Package: tryx (via r-universe)

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Title MR-TRYX (treasure your exceptions)

Version 0.2.0

Description Heterogeneity in MR analyses can arise due to horizontal pleiotropy. This package uses MR-Base to identify possible traits that can explain the heterogeneity, with a view to identifying novel putative associations, and adjusting for their influences to reduce heterogeneity and improve power.

Depends R (>= 3.6.0), TwoSampleMR, dplyr, RadialMR, magrittr, tidyr, ggplot2, glmnet, ggrepel

Suggests igraph, testthat

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Contents

`cochrans_q` *Cochran's Q statistic*

Description

Cochran's Q statistic

Usage

```
cochrans_q(b, se)
```

Arguments

`b`	vector of effecti
`se`	vector of standard errors

Value

q values

`strategy1` *MR Strategy 1*

Description

How to choose the result for a set of different MR analysies? Simple strategy: Use Wald ratio if only one SNP Use IVW if more than one SNP and heterogeneity is low Use weighted mode if more than some minimum number of SNPs and heterogeneity is high

Usage

```
strategy1(dat, het_threshold = 0.05, ivw_max_snp = 1)
```

Arguments

`dat`	Output from harmonise_data function
`het_threshold`	The p-value threshold for Cochran's Q - if lower than this threshold then run weighted mode. Default p = 0.05
`ivw_max_snp`	Maximum SNPs to allow IVW result even if heterogeneity is high. Default = 1

Tryx *Class for MR-TRYX analysis*

Description

A simple wrapper function. Using a summary set, find outliers in the MR analysis between the pair of trais. Find other 'candidate traits' associated with those outliers. Perform MR of each of those candidate traits with the original exposure and outcome.

Methods

Public methods:

- `Tryx$new()`
- `Tryx$print()`
- `Tryx$get_outliers()`
- `Tryx$set_candidate_traits()`
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- `Tryx$candidate_instruments()`
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- `Tryx$mr()`
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- `Tryx$analyse()`
- `Tryx$analyse.mv()`
- `Tryx$manhattan_plot()`
- `Tryx$clone()`

Method `new()`**:** Create a new dataset and initialise an R interface

Usage:

```
Tryx$new(dat)
```

Arguments:

`dat` Dataset from TwoSampleMR::harmonise_data

Method `print()`**:**

Usage:

```
Tryx$print(...)
```

Method `get_outliers()`**:** Detect outliers in exposure-outcome dataset.

Usage:

```
Tryx$get_outliers(
  dat = self$output$dat,
  outliers = "RadialMR",
  outlier_correction = "none",
 outlier_threshold = ifelse(outlier_correction == "none", 0.05/nrow(dat), 0.05)
)
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data. Note - only the first id.exposure - id.outcome pair will be used.

`outliers` Default is to use the RadialMR package to identify IVW outliers. Alternatively can providen an array of SNP names that are present in dat$SNP to use as outliers.

`outlier_correction` Defualt = "none", but can select from ("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none").

`outlier_threshold` If outlier_correction = "none" then the p-value threshold for detecting outliers is by default 0.05.

Method `set_candidate_traits()`**:** Set a list of GWAS IDs used.

Usage:

```
Tryx$set_candidate_traits(id_list = NULL)
```

Arguments:

`id_list` The list of trait IDs to search through for candidate associations. The default is the high priority traits in available_outcomes().

Method `scan()`**:** Search for candidate traits associated with outliers.

Usage:

```
Tryx$scan(
  dat = self$output$dat,
  search_correction = "none",
  search_threshold = ifelse(search_correction == "none", 5e-08, 0.05),
  use_proxies = FALSE
)
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data.

`search_correction` Default = "none", but can select from ("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none.

`search_threshold` If search_correction = "none" then the p-value threshold for detecting an association between an outlier and a candidate trait is by default 5e-8. Otherwise it is 0.05.

`use_proxies` Whether to use proxies when looking up associations. FALSE by default for speed.

Method `candidate_instruments()`**:** Obtain instruments for the candidate traits.

Usage:

```
Tryx$candidate_instruments(
  candidate_instruments = NULL,
  include_outliers = FALSE
)
```

Arguments:

`candidate_instruments` Instruments for candidate traits.

`include_outliers` When performing MR of candidate traits against exposures or outcomes, whether to include the original outlier SNP. Default is FALSE.

Method `outcome_instruments()`**:** Extract instrument for candidate trait instruments for the original outcome.

Usage:

```
Tryx$outcome_instruments(
  candidate_outcome = NULL,
  dat = self$output$dat,
  use_proxies = FALSE
)
```

Arguments:

`candidate_outcome` Extracted instrument SNPs from outcome.

`dat` Output from TwoSampleMR::harmonise_data.

`use_proxies` Whether to use proxies when looking up associations. FALSE by default for speed.

Method `exposure_instruments()`**:** Extract instrument for candidate trait instruments for the original exposure.

Usage:

```
Tryx$exposure_instruments(
  candidate_exposure = NULL,
  dat = self$output$dat,
  use_proxies = FALSE
)
```

Arguments:

`candidate_exposure` Extracted instrument SNPs from exposure.

`dat` Output from TwoSampleMR::harmonise_data.

`use_proxies` Whether to use proxies when looking up associations. FALSE by default for speed.

Method `exposure_candidate_instruments()`**:** Extract instrument for the original exposure for the candidate traits.

Usage:

```
Tryx$exposure_candidate_instruments(
  exposure_candidate = NULL,
  dat = self$output$dat,
```

```
  use_proxies = FALSE,
  include_outliers = FALSE
)
```

Arguments:

`exposure_candidate` Extracted instrument SNPs from exposure.

`dat` Output from TwoSampleMR::harmonise_data.

`use_proxies` Whether to use proxies when looking up associations. FALSE by default for speed.

`include_outliers` When performing MR of candidate traits against exposures or outcomes, whether to include the original outlier SNP. Default is FALSE.

Method `extractions()`**:** Extract instruments for MR analyses.

Usage:

```
Tryx$extractions(
  dat = self$output$dat,
  candidate_instruments = NULL,
  candidate_outcome = NULL,
  candidate_exposure = NULL,
  exposure_candidate = NULL,
  include_outliers = FALSE,
  use_proxies = FALSE
)
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data.

`candidate_instruments` Instruments for candidate traits.

`candidate_outcome` Extracted instrument SNPs from outcome.

`candidate_exposure` Extracted instrument SNPs from exposure.

`exposure_candidate` Extracted instrument SNPs from exposure.

`include_outliers` When performing MR of candidate traits against exposures or outcomes, whether to include the original outlier SNP. Default is FALSE.

`use_proxies` Whether to use proxies when looking up associations. FALSE by default for speed.

Method `candidate_outcome_dat()`**:** Make a dataset for the candidate traits and the original outcome.

Usage:

```
Tryx$candidate_outcome_dat(dat = self$output$dat)
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data.

Method `candidate_exposure_dat()`**:** Make a dataset for the candidate traits and the original exposure.

Usage:

```
Tryx$candidate_exposure_dat(dat = self$output$dat)
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data.

Method `exposure_candidate_dat()`**:** Make a dataset for the original exposure and the candidate traits.

Usage:

```
Tryx$exposure_candidate_dat(dat = self$output$dat)
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data.

Method `harmonise()`**:** Harmonised exposure - outcome dataset.

Usage:

```
Tryx$harmonise(dat = self$output$dat)
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data.

Method `mr()`**:** Perform MR anlayses of 1) candidate traits-outcome 2) candidate traits-exposure 3) exposure-candidate traits.

Usage:

```
Tryx$mr(dat = self$output$dat, mr_method = "mr_ivw")
```

Arguments:

`dat` Output from TwoSampleMR::harmonise_data.

`mr_method` Method to use for candidate trait - exposure/outcome analysis. Default is mr_ivw. Can also provide basic MR methods e.g. mr_weighted_mode, mr_weighted_median etc. Also possible to use "strategy1" which performs IVW in the first instance, but then weighted mode for associations with high heterogeneity.

Method `mrtryx()`**:** All-in-one: 1) Detect outlier 2) Search candidate traits 3) Perform MR of candidate traits and the outcome / exposure.

Usage:

```
Tryx$mrtryx(
  dat = self$output$dat,
  outliers = "RadialMR",
  outlier_correction = "none",
 outlier_threshold = ifelse(outlier_correction == "none", 0.05/nrow(dat), 0.05),
  use_proxies = FALSE,
  search_correction = "none",
  search_threshold = ifelse(search_correction == "none", 5e-08, 0.05),
  include_outliers = FALSE,
  mr_method = "mr_ivw"
)
```

Arguments:

`dat` Output from harmonise_data. Note - only the first id.exposure - id.outcome pair will be used.

`outliers` Default is to use the RadialMR package to identify IVW outliers. Alternatively can providen an array of SNP names that are present in dat$SNP to use as outliers.

`outlier_correction` Defualt = "none", but can select from ("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none").

`outlier_threshold` If outlier_correction = "none" then the p-value threshold for detecting outliers is by default 0.05.

`use_proxies` Whether to use proxies when looking up associations. FALSE by default for speed.

`search_correction` Default = "none", but can select from ("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none").

`search_threshold` If search_correction = "none" then the p-value threshold for detecting an association between an outlier and a candidate trait is by default 5e-8. Otherwise it is 0.05.

`include_outliers` When performing MR of candidate traits against exposures or outcomes, whether to include the original outlier SNP. Default is FALSE.

`mr_method` Method to use for candidate trait - exposure/outcome analysis. Default is mr_ivw. Can also provide basic MR methods e.g. mr_weighted_mode, mr_weighted_median etc. Also possible to use "strategy1" which performs IVW in the first instance, but then weighted mode for associations with high heterogeneity.

Method `tryx.sig()`**:** Identify putatively significant associations in the outlier scan.

Usage:

```
Tryx$tryx.sig(mr_threshold_method = "fdr", mr_threshold = 0.05)
```

Arguments:

`mr_threshold_method` This is the argument to be passed to `p.adjust`. Default is "fdr". If no p-value adjustment is to be applied then specify "unadjusted".

`mr_threshold` Threshold to declare significance

Method `adjustment()`**:** Outlier adjustment estimation - How much of the heterogeneity due to the outlier can be explained by alternative pathways?

Usage:

```
Tryx$adjustment(tryxscan = self$output, id_remove = NULL)
```

Arguments:

`tryxscan` Output from `x$mrtryx()`

`id_remove` List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.

`dat` Output from harmonise_data. Note - only the first id.exposure - id.outcome pair will be used.

Method `adjustment.mv()`**:** Similar to adjusment, but when there are multiple traits associated with a single variant.

Usage:

```
Tryx$adjustment.mv(
  tryxscan = self$output,
  lasso = TRUE,
  id_remove = NULL,
  proxies = FALSE
)
```

Arguments:

`tryxscan` Output from `x$scan()`

`lasso` Whether to shrink the estimates of each trait within SNP. Default=TRUE.

`id_remove` List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.

`proxies` Look for proxies in the MVMR methods. Default = FALSE.

`dat` Output from harmonise_data. Note - only the first id.exposure - id.outcome pair will be used.

Method `analyse()`**:** This returns various heterogeneity statistics, IVW estimates for raw, adjusted and outlier removed datasets, and summary of peripheral traits detected etc.

Usage:

```
Tryx$analyse(
  tryxscan = self$output,
  plot = TRUE,
  id_remove = NULL,
  filter_duplicate_outliers = TRUE
)
```

Arguments:

`tryxscan` Output from `x$scan()`.

`plot` Whether to plot or not. Default is TRUE.

`id_remove` List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.

`duplicate_outliers_method` Sometimes more than one trait will associate with a particular outlier. TRUE = only keep the trait that has the biggest influence on heterogeneity.

Method `analyse.mv()`**:** Similar to analyse, but when there are multiple traits associated with a single variant.

Usage:

```
Tryx$analyse.mv(
  tryxscan = self$output,
  lasso = TRUE,
```

```
  plot = TRUE,
  id_remove = NULL,
  proxies = FALSE
)
```

Arguments:

`tryxscan` Output from `x$scan()`

`lasso` Whether to shrink the estimates of each trait within SNP. Default=TRUE.

`id_remove` List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.

`proxies` Look for proxies in the MVMR methods. Default = FALSE.

Method `manhattan_plot()`**:** Draw a Manhattan style plot for candidate traits-outcome/exposure associations.

Usage:

```
Tryx$manhattan_plot(
  what = "outcome",
  id_remove = NULL,
  y_scale = NULL,
  label = TRUE
)
```

Arguments:

`what` Analyse candidate-exposure ('exposure') or candidate-outcome ('outcome') associations

`id_remove` List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.

`y_scale` The scaling function to be applied to y scale.

`label` Display the names of the traits on the graph.

Method `clone()`**:** The objects of this class are cloneable with this method.

Usage:

```
Tryx$clone(deep = FALSE)
```

Arguments:

`deep` Whether to make a deep clone.

tryx.adjustment *Outlier adjustment estimation*

Description

How much of the heterogeneity due to the outlier can be explained by alternative pathways?

Usage

```
tryx.adjustment(tryxscan, id_remove = NULL)
```

Arguments

tryxscan	Output from tryx.scan
id_remove	List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.

Value

data frame of adjusted effect estimates and heterogeneity stats

tryx.analyse *Analyse tryx results*

Description

This returns various heterogeneity statistics, IVW estimates for raw, adjusted and outlier removed datasets, and summary of peripheral traits detected etc.

Usage

```
tryx.analyse(
  tryxscan,
  plot = TRUE,
  id_remove = NULL,
  filter_duplicate_outliers = TRUE
)
```

Arguments

tryxscan	Output from tryx.scan
plot	Whether to plot or not. Default is TRUE
id_remove	List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.
duplicate_outliers_method	Sometimes more than one trait will associate with a particular outlier. TRUE = only keep the trait that has the biggest influence on heterogeneity

Value

List of - adj_full: data frame of SNP adjustments for all candidate traits - adj: The results from adj_full selected to adjust the exposure-outcome model - Q: Heterogeneity stats - estimates: Adjusted and unadjested exposure-outcome effects - plot: Radial plot showing the comparison of different methods and the changes in SNP effects ater adjustment

---

tryx.analyse.mv *Analyse tryx results*

Description

This returns various heterogeneity statistics, IVW estimates for raw, adjusted and outlier removed datasets, and summary of peripheral traits detected etc.

Usage

```
tryx.analyse.mv(
  tryxscan,
  lasso = TRUE,
  plot = TRUE,
  id_remove = NULL,
  proxies = FALSE
)
```

Arguments

tryxscan	Output from tryx.scan
lasso	Whether to shrink the estimates of each trait within SNP. Default=TRUE.
plot	Whether to plot or not. Default is TRUE

`id_remove` List of IDs to exclude from the adjustment analysis. It is possible that in the outlier search a candidate trait will come up which is essentially just a surrogate for the outcome trait (e.g. if you are analysing coronary heart disease as the outcome then a variable related to heart disease medication might come up as a candidate trait). Adjusting for a trait which is essentially the same as the outcome will erroneously nullify the result, so visually inspect the candidate trait list and remove those that are inappropriate.

`proxies` Look for proxies in the MVMR methods. Default = FALSE.

`filter_duplicate_outliers`
Whether to only allow each putative outlier to be adjusted by a single trait (in order of largest divergence). Default is TRUE.

Value

List of - adj_full: data frame of SNP adjustments for all candidate traits - adj: The results from adj_full selected to adjust the exposure-outcome model - Q: Heterogeneity stats - estimates: Adjusted and unadjested exposure-outcome effects - plot: Radial plot showing the comparison of different methods and the changes in SNP effects ater adjustment Adjust and analyse the tryx results

Similar to tryx.analyse, but when there are multiple traits associated with a single variant then we use a LASSO-based multivariable approach

List of - adj_full: data frame of SNP adjustments for all candidate traits - adj: The results from adj_full selected to adjust the exposure-outcome model - Q: Heterogeneity stats - estimates: Adjusted and unadjested exposure-outcome effects - plot: Radial plot showing the comparison of different methods and the changes in SNP effects ater adjustment

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`tryx.network` *Plot results from outlier_scan in a network*

Description

Creates a simple network depicting the connections between outlier instruments, the original exposure and outcome traits, and the detected candidate associations

Usage

```
tryx.network(tryxscan)
```

Arguments

`tryxscan` Output from outlier_scan function

Value

Prints plot, and returns dataframe of the connections

`tryx.scan` *Outlier scan*

Description

A simple wrapper function. Using a summary set, find outliers in the MR analysis between the pair of trais. Find other 'candidate traits' associated with those outliers. Perform MR of each of those candidate traits with the original exposure and outcome

Usage

```
tryx.scan(
  dat,
  outliers = "RadialMR",
  outlier_correction = "none",
  outlier_threshold = ifelse(outlier_correction == "none", 0.05/nrow(dat), 0.05),
  use_proxies = FALSE,
  search_correction = "none",
  search_threshold = ifelse(search_correction == "none", 5e-08, 0.05),
  id_list = "default",
  include_outliers = FALSE,
  mr_method = "mr_ivw"
)
```

Arguments

`dat`	Output from harmonise_data. Note - only the first id.exposure - id.outcome pair will be used.
`outliers`	Default is to use the RadialMR package to identify IVW outliers. Alternatively can providen an array of SNP names that are present in dat$SNP to use as outliers.
`outlier_correction`	Defualt = "none", but can select from ("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none").
`outlier_threshold`	If outlier_correction = "none" then the p-value threshold for detecting outliers is by default 0.05.
`use_proxies`	Whether to use proxies when looking up associations. FALSE by default for speed.
`search_correction`	Default = "none", but can select from ("holm", "hochberg", "hommel", "bonferroni", "BH", "BY", "fdr", "none").
`search_threshold`	If search_correction = "none" then the p-value threshold for detecting an association between an outlier and a candidate trait is by default 5e-8. Otherwise it is 0.05.

`id_list` The list of trait IDs to search through for candidate associations. The default is the high priority traits in available_outcomes().

`include_outliers` When performing MR of candidate traits against exposures or outcomes, whether to include the original outlier SNP. Default is FALSE.

`mr_method` Method to use for candidate trait - exposure/outcome analysis. Default is mr_ivw. Can also provide basic MR methods e.g. mr_weighted_mode, mr_weighted_median etc. Also possible to use "strategy1" which performs IVW in the first instance, but then weighted mode for associations with high heterogeneity.

Value

List dat Cleaned dat input radialmr Results from RadialMR analysis outliers List of outliers used id_list List of GWAS IDs used search Result from search of outliers against GWAS IDs candidate_instruments Instruments for candidate traits candidate_outcome Extracted instrument SNPs from outcome candidate_outcome_dat Harmonised candidate - outcome dataset candidate_outcome_mr MR analysis of candidates against outcome candidate_exposure Extracted instrument SNPs from exposure candidate_exposure_dat Harmonised candidate - exposure dataset candidate_exposure_mr MR analysis of candidates against exposure

---

`tryx.sig` *Identify putatively significant associations in the outlier scan*

Description

Identify putatively significant associations in the outlier scan

Usage

```
tryx.sig(tryxscan, mr_threshold_method = "fdr", mr_threshold = 0.05)
```

Arguments

`mr_threshold_method` This is the argument to be passed to `p.adjust`. Default is "fdr". If no p-value adjustment is to be applied then specify "unadjusted"

`mr_threshold` Threshold to declare significance

Value

Same as outlier_scan but the candidate_exposure_mr and candidate_outcome_mr objects have an extra pval_adj and sig column each

`tryx.simulate` *Simulate data to test tryx*

Description

Create data using model here: https://www.draw.io/#G1VqjTd4iH2de7sXI4PhUrxazBnYLduH_w. Create summary data for all necessary traits, then perform tryx scan x = exposure y = outcome u1 = confounder of x and y u2 = mediator of horizontal pleiotropy from gx to y. One for each gx u3 = mediator between x and y

Usage

```
tryx.simulate(
  nid = 10000,
  ngx = 30,
  ngu1 = 30,
  ngu2 = 30,
  nu2 = 2,
  ngu3 = 30,
  vgx = 0.2,
  vgu1 = 0.6,
  vgu2 = 0.2,
  vgu3 = 0.2,
  bxy = 0,
  bu1x = 0.6,
  bu1y = 0.4,
  bxu3 = 0.3,
  bu3y = 0,
  vgxu2 = 0.2,
  vu2y = 0.2,
  ngxu3 = 0,
  vgxu3 = 0,
  mininum_instruments = 10,
  instrument_threshold = "bonferroni",
  outlier_threshold = "bonferroni",
  outliers_known = "detected",
  directional_bias = FALSE
)
```

Arguments

`nid`	= 10000 Number of samples
`ngx`	= 30 Number of direct instruments to x
`ngu1`	= 30 Number of instruments influencing confounder of x and y
`ngu2`	= 30 Number of instruments per mediating
`nu2`	= 2 Number of gx that are pleiotropic

`ngu3` = 30 Number of instruments for u3 mediator

`vgx` = 0.2 Variance explained by gx instruments

`vgu1` = 0.6 Variance explained by u1 instruments

`vgu2` = 0.2 Variance explained by u2 instruments

`vgu3` = 0.2 Variance explained by u3 instruments

`bxy` = 0 Causal effect of x on y

`bu1x` = 0.6 Effect of u1 on x

`bu1y` = 0.4 Effect of u1 on y

`bxu3` = 0.3 Effect of x on u3

`bu3y` = 0 Effect of u3 on y

`vgxu2` = 0.2 Variance explained by each gx instrument on each u2 mediator

`vu2y` = 0.2 Variance explained by all u2 mediators on y

`ngxu3` = 0 Number of gx instruments that pleiotropically associate with u3 mediator

`mininum_instruments` = 10 Minimum number of instruments required to have been detected to run simulation

`instrument_threshold` = "bonferroni" Threshold, either numeric or 'bonferroni'

`outlier_threshold` = "bonferroni" Threshold, either numeric or 'bonferroni'

`outliers_known` = "detected" Either detected = using radial mr to find heterogeneity outliers; known = adjust for all known invalid instruments; all = adjust for all instruments

`directional_bias` = FALSE Is the pleiotropic effect randomly centered around 0 (FALSE) or does it have a non-0 mean (TRUE)

`vgxu3y` = 0 Variance explained by all gx variants directly on u3 mediator

Value

list for tryx.analyse

`volcano_plot` *Plot volcano plot of many MR analyses*

Description

Plot volcano plot of many MR analyses

Usage

```
volcano_plot(res, what = "exposure")
```

Arguments

res	Dataframe similar to output from mr() function, requiring id.exposure, id.outcome. Ideally only provide one MR estimate for each exposure-outcome hypothesis. Also provide a sig column of TRUE/FALSE to determine if that association is to be labelled
what	Whether to plot many exposures against few outcomes (default: exposure) or few exposures against many outcomes (outcome). If e.g. 'exposure' and there are multiple outcomes then will facet by outcome

Value

ggplot of volcano plots

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