Package 'LocalControlStrategy'

August 30, 2019

Title Local Control Strategy for Robust Analysis of Cross-Sectional Data

Version 1.3.3

Date 2019-09-01

Author Bob Obenchain

Maintainer Bob Obenchain <wizbob@att.net>

Depends cluster, lattice

Description Especially when cross-sectional data are observational, effects of treatment selection bias and confounding are revealed by using the Nonparametric and Unsupervised "preprocessing" methods central to Local Control (LC) Strategy. The LC objective is to estimate the ``effect-size distribution" that best quantifies a potentially causal relationship between a numeric y-Outcome variable and a t-Treatment variable. This t-variable may be either binary $\{1 = \text{``new''} \text{ vs } 0 = \text{``control''}\}\)$ or a numeric measure of Exposure level. LC Strategy starts by CLUSTERING experimental units (patients) on their pre-exposure X-Covariates, forming mutually exclusive and exhaustive BLOCKS of relatively well-matched units. The implicit statistical model for LC is thus simple one-way ANOVA. The Within-Block measures of effect-size are Local Rank Correlations (LRCs) when Exposure is numeric with more than two levels. Otherwise, Treatment choice is Nested within BLOCKS, and effect-sizes are LOCAL Treatment Differences (LTDs) between within-cluster y-Outcome Means [``new" minus ``control"]. An Instrumental Variable (IV) method is also provided so that Local Average y-Outcomes (LAOs) within BLOCKS may also contribute information for effect-size inferences ... assuming that X-Covariates influence only Treatment choice or Exposure level and otherwise have no direct effects on y-Outcome. Finally, a "Most-Like-Me" function provides histograms of effect-size distributions to aid Doctor-Patient communications about Personalized Medicine.

License GPL-2

URL https://www.R-project.org, http://localcontrolstatistics.org

NeedsCompilation no

Repository CRAN

Date/Publication 2019-08-29 23:10:09 UTC

R topics documented:

	LocalControlStrategy-package
	confirm
	ivadj
	KSperm
	LCcluster
	LCcompare
	LCsetup
	lrcagg
	ltdagg
	mlme
	mlme.stats
	pci15k
	plot.ivadj
	plot.lrcagg
	plot.ltdagg
	plot.mlme
	print.mlme
	radon
	reveal.data
Index	2'

LocalControlStrategy-package

LocalControlStrategy: Unsupervised, Nonparametric Adjustment for Bias and Confounding

Description

LC Strategy defines Local Treatment Differences (LTDs) or Local Rank Correlations (LRCs) within Clusters of experimental units (patients) who have been relatively well-matched on their baseline x-Covariates. The resulting distribution of LTD/LRC effect-size estimates can be interpreted much like a Bayesian posterior. Yet these distributions have been formed, via Nonparametric Preprocessing, in purely Objective Ways.

Details

Package: LocalControlStrategy

Type: Package Version: 1.3.3 Date: 2019-09-01 License: GPL-2 Multiple calls to ltdagg(K) or lrcagg(K) for varying numbers of clusters, K, are typically made after first invoking LCcluster() to hierarchically cluster patients in X-space and invoking LCsetup() to specify a numeric y-Outcome variable and a numeric treatment choice or exposure level measure, trex.

UNSUPERVISED INSTRUMENTAL VARIABLES = LOCAL AVERAGE y-OUTCOME EFFECTS:

An observed Propensity Score (PS) is defined here to be either (i) the local (within-cluster) fraction of experimental units (patients) receiving trex==1 (new) rather than trex==0 (control) or else (ii) a measure of "relative exposure" when the numeric trex measure has (many) more than 2 observed levels. Multiple calls to ivadj(K) for varying numbers of clusters, K, then yield alternative scatters of Local Average Outcomes (LAOs) for Clusters when plotted against their PS estimates and, thus, different possible linear fits or smooth.splines() yielding potentially different inferences about across-cluster Treatment or Exposure Effects.

CONFIRMATION and SENSITIVITY ANALYSES of LOCAL EFFECT-SIZE DISTRIBUTIONS:

For a given value of K = Number of Clusters requested, the output object from Itdagg(K) or Ircagg(K) can be input to confirm() to use (nonparametric) permutation theory to display visual evidence (empirical CDF comparisons) concerning the Question: Does x-matching Truly Matter? The NULL hypothesis here is that the x-Covariates used in Clustering / Matching of Experimental Units are actually IGNORABLE. Evidence against this hypothesis is provided when the observed LOCAL Effect-Size Distribution clearly deviates from the purely RANDOM, NULL distribution computed (to any desired precision) by randomly PERMUTING cluster ID labels across experimental units. Furthermore, the statistical significance of differences between the observed and random NULL distributions can be estimated using KSperm(), which simulates the random permutation distribution of the Kolmogorov-Smirnov D-statistic when many tied values occur in both distributions being compared. Finally, the LCcompare() function helps users of LC Strategy decide which Number of Clusters, K, optimizes Variance-Bias trade-offs. Larger values of K tend to yield smaller clusters with better matches and, thus, potentially reduced BIAS. On the other hand, smaller values of K usually yield local effect-size estimates with much lower Variability (higher Precision).

"Most-Like-Me" HISTOGRAMS for DOCTOR-PATIENT discussions of PERSONALIZED MEDICINE:

For a specified vector, xvec, of numerical values of the X-confounder variables used in the current CLUSTERING of eUnits, display histograms of observed LTD or LRC effect-sizes for (i) all available patients and (ii) for the specified number, NN, of "Nearest-Neighbors" in X-confounder space of the TARGET eUnit ...i.e. xvec defines "Me".

Author(s)

Bob Obenchain <wizbob@att.net>

References

McClellan M, McNeil BJ, Newhouse JP. (1994) Does More Intensive Treatment of Myocardial Infarction in the Elderly Reduce Mortality?: Analysis Using Instrumental Variables. *JAMA* **272**: 859-866.

Obenchain RL. (2010) The Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary*, *NC:SAS Press*, pages 151-192.

Obenchain RL, Young SS. (2013) Advancing Statistical Thinking in Observational Health Care Research. *J. Stat. Theory and Practice*, 7: 456-469, doi: 10.1080/15598608.2013.772821.

4 confirm

Lopiano KK, Obenchain RL, Young SS. (2014) Fair treatment comparisons in observational research. *Statistical Analysis and Data Mining*, 7: 376-384, doi: 10.1002/sam.11235.

Obenchain RL. LocalControlStrategy-vignette. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

Rosenbaum PR, Rubin RB. (1983) The Central Role of the Propensity Score in Observational Studies for Causal Effects. *Biometrika* **70**: 41-55.

Rosenbaum PR, Rubin RB. (1984) Reducing Bias in Observational Studies Using Subclassification on a Propensity Score. *JASA* **79**: 516-524.

Rubin DB. (1980) Bias reduction using Mahalanobis metric matching. Biometrics 36: 293-298.

Stuart EA. (2010) Matching Methods for Causal Inference: A Review and a Look Forward. *Statistical Science* **25**: 1-21.

confirm Confirm that Clustering in Covariate X-space yields an "adjusted" LTD/LRC effect-size Distribution

Description

For a given Number of Clusters, K, confirm() compares the observed distribution of LTDs or LRCs from relatively well-matched experimental units with the corresponding distribution from Purely Random Clusterings of experimental units. The larger are differences between the (blue) observed empirical CDF of effect-sizes and the (red) Purely Random CDF, the more potentially IMPORTANT are the "adjustments" resulting from focusing upon clustering (matching) of experimental units in X-space.

Usage

confirm(x, reps=100, seed=12345)

Arguments

X	An output object from ltdagg() or lrcagg() for a specified number of clusters, K.
reps	Number of simulation Replications, each with the same number, K, and sizes, N1, N2,, NK of Purely Random clusters.
seed	This (arbitrary) integer argument will be passed to the R set.seed() function. Knowing the value of this seed makes the output from confirm() reproducible.

Details

Making calls to confirm() for ltdagg() or lrcagg() objects resulting from different choices of K = Numbers of Clusters help the analyst decide which observed LTD or LRC effect-size distributions are (or are not) meaningfully different from Purely Random. When the X-covariates used in LC-cluster() are truly "ignorable," then [i] all X-based clusters will be Purely Random, and [ii] both the number (K) and the sizes (N1, N2, ...,NK) of clusters formed will be meaningless and arbitrary. Thus the LC Strategy confirm() function simulates the empirical CDF for LTDs or LRCs resulting from purely random permutations of the Cluster ID numbers (1, 2, ...,K) assigned by ltdagg()

confirm 5

or lrcagg(). Each permutation yields K artificial "clusters" of sizes N1, N2, ..., NK. Simulation results are accumulated for the total number of random permutations specified in the "reps=" argument of confirm(). Calls to print.confirm() and plot.confirm() provide information on comparisons of empirical CDFs for the Observed and Purely Random LTD/LRC distributions, including calculation of an observed two-sample Kolmogorov-Smirnov D-statistic using stats::ks.test. This is a non-standard use of ks.test() because the distributions being compared are DISCRETE; both contain many within-cluster TIED effect-size estimates. The p-value computed by ks.test() is not reported or saved because it is badly biased downwards due to TIED estimates. Researchers wishing to simulate a p-value for the observed KS D-statistic that is adjusted for TIES can invoke KSperm(confirm()).

Value

An output list object of class confirm:

hiclus Hierarchical clustering object created by the designated method.

dframe Name of data.frame containing X, trex & Y variables.

trtm Name of numerical trex variable.

yvar Name of numerical Y-outcome variable.

reps Number of overall Replications, each with the same numbers of requested clus-

ters.

seed Integer argument passed to set.seed(). Knowing which seed value was used in

the call to confirm() makes not only the NULL distribution of observed LTDs or LRCs reproducible but also makes the NULL distribution of D-statistics (ad-

justed for ties) from a subsequent call to KSperm() reproducible.

nclus Number of clusters requested.

units Number of experimental units or patients.

Type 1 ==> LTDs, otherwise LRCs.

LCmean Weighted Local Mean across Clusters.

LCstde Weighted Std. Error across Clusters.

RPmean Weighted Random Permutation Mean across Clusters.

RPstde Weighted Random Permutation Std. Error across Clusters.

KSobsD Output from print(ks.test()).

LCdist data.frame of 5 key variables for all experimental units.

dfconf data.frame of lstat = LTD or LRC values of max(length) = reps*units.

Author(s)

Bob Obenchain <wizbob@att.net>

References

Obenchain RL. (2010) The Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary*, *NC:SAS Press*, pages 151-192.

Obenchain RL. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

6 ivadj

See Also

1tdagg and 1rcagg.

ivadj

Instrumental Variable LAO Fitting and Smoothing

Description

For a given number of patient clusters in baseline X-covariate space and a specified Y-outcome variable, smooth the distribution of Local Average Outcomes (LAOs) plotted versus Within-Cluster Propensity-like Scores: the Treatment Selection Fraction or the Relative Exposure Level.

Usage

ivadj(x)

Arguments

Х

An output object from ltdagg() or lrcagg() using K Clusters in X-covariate space.

Details

Multiple invocations of ivadj(ltdagg()) or ivadj(lrgagg()) using varying numbers of clusters, K, can be made. Each invocation of ivadj() displays a linear lm() fit and a smooth.spline() fit to the scatter of LAO estimates plotted versus their within-cluster propensity-like score estimates.

Value

An output list object of class ivadj:

hclobj Name of clustering object output by LCcluster().

dframe Name of data.frame containing X, trtm & Y variables.

trtm Name of the numeric treatment variable.

yvar Name of the numeric outcome Y variable.

K Number of Clusters Requested.

actclust Number of Clusters actually produced.

Author(s)

Bob Obenchain <wizbob@att.net>

KSperm 7

References

McClellan M, McNeil BJ, Newhouse JP. (1994) Does More Intensive Treatment of Myocardial Infarction in the Elderly Reduce Mortality?: Analysis Using Instrumental Variables. *JAMA* **272**: 859-866.

Obenchain RL. (2010) Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary*, *NC:SAS Press*, pages 151-192.

Obenchain RL. (2018) LCstrategy_in_R.pdf http://localcontrolstatistics.org

Rosenbaum PR, Rubin RB. (1983) The Central Role of the Propensity Score in Observational Studies for Causal Effects. *Biometrika* **70**: 41-55.

See Also

1tdagg, 1rcagg and LCcompare.

Examples

```
## Not run:
# Long running example...
data(pci15k)
xvars <- c("stent", "height", "female", "diabetic", "acutemi", "ejfract", "ves1proc")
hclobj <- LCcluster(pci15k, xvars)
LC.env <- LCsetup(hclobj, pci15k, thin, surv6mo)
surv050 <- ltdagg(50, LC.env)
iv050 <- ivadj(surv050)
iv050
plot(iv050)
## End(Not run)</pre>
```

KSperm

Simulate a p-value for the significance of the Kolmogorov-Smirnov D-statistic from confirm().

Description

For a given confirm() output object, KSperm() simulates the NULL distribution of LTDs or LRCs resulting from Purely Random Clusterings of experimental units within the parent data.frame. This NULL distribution is discrete because Local Effect-Size estimates are TIED within-clusters. The observed D-Statistic from confirm() is compared with new NULL order statistics computed by KSperm(), again using stats::ks.test. When KSperm() is called immediately after confirm() and the seed value used in confirm() is known, then both the simulated p-value and the additional NULL KS-D order statistics generated by KSperm() will all be reproducible.

Usage

```
KSperm(x, reps=100)
```

8 KSperm

Arguments

x An output object from confirm().

reps This is the number of new NULL KS-D statistics to generated. Each experi-

mental unit is used at most once within each full replication. No clusters will be

empty, but some may be "uninformative".

Details

The observed value of the Kolmogorov-Smirnov D-statistic from confirm() is used here, but its "p.value" from ks.test() is not because it is badly biased downwards. This bias results because the distribution of LTDs or LRCs across clusters is always discrete, due to TIED values within clusters that typically also vary in size. Thus, KSperm() generates "reps" additional, independent, NULL values of KS-D and saves their order statistics. Finally, KSperm() compares the Observed KS-D from confirm() with its simulated NULL order statistics to estimate an appropriately "adjusted" p-value, pv.adj. Note that the simulated pv.adj value estimate cannot be less than 1/(reps).

Value

An output list object of class KSperm:

hiclus Hierarchical clustering object created by the designated method.

dframe Name of data.frame containing X, t & Y variables.

trtm Name of numerical treatment/exposure variable.

yvar Name of numerical y-Outcome variable.

Type 1 ==> LTDs, otherwise LRCs.

reps Number of overall Replications, each with the same number, K, of requested

clusters.

nclus Number of clusters requested.

units Number of experimental units or patients.

obsD Observed numerical value of KS D-statistic from confirm()

Dvec Vector of order statistics for simulated NULL KS D-statistics.

pv.adj Simulated p-value adjusted for TIES within discrete LTD/LRC distributions.

Author(s)

Bob Obenchain <wizbob@att.net>

References

Obenchain RL. (2010) Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary*, *NC:SAS Press*, pages 151-192.

Obenchain RL. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

See Also

confirm, 1tdagg and 1rcagg.

LCcluster 9

LCcluster	Hierarchical Clustering of experimental units (such as patients) in X-covariate Space

Description

Form the full, hierarchical clustering tree (dendrogram) for all units (regardless of Treatment/Exposure status) using Mahalonobis distances computed from specified baseline X-covariate characteristics.

Usage

```
LCcluster(dframe, xvars, method="ward.D")
```

Arguments

dframe Name of data.frame containing baseline X covariates.

xvars List of names of X variable(s).

method Hierarchical Clustering Method of "diana", "ward.D", "ward.D2", "complete",

"average", "mcquitty", "median" or "centroid".

Details

The first step in applying Local Control Strategy to data is to hierarchically cluster experimental units in baseline X-covariate space ...thereby creating "Blocks" of relatively well-matched units. LCcluster first calls stats::prcomp() to calculate Mahalanobis distances using standardized and orthogonal Principal Coordinates. LCcluster then uses either the divisive cluster::diana() method or one of seven agglomerative methods from stats::hclust() to compute a dendrogram tree. The hclust function is based on Fortran code contributed to STATLIB by F. Murtagh.

Value

An output list object of class LCcluster, derived from cluster::diana or stats::hclust.

dframe Name of data.frame containing all baseline X-covariates.

xvars List of 1 or more X-variable names.

method Hierarchical Clustering Method: "diana", "ward.D", "ward.D2", "complete",

"average", "mcquitty", "median" or "centroid".

hclobj Hierarchical clustering object created by the designated method.

Author(s)

Bob Obenchain <wizbob@att.net>

10 LCcompare

References

Kaufman L, Rousseeuw PJ. (1990) **Finding Groups in Data. An Introduction to Cluster Analysis**. New York: John Wiley and Sons.

Kereiakes DJ, Obenchain RL, Barber BL, et al. (2000) Abciximab provides cost effective survival advantage in high volume interventional practice. *Am Heart J* **140**: 603-610.

Murtagh F. (1985) Multidimensional Clustering Algorithms. COMPSTAT Lectures 4.

Obenchain RL. (2010) Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary, NC:SAS Press*, pages 151-192.

Rubin DB. (1980) Bias reduction using Mahalanobis metric matching. *Biometrics* 36: 293-298.

See Also

```
LCsetup, 1tdagg and 1rcagg.
```

Examples

```
data(radon)
xvars <- c("obesity", "over65", "cursmoke")
hclobj <- LCcluster(radon, xvars) # ...using default method = "ward.D"
plot(hclobj)</pre>
```

LCcompare

Display LC Sensitivity Graphic for help in choice of K = Number of Clusters

Description

This function displays Box-Whisker diagrams that compare Treatment Effect-Size distributions for different values of K = Number of Clusters requested in X-covariate space. After an initial call to LCsetup(), the analyst typically makes multiple calls to either ltdagg() or lrcagg() for different values of K. The analyst then invokes LCcompare() to see how choice of K changes the location, spread and/or skewness of the distribution of Treatment Effect-Size estimates across Clusters. Variance-Bias trade-offs occur as K increases; large values of K may reduce Bias, but they definitely inflate the Variance of LTD and LRC distributions.

Usage

```
LCcompare(envir)
```

Arguments

envir

R environment output by an earlier call to LCsetup().

LCcompare 11

Details

The third phase of Local Control Strategy is called EXPLORE and uses graphical Sensitivity Analyses to show how Treatment Effect-Size distributions change with choice of LC parameter settings. Choice of K = Number of Clusters requested is guided, primarily, by LCcompare() graphics. Equally important are the analyst's choices of (i) which [and how many] of the available baseline X-covariates to "adjust for" and (ii) which clustering algorithm and dissimilarity metric to use. Unfortunately, changing these latter choices requires the analyst to essentially "start over" ...i.e. invoking LCcluster() with changed arguments, followed by an invocation of LCsetup() with a different 1st argument. To change only one's choice of y-Outcome variable and/or the Treatment/Exposure variable, a new LCsetup() invocation is all that is needed.

Value

NULL

Author(s)

Bob Obenchain <wizbob@att.net>

References

Obenchain RL. (2010) Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary*, *NC:SAS Press*, pages 151-192.

Obenchain RL. (2015) LC_Confirm_Guidelines.pdf http://localcontrolstatistics.org

Obenchain RL. (2019) LCstrategy in R.pdf http://localcontrolstatistics.org

Rubin DB. (1980) Bias reduction using Mahalanobis metric matching. Biometrics 36: 293-298.

Tukey JW. (1977) Exploratory Data Analysis, New York: Addison-Wesley, Section 2C.

See Also

```
ltdagg, ivadj and lrcagg.
```

Examples

```
## Not run:
# Long running example...
data(pci15k)
xvars <- c("stent", "height", "female", "diabetic", "acutemi", "ejfract", "ves1proc")
hclobj <- LCcluster(pci15k, xvars)
LC.env <- LCsetup(hclobj, pci15k, thin, surv6mo)
surv050 <- ltdagg( 50, LC.env)
surv100 <- ltdagg(100, LC.env)
surv200 <- ltdagg(200, LC.env)
LCcompare(LC.env)
## End(Not run)</pre>
```

12 LCsetup

LCsetup	Specify KEY parameters used in Local Control (LC) Strategy to "de-
	sign" analyses of Observational Data.
	sign unityses of Observational Data.

Description

Invoke LCsetup() to specify the name of the Hierarchical Clustering object output by LCcluster() and the name of the data.frame containing all desired X-covariates, the Treatment/Exposure variable and the Y-Outcome variable. It is ESSENTIAL to save the Environment output by LCsetup() as a named object within the user's .GlobalEnv space.

Usage

```
LCsetup(hclobj, dframe, trex, yvar)
```

Arguments

hclobj	Name of a LCcluster() output object created using a cluster::diana or stats::hclust

method.

dframe Name of the data.frame containing all X-covariates, the Treatment/Exposure

variable and the Y-Outcome variable.

trex Name of the numerical Treatment/Exposure variable.

yvar Name of the numerical Y-Outcome variable.

Value

The environment output by LCsetup() must be saved to the user's .GlobalEnv space. It's contents will be automatically updated by calls to other LocalControlStrategy functions:

aggdf data.frame with 4 columns and 1 row for each call to ltdagg() or lrcagg().

aggdf\$Label Factor value of "LTD" or "LRC".

aggdf\$Blocks K = integer Number of Clusters requested.

aggdf\$LTDmean or aggdf\$LRCmean

numerical value of cluster mean of LTD or LRC estimates.

aggdf\$LTDstde or aggdf\$LRCstde

numerical value of the within-cluster standard deviation.

boxdf data.frame of 2 variables ...for input to boxplot() by LCcompare().

boxdf\$LCstat LTD or LRC estimate for a single experimental unit from ltdagg() or lrcagg().

boxdf\$K Number of Cluters used in forming the LTD or LRC estimate for each Experi-

mental Unit.

Kmax Maximum Number of Clusters so that Average Size will be >= 12 experimental

units.

LTDmax or LRCmax

Maximum Treatment Effect-Size estimate across Clusters.

lrcagg 13

1	ТΓ	∩m i	n	or	LRCmin
ᆫ	I L	ノハハエ	11	O1	LIVCIIITII

	Minimum Treatment Effect-Size estimate across Clusters.
NumLevels	Integer number of distinct Levels of the Treatment/Exposure variable: trex.
pars	Character data.frame with 4 columns and 1 row.
pars[1,1]	Name of the diana or helust object created by LCcluster().
pars[1,2]	Name of data.frame containing the X , Treatment/Exposure and Y variables.
pars[1,3]	Name of Treatment/Exposure variable within data.frame pars[1,2].
pars[1.4]	Name of Y-outcome variable within data.frame pars[1,2].

Author(s)

Bob Obenchain <wizbob@att.net>

References

Obenchain RL. (2010) Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary, NC:SAS Press*, pages 151-192.

Obenchain RL. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

See Also

```
ltdagg, ivadj and lrcagg.
```

Examples

```
## Not run:
# Long running example...
data(pci15k)
xvars <- c("stent", "height", "female", "diabetic", "acutemi", "ejfract", "ves1proc")
hclobj <- LCcluster(pci15k, xvars)
LCe <- LCsetup(hclobj, pci15k, thin, surv6mo)
ls.str(LCe)
## End(Not run)</pre>
```

lrcagg

Calculate the observed Distribution of LRCs in Local Control Strategy

Description

For a given number, K, of Clusters of Experimental Units in baseline X-covariate space, lrcagg() calculates the observed distribution of "Local Rank Correlations" (LRCs) across Clusters ...where each LRC = cor(trex, Y, method = "spearman") within a Cluster, trex is a numeric measure of Exposure, and Y is a numeric measure of Outcome.

14 lrcagg

Usage

lrcagg(K, envir)

Arguments

K Number of Clusters in baseline X-covariate space.
envir R environment output by a previous call to LCsetup().

Details

Multiple calls to lrcagg(K) for varying numbers of clusters, K, are typically made after first invoking LCcluster() to hierarchically cluster patients in X-space and then invoking LCsetup() to specify a Y Outcome variable and a continuous, numerical treatment Exposure: trex. lrcagg() computes an observed LRC Distribution, updates information stored in its envir object, and outputs an object that is typically saved in the user's .GlobalEnv to allow subsequent use by print.lrcagg(), plot.lrcagg(), confirm() or KSperm(). Uninformative Clusters (those containing only 1 or 2 experimental units) contribute NA values to the LRCtabl\$LRC and LRCdist\$LRC objects within the lrcagg() output list.

Value

An output list of 12 objects, of class lreagg:

hclobj Name of clustering dendrogram object created by LCcluster().

dframe Name of data.frame containing X, trex & Y variables.

trex Name of numerical treatment/exposure level variable.

yvar Name of outcome Y variable.

K Number of Clusters Requested.

actclust Number of Clusters delivered.

LRCtabl data.frame with 5 columns and K rows for Clusters.

LRCtabl\$c Cluster ID Factor, "1", "2", ..., "K".

LRCtabl\$LRC Numerical value of Local Treatment Difference for a Cluster.

LRCtabl\$w Integer value of "weight" = Cluster Size.

LRCtabl\$LAO Numerical value of within-cluster Local Average Outcome (Y-value).

LRCtabl\$PS Numerical value of Local Relative Propensity for Exposure, 0.0 to 1.0.

LRCdist data.frame with 4 columns and same number of rows as the data: dframe.

LRCdist\$c.K Name for the Cluster ID Variable of the form: "c.K"

LRCdist\$y Numerical value of the Y-Outcome for an Experimental Unit.

LRCdist\$t Numerical value of trex Exposure Level for an Experimental Unit.

LRCdist\$LRC Numerical value of the LRC for the Cluster containing each Experimental Unit.

infoclus Integer value of Number of Informative Clusters.

infounits Integer value of Number of Units within Informative Clusters.

LRCmean Numerical value of mean(LRCdist\$LRC) = Weighted Average of LRCtabl\$LRC

values.

LRCstde Numerical value of sqrt(var(LRCdist\$LRC)) = Weighted Standard Deviation of

LRCtabl\$LRC values.

ltdagg 15

Author(s)

Bob Obenchain <wizbob@att.net>

References

Obenchain RL. (2010) The Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary, NC:SAS Press*, pages 151-192.

Obenchain RL. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

See Also

```
ivadj, 1tdagg and LCcompare.
```

Examples

```
data(radon)
xvars <- c("obesity", "over65", "cursmoke")
hclobj <- LCcluster(radon, xvars)
e <- LCsetup(hclobj, radon, lnradon, lcanmort)
lrc050 <- lrcagg(50, e)
lrc050
plot(lrc050, e)</pre>
```

1tdagg

Calculate the Observed Distribution of LTDs in Local Control Strategy

Description

For a given number, K, of Clusters of Experimental Units in baseline X-covariate space, ltdagg() calculates the observed distribution of "Local Treatment Differences" (LTDs) of the form LTD = ((mean(Y) for units receiving trtm==1) - (mean(Y) for units receiving trtm==0)).

Usage

```
ltdagg(K, envir)
```

Arguments

K Number of Clusters in baseline X-covariate space.

envir R environment output by a previous call to LCsetup().

16 ltdagg

Details

Multiple calls to Itdagg(K) for varying numbers of clusters, K, are typically made after first invoking LCcluster() to hierarchically cluster patients in X-space and then invoking LCsetup() to specify a Y Outcome variable and a two-level, numerical treatment variable: trtm. Itdagg() computes an observed LTD Distribution, updates information stored in its envir object, and outputs an object that is typically saved in the user's .GlobalEnv to allow subsequent use by print.Itdagg(), plot.Itdagg(), confirm() or KSperm(). Uninformative Clusters (those containing either only trtm==1 units or else only trtm==0 units) contribute NA values to the LTDtabl\$LTD and LTDdist\$LTD objects within the Itdagg() output list object.

Value

An output list of 12 objects, of class ltdagg:

hiclus Name of clustering object created by LCcluster().

dframe Name of data.frame containing X, trtm & Y variables.

trtm Name of treatment factor variable.

yvar Name of outcome Y variable.

K Number of Clusters Requested.

actclust Number of Clusters delivered.

LTDtabl data.frame with 5 columns and K rows for Clusters.

LTDtabl\$c Cluster ID Factor, "1", "2", ..., "K".

LTDtabl\$w Integer value of "weight" = Cluster Size.

LTDtab1\$LAO Numerical value of within-cluster Local Average Outcome (Y-value).

receiving trtm==1; $0.0 \le PS \le 1.0$.

LTDdist data.frame with 4 columns and same number of rows as the data: dframe.

LTDdist\$c.K Factor values within c("1", "2", ..., "K").

LTDdist\$y Numerical value of the Y-Outcome for an Experimental Unit.

LTDdist\$t Numerical value of trtm (0 or 1) for an Experimental Unit.

infoclus Integer value of Number of Informative Clusters.

infounits Integer value of Number of Units within Informative Clusters.

LTDmean Numerical value of mean(LTDdist\$LTD) = Weighted Average of LTDtabl\$LTD

values.

 $\label{eq:local_local_local_local} \mbox{LTDstde} \qquad \mbox{Numerical value of } \mbox{sqrt}(\mbox{var}(\mbox{LTDdist}\mbox{\$LTD})) = \mbox{Weighted Standard Deviation of } \mbox{}$

LTDtabl\$LTD values.

Author(s)

Bob Obenchain <wizbob@att.net>

mlme 17

References

Obenchain RL. (2010) Local Control Approach using JMP. Chapter 7 of **Analysis of Observational Health Care Data using SAS**, *Cary, NC:SAS Press*, pages 151-192.

Obenchain RL. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

See Also

```
ivadj, 1rcagg and LCcompare.
```

Examples

```
## Not run:
# Long running example...
data(pci15k)
  xvars <- c("stent", "height", "female", "diabetic", "acutemi", "ejfract", "ves1proc")
  hclobj <- LCcluster(pci15k, xvars)
  LCe <- LCsetup(hclobj, pci15k, thin, surv6mo)
  surv050 <- ltdagg(50, LCe)
  surv050
  plot(surv050, LCe)

## End(Not run)</pre>
```

mlme

Create a «Most-Like-Me» data.frame for a specified X-Confounder vector: xvec

Description

For a Given X-confounder Vector (xvec), sort all experimental units (eUnits) in an Itdagg() or Ircagg() output object into the strictly non-decreasing order of their distances from this X-Vector, which defines the TARGET eUnit: "Me". Plots of mlme() objects and displays of mlme.stats() are then used to Visualize and Summarize "Mini-" « LOCAL effect-size Distributions » for different Numbers of "Nearest Neighbor" eUnits.

Usage

```
mlme(envir, hcl, LCagg, xvec )
```

Arguments

envir	Environment output by a call to the LCsetup() function.
hcl	Name of a LCcluster() output object created using a cluster::diana or stats::hclust method.
LCagg	A data.frame object output by ltdagg() or lrcagg() containing LOCAL effect-size Estimates for eUnits within Clusters defined in X-covariate space.
xvec	A suitable vector of the Numerical values for the X-Confounder variables, used in the current CLUSTERING, that define the eUnit: "Me".

18 mlme

Details

For example, in demo(radon), the eUnits are 2881 US "Counties", and the LCagg object is of type lrcagg() because radon exposure is a continuous variable. But, in demo(pci15k), the eUnits are 15487 "Patients," and the LCagg object is of type ltdagg() because treatment choice (thin) is Binary (0 = "No", 1 = "Yes").

Value

An output list object of class mlme:

xvec The xvec vector input to mlme().

Type Either "LTD" or "LRC".

xvars Names of the X-Confounder variables specified in LCsetup().

varx The vector of Variances of the xvars variabes, used in rescaling distances.

outdf The output data.frame of sorted "Nearest Neighbor" candidate eUnits.

Author(s)

Bob Obenchain <wizbob@att.net>

References

Obenchain RL. LocalControlStrategy-vignette. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

See Also

```
plot.mlme,print.mlme,mlme.stats
```

Examples

```
## Not run:
# Long running example...
data(pci15k)
xvars <- c("stent", "height", "female", "diabetic", "acutemi", "ejfract", "ves1proc")
hclobj <- LCcluster(pci15k, xvars)
LC.env <- LCsetup(hclobj, pci15k, thin, surv6mo)
surv0500 <- ltdagg(500, LC.env)
xvec11870 <- c( 0, 162, 1, 1, 0, 57, 1)
mlmeC5H <- mlme(envir = LC.env, hcl = hclobj, LCagg = surv0500, xvec = xvec11870 )
plot(mlmeC5H) # using default "NN" and "breaks" settings...
## End(Not run)</pre>
```

mlme.stats 19

Pairs.	mlme.stats	Print Summary Statistics for One or More "Most-Like-Me" Histogram Pairs.
--------	------------	---

Description

Print Summary Statistics for Local effect-size (LTD or LRC) Distributions associated with given Numbers of "Nearest-Neighbors" in X-confounder Space.

Usage

```
mlme.stats(x, NN = 50, ...)
```

Arguments

x An object output by mlme.data().

NN Number(s) of "Nearest Neighbors" displayed in Histogram(s). NN can be either

a single integer like NN = 40 or a combination of integers like NN = c(50, 250,

2500).

. . . Other arguments passed on to print().

Value

NULL

Author(s)

Bob Obenchain <wizbob@att.net>

See Also

```
plot.mlme,print.mlme,mlme
```

pci15k	Six-month Survival,	Cardiac co	ost and	Baseline	Covariate	data for
	15,487 PCI patients.					

Description

Using observational data on 996 patients who received a Percutaneous Coronary Intervention (PCI) at Ohio Heart Health, Lindner Center, Christ Hospital, Cincinnati (Kereiakes et al, 2000), we generated this much larger dataset via "plasmode simulation."

Usage

```
data(pci15k)
```

20 plot.ivadj

Format

A data frame of 11 variables on 15,487 patients; no NAs.

patid Patient ID number: 1 to 15487.

surv6mo Binary PCI Survival variable: 1 => Survival for at least 6 months following PCI, 0 => Survival for less than 6 months.

cardcost Cardiac related costs incurred within 6 months of patient's initial PCI; numeric value in 1998 dollars; costs were truncated by death for the 404 patients with surv6mo == 0.

thin Numeric treatment selection indicator: thin = 0 implies usual PCI care alone; thin = 1 implies usual PCI care augmented by either planned or rescue treatment with a new blood thinning agent.

stent Coronary stent deployment; numeric, with 1 meaning YES and 0 meaning NO.

height Height in centimeters; numeric integer from 133 to 198.

female Female gender; numeric, with 1 meaning YES and 0 meaning NO.

diabetic Diabetes mellitus diagnosis; numeric, with 1 meaning YES and 0 meaning NO.

acutemi Acute myocardial infarction within the previous 7 days; numeric, with 1 meaning YES and 0 meaning NO.

ejfract Left ejection fraction; numeric value from 17 percent to 77 percent.

ves1proc Number of vessels involved in the patient's initial PCI procedure; numeric integer from 0 to 5.

References

Kereiakes DJ, Obenchain RL, Barber BL, et al. Abciximab provides cost effective survival advantage in high volume interventional practice. *Am Heart J* 2000; **140**: 603-610.

Gadbury GL, Xiang Q, Yang L, Barnes S, Page GP, Allison DB. Evaluating Statistical Methods Using Plasmode Data Sets in the Age of Massive Public Databases: An Illustration Using False Discovery Rates. *PLOS Genetics* 2008; **4**: 1-8, e1000098 (Open Access).

Obenchain RL. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

Examples

data(pci15k)
str(pci15k)

plot.ivadj Display an Instrumental Variable (LAO) plot with Linear and smooth.spline Fits

Description

For a given number of patient clusters, K, in baseline X-covariate space and a specified Y-outcome variable, display the distribution of Local Average Outcomes (LAOs) plotted versus Within-Cluster Propensity-like Scores: Treatment Selection Fractions or Relative Exposure Levels.

plot.lrcagg 21

Usage

```
## S3 method for class 'ivadj'
plot(x, maxsiz = 0.15, ...)
```

Arguments

An object output by ivadj() for K given Clusters in baseline X-covariate space.
 Radius of the Circle plotting symbol for the largest Cluster. Usually < 0.6
 Other arguments passed on to plot().

Value

NULL

Author(s)

Bob Obenchain <wizbob@att.net>

See Also

```
plot.ltdagg, plot.lrcagg
```

plot.lrcagg	Display Visualizations of an Observed LRC Distribution in Local Con-
	trol Strategy

Description

Display a Histogram, Box-Whisker Diagram and/or empirical Cumulative Distribution Function depicting the Observed Local Rank Correlation (LRC) Distribution across K Clusters.

Usage

```
## S3 method for class 'lrcagg'
plot(x, envir, show="all", breaks="Sturges", ...)
```

Arguments

X	An object output by $lrcagg()$ for $K = Number$ of Clusters in baseline X-covariate space.
envir	R environment output by a previous call to LCsetup().
show	Choice of "all", "seq", "hist", "boxp", or "ecdf".
breaks	Parameter setting for hist(); May be an integer valuelike 25 or 50.
	Other arguments passed on to plot().

22 plot.ltdagg

Value

NULL

Author(s)

Bob Obenchain <wizbob@att.net>

See Also

```
plot.ltdagg
```

plot.ltdagg	Display Visualizations of an Observed LTD Distribution in Local Con-
	trol Strategy

Description

Display a Histogram, Box-Whisker Diagram and/or empirical Cumulative Distribution Function depicting the Observed Local Treatment Difference (LTD) Distribution across K Clusters.

Usage

```
## S3 method for class 'ltdagg'
plot(x, envir, show="all", breaks="Sturges", ...)
```

Arguments

X	An object output by $ltdagg()$ for $K = Number$ of Clusters in baseline X-covariate
	space.
envir	R environment output by a previous call to LCsetup().
show	Choice of "all", "seq", "hist", "boxp", or "ecdf".
breaks	Parameter setting for hist(); May be an integer valuelike 25 or 50.
	Other arguments passed on to plot().

Value

NULL

Author(s)

Bob Obenchain <wizbob@att.net>

See Also

```
plot.lrcagg
```

plot.mlme 23

plot.mlme	Display a Pair (or Pairs) of Histograms showing LOCAL effect-sizes for Patients "Most-Like-Me".
	jor Panents Most-Like-Me .

Description

Display Pair(s) of Histograms of Local effect-size (LTD or LRC) Distributions for a specified Number (or combinations of Numbers) of "Nearest-Neighbors in X-confounder Space.

Usage

```
## S3 method for class 'mlme'
plot(x, NN=50, breaks=50, ...)
```

Arguments

V	An object output by mlme()	١
Λ	All object output by million	,.

NN Number(s) of Nearest Neighbors displayed in Bottom Histogram(s). NN can be

a single integer like NN = 40 or a combination of integers like NN = c(50, 250,

2500).

breaks Integer number of breaks in the Top Histogram for the full LTD or LRC distribu-

tion. Because the Bottom Histogram may include only a few Nearest Neighbors,

it is always displayed using breaks = "Sturges".

... Other arguments passed on to plot().

Value

NULL

Author(s)

Bob Obenchain <wizbob@att.net>

See Also

```
mlme.stats,print.mlme,mlme
```

24 radon

print.mlme	Print Summary Statistics on Local effect-size Estimates for Patients "Most-Like-Me".

Description

Display "Most-Like-Me" Summary Statistics for LOCAL effect-size (LTD or LRC) Distributions of "Nearest-Neighbors" in X-confounder Space.

Usage

```
## S3 method for class 'mlme'
print(x, ...)
```

Arguments

x An object output by mlme().

... Other arguments passed on to print().

Value

NULL

Author(s)

Bob Obenchain <wizbob@att.net>

See Also

```
mlme.stats,plot.mlme,mlme
```

radon

Radon exposure and lung cancer mortality data for 2,881 US counties in 46 States.

Description

Federal EPA and state government agencies have been reporting observational data at the US County level since about 1980. The data given here include 5 potential X-confounder variables of the relationship between lung cancer mortality and radon exposure; they were amassed and checked by Goran Krstic, Fraser Health Authority, Vancouver, BC, Canada.

Usage

```
data(radon)
```

reveal.data 25

Format

A data frame of 11 variables for 2881 US counties. One Missing Value; row 778 for Shannon County, SD, fips == 46113, has hhincome == NA.

fips County FIPS code. Codes are 4 or 5 digit integers; 2881 unique values.

state State Factor variable (2-character codes); 46 unique levels.

county County or Parish Factor variable (character codes); 1703 unique levels.

Icanmort Lung Cancer Mortality rate (deaths per 100,000 person-years), 1980-2004.

radon County Radon Exposure level in picocuries per liter (pCi/L) for some unspecified period within 1986-1992; rounded to nearest single decimal place.

Inradon Natural logarithm of County Radon Exposure level. Radon levels reported as 0.0 for 10 US counties are Windsorized here to ln(0.05), which is roughly -3.

obesity Percentage of County Residents considered Obese (age adjusted), 2008.

over65 Percentage of County Residents of Age 65 and over, 2000 Census.

cursmoke Percentage of County Residents who Currently Smoke, 1997-2003.

evrsmoke Percentage of County Residents who Ever Smoked, 1997-2003.

hhincome Average Median HouseHold Income in Thousands (\$1,000), 1989-2004.

References

Krstic G, Obenchain RL. (2016) Radon dataset documentation and downloads. http://localcontrolstatistics.org Obenchain RL. (2018) **RADON_short.pdf** http://localcontrolstatistics.org 40 PPT Slides and Commentary in Notes Pages format.

Examples

data(radon)
str(radon)

reveal.data

Create a data.frame for use in Prediction of a LTD/LRC effect-size Distribution

Description

reveal.data() forms a data.frame by sorting and appending the LTD or LRC treatment effect-size measures from ltdagg() or lrcagg() – as well as a Cluster membership-number variable – to a copy of the data.frame specified in LCsetup(). In the fourth and final REVEAL Phase of Local Control Strategy, a stretch-goal is to predict variation in LTD/LRC effect-size distributions using the known (baseline) X-covariate characteristics of experimental units. For example, the data.frame output by reveal.data() is suitable for input to party::ctree() as well as to a number of other "less Visual" prediction methods available in **R**.

26 reveal.data

Usage

```
reveal.data(x, clus.var="Clus", effe.var="eSiz")
```

Arguments

x An output object resulting from a call to ltdagg() or lrcagg().

clus.var Quoted NAME for the Cluster-Number variable.

effe.var Quoted NAME for the LTD/LRC effect-size variable.

Value

The desired data.frame:

outdf A data.frame containing clus.var, effe.var plus (X, trex & Y) variables.

Author(s)

Bob Obenchain <wizbob@att.net>

References

Obenchain RL. (2019) LCstrategy_in_R.pdf http://localcontrolstatistics.org

See Also

1tdagg, 1rcagg, and LCsetup.

Index

```
*Topic cluster
                                                  pci15k, 19
    LCcluster, 9
                                                  plot.ivadj, 20
*Topic datasets
                                                  plot.lrcagg, 21, 21, 22
    pci15k, 19
                                                  plot.ltdagg, 21, 22, 22
    radon, 24
                                                  plot.mlme, 18, 19, 23, 24
*Topic design
                                                  print.mlme, 18, 19, 23, 24
    LCcluster, 9
                                                  radon, 24
    LCsetup, 12
                                                  reveal.data, 25
*Topic methods
    mlme.stats, 19
    plot.ivadj, 20
    plot.lrcagg, 21
    plot.ltdagg, 22
    plot.mlme, 23
    print.mlme, 24
*Topic nonparametric
    confirm, 4
    ivadj, 6
    KSperm, 7
    1rcagg, 13
    1tdagg, 15
    mlme, 17
*Topic package
    LocalControlStrategy-package, 2
confirm, 4, 8
ivadj, 6, 11, 13, 15, 17
KSperm, 7
LCcluster, 9
LCcompare, 7, 10, 15, 17
LCsetup, 10, 12, 26
LocalControlStrategy-package, 2
lrcagg, 6–8, 10, 11, 13, 13, 17, 26
1tdagg, 6–8, 10, 11, 13, 15, 15, 26
mlme, 17, 19, 23, 24
mlme.stats, 18, 19, 23, 24
```