

# Package ‘drMAIC’

March 29, 2026

**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)

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bootstrap_ci	<i>Bootstrap Confidence Intervals for DR-MAIC</i>
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## 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 <code>dr_maic()</code> .
R	Integer; number of bootstrap replicates. Default 1000. Use $R \geq 2000$ 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(nslc_ipd); data(nslc_agd)
w <- compute_weights(nslc_ipd,
  c(age = nslc_agd$mean_age, ecog = nslc_agd$prop_ecog1,
    smoker = nslc_agd$prop_smoker), c("age", "ecog", "smoker"))
res <- dr_maic(w, "response", "binary",
  comparator_estimate = nslc_agd$response_rate,
  comparator_se       = nslc_agd$response_se)
boot_res <- bootstrap_ci(res, R = 500, seed = 42)
print(boot_res)
boot_res$boot_plot

```

---

check_assumptions	<i>Check Assumptions for DR-MAIC</i>
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---

**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	<i>Compute MAIC Weights via Entropy Balancing</i>
-----------------	---

---

## 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 <code>stats::optim()</code> . 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  $X_i, i = 1, \dots, n$  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 <code>compute_weights()</code> .
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 <code>binomial()</code> for binary outcomes, <code>gaussian()</code> 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  $\omega_i$  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  $\hat{m}(X_i) = \hat{E}[Y | X_i]$  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  $\omega_i$  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 ( $Y_i - \hat{m}_i$ ).  
 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  $|SMD| < \text{threshold}$  after weighting.

**love\_plot** ggplot2 Love plot object.

**weight\_plot** ggplot2 weight distribution plot.

**all\_balanced** Logical; TRUE if all  $|SMD| < \text{threshold}$  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 <code>bootstrap_ci()</code> .
sensitivity_result	Optional object of class "maic_sensitivity" from <code>sensitivity_analysis()</code> .
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(nslc_ipd); data(nslc_agd)
w <- compute_weights(nslc_ipd,
  c(age = nslc_agd$mean_age, ecog = nslc_agd$prop_ecog1,
    smoker = nslc_agd$prop_smoker), c("age", "ecog", "smoker"))
res <- dr_maic(w, "response", "binary",
  comparator_estimate = nslc_agd$response_rate,
  comparator_se       = nslc_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")
```

---

nslc\_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

```
nslc_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  $\geq 50\%$ .

**prop\_prior\_lines** Proportion with  $\geq 1$  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(nslc_agd)
str(nslc_agd)
```

---

nslc\_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**

```
nslc_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  $\geq 50\%$  (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(nslc_ipd)
head(nslc_ipd)
summary(nslc_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:

evaluate E-value for the main DR-MAIC estimate.

evaluate\_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.

evaluate\_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$response_se)
sa <- sensitivity_analysis(res)
sa$evaluate
sa$trim_plot
```

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