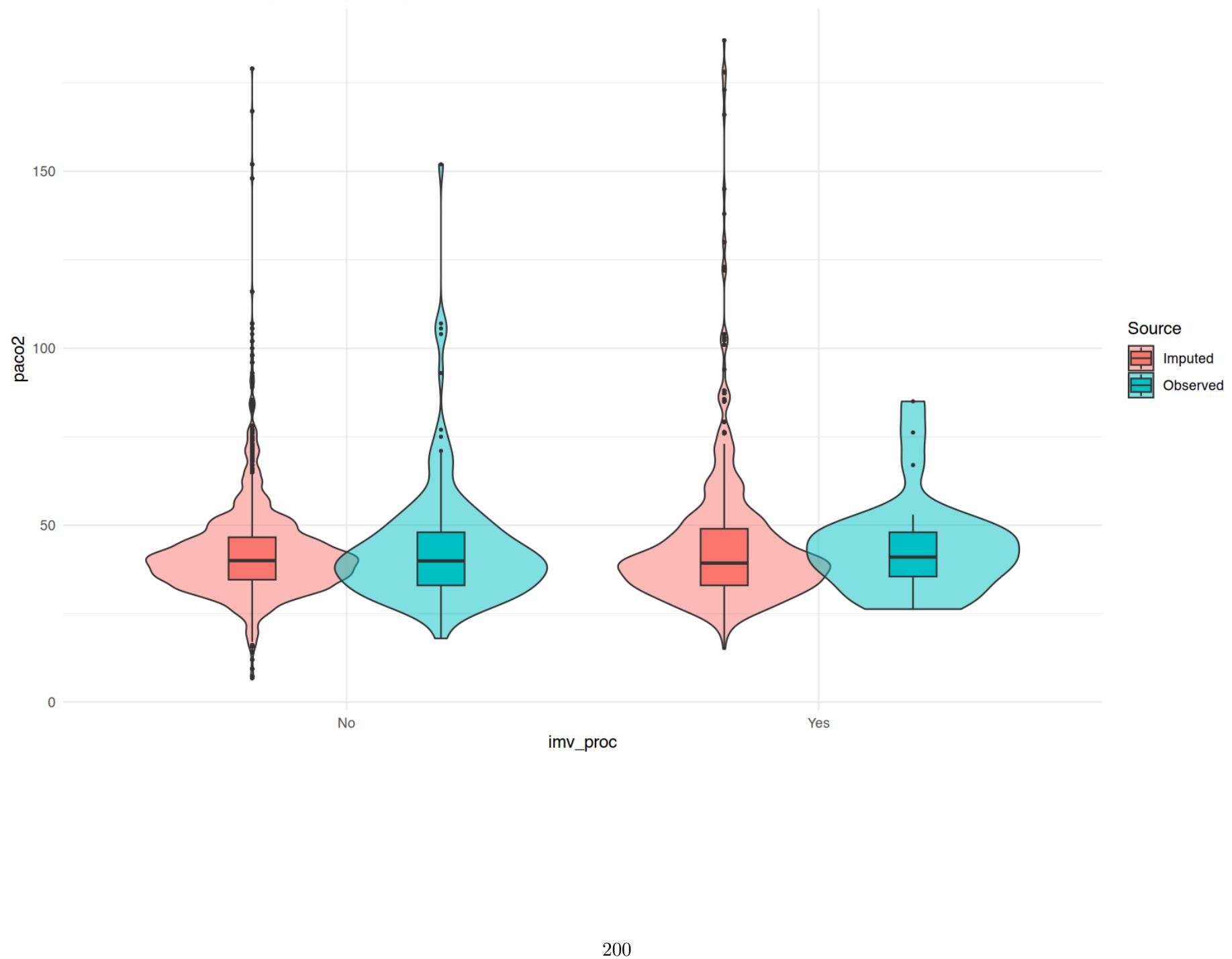
Observed vs imputed: vbg_o2sat by imv_proc



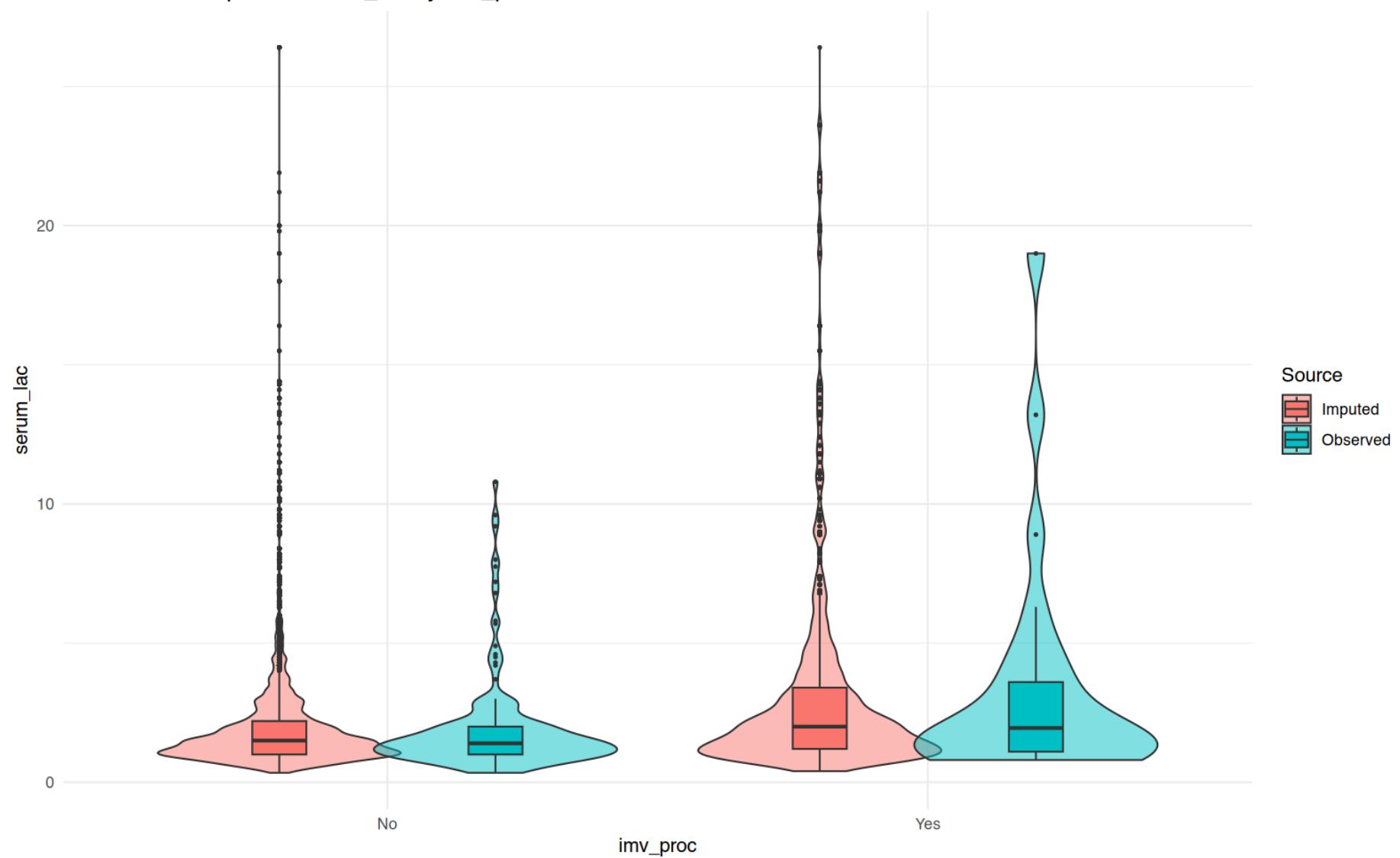
Observed vs imputed: vbg_co2 by imv_proc



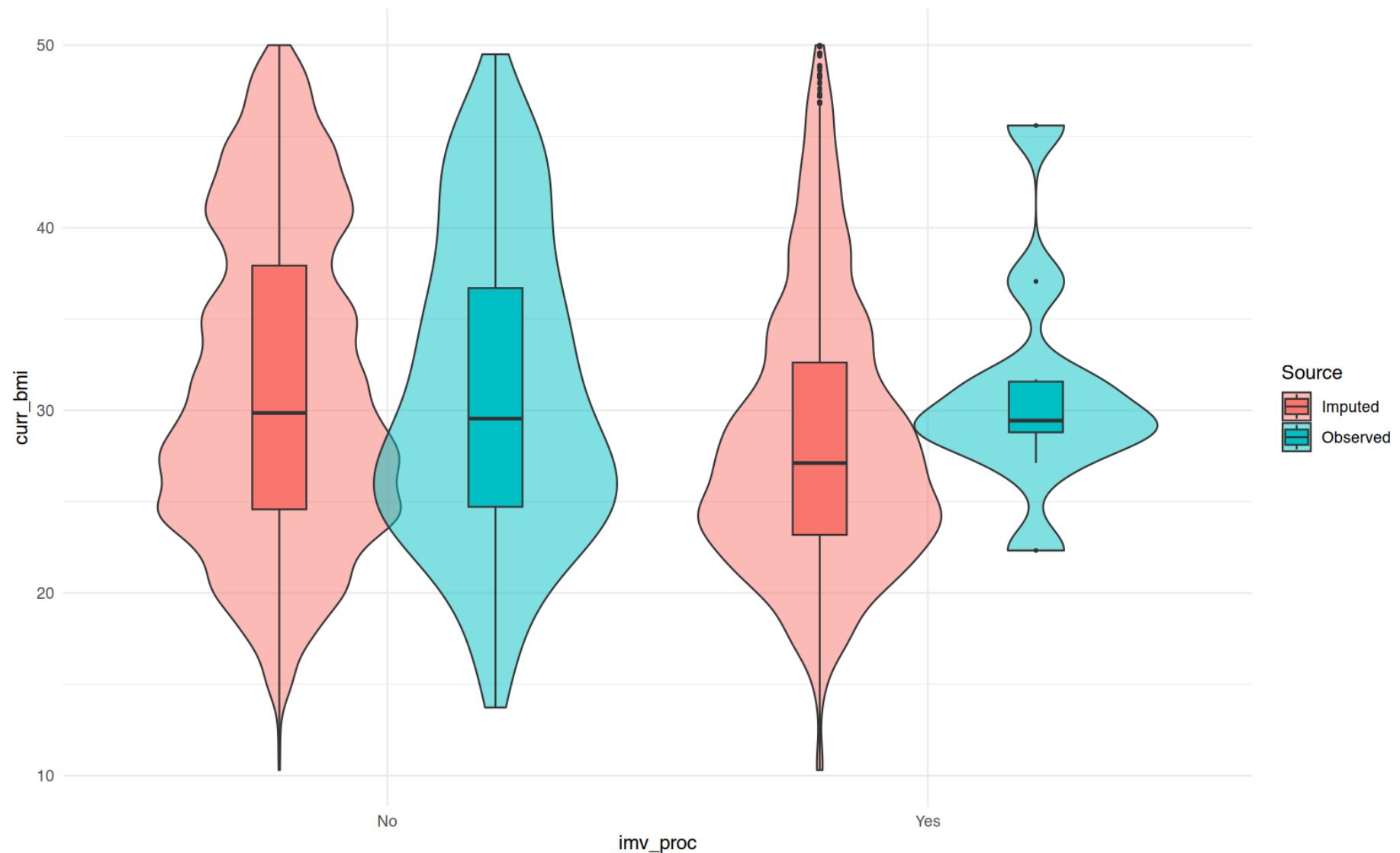
Observed vs imputed: paco2 by imv_proc



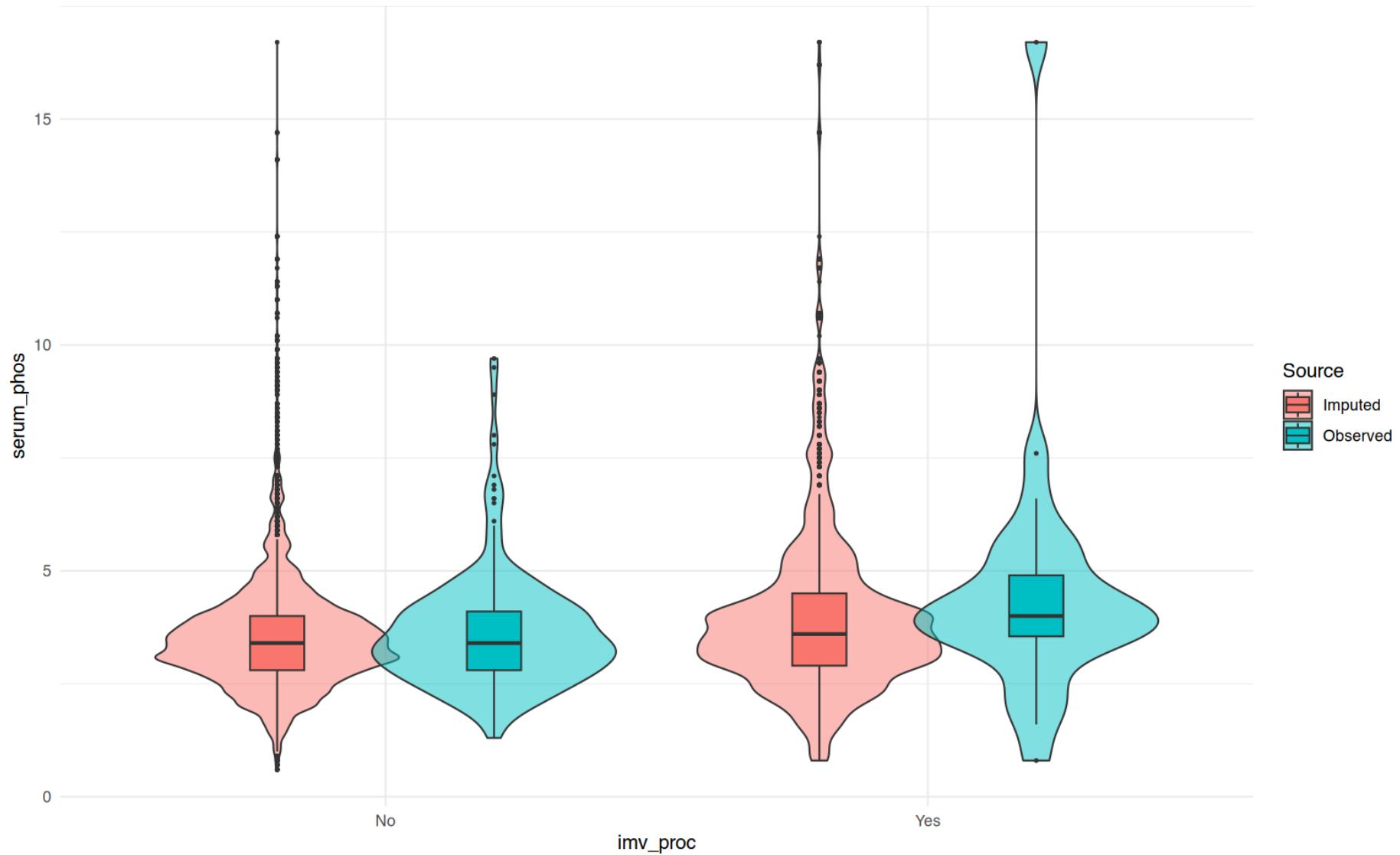
Observed vs imputed: serum_lac by imv_proc



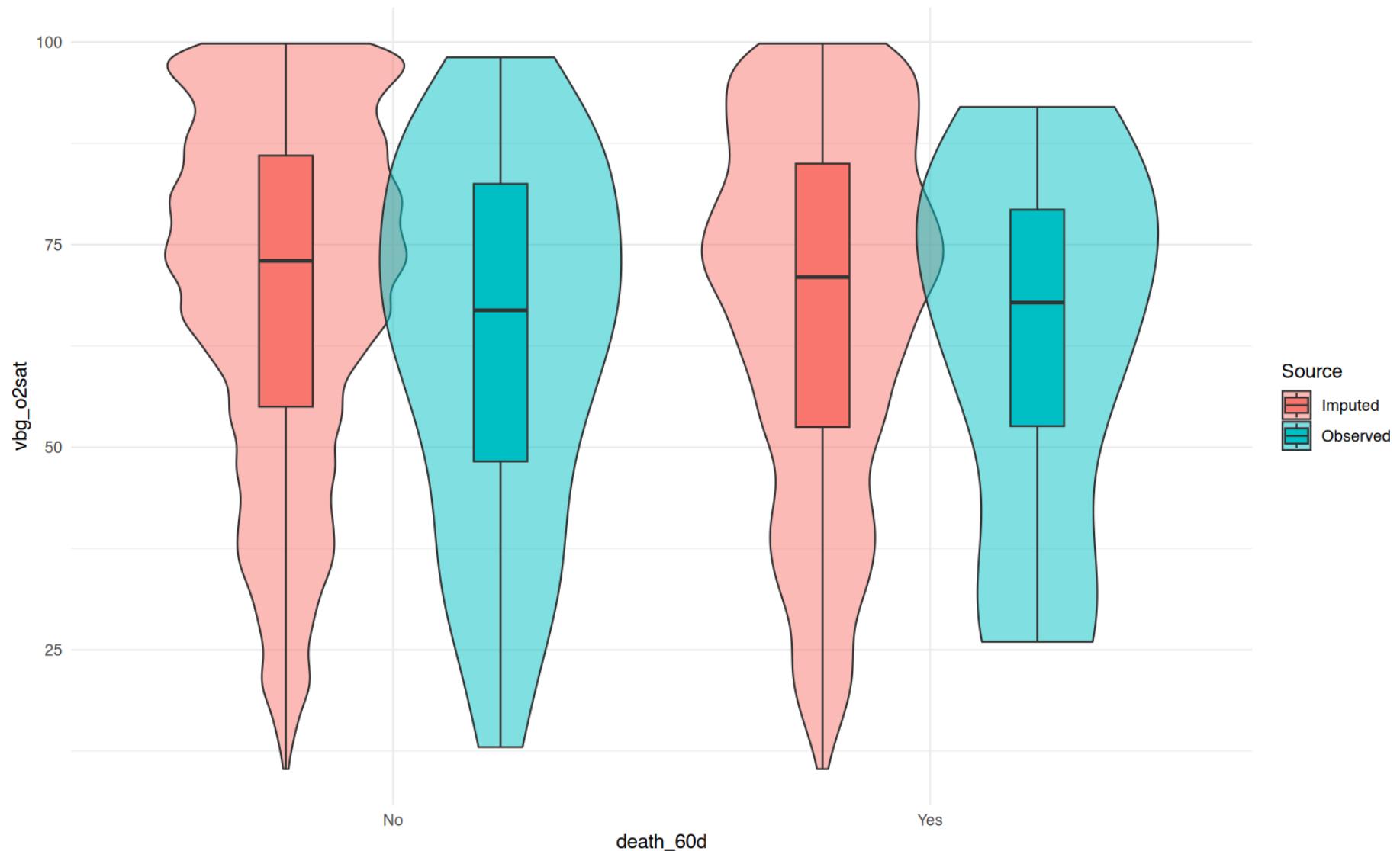
Observed vs imputed: curr_bmi by imv_proc



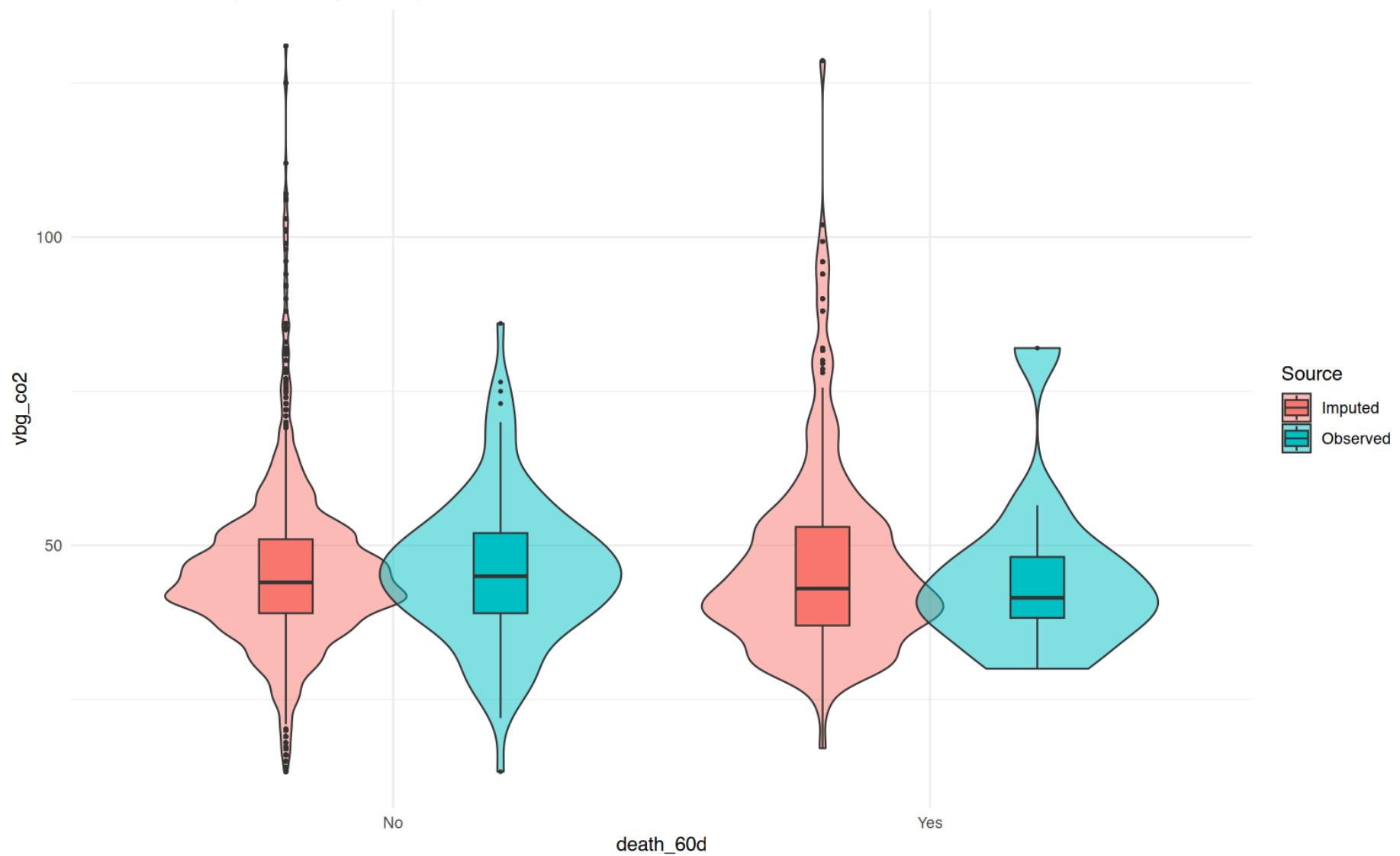
Observed vs imputed: serum_phos by imv_proc



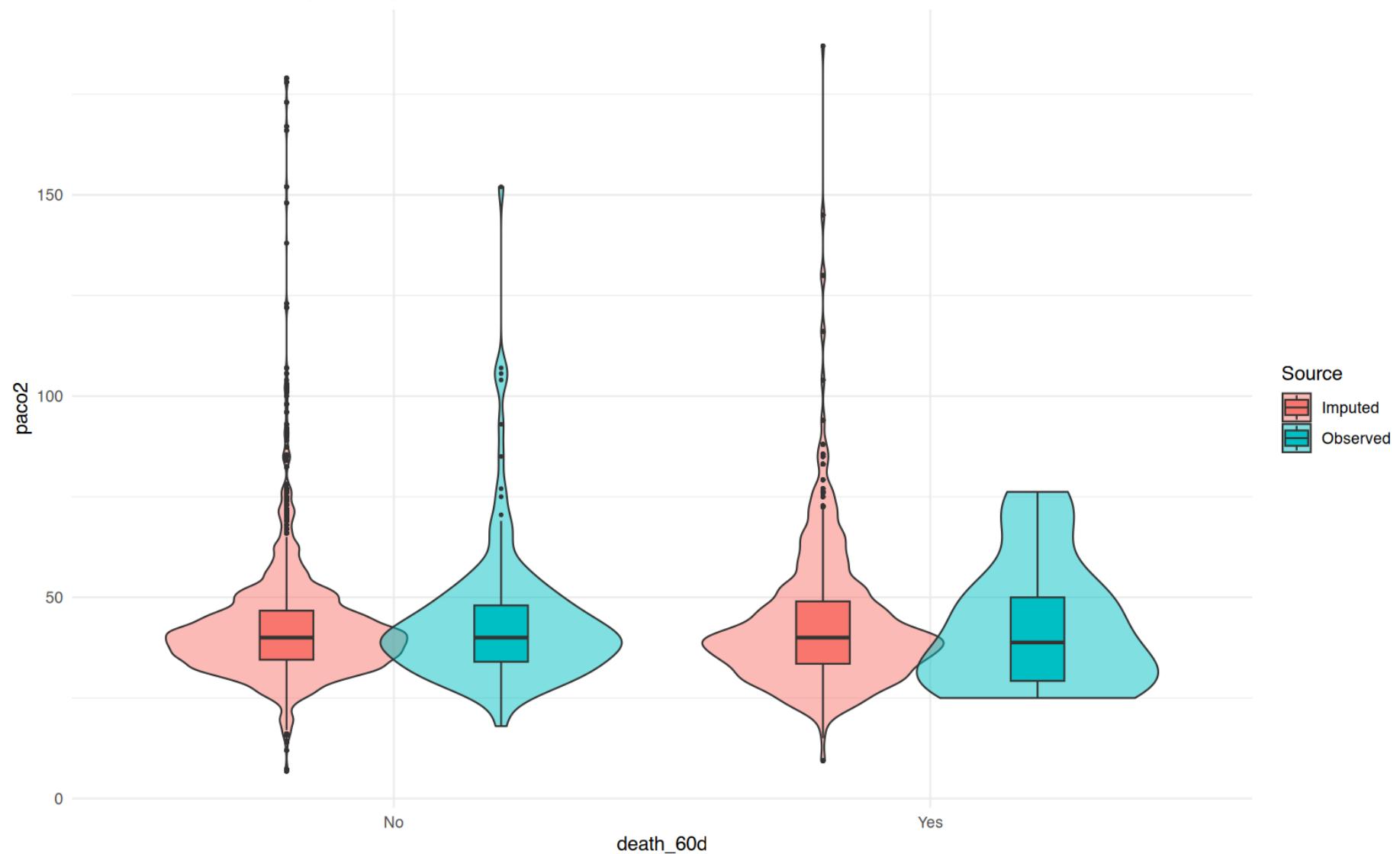
Observed vs imputed: vbg_o2sat by death_60d



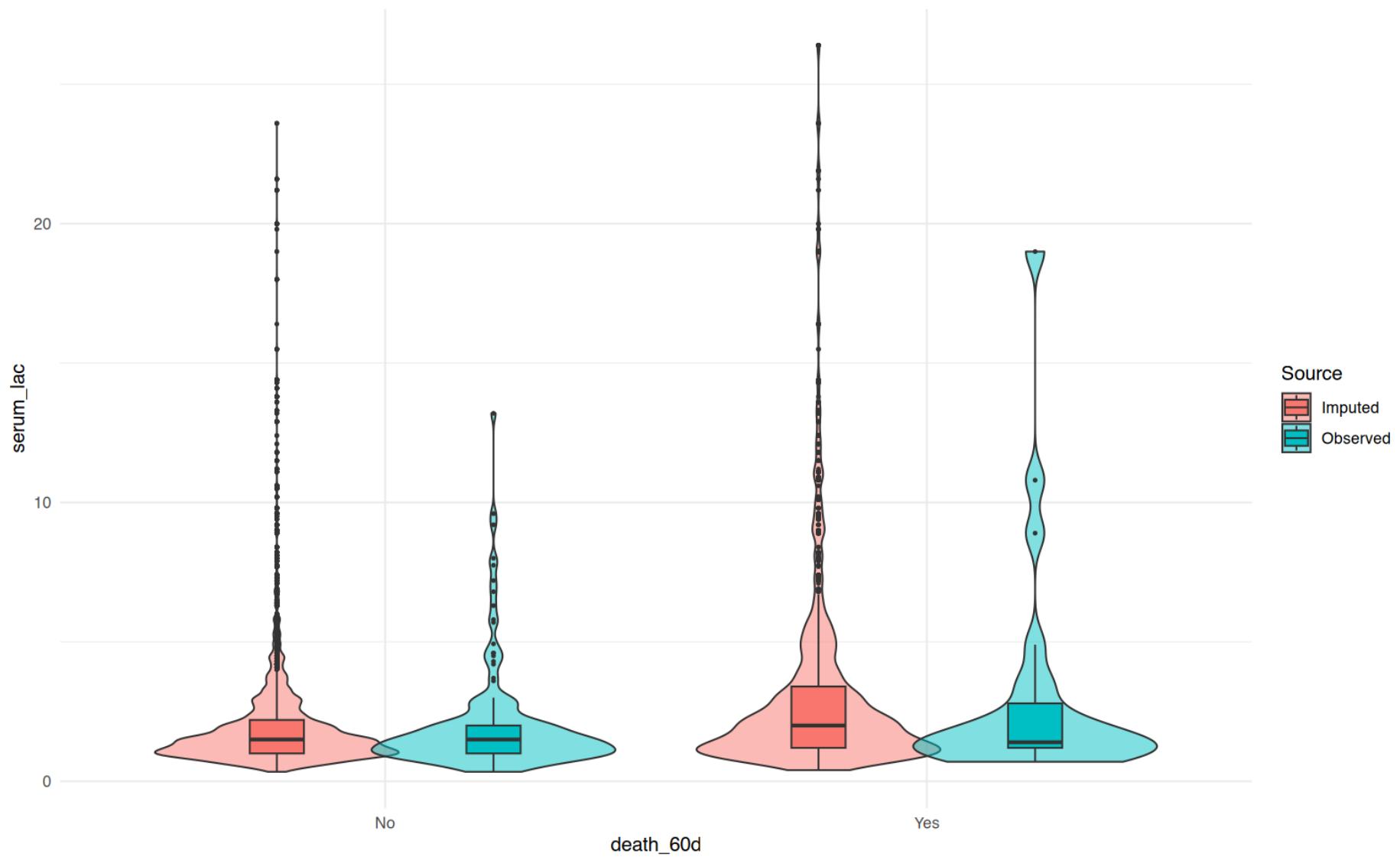
Observed vs imputed: vbg_co2 by death_60d



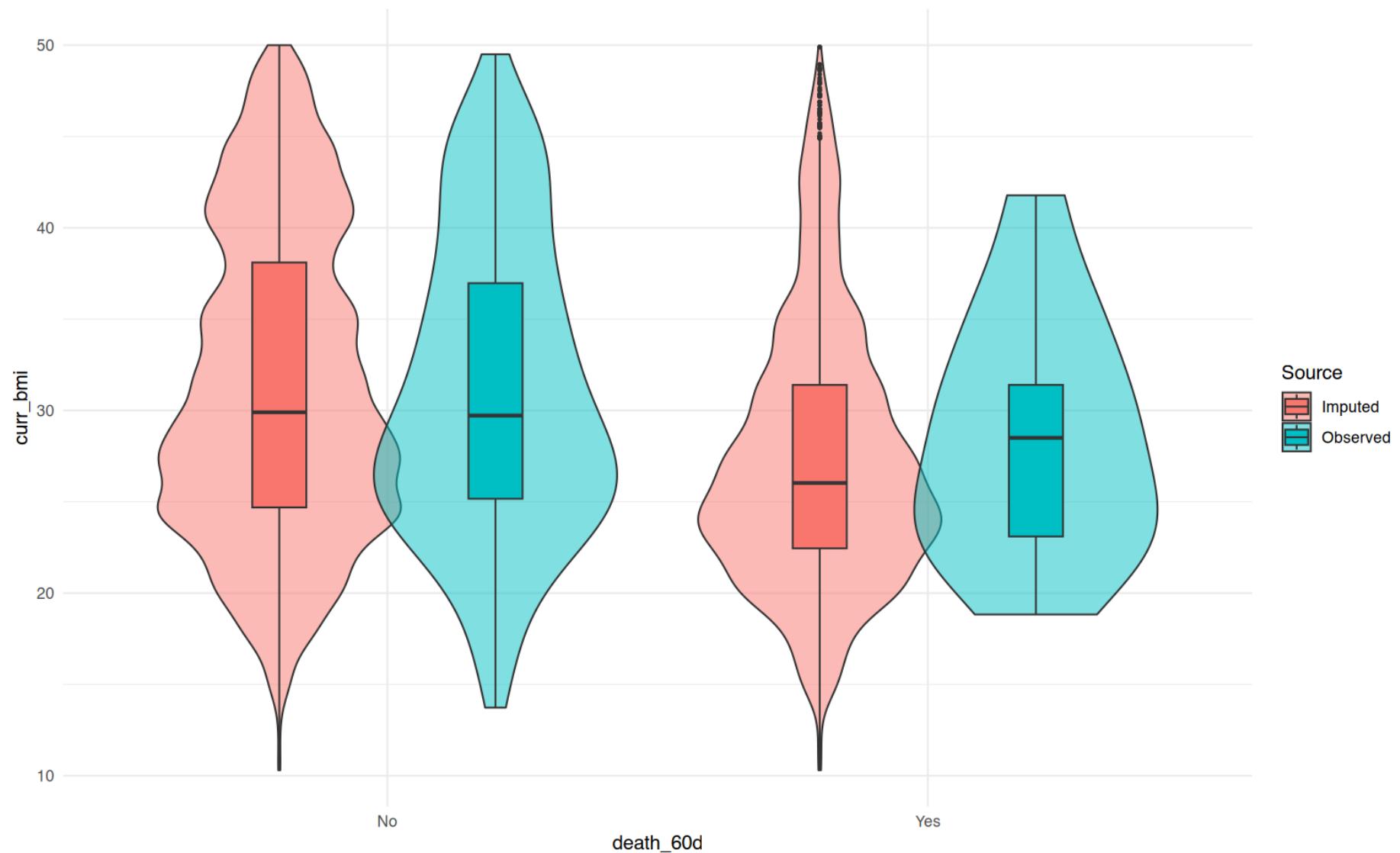
Observed vs imputed: paco2 by death_60d



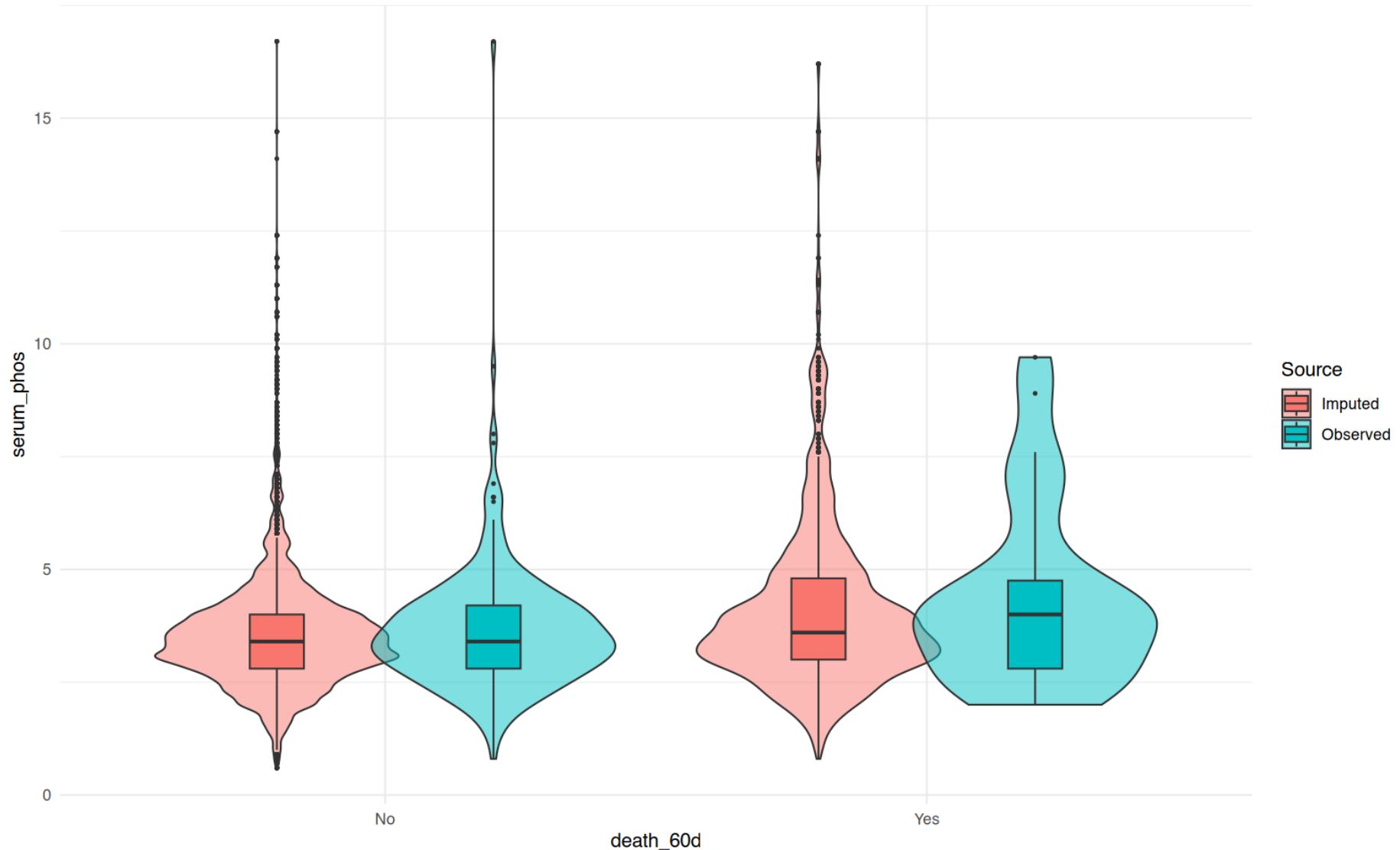
Observed vs imputed: serum_lac by death_60d



Observed vs imputed: curr_bmi by death_60d



Observed vs imputed: serum_phos by death_60d



```
mc_file <- results_path("mi_mcerr_progress.csv")
stopifnot(file.exists(mc_file))
mc_prog <- utils:::read.csv(mc_file)
render_table_pdf_maybe(
```

```

mc_prog,
caption = "MC error progress by m (early-stop diagnostic)",
file_stub = "mi_mcerr_progress",
digits = 3,
show = SHOW_LOW_VALUE_TABLES
)

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

stopifnot(exists("imp"))

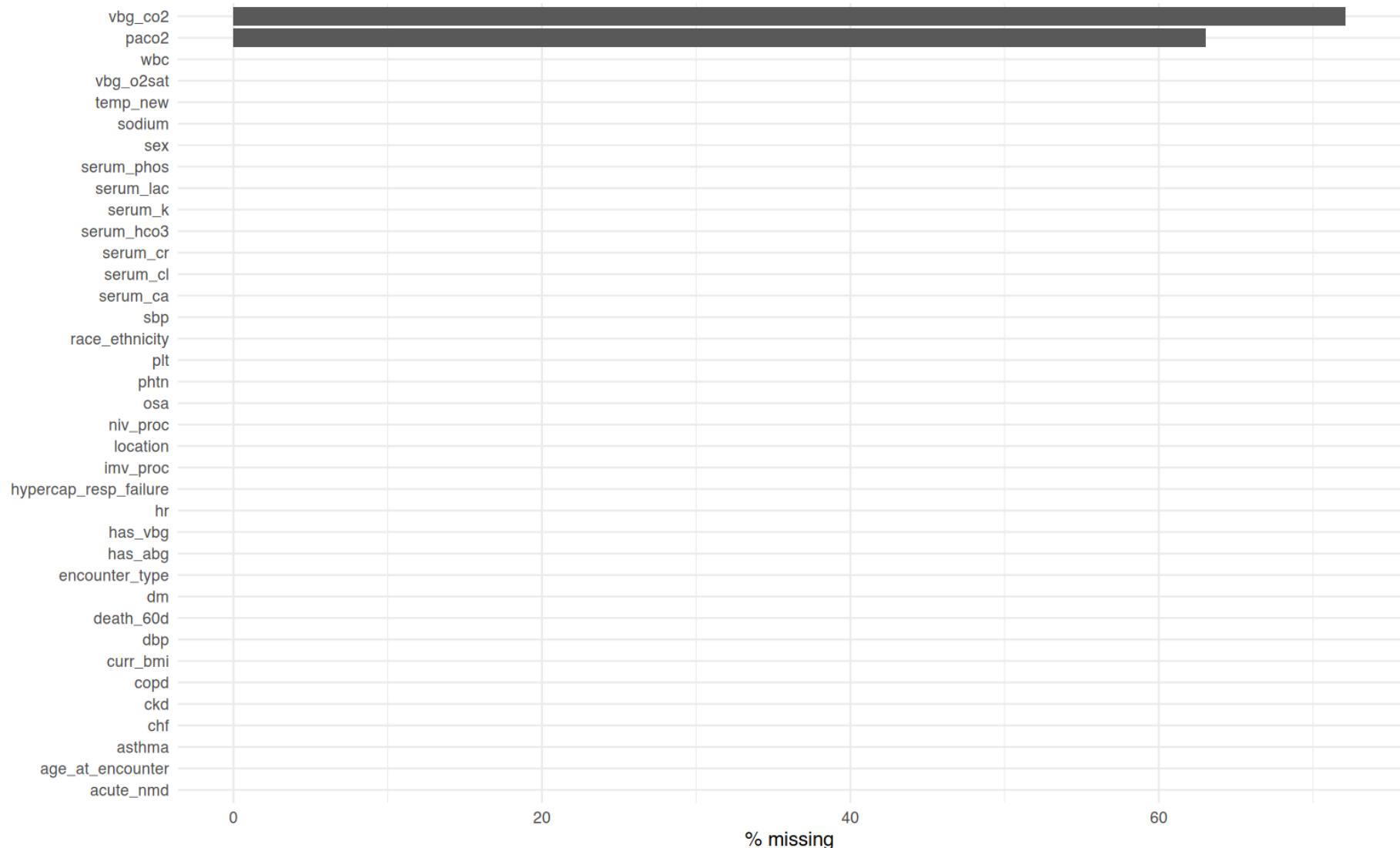
dat_imp <- mice::complete(imp, action = 1, include = FALSE)

# 1) Tabular summary on completed data (should be near 0% by design)
miss_tbl <- naniar::miss_var_summary(dat_imp) %>% arrange(desc(pct_miss))
render_table_pdf_maybe(
  miss_tbl,
  caption = "Missingness after MI (completed data)",
  file_stub = "missingness_after_mi",
  digits = 2,
  show = SHOW_LOW_VALUE_TABLES
)

# 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)

```

Top missing variables (after MI)

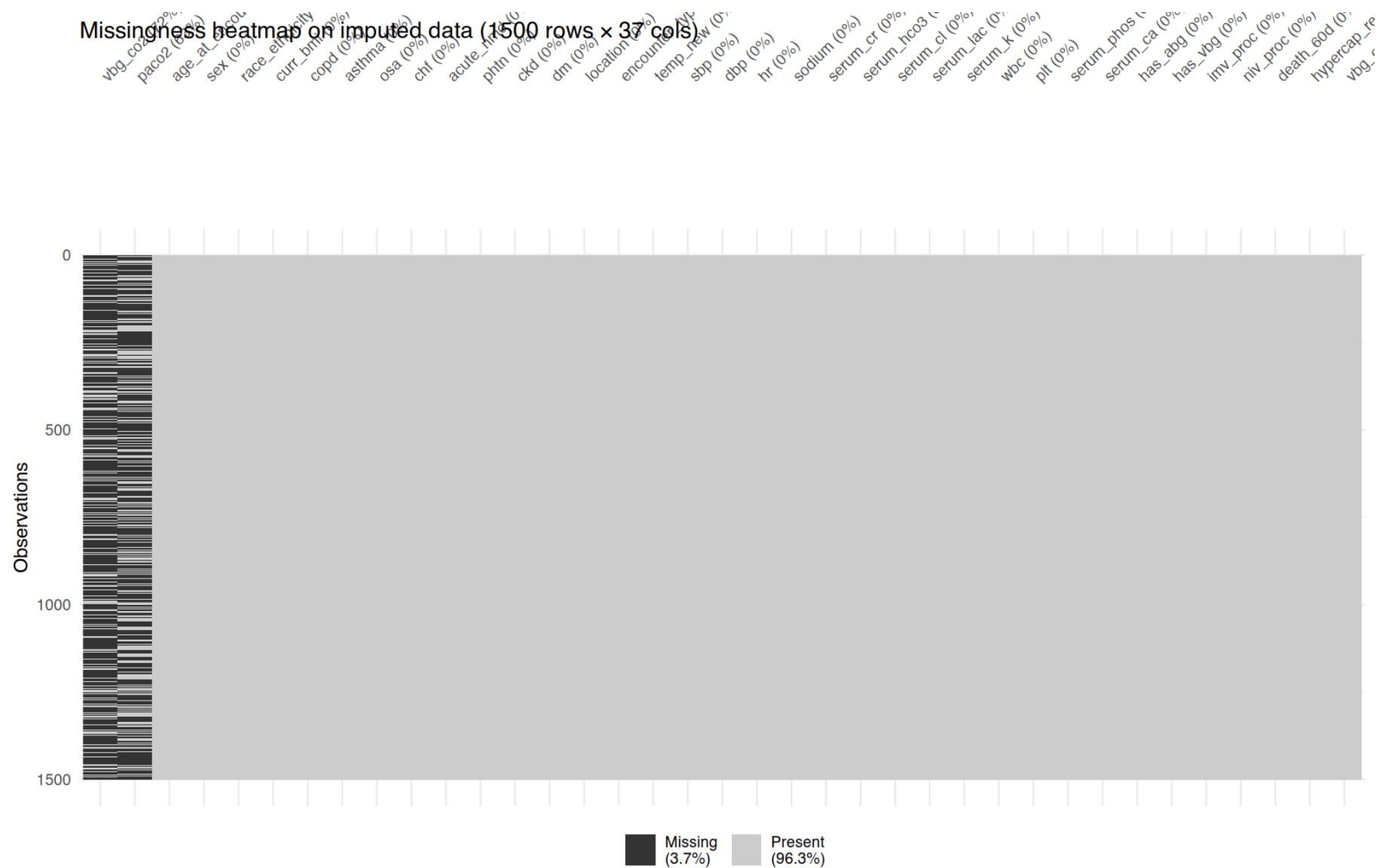


```
# 3) Small heatmap on imputed data (rows/cols sampled)
M <- 60
R <- min(1500, nrow(dat_imp))
cols_heat <- head(top_vars, M)
```

```
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)
```

Missingness heatmap on imputed data (1500 rows x 37 cols)



```
# 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))
```

3.3 10) Refit propensity models within each imputation

MI propensity scores use logistic regression with restricted cubic splines (`rms::rcs`, 4 knots by default) for continuous covariates; the same covariate set used in non-MI models is reused here (`covars_ps`). IPSW truncation rules are unchanged.

Note: the MI computations below run in a single pass per imputation (weights, balance, cat3, spline). Subsequent MI sections reuse those outputs and will stop if they are missing.

3.3.1 FAIL-FAST CHECKS

```
if (M_IMP < 50) {
  stop("M_IMP must be >= 50. Current M_IMP = ", M_IMP)
}

stopifnot(exists("imp"))

if (imp$m < 50) {
  stop("imp$m must be >= 50. Current imp$m = ", imp$m)
}

# Ensure no missing covariates in each imputation for WeightIt
for (i in seq_len(imp$m)) {
  di <- get_imp(i)
  assert_no_na_covars(di, covars_ps, context = paste0("imputation ", i))
}

# This single-pass loop computes MI weights, target balance, 3-level outcomes,
# and spline outcomes in one traversal of imputations to avoid repeated
# mice::complete() calls and re-normalization.

stopifnot(exists("imp"))
imp_n <- imp$m
mi_single_pass_t0 <- Sys.time()

# --- Helper: fit ABG/VBG weights for a single imputation -----
```

```

fit_abg_one <- function(d, imp_index) {
  d <- normalize_types(d, levels_ref)
  d_ps <- d[, c("has_abg", "has_vbg", covars_ps), drop = FALSE]
  d_ps <- droplevels_all(d_ps)
  write_factor_levels_diag(d_ps, covars_ps, "abg", file_prefix = "mi_logistic_ps_factor_levels")
  assert_no_na_covars(d_ps, covars_ps, context = "ABG MI PS (glm)")
  ps_fit <- fit_mi_ps_glm(
    d_ps, "has_abg", covars_ps,
    k = MI_PS_SPLINE_K, maxit = MI_GLM_MAXIT,
    context = make_context(
      stage = "MI", component = "mi_ps_glm",
      analysis_variant = "weighted_imputed",
      model_type = "ps",
      group = "ABG",
      outcome = NA_character_,
      imputation = imp_index,
      batch = NA_integer_
    )
  )
  if (!is.null(ps_fit$error)) {
    stop("MI PS model failed (ABG, imp ", imp_index, "): ", ps_fit$error)
  }
  ipow <- compute_ipow_weights(
    ps_fit,
    treat = to01(d_ps$has_abg),
    ps_floor_quantile = ps_trunc_quantile,
    stabilize = TRUE
  )
  assert_finite_weights(ipow$weights[d_ps$has_abg == 1], "w_abg")
  ps_fit$weights <- ipow$weights
  ps_fit$ipow_info <- list(
    ps_floor = ipow$ps_floor,
    cap = ipow$cap,
    trunc_rate = mean(ipow$truncated, na.rm = TRUE)
  )
  ps_fit
}

```

```

}

fit_vbg_one <- function(d, imp_index) {
  d <- normalize_types(d, levels_ref)
  d_ps <- d[, c("has_abg", "has_vbg", covars_ps), drop = FALSE]
  d_ps <- droplevels_all(d_ps)
  write_factor_levels_diag(d_ps, covars_ps, "vbg", file_prefix = "mi_logistic_ps_factor_levels")
  assert_no_na_covars(d_ps, covars_ps, context = "VBG MI PS (glm)")
  ps_fit <- fit_mi_ps_glm(
    d_ps, "has_vbg", covars_ps,
    k = MI_PS_SPLINE_K, maxit = MI_GLM_MAXIT,
    context = make_context(
      stage = "MI", component = "mi_ps_glm",
      analysis_variant = "weighted_imputed",
      model_type = "ps",
      group = "VBG",
      outcome = NA_character_,
      imputation = imp_index,
      batch = NA_integer_
    )
  )
  if (!is.null(ps_fit$error)) {
    stop("MI PS model failed (VBG, imp ", imp_index, "): ", ps_fit$error)
  }
  ipow <- compute_ipow_weights(
    ps_fit,
    treat = to01(d_ps$has_vbg),
    ps_floor_quantile = ps_trunc_quantile,
    stabilize = TRUE
  )
  assert_finite_weights(ipow$weights[d_ps$has_vbg == 1], "w_vbg")
  ps_fit$weights <- ipow$weights
  ps_fit$ipow_info <- list(
    ps_floor = ipow$ps_floor,
    cap = ipow$cap,
    trunc_rate = mean(ipow$truncated, na.rm = TRUE)
  )
}

```

```

)
ps_fit
}

# --- Helper: target balance (treated vs target) -----
target_balance_table <- function(data, treat_var, weights, covars, levels_ref = NULL) {
  stopifnot(length(weights) == nrow(data))
  treat <- to01(data[[treat_var]]) == 1L
  treat[is.na(treat)] <- FALSE
  w <- as.numeric(weights)

  w_mean <- function(x, wts) {
    ok <- is.finite(x) & is.finite(wts)
    if (!any(ok)) return(NA_real_)
    sum(wts[ok] * x[ok]) / sum(wts[ok])
  }

  out <- lapply(covars, function(v) {
    x <- data[[v]]
    if (is.character(x)) {
      if (!is.null(levels_ref) && !is.null(levels_ref[[v]])) {
        x <- factor(x, levels = levels_ref[[v]])
      } else {
        x <- factor(x)
      }
    }

    if (is.factor(x)) {
      levs <- levels(x)
      lapply(levs, function(lv) {
        ind <- as.integer(x == lv)
        p_target <- mean(ind, na.rm = TRUE)
        sd_target <- sqrt(p_target * (1 - p_target))
        ind_treat <- ind[treat]
        w_treat <- w[treat]
        pre <- mean(ind_treat, na.rm = TRUE)
      })
    }
  })
}

```

```

post <- w_mean(ind_treat, w_treat)
smd_pre <- if (is.finite(sd_target) && sd_target > 0) (pre - p_target) / sd_target else NA_real_
smd_post <- if (is.finite(sd_target) && sd_target > 0) (post - p_target) / sd_target else NA_real_
data.frame(
  variable = v,
  level = lv,
  type = "factor",
  smd_pre = smd_pre,
  smd_post = smd_post,
  stringsAsFactors = FALSE
)
}) |> dplyr::bind_rows()
} else {
  x_num <- suppressWarnings(as.numeric(x))
  mean_target <- mean(x_num, na.rm = TRUE)
  sd_target <- stats::sd(x_num, na.rm = TRUE)
  x_treat <- x_num[treat]
  w_treat <- w[treat]
  mean_pre <- mean(x_treat, na.rm = TRUE)
  mean_post <- w_mean(x_treat, w_treat)
  smd_pre <- if (is.finite(sd_target) && sd_target > 0) (mean_pre - mean_target) / sd_target else NA_real_
  smd_post <- if (is.finite(sd_target) && sd_target > 0) (mean_post - mean_target) / sd_target else NA_real_
  data.frame(
    variable = v,
    level = NA_character_,
    type = "numeric",
    smd_pre = smd_pre,
    smd_post = smd_post,
    stringsAsFactors = FALSE
  )
}
})
dplyr::bind_rows(out)
}

# --- Helper: fit 3-level outcome per imputation -----

```

```

fit_cat3_imp <- function(d, weights, outcome_var, co2_var, treat_var,
                           low_cut, high_cut, group_label, imp_index) {
  stopifnot(co2_var %in% names(d))
  d[[co2_var]] <- coerce_num(d[[co2_var]])
  g <- d[[treat_var]] == 1 & is.finite(d[[co2_var]])
  if (!any(g)) {
    return(list(error = "No treated rows with finite CO2"))
  }

  d2 <- d[g, , drop = FALSE]
  w <- weights[g]
  w[!is.finite(w)] <- NA_real_
  ok <- is.finite(w)
  if (!all(ok)) {
    d2 <- d2[ok, , drop = FALSE]
    w <- w[ok]
    if (nrow(d2) == 0L) return(list(error = "All weights non-finite"))
  }

  d2$co2_cat <- make_co2_cat3(d2[[co2_var]], low_cut, high_cut)
  d2$co2_cat <- stats::relevel(base::droplevels(d2$co2_cat), ref = "Normal")
  if (nlevels(d2$co2_cat) < 2) {
    return(list(error = "co2_cat has <2 levels"))
  }

  d2[[outcome_var]] <- to01(d2[[outcome_var]])
  des <- survey::svydesign(ids = ~1, weights = ~w, data = d2)
  fml <- stats::reformulate(c("co2_cat", adj_core), response = outcome_var)
  fit_res <- fit_with_diagnostics(
    function() survey::svyglm(fml, design = des, family = quasibinomial(),
                               control = stats::glm.control(maxit = 50)),
    context = make_context(
      stage = "outcome",
      component = "cat3",
      analysis_variant = "mi_ipw",
      model_type = "cat3",

```

```

group = group_label,
outcome = outcome_var,
imputation = imp_index,
batch = NA_integer_
)
)
diag <- fit_res$diag
if (!is.null(diag) && nrow(diag)) {
  diag$n_used <- nrow(d2)
  diag$events <- sum(d2[[outcome_var]] == 1, na.rm = TRUE)
}
list(fit = fit_res$fit, diag = diag, warnings = fit_res$warnings)
}

# --- Pool terms across imputations (robust svyglm) -----
pool_terms <- function(fits, term_prefix = NULL, term_pattern = NULL, min_ok_frac = 0.9) {
  ok <- vapply(fits, function(x) inherits(x, "svyglm"), logical(1))
  fits <- fits[ok]
  m_tot <- length(ok)
  m_ok <- length(fits)
  if (m_ok == 0L) {
    stop("pool_terms: no successful svyglm fits; check per-imputation diagnostics.")
  }
  if (m_ok < ceiling(min_ok_frac * m_tot)) {
    warning("pool_terms: only ", m_ok, " / ", m_tot,
           " fits succeeded (below min_ok_frac).", call. = FALSE)
  }
  if (!all(vapply(fits, inherits, logical(1), "svyglm"))) {
    stop("pool_terms expects svyglm fits so pooled vcov is robust.")
  }
  results <- lapply(fits, coef)
  variances <- lapply(fits, vcov)
  pooled <- mitools::MIcombine(results = results, variances = variances)
  pooled_mi_vcov_check(pooled)
  est <- as.numeric(coef(pooled))
  se <- sqrt(diag(pooled$variance))
}

```

```

term <- names(coef(pooled))
out <- data.frame(
  term = term,
  logOR = est,
  estimate = exp(est),
  SE = se,
  LCL = exp(est - 1.96 * se),
  UCL = exp(est + 1.96 * se),
  stringsAsFactors = FALSE
)
if (!is.null(term_prefix)) {
  out <- out[grep0("^", term_prefix), out$term], , drop = FALSE]
}
if (!is.null(term_pattern)) {
  out <- out[grep0(term_pattern, out$term), , drop = FALSE]
}
out
}

# --- Fit spline model on treated cohort only (IPSW) -----
fit_spline_imp <- function(data, weights, outcome, co2_var, treat_var,
                            adj_vars = NULL,
                            spline_df = SPLINE_DF,
                            spline_basis = SPLINE_BASIS,
                            grid_df = NULL,
                            ref_idx = NULL,
                            imp_index = NA_integer_) {
  spline_basis <- match.arg(spline_basis, c("ns", "rcs"))
  stopifnot(is.data.frame(data))
  stopifnot(length(weights) == nrow(data))
  stopifnot(all(c(outcome, co2_var, treat_var) %in% names(data)))
  if (!is.null(adj_vars) && length(adj_vars)) {
    missing_adj <- setdiff(adj_vars, names(data))
    if (length(missing_adj)) {
      return(list(error = paste0("Missing adj_core vars: ", paste(missing_adj, collapse = ", "))))
    }
  }
}

```

```
}
```

```
data[[treat_var]] <- to01(data[[treat_var]])
data[[outcome]]   <- to01(data[[outcome]])
data[[co2_var]]   <- coerce_num(data[[co2_var]])
w <- suppressWarnings(as.numeric(weights))

keep <- (data[[treat_var]] == 1L) &
  is.finite(data[[co2_var]]) &
  !is.na(data[[outcome]]) &
  is.finite(w) & (w > 0)

if (!any(keep)) {
  return(list(error = "No eligible treated rows after filtering (treated==1, finite CO2, non-missing outcome, finite positive weight)"))
}

d2 <- data[keep, , drop = FALSE]
w2 <- w[keep]
d2$w <- w2

if (length(unique(d2[[outcome]])) < 2L) {
  return(list(error = paste0("Outcome has one level in treated sample after filtering: outcome=", outcome, ", n=", nrow(d2),
                             ", events=", sum(d2[[outcome]] == 1, na.rm = TRUE))))
}

des <- survey::svydesign(ids = ~1, weights = ~w, data = d2)
if (spline_basis == "ns") {
  rhs_terms <- c(sprintf("splines::ns(%s, %d)", co2_var, spline_df), adj_vars)
  fml <- stats::as.formula(paste(outcome, "~", paste(rhs_terms, collapse = " + ")))
} else {
  dd <- rms::datadist(d2)
  old_opt <- options(datadist = ".__dd_tmp__")
  assign(".__dd_tmp__", dd, envir = .GlobalEnv)
  on.exit({
    options(old_opt)
  })
}
```

```

    rm(list = ".__dd_tmp__", envir = .GlobalEnv)
}, add = TRUE)
rhs_terms <- c(sprintf("rms::rcs(%s, %d)", co2_var, spline_df), adj_vars)
fml <- stats::as.formula(paste(outcome, "~", paste(rhs_terms, collapse = " + ")))
}

group_label <- if (identical(treat_var, "has_abg")) "ABG" else if (identical(treat_var, "has_vbg")) "VBG" else treat_var
fit_res <- fit_with_diagnostics(
  function() survey::svyglm(fml, design = des, family = quasibinomial(),
                            control = stats::glm.control(maxit = 50)),
  context = make_context(
    stage = "outcome",
    component = "spline",
    analysis_variant = "mi_ipw",
    model_type = "spline",
    group = group_label,
    outcome = outcome,
    imputation = imp_index,
    batch = NA_integer_
  )
)
fit <- fit_res$fit
warns <- fit_res$warnings
diag <- fit_res$diag
if (!is.null(diag) && nrow(diag)) {
  diag$n_used <- nrow(d2)
  diag$events <- sum(d2[[outcome]] == 1, na.rm = TRUE)
}
if (is.null(fit)) {
  err_msg <- if (!is.null(diag$error_message) && is.finite(nchar(diag$error_message))) diag$error_message else "svyglm error"
  return(list(error = err_msg,
             warnings = warns,
             diag = diag,
             n_used = nrow(d2),
             events = sum(d2[[outcome]] == 1, na.rm = TRUE)))
}

```

```

if (!is.null(grid_df)) {
  if (is.null(ref_idx)) {
    return(list(error = "ref_idx is required when grid_df is provided.",
               warnings = warns, diag = diag))
  }
  pr <- tryCatch(
    predict_or_curve_from_fit(fit, grid_df, ref_idx, co2_var),
    error = function(e) list(error = paste0("predict error: ", conditionMessage(e)))
  )
  if (!is.null(pr$error)) return(list(error = pr$error,
                                         warnings = warns,
                                         diag = diag,
                                         n_used = nrow(d2),
                                         events = sum(d2[[outcome]] == 1, na.rm = TRUE)))
  return(list(
    fit = fit,
    logOR = pr$logOR,
    var_logOR = pr$var_logOR,
    warnings = warns,
    diag = diag,
    n_used = nrow(d2),
    events = sum(d2[[outcome]] == 1, na.rm = TRUE)
  ))
}

list(fit = fit, warnings = warns, diag = diag,
      n_used = nrow(d2),
      events = sum(d2[[outcome]] == 1, na.rm = TRUE))
}

# --- Pool spline coefficients across imputations -----
pool_spline_coefs <- function(fit_list, min_ok_frac = 0.9) {
  fits <- lapply(fit_list, function(x) if (is.list(x) && !is.null(x$fit)) x$fit else if (inherits(x, "svyglm")) x else NULL)
  ok <- !vapply(fits, is.null, logical(1))
  m_tot <- length(ok)
}

```

```

m_ok <- sum(ok)
if (m_ok < ceiling(min_ok_frac * m_tot)) {
  stop("Too many failed spline fits: m_ok=", m_ok, " / m_total=", m_tot)
}
fits <- fits[ok]
results <- lapply(fits, coef)
variances <- lapply(fits, vcov)
pooled <- mitools::MIcombine(results = results, variances = variances)
pooled_mi_vcov_check(pooled)
est <- as.numeric(coef(pooled))
se <- sqrt(diag(pooled$variance))
data.frame(
  term = names(coef(pooled)),
  estimate = est,
  SE = se,
  LCL = est - 1.96 * se,
  UCL = est + 1.96 * se,
  m_used = m_ok,
  m_total = m_tot,
  row.names = NULL
)
}

# --- Pool spline curves (pointwise Rubin pooling on log-OR scale) -----
pool_spline_curve <- function(fit_list, grid_df, ref_idx, co2_ref, min_ok_frac = 0.9) {
  n_grid <- nrow(grid_df)
  ok <- vapply(fit_list, function(x) {
    is.list(x) && is.null(x$error) &&
      !is.null(x$logOR) && !is.null(x$var_logOR) &&
      length(x$logOR) == n_grid && length(x$var_logOR) == n_grid
  }, logical(1))
  m_tot <- length(ok)
  m_ok <- sum(ok)
  if (m_ok < ceiling(min_ok_frac * m_tot)) {
    stop("Too many failed spline fits: m_ok=", m_ok, " / m_total=", m_tot)
  }
}

```

```

logOR_mat <- matrix(NA_real_, nrow = n_grid, ncol = m_ok)
var_mat <- matrix(NA_real_, nrow = n_grid, ncol = m_ok)
ok_idx <- which(ok)
for (i in seq_along(ok_idx)) {
  fit_i <- fit_list[[ok_idx[i]]]
  logOR_mat[, i] <- fit_i$logOR
  var_mat[, i] <- fit_i$var_logOR
}
Qbar <- rowMeans(logOR_mat, na.rm = TRUE)
Ubar <- rowMeans(var_mat, na.rm = TRUE)
B <- apply(logOR_mat, 1, stats::var, na.rm = TRUE)
Tvar <- Ubar + (1 + 1 / m_ok) * B
se <- sqrt(Tvar)
if (!is.na(ref_idx) && is.finite(ref_idx)) {
  if (abs(exp(Qbar[ref_idx]) - 1) > 1e-6) {
    warning("Pooled spline OR at reference differs from 1 (check ref_idx/co2_ref).", call. = FALSE)
  }
}
data.frame(
  grid_df,
  logOR = Qbar,
  SE_logOR = se,
  OR = exp(Qbar),
  LCL = exp(Qbar - 1.96 * se),
  UCL = exp(Qbar + 1.96 * se),
  co2_ref = co2_ref,
  m_used = m_ok,
  m_total = m_tot,
  row.names = NULL
)
# --- Single-pass loop -----
cat3_outcomes <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")
cat3_labels <- c(

```

```

imv_proc = "IMV",
niv_proc = "NIV",
death_60d = "Death60d",
hypercap_resp_failure = "HCRF"
)

abg_co2_obs <- subset_data$paco2[subset_data$has_abg == 1 & !is.na(subset_data$paco2)]
if (length(abg_co2_obs) < 10) stop("ABG spline: not enough observed PaCO2 values.")
q_abg <- stats::quantile(abg_co2_obs, probs = c(0.02, 0.98), na.rm = TRUE)
grid_abg_info_mi <- make_co2_grid_ref(
  "paco2",
  seq(q_abg[1], q_abg[2], length.out = SPLINE_GRID_N),
  x_ref_abg,
  ABG_CO2_REF
)
grid_abg_mi <- grid_abg_info_mi$grid
ref_idx_abg_mi <- grid_abg_info_mi$ref_idx
co2_ref_abg_mi <- grid_abg_info_mi$co2_ref

vbg_co2_obs <- subset_data$vbg_co2[subset_data$has_vbg == 1 & !is.na(subset_data$vbg_co2)]
if (length(vbg_co2_obs) < 10) stop("VBG spline: not enough observed VBG CO2 values.")
q_vbg <- stats::quantile(vbg_co2_obs, probs = c(0.02, 0.98), na.rm = TRUE)
grid_vbg_info_mi <- make_co2_grid_ref(
  "vbg_co2",
  seq(q_vbg[1], q_vbg[2], length.out = SPLINE_GRID_N),
  x_ref_vbg,
  VBG_CO2_REF
)
grid_vbg_mi <- grid_vbg_info_mi$grid
ref_idx_vbg_mi <- grid_vbg_info_mi$ref_idx
co2_ref_vbg_mi <- grid_vbg_info_mi$co2_ref

covars_use <- intersect(covars_ps, names(subset_data))
covars_use_abg <- covars_use
covars_use_vbg <- covars_use

```

```

# MI PS covariate typing (continuous vs categorical) for transparency
mi_logistic_ps_type_file <- results_path("mi_logistic_ps_covariate_types.csv")
d_ps_tmp <- get_imp(1)
d_ps_tmp <- normalize_types(d_ps_tmp, levels_ref)
d_ps_tmp <- d_ps_tmp[, c("has_abg", "has_vbg", covars_ps), drop = FALSE]
d_ps_tmp <- droplevels_all(d_ps_tmp)
cont_vars <- covars_ps[vapply(covars_ps, ps_is_continuous, logical(1), df = d_ps_tmp)]
cat_vars_ps <- setdiff(covars_ps, cont_vars)
mi_logistic_ps_types <- dplyr::bind_rows(
  data.frame(variable = cont_vars, type = "continuous", stringsAsFactors = FALSE),
  data.frame(variable = cat_vars_ps, type = "categorical", stringsAsFactors = FALSE)
)
write_csv_safely(mi_logistic_ps_types, mi_logistic_ps_type_file, row_names = FALSE)
rm(d_ps_tmp, cont_vars, cat_vars_ps, mi_logistic_ps_types)
gc()

```

	used (Mb)	gc trigger (Mb)	limit (Mb)	max used (Mb)
Ncells	6790520	362.7	13033026	696.1
Vcells	500219294	3816.4	1121950078	8559.8
			16384	1121657427
				8557.6

```

mi_logistic_ps_abg_list <- vector("list", imp_n)
mi_logistic_ps_vbg_list <- vector("list", imp_n)
bal_rows_abg <- vector("list", imp_n)
bal_rows_vbg <- vector("list", imp_n)
cat3_fits_abg <- setNames(lapply(cat3_outcomes, function(x) vector("list", imp_n)), cat3_outcomes)
cat3_fits_vbg <- setNames(lapply(cat3_outcomes, function(x) vector("list", imp_n)), cat3_outcomes)
spline_fits_abg <- setNames(lapply(cat3_outcomes, function(x) vector("list", imp_n)), cat3_outcomes)
spline_fits_vbg <- setNames(lapply(cat3_outcomes, function(x) vector("list", imp_n)), cat3_outcomes)

cat3_diag_rows <- list()
spline_diag_rows <- list()
weight_diag_abg <- vector("list", imp_n)
weight_diag_vbg <- vector("list", imp_n)

message("MI single-pass: running ", imp_n, " imputations sequentially.")

```

```

for (i in seq_len(imp_n)) {
  d <- get_imp(i)

  set.seed(20251206 + i)
  mi_logistic_ps_abg_list[[i]] <- fit_abg_one(d, i)
  set.seed(30251206 + i)
  mi_logistic_ps_vbg_list[[i]] <- fit_vbg_one(d, i)

  bal_rows_abg[[i]] <- target_balance_table(
    d, "has_abg", mi_logistic_ps_abg_list[[i]]$weights, covars_use_abg, levels_ref
  ) |>
    dplyr::mutate(group = "ABG", imp = i)
  bal_rows_vbg[[i]] <- target_balance_table(
    d, "has_vbg", mi_logistic_ps_vbg_list[[i]]$weights, covars_use_vbg, levels_ref
  ) |>
    dplyr::mutate(group = "VBG", imp = i)

  for (outcome_var in cat3_outcomes) {
    fit_abg_cat <- fit_cat3_imp(
      d, mi_logistic_ps_abg_list[[i]]$weights, outcome_var, "paco2", "has_abg",
      ABG_CO2_LOW, ABG_CO2_HIGH, "ABG", i
    )
    cat3_fits_abg[[outcome_var]][[i]] <- fit_abg_cat$fit
    if (!is.null(fit_abg_cat$diag)) cat3_diag_rows[[length(cat3_diag_rows) + 1L]] <- fit_abg_cat$diag

    fit_vbg_cat <- fit_cat3_imp(
      d, mi_logistic_ps_vbg_list[[i]]$weights, outcome_var, "vbg_co2", "has_vbg",
      VBG_CO2_LOW, VBG_CO2_HIGH, "V ро", i
    )
    cat3_fits_vbg[[outcome_var]][[i]] <- fit_vbg_cat$fit
    if (!is.null(fit_vbg_cat$diag)) cat3_diag_rows[[length(cat3_diag_rows) + 1L]] <- fit_vbg_cat$diag
  }

  for (outcome_var in cat3_outcomes) {
    spline_abg <- fit_spline_imp(
      d, mi_logistic_ps_abg_list[[i]]$weights, outcome_var, "paco2", "has_abg",

```

```

adj_vars = adj_core, spline_df = SPLINE_DF, spline_basis = SPLINE_BASIS,
grid_df = grid_abg_mi, ref_idx = ref_idx_abg_mi, imp_index = i
)
spline_fits_abg[[outcome_var]][[i]] <- spline_abg
if (!is.null(spline_abg$diag)) spline_diag_rows[[length(spline_diag_rows) + 1L]] <- spline_abg$diag

spline_vbg <- fit_spline_imp(
  d, mi_logistic_ps_vbg_list[[i]]$weights, outcome_var, "vbg_co2", "has_vbg",
  adj_vars = adj_core, spline_df = SPLINE_DF, spline_basis = SPLINE_BASIS,
  grid_df = grid_vbg_mi, ref_idx = ref_idx_vbg_mi, imp_index = i
)
spline_fits_vbg[[outcome_var]][[i]] <- spline_vbg
if (!is.null(spline_vbg$diag)) spline_diag_rows[[length(spline_diag_rows) + 1L]] <- spline_vbg$diag
}

weight_diag_abg[[i]] <- {
  w <- mi_logistic_ps_abg_list[[i]]$weights
  t <- d$has_abg
  w <- w[t == 1]
  c(
    n = length(w),
    min = min(w, na.rm = TRUE),
    p99 = stats::quantile(w, 0.99, na.rm = TRUE),
    max = max(w, na.rm = TRUE),
    ess = sum(w^2) / sum(w^2)
  )
}
weight_diag_vbg[[i]] <- {
  w <- mi_logistic_ps_vbg_list[[i]]$weights
  t <- d$has_vbg
  w <- w[t == 1]
  c(
    n = length(w),
    min = min(w, na.rm = TRUE),
    p99 = stats::quantile(w, 0.99, na.rm = TRUE),
    max = max(w, na.rm = TRUE),
    ess = sum(w^2) / sum(w^2)
  )
}

```

```

    ess = sum(w)^2 / sum(w^2)
  )
}

rm(d)
invisible(gc())
}

append_outcome_diag(dplyr::bind_rows(cat3_diag_rows, spline_diag_rows))

bal_imp_abg <- list(
  bal_long = dplyr::bind_rows(bal_rows_abg)
)
bal_imp_abg$bal_imp_summary <- bal_imp_abg$bal_long |>
  dplyr::group_by(group, imp) |>
  dplyr::summarise(
    max_abs_post = max(abs(smd_post), na.rm = TRUE),
    mean_abs_post = mean(abs(smd_post), na.rm = TRUE),
    .groups = "drop"
  )
bal_imp_abg$worst_rows_overall <- bal_imp_abg$bal_long |>
  dplyr::mutate(abs_post = abs(smd_post)) |>
  dplyr::arrange(desc(abs_post)) |>
  dplyr::ungroup()
bal_imp_abg$worst_by_imp <- bal_imp_abg$bal_long |>
  dplyr::mutate(term = ifelse(is.na(level), variable, paste0(variable, ":", level)),
    abs_post = abs(smd_post)) |>
  dplyr::group_by(group, imp) |>
  dplyr::slice_max(abs_post, n = 1, with_ties = FALSE) |>
  dplyr::ungroup() |>
  dplyr::select(group, imp, term, smd_pre, smd_post, abs_post)
bal_imp_abg$worst_terms_by_imp <- bal_imp_abg$bal_long |>
  dplyr::mutate(term = ifelse(is.na(level), variable, paste0(variable, ":", level)),
    abs_post = abs(smd_post)) |>
  dplyr::group_by(group, imp) |>
  dplyr::slice_max(abs_post, n = 10, with_ties = FALSE) |>

```

```

dplyr::ungroup() |>
dplyr::select(group, imp, term, smd_pre, smd_post, abs_post)

bal_imp_vbg <- list(
  bal_long = dplyr::bind_rows(bal_rows_vbg)
)
bal_imp_vbg$bal_imp_summary <- bal_imp_vbg$bal_long |>
  dplyr::group_by(group, imp) |>
  dplyr::summarise(
    max_abs_post = max(abs(smd_post), na.rm = TRUE),
    mean_abs_post = mean(abs(smd_post), na.rm = TRUE),
    .groups = "drop"
  )
bal_imp_vbg$worst_rows_overall <- bal_imp_vbg$bal_long |>
  dplyr::mutate(abs_post = abs(smd_post)) |>
  dplyr::arrange(desc(abs_post)) |>
  dplyr::ungroup()
bal_imp_vbg$worst_by_imp <- bal_imp_vbg$bal_long |>
  dplyr::mutate(term = ifelse(is.na(level), variable, paste0(variable, ":", level)),
                abs_post = abs(smd_post)) |>
  dplyr::group_by(group, imp) |>
  dplyr::slice_max(abs_post, n = 1, with_ties = FALSE) |>
  dplyr::ungroup() |>
  dplyr::select(group, imp, term, smd_pre, smd_post, abs_post)
bal_imp_vbg$worst_terms_by_imp <- bal_imp_vbg$bal_long |>
  dplyr::mutate(term = ifelse(is.na(level), variable, paste0(variable, ":", level)),
                abs_post = abs(smd_post)) |>
  dplyr::group_by(group, imp) |>
  dplyr::slice_max(abs_post, n = 10, with_ties = FALSE) |>
  dplyr::ungroup() |>
  dplyr::select(group, imp, term, smd_pre, smd_post, abs_post)

mi_weight_diag_abg <- dplyr::bind_rows(lapply(weight_diag_abg, function(x) {
  as.data.frame(as.list(x), stringsAsFactors = FALSE)
}()))
mi_weight_diag_vbg <- dplyr::bind_rows(lapply(weight_diag_vbg, function(x) {

```

```

    as.data.frame(as.list(x), stringsAsFactors = FALSE)
}))

abg_cat_results <- dplyr::bind_rows(lapply(cat3_outcomes, function(outcome_var) {
  pool_terms(cat3_fits_abg[[outcome_var]], term_prefix = "co2_cat") |>
    dplyr::mutate(
      outcome = cat3_labels[[outcome_var]],
      group = "ABG",
      OR = estimate
    )
}))

vbg_cat_results <- dplyr::bind_rows(lapply(cat3_outcomes, function(outcome_var) {
  pool_terms(cat3_fits_vbg[[outcome_var]], term_prefix = "co2_cat") |>
    dplyr::mutate(
      outcome = cat3_labels[[outcome_var]],
      group = "VBG",
      OR = estimate
    )
}))

abg_spline <- list(
  curves = dplyr::bind_rows(lapply(cat3_outcomes, function(outcome_var) {
    pool_spline_curve(spline_fits_abg[[outcome_var]], grid_abg_mi, ref_idx_abg_mi, co2_ref_abg_mi) |>
      dplyr::mutate(outcome = outcome_var, group = "ABG")
  })),
  coefs = dplyr::bind_rows(lapply(cat3_outcomes, function(outcome_var) {
    pool_spline_coefs(spline_fits_abg[[outcome_var]]) |>
      dplyr::mutate(outcome = outcome_var, group = "ABG")
  }))
)

vbg_spline <- list(
  curves = dplyr::bind_rows(lapply(cat3_outcomes, function(outcome_var) {
    pool_spline_curve(spline_fits_vbg[[outcome_var]], grid_vbg_mi, ref_idx_vbg_mi, co2_ref_vbg_mi) |>
      dplyr::mutate(outcome = outcome_var, group = "VBG")
  })),
  coefs = dplyr::bind_rows(lapply(cat3_outcomes, function(outcome_var) {

```

```

    pool_spline_coefs(spline_fits_vbg[[outcome_var]]) |>
      dplyr::mutate(outcome = outcome_var, group = "VBG")
  }))

abg_curves <- abg_spline$curves
abg_coefs  <- abg_spline$coefs
vbg_curves <- vbg_spline$curves
vbg_coefs  <- vbg_spline$coefs

write_csv_safely(abg_curves, results_path("mi_spline_curve_abg.csv"), row_names = FALSE)
write_csv_safely(abg_coefs,  results_path("mi_spline_coef_abg.csv"), row_names = FALSE)
write_csv_safely(vbg_curves, results_path("mi_spline_curve_vbg.csv"), row_names = FALSE)
write_csv_safely(vbg_coefs,  results_path("mi_spline_coef_vbg.csv"), row_names = FALSE)

mi_single_pass_t1 <- Sys.time()
stopifnot(exists("runtime_log"))
runtime_log <- dplyr::bind_rows(
  runtime_log,
  data.frame(
    step_name = "mi_single_pass",
    seconds = as.numeric(difftime(mi_single_pass_t1, mi_single_pass_t0, units = "secs")),
    start_time = as.character(mi_single_pass_t0),
    end_time = as.character(mi_single_pass_t1),
    notes = paste0("m=", imp_n),
    run_id = runtime_run_id,
    run_mode = RUN_MODE,
    n_subset = nrow(subset_data),
    stringsAsFactors = FALSE
  )
)

mi_single_pass_done <- TRUE

```

3.3.2 10.1 ABG propensity (has_abg)

```
stopifnot(exists("mi_single_pass_done"), isTRUE(mi_single_pass_done))
stopifnot(exists("mi_logistic_ps_abg_list"))
message("ABG MI weights were computed in the single-pass MI loop above.")
```

3.3.3 10.2 Balance diagnostics across imputations

```
stopifnot(exists("target_balance_table"))

# Use a fixed x-axis max so ABG/VBG balance plots are directly comparable.

stopifnot(exists("bal_imp_abg"))

bal_abg_pooled <- bal_imp_abg$bal_long |>
  mutate(label = ifelse(is.na(level), variable, paste0(variable, ":", level))) |>
  group_by(label) |>
  summarise(
    pre_med = median(abs(smd_pre), na.rm = TRUE),
    post_med = median(abs(smd_post), na.rm = TRUE),
    pre_mean = mean(abs(smd_pre), na.rm = TRUE),
    post_mean = mean(abs(smd_post), na.rm = TRUE),
    post_max = max(abs(smd_post), na.rm = TRUE),
    .groups = "drop"
  )

bal_abg_plot <- bal_abg_pooled |>
  mutate(label = factor(label, levels = label[order(post_med, decreasing = TRUE)])) |>
  pivot_longer(c(pre_med, post_med), names_to = "type", values_to = "smd") |>
  mutate(type = recode(type, pre_med = "Pre", post_med = "Post"))

p_abg <- ggplot(bal_abg_plot, aes(x = smd, y = label, shape = type)) +
  geom_vline(xintercept = 0.1, linetype = 2, linewidth = 0.3) +
```

```

geom_point(size = 1.2) +
  labs(title = "MI target balance (ABG): pooled |SMD|", x = "|Target SMD|", y = NULL, shape = "Stage") +
  scale_x_continuous(limits = c(0, BAL_XLIM_MAX),
                     expand = expansion(mult = c(0, 0.02))) +
  theme_minimal(base_size = 10)
save_diag_plot(p_abg, results_path("figs", "diag-mi-balance-pooled-abg.png"), width = 7, height = 6)

render_table_pdf_maybe(
  bal_imp_abg$worst_rows_overall,
  caption = "ABG: target SMD rows across imputations (sorted by |SMD|)",
  file_stub = "abg_worst_target_smd_rows",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)

abg_imp_summary <- bal_imp_abg$bal_imp_summary |>
  summarise(
    med = median(max_abs_post, na.rm = TRUE),
    p90 = quantile(max_abs_post, 0.9, na.rm = TRUE),
    max = max(max_abs_post, na.rm = TRUE)
  )
render_table_pdf_maybe(
  abg_imp_summary,
  caption = "ABG: max |Target SMD| summary across imputations",
  file_stub = "abg_target_smd_summary",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)

```

3.3.4 10.3 VBG propensity (has_vbg)

```

stopifnot(exists("mi_single_pass_done"), isTRUE(mi_single_pass_done))
stopifnot(exists("mi_logistic_ps_vbg_list"))
message("VBG MI weights were computed in the single-pass MI loop above.")

```

3.3.5 10.4 VBG balance

```
stopifnot(exists("bal_imp_vbg"))

bal_vbg_pooled <- bal_imp_vbg$bal_long |>
  mutate(label = ifelse(is.na(level), variable, paste0(variable, ":", level))) |>
  group_by(label) |>
  summarise(
    pre_med = median(abs(smd_pre), na.rm = TRUE),
    post_med = median(abs(smd_post), na.rm = TRUE),
    pre_mean = mean(abs(smd_pre), na.rm = TRUE),
    post_mean = mean(abs(smd_post), na.rm = TRUE),
    post_max = max(abs(smd_post), na.rm = TRUE),
    .groups = "drop"
  )

bal_vbg_plot <- bal_vbg_pooled |>
  mutate(label = factor(label, levels = label[order(post_med, decreasing = TRUE)])) |>
  pivot_longer(c(pre_med, post_med), names_to = "type", values_to = "smd") |>
  mutate(type = recode(type, pre_med = "Pre", post_med = "Post"))

p_vbg <- ggplot(bal_vbg_plot, aes(x = smd, y = label, shape = type)) +
  geom_vline(xintercept = 0.1, linetype = 2, linewidth = 0.3) +
  geom_point(size = 1.2) +
  labs(title = "MI target balance (VBG): pooled |SMD|", x = "|Target SMD|", y = NULL, shape = "Stage") +
  scale_x_continuous(limits = c(0, BAL_XLIM_MAX),
                     expand = expansion(mult = c(0, 0.02))) +
  theme_minimal(base_size = 10)
save_diag_plot(p_vbg, results_path("figs", "diag-mi-balance-pooled-vbg.png"), width = 7, height = 6)

render_table_pdf_maybe(
  bal_imp_vbg$worst_rows_overall,
  caption = "VBG: target SMD rows across imputations (sorted by |SMD|)",
  file_stub = "vbg_worst_target_smd_rows",
  digits = 3,
```

```

    show = SHOW_LOW_VALUE_TABLES
)

vbg_imp_summary <- bal_imp_vbg$bal_imp_summary |>
  summarise(
    med = median(max_abs_post, na.rm = TRUE),
    p90 = quantile(max_abs_post, 0.9, na.rm = TRUE),
    max = max(max_abs_post, na.rm = TRUE)
  )
render_table_pdf_maybe(
  vbg_imp_summary,
  caption = "VBG: max |Target SMD| summary across imputations",
  file_stub = "vbg_target_smd_summary",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)

```

3.4 11) Weighted outcome models within each imputation + pooling

Within each imputation, fit covariate-adjusted CO₂ spline outcome models **only in the measured cohort** (has_abg==1 for PaCO₂; has_vbg==1 for VBG CO₂), using IPSW weights to address nonrandom testing. Curves are pooled pointwise across imputations (Rubin's rules on the log-OR scale) and displayed as odds ratios relative to CO₂_ref at a reference covariate profile.

3.4.1 11.1 Helper: fit + extract log-OR and SE from svyglm

```

stopifnot(exists("fit_spline_imp"), exists("pool_spline_curve"),
          exists("pool_spline_coefs"), exists("pool_terms"))

stopifnot(exists("mi_single_pass_done"), isTRUE(mi_single_pass_done))
stopifnot(exists("abg_spline"), exists("abg_curves"), exists("abg_coefs"))
message("ABG MI spline results were computed in the single-pass MI loop above.")

```

3.4.2 11.3 VBG: MI pooled spline models (treated cohort only)

```
stopifnot(exists("mi_single_pass_done"), isTRUE(mi_single_pass_done))
stopifnot(exists("vbg_spline"), exists("vbg_curves"), exists("vbg_coefs"))
message("VBG MI spline results were computed in the single-pass MI loop above.")
```

3.5 12) Explainability on one representative imputation

MI propensity scores are estimated via logistic regression with splines; SHAP summaries are not computed for the MI PS model. A placeholder diagnostic file is written for audit completeness.

```
shap_stability_file <- results_path("diag-ps-shap-stability.csv")
shap_stub <- data.frame(
  cohort = character(),
  feature = character(),
  mean_abs_seed1 = numeric(),
  mean_abs_seed2 = numeric(),
  run_id = character(),
  stringsAsFactors = FALSE
)
write_csv_safely(shap_stub, shap_stability_file, row_names = FALSE)
```

3.6 13) MI three-level PCO2 helpers and checks

```
stopifnot(exists("pool_terms"))
message("MI 3-level helpers defined in the single-pass MI section.")
```

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

3.7.1 ABG: MI + IPW, three-level PCO2 outcomes

```
stopifnot(exists("mi_single_pass_done"), isTRUE(mi_single_pass_done))
stopifnot(exists("abg_cat_results"))

mi_abg_cat_forms <- list(
  "MI IPW ABG 3-level: IMV ~ CO2 category + X"      = reformulate(c("co2_cat", adj_core), response = "imv_proc"),
  "MI IPW ABG 3-level: NIV ~ CO2 category + X"      = reformulate(c("co2_cat", adj_core), response = "niv_proc"),
  "MI IPW ABG 3-level: Death60d ~ CO2 category + X" = reformulate(c("co2_cat", adj_core), response = "death_60d"),
  "MI IPW ABG 3-level: HCRF ~ CO2 category + X"     = reformulate(c("co2_cat", adj_core), response = "hypercap_resp_failure")
)
register_model_diagrams(mi_abg_cat_forms)
message("ABG MI 3-level results were computed in the single-pass MI loop above.")
```

3.7.2 VBG: MI + IPW, three-level PCO2 outcomes

```
stopifnot(exists("mi_single_pass_done"), isTRUE(mi_single_pass_done))
stopifnot(exists("vbg_cat_results"))

mi_vbg_cat_forms <- list(
  "MI IPW VBG 3-level: IMV ~ CO2 category + X"      = reformulate(c("co2_cat", adj_core), response = "imv_proc"),
  "MI IPW VBG 3-level: NIV ~ CO2 category + X"      = reformulate(c("co2_cat", adj_core), response = "niv_proc"),
  "MI IPW VBG 3-level: Death60d ~ CO2 category + X" = reformulate(c("co2_cat", adj_core), response = "death_60d"),
  "MI IPW VBG 3-level: HCRF ~ CO2 category + X"     = reformulate(c("co2_cat", adj_core), response = "hypercap_resp_failure")
)
register_model_diagrams(mi_vbg_cat_forms)
message("VBG MI 3-level results were computed in the single-pass MI loop above.")
```

3.7.3 Table 3: MI-pooled IPW associations (3-level CO2)

```
stopifnot(exists("abg_cat_results"), exists("vbg_cat_results"))

mi_threel level_results <- dplyr::bind_rows(
  dplyr::mutate(abg_cat_results, group = "ABG"),
  dplyr::mutate(vbg_cat_results, group = "V рG")
) |>
  dplyr::mutate(method = "IPW + MI adjusted")

table3_df <- dplyr::bind_rows(
  dplyr::mutate(abg_cat_results, group = "ABG"),
  dplyr::mutate(vbg_cat_results, group = "V рG")
) |>
  dplyr::mutate(
    exposure = gsub("^co2_cat", "", term),
    contrast = dplyr::recode(exposure,
      Low = "Low vs normal",
      High = "High vs normal",
      .default = exposure),
    outcome_label = dplyr::recode(
      outcome,
      IMV = "IMV",
      NIV = "NIV",
      Death60d = "Death (60d)",
      HCRF = "Hypercapnic RF"
    ),
    or_ci = sprintf("%.2f (%.2f, %.2f)", OR, LCL, UCL)
  ) |>
  dplyr::select(group, outcome_label, contrast, or_ci)

table3_wide <- table3_df |>
  tidyr::pivot_wider(names_from = contrast, values_from = or_ci) |>
  dplyr::arrange(
    factor(group, levels = c("ABG", "V рG")),
```

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

Cohort	Outcome	Low vs normal OR (95% CI)	High vs normal OR (95% CI)
ABG	IMV	1.41 (1.04, 1.90)	1.26 (0.93, 1.72)
ABG	NIV	1.04 (0.63, 1.74)	3.05 (1.98, 4.70)
ABG	Death (60d)	1.57 (1.09, 2.26)	1.52 (1.07, 2.15)
ABG	Hypercapnic RF	1.28 (0.71, 2.31)	9.24 (5.76, 14.83)
VBG	IMV	1.26 (0.78, 2.04)	1.64 (1.04, 2.59)
VBG	NIV	0.78 (0.39, 1.59)	2.71 (1.47, 4.98)
VBG	Death (60d)	1.08 (0.67, 1.74)	1.11 (0.70, 1.77)
VBG	Hypercapnic RF	0.71 (0.31, 1.63)	6.36 (3.51, 11.51)

Weighted survey GLMs adjusted for baseline covariates; weights = MI-specific GLM (RCS) IPW; m = 80 imputations (seed 20251206); reference = Normal.

```

    factor(outcome_label, levels = c("IMV", "NIV", "Death (60d)", "Hypercapnic RF"))

)

gt::gt(table3_wide) |>
  gt::tab_header(title = "Table 3. MI-pooled IPW associations between CO\u2082 category and outcomes (adjusted)") |>
  gt::cols_label(
    group      = "Cohort",
    outcome_label  = "Outcome",
    `Low vs normal` = "Low vs normal OR (95% CI)",
    `High vs normal` = "High vs normal OR (95% CI)"
  ) |>
  gt::fmt_missing(columns = gt::everything(), missing_text = "-") |>
  gt::tab_source_note(
    paste0(
      "Weighted survey GLMs adjusted for baseline covariates; weights = MI-specific GLM (RCS) IPW; m = ", M_IMP,
      " imputations (seed ", MI_SEED, "); reference = Normal."
    )
  )
)

```

3.7.4 Summary: adjusted CO2-category associations across analysis tracks

```
label_outcome <- function(x) {
  dplyr::recode(
    x,
    imv_proc = "IMV",
    niv_proc = "NIV",
    death_60d = "Death (60d)",
    hypercap_resp_failure = "Hypercapnic RF",
    IMV = "IMV",
    NIV = "NIV",
    Death60d = "Death (60d)",
    HCRF = "Hypercapnic RF"
  )
}

map_contrast <- function(term) {
  dplyr::case_when(
    grepl("Low", term) ~ "Low vs normal",
    grepl("High", term) ~ "High vs normal",
    TRUE ~ NA_character_
  )
}

prep_threellevel <- function(df, estimate_col, lcl_col, ucl_col, method_label) {
  df |>
    dplyr::mutate(
      contrast = map_contrast(term),
      outcome_label = label_outcome(outcome),
      OR = .data[[estimate_col]],
      LCL = .data[[lcl_col]],
      UCL = .data[[ucl_col]],
      method = method_label
    ) |>
    dplyr::filter(!is.na(contrast)) |>
```

```

dplyr::select(method, group, outcome_label, contrast, OR, LCL, UCL)
}

count_model <- function(data, outcome, exposure, adj_vars,
                        treat_var = NULL, weight_var = NULL) {
  d <- data
  if (!is.null(treat_var)) d <- d[d[[treat_var]] == 1, , drop = FALSE]
  vars <- c(outcome, exposure, adj_vars)
  if (!is.null(weight_var)) vars <- c(vars, weight_var)
  d <- d[, vars, drop = FALSE]
  d <- d[complete.cases(d), , drop = FALSE]
  if (!is.null(weight_var)) {
    w <- suppressWarnings(as.numeric(d[[weight_var]]))
    d <- d[is.finite(w) & w > 0, , drop = FALSE]
  }
  if (nrow(d) == 0L) {
    return(tibble::tibble(n_model = 0L, events = 0L))
  }
  d[[outcome]] <- to01(d[[outcome]])
  tibble::tibble(
    n_model = nrow(d),
    events = sum(d[[outcome]] == 1, na.rm = TRUE)
  )
}

count_group <- function(group, method) {
  exp_var <- if (group == "ABG") "pc02_cat_abg" else "pc02_cat_vbg"
  treat_var <- if (group == "ABG") "has_abg" else "has_vbg"
  weight_var <- if (method == "IPW adjusted") {
    if (group == "ABG") "w_abg" else "w_vbg"
  } else {
    NULL
  }
  outcomes <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")
  purrr::map_dfr(outcomes, function(outcome) {
    cnt <- count_model(subset_data, outcome, exp_var, adj_core,

```

```

            treat_var = treat_var, weight_var = weight_var)
dplyr::mutate(cnt,
              method = method,
              group = group,
              outcome_label = label_outcome(outcome)))
})
}

mi_counts_threelvel <- function(outcome, group) {
  imp_n <- imp$m
  counts <- lapply(seq_len(imp_n), function(i) {
    d <- get_imp(i)
    if (group == "ABG") {
      co2_var <- "paco2"
      treat_var <- "has_abg"
      w <- mi_logistic_ps_abg_list[[i]]$weights
      low_cut <- ABG_CO2_LOW
      high_cut <- ABG_CO2_HIGH
    } else {
      co2_var <- "vbg_co2"
      treat_var <- "has_vbg"
      w <- mi_logistic_ps_vbg_list[[i]]$weights
      low_cut <- VBG_CO2_LOW
      high_cut <- VBG_CO2_HIGH
    }
    d[[co2_var]] <- suppressWarnings(as.numeric(d[[co2_var]]))
    keep <- d[[treat_var]] == 1 & is.finite(d[[co2_var]])
    if (!any(keep)) return(c(n_model = 0, events = 0))
    d2 <- d[keep, , drop = FALSE]
    w2 <- w[keep]
    d2$co2_cat <- make_co2_cat3(d2[[co2_var]], low_cut, high_cut)
    keep2 <- !is.na(d2$co2_cat)
    d2 <- d2[keep2, , drop = FALSE]
    w2 <- w2[keep2]
    if (nrow(d2) == 0L) return(c(n_model = 0, events = 0))
    d2[[outcome]] <- to01(d2[[outcome]])
  })
}

```

```

complete_ok <- complete.cases(d2[, c(outcome, adj_core, "co2_cat")], drop = FALSE)
w_ok <- is.finite(w2) & w2 > 0
d2 <- d2[complete_ok & w_ok, , drop = FALSE]
if (nrow(d2) == 0L) return(c(n_model = 0, events = 0))
c(n_model = nrow(d2), events = sum(d2[[outcome]] == 1, na.rm = TRUE))
})
n_vals <- vapply(counts, `[[`, numeric(1), "n_model")
e_vals <- vapply(counts, `[[`, numeric(1), "events")
tibble::tibble(
  n_model = round(stats::median(n_vals, na.rm = TRUE)),
  events = round(stats::median(e_vals, na.rm = TRUE))
)
}

mi_counts <- function(group) {
  outcomes <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")
  purrr::map_dfr(outcomes, function(outcome) {
    cnt <- mi_counts_threel level(outcome, group)
    dplyr::mutate(cnt,
                  method = "IPW + MI adjusted",
                  group = group,
                  outcome_label = label_outcome(outcome))
  })
}

counts_tbl <- dplyr::bind_rows(
  count_group("ABG", "Unweighted adjusted"),
  count_group("VBG", "Unweighted adjusted"),
  count_group("ABG", "IPW adjusted"),
  count_group("VBG", "IPW adjusted"),
  mi_counts("ABG"),
  mi_counts("VBG")
)

or_all <- dplyr::bind_rows(
  prep_threel level(unw_threel level_results, "estimate", "conf.low", "conf.high", "Unweighted adjusted"),

```

```

prep_threelvel(ipw_threelvel_results, "estimate", "conf.low", "conf.high", "IPW adjusted"),
prep_threelvel(mi_threelvel_results, "OR", "LCL", "UCL", "IPW + MI adjusted")
) |>
dplyr::left_join(counts_tbl, by = c("method", "group", "outcome_label"))

table_summary <- or_all |>
dplyr::mutate(or_ci = sprintf("%.2f (%.2f, %.2f)", OR, LCL, UCL)) |>
dplyr::select(method, group, outcome_label, n_model, events, contrast, or_ci) |>
tidyrr::pivot_wider(names_from = contrast, values_from = or_ci) |>
dplyr::arrange(
  factor(method, levels = c("Unweighted adjusted", "IPW adjusted", "IPW + MI adjusted")),
  factor(group, levels = c("ABG", "VBG")),
  factor(outcome_label, levels = c("IMV", "NIV", "Death (60d)", "Hypercapnic RF"))
)

render_table_pdf(
  table_summary,
  caption = "Adjusted odds ratios (low/high vs normal) across analysis tracks; n/events reflect model sample size (median across
file_stub = "table_summary_adjusted_threelvel",
digits = 2
)

```

Table 10: Adjusted odds ratios (low/high vs normal) across analysis tracks; n/events reflect model sample size (median across imputations for MI). (Part A)

method	group	outcome_label	n_model	events	Low vs normal
Unweighted adjusted	ABG	IMV	1911	463	1.39 (1.07, 1.80)
Unweighted adjusted	ABG	NIV	1911	183	0.99 (0.64, 1.52)
Unweighted adjusted	ABG	Death (60d)	1911	322	1.76 (1.29, 2.39)
Unweighted adjusted	ABG	Hypercapnic RF	1911	206	1.37 (0.81, 2.30)
Unweighted adjusted	VBG	IMV	1445	208	1.27 (0.87, 1.85)
Unweighted adjusted	VBG	NIV	1445	100	1.00 (0.56, 1.77)
Unweighted adjusted	VBG	Death (60d)	1445	200	1.53 (1.04, 2.25)
Unweighted adjusted	VBG	Hypercapnic RF	1445	133	0.84 (0.43, 1.58)
IPW adjusted	ABG	IMV	1911	463	1.40 (1.06, 1.86)
IPW adjusted	ABG	NIV	1911	183	1.04 (0.65, 1.69)
IPW adjusted	ABG	Death (60d)	1911	322	1.52 (1.08, 2.16)
IPW adjusted	ABG	Hypercapnic RF	1911	206	1.54 (0.84, 2.82)
IPW adjusted	VBG	IMV	1445	208	1.34 (0.89, 2.03)
IPW adjusted	VBG	NIV	1445	100	0.88 (0.47, 1.67)
IPW adjusted	VBG	Death (60d)	1445	200	1.38 (0.91, 2.10)
IPW adjusted	VBG	Hypercapnic RF	1445	133	0.76 (0.37, 1.56)
IPW + MI adjusted	ABG	IMV	1911	463	1.41 (1.04, 1.90)
IPW + MI adjusted	ABG	NIV	1911	183	1.04 (0.63, 1.74)
IPW + MI adjusted	ABG	Death (60d)	1911	322	1.57 (1.09, 2.26)
IPW + MI adjusted	ABG	Hypercapnic RF	1911	206	1.28 (0.71, 2.31)
IPW + MI adjusted	VBG	IMV	1445	208	1.26 (0.78, 2.04)
IPW + MI adjusted	VBG	NIV	1445	100	0.78 (0.39, 1.59)
IPW + MI adjusted	VBG	Death (60d)	1445	200	1.08 (0.67, 1.74)
IPW + MI adjusted	VBG	Hypercapnic RF	1445	133	0.71 (0.31, 1.63)

Table 11: Adjusted odds ratios (low/high vs normal) across analysis tracks; n/events reflect model sample size (median across imputations for MI). (Part B)

High vs normal
1.25 (0.96, 1.61)
2.62 (1.83, 3.78)
1.54 (1.14, 2.08)
8.50 (5.76, 12.89)
1.61 (1.11, 2.33)
2.80 (1.71, 4.68)
1.29 (0.87, 1.89)
7.09 (4.49, 11.55)
1.14 (0.85, 1.52)
2.82 (1.90, 4.17)
1.46 (1.05, 2.02)
9.39 (5.99, 14.73)
1.58 (1.06, 2.37)
2.77 (1.62, 4.75)
1.31 (0.87, 1.98)
7.58 (4.54, 12.67)
1.26 (0.93, 1.72)
3.05 (1.98, 4.70)
1.52 (1.07, 2.15)
9.24 (5.76, 14.83)
1.64 (1.04, 2.59)
2.71 (1.47, 4.98)
1.11 (0.70, 1.77)
6.36 (3.51, 11.51)

```

append_mem_snapshot("stage1", "end", "post")
stage1_rm <- c(
  "unw_results_crude", "unw_results_adj", "unw_threel level_results",
  "unw_combined_or_df", "unw_plot_df", "unw_p_or", "unw_axis_spec", "outcomes_unw"
)
missing_stage1 <- setdiff(stage1_rm, ls())
stopifnot(length(missing_stage1) == 0)
rm(list = stage1_rm)
invisible(gc())
append_mem_snapshot("stage1", "cleanup", "post")

```

3.8 Manuscript outputs summary

```

# Cohort flow / sample sizes
flow_tbl <- tibble::tibble(
  metric = c(
    "Full cohort (raw)",
    "Analytic subset",
    "ABG tested",
    "ABG with PaCO2",
    "VBG tested",
    "VBG with VBG CO2"
  ),
  n = c(
    nrow(stata_data),
    nrow(subset_data),
    sum(subset_data$has_abg == 1, na.rm = TRUE),
    sum(subset_data$has_abg == 1 & !is.na(subset_data$paco2), na.rm = TRUE),
    sum(subset_data$has_vbg == 1, na.rm = TRUE),
    sum(subset_data$has_vbg == 1 & !is.na(subset_data$vbg_co2), na.rm = TRUE)
  )
)
render_table_pdf_maybe(flow_tbl, "Cohort flow summary", "cohort_flow_summary",
  digits = 0, show = SHOW_LOW_VALUE_TABLES)

```

```

# Event counts by cohort
outcome_vars <- c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")
outcome_labels <- c(
  imv_proc = "IMV",
  niv_proc = "NIV",
  death_60d = "Death (60d)",
  hypercap_resp_failure = "Hypercapnic RF"
)
event_tbl <- dplyr::bind_rows(
  lapply(outcome_vars, function(o) {
    dplyr::tibble(
      outcome = outcome_labels[[o]],
      group = "ABG",
      n = sum(subset_data$has_abg == 1 & !is.na(subset_data[[o]]), na.rm = TRUE),
      events = sum(subset_data$has_abg == 1 & subset_data[[o]] == 1, na.rm = TRUE)
    )
  }),
  lapply(outcome_vars, function(o) {
    dplyr::tibble(
      outcome = outcome_labels[[o]],
      group = "VBG",
      n = sum(subset_data$has_vbg == 1 & !is.na(subset_data[[o]]), na.rm = TRUE),
      events = sum(subset_data$has_vbg == 1 & subset_data[[o]] == 1, na.rm = TRUE)
    )
  })
)
event_tbl <- event_tbl |>
  dplyr::mutate(pct = ifelse(n > 0, 100 * events / n, NA_real_))
render_table_pdf_maybe(event_tbl,
  "Outcome counts by cohort (ABG/VBG tested)",
  "outcome_counts_by_cohort",
  digits = 1, show = SHOW_LOW_VALUE_TABLES)

# Weighting diagnostics (non-MI weights)
stopifnot(all(c("w_abg", "w_vbg", "ps_abg", "ps_vbg") %in% names(subset_data)))

```

```

wt_abg <- subset_data$w_abg[subset_data$has_abg == 1]
wt_vbg <- subset_data$w_vbg[subset_data$has_vbg == 1]
ps_abg <- subset_data$ps_abg[subset_data$has_abg == 1]
ps_vbg <- subset_data$ps_vbg[subset_data$has_vbg == 1]
trunc_abg <- subset_data$trunc_abg[subset_data$has_abg == 1]
trunc_vbg <- subset_data$trunc_vbg[subset_data$has_vbg == 1]

wt_sum <- dplyr::bind_rows(
  weight_summary(wt_abg, ps = ps_abg, ps_floor = ps_floor_abg,
    truncated = trunc_abg) |>
    dplyr::mutate(group = "ABG"),
  weight_summary(wt_vbg, ps = ps_vbg, ps_floor = ps_floor_vbg,
    truncated = trunc_vbg) |>
    dplyr::mutate(group = "VBG")
)
wt_sum_display <- wt_sum |>
  dplyr::select(group, n, ess, min, p99, max, trunc_rate, ps_p01) |>
  dplyr::rename(
    trunc = trunc_rate,
    p01_ps = ps_p01
  )
render_table_pdf_maybe(wt_sum_display,
  "Weighting diagnostics summary (non-MI)",
  "weighting_diagnostics_non_mi",
  wide = TRUE,
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES)

# Missingness + MI spec summary
miss_vars <- c(covars_ps, "paco2", "vbg_co2",
  "imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure")
miss_vars <- intersect(miss_vars, names(subset_data_raw))
miss_tbl <- subset_data_raw |>
  dplyr::summarise(dplyr::across(dplyr::all_of(miss_vars), ~ mean(is.na(.)) * 100)) |>
  tidyr::pivot_longer(dplyr::everything(), names_to = "variable", values_to = "pct_missing") |>
  dplyr::arrange(dplyr::desc(pct_missing))

```

```

render_table_pdf_maybe(miss_tbl,
                      "Variables by missingness (pre-imputation)",
                      "missingness_all",
                      digits = 1,
                      show = SHOW_LOW_VALUE_TABLES)

mi_spec_tbl <- tibble::tibble(
  m = imp$m,
  maxit = MAXIT_MI,
  methods = paste(unique(imp$method[imp$method != ""]),
                  collapse = ", "),
  ps_model = MI_PS_METHOD,
  ps_spline_k = MI_PS_SPLINE_K,
  ps_glm_maxit = MI_GLM_MAXIT
)
render_table_pdf_maybe(mi_spec_tbl,
                      "MI specification (methods used)",
                      "mi_specification",
                      show = SHOW_LOW_VALUE_TABLES)

```

```

stopifnot(exists("imp"))
imp_n <- imp$m
get_imp <- function(i, imp_obj = imp) { normalize_types(mice::complete(imp_obj, action = i), levels_ref) }

# 1) must exist and be numeric
d1 <- get_imp(1)
stopifnot(all(c("paco2", "vbg_co2") %in% names(d1)))
stopifnot(is.numeric(d1$paco2), is.numeric(d1$vbg_co2))

# 2) confirm at least two PaCO2 levels among those with ABG in each imputation
table(vapply(seq_len(imp_n), function(i) {
  d <- get_imp(i)
  dplyr::n_distinct(d$paco2[d$has_abg == 1 & is.finite(d$paco2)])
}, integer(1)) > 1)

```

```
TRUE  
80
```

```
# 3) light sanity check: ensure pooled MI cat3 results exist  
stopifnot(exists("abg_cat_results"), nrow(abg_cat_results) > 0)
```

3.8.1 Visualization: pooled three-level ORs

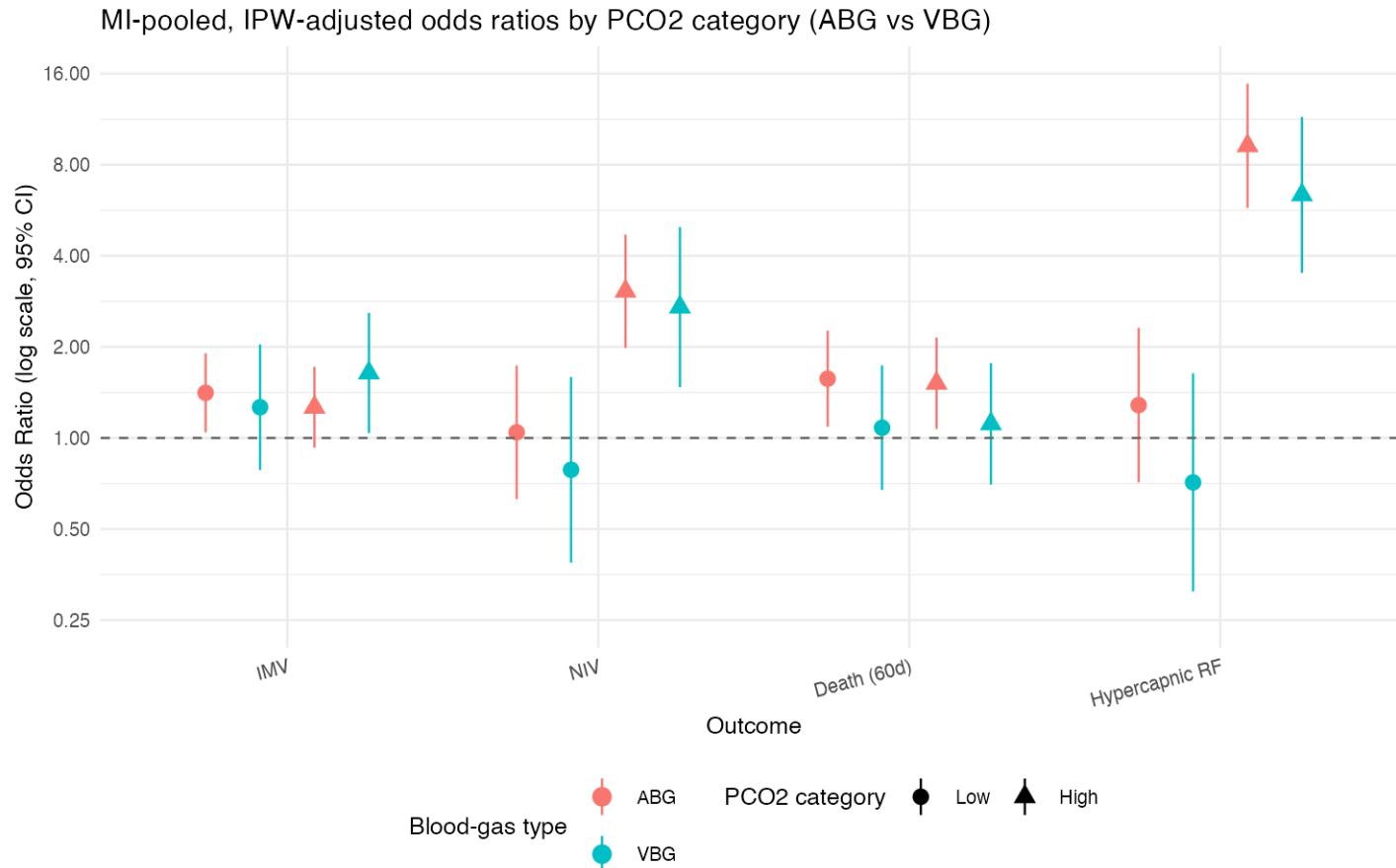
```
stopifnot(exists("abg_cat_results"), exists("vbg_cat_results"))

mi_combined_or_df <- dplyr::bind_rows(  
  dplyr::mutate(abg_cat_results, group = "ABG"),  
  dplyr::mutate(vbg_cat_results, group = "VBG")  
) |>  
  dplyr::mutate(  
    outcome = factor(outcome,  
      levels = c("IMV", "NIV", "Death60d", "HCRF"),  
      labels = c("IMV", "NIV", "Death (60d)", "Hypercapnic RF")),  
    group = factor(group, levels = c("ABG", "VBG"))  
)  
  
mi_combined_or_df <- map_or_exposure(mi_combined_or_df, "or-plot-mi-weighted")  
mi_plot_df <- mi_combined_or_df |>  
  dplyr::mutate(estimate = OR, conf.low = LCL, conf.high = UCL) |>  
  dplyr::select(-OR, -LCL, -UCL)  
  
mi_plot_df <- build_or_plot_df(  
  mi_plot_df,  
  "or-plot-mi-weighted",  
  expected_exposure_levels = CO2_CAT_CONTRAST_LEVELS  
)  
mi_axis_spec <- compute_or_axis_spec(list(mi_plot_df), lo_col = "conf.low", hi_col = "conf.high")  
  
mi_p_or <- plot_or_safe(
```

```

mi_plot_df,
plot_name = "or-plot-mi-weighted",
axis_spec = mi_axis_spec,
title = "MI-pooled, IPW-adjusted odds ratios by PCO2 category (ABG vs VBG)"
)
print_plot_once(mi_p_or, "or-plot-mi-weighted", width = 7.5, height = 4.8)

```



3.8.2 Visualization

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

mi_ipw_rcs_forms <- list(
  "MI IPW spline (adjusted) ABG: IMV ~ CO2 spline + X"      = make_spline_fml("imv_proc", "paco2", adj_core),
  "MI IPW spline (adjusted) ABG: NIV ~ CO2 spline + X"      = make_spline_fml("niv_proc", "paco2", adj_core),
  "MI IPW spline (adjusted) ABG: Death60d ~ CO2 spline + X" = make_spline_fml("death_60d", "paco2", adj_core),
  "MI IPW spline (adjusted) ABG: HCRF ~ CO2 spline + X"     = make_spline_fml("hypercap_resp_failure", "paco2", adj_core),
  "MI IPW spline (adjusted) VBG: IMV ~ CO2 spline + X"      = make_spline_fml("imv_proc", "vbg_co2", adj_core),
  "MI IPW spline (adjusted) VBG: NIV ~ CO2 spline + X"      = make_spline_fml("niv_proc", "vbg_co2", adj_core),
  "MI IPW spline (adjusted) VBG: Death60d ~ CO2 spline + X" = make_spline_fml("death_60d", "vbg_co2", adj_core),
  "MI IPW spline (adjusted) VBG: HCRF ~ CO2 spline + X"     = make_spline_fml("hypercap_resp_failure", "vbg_co2", adj_core)
)
register_model_diagrams(mi_ipw_rcs_forms)

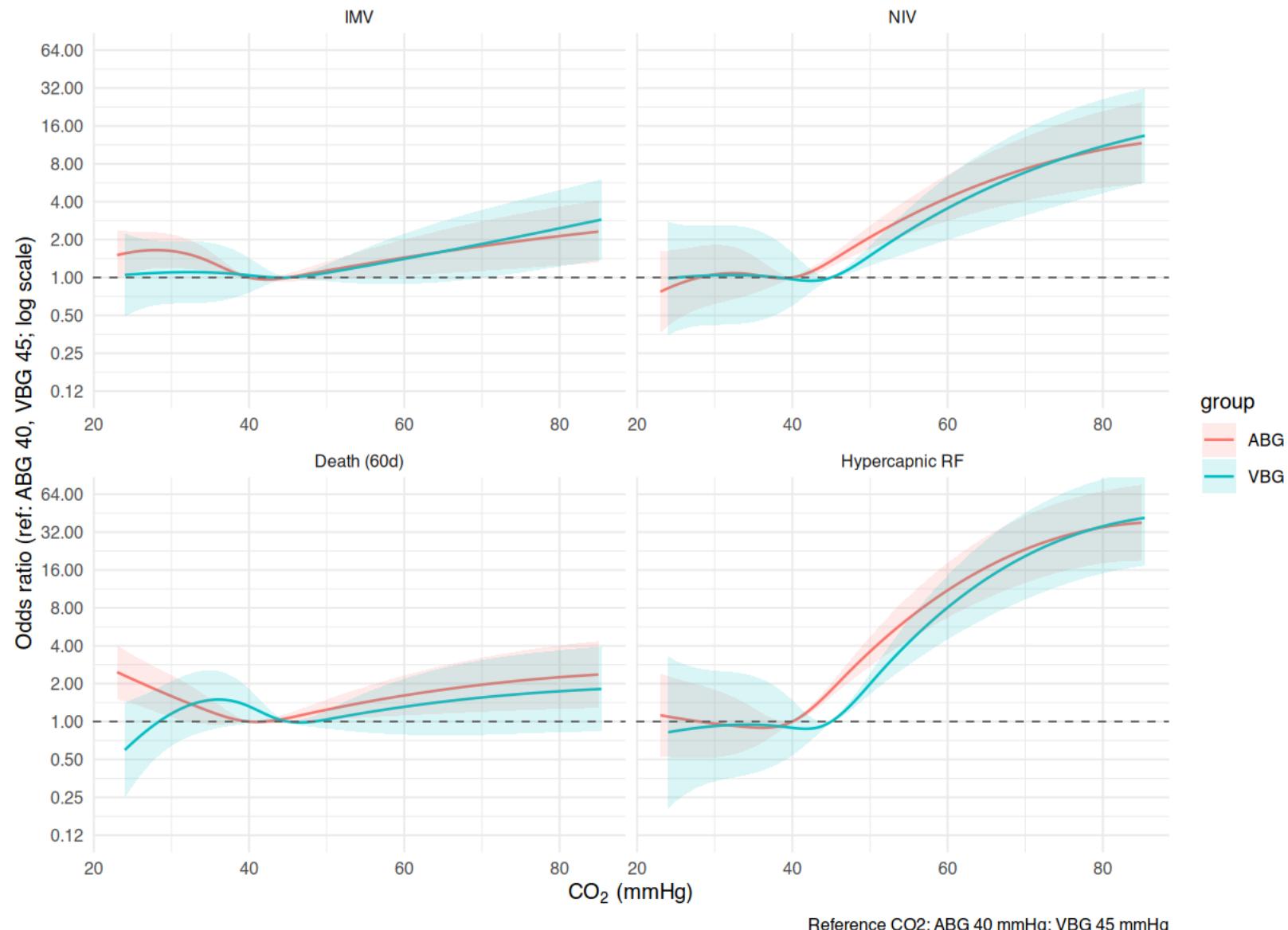
stopifnot(exists("abg_curves"), exists("vbg_curves"))

curve_abg <- abg_curves |>
  mutate(co2 = paco2) |>
  select(-paco2)
curve_vbg <- vbg_curves |>
  mutate(co2 = vbg_co2) |>
  select(-vbg_co2)
curve_all <- bind_rows(curve_abg, curve_vbg) |>
  mutate(outcome = factor(outcome,
                          levels = c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure"),
                          labels = c("IMV", "NIV", "Death (60d)", "Hypercapnic RF")))
axis_mi_ipw <- compute_or_axis_spec(list(curve_abg, curve_vbg), lo_col = "LCL", hi_col = "UCL")

ggplot(curve_all, aes(x = co2, y = OR, color = group, fill = group)) +
  geom_line(linewidth = 0.6) +
```

```
geom_ribbon(aes(ymin = LCL, ymax = UCL), alpha = 0.15, color = NA) +
  geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
  or_axis_scale(axis_mi_ipw) +
  facet_wrap(~ outcome, scales = "free_x") +
  labs(
    title = expression(
      paste("MI-pooled, IPSW-adjusted spline odds ratios: ABG vs VBG CO"[2]))
  ),
  x = expression(CO[2]~"(mmHg)"),
  y = paste0("Odds ratio (ref: ABG ", ABG_CO2_REF, ", VBG ", VBG_CO2_REF, "; log scale)"),
  caption = paste0("Reference CO2: ABG ", ABG_CO2_REF, " mmHg; VBG ", VBG_CO2_REF, " mmHg")
) +
  theme_minimal(base_size = 10)
```

MI-pooled, IPSW-adjusted spline odds ratios: ABG vs VBG CO₂



3.9 Diagnostics

```
stopifnot(gbm_params$stop.method == "smd.max")
stopifnot(exists("M_IMP"), exists("MAXIT_MI"), exists("MI_SEED"))
stopifnot(exists("imp"))
stopifnot(exists("mi_logistic_ps_abg_list"), exists("mi_logistic_ps_vbg_list"))
meth <- imp$method

diag_fig_dir <- results_path("figs")
fs::dir_create(diag_fig_dir)
```

```
library(dplyr)
library(tidyr)
library(naniar)

extra_miss_vars <- intersect(c("bnp", "spo2"), names(subset_data_raw))
miss_vars <- intersect(
  covars_ps, extra_miss_vars, "paco2", "vbg_co2", "vbg_o2sat",
  "imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure"),
  names(subset_data_raw)
)

miss_overall <- subset_data_raw |>
  summarise(across(all_of(miss_vars), ~ mean(is.na(.)) * 100)) |>
  pivot_longer(everything(), names_to = "variable", values_to = "pct_missing_overall") |>
  arrange(desc(pct_missing_overall))

miss_overall_file <- results_path("diagnostics_missingness.csv")
write_csv_safely(miss_overall, miss_overall_file, row_names = FALSE)

miss_by_strata <- bind_rows(
  subset_data_raw |>
    group_by(has_abg) |>
    summarise(across(all_of(miss_vars), ~ mean(is.na(.)) * 100), .groups = "drop") |>
    pivot_longer(-has_abg, names_to = "variable", values_to = "pct_missing") |>
```

```

    mutate(stratum = "has_abg", level = as.character(has_abg)) |>
    select(stratum, level, variable, pct_missing),
    subset_data_raw |>
    group_by(has_vbg) |>
    summarise(across(all_of(miss_vars), ~ mean(is.na(.)) * 100), .groups = "drop") |>
    pivot_longer(-has_vbg, names_to = "variable", values_to = "pct_missing") |>
    mutate(stratum = "has_vbg", level = as.character(has_vbg)) |>
    select(stratum, level, variable, pct_missing)
)

miss_by_strata_file <- results_path("diagnostics_missingness-by-strata.csv")
write_csv_safely(miss_by_strata, miss_by_strata_file, row_names = FALSE)

md_fig_file <- results_path("figs", "diag-mi-missingness-pattern.png")
grDevices::png(md_fig_file, width = 1800, height = 1200, res = 200)
mice::md.pattern(imp$data, plot = TRUE)
grDevices::dev.off()

if (nrow(miss_overall) > 0) {
  top_vars <- miss_overall |>
    slice_head(n = min(20, nrow(miss_overall))) |>
    pull(variable)
  miss_sample <- subset_data_raw |>
    select(all_of(top_vars)) |>
    slice_sample(n = min(1000, nrow(subset_data_raw)))

  p_miss <- naniar::vis_miss(miss_sample, sort_miss = TRUE) +
    theme_minimal(base_size = 10) +
    labs(title = "Missingness heatmap (top 20 variables)")
  save_diag_plot(p_miss, results_path("figs", "diag-mi-missingness-heatmap.png"),
                 width = 10, height = 6)
}

```

3.9.1 MI convergence and mixing

```
stopifnot(exists("imp"))

log_events_summary_file <- results_path("mice_logged_events_summary.csv")
stopifnot(file.exists(log_events_summary_file))
log_events_summary <- tryCatch(
  utils::read.csv(log_events_summary_file, stringsAsFactors = FALSE),
  error = function(e) data.frame()
)
if (nrow(log_events_summary) && !("empty" %in% names(log_events_summary) && all(log_events_summary$empty))) {
  render_table_pdf_maybe(
    log_events_summary,
    caption = "Logged events (MI)",
    file_stub = "mice_logged_events_summary",
    digits = 0,
    show = SHOW_LOW_VALUE_TABLES
)

stopifnot(all(c("variable", "n") %in% names(log_events_summary)))
total_events <- sum(log_events_summary$n, na.rm = TRUE)
if (is.finite(total_events) && total_events > 1000) {
  warning("MI loggedEvents count is high (", total_events, "). Review mice_logged_events_summary.csv.", call. = FALSE)
}
by_var <- log_events_summary |>
  dplyr::group_by(variable) |>
  dplyr::summarise(n = sum(n), .groups = "drop") |>
  dplyr::arrange(dplyr::desc(n))
if (nrow(by_var) && is.finite(total_events) && total_events > 0) {
  top_share <- by_var$n[1] / total_events
  if (top_share > 0.5) {
    warning("MI loggedEvents dominated by variable '", by_var$variable[1],
           "' (", round(100 * top_share, 1), "% of events).", call. = FALSE)
  }
}
```

```

} else {
  message("No logged events to summarize.")
}

stopifnot(exists("chain_diag"))
stopifnot(nrow(chain_diag) > 0)
n_imputed <- chain_diag_stats$n_imputed_vars
n_with_tail <- chain_diag_stats$n_with_drift_tail
message("Chain diagnostics: drift_tail available for ", n_with_tail, " / ", n_imputed, " imputed variables.")
stopifnot("drift_tail_scaled" %in% names(chain_diag))
frac_flagged <- mean(chain_diag$flag %in% TRUE, na.rm = TRUE)
med_scaled <- stats::median(chain_diag$drift_tail_scaled, na.rm = TRUE)
max_scaled <- max(chain_diag$drift_tail_scaled, na.rm = TRUE)
message("Chain diagnostics (scaled): flagged=", round(frac_flagged, 3),
       "; median drift_tail_scaled=", signif(med_scaled, 3),
       "; max drift_tail_scaled=", signif(max_scaled, 3))

top_flagged <- chain_diag |>
  dplyr::filter(flag %in% TRUE) |>
  dplyr::arrange(dplyr::desc(abs(drift_tail_scaled)))
if (nrow(top_flagged)) {
  render_table_pdf_maybe(
    top_flagged |>
      dplyr::select(variable, method, drift_tail, drift_tail_scaled, slope, slope_scaled,
                    tail_n_finite, tail_window_na_frac, flag_reason),
    caption = "MICE chain diagnostics (flagged drift)",
    file_stub = "mice_chain_diagnostics_flagged",
    digits = 3,
    show = SHOW_LOW_VALUE_TABLES
  )
} else {
  message("No flagged drift in chain diagnostics.")
}

top_tail_na <- chain_diag |>
  dplyr::arrange(dplyr::desc(tail_window_na_frac))

```

```

if (nrow(top_tail_na)) {
  render_table_pdf_maybe(
    top_tail_na,
    caption = "MICE chain diagnostics (tail NA fraction)",
    file_stub = "mice_chain_diagnostics_tail_na",
    digits = 3,
    show = SHOW_LOW_VALUE_TABLES
  )
}

trace_vars <- intersect(c("curr_bmi", "serum_hco3", "hr", "sodium", "serum_cr"),
                        names(imp$data))

imp_trace <- imp
if (imp$m > 10) {
  set.seed(MI_SEED)
  idx <- sort(sample(seq_len(imp$m), 10))
  imp_trace$imp <- lapply(imp$imp, function(x) x[, idx, drop = FALSE])
  imp_trace$m <- length(idx)
}

if (length(trace_vars)) {
  tr_file <- results_path("figs", "diag-mi-trace-selected.png")
  grDevices::png(tr_file, width = 1800, height = 1200, res = 200)
  plot(imp_trace, trace_vars)
  grDevices::dev.off()
}

png
2

message("Using memory-safe observed vs imputed plots from mi-diagnostics (no mids densityplot/striplplot).")

```

3.9.2 MI stability across m

```
stopifnot(exists("imp"))
stopifnot(exists("mi_logistic_ps_abg_list"), exists("mi_logistic_ps_vbg_list"))
library(dplyr)

subset_mids <- function(imp_obj, m_keep) {
  if (imp_obj$m == m_keep) return(imp_obj)
  idx <- seq_len(m_keep)
  imp_new <- imp_obj
  imp_new$imp <- lapply(imp_obj$imp, function(x) x[, idx, drop = FALSE])
  imp_new$m <- m_keep
  imp_new
}

m_vals <- sort(unique(c(20, 50, M_IMP)))
m_vals <- m_vals[m_vals <= imp$m]

med_abg <- median(subset_data$paco2[subset_data$has_abg == 1 & !is.na(subset_data$paco2)], na.rm = TRUE)
med_vbg <- median(subset_data$vbg_co2[subset_data$has_vbg == 1 & !is.na(subset_data$vbg_co2)], na.rm = TRUE)
if (!is.finite(med_abg)) med_abg <- ABG_CO2_REF
if (!is.finite(med_vbg)) med_vbg <- VBG_CO2_REF
grid_abg_info_m <- make_co2_grid_ref("paco2", c(med_abg, ABG_CO2_REF), x_ref_abg, ABG_CO2_REF)
grid_vbg_info_m <- make_co2_grid_ref("vbg_co2", c(med_vbg, VBG_CO2_REF), x_ref_vbg, VBG_CO2_REF)
grid_abg_m <- grid_abg_info_m$grid
grid_vbg_m <- grid_vbg_info_m$grid
ref_idx_abg_m <- grid_abg_info_m$ref_idx
ref_idx_vbg_m <- grid_vbg_info_m$ref_idx
med_idx_abg <- match(med_abg, grid_abg_m$paco2)
med_idx_vbg <- match(med_vbg, grid_vbg_m$vbg_co2)
if (is.na(med_idx_abg)) med_idx_abg <- which.min(abs(grid_abg_m$paco2 - med_abg))
if (is.na(med_idx_vbg)) med_idx_vbg <- which.min(abs(grid_vbg_m$vbg_co2 - med_vbg))

stab_rows <- lapply(m_vals, function(mv) {
  imp_m <- subset_mids(imp, mv)
```

```

get_imp_m <- function(i) normalize_types(mice::complete(imp_m, action = i), levels_ref)

fits_abg <- lapply(seq_len(mv), function(i) {
  d <- get_imp_m(i)
  d <- d[, c("imv_proc", "has_abg", "paco2", adj_core), drop = FALSE]
  tryCatch(
    fit_spline_imp(
      d, mi_logistic_ps_abg_list[[i]]$weights, "imv_proc", "paco2", "has_abg",
      adj_vars = adj_core,
      spline_df = SPLINE_DF, spline_basis = SPLINE_BASIS, grid_df = grid_abg_m,
      ref_idx = ref_idx_abg_m,
      imp_index = i
    ),
    error = function(e) list(error = conditionMessage(e))
  )
})
collect_warnings_from_list(fits_abg)
curve_abg <- pool_spline_curve(fits_abg, grid_abg_m, ref_idx_abg_m, ABG_CO2_REF,
                                 min_ok_frac = 0.9)

fits_vbg <- lapply(seq_len(mv), function(i) {
  d <- get_imp_m(i)
  d <- d[, c("imv_proc", "has_vbg", "vbg_co2", adj_core), drop = FALSE]
  tryCatch(
    fit_spline_imp(
      d, mi_logistic_ps_vbg_list[[i]]$weights, "imv_proc", "vbg_co2", "has_vbg",
      adj_vars = adj_core,
      spline_df = SPLINE_DF, spline_basis = SPLINE_BASIS, grid_df = grid_vbg_m,
      ref_idx = ref_idx_vbg_m,
      imp_index = i
    ),
    error = function(e) list(error = conditionMessage(e))
  )
})
collect_warnings_from_list(fits_vbg)
curve_vbg <- pool_spline_curve(fits_vbg, grid_vbg_m, ref_idx_vbg_m, VBG_CO2_REF,

```

```

    min_ok_frac = 0.9)

bind_rows(
  tibble::tibble(group = "ABG", m = mv, OR = curve_abg$OR[med_idx_abg]),
  tibble::tibble(group = "VBG", m = mv, OR = curve_vbg$OR[med_idx_vbg])
)
})

stab_df <- bind_rows(stab_rows)
ref <- stab_df |> filter(m == max(m_vals)) |> select(group, OR) |> rename(OR_ref = OR)
stab_df <- stab_df |>
  left_join(ref, by = "group") |>
  mutate(abs_diff = OR - OR_ref,
        pct_diff = 100 * (OR - OR_ref) / OR_ref)

stab_file <- results_path("mi_m_stability.csv")
write_csv_safely(stab_df, stab_file, row_names = FALSE)

# FMI / relative efficiency for a representative unweighted model
cap_fmi <- capture_warnings(
  summary(mice::pool(with(imv, glm(imv_proc ~ has_abg + age_at_encounter + sex,
                                    family = binomial())))),
  context = make_context(
    stage = "diagnostics",
    component = "mi_fmi_glm",
    analysis_variant = "mi",
    model_type = "glm",
    group = NA_character_,
    outcome = "imv_proc",
    imputation = NA_integer_,
    batch = NA_integer_
  )
)
append_warnings(cap_fmi$warnings)
fmi_tab <- cap_fmi$value
fmi_abg <- fmi_tab |> filter(term == "has_abg")

```

```

if (is.null(fmi_tab) || !"fmi" %in% names(fmi_tab)) {
  warning("FMI not available from mice::pool() summary; leaving FMI as NA.", call. = FALSE)
  fmi_abg <- fmi_abg |> mutate(fmi = NA_real_)
}
fmi_abg$rel_eff <- if (is.finite(fmi_abg$fmi[1])) 1 / (1 + fmi_abg$fmi[1] / M_IMP) else NA_real_

```

3.9.3 MI maxit sensitivity (sampled)

```

run_maxit_sensitivity <- TRUE
if (run_maxit_sensitivity) {
  stopifnot(exists("mi_df"), exists("meth"), exists("pred"))
  set.seed(MI_SEED)
  idx <- sample(seq_len(nrow(mi_df)), min(2000, nrow(mi_df)))
  mi_df_sens <- mi_df[idx, , drop = FALSE]

  m_sens <- min(20, M_IMP)
  maxit_short <- max(5, floor(MAXIT_MI / 2))

  cap_short <- capture_warnings(
    mice::mice(
      data          = mi_df_sens,
      m             = m_sens,
      maxit         = maxit_short,
      predictorMatrix = pred,
      method        = meth,
      printFlag     = FALSE,
      seed          = MI_SEED
    ),
    context = make_context(
      stage = "MI",
      component = "mice_maxit_short",
      analysis_variant = "mi",
      model_type = "mice",
      group = NA_character_
    )
  )
}
```

```

    outcome = NA_character_,
    imputation = NA_integer_,
    batch = NA_integer_
  )
)
append_warnings(cap_short$warnings)
imp_short <- cap_short$value
le_short <- as.data.frame(imp_short$loggedEvents)
if (nrow(le_short)) {
  le_short$run_type <- "maxit_short"
}
write_csv_safely(le_short, results_path("mice_logged_events_maxit_short.csv"), row_names = FALSE)

cap_long <- capture_warnings(
  mice::mice(
    data          = mi_df_sens,
    m             = m_sens,
    maxit         = MAXIT_MI,
    predictorMatrix = pred,
    method        = meth,
    printFlag     = FALSE,
    seed          = MI_SEED + 1
  ),
  context = make_context(
    stage = "MI",
    component = "mice_maxit_long",
    analysis_variant = "mi",
    model_type = "mice",
    group = NA_character_,
    outcome = NA_character_,
    imputation = NA_integer_,
    batch = NA_integer_
  )
)
append_warnings(cap_long$warnings)
imp_long <- cap_long$value

```

```

le_long <- as.data.frame(imp_long$loggedEvents)
if (nrow(le_long)) {
  le_long$run_type <- "maxit_long"
}
write_csv_safely(le_long, results_path("mice_logged_events_maxit_long.csv"), row_names = FALSE)

mean_across_imps <- function(imp_obj, var) {
  means <- vapply(seq_len(imp_obj$m), function(i) {
    d <- mice::complete(imp_obj, action = i)
    mean(d[[var]], na.rm = TRUE)
  }, numeric(1))
  mean(means, na.rm = TRUE)
}

key_vars <- intersect(c("curr_bmi", "serum_hco3", "sodium", "serum_cr"), names(mi_df_sens))
sens_df <- lapply(key_vars, function(v) {
  m_short <- mean_across_imps(imp_short, v)
  m_long <- mean_across_imps(imp_long, v)
  data.frame(
    variable = v,
    mean_short = m_short,
    mean_long = m_long,
    diff = m_long - m_short,
    stringsAsFactors = FALSE
  )
}) |> bind_rows()

sens_file <- results_path("mi_maxit_sensitivity.csv")
write_csv_safely(sens_df, sens_file, row_names = FALSE)
}

stopifnot(all(c("w_abg", "w_vbg") %in% names(subset_data)))

wt_abg <- subset_data$w_abg[subset_data$has_abg == 1]
wt_vbg <- subset_data$w_vbg[subset_data$has_vbg == 1]
ps_abg <- subset_data$ps_abg[subset_data$has_abg == 1]

```

```

ps_vbg <- subset_data$ps_vbg[subset_data$has_vbg == 1]
trunc_abg <- subset_data$trunc_abg[subset_data$has_abg == 1]
trunc_vbg <- subset_data$trunc_vbg[subset_data$has_vbg == 1]

wt_sum <- bind_rows(
  weight_summary(wt_abg, ps = ps_abg, ps_floor = ps_floor_abg,
                 truncated = trunc_abg) |>
    mutate(group = "ABG"),
  weight_summary(wt_vbg, ps = ps_vbg, ps_floor = ps_floor_vbg,
                 truncated = trunc_vbg) |>
    mutate(group = "VBG")
)
wt_sum_file <- results_path("weight_summary.csv")
write_csv_safely(wt_sum, wt_sum_file, row_names = FALSE)

ps_stat <- function(ps, group) {
  ps_ok <- ps[is.finite(ps)]
  if (!length(ps_ok)) {
    return(data.frame(
      group = group,
      ps_min = NA_real_,
      ps_p01 = NA_real_,
      ps_p50 = NA_real_,
      ps_p99 = NA_real_,
      ps_max = NA_real_,
      stringsAsFactors = FALSE
    ))
  }
  data.frame(
    group = group,
    ps_min = min(ps_ok, na.rm = TRUE),
    ps_p01 = stats::quantile(ps_ok, 0.01, na.rm = TRUE),
    ps_p50 = stats::median(ps_ok, na.rm = TRUE),
    ps_p99 = stats::quantile(ps_ok, 0.99, na.rm = TRUE),
    ps_max = max(ps_ok, na.rm = TRUE),
    stringsAsFactors = FALSE
  )
}

```

```

    )
}

ps_summary <- dplyr::bind_rows(
  ps_stat(ps_abg, "ABG"),
  ps_stat(ps_vbg, "VBG")
)
write_csv_safely(ps_summary, results_path("ps_overlap_summary.csv"), row_names = FALSE)
render_table_pdf_maybe(
  ps_summary,
  caption = "Propensity score overlap (tested cohort)",
  file_stub = "ps_overlap_summary",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)

wt_df <- bind_rows(
  tibble::tibble(group = "ABG", ps = ps_abg, weight = wt_abg),
  tibble::tibble(group = "VBG", ps = ps_vbg, weight = wt_vbg)
) |>
  filter(is.finite(weight), is.finite(ps))

plot_hist <- function(df, title) {
  ggplot(df, aes(x = weight)) +
    geom_histogram(bins = 40, fill = "grey70", color = "white") +
    labs(title = title, x = "Weight", y = "Count") +
    theme_minimal(base_size = 10)
}

p_hist_abg <- plot_hist(filter(wt_df, group == "ABG"), "ABG weight distribution")
p_hist_vbg <- plot_hist(filter(wt_df, group == "VBG"), "VBG weight distribution")
save_diag_plot(p_hist_abg, results_path("figs", "diag-wt-weights-hist-abg.png"), width = 7, height = 5)
save_diag_plot(p_hist_vbg, results_path("figs", "diag-wt-weights-hist-vbg.png"), width = 7, height = 5)

plot_scatter <- function(df, title) {
  top_wt <- df |>

```

```

    slice_max(order_by = weight, n = min(20, nrow(df)))
  ggplot(df, aes(x = ps, y = weight)) +
    geom_point(alpha = 0.3, size = 0.7) +
    geom_point(data = top_wt, color = "red", size = 1.2) +
    scale_y_log10() +
    labs(title = title, x = "Propensity score", y = "Weight (log10)") +
    theme_minimal(base_size = 10)
}

p_scatter_abg <- plot_scatter(filter(wt_df, group == "ABG"),
                               "ABG weights vs propensity (top 20 highlighted)")
p_scatter_vbg <- plot_scatter(filter(wt_df, group == "VBG"),
                               "VBG weights vs propensity (top 20 highlighted)")
save_diag_plot(p_scatter_abg, results_path("figs", "diag-wt-weights-vs-ps-abg.png"), width = 7, height = 5)
save_diag_plot(p_scatter_vbg, results_path("figs", "diag-wt-weights-vs-ps-vbg.png"), width = 7, height = 5)

```

3.9.4 Balance diagnostics

```

stopifnot(exists("target_balance_table"))

covars_use <- intersect(covars_ps, names(subset_data))

bal_target_abg <- target_balance_table(subset_data, "has_abg", subset_data$w_abg, covars_use, levels_ref) |>
  mutate(group = "ABG")
bal_target_vbg <- target_balance_table(subset_data, "has_vbg", subset_data$w_vbg, covars_use, levels_ref) |>
  mutate(group = "VBG")

bal_target <- bind_rows(bal_target_abg, bal_target_vbg)
write_csv_safely(bal_target, results_path("balance_table.csv"), row_names = FALSE)

bal_target_sum <- bal_target |>
  group_by(group, variable) |>
  summarise(
    max_abs_pre = max(abs(smd_pre), na.rm = TRUE),
    max_abs_smd = max(abs(smd), na.rm = TRUE),
    max_abs_zscore = max(abs(zscore), na.rm = TRUE)
  )

```

```

max_abs_post = max(abs(smd_post), na.rm = TRUE),
  .groups = "drop"
)
bal_worst <- bal_target_sum |>
  group_by(group) |>
  arrange(desc(max_abs_post)) |>
  ungroup()
write_csv_safely(bal_worst, results_path("balance_worst10.csv"), row_names = FALSE)
render_table_pdf_maybe(
  bal_worst,
  caption = "Target balance by covariate (sorted by max |SMD|)",
  file_stub = "balance_worst",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)

bal_plot_df <- bal_target |>
  mutate(label = ifelse(is.na(level), variable, paste0(variable, ":", level))) |>
  tidyr::pivot_longer(
    cols = c(smd_pre, smd_post),
    names_to = "stage",
    values_to = "smd"
  ) |>
  mutate(stage = recode(stage, smd_pre = "Pre", smd_post = "Post"))

p_bal_abg <- ggplot(filter(bal_plot_df, group == "ABG"),
                      aes(x = reorder(label, abs(smd)), y = smd, color = stage, shape = stage)) +
  geom_point(size = 1) +
  geom_hline(yintercept = c(-0.1, 0.1), linetype = 2, linewidth = 0.3) +
  geom_hline(yintercept = c(-0.05, 0.05), linetype = 3, linewidth = 0.3) +
  coord_flip() +
  labs(x = NULL, y = "Target SMD", title = "ABG target balance") +
  theme_minimal(base_size = 10)

p_bal_vbg <- ggplot(filter(bal_plot_df, group == "VBG"),
                      aes(x = reorder(label, abs(smd)), y = smd, color = stage, shape = stage)) +

```

```

geom_point(size = 1) +
  geom_hline(yintercept = c(-0.1, 0.1), linetype = 2, linewidth = 0.3) +
  geom_hline(yintercept = c(-0.05, 0.05), linetype = 3, linewidth = 0.3) +
  coord_flip() +
  labs(x = NULL, y = "Target SMD", title = "VBG target balance") +
  theme_minimal(base_size = 10)

save_diag_plot(p_bal_abg, results_path("figs", "diag-balance-loveplot-abg.png"), width = 9, height = 7)
save_diag_plot(p_bal_vbg, results_path("figs", "diag-balance-loveplot-vbg.png"), width = 9, height = 7)

# MI target balance summaries across imputations
stopifnot(exists("bal_imp_abg"), exists("bal_imp_vbg"))
bal_imp <- bind_rows(bal_imp_abg$bal_long, bal_imp_vbg$bal_long)
bal_imp_summary <- bind_rows(bal_imp_abg$bal_imp_summary, bal_imp_vbg$bal_imp_summary)
worst_rows <- bind_rows(bal_imp_abg$worst_rows_overall, bal_imp_vbg$worst_rows_overall)
worst_by_imp <- bind_rows(bal_imp_abg$worst_by_imp, bal_imp_vbg$worst_by_imp)
worst_terms_by_imp <- bind_rows(bal_imp_abg$worst_terms_by_imp, bal_imp_vbg$worst_terms_by_imp)

write_csv_safely(bal_imp, results_path("balance_target_by_imp.csv"), row_names = FALSE)
write_csv_safely(bal_imp_summary, results_path("balance_target_imp_summary.csv"), row_names = FALSE)
write_csv_safely(worst_rows, results_path("balance_target_worst_rows.csv"), row_names = FALSE)
render_table_pdf_maybe(
  worst_rows,
  caption = "Target SMD rows across imputations (sorted by |SMD|)",
  file_stub = "balance_target_worst_rows",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)
write_csv_safely(worst_by_imp, results_path("balance_max_smd_by_imp.csv"), row_names = FALSE)
write_csv_safely(worst_terms_by_imp, results_path("balance_worst_terms.csv"), row_names = FALSE)
if (any(bal_imp_summary$max_abs_post > 0.10, na.rm = TRUE)) {
  warning("Target balance: max |SMD| > 0.10 in at least one imputation.", call. = FALSE)
}
if (nrow(bal_imp_summary)) {
  dist_tbl <- bal_imp_summary |>
    dplyr::group_by(group) |>

```

```

dplyr::summarise(
  med = median(max_abs_post, na.rm = TRUE),
  iqr = IQR(max_abs_post, na.rm = TRUE),
  max = max(max_abs_post, na.rm = TRUE),
  .groups = "drop"
)
render_table_pdf_maybe(
  dist_tbl,
  caption = "Distribution of max |Target SMD| across imputations",
  file_stub = "balance_target_max_smd_distribution",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)
}
if (nrow(worst_terms_by_imp)) {
  worst_freq <- worst_terms_by_imp |>
    dplyr::count(group, term, sort = TRUE) |>
    dplyr::ungroup()
  render_table_pdf_maybe(
    worst_freq,
    caption = "Most frequent worst-balance terms",
    file_stub = "balance_worst_terms_freq",
    digits = 0,
    show = SHOW_LOW_VALUE_TABLES
)
}

n_abg <- sum(subset_data$has_abg == 1, na.rm = TRUE)
n_vbg <- sum(subset_data$has_vbg == 1, na.rm = TRUE)

stopifnot(exists("wt_sum"))
ess_abg <- wt_sum$ess[wt_sum$group == "ABG"]
ess_vbg <- wt_sum$ess[wt_sum$group == "VBG"]

if (is.finite(ess_abg) && is.finite(n_abg) && ess_abg < 0.2 * n_abg) {
  warning("ABG balance: ESS < 0.2 * n_abg (", round(ess_abg, 1), " vs ", n_abg, ".)", call. = FALSE)
}

```

```

}

if (is.finite(ess_vbg) && is.finite(n_vbg) && ess_vbg < 0.2 * n_vbg) {
  warning("VBG balance: ESS < 0.2 * n_vbg (", round(ess_vbg, 1), " vs ", n_vbg, ".)", call. = FALSE)
}

```

3.9.5 Outcome diagnostics

```

stopifnot(exists("abg_curves"), exists("vbg_curves"))
curve_abg <- abg_curves |>
  mutate(co2 = paco2) |>
  select(-paco2)
curve_vbg <- vbg_curves |>
  mutate(co2 = vbg_co2) |>
  select(-vbg_co2)
curve_all <- bind_rows(curve_abg, curve_vbg) |>
  mutate(outcome = factor(outcome,
                          levels = c("imv_proc", "niv_proc", "death_60d", "hypercap_resp_failure"),
                          labels = c("IMV", "NIV", "Death (60d)", "Hypercapnic RF")))
axis_mi_outcome <- compute_or_axis_spec(list(curve_abg, curve_vbg), lo_col = "LCL", hi_col = "UCL")

p_outcome <- ggplot(curve_all, aes(x = co2, y = OR, color = group, fill = group)) +
  geom_line(linewidth = 0.6) +
  geom_ribbon(aes(ymin = LCL, ymax = UCL), alpha = 0.15, color = NA) +
  geom_hline(yintercept = 1, linetype = "dashed", color = "grey40") +
  or_axis_scale(axis_mi_outcome) +
  facet_wrap(~ outcome, scales = "free_x") +
  labs(
    title = "MI-pooled IPSW spline odds ratios: ABG vs VBG",
    x = expression(CO[2]~"(mmHg)"),
    y = paste0("Odds ratio (ref: ABG ", ABG_CO2_REF, ", VBG ", VBG_CO2_REF, "; log scale)"),
    caption = paste0("Reference CO2: ABG ", ABG_CO2_REF, " mmHg; VBG ", VBG_CO2_REF, " mmHg")
  ) +
  theme_minimal(base_size = 10)

```

```
save_diag_plot(p_outcome, results_path("figs", "diag-outcome-or-vs-paco2.png"),
               width = 10, height = 8)
```

3.9.6 Diagnostics summary and audit

```
stopifnot(exists("bal_imp_summary"), exists("wt_sum"), exists("chain_diag_stats"))
target_abg_med <- median(bal_imp_summary$max_abs_post[bal_imp_summary$group == "ABG"], na.rm = TRUE)
target_abg_max <- max(bal_imp_summary$max_abs_post[bal_imp_summary$group == "ABG"], na.rm = TRUE)
target_vbg_med <- median(bal_imp_summary$max_abs_post[bal_imp_summary$group == "VBG"], na.rm = TRUE)
target_vbg_max <- max(bal_imp_summary$max_abs_post[bal_imp_summary$group == "VBG"], na.rm = TRUE)

runtime_proj_total_hrs <- NA_real_
if (is.finite(PILOT_FRAC) && PILOT_FRAC > 0 && PILOT_FRAC < 1) {
  runtime_log_curr <- runtime_log
  runtime_log_curr <- runtime_log_curr[runtime_log_curr$run_id == runtime_run_id, , drop = FALSE]
  scalable_steps <- c("mice_imputation", "mi_single_pass")
  scalable_secs <- runtime_log_curr |>
    dplyr::filter(step_name %in% scalable_steps) |>
    dplyr::summarise(total = sum(seconds, na.rm = TRUE)) |>
    dplyr::pull(total)
  if (length(scalable_secs) && is.finite(scalable_secs)) {
    runtime_proj_total_hrs <- scalable_secs / PILOT_FRAC / 3600
  }
}

get_wt_row <- function(group) {
  row <- wt_sum[wt_sum$group == group, , drop = FALSE]
  if (nrow(row) == 0L) {
    stop("Weight summary missing for group: ", group)
  }
  row[, c("ps_floor", "p01", "p05", "p95", "p99", "max", "sum_w", "ess",
         "top01_weight_share", "trunc_rate"), drop = FALSE]
}
```

```

wt_abg_row <- get_wt_row("ABG")
wt_vbg_row <- get_wt_row("VBG")

diag_summary <- bind_rows(
  tibble::tibble(
    block = "ABG weights",
    run_mode = RUN_MODE,
    m = M_IMP,
    maxit = MAXIT_MI,
    pilot_frac = PILOT_FRAC,
    stop_method = gbm_params$stop.method,
    ps_floor_quantile = ps_trunc_quantile,
    ps_floor = wt_abg_row$ps_floor,
    weight_p01 = wt_abg_row$p01,
    weight_p05 = wt_abg_row$p05,
    weight_p95 = wt_abg_row$p95,
    weight_p99 = wt_abg_row$p99,
    weight_max = wt_abg_row$max,
    sum_w = wt_abg_row$sum_w,
    ess = wt_abg_row$ess,
    top1_weight_share = wt_abg_row$top01_weight_share,
    trunc_rate = wt_abg_row$trunc_rate,
    target_max_smd_post_med = target_abg_med,
    target_max_smd_post_max = target_abg_max,
    runtime_proj_total_hrs = runtime_proj_total_hrs,
    chain_diag_n_imputed_vars = chain_diag_stats$n_imputed_vars,
    chain_diag_n_with_chainMean = chain_diag_stats$n_with_chainMean,
    chain_diag_n_with_drift_tail = chain_diag_stats$n_with_drift_tail,
    chain_diag_drift_tail_na_frac = chain_diag_stats$drift_tail_na_frac,
    chain_diag_tail_window_na_mean = chain_diag_stats$tail_window_na_mean
  ),
  tibble::tibble(
    block = "V ресурсов",
    run_mode = RUN_MODE,
    m = M_IMP,
    maxit = MAXIT_MI,
  )
)

```

```

pilot_frac = PILOT_FRAC,
stop_method = gbm_params$stop.method,
ps_floor_quantile = ps_trunc_quantile,
ps_floor = wt_vbg_row$ps_floor,
weight_p01 = wt_vbg_row$p01,
weight_p05 = wt_vbg_row$p05,
weight_p95 = wt_vbg_row$p95,
weight_p99 = wt_vbg_row$p99,
weight_max = wt_vbg_row$max,
sum_w = wt_vbg_row$sum_w,
ess = wt_vbg_row$ess,
top1_weight_share = wt_vbg_row$top01_weight_share,
trunc_rate = wt_vbg_row$trunc_rate,
target_max_smd_post_med = target_vbg_med,
target_max_smd_post_max = target_vbg_max,
runtime_proj_total_hrs = runtime_proj_total_hrs,
chain_diag_n_imputed_vars = chain_diag_stats$n_imputed_vars,
chain_diag_n_with_chainMean = chain_diag_stats$n_with_chainMean,
chain_diag_n_with_drift_tail = chain_diag_stats$n_with_drift_tail,
chain_diag_drift_tail_na_frac = chain_diag_stats$drift_tail_na_frac,
chain_diag_tail_window_na_mean = chain_diag_stats$tail_window_na_mean
),
tibble::tibble(
  block = "ABG outcomes",
  run_mode = RUN_MODE,
  m = M_IMP,
  maxit = MAXIT_MI,
  pilot_frac = PILOT_FRAC,
  stop_method = gbm_params$stop.method,
  ps_floor_quantile = ps_trunc_quantile,
  ps_floor = wt_abg_row$ps_floor,
  weight_p01 = wt_abg_row$p01,
  weight_p05 = wt_abg_row$p05,
  weight_p95 = wt_abg_row$p95,
  weight_p99 = wt_abg_row$p99,
  weight_max = wt_abg_row$max,

```

```

sum_w = wt_abg_row$sum_w,
ess = wt_abg_row$ess,
top1_weight_share = wt_abg_row$top01_weight_share,
trunc_rate = wt_abg_row$trunc_rate,
target_max_smd_post_med = target_abg_med,
target_max_smd_post_max = target_abg_max,
runtime_proj_total_hrs = runtime_proj_total_hrs,
chain_diag_n_imputed_vars = chain_diag_stats$n_imputed_vars,
chain_diag_n_with_chainMean = chain_diag_stats$n_with_chainMean,
chain_diag_n_with_drift_tail = chain_diag_stats$n_with_drift_tail,
chain_diag_drift_tail_na_frac = chain_diag_stats$drift_tail_na_frac,
chain_diag_tail_window_na_mean = chain_diag_stats$tail_window_na_mean
),
tibble::tibble(
  block = "V рг outcomes",
  run_mode = RUN_MODE,
  m = M_IMP,
  maxit = MAXIT_MI,
  pilot_frac = PILOT_FRAC,
  stop_method = gbm_params$stop.method,
  ps_floor_quantile = ps_trunc_quantile,
  ps_floor = wt_vbg_row$ps_floor,
  weight_p01 = wt_vbg_row$p01,
  weight_p05 = wt_vbg_row$p05,
  weight_p95 = wt_vbg_row$p95,
  weight_p99 = wt_vbg_row$p99,
  weight_max = wt_vbg_row$max,
  sum_w = wt_vbg_row$sum_w,
  ess = wt_vbg_row$ess,
  top1_weight_share = wt_vbg_row$top01_weight_share,
  trunc_rate = wt_vbg_row$trunc_rate,
  target_max_smd_post_med = target_vbg_med,
  target_max_smd_post_max = target_vbg_max,
  runtime_proj_total_hrs = runtime_proj_total_hrs,
  chain_diag_n_imputed_vars = chain_diag_stats$n_imputed_vars,
  chain_diag_n_with_chainMean = chain_diag_stats$n_with_chainMean,

```

```

chain_diag_n_with_drift_tail = chain_diag_stats$n_with_drift_tail,
chain_diag_drift_tail_na_frac = chain_diag_stats$drift_tail_na_frac,
chain_diag_tail_window_na_mean = chain_diag_stats$tail_window_na_mean
)
)

check_abg <- bal_imp_summary |>
  dplyr::filter(group == "ABG") |>
  dplyr::summarise(x = max(max_abs_post, na.rm = TRUE), .groups = "drop") |>
  dplyr::pull(x)
check_vbg <- bal_imp_summary |>
  dplyr::filter(group == "VBG") |>
  dplyr::summarise(x = max(max_abs_post, na.rm = TRUE), .groups = "drop") |>
  dplyr::pull(x)
diag_abg <- diag_summary$target_max_smd_post_max[diag_summary$block == "ABG weights"]
diag_vbg <- diag_summary$target_max_smd_post_max[diag_summary$block == "V рг weights"]
if (length(diag_abg) && is.finite(check_abg)) {
  stopifnot(isTRUE(all.equal(check_abg, diag_abg, tolerance = 1e-8)))
}
if (length(diag_vbg) && is.finite(check_vbg)) {
  stopifnot(isTRUE(all.equal(check_vbg, diag_vbg, tolerance = 1e-8)))
}
stopifnot(exists("covars_use_abg"), exists("covars_use_vbg"))
stopifnot(setequal(covars_use_abg, covars_use_vbg))

diag_summary_file <- results_path("diagnostics_summary.csv")
write_csv_safely(diag_summary, diag_summary_file, row_names = FALSE)

diag_summary_display <- diag_summary |>
  dplyr::select(
    block,
    m,
    ess,
    trunc_rate,
    target_max_smd_post_med,
    target_max_smd_post_max

```

```

) |>
dplyr::rename(
  `trunc` = trunc_rate,
  `med_max_smd` = target_max_smd_post_med,
  `max_max_smd` = target_max_smd_post_max
)
render_table_pdf_maybe(diag_summary_display,
  "Diagnostics summary (IPSW + MI)",
  "diagnostics_summary_display",
  wide = TRUE,
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES)

audit_lines <- c(
  "# Diagnostics Audit",
  "",
  "## A1. MI workflow",
  "- Impute -> single-pass per-imputation loop (weights, target balance, 3-level outcomes, spline outcomes) -> pool curves and co."
  "## A2. MI settings",
  paste0("- m = ", M_IMP, ", maxit = ", MAXIT_MI, ", seed = ", MI_SEED,
    "; treatments/outcomes/PaC02/VBG C02 are not imputed but are predictors (`mi-exec`)."),
  "## A3. Propensity weighting",
  "- Unimputed weighting uses WeightIt with method = \"gbm\" and balance-based stopping (stop.method = \"smd.max\"); no AUC-based",
  "- MI weighting uses logistic PS with restricted cubic splines (glm + rcs); no SHAP is computed for MI.",
  "## A4. One-sided IPSW + truncation",
  "- Weights are 1/ps for observed tests (ABG or VBG), truncated only for very small propensities (ps floor = 1st percentile), the",
  "## A5. Robust variance",
  "- Outcome models are survey::svyglm with svydesign (robust SEs), using spline(C02) + X adjustment; ABG and VBG are fit separately",
  "## A6. Pooling",
  "- mitools::MIcombine pools coefficients and robust vcov from svyglm; spline curves are pooled pointwise on the log-OR scale rather than the raw scale",
  "",
  "## Potential mismatches / risks",
  "- Target balance diagnostics compare weighted treated cohort to the full analytic sample (no treated-vs-control balance).",
  "- MI stability across m uses subsets of the first m imputations from the main mids object (not full re-imputation at each m).",
  "- Unweighted analyses remain earlier in the notebook for context; primary inference is based on weighted spline models."
)

```

```
audit_file <- results_path("diagnostics_audit.md")
write_diag_lines(audit_lines, audit_file)
```

3.9.7 Performance / runtime log

```
stopifnot(exists("mi_warn_log"), exists("mi_info_log"))
warn_df <- mi_warn_log
write_csv_safely(warn_df, results_path("mi_warnings_log.csv"), row_names = FALSE)
write_csv_safely(warn_df, results_path("warnings_log.csv"), row_names = FALSE)
write_csv_safely(mi_info_log, results_path("mi_info_log.csv"), row_names = FALSE)

if (nrow(warn_df)) {
  msg_counts <- warn_df |>
    dplyr::count(stage, component, message, sort = TRUE)
  render_table_pdf_maybe(
    msg_counts,
    caption = "Warning messages by stage/component",
    file_stub = "warnings_by_stage_component",
    digits = 0,
    show = SHOW_LOW_VALUE_TABLES
  )

  nonconv <- warn_df |>
    dplyr::filter(grepl("glm.fit: algorithm did not converge", message, fixed = TRUE))
  if (nrow(nonconv)) {
    nonconv_ctx <- nonconv |>
      dplyr::count(stage, component, analysis_variant, model_type, outcome, group, imputation, sort = TRUE)
    render_table_pdf_maybe(
      nonconv_ctx,
      caption = "Nonconvergence contexts",
      file_stub = "nonconvergence_contexts",
      digits = 0,
      show = SHOW_LOW_VALUE_TABLES
    )
  }
}
```

```

    }
} else {
  message("No captured warnings.")
}

write_csv_safely(plot_drop_log(), results_path("plot_drop_log.csv"), row_names = FALSE)

```

```

stopifnot(exists("mi_outcome_diag"))
if (nrow(mi_outcome_diag) == 0L) {
  stop("mi_outcome_diag is empty; outcome diagnostics were not captured.")
}
out_diag_file <- results_path("model_fit_diagnostics.csv")
write_csv_safely(mi_outcome_diag, out_diag_file)
write_csv_safely(mi_outcome_diag, results_path("mi_outcome_fit_diagnostics.csv"))

nonconv <- mi_outcome_diag |>
  dplyr::filter(isTRUE(nonconv_flag) | isFALSE(converged))
sep <- mi_outcome_diag |>
  dplyr::filter(isTRUE(sep_flag))

if (nrow(nonconv)) {
  nonconv_counts <- nonconv |>
    dplyr::count(analysis_variant, group, outcome, model_type, sort = TRUE)
  render_table_pdf_maybe(
    nonconv_counts,
    caption = "Nonconverged fits by variant/group/outcome",
    file_stub = "nonconverged_fits_by_variant",
    digits = 0,
    show = SHOW_LOW_VALUE_TABLES
  )

  worst_imps <- nonconv |>
    dplyr::count(imputation, sort = TRUE)
  render_table_pdf_maybe(
    worst_imps,
    caption = "Imputations with most nonconverged fits",
  )
}

```

```

file_stub = "nonconverged_imputations",
digits = 0,
show = SHOW_LOW_VALUE_TABLES
)
} else {
  message("No nonconverged outcome fits recorded.")
}

if (nrow(sep)) {
  sep_counts <- sep |>
    dplyr::count(analysis_variant, group, outcome, model_type, sort = TRUE)
  render_table_pdf_maybe(
    sep_counts,
    caption = "Separation flags by variant/group/outcome",
    file_stub = "separation_flags_by_variant",
    digits = 0,
    show = SHOW_LOW_VALUE_TABLES
  )
} else {
  message("No separation flags recorded.")
}

worst_phat <- mi_outcome_diag |>
  dplyr::filter(is.finite(min_phat) | is.finite(max_phat)) |>
  dplyr::mutate(extreme = pmin(min_phat, 1 - max_phat, na.rm = TRUE)) |>
  dplyr::arrange(extreme)

if (nrow(worst_phat)) {
  render_table_pdf_maybe(
    worst_phat,
    caption = "Worst fitted-probability extremes",
    file_stub = "worst_phat_extremes",
    digits = 3,
    show = SHOW_LOW_VALUE_TABLES
  )
}

```

```

diag_df <- mi_outcome_diag
diag_df$sep_warn <- grepl("fitted probabilities numerically 0 or 1",
                           diag_df$top_warning, fixed = TRUE) |
  grepl("separat", diag_df$top_warning, ignore.case = TRUE)
diag_df$phat_extreme <- (diag_df$min_phat < PROB_EPS) |
  (diag_df$max_phat > 1 - PROB_EPS)
diag_df$sep_flag <- dplyr::coalesce(as.logical(diag_df$sep_flag), FALSE)
diag_df$nonconv_flag <- dplyr::coalesce(as.logical(diag_df$nonconv_flag), FALSE) |
  dplyr::coalesce(!as.logical(diag_df$converged), FALSE)

mi_variants <- intersect(c("mi_ipw", "weighted_imputed"), unique(diag_df$analysis_variant))
if (!length(mi_variants)) mi_variants <- unique(diag_df$analysis_variant)

issue_summary <- diag_df |>
  dplyr::filter(analysis_variant %in% mi_variants) |>
  dplyr::group_by(group, outcome, component, analysis_variant) |>
  dplyr::summarise(
    n_fits = dplyr::n(),
    n_nonconv = sum(nonconv_flag %in% TRUE, na.rm = TRUE),
    n_sep_warn = sum(sep_warn %in% TRUE, na.rm = TRUE),
    n_phat_extreme = sum(phat_extreme %in% TRUE, na.rm = TRUE),
    n_sep_flag = sum(sep_flag %in% TRUE, na.rm = TRUE),
    .groups = "drop"
  )
write_csv_safely(issue_summary, results_path("mi_fit_issue_summary.csv"))

# Top warning messages by stage/component
if (nrow(mi_warn_log)) {
  warn_top <- mi_warn_log |>
    dplyr::count(stage, component, analysis_variant, model_type, message, sort = TRUE)
  render_table_pdf_maybe(
    warn_top,
    caption = "Warnings by stage/component",
    file_stub = "warnings_by_stage_component_full",
    digits = 0,
    show = SHOW_LOW_VALUE_TABLES
  )
}

```

```

    )
}

# Top MICE loggedEvents drivers
stopifnot(exists("log_events_summary"))
if (nrow(log_events_summary)) {
  render_table_pdf_maybe(
    log_events_summary,
    caption = "MICE loggedEvents drivers",
    file_stub = "mice_logged_events_drivers",
    digits = 0,
    show = SHOW_LOW_VALUE_TABLES
  )
}

# Replay debug mode (off by default)
MI_DEBUG_REPLAY <- FALSE
if (MI_DEBUG_REPLAY) {
  stopifnot(file.exists(results_path("model_fit_diagnostics.csv")))
  diag_df <- read.csv(results_path("model_fit_diagnostics.csv"), stringsAsFactors = FALSE)
  bad <- diag_df[isFALSE(diag_df$converged), , drop = FALSE]
  if (nrow(bad)) {
    row <- bad[1, , drop = FALSE]
    message("Replaying: group=", row$group, ", outcome=", row$outcome,
            ", model_type=", row$model_type, ", imputation=", row$imputation)
    options(warn = 1)
    stopifnot(exists("imp"))
    get_imp <- function(i, imp_obj = imp) {
      normalize_types(mice::complete(imp_obj, action = i), levels_ref)
    }
    d_dbg <- get_imp(row$imputation)
    if (row$group == "ABG") {
      d_dbg <- d_dbg[d_dbg$has_abg == 1 & is.finite(d_dbg$paco2), , drop = FALSE]
      w_dbg <- mi_logistic_ps_abg_list[[row$imputation]]$weights[d_dbg$has_abg == 1 & is.finite(d_dbg$paco2)]
      if (row$model_type == "spline") {
        d_dbg <- d_dbg[, c(row$outcome, "has_abg", "paco2", adj_core), drop = FALSE]
      }
    }
  }
}

```

```

    fit_spline_imp(d_dbg, w_dbg, row$outcome, "paco2", "has_abg",
                    adj_vars = adj_core, spline_df = SPLINE_DF, spline_basis = SPLINE_BASIS,
                    grid_df = NULL, ref_idx = NULL, imp_index = row$imputation)
} else {
  d_dbg$co2_cat <- make_co2_cat3(d_dbg$paco2, ABG_CO2_LOW, ABG_CO2_HIGH)
  d_dbg$co2_cat <- stats::relevel(base::droplevels(d_dbg$co2_cat), ref = "Normal")
  d_dbg[[row$outcome]] <- to01(d_dbg[[row$outcome]])
  des <- survey::svydesign(ids = ~1, weights = ~w_dbg, data = d_dbg)
  fml <- stats::reformulate(c("co2_cat", adj_core), response = row$outcome)
  survey::svyglm(fml, design = des, family = quasibinomial(),
                 control = stats::glm.control(maxit = 50))
}
} else if (row$group == "VBG") {
  d_dbg <- d_dbg[d_dbg$has_vbg == 1 & is.finite(d_dbg$vbg_co2), , drop = FALSE]
  w_dbg <- mi_logistic_ps_vbg_list[[row$imputation]]$weights[d_dbg$has_vbg == 1 & is.finite(d_dbg$vbg_co2)]
  if (row$model_type == "spline") {
    d_dbg <- d_dbg[, c(row$outcome, "has_vbg", "vbg_co2", adj_core), drop = FALSE]
    fit_spline_imp(d_dbg, w_dbg, row$outcome, "vbg_co2", "has_vbg",
                   adj_vars = adj_core, spline_df = SPLINE_DF, spline_basis = SPLINE_BASIS,
                   grid_df = NULL, ref_idx = NULL, imp_index = row$imputation)
  } else {
    d_dbg$co2_cat <- make_co2_cat3(d_dbg$vbg_co2, VBG_CO2_LOW, VBG_CO2_HIGH)
    d_dbg$co2_cat <- stats::relevel(base::droplevels(d_dbg$co2_cat), ref = "Normal")
    d_dbg[[row$outcome]] <- to01(d_dbg[[row$outcome]])
    des <- survey::svydesign(ids = ~1, weights = ~w_dbg, data = d_dbg)
    fml <- stats::reformulate(c("co2_cat", adj_core), response = row$outcome)
    survey::svyglm(fml, design = des, family = quasibinomial(),
                   control = stats::glm.control(maxit = 50))
  }
}
options(warn = 0)
} else {
  message("MI_DEBUG_REPLY=TRUE but no nonconverged rows found.")
}
}

```

3.9.8 Performance / runtime log

```
stopifnot(exists("runtime_log"), nrow(runtime_log) > 0)
runtime_log_curr <- runtime_log
runtime_log_curr <- runtime_log_curr[runtime_log_curr$run_id == runtime_run_id, , drop = FALSE]
runtime_log_file <- results_path("runtime_log.csv")
write_csv_safely(runtime_log_curr, runtime_log_file, row_names = FALSE)
top_steps <- runtime_log_curr |>
  arrange(desc(seconds))
top15_file <- results_path("runtime_summary_top15.csv")
write_csv_safely(top_steps, top15_file, row_names = FALSE)
render_table_pdf_maybe(
  top_steps,
  caption = "Runtime steps (seconds)",
  file_stub = "runtime_steps",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)

total_seconds <- sum(runtime_log_curr$seconds, na.rm = TRUE)
runtime_summary <- bind_rows(
  tibble::tibble(step_name = "TOTAL", seconds = total_seconds),
  runtime_log_curr |>
    arrange(desc(seconds)) |>
    select(step_name, seconds)
)
runtime_summary_file <- results_path("runtime_summary.csv")
write_csv_safely(runtime_summary, runtime_summary_file, row_names = FALSE)
render_table_pdf_maybe(
  runtime_summary,
  caption = "Runtime summary (total + all steps)",
  file_stub = "runtime_summary",
  digits = 3,
  show = SHOW_LOW_VALUE_TABLES
)
```

```

# GBM preflight diagnostics (CSV only)
write_csv_safely(memory_snapshots, results_path("memory_snapshots.csv"), row_names = FALSE)
write_csv_safely(gbm_preflight_design_dims, results_path("gbm_preflight_design_dims.csv"), row_names = FALSE)
write_csv_safely(gbm_preflight_warnings, results_path("gbm_preflight_warnings.csv"), row_names = FALSE)

if (is.finite(PILOT_FRAC) && PILOT_FRAC > 0 && PILOT_FRAC < 1) {
  scalable_steps <- c("mice_imputation", "mi_single_pass")
  proj <- runtime_log_curr |>
    filter(step_name %in% scalable_steps) |>
    mutate(projected_seconds = seconds / PILOT_FRAC,
           projected_hours = projected_seconds / 3600)
  proj_total <- sum(proj$projected_hours, na.rm = TRUE)
  render_table_pdf_maybe(
    proj |> select(step_name, seconds, projected_hours),
    caption = paste0("Runtime projection (scalable steps; pilot_frac = ", PILOT_FRAC, ")"),
    file_stub = "runtime_projection",
    digits = 3,
    show = SHOW_LOW_VALUE_TABLES
  )
  if (is.finite(proj_total) && proj_total > 10) {
    warning("Projected full-run time exceeds 10 hours (", round(proj_total, 1), "h).",
           call. = FALSE)
  }
} else {
  message("Runtime projection skipped because PILOT_FRAC == 1 (full run).")
}

stopifnot(exists("get_imp_stats"))
get_imp_df <- data.frame(
  count = get_imp_stats$count,
  seconds = get_imp_stats$seconds,
  seconds_per_call = if (get_imp_stats$count > 0) get_imp_stats$seconds / get_imp_stats$count else NA_real_,
  run_id = runtime_run_id,
  run_mode = RUN_MODE,
  n_subset = nrow(subset_data),

```

```

    stringsAsFactors = FALSE
)
write_csv_safely(get_imp_df, results_path("get_imp_usage.csv"), row.names = FALSE)

expected_diag <- c(
  "runtime_log.csv", "runtime_summary.csv", "runtime_summary_top15.csv",
  "warnings_log.csv", "mi_warnings_log.csv", "mi_info_log.csv",
  "diagnostics_summary.csv", "diagnostics_missingness.csv",
  "diagnostics_missingness-by-strata.csv",
  "balance_target_imp_summary.csv", "balance_target_by_imp.csv",
  "balance_target_worst_rows.csv", "balance_max_smd_by_imp.csv",
  "balance_worst_terms.csv", "balance_worst10.csv", "balance_table.csv",
  "weight_summary.csv", "ps_overlap_summary.csv",
  "model_fit_diagnostics.csv", "mi_outcome_fit_diagnostics.csv",
  "mi_fit_issue_summary.csv", "mi_m_stability.csv", "mi_maxit_sensitivity.csv",
  "mi_obs_vs_imp_summary.csv", "mi_spline_curve_abg.csv",
  "mi_spline_curve_vbg.csv", "mi_spline_coef_abg.csv",
  "mi_spline_coef_vbg.csv", "diag-ps-shap-stability.csv",
  "mice_logged_events_raw.csv", "mice_logged_events_summary.csv",
  "mice_pred_width_preflight.csv", "mice_chain_diagnostics.csv",
  "mice_batches_log.csv", "missingness-by-strata.csv",
  "missingness-drivers.csv", "missingness-pattern.csv", "plot_drop_log.csv",
  "mice_smoketest.log"
)
missing_files <- expected_diag[!file.exists(results_path(expected_diag))]
stopifnot(length(missing_files) == 0)

run_id_mismatch <- character()
for (f in expected_diag) {
  path <- results_path(f)
  if (grepl("\\\\.csv$", f)) {
    df <- tryCatch(read.csv(path, nrows = 1), error = function(e) NULL)
    stopifnot(!is.null(df))
    stopifnot("run_id" %in% names(df))
    if (nrow(df) > 0 && !identical(as.character(df$run_id[1]), diag_run_id)) {
      run_id_mismatch <- c(run_id_mismatch, f)
    }
  }
}

```

```

    }
  }
}

if (length(missing_files) || length(run_id_mismatch)) {
  msg <- paste0(
    "Diagnostics completeness check failed: missing files [",
    paste(missing_files, collapse = ", "),
    "] ; run_id mismatch [",
    paste(run_id_mismatch, collapse = ", "),
    "] ."
  )
  stop(msg)
}

```

3.10 16) Save, export, and session info

```

audit_script <- here::here("R", "diagnostics_audit.R")
audit_md <- results_path("diagnostics_audit.md")
stopifnot(file.exists(audit_script))

audit_out <- tryCatch(
  system2(
    "Rscript",
    args = c(shQuote(audit_script)),
    env = c(paste0("DIAG_RESULTS_DIR=", results_dir)),
    stdout = TRUE,
    stderr = TRUE
  ),
  error = function(e) e
)
if (inherits(audit_out, "error")) {
  warning("diagnostics_audit.R failed: ", conditionMessage(audit_out), call. = FALSE)
} else {

```

```

status <- attr(audit_out, "status")
if (!is.null(status) && status != 0) {
  warning("diagnostics_audit.R exited with status ", status, ".", call. = FALSE)
}
}

audit_issues <- results_path("diagnostics_audit_issues.csv")
if (file.exists(audit_issues)) {
  issues_df <- read.csv(audit_issues)
  issues_df <- issues_df |>
    dplyr::arrange(factor(severity, levels = c("blocker", "high", "medium", "low")))
  render_table_pdf_maybe(
    issues_df,
    caption = "Diagnostics audit issues (see Results/diagnostics_audit.md for details)",
    file_stub = "diagnostics_audit_issues",
    digits = 2,
    show = SHOW_LOW_VALUE_TABLES
  )
} else {
  cat("Diagnostics audit summary not available.\n")
}

stopifnot(exists("abg_curves"), exists("vbg_curves"), exists("abg_coefs"), exists("vbg_coefs"))
saveRDS(
  list(
    abg_curves = abg_curves,
    vbg_curves = vbg_curves,
    abg_coefs = abg_coefs,
    vbg_coefs = vbg_coefs
  ),
  mi_pooled_file
)

writeLines(capture.output(sessionInfo()), results_path("sessionInfo.txt"))

```

```
cat("Software: R ", as.character(getRversion()),  
    "; key packages: mice, WeightIt, cobalt, survey, rms.\n")
```

Software: R 4.5.2 ; key packages: mice, WeightIt, cobalt, survey, rms.

```
pdf_input <- knitr::current_input()  
if (is.null(pdf_input) || !nzchar(pdf_input)) {  
  pdf_input <- "ABG-VBG analysis 2025-12-11.qmd"  
}  
pdf_file <- results_path(paste0(tools::file_path_sans_ext(basename(pdf_input)), ".pdf"))  
scan_out <- results_path("pdf_hygiene_scan.csv")  
pdftotext_bin <- Sys.which("pdftotext")  
if (!nzchar(pdftotext_bin) || !file.exists(pdf_file)) {  
  write_csv_safely(data.frame(line = character()), scan_out, row_names = FALSE)  
} else {  
  tmp_txt <- tempfile(fileext = ".txt")  
  system2(pdftotext_bin, c(pdf_file, tmp_txt))  
  txt <- readLines(tmp_txt, warn = FALSE)  
  bad <- txt[grep1("/Users/[A-Z]:\\\\\\\\\\\\\\", txt)]  
  scan_df <- data.frame(line = bad, stringsAsFactors = FALSE)  
  write_csv_safely(scan_df, scan_out, row_names = FALSE)  
  if (RUN_MODE == "full" && nrow(scan_df) > 0) {  
    stop("PDF hygiene scan detected absolute paths; see ", scan_out)  
  }  
}
```