Package 'drMAIC'

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Language en-GB

Title Doubly Robust Matching-Adjusted Indirect Comparison for HTA

Version 0.1.0

Description Implements Doubly Robust Matching-Adjusted Indirect Comparison (DR-MAIC) for population-adjusted indirect treatment comparisons in health technology appraisal (HTA). The package provides: (1) standard MAIC via entropy balancing / exponential tilting; (2) augmented/doubly robust MAIC combining inverse probability weighting with outcome regression; (3) comprehensive covariate balance diagnostics including standardised mean differences, Love plots, and effective sample size; (4) sensitivity analyses including E-values, weight trimming, and variable exclusion analyses; (5) bootstrap confidence intervals; and (6) submission-ready outputs aligned with NICE Decision Support Unit Technical Support Document 18, Cochrane Handbook guidance on indirect comparisons, and ISPOR best practice guidelines. Supports binary (risk difference, risk ratio, odds ratio) and time-to-event (hazard ratio) outcomes.

License GPL (>= 3)

Encoding UTF-8

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Depends R (>= 4.0.0)

Imports stats, survival, boot, ggplot2

Suggests knitr, rmarkdown, testthat (>= 3.0.0)

VignetteBuilder knitr

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LazyData true

URL https://github.com/Anupama-Singh01/drMAIC

BugReports https://github.com/Anupama-Singh01/drMAIC/issues

NeedsCompilation no

Author Anupama Singh [aut, cre]

Maintainer Anupama Singh <anupama.singh@pharmacoevidence.com>

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Contents

`bootstrap_ci` *Bootstrap Confidence Intervals for DR-MAIC*

Description

Computes non-parametric bootstrap confidence intervals for the DR-MAIC indirect treatment comparison estimate. Three interval types are available: percentile, basic (Hall), and bias-corrected and accelerated (BCa).

Usage

```
bootstrap_ci(
  dr_maic_result,
  R = 1000L,
  ci_type = c("bca", "perc", "norm"),
  alpha = 0.05,
  seed = NULL,
  parallel = FALSE,
  verbose = TRUE
)
```

Arguments

`dr_maic_result`	An object of class `"dr_maic"` from `dr_maic()`.
`R`	Integer; number of bootstrap replicates. Default 1000. Use R >= 2000 for stable BCa intervals.
`ci_type`	Character; bootstrap CI type: `"bca"` (default), `"perc"`, or `"norm"`.
`alpha`	Numeric; significance level. Default 0.05.
`seed`	Integer; random seed for reproducibility.

parallel	Logical; use parallel computation if parallel package is available. Default FALSE.
verbose	Logical; show progress. Default TRUE.

Details

Bootstrap procedure: The IPD are resampled with replacement B times. For each bootstrap replicate:

1. MAIC weights are recomputed on the resampled IPD.
2. The DR-MAIC estimator is evaluated.
3. The ITC is computed.

Bootstrap resampling captures variance from both the weight estimation and outcome regression steps, providing honest uncertainty quantification for the doubly robust estimator.

Bootstrap CI methods (per Efron and Tibshirani, 1993):

- **Percentile**: uses the 2.5th and 97.5th percentiles of the bootstrap distribution.
- **BCa** (Bias-Corrected and Accelerated): adjusts for bias and skewness. Recommended method per ISPOR guidance.
- **Normal**: uses bootstrap standard error with normal quantiles.

NICE guidance alignment: NICE DSU TSD 18 recommends bootstrap CIs for MAIC to capture parameter uncertainty from the weight estimation step.

Value

A list of class "maic_bootstrap" containing:

ci_maic Bootstrap CI for standard MAIC ITC.

ci_stc Bootstrap CI for STC ITC.

ci_dr Bootstrap CI for DR-MAIC ITC.

se_boot_dr Bootstrap SE for DR-MAIC.

boot_distribution Data frame of bootstrap replicate estimates.

boot_plot ggplot2 bootstrap distribution plot.

ci_type CI type used.

R Number of bootstrap replicates.

References

Efron B, Tibshirani RJ. (1993). *An Introduction to the Bootstrap.* Chapman and Hall/CRC.

Phillippo DM, et al. (2016). *NICE DSU TSD 18*.

Examples

```
data(nsclc_ipd); data(nsclc_agd)
w   <- compute_weights(nsclc_ipd,
         c(age = nsclc_agd$mean_age, ecog = nsclc_agd$prop_ecog1,
           smoker = nsclc_agd$prop_smoker), c("age","ecog","smoker"))
res <- dr_maic(w, "response", "binary",
               comparator_estimate = nsclc_agd$response_rate,
               comparator_se       = nsclc_agd$response_se)
boot_res <- bootstrap_ci(res, R = 500, seed = 42)
print(boot_res)
boot_res$boot_plot
```

`check_assumptions` *Check Assumptions for DR-MAIC*

Description

Runs a structured check of the key assumptions required for valid DR-MAIC inference, aligned with NICE DSU TSD 18 and Cochrane guidance.

Usage

```
check_assumptions(
  maic_weights,
  dr_maic_result = NULL,
  ess_threshold = 30,
  smd_threshold = 0.1
)
```

Arguments

`maic_weights`	A `maic_weights` object from `compute_weights()`.
`dr_maic_result`	Optional `dr_maic` object for outcome model checks.
`ess_threshold`	Minimum acceptable ESS% threshold. Default 30.
`smd_threshold`	Maximum acceptable |SMD| after weighting. Default 0.1.

Value

A data frame summarising assumption check results (invisibly). Prints a structured checklist to the console.

compute_weights *Compute MAIC Weights via Entropy Balancing*

Description

Estimates matching-adjusted indirect comparison (MAIC) weights by solving the entropy balancing / exponential tilting problem. Weights are chosen so that the weighted moments of the IPD covariates match the aggregate data (AgD) target moments. The method follows the approach described in Signorovitch et al. (2010) and formalised by Phillippo et al. (2016) and NICE DSU TSD 18.

Usage

```
compute_weights(
  ipd,
  target_moments,
  match_vars = NULL,
  match_var_types = NULL,
  optimizer = "BFGS",
  maxit = 10000L,
  verbose = TRUE
)
```

Arguments

ipd	A data frame of individual patient data from the index trial. Must contain the covariates listed in match_vars.
target_moments	A named numeric vector or list of target aggregate statistics (means, and optionally variances/proportions) from the comparator study AgD. Names must match column names in ipd.
match_vars	Character vector of covariate names to match. If NULL, uses all names in target_moments.
match_var_types	Named character vector specifying the type of each matching variable: "mean" (continuous, match on mean), "mean_sd" (continuous, match on mean AND standard deviation via second moment), or "proportion" (binary, match on proportion). Defaults to "mean" for all variables.
optimizer	Optimisation algorithm passed to stats::optim(). Default "BFGS". Use "Nelder-Mead" if BFGS fails to converge.
maxit	Maximum iterations for optimiser. Default 10000.
verbose	Logical; print convergence information. Default TRUE.

Details

Statistical method: Given individual patient data (IPD) from study A (index trial) with covariates $X_i, i = 1, \ldots, n$ and target aggregate statistics $\bar{X}_{target}$ from study B (comparator), MAIC weights are defined by exponential tilting:

$$w_i = \exp(X_i^\top \hat{\lambda})$$

where $\hat{\lambda}$ solves the moment-matching equations:

$$\sum_{i=1}^{n} w_i X_i = n \bar{X}_{target}$$

Equivalently, $\hat{\lambda}$ minimises the convex objective:

$$Q(\lambda) = \sum_{i=1}^{n} \exp(X_i^\top \lambda) - n \lambda^\top \bar{X}_{target}$$

Weights are returned in two forms: raw (unnormalized, sum to n_eff) and normalized (sum to 1). The normalized weights are used for estimation.

NICE alignment: The weight computation follows NICE DSU TSD 18 (Phillippo et al., 2016, 2020) guidance on MAIC for population-adjusted ITC.

Value

A list of class `"maic_weights"` containing:

`weights` Numeric vector of normalized weights (sum to 1), length n.

`weights_raw` Numeric vector of unnormalized weights.

`lambda` Estimated Lagrange multiplier vector $\hat{\lambda}$.

`ess` Effective sample size.

`ess_pct` ESS as percentage of original n.

`n_original` Original sample size.

`convergence` Convergence code from `stats::optim()` (0 = success).

`balance_before` SMD before weighting (named vector).

`balance_after` SMD after weighting (named vector).

`match_vars` Character vector of matched variables.

`target_moments` Target moments used for matching.

`ipd` Original IPD data frame (stored for downstream functions).

References

Signorovitch JE, Wu EQ, Yu AP, et al. (2010). Comparative effectiveness without head-to-head trials: a method for matching-adjusted indirect comparisons applied to psoriasis treatment with adalimumab or etanercept. *PharmacoEconomics*, 28(10), 935-945.

Phillippo DM, Ades AE, Dias S, et al. (2016). Methods for population-adjusted indirect comparisons in submissions to NICE. *NICE Decision Support Unit TSD 18*.

Phillippo DM, Ades AE, Dias S, et al. (2020). Population adjustment methods for indirect comparisons: A review of national institute for health and care excellence technology appraisals. *International Journal of Technology Assessment in Health Care*, 36(5), 454-461.

Examples

```
# Load example NSCLC dataset
data(nsclc_ipd)
data(nsclc_agd)

# Target moments from AgD comparator trial
target <- c(
  age     = nsclc_agd$mean_age,
  ecog    = nsclc_agd$prop_ecog1,
  smoker  = nsclc_agd$prop_smoker
)

# Compute MAIC weights
w <- compute_weights(
  ipd            = nsclc_ipd,
  target_moments = target,
  match_vars     = c("age", "ecog", "smoker")
)
print(w)
summary(w)
```

`dr_maic` *Doubly Robust MAIC Estimation*

Description

Estimates a population-adjusted treatment effect using the doubly robust (augmented) MAIC estimator. This combines inverse probability weighting (MAIC) with outcome regression (parametric g-computation / STC) into a single estimator that is consistent if *either* the weight model *or* the outcome model is correctly specified.

Usage

```
dr_maic(
  maic_weights,
  outcome_var,
  outcome_type = c("binary", "continuous", "tte"),
  time_var = NULL,
  comparator_estimate,
  comparator_se = NULL,
  effect_measure = NULL,
  outcome_model_formula = NULL,
  outcome_model_family = NULL,
  additional_covariates = NULL,
  alpha = 0.05
)
```

Arguments

`maic_weights`	An object of class `"maic_weights"` from `compute_weights()`.
`outcome_var`	Character string; name of the outcome column in the IPD.
`outcome_type`	Character string; type of outcome: `"binary"` (default), `"continuous"`, or `"tte"` (time-to-event).
`time_var`	Character string; for `outcome_type = "tte"`, the name of the time variable in the IPD.
`comparator_estimate`	Numeric; the outcome estimate from the comparator (AgD) study B. For binary outcomes, a proportion; for TTE, a median survival or log-HR depending on `effect_measure`.
`comparator_se`	Numeric; standard error of `comparator_estimate`. Used for variance estimation of the ITC.
`effect_measure`	Character string; scale for the treatment effect: `"RD"` (risk difference), `"RR"` (risk ratio), `"OR"` (odds ratio), `"HR"` (hazard ratio). Default is `"OR"` for binary, `"HR"` for TTE, `"MD"` (mean difference) for continuous.
`outcome_model_formula`	A formula for the outcome regression model. If `NULL` (default), uses all matched covariates as predictors.
`outcome_model_family`	GLM family for outcome model. Default `binomial()` for binary outcomes, `gaussian()` for continuous.
`additional_covariates`	Character vector of additional prognostic covariates to include in the outcome model (beyond matched variables). These improve efficiency but are not required for the DR property.
`alpha`	Significance level for confidence intervals. Default 0.05.

Details

Statistical framework:

Let study A (index) provide IPD with outcome Y_i and covariates X_i, and study B (comparator) provide AgD with outcome summary statistic $\hat{\theta}_B$. MAIC weights ω_i target the covariate distribution of population B.

Three estimators are implemented:

(1) Standard MAIC (IPW):

$$\hat{\theta}_{MAIC} = \frac{\sum_i \omega_i Y_i}{\sum_i \omega_i}$$

(2) Standardised Treatment Comparison / g-computation (STC):

$$\hat{\theta}_{STC} = \frac{\sum_i \omega_i \hat{m}(X_i)}{\sum_i \omega_i}$$

where $\hat{m}(X_i) = \hat{E}[Y \mid X_i]$ from an outcome regression model fitted on the IPD.

(3) Doubly Robust / Augmented estimator (DR-MAIC):

$$\hat{\theta}_{DR} = \hat{\theta}_{STC} + \frac{\sum_i \omega_i (Y_i - \hat{m}(X_i))}{\sum_i \omega_i}$$

The DR estimator equals the MAIC estimator plus a bias-correction term based on outcome model residuals, weighted towards population B. It is consistent if either (i) the weights ω_i correctly balance covariates (outcome model may be misspecified), or (ii) the outcome model $\hat{m}$ is correctly specified (weights may be misspecified) — the double robustness property (Lunceford and Davidian, 2004; Tan, 2010; Remiro-Azocar, 2022).

The indirect treatment comparison is then:

$$\hat{\Delta} = \hat{\theta}_{DR,A} - \hat{\theta}_B$$

For binary outcomes the comparison can be on the risk difference, log-risk ratio, or log-odds ratio scale. For time-to-event outcomes, the log-hazard ratio is estimated via a weighted Cox model (or Weibull regression).

Alignment with guidelines:

- NICE DSU TSD 18 (Phillippo et al., 2016; 2020)
- Cochrane Handbook Chapter 23 (Dias et al.)
- ISPOR Task Force on Indirect Treatment Comparisons
- Remiro-Azócar et al. (2022) *Statistics in Medicine*

Value

A list of class `"dr_maic"` containing:

`theta_maic` MAIC (IPW) estimate in population B.

`theta_stc` STC (g-computation) estimate in population B.

`theta_dr` Doubly robust estimate in population B.

`theta_comparator` Comparator estimate (from AgD).

`itc_maic` Indirect treatment comparison (MAIC): A vs B effect.

`itc_stc` Indirect treatment comparison (STC): A vs B effect.

`itc_dr` Indirect treatment comparison (DR): A vs B effect.

`effect_measure` Effect measure used.

`outcome_model` Fitted outcome model object.

`residuals` Outcome model residuals (Y_i - m_hat_i).

`dr_correction` The augmentation term (STC correction).

`maic_weights` The `maic_weights` object used.

`n` Original sample size.

`ess` Effective sample size.

References

Remiro-Azócar A, Heath A, Baio G. (2022). Methods for population-adjusted indirect comparisons in health technology appraisal. *Medical Decision Making*, 42(3), 386-401.

Lunceford JK, Davidian M. (2004). Stratification and weighting via the propensity score in estimation of causal treatment effects. *Statistics in Medicine*, 23(19), 2937-2960.

Tan Z. (2010). Bounded, efficient and doubly robust estimation with inverse weighting. *Biometrika*, 97(3), 661-682.

Phillippo DM, Ades AE, Dias S, et al. (2016). *NICE DSU Technical Support Document 18: Methods for population-adjusted indirect comparisons in submissions to NICE*.

Examples

```
data(nsclc_ipd)
data(nsclc_agd)

# Step 1: Compute weights
w <- compute_weights(
  ipd            = nsclc_ipd,
  target_moments = c(age = nsclc_agd$mean_age,
                     ecog   = nsclc_agd$prop_ecog1,
                     smoker = nsclc_agd$prop_smoker),
  match_vars     = c("age", "ecog", "smoker")
)

# Step 2: DR-MAIC for binary outcome
res <- dr_maic(
  maic_weights         = w,
  outcome_var          = "response",
  outcome_type         = "binary",
  comparator_estimate  = nsclc_agd$response_rate,
  comparator_se        = nsclc_agd$response_se,
  effect_measure       = "OR"
)
print(res)
summary(res)
```

`maic_diagnostics` *Covariate Balance Diagnostics for MAIC*

Description

Produces covariate balance diagnostics following NICE DSU TSD 18 and Cochrane guidance. Includes: standardised mean differences (SMD) before and after weighting, Love plot, weight distribution visualisations, and effective sample size reporting.

Usage

```
maic_diagnostics(
  maic_weights,
  plot_type = "all",
  threshold = 0.1,
  title_suffix = NULL
)
```

Arguments

maic_weights	An object of class "maic_weights" from compute_weights().
plot_type	Character vector specifying which plots to produce: "love" (Love plot of SMDs), "weights" (weight distribution), "balance" (balance table), "all" (default — produces all).
threshold	Numeric; SMD threshold line on Love plot. Default 0.1 (standard threshold used by NICE and Austin and Stuart, 2015).
title_suffix	Optional character string appended to plot titles.

Details

Standardised Mean Difference (SMD):

$$SMD_j = \frac{\bar{X}_{j,weighted} - \mu_{j,target}}{s_j}$$

where s_j is the unweighted standard deviation of covariate j in the IPD (per NICE DSU TSD 18 recommendation). |SMD| < 0.1 indicates good balance.

Effective Sample Size (ESS):

$$ESS = \frac{(\sum_i w_i)^2}{\sum_i w_i^2}$$

ESS should be interpreted relative to the original n. ESS < 30% of n is a warning threshold per NICE guidance.

Value

A list of class "maic_diagnostics" containing:

balance_table Data frame with SMD before/after weighting.

ess Effective sample size.

ess_pct ESS as % of original n.

n_balanced Number of variables with |SMD| < threshold after weighting.

love_plot ggplot2 Love plot object.

weight_plot ggplot2 weight distribution plot.

all_balanced Logical; TRUE if all |SMD| < threshold after weighting.

References

Austin PC, Stuart EA. (2015). Moving towards best practice when using inverse probability of treatment weighting (IPTW) using the propensity score to estimate causal treatment effects in observational studies. *Statistics in Medicine*, 34(28), 3661-3679.

Phillippo DM, Ades AE, Dias S, et al. (2016). *NICE DSU TSD 18*.

Examples

```
data(nsclc_ipd)
data(nsclc_agd)

w <- compute_weights(
  ipd            = nsclc_ipd,
  target_moments = c(age = nsclc_agd$mean_age,
                     ecog = nsclc_agd$prop_ecog1,
                     smoker = nsclc_agd$prop_smoker),
  match_vars     = c("age", "ecog", "smoker")
)

diag <- maic_diagnostics(w)
print(diag)
diag$love_plot
diag$weight_plot
```

---

nice_report *Generate NICE/HTA Submission-Ready Report*

Description

Produces a structured, submission-ready report of the DR-MAIC analysis aligned with NICE DSU TSD 18, Cochrane Handbook Chapter 23, and ISPOR best practice guidance for population-adjusted indirect treatment comparisons.

Usage

```
nice_report(
  dr_maic_result,
  bootstrap_result = NULL,
  sensitivity_result = NULL,
  study_a_name = "Study A",
  study_b_name = "Study B",
  indication = "",
  treatment_a = "Treatment A",
  treatment_b = "Treatment B",
  submission_date = format(Sys.Date(), "%d %B %Y"),
  output_format = "console"
)
```

Arguments

`dr_maic_result`	An object of class `"dr_maic"`.
`bootstrap_result`	Optional object of class `"maic_bootstrap"` from `bootstrap_ci()`.
`sensitivity_result`	Optional object of class `"maic_sensitivity"` from `sensitivity_analysis()`.
`study_a_name`	Character; name of the index trial (Study A). Default `"Study A"`.
`study_b_name`	Character; name of the comparator trial (Study B). Default `"Study B"`.
`indication`	Character; disease indication. Default `""`.
`treatment_a`	Character; treatment in index trial.
`treatment_b`	Character; treatment in comparator trial.
`submission_date`	Character; date of submission. Default: today's date.
`output_format`	Character; `"console"` (default) or `"list"`.

Details

The report includes the following sections:

1. **Study and population characteristics** - IPD summary and AgD target moments
2. **Weight estimation** - ESS, convergence, moment-matching results
3. **Covariate balance** - SMD table (NICE TSD 18 format)
4. **Treatment effect estimates** - MAIC, STC, and DR-MAIC ITCs
5. **Uncertainty** - Bootstrap CIs (if provided)
6. **Sensitivity analysis** - E-values and trimming (if provided)
7. **Assumptions and limitations** - per NICE and Cochrane guidance
8. **Methods description** - citable methods paragraph

Value

A list of class `"nice_report"` (invisibly) containing all formatted sections. Also prints to console.

References

Phillippo DM, Ades AE, Dias S, et al. (2016). *NICE DSU TSD 18*.

Dias S, Sutton AJ, Ades AE, Welton NJ. (2013). A generalised linear modelling framework for pairwise and network meta-analysis of randomised controlled trials. *Statistics in Medicine*, 32(13), 2312-2330.

Higgins JPT, et al. (2023). *Cochrane Handbook for Systematic Reviews of Interventions*, Version 6.4. Chapter 23.

ISPOR Task Force. (2014). Indirect treatment comparison/network meta-analysis study questionnaire to assess relevance and credibility. *Value in Health*.

Examples

```
data(nsclc_ipd); data(nsclc_agd)
w   <- compute_weights(nsclc_ipd,
         c(age = nsclc_agd$mean_age, ecog = nsclc_agd$prop_ecog1,
           smoker = nsclc_agd$prop_smoker), c("age","ecog","smoker"))
res <- dr_maic(w, "response", "binary",
               comparator_estimate = nsclc_agd$response_rate,
               comparator_se       = nsclc_agd$response_se)
nice_report(res,
            study_a_name  = "KEYNOTE-024",
            study_b_name  = "IMpower150",
            indication    = "Advanced NSCLC",
            treatment_a   = "Pembrolizumab",
            treatment_b   = "Atezolizumab + Bevacizumab + Chemo")
```

---

nsclc_agd *Simulated NSCLC Aggregate Data (Study B — Comparator)*

Description

Simulated aggregate data (AgD) representing published summary statistics from a hypothetical comparator trial in advanced NSCLC.

Usage

```
nsclc_agd
```

Format

A list with the following elements:

mean_age Mean age of trial population.

prop_ecog1 Proportion with ECOG 1/2.

prop_smoker Proportion with smoking history.

prop_pdl1_high Proportion with PD-L1 >=50%.

prop_prior_lines Proportion with >= 1 prior line.

response_rate Observed response rate (proportion).

response_se Standard error of response rate.

n_agd Sample size of comparator trial.

os_median Median OS in months.

os_hr_ref Log-HR (vs common reference arm, if available).

Source

Simulated data. Not based on any real trial. For illustration only.

Examples

```
data(nsclc_agd)
str(nsclc_agd)
```

`nsclc_ipd` *Simulated NSCLC Individual Patient Data (Study A)*

Description

A simulated individual patient dataset (IPD) representing a hypothetical single-arm trial of an immunotherapy agent in advanced non-small cell lung cancer (NSCLC). Created for demonstration of the drMAIC package.

Usage

```
nsclc_ipd
```

Format

A data frame with 200 rows and 8 variables:

patient_id Patient identifier.

age Age in years (continuous).

ecog ECOG performance status (binary: 0 = ECOG 0, 1 = ECOG 1/2).

smoker Smoking history (binary: 1 = ever-smoker, 0 = never-smoker).

pdl1_high PD-L1 expression >=50% (binary: 1 = high, 0 = low/negative).

prior_lines Number of prior lines of therapy (0 or 1).

response Objective response (binary: 1 = responder, 0 = non-responder).

os_time Overall survival time in months (censored).

os_event Overall survival event indicator (1 = death, 0 = censored).

Source

Simulated data. Not based on any real trial. For illustration only.

Examples

```
data(nsclc_ipd)
head(nsclc_ipd)
summary(nsclc_ipd)
```

`sensitivity_analysis` *Sensitivity Analysis for DR-MAIC*

Description

Conducts pre-specified sensitivity analyses for the DR-MAIC indirect treatment comparison, including: (1) E-value analysis for unmeasured confounding; (2) weight trimming sensitivity; (3) variable exclusion (leave-one-out) analysis; and (4) outcome model specification sensitivity.

Usage

```
sensitivity_analysis(
  dr_maic_result,
  trim_percentiles = c(0.9, 0.95, 0.99),
  lovo = TRUE,
  outcome_model_specs = NULL,
  alpha = 0.05
)
```

Arguments

`dr_maic_result`	An object of class `"dr_maic"` from `dr_maic()`.
`trim_percentiles`	Numeric vector of weight trimming percentiles (0-1). Default `c(0.90, 0.95, 0.99)`.
`lovo`	Logical; run leave-one-variable-out analysis. Default `TRUE`.
`outcome_model_specs`	Optional list of alternative outcome model formulas for specification sensitivity.
`alpha`	Significance level. Default 0.05.

Details

E-value analysis: The E-value quantifies the minimum strength of unmeasured confounding required to explain away the observed treatment effect (VanderWeele & Ding, 2017). For an observed risk ratio RR:

$$E\text{-value} = RR + \sqrt{RR(RR-1)}$$

For OR, the converted RR = $OR^{0.5}$ is used (when outcome is not rare). A large E-value indicates the result is robust to unmeasured confounding.

Weight trimming sensitivity: Extreme weights are trimmed at specified percentiles, and the effect estimate is recomputed. This assesses the influence of patients with extreme weights on the ITC.

Leave-one-variable-out (LOVO): Each matched variable is excluded in turn, and the full DR-MAIC analysis is re-run. This assesses which variables most influence the estimate.

Assumptions tested (per NICE DSU TSD 18 and Cochrane guidance):

- Transportability: the matched population is exchangeable with target B

- No unmeasured effect modifiers: E-value addresses this
- Positivity: overlap between IPD and target assessed via weight distribution
- SUTVA: assumed throughout

Value

A list of class `"maic_sensitivity"` containing:

`evalue` E-value for the main DR-MAIC estimate.

`evalue_ci` E-value for the confidence interval boundary.

`trim_results` Data frame of trimming sensitivity results.

`lovo_results` Data frame of leave-one-variable-out results.

`evalue_plot` ggplot2 E-value plot.

`trim_plot` ggplot2 trimming sensitivity plot.

`lovo_plot` ggplot2 LOVO plot.

References

VanderWeele TJ, Ding P. (2017). Sensitivity analysis in observational research: introducing the E-value. *Annals of Internal Medicine*, 167(4), 268-274.

Phillippo DM, et al. (2016). *NICE DSU TSD 18*.

Cochrane Handbook, Chapter 23: Including variants on randomized trials.

Examples

```
data(nsclc_ipd)
data(nsclc_agd)

w   <- compute_weights(nsclc_ipd,
         c(age = nsclc_agd$mean_age, ecog = nsclc_agd$prop_ecog1,
           smoker = nsclc_agd$prop_smoker),
         c("age","ecog","smoker"))
res <- dr_maic(w, "response", "binary",
               comparator_estimate = nsclc_agd$response_rate,
               comparator_se       = nsclc_agd$response_se)
sa  <- sensitivity_analysis(res)
sa$evalue
sa$trim_plot
```

Index