

Package: simml (via r-universe)

September 3, 2024

Type Package

Title Single-Index Models with Multiple-Links

Version 0.3.0

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Description A major challenge in estimating treatment decision rules from a randomized clinical trial dataset with covariates measured at baseline lies in detecting relatively small treatment effect modification-related variability (i.e., the treatment-by-covariates interaction effects on treatment outcomes) against a relatively large non-treatment-related variability (i.e., the main effects of covariates on treatment outcomes). The class of Single-Index Models with Multiple-Links is a novel single-index model specifically designed to estimate a single-index (a linear combination) of the covariates associated with the treatment effect modification-related variability, while allowing a nonlinear association with the treatment outcomes via flexible link functions. The models provide a flexible regression approach to developing treatment decision rules based on patients' data measured at baseline. We refer to Park, Petkova, Tarpey, and Ogden (2020) <[doi:10.1016/j.jspi.2019.05.008](https://doi.org/10.1016/j.jspi.2019.05.008)> and Park, Petkova, Tarpey, and Ogden (2020) <[doi:10.1111/biom.13320](https://doi.org/10.1111/biom.13320)> (that allows an unspecified X main effect) for detail of the method. The main function of this package is `simml()`.

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Imports mgcv

Encoding UTF-8

RoxygenNote 6.1.1

NeedsCompilation no

Repository CRAN

Date/Publication 2021-05-25 06:50:02 UTC

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der.link	<i>A subfunction used in estimation</i>
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Description

This function computes the 1st derivative of the treatment-specific link function with respect to the single index, using finite difference.

Usage

```
der.link(g.fit, eps = 10-6)
```

Arguments

<code>g.fit</code>	a <code>mgcv::gam</code> object
<code>eps</code>	a small finite difference used in numerical differentiation.

See Also

`fit.simml`, `simml`

fit.simml	<i>Single-index models with multiple-links (workhorse function)</i>
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Description

`fit.simml` is the workhorse function for Single-index models with multiple-links (SIMML). The function estimates a linear combination (a single-index) of covariates X , and models the treatment-specific outcome y , via treatment-specific nonparametrically-defined link functions.

Usage

```
fit.simml(y, A, X, Xm = NULL, aug = NULL, rho = 0,
  family = "gaussian", R = NULL, bs = "ps", k = 8, sp = NULL,
  linear.link = FALSE, method = "GCV.Cp", gamma = 1, max.iter = 20,
  eps.iter = 0.01, trace.iter = TRUE, ind.to.be.positive = NULL,
  scale.si.01 = FALSE, lambda = 0, pen.order = 0, scale.X = TRUE,
  center.X = TRUE, ortho.constr = TRUE, beta.ini = NULL,
  si.main.effect = FALSE, random.effect = FALSE, z = NULL,
  plots = FALSE)
```

Arguments

y	a n-by-1 vector of treatment outcomes; y is a member of the exponential family; any distribution supported by <code>mgcv::gam</code> ; y can also be an ordinal categorical response with R categories taking a value from 1 to R.
A	a n-by-1 vector of treatment variable; each element is assumed to take a value on a continuum.
X	a n-by-p matrix of baseline covarates.
Xm	a n-by-q design matrix associated with an X main effect model; the default is NULL and it is taken as a vector of zeros
aug	a n-by-1 additional augmentation vector associated with the X main effect; the default is NULL and it is taken as a vector of zeros
rho	a tuning parameter associated with the additional augmentation vector aug; the default is 0.
family	specifies the distribution of y; e.g., "gaussian", "binomial", "poisson"; can be any family supported by <code>mgcv::gam</code> ; can also be "ordinal", for an ordinal categorical response y.
R	the number of response categories for the case of family = "ordinal".
bs	basis type for the treatment (A) and single-index domains, respectively; the default is "ps" (p-splines); any basis supported by <code>mgcv::gam</code> can be used, e.g., "cr" (cubic regression splines); see <code>mgcv::s</code> for detail.
k	basis dimension for the treatment (A) and single-index domains, respectively.
sp	smoothing paramter for the treatment-specific link functions; if NULL, then estimated from the data.
linear.link	if TRUE, the link function is restricted to be linear.
method	the smoothing parameter estimation method; "GCV.Cp" to use GCV for unknown scale parameter and Mallows' Cp/UBRE/AIC for known scale; any method supported by <code>mgcv::gam</code> can be used.
gamma	increase this beyond 1 to produce smoother models. gamma multiplies the effective degrees of freedom in the GCV or UBRE/AIC (see <code>mgcv::gam</code> for detail); the default is 1.
max.iter	an integer specifying the maximum number of iterations for beta.coef update.
eps.iter	a value specifying the convergence criterion of algorithm.

<code>trace.iter</code>	if TRUE, trace the estimation process and print the differences in <code>beta.coef</code> .
<code>ind.to.be.positive</code>	for identifiability of the solution <code>beta.coef</code> , the user can restrict the j th (e.g., $j=1$) component of <code>beta.coef</code> to be positive; by default, we match the "overall" sign of <code>beta.coef</code> with that of the linear estimate (i.e., the initial estimate), by restricting the inner product between the two to be positive.
<code>scale.si.01</code>	if TRUE, re-scale the index coefficients to restrict the index to the interval $[0,1]$; in such a case, an intercept term is induced.
<code>lambda</code>	a regularization parameter associated with the penalized LS for <code>beta.coef</code> update.
<code>pen.order</code>	0 indicates the ridge penalty; 1 indicates the 1st difference penalty; 2 indicates the 2nd difference penalty, used in a penalized least squares (LS) estimation of <code>beta.coef</code> .
<code>scale.X</code>	if TRUE, scale X to have unit variance.
<code>center.X</code>	if TRUE, center X to have zero mean.
<code>ortho.constr</code>	separates the interaction effects from the main effect (without this, the interaction effect can be confounded by the main effect; the default is TRUE).
<code>beta.ini</code>	an initial value for <code>beta.coef</code> ; a p -by-1 vector; the default is NULL, in which case a linear model estimate is used.
<code>si.main.effect</code>	if TRUE, once the convergence in the estimates of <code>beta.coef</code> is reached, include the main effect associated with the fitted single-index ($\text{beta.coef}'X$) to the final fit; the default is FALSE.
<code>random.effect</code>	if TRUE, as part of the main effects, the user can incorporate z -specific random intercepts.
<code>z</code>	a factor that specifies the random intercepts when <code>random.effect = TRUE</code> .
<code>plots</code>	if TRUE, produce a plot for the estimated effect contrast (for binary treatment cases) (on a linear predictor scale).

Details

SIMML captures the effect of covariates via a single-index and their interaction with the treatment via nonparametric link functions. Interaction effects are determined by distinct shapes of the link functions. The estimated single-index is useful for comparing differential treatment efficacy. The resulting `simml` object can be used to estimate an optimal treatment decision rule for a new patient with pretreatment clinical information.

Value

a list of information of the fitted SIMML including

<code>beta.coef</code>	the estimated single-index coefficients.
<code>g.fit</code>	a <code>mgcv:gam</code> object containing information about the estimated treatment-specific link functions.
<code>beta.ini</code>	the initial value used in the estimation of <code>beta.coef</code>
<code>beta.path</code>	solution path of <code>beta.coef</code> over the iterations

d.beta	records the change in beta.coef over the solution path, beta.path
scale.X	sd of pretreatment covariates X
center.X	mean of pretreatment covariates X
L	number of different treatment options
p	number of pretreatment covariates X
n	number of subjects
boot.ci	(1-boot.alpha/2) percentile bootstrap CIs (LB, UB) associated with beta.coef

Author(s)

Park, Petkova, Tarpey, Ogden

See Also

pred.simml, simml

generate.data	<i>A data generation function</i>
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Description

generate.data generates an example dataset from a mean model that has a "main" effect component and a treatment-by-covariates interaction effect component (and a random component for noise).

Usage

```
generate.data(n = 200, p = 10, family = "gaussian",
  correlationX = 0, sigmaX = 1, sigma = 0.4, s = 2, delta = 1,
  pi.1 = 0.5, true.beta = NULL, true.eta = NULL)
```

Arguments

n	sample size.
p	dimension of covariates.
family	specifies the distribution of the outcome y; "gaussian", "binomial", "poisson"; the default is "gaussian"
correlationX	correlation among the covariates.
sigmaX	standard deviation of the covariates.
sigma	standard deviation of the random noise term (for gaussian response).
s	controls the nonliarity of the treatment-specific link functions that define the interaction effect component.
	s=1 linear

	s=2 nonlinear
delta	controls the intensity of the main effect; can take any intermediate value, e.g., delta= 1.4. delta=1 moderate main effect delta=2 big main effect
pi.1	probability of being assigned to the treatment 1
true.beta	a p-by-1 vector of the true single-index coefficients (associated with the interaction effect component); if NULL, true.beta is set to be (1, 0.5, 0.25, 0.125, 0, ... 0)' (only the first 4 elements are nonzero).
true.eta	a p-by-1 vector of the true main effect coefficients; if NULL, true.eta is set to be (0, ..., 0.125, 0.25, 0.25, 1)' (only the last 4 elements are nonzero).

Value

y	a n-by-1 vector of treatment outcomes.
A	a n-by-1 vector of treatment indicators.
X	a n-by-p matrix of pretreatment covariates.
SNR	the "signal" (interaction effect) to "nuisance" (main effect) variance ratio (SNR) in the canonical parameter function.
true.beta	the true single-index coefficient vector.
true.eta	the true main effect coefficient vector.
optTr	a n-by-1 vector of treatments, indicating the optimal treatment selections.
value.opt	the "value" implied by the optimal treatment decision rule, optTr.

ordinal.data

*A function for ordinal categorical response data generation.***Description**

ordinal.data generates ordered category response data (with p covariates and a treatment variable).

Usage

```
ordinal.data(n = 400, p = 10, R = 11, delta = 1, s = "nonlinear",
            sigma = 0)
```

Arguments

n	sample size.
p	dimension of covariates.
R	number of response levels in y
delta	magnitude of "main" effect (i.e., "nuisance" effect) of the covariates; a large delta means a larger "nuisance" variance.
s	type of the treatment-by-covariates interaction effect ("linear" or "nonlinear")
sigma	noise sd in the latent variable representation

Value

y	a n-by-1 vector of treatment outcomes.
A	a n-by-1 vector of treatment indicators.
X	a n-by-p matrix of pretreatment covariates.
SNR	the "signal" (interaction effect) to "nuisance" (main effect) variance ratio (SNR) in the canonical parameter function.
true.beta	the true single-index coefficient vector.
delta	magnitude of "main" effect.
s	type of the treatment-by-covariates interaction effect.

pred.simml	<i>SIMML prediction function</i>
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Description

This function makes predictions from an estimated SIMML, given a (new) set of pretreatment covariates. The function returns a set of predicted outcomes for each treatment condition and a set of recommended treatment assignments (assuming a larger value of the outcome is better).

Usage

```
pred.simml(simml.obj, newX = NULL, newA = NULL, newXm = NULL,
  single.index = NULL, type = "link", maximize = TRUE)
```

Arguments

simml.obj	a simml object
newX	a (n-by-p) matrix of new values for the covariates X at which predictions are to be made.
newA	a (n-by-L) matrix of new values for the treatment A at which predictions are to be made.
newXm	a (n-by-q) matrix of new values for the covariates associated with the fitted main effect Xm at which predictions are to be made.
single.index	a length n vector specifying new values for the single-index at which predictions are to be made; the default is NULL.
type	the type of prediction required; the default "response" is on the scale of the response variable; the alternative "link" is on the scale of the linear predictors.
maximize	the default is TRUE, assuming a larger value of the outcome is better; if FALSE, a smaller value is assumed to be preferred.

Value

pred.new	a (n-by-L) matrix of predicted values; each column represents a treatment option.
trt.rule	a (n-by-1) vector of suggested treatment assignments

Author(s)

Park, Petkova, Tarpey, Ogden

See Also

simml, fit.simml

simml

Single-index models with multiple-links (main function)

Description

simml is the wrapper function for Single-index models with multiple-links (SIMML). The function estimates a linear combination (a single-index) of covariates X , and models the treatment-specific outcome y , via treatment-specific nonparametrically-defined link functions.

Usage

```
simml(y, A, X, Xm = NULL, aug = NULL, family = "gaussian",
      R = NULL, bs = "cr", k = 8, sp = NULL, linear.link = FALSE,
      method = "GCV.Cp", gamma = 1, rho = 0, beta.ini = NULL,
      ind.to.be.positive = NULL, scale.si.01 = FALSE, max.iter = 20,
      eps.iter = 0.01, trace.iter = TRUE, lambda = 0, pen.order = 0,
      scale.X = TRUE, center.X = TRUE, ortho.constr = TRUE,
      si.main.effect = FALSE, random.effect = FALSE, z = NULL,
      plots = FALSE, bootstrap = FALSE, nboot = 200, boot.conf = 0.95,
      seed = 1357)
```

Arguments

<code>y</code>	a n -by-1 vector of treatment outcomes; y is a member of the exponential family; any distribution supported by <code>mgcv::gam</code> ; y can also be an ordinal categorical response with R categories taking a value from 1 to R .
<code>A</code>	a n -by-1 vector of treatment variable; each element is assumed to take a value in a finite discrete space.
<code>X</code>	a n -by- p matrix of baseline covariates.
<code>Xm</code>	a n -by- q design matrix associated with an X main effect model; the default is <code>NULL</code> and it is taken as a vector of zeros
<code>aug</code>	a n -by-1 additional augmentation vector associated with the X main effect; the default is <code>NULL</code> and it is taken as a vector of zeros
<code>family</code>	specifies the distribution of y ; e.g., "gaussian", "binomial", "poisson"; can be any family supported by <code>mgcv::gam</code> ; can also be "ordinal", for an ordinal categorical response y .
<code>R</code>	the number of response categories for the case of <code>family = "ordinal"</code> .

<code>bs</code>	basis type for the treatment (A) and single-index joint effect; the default is "ps" (p-splines); any basis supported by <code>mgcv : : gam</code> can be used, e.g., "cr" (cubic regression splines); see <code>mgcv : : s</code> for detail.
<code>k</code>	basis dimension for the spline-type-represented treatment-specific link functions.
<code>sp</code>	smoothing parameter for the treatment-specific link functions; if NULL, then estimated from the data.
<code>linear.link</code>	if TRUE, the link function is restricted to be linear.
<code>method</code>	the smoothing parameter estimation method; "GCV.Cp" to use GCV for unknown scale parameter and Mallows' Cp/UBRE/AIC for known scale; any method supported by <code>mgcv : : gam</code> can be used.
<code>gamma</code>	increase this beyond 1 to produce smoother models. <code>gamma</code> multiplies the effective degrees of freedom in the GCV or UBRE/AIC (see <code>mgcv : : gam</code> for detail); the default is 1.
<code>rho</code>	a tuning parameter associated with the additional augmentation vector <code>aug</code> ; the default is 0.
<code>beta.ini</code>	an initial value for <code>beta.coef</code> ; a p-by-1 vector; the default is NULL, in which case a linear model estimate is used.
<code>ind.to.be.positive</code>	for identifiability of the solution <code>beta.coef</code> , the user can restrict the <code>j</code> th (e.g., <code>j=1</code>) component of <code>beta.coef</code> to be positive; by default, we match the "overall" sign of <code>beta.coef</code> with that of the linear estimate (i.e., the initial estimate), by restricting the inner product between the two to be positive.
<code>scale.si.01</code>	if TRUE, re-scale the index coefficients to restrict the index to the interval [0,1]; in such a case, an intercept term is induced.
<code>max.iter</code>	an integer specifying the maximum number of iterations for <code>beta.coef</code> update.
<code>eps.iter</code>	a value specifying the convergence criterion of algorithm.
<code>trace.iter</code>	if TRUE, trace the estimation process and print the differences in <code>beta.coef</code> .
<code>lambda</code>	a regularization parameter associated with the penalized LS for <code>beta.coef</code> update; the default is 0, and the index coefficients are not penalized.
<code>pen.order</code>	0 indicates the ridge penalty; 1 indicates the 1st difference penalty; 2 indicates the 2nd difference penalty, used in a penalized least squares (LS) estimation of <code>beta.coef</code> .
<code>scale.X</code>	if TRUE, scale <code>X</code> to have unit variance.
<code>center.X</code>	if TRUE, center <code>X</code> to have zero mean.
<code>ortho.constr</code>	separates the interaction effects from the main effect (without this, the interaction effect can be confounded by the main effect; the default is TRUE).
<code>si.main.effect</code>	if TRUE, once the convergence in the estimates of <code>beta.coef</code> is reached, include the main effect associated with the fitted single-index (<code>beta.coef'X</code>) to the final fit; the default is FALSE.
<code>random.effect</code>	if TRUE, as part of the main effects, the user can incorporate z-specific random intercepts.
<code>z</code>	a factor that specifies the random intercepts when <code>random.effect = TRUE</code> .

<code>plots</code>	if TRUE, produce a plot for the estimated effect contrast (for binary treatment cases) (on a linear predictor scale).
<code>bootstrap</code>	if TRUE, compute bootstrap confidence intervals for the single-index coefficients, <code>beta.coef</code> ; the default is FALSE.
<code>nboot</code>	when <code>bootstrap=TRUE</code> , a value specifying the number of bootstrap replications.
<code>boot.conf</code>	a value specifying the confidence level of the bootstrap confidence intervals; the default is <code>boot.conf = 0.95</code> .
<code>seed</code>	when <code>bootstrap=TRUE</code> , randomization seed used in bootstrap resampling.

Details

SIMML captures the effect of covariates via a single-index and their interaction with the treatment via nonparametric link functions. Interaction effects are determined by distinct shapes of the link functions. The estimated single-index is useful for comparing differential treatment efficacy. The resulting `simml` object can be used to estimate an optimal treatment decision rule for a new patient with pretreatment clinical information.

Value

a list of information of the fitted SIMML including

<code>beta.coef</code>	the estimated single-index coefficients.
<code>g.fit</code>	a <code>mgcv:gam</code> object containing information about the estimated treatment-specific link functions.
<code>beta.ini</code>	the initial value used in the estimation of <code>beta.coef</code>
<code>beta.path</code>	solution path of <code>beta.coef</code> over the iterations
<code>d.beta</code>	records the change in <code>beta.coef</code> over the solution path, <code>beta.path</code>
<code>scale.X</code>	sd of pretreatment covariates X
<code>center.X</code>	mean of pretreatment covariates X
<code>L</code>	number of different treatment options
<code>p</code>	number of pretreatment covariates X
<code>n</code>	number of subjects
<code>boot.ci</code>	($1-\text{boot.alpha}/2$) percentile bootstrap CIs (LB, UB) associated with <code>beta.coef</code>

Author(s)

Park, Petkova, Tarpey, Ogden

See Also

`pred.simml`, `fit.simml`

Examples

```

family <- "gaussian" # "poisson"
delta = 1           # moderate main effect
s=2                # if s=2 (s=1), a nonlinear (linear) contrast function
n=500              # number of subjects
p=10               # number of pretreatment covariates

# generate training data
data <- generate.data(n= n, p=p, delta = delta, s= s, family = family)
data$SNR # the ratio of interactions("signal") vs. main effects("noise")
A <- data$A
y <- data$y
X <- data$X

# generate testing data
data.test <- generate.data(n=10^5, p=p, delta = delta, s= s, family = family)
A.test <- data.test$A
y.test <- data.test$y
X.test <- data.test$X
data.test$value.opt # the optimal "value"

# fit SIMML
#1) SIMML without X main effect
simml.obj1 <- simml(y, A, X, family = family)

#2) SIMML with X main effect (estimation efficiency for the g term of SIMML can be improved)
simml.obj2 <- simml(y, A, X, Xm = X, family = family)

# apply the estimated SIMML to the testing set and obtain treatment assignment rules.
simml.trt.rule1 <- pred.simml(simml.obj1, newX= X.test)$trt.rule
# "value" estimation (estimated by IPWE)
simml.value1 <- mean(y.test[simml.trt.rule1 == A.test])
simml.value1

simml.trt.rule2 <- pred.simml(simml.obj2, newX= X.test)$trt.rule
simml.value2 <- mean(y.test[simml.trt.rule2 == A.test])
simml.value2

# compare these to the optimal "value"
data.test$value.opt

# fit MC (modified covariates) model of Tien et al 2014
n.A <- summary(as.factor(A)); pi.A <- n.A/sum(n.A)
mc <- (as.numeric(A) + pi.A[1] -2) *cbind(1, X) # 0.5*(-1)^as.numeric(A) *cbind(1, X)
mc.coef <- coef(glm(y ~ mc, family = family))
mc.trt.rule <- (cbind(1, X.test) %*% mc.coef[-1] > 0) +1
# "value" estimation (estimated by IPWE)

```

```

mc.value <- mean(y.test[mc.trt.rule == A.test])
mc.value

# visualization of the estimated link functions of SIMML
simml.obj1$beta.coef      # estimated single-index coefficients
g.fit <- simml.obj1$g.fit # estimated trt-specific link functions; "g.fit" is a mgcv::gam object.
#plot(g.fit)

# can improve visualization by using the package "mgcViz"
#install.packages("mgcViz")
# mgcViz depends on "rgl". "rgl" depends on XQuartz, which you can download from xquartz.org
#library(mgcViz)
# transform the "mgcv::gam" object to a "mgcViz" object (to improve visualization)
g.fit <- getViz(g.fit)

plot1 <- plot( sm(g.fit,1) ) # for treatment group 1
plot1 + l_fitLine(colour = "red") + l_rug(mapping = aes(x=x, y=y), alpha = 0.8) +
  l_ciLine(mul = 5, colour = "blue", linetype = 2) +
  l_points(shape = 19, size = 1, alpha = 0.1) +
  xlab(expression(paste("z = ", alpha*minute, "x"))) + ylab("y") +
  ggtitle("Treatment group 1 (Trt =1)") + theme_classic()

plot2 <- plot( sm(g.fit,2) ) # for treatment group 2
plot2 + l_fitLine(colour = "red") + l_rug(mapping = aes(x=x, y=y), alpha = 0.8) +
  l_ciLine(mul = 5, colour = "blue", linetype = 2) +
  l_points(shape = 19, size = 1, alpha = 0.1) +
  xlab(expression(paste("z = ", alpha*minute, "x"))) + ylab("y") +
  ggtitle("Treatment group 2 (Trt =2)") + theme_classic()

trans = function(x) x + g.fit$coefficients[2]
plotDiff(s1 = sm(g.fit, 2), s2 = sm(g.fit, 1), trans=trans) + l_ciPoly() +
  l_fitLine() + geom_hline(yintercept = 0, linetype = 2) +
  xlab(expression(paste("z = ", alpha*minute, "x"))) +
  ylab("(Treatment 2 effect) - (Treatment 1 effect)") +
  ggtitle("Contrast between two treatment effects") +
  theme_classic()

# yet another way of visualization, using ggplot2
#library(ggplot2)
dat <- data.frame(y= simml.obj1$g.fit$model$y,
                  x= simml.obj1$g.fit$model$single.index,
                  Treatment= simml.obj1$g.fit$model$A)
g.plot<- ggplot(dat, aes(x=x,y=y,color=Treatment,shape=Treatment,linetype=Treatment))+
  geom_point(aes(color=Treatment, shape=Treatment), size=1, fill="white") +
  scale_colour_brewer(palette="Set1", direction=-1) +
  xlab(expression(paste(beta*minute, "x"))) + ylab("y")
g.plot + geom_smooth(method=gam, formula= y~ s(x, bs=simml.obj1$bs, k=simml.obj1$k),
                    se=TRUE, fullrange=TRUE, alpha = 0.35)

```

```

# can obtain bootstrap CIs for beta.coef.
simml.obj <- simml(y,A,X,Xm=X, family=family,bootstrap=TRUE,nboot=15) #nboot=500.
simml.obj$beta.coef
round(simml.obj$boot.ci,3)

# compare the estimates to the true beta.coef.
data$true.beta

# an application to data with ordinal categorical response
dat <- ordinal.data(n=500, p=5, R = 11, # 11 response levels
                    s = "nonlinear", # nonlinear interactions
                    delta = 1)
dat$SNR
y <- dat$y # ordinal response
X <- dat$X # X matrix
A <- dat$A # treatment
dat$true.beta # the "true" single-index coefficient

# 1) fit a cumulative logit simml, with a flexible link function
res <- simml(y,A,X, family="ordinal", R=11)
res$beta.coef # single-index coefficients.
res$g.fit$family$getTheta(TRUE) # the estimated R-1 threshold values.

# 2) fit a cumulative logit simml, with a linear link function
res2 <- simml(y,A,X, family="ordinal", R=11, linear.link = TRUE)
res2$beta.coef # single-index coefficients.

family = mgcv::ocat(R=11) # ocat: ordered categorical response family, with R categories.
# the treatment A's effect.
tmp <- mgcv::gam(y ~ A, family =family)
exp(coef(tmp)[2]) #odds ratio (OR) comparing treatment A=2 vs. A=1.

ind2 <- pred.simml(res)$trt.rule ==2 # subgroup recommended with A=2 under SIMML ITR
tmp2 <- mgcv::gam(y[ind2] ~ A[ind2], family = family)
exp(coef(tmp2)[2]) #OR comparing treatment A=2 vs. A=1, for subgroup recommended with A=2

ind1 <- pred.simml(res)$trt.rule ==1 # subgroup recommended with A=1 under SIMML ITR
tmp1 <- mgcv::gam(y[ind1] ~ A[ind1], family = family)
exp(coef(tmp1)[2]) #OR comparing treatment A=2 vs. A=1, for subgroup recommended with A=2

```

Index

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