

Introduction to dtametaTMB

This vignette introduces the main functionality of the `dtametaTMB` package for meta-analysis of diagnostic test accuracy (DTA) studies. We demonstrate how to fit three commonly used models:

- the Reitsma bivariate model
- the Rutter and Gatsonis (HSROC) model
- the Hoyer model for multiple thresholds

using real datasets included in the package.

Subgroup analyses, meta-regression, and latent class analysis allowing for an imperfect reference standard are covered in separate vignettes.

Note: Rendering forest plots via `forest` may take longer in an interactive R session due to the underlying grid graphics. Performance is typically faster when knitting the vignette (e.g. via RMarkdown or Quarto).

How do I load the package?

```
#install.packages("dtametaTMB")  
library(dtametaTMB)
```

Which model should I use?

- **Reitsma model:** single threshold per study: use when studies apply similar thresholds.
- **Rutter and Gatsonis model:** single threshold per study: use when thresholds vary between studies
- **Hoyer model:** multiple thresholds per study

The Reitsma and Rutter-Gatsonis model classes support parameter constraints for simplified analyses and sparse datasets.

Validation

The implementations reproduce benchmark results from the Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy (including parameter estimates, standard errors, and graphical outputs) for standard datasets such as the Anti-CCP and RF examples.

How do I use the Reitsma model?

Unlike the `mada` package, `dtametaTMB` uses the binomial likelihood to model the within study distribution as recommended by The Cochrane Handbook.

For sensitivity in study i , we have the number of diseased individuals testing positive: $y_{Ai} \sim \mathcal{B}(n_{Ai}, \pi_{Ai})$.

Similarly for specificity, we have the number of non-diseased individuals testing negative: $y_{Bi} \sim \mathcal{B}(n_{Bi}, \pi_{Bi})$.

At the study level, we have

$$\begin{pmatrix} \text{logit}(\pi_{Ai}) \\ \text{logit}(\pi_{Bi}) \end{pmatrix} = \begin{pmatrix} \mu_{Ai} \\ \mu_{Bi} \end{pmatrix} \sim \mathcal{N} \left(\begin{pmatrix} \mu_A \\ \mu_B \end{pmatrix}, \Sigma \right), \quad \text{with} \quad \Sigma = \begin{pmatrix} \sigma_A^2 & \sigma_{AB} \\ \sigma_{AB} & \sigma_B^2 \end{pmatrix}.$$

```
data("anticcp")
reitsma <- fitReitsma(data=anticcp,
                     TP=TP,
                     FP=FP,
                     FN=FN,
                     TN=TN,
                     study=study)

reitsma
#>
#> Reitsma Model
#> -----
#>
#> Number of studies : 37
#> Optimizer          : Converged
#> Hessian            : Positive definite
#> Max |grad|         : 0.0001136795
#> -2 log likelihood  : 545.56 ( df = 5 )
#> AIC                : 555.56
#> BIC                : 563.614
#>
#> mu_A (logitsens)   : 0.653
```

```

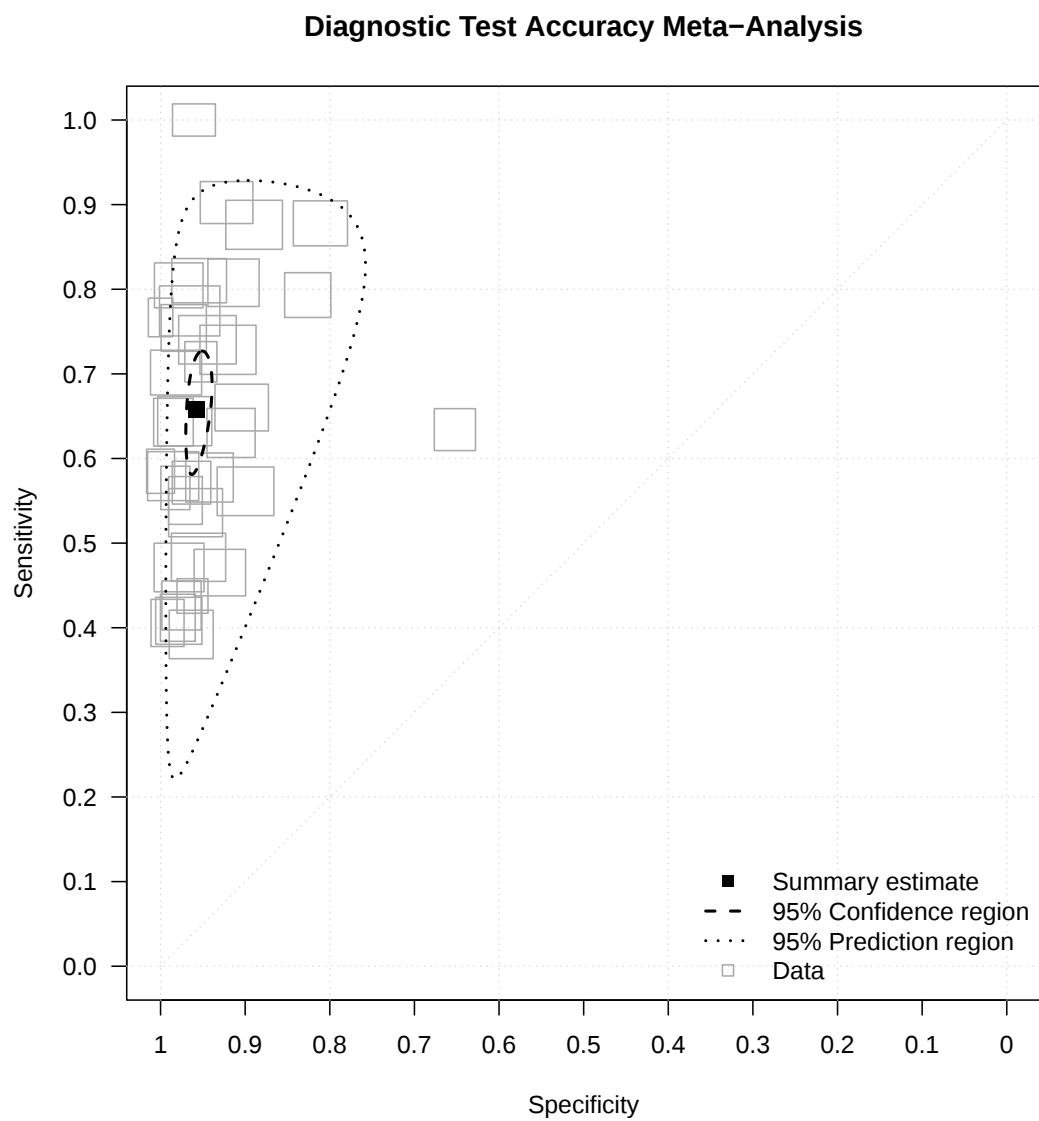
#> mu_B (logitspec) : 3.109
#>
#> Use summary() for parameter estimates.
summary(reitsma)
#>
#> Summary: Reitsma Model
#> -----
#>
#> Parameter estimates
#> -----
#>
#> Estimate Std_Error
#> mu_A.sens 0.65340288 0.12748659
#> mu_B.spec 3.10899060 0.14588466
#> sigma2_A.sens 0.54263975 0.14634780
#> sigma2_B.spec 0.57170193 0.18732112
#> sigma_AB -0.27041482 0.11985200
#>
#> Sensitivity / specificity
#> -----
#>
#> Estimate conflevel CI_Lower CI_Upper
#> sens 0.65777688 0.95 0.59953639 0.71162144
#> spec 0.95726208 0.95 0.94390940 0.96754537
#>
#> Recovered HSR0C parameters (Rutter-Gatsonis)
#> -----
#>
#> Lambda Theta beta sigma2_alpha sigma2_theta
#> Estimate (recovered) 3.7306844 -1.2033611 0.026086047 0.573133 0.41369807

```

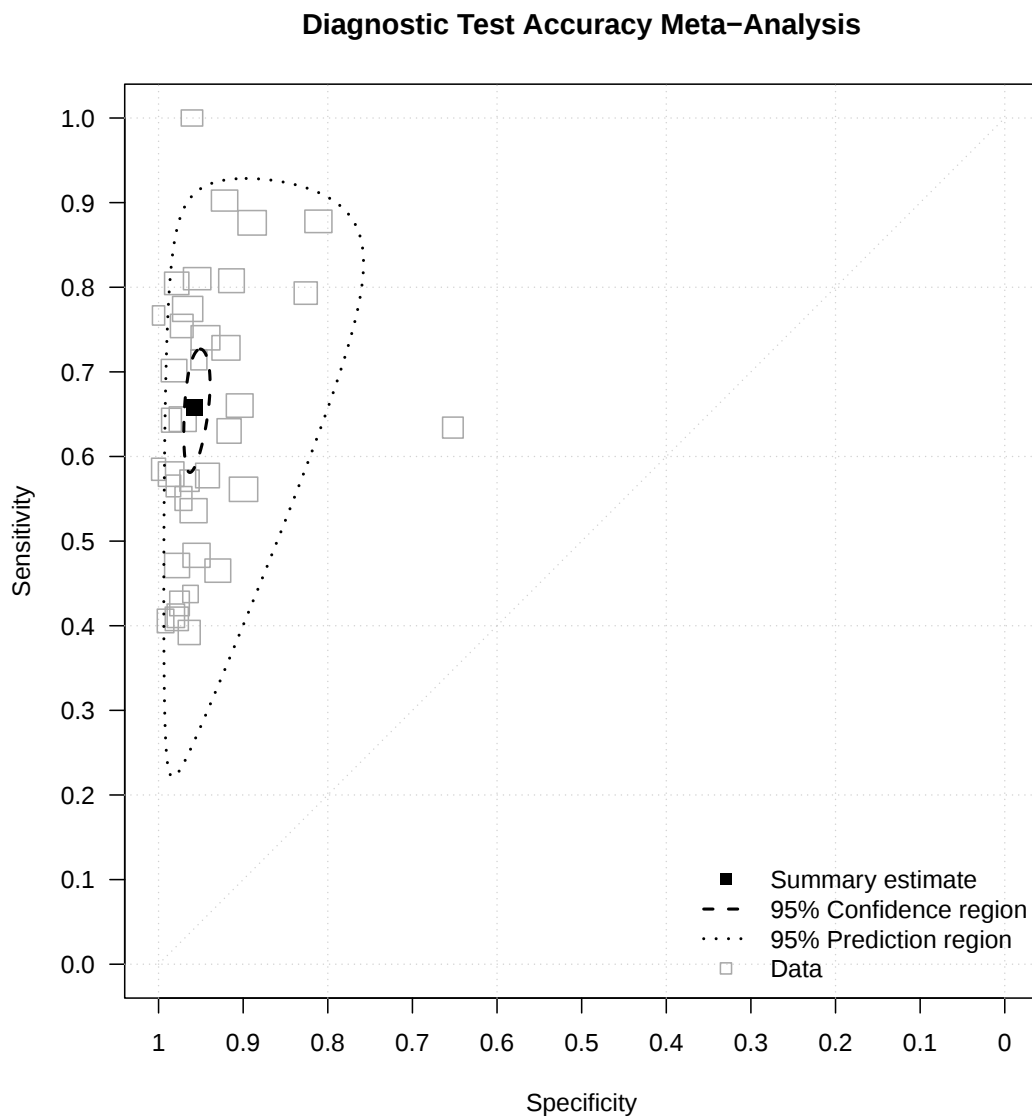
How do I get a summary plot of the Reitsma model?

The confidence region reflects uncertainty in the estimated summary point, whereas the prediction region reflects the likely location of a future study.

```
plot(reitsma)
```



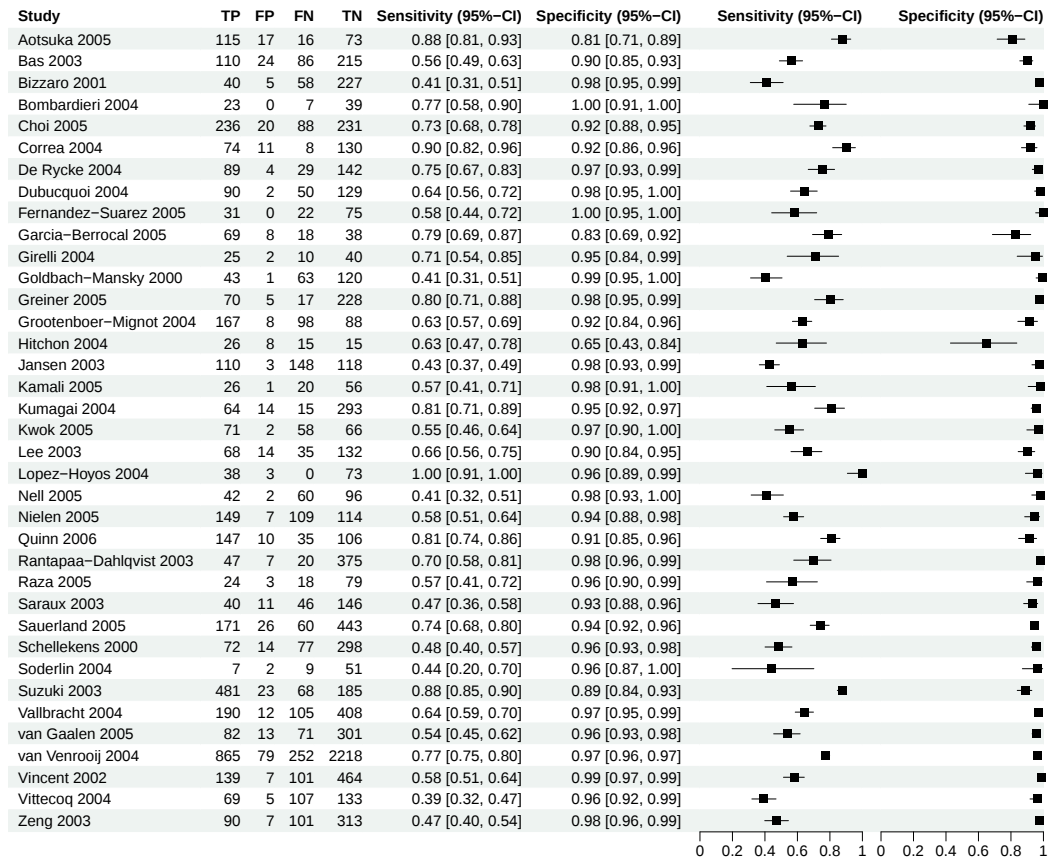
```
plot(reitsma,scale=0.01)
```



How do I get a coupled forest plot?

Note: Rendering forest plots may take longer in an interactive R session due to the underlying grid graphics. Performance is typically faster when knitting the vignette (e.g. via RMarkdown or Quarto).

```
forest(reitsma)
```



How do I export results to RevMan?

```
as_revman(reitsma)
#>      Externally_Calculated_Parameters      Parameter      Estimate
#> 1          HSROC model parameters          Lambda 3.730684359
#> 2          HSROC model parameters          Theta -1.203361126
#> 3          HSROC model parameters          beta 0.026086047
#> 4          HSROC model parameters Var(accuracy) 0.573132997
#> 5          HSROC model parameters Var(threshold) 0.413698071
```

```

#> 6      Bivariate model parameters      E(logitSe) 0.653402883
#> 7      Bivariate model parameters      E(logitSp) 3.108990638
#> 8      Bivariate model parameters      Var(logitSe) 0.542639749
#> 9      Bivariate model parameters      Var(logitSp) 0.571701927
#> 10     Bivariate model parameters      Cov(logits) -0.270414821
#> 11     Bivariate model parameters      Corr(logits) -0.485500701
#> 12 Confidence and prediction regions SE(E(logitSe)) 0.127486590
#> 13 Confidence and prediction regions SE(E(logitSp)) 0.145884662
#> 14 Confidence and prediction regions      Cov(Es) -0.007412423
#> 15 Confidence and prediction regions      Studies 37.000000000

```

How do I use the Rutter and Gatsonis model?

The number of diseased individuals from study i who test positive is denoted by $y_{i1} \sim \mathcal{B}(n_{i1}, \pi_{i1})$.

Similarly, the number of non-diseased individuals who test positive is $y_{i2} \sim \mathcal{B}(n_{i2}, \pi_{i2})$.

At the study level, we have

$$\text{logit}(\pi_{ij}) = (\theta_i + \alpha_i x_{ij}) \exp(-\beta x_{ij}), \quad \alpha_i \sim \mathcal{N}(\Lambda, \sigma_\alpha^2), \quad \theta_i \sim \mathcal{N}(\Theta, \sigma_\theta^2),$$

where

$$x_{ij} = \begin{cases} -0.5 & \text{for non-diseased individuals,} \\ 0.5 & \text{for diseased individuals.} \end{cases}$$

In this parameterization Λ corresponds to accuracy, Θ to threshold, and β controls the shape of the HSROC curve.

```

data("RF")
ruttergatsonis <- fitRutterGatsonis(data=RF,
                                   TP=TP,
                                   FP=FP,
                                   FN=FN,
                                   TN=TN,
                                   study=study)

```

```

ruttergatsonis
#>
#> Rutter & Gatsonis Model
#> -----

```

```

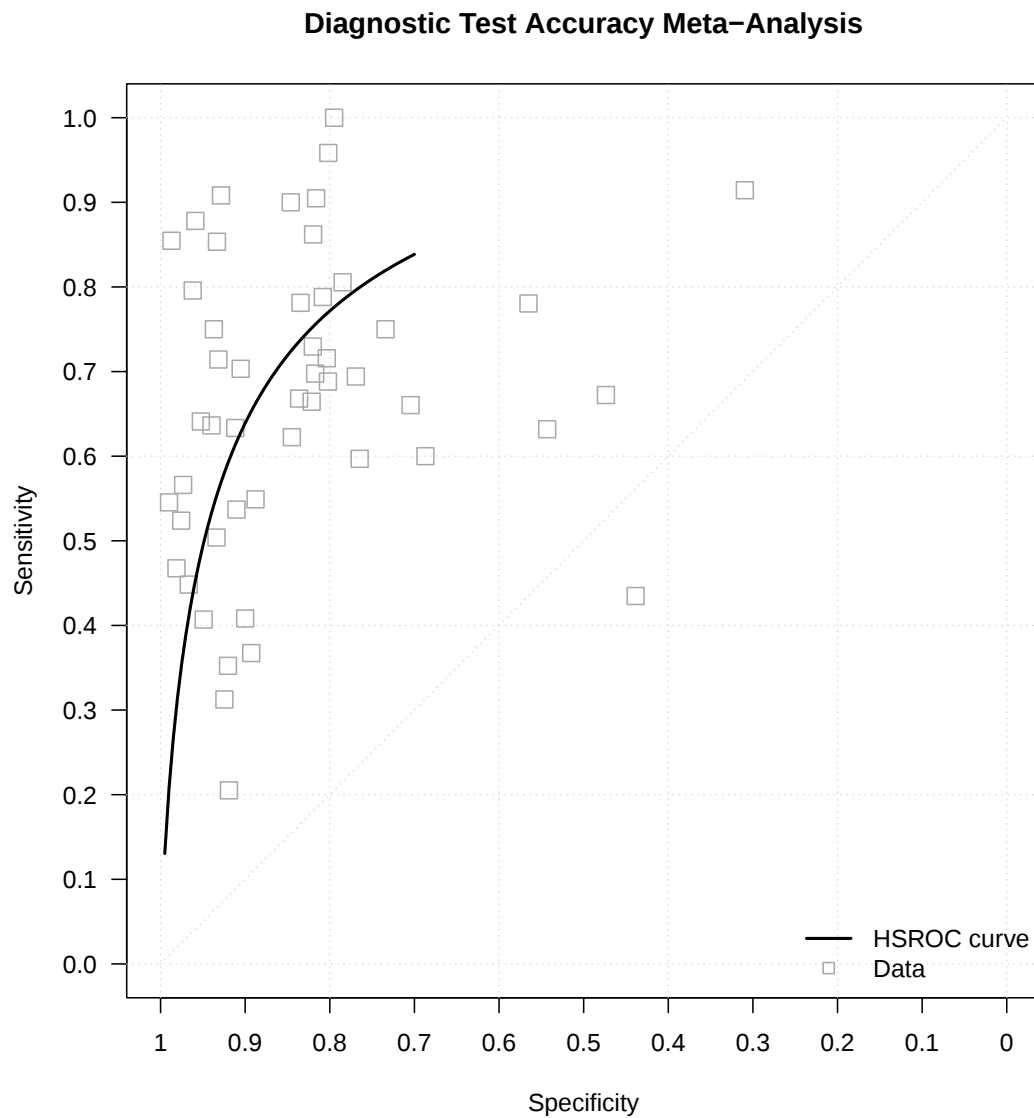
#>
#> Number of studies : 50
#> Optimizer          : Converged
#> Hessian            : Positive definite
#> Max |grad|         : 0.0004717637
#> -2 log likelihood  : 806.934 ( df = 5 )
#> AIC                : 816.934
#> BIC                : 826.494
#>
#> Lambda             : 2.602
#> Theta              : -0.437
#> beta               : 0.227
#>
#> Use summary() for parameter estimates.
summary(ruttergatsonis)
#>
#> Summary: Rutter & Gatsonis Model
#> -----
#>
#> Parameter estimates
#> -----
#>               Estimate Std. Error
#> Lambda         2.60159850 0.186166910
#> Theta         -0.43701666 0.146851770
#> beta          0.22668487 0.162369920
#> sigma2_alpha  1.30140570 0.304559180
#> sigma2_theta  0.54229651 0.123662560
#> logitsens     0.82868835 0.155394390
#> sens          0.69607752 0.032874245
#>
#> Sensitivity / specificity
#> -----
#>          spec conflevel logitsens Std_Error CI_Lower CI_Upper      Sens
#> 1 0.86695447      0.95 0.82868835 0.15539439 0.52412093 1.1332558 0.69607752
#>   SensCI_Lower SensCI_Upper
#> 1   0.62811087   0.75643924
#>
#> Recovered bivariate parameters (Reitsma)
#> -----
#>               mu_A.sens mu_B.spec sigma2_A.sens sigma2_B.spec
#> Estimate (recovered) 0.77122384 1.9463806      0.69166461      1.0884075
#>               sigma_AB

```

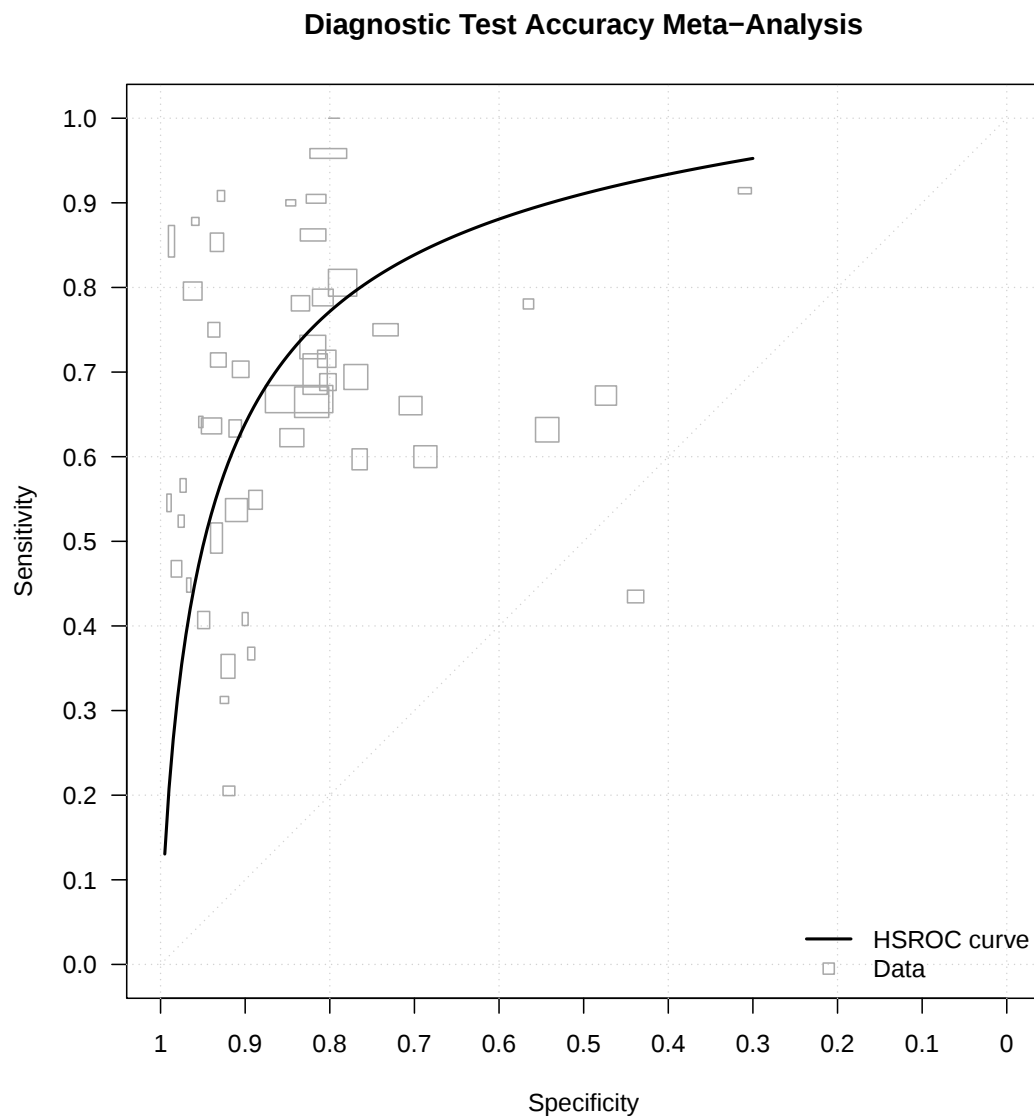
```
#> Estimate (recovered) -0.21694508
```

How do I get a summary plot of the Rutter and Gatsonis model?

```
plot(ruttergatsonis)
```



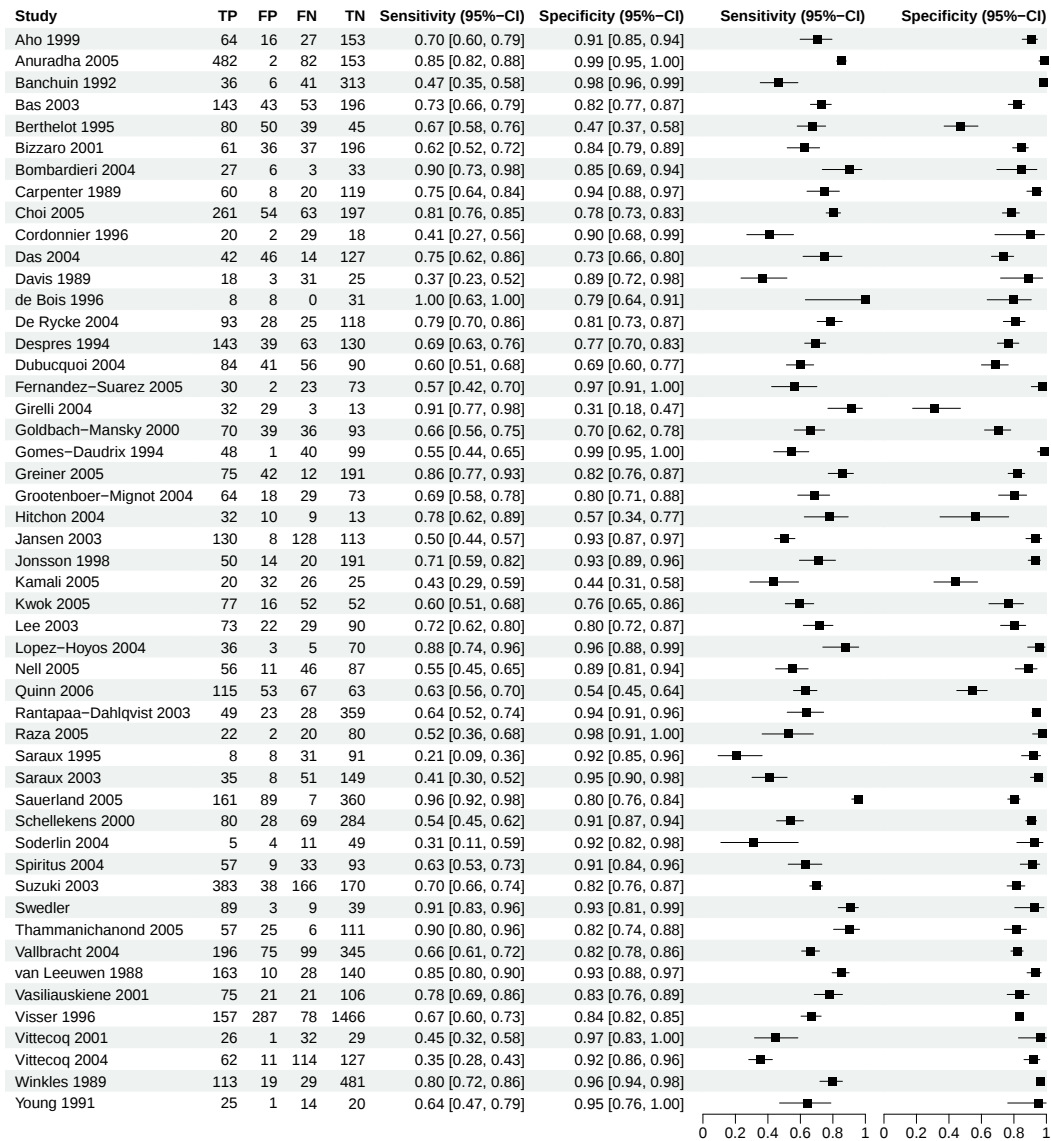
```
plot(ruttergatsonis,size="se",specrange=c(0.3,0.995),scale=0.01)
```



How do I get a coupled forest plot?

Note: Rendering forest plots may take longer in an interactive R session due to the underlying grid graphics. Performance is typically faster when knitting the vignette (e.g. via RMarkdown or Quarto).

forest(ruttergatsonis)



How do I simplify the models via parameter constraints?

The package allows model parameters to be constrained to zero during estimation. This can be useful in meta-analysis of sparse data, when convergence is difficult, or when fitting simplified models as described in the Cochrane Handbook. For example,

```
reitsmacons <- fitReitsma(data = anticcp,
                          TP = TP,
                          FP = FP,
                          FN = FN,
                          TN = TN,
                          study = study,
                          constrain = "sigma_AB")

summary(reitsmacons)
#>
#> Summary: Reitsma Model
#> -----
#>
#> Parameter estimates
#> -----
#>
#>           Estimate Std_Error
#> mu_A.sens    0.65851744 0.12949978
#> mu_B.spec    3.10452410 0.14750046
#> sigma2_A.sens 0.56018928 0.15305457
#> sigma2_B.spec 0.58148188 0.19134252
#> sigma_AB      0.00000000 0.00000000
#>
#> Sensitivity / specificity
#> -----
#>
#>           Estimate conflevel   CI_Lower   CI_Upper
#> sens 0.65892727      0.95 0.59981697 0.71347719
#> spec 0.95707898      0.95 0.94350388 0.96750454
#>
#> Recovered HSROC parameters (Rutter-Gatsonis)
#> -----
#>
#>           Lambda      Theta      beta sigma2_alpha sigma2_theta
#> Estimate (recovered) 3.7403928 -1.2055087 0.018652545    1.1414726    0.28536815
```

fixed the between-study random-effects covariance at zero. Other options include `constrain="sigma2_A"`, `constrain=sigma2_B`, or `constrain=all`.

The Rutter and Gatsonis model allows for the constraint $\sigma_{\alpha}^2 = 0$, $\sigma_{\theta}^2 = 0$ and/or $\beta = 0$ (shape parameter). For example

```

ruttergatsoniscons <- fitRutterGatsonis(data = RF,
                                         TP = TP,
                                         FP = FP,
                                         FN = FN,
                                         TN = TN,
                                         study = study,
                                         constrain = c("sigma2_theta","shape"))

summary(ruttergatsoniscons)
#>
#> Summary: Rutter & Gatsonis Model
#> -----
#>
#> Parameter estimates
#> -----
#>
#>             Estimate Std. Error
#> Lambda      2.4745581e+00 0.164585260
#> Theta      -4.7568280e-01 0.022193047
#> beta        0.0000000e+00 0.000000000
#> sigma2_alpha 1.2121724e+00 0.275679630
#> sigma2_theta 4.9303807e-32 0.000000000
#> logitsens    6.0026296e-01 0.164585260
#> sens         6.4571647e-01 0.037651629
#>
#> Sensitivity / specificity
#> -----
#>
#>          spec conflevel logitsens Std_Error CI_Lower CI_Upper      Sens
#> 1 0.86695447      0.95 0.60026296 0.16458526 0.27768178 0.92284414 0.64571647
#>   SensCI_Lower SensCI_Upper
#> 1   0.56897779   0.71562126
#>
#> Recovered bivariate parameters (Reitsma)
#> -----
#>
#>             mu_A.sens mu_B.spec sigma2_A.sens sigma2_B.spec
#> Estimate (recovered) 0.76159623 1.7129618      0.30304311      0.30304311
#>
#>             sigma_AB
#> Estimate (recovered) 0.30304311

```

Note that we can also compare the constrained model with the full model using likelihood ratio tests.

```
anova(ruttergatsoniscons,ruttergatsonis)
#>      Df  logLik Df.diff Chisq Pr(>Chisq)
#> Model 1   3 -683.02
#> Model 2   5 -403.47      2 559.1 < 2.2e-16 ***
#> ---
#> Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

How do I use the Hoyer model?

The Hoyer model assumes that the diagnostic test measurement arises from a latent continuous variable Y_j , with $j = 0$ for the non-diseased individuals and $j = 1$ for the diseased, which follows a parametric survival distribution. The observed test results correspond to interval-censored observations of this latent variable due to the use of thresholds.

Which distributions does dtametaTMB support?

The latent variable Y_j is assumed to follow a location-scale family:

$$Y_j \sim F(\mu_j, \phi_j),$$

where:

- μ_j is a study-specific location parameter
- ϕ_j is a scale parameter

Common choices for F include:

Weibull distribution

$$f(y; \mu_j, \phi_j) = \mu_j \phi_j y^{\phi_j - 1} \exp(-\mu_j y^{\phi_j})$$

Log-normal distribution

$$f(y; \mu_j, \phi_j) = \frac{1}{\phi_j y} \varphi\left(\frac{\log(y) - \mu_j}{\phi_j}\right)$$

Log-logistic distribution

$$f(y; \mu_j, \phi_j) = \frac{\mu_j \phi_j y^{\phi_j - 1}}{(1 + \mu_j y^{\phi_j})^2}$$

Random effects structure

To account for between-study heterogeneity and the correlation between diseased and non-diseased groups, we introduce study-specific random effects:

$$\log(y_{0i}) = \beta_0 + \varepsilon_{0i} + u_{0i}, \quad \log(y_{1i}) = \beta_1 + \varepsilon_{1i} + u_{1i},$$

with

$$\begin{pmatrix} u_{0i} \\ u_{1i} \end{pmatrix} \sim \mathcal{N} \left(\begin{pmatrix} 0 \\ 0 \end{pmatrix}, \begin{pmatrix} \sigma_0^2 & \rho \sigma_0 \sigma_1 \\ \rho \sigma_0 \sigma_1 & \sigma_1^2 \end{pmatrix} \right).$$

Censoring mechanism

Because only thresholded outcomes (TN, TP, FN, FP) are observed, the latent variable Y_j is subject to censoring.

- Left censoring: $(-\infty, y_k^R]$
- Interval censoring between adjacent thresholds
- Right censoring: $(y_k^L, +\infty)$

where y_k^L and y_k^R denote finite threshold values.

How do I compute sensitivities and specificities?

We can model the ROC curve by predicting sensitivities and specificities (1 - false positive rates) at several threshold values y .

Weibull distribution

$$S_1(y) = \exp \left(-\exp \left(\frac{\log(y) - \beta_1}{\lambda_1} \right) \right), \quad \text{with } \beta_1 = -\log(\mu_1), \quad \lambda_1 = 1/\phi_1,$$
$$S_0(y) = \exp \left(-\exp \left(\frac{\log(y) - \beta_0}{\lambda_0} \right) \right), \quad \text{with } \beta_0 = -\log(\mu_0), \quad \lambda_0 = 1/\phi_0.$$

Log-normal distribution

$$S_1(y) = 1 - \Phi\left(\frac{\log(y) - \beta_1}{\lambda_1}\right), \quad \text{with } \beta_1 = \mu_1, \quad \lambda_1 = \phi_1,$$

$$S_0(y) = 1 - \Phi\left(\frac{\log(y) - \beta_0}{\lambda_0}\right), \quad \text{with } \beta_0 = \mu_0, \quad \lambda_0 = \phi_0.$$

Log-logistic distribution

$$S_1(y) = \left(1 + \exp\left(\frac{\log(y) - \beta_1}{\lambda_1}\right)\right)^{-1}, \quad \text{with } \beta_1 = -\phi_1^{-1} \log(\mu_1), \quad \lambda_1 = 1/\phi_1,$$

$$S_0(y) = \left(1 + \exp\left(\frac{\log(y) - \beta_0}{\lambda_0}\right)\right)^{-1}, \quad \text{with } \beta_0 = -\phi_0^{-1} \log(\mu_0), \quad \lambda_0 = 1/\phi_0.$$

How do I interpret test direction?

For tests where larger values indicate disease (`testdirection = "greater"`):

- $S_1(y)$ corresponds to **sensitivity** at threshold y
- $S_0(y)$ corresponds to the **false positive rate (FPR) = 1 - specificity**

For tests where smaller values indicate disease (`testdirection = "less"`):

- $S_1(y)$ corresponds to the **false negative rate (FNR) = 1 - sensitivity**
- $S_0(y)$ corresponds to **specificity**

In a nutshell

By modelling the diagnostic marker as a latent continuous outcome, the Hoyer model:

- naturally accommodates **multiple thresholds per study**
- provides a unified framework for **interval-censored diagnostic data**
- preserves the correlation between sensitivity and specificity

The following parameters have to be estimated: $\beta_0, \beta_1, \lambda_0, \lambda_1, \sigma_0^2, \sigma_1^2$, and ρ , where λ_0 and λ_1 are transformations of ϕ_0 and ϕ_1 .

To obtain initial values, it is necessary to specify a smallest (« $\min y$) and largest (» $\max y$) value across all studies, essentially replacing negative and positive infinity for the left and right censored intervals.

How do I fit the Hoyer model?

```
data("diabetes")
head(diabetes)
#>      study threshold  TP   TN   FP  FN   D   H originally_published
#> 1 Study 01         5.9 574 1389  682 262 836 2071                1
#> 2 Study 02         5.0 617 1005 7735  18 635 8740                0
#> 3 Study 02         5.1 607 1617 7123  28 635 8740                0
#> 4 Study 02         5.2 600 2438 6302  35 635 8740                0
#> 5 Study 02         5.3 581 3409 5331  54 635 8740                0
#> 6 Study 02         5.4 563 4422 4318  72 635 8740                0
summary(diabetes$threshold)
#>      Min. 1st Qu.  Median      Mean 3rd Qu.      Max.
#>  3.900   5.500   5.800   5.837   6.100   7.600
```

The argument `eval_threshold` specifies the values at which sensitivities and specificities are evaluated after model fitting.

```
hoyer <- fitHoyer(data=diabetes,
                  TP=TP,
                  FP=FP,
                  FN=FN,
                  TN=TN,
                  threshold=threshold,
                  study=study,
                  dist="loglogistic",
                  testdirection="greater",
                  eval_threshold=c(5.0,5.5,6.0,6.5,7.0,7.5),
                  smallest=2,
                  largest=10)
```

```
hoyer
#>
#> Hoyer Model
#> -----
#>
#> Number of studies : 38
#> Optimizer          : Converged
#> Hessian            : Positive definite
#> Max |grad|         : 0.03070981
#> -2 log likelihood : 209322 ( df = 7 )
```

```

#> AIC                : 209336
#> BIC                : 209347.4
#>
#> Distribution        : Loglogistic
#> Test direction      : greater
#>
#> Use summary() for parameter estimates.
summary(hoyer)
#>
#> Summary: Hoyer Model
#> -----
#>
#> Parameter estimates
#> -----
#>
#>           Estimate      Std. Error
#> beta0      1.7056911000 0.00956301460
#> lambda0    0.0395020040 0.00018572655
#> su0        0.0586486790 0.00677848700
#> beta1      1.8253371000 0.01456524000
#> lambda1    0.0563984790 0.00092447216
#> su1        0.0883206310 0.01095646100
#> rho        0.8630325700 0.04544108800
#> covu0u1    0.0044704124 0.00114172000
#> logitSurv1 3.8281031000 0.26350352000
#> logitSurv1 2.1381608000 0.25933476000
#> logitSurv1 0.5953642400 0.25807906000
#> logitSurv1 -0.8238709800 0.25910740000
#> logitSurv1 -2.1378776000 0.26190467000
#> logitSurv1 -3.3611884000 0.26605427000
#> logitSurv0 2.4366671000 0.24260400000
#> logitSurv0 0.0238736250 0.24209177000
#> logitSurv0 -2.1788343000 0.24208781000
#> logitSurv0 -4.2051291000 0.24247511000
#> logitSurv0 -6.0811851000 0.24316614000
#> logitSurv0 -7.8277515000 0.24409438000
#>
#> Sensitivity / specificity
#> -----
#>   threshold conflevel      Sens SensCI_Lower SensCI_Upper      Spec
#> 1         5.0        0.95 0.97871219 0.964826170 0.987189040 0.080419039
#> 2         5.5        0.95 0.89455725 0.836152370 0.933791700 0.494031880
#> 3         6.0        0.95 0.64459500 0.522369700 0.750482990 0.898332650

```

```

#> 4      6.5      0.95 0.30494258 0.208876300 0.421643620 0.985300440
#> 5      7.0      0.95 0.10546947 0.065915008 0.164577800 0.997719740
#> 6      7.5      0.95 0.03353069 0.020180626 0.055214536 0.999601640
#>   SpecCI_Lower SpecCI_Upper
#> 1 0.051555604 0.12334026
#> 2 0.377925030 0.61078605
#> 3 0.846102130 0.93421518
#> 4 0.976566740 0.99080968
#> 5 0.996332560 0.99858298
#> 6 0.999357390 0.99975307

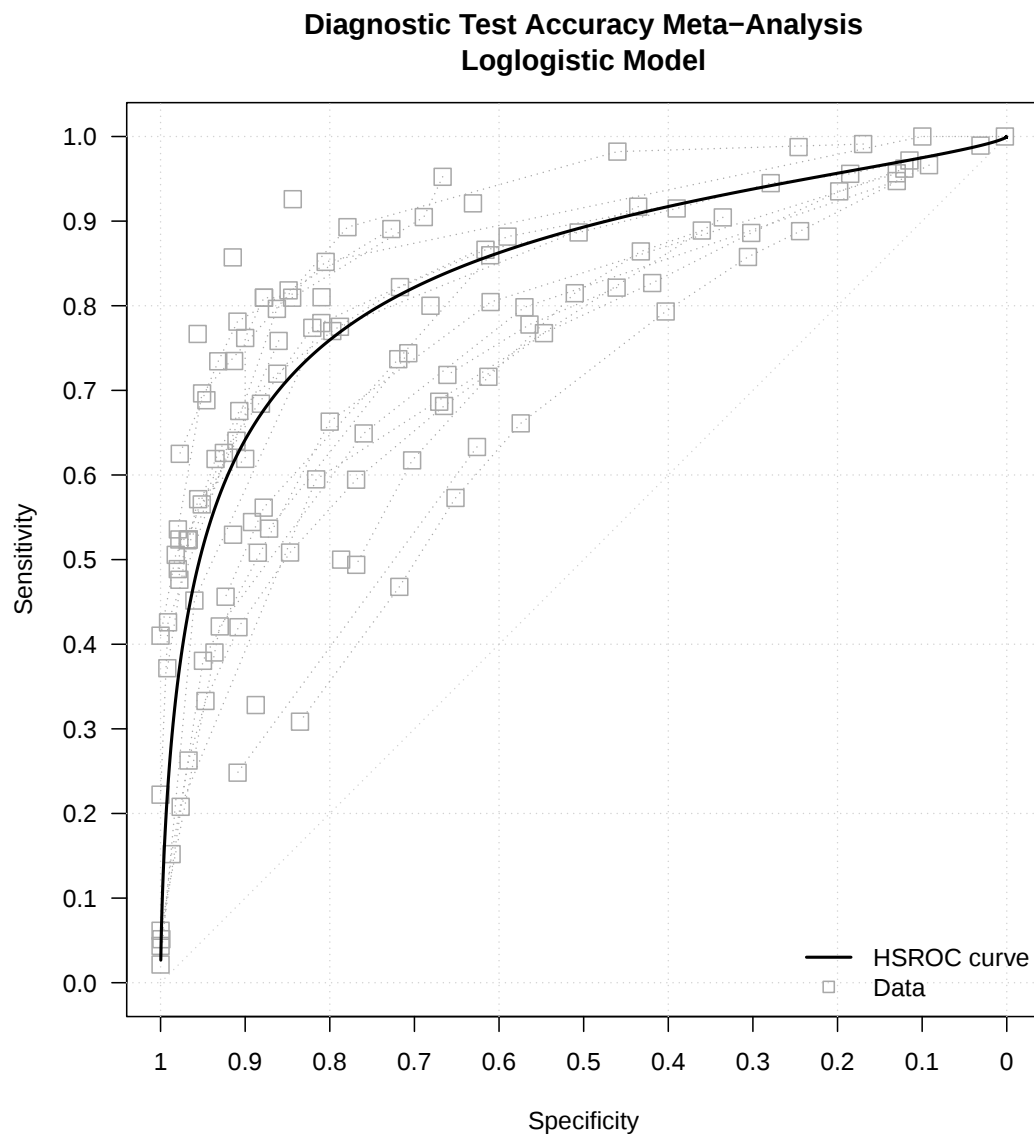
```

How do I get a summary plot of the Hoyer model?

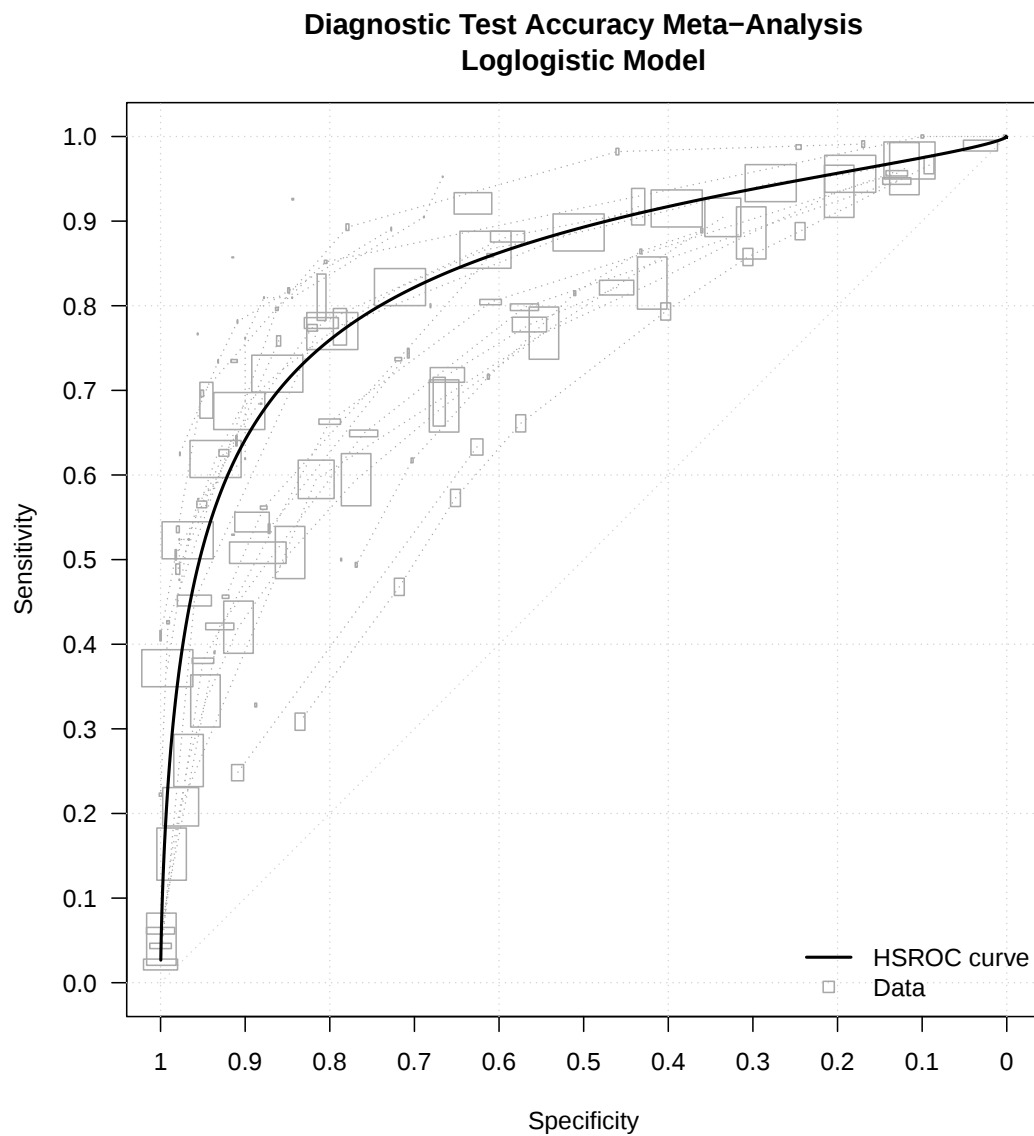
```

plot(hoyer,
      main="Diagnostic Test Accuracy Meta-Analysis\nLoglogistic Model")

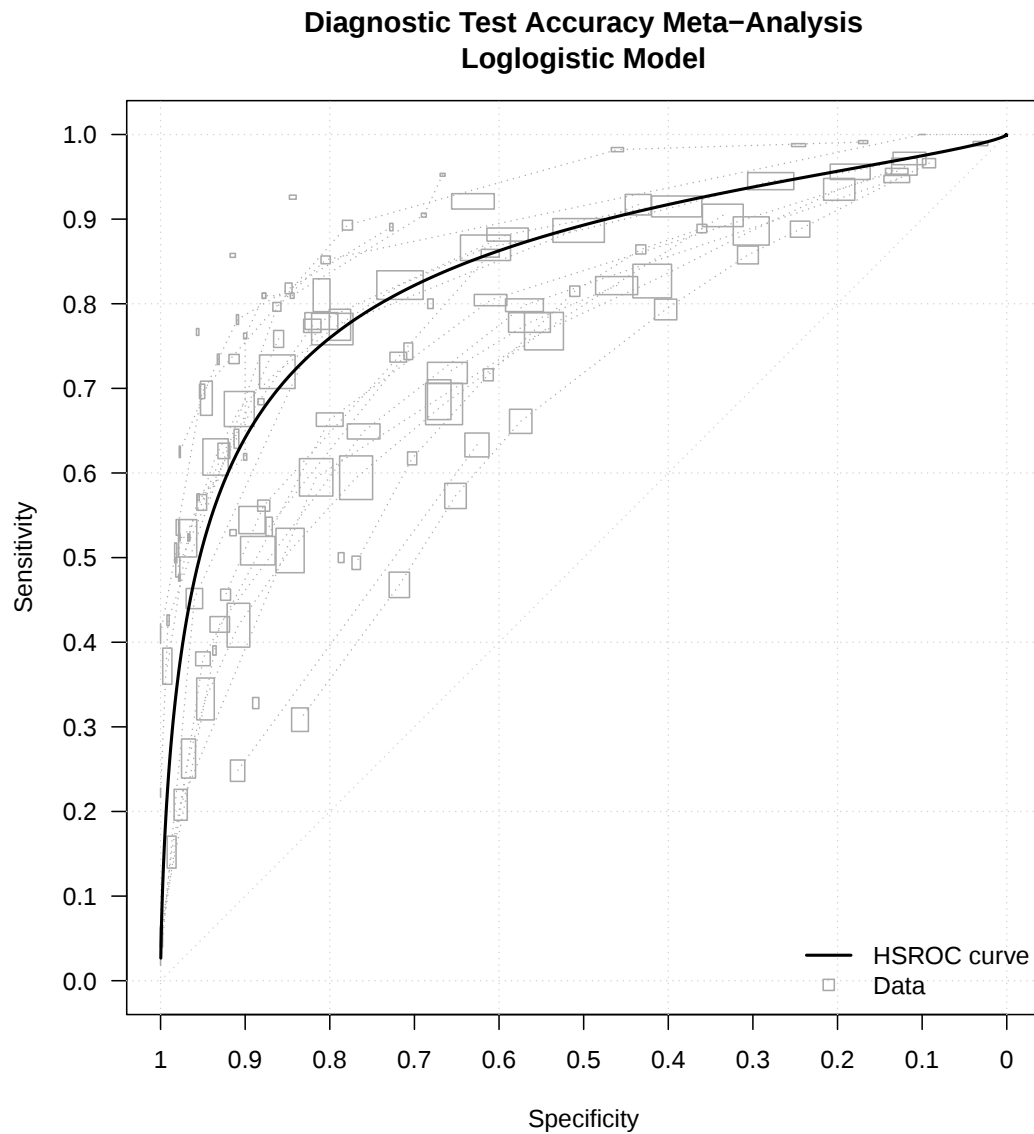
```



```
plot(hoyer,size="sampsize",scale=0.025,
     main="Diagnostic Test Accuracy Meta-Analysis\nLoglogistic Model")
```



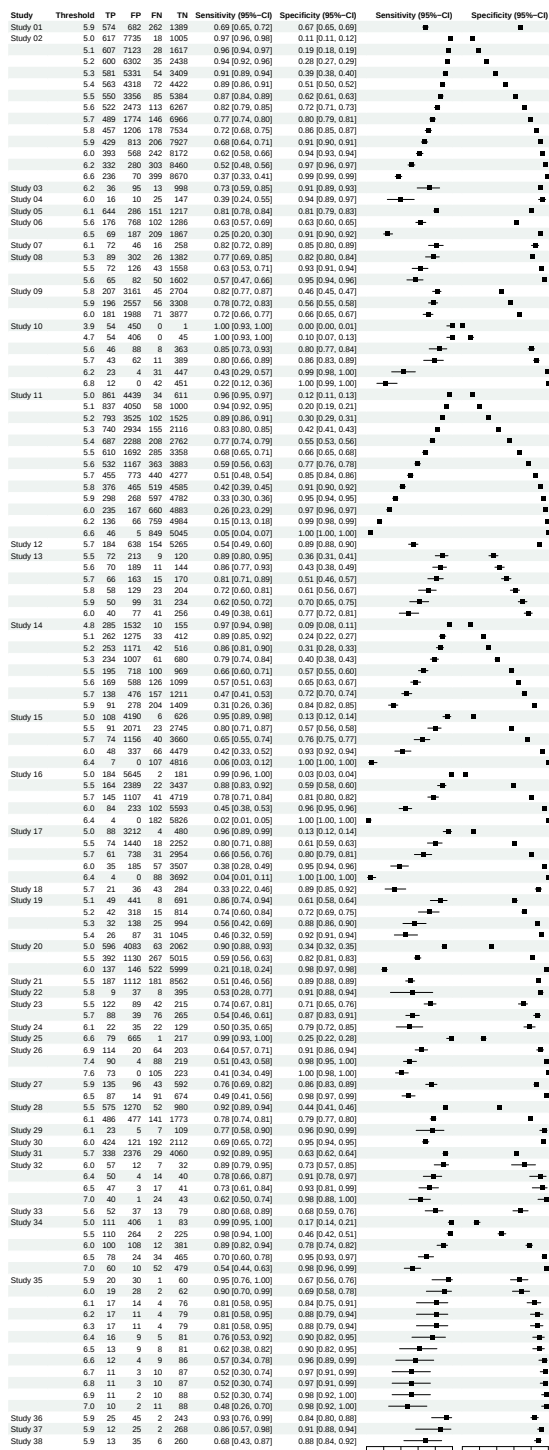
```
plot(hoyer,size="se",scale=0.025,  
     main="Diagnostic Test Accuracy Meta-Analysis\nLoglogistic Model")
```



How do I get a coupled forest plot?

Note: Rendering forest plots may take longer in an interactive R session due to the underlying grid graphics. Performance is typically faster when knitting the vignette (e.g. via RMarkdown or Quarto).

```
forest(hoyer)
```



How do I fit the Hoyer model to the FeNO dataset?

Note: The FeNO data are reproduced from the original source and the supplementary material accompanying the Cochrane Handbook. However, the study ‘Schneider 2013’ contains inconsistent diseased counts (TP + FN). To illustrate the Hoyer analysis, we modify the TP counts in rows 118–120 from 39 to 38, restoring a constant total of 154 diseased individuals. Other corrections restoring internal consistency are also conceivable.

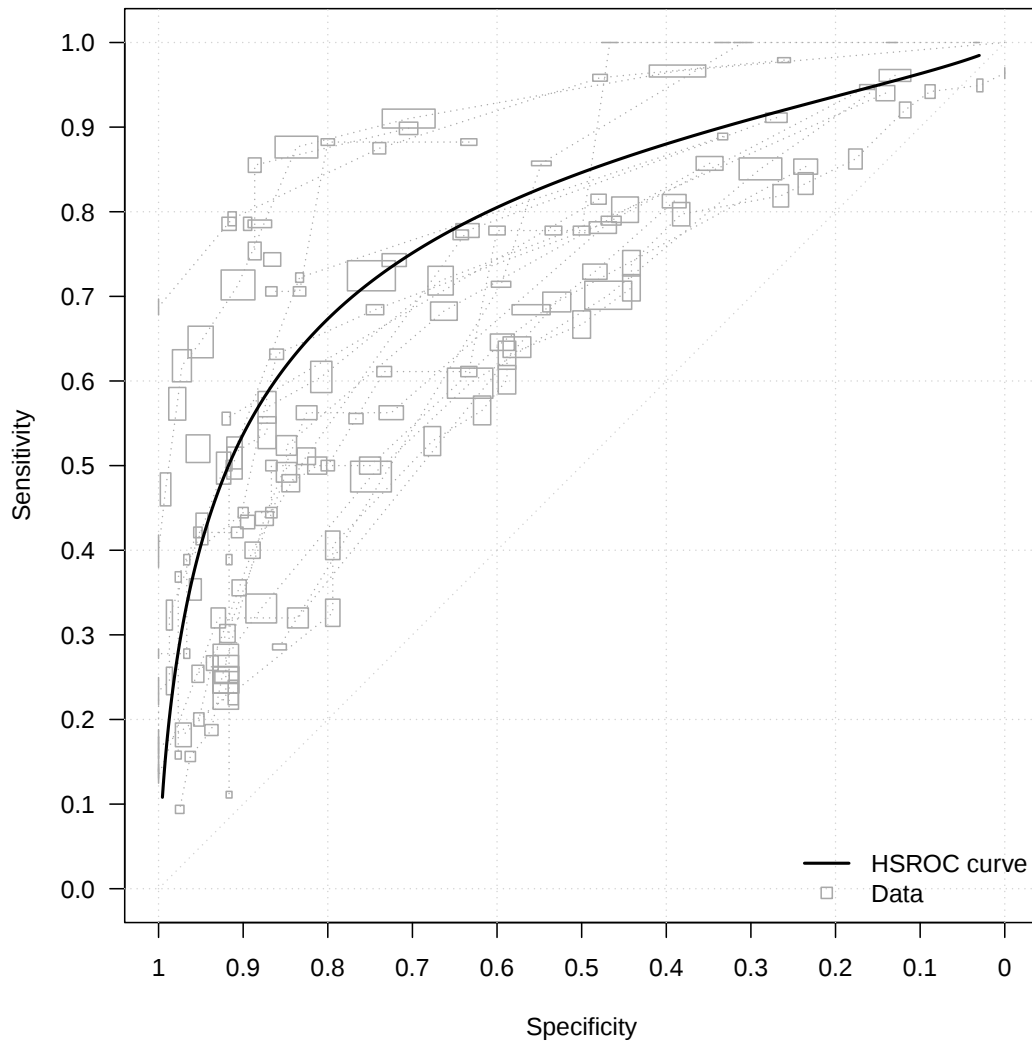
```
data("FENO")
head(FENO)
#>      study study_id cutoff  TP FN FP TN
#> 1 Arora 2006      1      6 133  5 34  0
#> 2 Arora 2006      1      7 131  7 33  1
#> 3 Arora 2006      1      8 130  8 31  3
#> 4 Arora 2006      1      9 127 11 30  4
#> 5 Arora 2006      1     10 119 19 28  6
#> 6 Arora 2006      1     11 115 23 26  8
summary(FENO$cutoff)
#>   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
#>   5.00  16.00  25.00  31.05  40.75 100.00
# feno <- fitHoyer(data=FENO,
#                   TP=TP,
#                   FP=FP,
#                   FN=FN,
#                   TN=TN,
#                   threshold=cutoff,
#                   study=study,
#                   dist="loglogistic",
#                   testdirection="greater",
#                   eval_threshold=seq(16,40,1),
#                   smallest=2,
#                   largest=120)
#Error in `FUN()`:
#| Inconsistent diseased counts (TP+FN) within study 'Schneider 2013'.
#Rows: 110, 111, 112, 113, 114, 115, 116, 117, 118, 119, 120, 121, 122
#Counts: 154, 155
#
# Let's check the Schneider 2013 study
check_schneider <- FENO[110:122,]
check_schneider$n1 <- with(check_schneider,TP+FN)
check_schneider$n0 <- with(check_schneider,TN+FP)
check_schneider
#>      study study_id cutoff  TP  FN  FP  TN  n1  n0
```

```

#> 110 Schneider 2013      11      9 148    6 208   31 154 239
#> 111 Schneider 2013      11     12 131   23 170   69 154 239
#> 112 Schneider 2013      11     16 108   46 127  112 154 239
#> 113 Schneider 2013      11     20  92   62  88 151 154 239
#> 114 Schneider 2013      11     25  75   79  60 179 154 239
#> 115 Schneider 2013      11     35  51  103  29 210 154 239
#> 116 Schneider 2013      11     41  42  112  19 220 154 239
#> 117 Schneider 2013      11     42  40  114  19 220 154 239
#> 118 Schneider 2013      11     43  39  116  19 220 155 239
#> 119 Schneider 2013      11     44  39  116  19 220 155 239
#> 120 Schneider 2013      11     45  39  116  19 220 155 239
#> 121 Schneider 2013      11     46  35  119  19 220 154 239
#> 122 Schneider 2013      11     71  28  126   7 232 154 239
# Inspection suggests that the TP and/or FN counts
# in rows 118, 119, 120 may need to be changed.
# Let's reduce the TP counts from 39 to 38.
# But other corrections are conceivable as well.
FENO[118:120,"TP"] <- 38
### Let's try again
feno <- fitHoyer(data=FENO,
  TP=TP,
  FP=FP,
  FN=FN,
  TN=TN,
  threshold=cutoff,
  study=study,
  dist="loglogistic",
  testdirection="greater",
  eval_threshold=seq(16,40,1),
  smallest=2,
  largest=120)
plot(feno,size="se",scale=0.03,
  main="Diagnostic Test Accuracy Meta-Analysis\nLoglogistic Model")

```

Diagnostic Test Accuracy Meta-Analysis Loglogistic Model



How does `testdirection="less"` work?

We use the synthetic anaemia data set. Smaller values in haemoglobin indicate disease.

```
data("anaemia")
summary(anaemia$threshold)
#>   Min. 1st Qu.  Median    Mean 3rd Qu.    Max.
#>   7.00   8.00   10.00  10.33  13.00   14.00
```

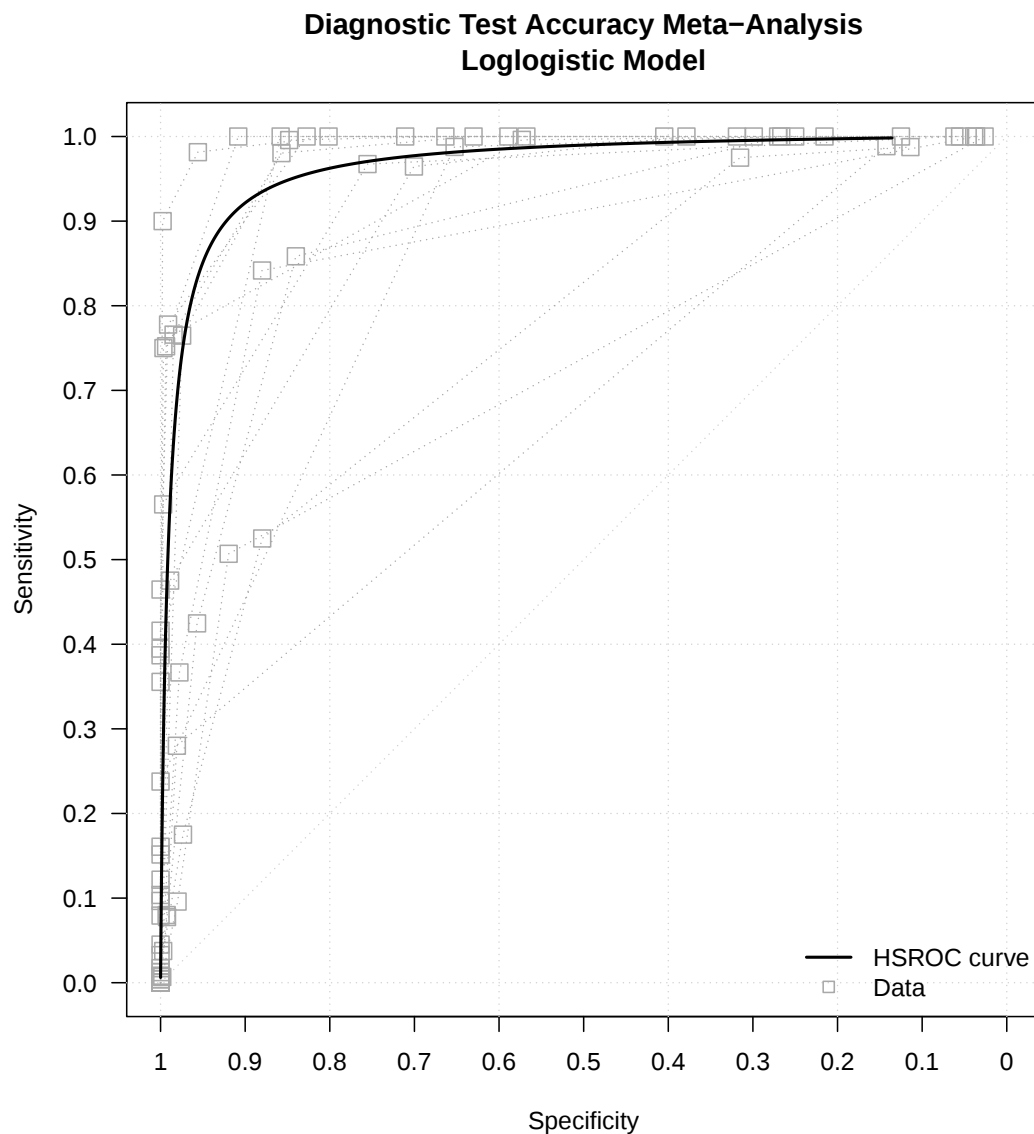
```
less <- fitHoyer(data=anaemia,
                 TP=TP,
                 FP=FP,
                 FN=FN,
                 TN=TN,
                 threshold=threshold,
                 study=study,
                 dist="loglogistic",
                 testdirection="less",
                 eval_threshold=c(8,9,10,11,12,13),
                 smallest=5,
                 largest=17)
```

```
less
#>
#> Hoyer Model
#> -----
#>
#> Number of studies : 15
#> Optimizer          : Converged
#> Hessian            : Positive definite
#> Max |grad|         : 0.03477329
#> -2 log likelihood : 19708.9 ( df = 7 )
#> AIC                : 19722.9
#> BIC                : 19727.86
#>
#> Distribution       : Loglogistic
#> Test direction     : less
#>
#> Use summary() for parameter estimates.
summary(less)
#>
#> Summary: Hoyer Model
#> -----
#>
#> Parameter estimates
#> -----
#>
#>           Estimate   Std. Error
#> beta0      2.5310712000 0.0169254100
#> lambda0    0.0583099970 0.0007979991
#> su0        0.0652667800 0.0120139560
#> beta1      2.2538212000 0.0147254380
```

```

#> lambda1      0.0605300340 0.0012263705
#> su1          0.0562794810 0.0105351710
#> rho          -0.4117582600 0.2194120800
#> covu0u1     -0.0015124624 0.0010422566
#> logitSurv1   2.8808784000 0.2497852800
#> logitSurv1   0.9350173500 0.2438804400
#> logitSurv1  -0.8056146700 0.2439346900
#> logitSurv1  -2.3802079000 0.2483362300
#> logitSurv1  -3.8176988000 0.2557856900
#> logitSurv1  -5.1400623000 0.2652905600
#> logitSurv0   7.7453210000 0.3083465400
#> logitSurv0   5.7253751000 0.3001481600
#> logitSurv0   3.9184720000 0.2948244800
#> logitSurv0   2.2839293000 0.2917357100
#> logitSurv0   0.7917087700 0.2903955800
#> logitSurv0  -0.5810010800 0.2904281500
#>
#> Sensitivity / specificity
#> -----
#>   threshold  conflevel      Sens SensCI_Lower SensCI_Upper      Spec
#> 1          8      0.95 0.053106947  0.033231895  0.083837892 0.99956742
#> 2          9      0.95 0.281907910  0.195759070  0.387692890 0.99674848
#> 3         10      0.95 0.691174230  0.581153750  0.783081980 0.98051575
#> 4         11      0.95 0.915305550  0.869151560  0.946187650 0.90753730
#> 5         12      0.95 0.978494340  0.964986080  0.986862110 0.68819812
#> 6         13      0.95 0.994176780  0.990244320  0.996529650 0.35870228
#>   SpecCI_Lower SpecCI_Upper
#> 1  0.99920865  0.99976358
#> 2  0.99415958  0.99819187
#> 3  0.96579655  0.98897297
#> 4  0.84711337  0.94561365
#> 5  0.55540748  0.79590165
#> 6  0.24044711  0.49705694
plot(less,main="Diagnostic Test Accuracy Meta-Analysis\nLoglogistic Model")

```



How does `fitHoyer` work internally? – Optional advanced workflow

Most users should use the high-level `fitHoyer` function. The lower-level functions are provided for advanced use and transparency.

Step 1: How do we restructure the data set?

```
res <- restructure_data(
  data = diabetes,
  TP = TP,
  FP = FP,
  FN = FN,
  TN = TN,
  study = study,
  threshold = threshold,
  testdirection = "greater",
  smallest = 2,
  largest = 10)
res
#> $restructured
#>
#>      study TP  TN  D   H threshold lowerB upperB events1 events0
#> Study 01.1 Study 01 574 1389 836 2071      5.9      NA      5.9      262      1389
#> Study 01.2 Study 01 574 1389 836 2071      5.9      5.9      NA      574      682
#> Study 02.1 Study 02 617 1005 635 8740      5.0      NA      5.0       18     1005
#> Study 02.2 Study 02 607 1617 635 8740      5.1      5.0      5.1       10      612
#> Study 02.3 Study 02 600 2438 635 8740      5.2      5.1      5.2        7      821
#> Study 02.4 Study 02 581 3409 635 8740      5.3      5.2      5.3       19      971
#> Study 02.5 Study 02 563 4422 635 8740      5.4      5.3      5.4       18     1013
#> Study 02.6 Study 02 550 5384 635 8740      5.5      5.4      5.5       13      962
#> Study 02.7 Study 02 522 6267 635 8740      5.6      5.5      5.6       28      883
#> Study 02.8 Study 02 489 6966 635 8740      5.7      5.6      5.7       33      699
#> Study 02.9 Study 02 457 7534 635 8740      5.8      5.7      5.8       32      568
#> Study 02.10 Study 02 429 7927 635 8740      5.9      5.8      5.9       28      393
#> Study 02.11 Study 02 393 8172 635 8740      6.0      5.9      6.0       36      245
#> Study 02.12 Study 02 332 8460 635 8740      6.2      6.0      6.2       61      288
#> Study 02.13 Study 02 236 8670 635 8740      6.6      6.2      6.6       96      210
#> Study 02.14 Study 02 236 8670 635 8740      6.6      6.6      NA      236       70
#> Study 03.1 Study 03  36  998  49 1093      6.2      NA      6.2       13      998
#> Study 03.2 Study 03  36  998  49 1093      6.2      6.2      NA       36       95
#> Study 04.1 Study 04  16  147  41  157      6.0      NA      6.0       25      147
#> Study 04.2 Study 04  16  147  41  157      6.0      6.0      NA       16       10
#> Study 05.1 Study 05 644 1217 795 1503      6.1      NA      6.1      151     1217
#> Study 05.2 Study 05 644 1217 795 1503      6.1      6.1      NA      644      286
#> Study 06.1 Study 06 176 1286 278 2054      5.6      NA      5.6      102     1286
#> Study 06.2 Study 06  69 1867 278 2054      6.5      5.6      6.5      107      581
#> Study 06.3 Study 06  69 1867 278 2054      6.5      6.5      NA       69      187
#> Study 07.1 Study 07  72  258  88  304      6.1      NA      6.1       16      258
```

#> Study 07.2	Study 07	72	258	88	304	6.1	6.1	NA	72	46
#> Study 08.1	Study 08	89	1382	115	1684	5.3	NA	5.3	26	1382
#> Study 08.2	Study 08	72	1558	115	1684	5.5	5.3	5.5	17	176
#> Study 08.3	Study 08	65	1602	115	1684	5.6	5.5	5.6	7	44
#> Study 08.4	Study 08	65	1602	115	1684	5.6	5.6	NA	65	82
#> Study 09.1	Study 09	207	2704	252	5865	5.8	NA	5.8	45	2704
#> Study 09.2	Study 09	196	3308	252	5865	5.9	5.8	5.9	11	604
#> Study 09.3	Study 09	181	3877	252	5865	6.0	5.9	6.0	15	569
#> Study 09.4	Study 09	181	3877	252	5865	6.0	6.0	NA	181	1988
#> Study 10.1	Study 10	54	1	54	451	3.9	NA	3.9	0	1
#> Study 10.2	Study 10	54	45	54	451	4.7	3.9	4.7	0	44
#> Study 10.3	Study 10	46	363	54	451	5.6	4.7	5.6	8	318
#> Study 10.4	Study 10	43	389	54	451	5.7	5.6	5.7	3	26
#> Study 10.5	Study 10	23	447	54	451	6.2	5.7	6.2	20	58
#> Study 10.6	Study 10	12	451	54	451	6.8	6.2	6.8	11	4
#> Study 10.7	Study 10	12	451	54	451	6.8	6.8	NA	12	0
#> Study 11.1	Study 11	861	611	895	5050	5.0	NA	5.0	34	611
#> Study 11.2	Study 11	837	1000	895	5050	5.1	5.0	5.1	24	389
#> Study 11.3	Study 11	793	1525	895	5050	5.2	5.1	5.2	44	525
#> Study 11.4	Study 11	740	2116	895	5050	5.3	5.2	5.3	53	591
#> Study 11.5	Study 11	687	2762	895	5050	5.4	5.3	5.4	53	646
#> Study 11.6	Study 11	610	3358	895	5050	5.5	5.4	5.5	77	596
#> Study 11.7	Study 11	532	3883	895	5050	5.6	5.5	5.6	78	525
#> Study 11.8	Study 11	455	4277	895	5050	5.7	5.6	5.7	77	394
#> Study 11.9	Study 11	376	4585	895	5050	5.8	5.7	5.8	79	308
#> Study 11.10	Study 11	298	4782	895	5050	5.9	5.8	5.9	78	197
#> Study 11.11	Study 11	235	4883	895	5050	6.0	5.9	6.0	63	101
#> Study 11.12	Study 11	136	4984	895	5050	6.2	6.0	6.2	99	101
#> Study 11.13	Study 11	46	5045	895	5050	6.6	6.2	6.6	90	61
#> Study 11.14	Study 11	46	5045	895	5050	6.6	6.6	NA	46	5
#> Study 12.1	Study 12	184	5265	338	5903	5.7	NA	5.7	154	5265
#> Study 12.2	Study 12	184	5265	338	5903	5.7	5.7	NA	184	638
#> Study 13.1	Study 13	72	120	81	333	5.5	NA	5.5	9	120
#> Study 13.2	Study 13	70	144	81	333	5.6	5.5	5.6	2	24
#> Study 13.3	Study 13	66	170	81	333	5.7	5.6	5.7	4	26
#> Study 13.4	Study 13	58	204	81	333	5.8	5.7	5.8	8	34
#> Study 13.5	Study 13	50	234	81	333	5.9	5.8	5.9	8	30
#> Study 13.6	Study 13	40	256	81	333	6.0	5.9	6.0	10	22
#> Study 13.7	Study 13	40	256	81	333	6.0	6.0	NA	40	77
#> Study 14.1	Study 14	285	155	295	1687	4.8	NA	4.8	10	155
#> Study 14.2	Study 14	262	412	295	1687	5.1	4.8	5.1	23	257
#> Study 14.3	Study 14	253	516	295	1687	5.2	5.1	5.2	9	104

#> Study 14.4	Study 14	234	680	295	1687	5.3	5.2	5.3	19	164
#> Study 14.5	Study 14	195	969	295	1687	5.5	5.3	5.5	39	289
#> Study 14.6	Study 14	169	1099	295	1687	5.6	5.5	5.6	26	130
#> Study 14.7	Study 14	138	1211	295	1687	5.7	5.6	5.7	31	112
#> Study 14.8	Study 14	91	1409	295	1687	5.9	5.7	5.9	47	198
#> Study 14.9	Study 14	91	1409	295	1687	5.9	5.9	NA	91	278
#> Study 15.1	Study 15	108	626	114	4816	5.0	NA	5.0	6	626
#> Study 15.2	Study 15	91	2745	114	4816	5.5	5.0	5.5	17	2119
#> Study 15.3	Study 15	74	3660	114	4816	5.7	5.5	5.7	17	915
#> Study 15.4	Study 15	48	4479	114	4816	6.0	5.7	6.0	26	819
#> Study 15.5	Study 15	7	4816	114	4816	6.4	6.0	6.4	41	337
#> Study 15.6	Study 15	7	4816	114	4816	6.4	6.4	NA	7	0
#> Study 16.1	Study 16	184	181	186	5826	5.0	NA	5.0	2	181
#> Study 16.2	Study 16	164	3437	186	5826	5.5	5.0	5.5	20	3256
#> Study 16.3	Study 16	145	4719	186	5826	5.7	5.5	5.7	19	1282
#> Study 16.4	Study 16	84	5593	186	5826	6.0	5.7	6.0	61	874
#> Study 16.5	Study 16	4	5826	186	5826	6.4	6.0	6.4	80	233
#> Study 16.6	Study 16	4	5826	186	5826	6.4	6.4	NA	4	0
#> Study 17.1	Study 17	88	480	92	3692	5.0	NA	5.0	4	480
#> Study 17.2	Study 17	74	2252	92	3692	5.5	5.0	5.5	14	1772
#> Study 17.3	Study 17	61	2954	92	3692	5.7	5.5	5.7	13	702
#> Study 17.4	Study 17	35	3507	92	3692	6.0	5.7	6.0	26	553
#> Study 17.5	Study 17	4	3692	92	3692	6.4	6.0	6.4	31	185
#> Study 17.6	Study 17	4	3692	92	3692	6.4	6.4	NA	4	0
#> Study 18.1	Study 18	21	284	64	320	5.7	NA	5.7	43	284
#> Study 18.2	Study 18	21	284	64	320	5.7	5.7	NA	21	36
#> Study 19.1	Study 19	49	691	57	1132	5.1	NA	5.1	8	691
#> Study 19.2	Study 19	42	814	57	1132	5.2	5.1	5.2	7	123
#> Study 19.3	Study 19	32	994	57	1132	5.3	5.2	5.3	10	180
#> Study 19.4	Study 19	26	1045	57	1132	5.4	5.3	5.4	6	51
#> Study 19.5	Study 19	26	1045	57	1132	5.4	5.4	NA	26	87
#> Study 20.1	Study 20	596	2062	659	6145	5.0	NA	5.0	63	2062
#> Study 20.2	Study 20	392	5015	659	6145	5.5	5.0	5.5	204	2953
#> Study 20.3	Study 20	137	5999	659	6145	6.0	5.5	6.0	255	984
#> Study 20.4	Study 20	137	5999	659	6145	6.0	6.0	NA	137	146
#> Study 21.1	Study 21	187	8562	368	9674	5.5	NA	5.5	181	8562
#> Study 21.2	Study 21	187	8562	368	9674	5.5	5.5	NA	187	1112
#> Study 22.1	Study 22	9	395	17	432	5.8	NA	5.8	8	395
#> Study 22.2	Study 22	9	395	17	432	5.8	5.8	NA	9	37
#> Study 23.1	Study 23	122	215	164	304	5.5	NA	5.5	42	215
#> Study 23.2	Study 23	88	265	164	304	5.7	5.5	5.7	34	50
#> Study 23.3	Study 23	88	265	164	304	5.7	5.7	NA	88	39

#> Study 24.1	Study 24	22	129	44	164	6.1	NA	6.1	22	129
#> Study 24.2	Study 24	22	129	44	164	6.1	6.1	NA	22	35
#> Study 25.1	Study 25	79	217	80	882	6.6	NA	6.6	1	217
#> Study 25.2	Study 25	79	217	80	882	6.6	6.6	NA	79	665
#> Study 26.1	Study 26	114	203	178	223	6.9	NA	6.9	64	203
#> Study 26.2	Study 26	90	219	178	223	7.4	6.9	7.4	24	16
#> Study 26.3	Study 26	73	223	178	223	7.6	7.4	7.6	17	4
#> Study 26.4	Study 26	73	223	178	223	7.6	7.6	NA	73	0
#> Study 27.1	Study 27	135	592	178	688	5.9	NA	5.9	43	592
#> Study 27.2	Study 27	87	674	178	688	6.5	5.9	6.5	48	82
#> Study 27.3	Study 27	87	674	178	688	6.5	6.5	NA	87	14
#> Study 28.1	Study 28	575	980	627	2250	5.5	NA	5.5	52	980
#> Study 28.2	Study 28	486	1773	627	2250	6.1	5.5	6.1	89	793
#> Study 28.3	Study 28	486	1773	627	2250	6.1	6.1	NA	486	477
#> Study 29.1	Study 29	23	109	30	114	6.1	NA	6.1	7	109
#> Study 29.2	Study 29	23	109	30	114	6.1	6.1	NA	23	5
#> Study 30.1	Study 30	424	2112	616	2233	6.0	NA	6.0	192	2112
#> Study 30.2	Study 30	424	2112	616	2233	6.0	6.0	NA	424	121
#> Study 31.1	Study 31	338	4060	367	6436	5.7	NA	5.7	29	4060
#> Study 31.2	Study 31	338	4060	367	6436	5.7	5.7	NA	338	2376
#> Study 32.1	Study 32	57	32	64	44	6.0	NA	6.0	7	32
#> Study 32.2	Study 32	50	40	64	44	6.4	6.0	6.4	7	8
#> Study 32.3	Study 32	47	41	64	44	6.5	6.4	6.5	3	1
#> Study 32.4	Study 32	40	43	64	44	7.0	6.5	7.0	7	2
#> Study 32.5	Study 32	40	43	64	44	7.0	7.0	NA	40	1
#> Study 33.1	Study 33	52	79	65	116	5.6	NA	5.6	13	79
#> Study 33.2	Study 33	52	79	65	116	5.6	5.6	NA	52	37
#> Study 34.1	Study 34	111	83	112	489	5.0	NA	5.0	1	83
#> Study 34.2	Study 34	110	225	112	489	5.5	5.0	5.5	1	142
#> Study 34.3	Study 34	100	381	112	489	6.0	5.5	6.0	10	156
#> Study 34.4	Study 34	78	465	112	489	6.5	6.0	6.5	22	84
#> Study 34.5	Study 34	60	479	112	489	7.0	6.5	7.0	18	14
#> Study 34.6	Study 34	60	479	112	489	7.0	7.0	NA	60	10
#> Study 35.1	Study 35	20	60	21	90	5.9	NA	5.9	1	60
#> Study 35.2	Study 35	19	62	21	90	6.0	5.9	6.0	1	2
#> Study 35.3	Study 35	17	76	21	90	6.1	6.0	6.1	2	14
#> Study 35.4	Study 35	17	79	21	90	6.2	6.1	6.2	0	3
#> Study 35.5	Study 35	17	79	21	90	6.3	6.2	6.3	0	0
#> Study 35.6	Study 35	16	81	21	90	6.4	6.3	6.4	1	2
#> Study 35.7	Study 35	13	81	21	90	6.5	6.4	6.5	3	0
#> Study 35.8	Study 35	12	86	21	90	6.6	6.5	6.6	1	5
#> Study 35.9	Study 35	11	87	21	90	6.7	6.6	6.7	1	1

```

#> Study 35.10 Study 35 11 87 21 90 6.8 6.7 6.8 0 0
#> Study 35.11 Study 35 11 88 21 90 6.9 6.8 6.9 0 1
#> Study 35.12 Study 35 10 88 21 90 7.0 6.9 7.0 1 0
#> Study 35.13 Study 35 10 88 21 90 7.0 7.0 NA 10 2
#> Study 36.1 Study 36 25 243 27 288 5.9 NA 5.9 2 243
#> Study 36.2 Study 36 25 243 27 288 5.9 5.9 NA 25 45
#> Study 37.1 Study 37 12 268 14 293 5.9 NA 5.9 2 268
#> Study 37.2 Study 37 12 268 14 293 5.9 5.9 NA 12 25
#> Study 38.1 Study 38 13 260 19 295 5.9 NA 5.9 6 260
#> Study 38.2 Study 38 13 260 19 295 5.9 5.9 NA 13 35
#> ctype lcutmean
#> Study 01.1 1 1.234050
#> Study 01.2 3 2.038769
#> Study 02.1 1 1.151293
#> Study 02.2 2 1.619339
#> Study 02.3 2 1.638950
#> Study 02.4 2 1.658183
#> Study 02.5 2 1.677053
#> Study 02.6 2 1.695574
#> Study 02.7 2 1.713757
#> Study 02.8 2 1.731616
#> Study 02.9 2 1.749162
#> Study 02.10 2 1.766405
#> Study 02.11 2 1.783356
#> Study 02.12 2 1.808154
#> Study 02.13 2 1.855809
#> Study 02.14 3 2.094827
#> Study 03.1 1 1.258848
#> Study 03.2 3 2.063567
#> Study 04.1 1 1.242453
#> Study 04.2 3 2.047172
#> Study 05.1 1 1.250718
#> Study 05.2 3 2.055437
#> Study 06.1 1 1.207957
#> Study 06.2 2 1.797284
#> Study 06.3 3 2.087194
#> Study 07.1 1 1.250718
#> Study 07.2 3 2.055437
#> Study 08.1 1 1.180427
#> Study 08.2 2 1.686227
#> Study 08.3 2 1.713757
#> Study 08.4 3 2.012676

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```
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#> Study 09.2      2 1.766405
#> Study 09.3      2 1.783356
#> Study 09.4      3 2.047172
#> Study 10.1      1 1.027062
#> Study 10.2      2 1.454270
#> Study 10.3      2 1.635165
#> Study 10.4      2 1.731616
#> Study 10.5      2 1.782508
#> Study 10.6      2 1.870736
#> Study 10.7      3 2.109754
#> Study 11.1      1 1.151293
#> Study 11.2      2 1.619339
#> Study 11.3      2 1.638950
#> Study 11.4      2 1.658183
#> Study 11.5      2 1.677053
#> Study 11.6      2 1.695574
#> Study 11.7      2 1.713757
#> Study 11.8      2 1.731616
#> Study 11.9      2 1.749162
#> Study 11.10     2 1.766405
#> Study 11.11     2 1.783356
#> Study 11.12     2 1.808154
#> Study 11.13     2 1.855809
#> Study 11.14     3 2.094827
#> Study 12.1      1 1.216807
#> Study 12.2      3 2.021526
#> Study 13.1      1 1.198948
#> Study 13.2      2 1.713757
#> Study 13.3      2 1.731616
#> Study 13.4      2 1.749162
#> Study 13.5      2 1.766405
#> Study 13.6      2 1.783356
#> Study 13.7      3 2.047172
#> Study 14.1      1 1.130882
#> Study 14.2      2 1.598928
#> Study 14.3      2 1.638950
#> Study 14.4      2 1.658183
#> Study 14.5      2 1.686227
#> Study 14.6      2 1.713757
#> Study 14.7      2 1.731616
#> Study 14.8      2 1.757709
```

```
#> Study 14.9      3 2.038769
#> Study 15.1      1 1.151293
#> Study 15.2      2 1.657093
#> Study 15.3      2 1.722607
#> Study 15.4      2 1.766113
#> Study 15.5      2 1.824029
#> Study 15.6      3 2.079442
#> Study 16.1      1 1.151293
#> Study 16.2      2 1.657093
#> Study 16.3      2 1.722607
#> Study 16.4      2 1.766113
#> Study 16.5      2 1.824029
#> Study 16.6      3 2.079442
#> Study 17.1      1 1.151293
#> Study 17.2      2 1.657093
#> Study 17.3      2 1.722607
#> Study 17.4      2 1.766113
#> Study 17.5      2 1.824029
#> Study 17.6      3 2.079442
#> Study 18.1      1 1.216807
#> Study 18.2      3 2.021526
#> Study 19.1      1 1.161194
#> Study 19.2      2 1.638950
#> Study 19.3      2 1.658183
#> Study 19.4      2 1.677053
#> Study 19.5      3 1.994492
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#> Study 20.2      2 1.657093
#> Study 20.3      2 1.748254
#> Study 20.4      3 2.047172
#> Study 21.1      1 1.198948
#> Study 21.2      3 2.003667
#> Study 22.1      1 1.225503
#> Study 22.2      3 2.030222
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#> Study 23.2      2 1.722607
#> Study 23.3      3 2.021526
#> Study 24.1      1 1.250718
#> Study 24.2      3 2.055437
#> Study 25.1      1 1.290108
#> Study 25.2      3 2.094827
#> Study 26.1      1 1.312334
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#> Study 26.3      2 2.014814
#> Study 26.4      3 2.165367
#> Study 27.1      1 1.234050
#> Study 27.2      2 1.823377
#> Study 27.3      3 2.087194
#> Study 28.1      1 1.198948
#> Study 28.2      2 1.756518
#> Study 28.3      3 2.055437
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#> Study 29.2      3 2.055437
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#> Study 30.2      3 2.047172
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#> Study 31.2      3 2.021526
#> Study 32.1      1 1.242453
#> Study 32.2      2 1.824029
#> Study 32.3      2 1.864050
#> Study 32.4      2 1.908856
#> Study 32.5      3 2.124248
#> Study 33.1      1 1.207957
#> Study 33.2      3 2.012676
#> Study 34.1      1 1.151293
#> Study 34.2      2 1.657093
#> Study 34.3      2 1.748254
#> Study 34.4      2 1.831781
#> Study 34.5      2 1.908856
#> Study 34.6      3 2.124248
#> Study 35.1      1 1.234050
#> Study 35.2      2 1.783356
#> Study 35.3      2 1.800024
#> Study 35.4      2 1.816419
#> Study 35.5      2 1.832549
#> Study 35.6      2 1.848424
#> Study 35.7      2 1.864050
#> Study 35.8      2 1.879436
#> Study 35.9      2 1.894589
#> Study 35.10     2 1.909515
#> Study 35.11     2 1.924222
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#> Study 35.13     3 2.124248
#> Study 36.1      1 1.234050

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#> Study 36.2      3 2.038769
#> Study 37.1      1 1.234050
#> Study 37.2      3 2.038769
#> Study 38.1      1 1.234050
#> Study 38.2      3 2.038769
#>
#> $original
#>      study TP   TN   FP  FN threshold  n1   n0 testdirection      sens
#> 1  Study 01 574 1389  682 262      5.9 836 2071      greater 0.68660287
#> 2  Study 02 617 1005 7735  18      5.0 635 8740      greater 0.97165354
#> 3  Study 02 607 1617 7123  28      5.1 635 8740      greater 0.95590551
#> 4  Study 02 600 2438 6302  35      5.2 635 8740      greater 0.94488189
#> 5  Study 02 581 3409 5331  54      5.3 635 8740      greater 0.91496063
#> 6  Study 02 563 4422 4318  72      5.4 635 8740      greater 0.88661417
#> 7  Study 02 550 5384 3356  85      5.5 635 8740      greater 0.86614173
#> 8  Study 02 522 6267 2473 113      5.6 635 8740      greater 0.82204724
#> 9  Study 02 489 6966 1774 146      5.7 635 8740      greater 0.77007874
#> 10 Study 02 457 7534 1206 178      5.8 635 8740      greater 0.71968504
#> 11 Study 02 429 7927  813 206      5.9 635 8740      greater 0.67559055
#> 12 Study 02 393 8172  568 242      6.0 635 8740      greater 0.61889764
#> 13 Study 02 332 8460  280 303      6.2 635 8740      greater 0.52283465
#> 14 Study 02 236 8670   70 399      6.6 635 8740      greater 0.37165354
#> 15 Study 03  36  998   95  13      6.2  49 1093      greater 0.73469388
#> 16 Study 04  16  147   10  25      6.0  41  157      greater 0.39024390
#> 17 Study 05 644 1217  286 151      6.1 795 1503      greater 0.81006289
#> 18 Study 06 176 1286  768 102      5.6 278 2054      greater 0.63309353
#> 19 Study 06  69 1867  187 209      6.5 278 2054      greater 0.24820144
#> 20 Study 07  72  258   46  16      6.1  88  304      greater 0.81818182
#> 21 Study 08  89 1382  302  26      5.3 115 1684      greater 0.77391304
#> 22 Study 08  72 1558  126  43      5.5 115 1684      greater 0.62608696
#> 23 Study 08  65 1602   82  50      5.6 115 1684      greater 0.56521739
#> 24 Study 09 207 2704 3161  45      5.8 252 5865      greater 0.82142857
#> 25 Study 09 196 3308 2557  56      5.9 252 5865      greater 0.77777778
#> 26 Study 09 181 3877 1988  71      6.0 252 5865      greater 0.71825397
#> 27 Study 10  54   1  450   0      3.9  54  451      greater 1.00000000
#> 28 Study 10  54  45  406   0      4.7  54  451      greater 1.00000000
#> 29 Study 10  46  363   88   8      5.6  54  451      greater 0.85185185
#> 30 Study 10  43  389   62  11      5.7  54  451      greater 0.79629630
#> 31 Study 10  23  447    4  31      6.2  54  451      greater 0.42592593
#> 32 Study 10  12  451    0  42      6.8  54  451      greater 0.22222222
#> 33 Study 11 861  611 4439  34      5.0 895 5050      greater 0.96201117
#> 34 Study 11 837 1000 4050  58      5.1 895 5050      greater 0.93519553

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#> 35	Study 11	793	1525	3525	102	5.2	895	5050	greater	0.88603352
#> 36	Study 11	740	2116	2934	155	5.3	895	5050	greater	0.82681564
#> 37	Study 11	687	2762	2288	208	5.4	895	5050	greater	0.76759777
#> 38	Study 11	610	3358	1692	285	5.5	895	5050	greater	0.68156425
#> 39	Study 11	532	3883	1167	363	5.6	895	5050	greater	0.59441341
#> 40	Study 11	455	4277	773	440	5.7	895	5050	greater	0.50837989
#> 41	Study 11	376	4585	465	519	5.8	895	5050	greater	0.42011173
#> 42	Study 11	298	4782	268	597	5.9	895	5050	greater	0.33296089
#> 43	Study 11	235	4883	167	660	6.0	895	5050	greater	0.26256983
#> 44	Study 11	136	4984	66	759	6.2	895	5050	greater	0.15195531
#> 45	Study 11	46	5045	5	849	6.6	895	5050	greater	0.05139665
#> 46	Study 12	184	5265	638	154	5.7	338	5903	greater	0.54437870
#> 47	Study 13	72	120	213	9	5.5	81	333	greater	0.88888889
#> 48	Study 13	70	144	189	11	5.6	81	333	greater	0.86419753
#> 49	Study 13	66	170	163	15	5.7	81	333	greater	0.81481481
#> 50	Study 13	58	204	129	23	5.8	81	333	greater	0.71604938
#> 51	Study 13	50	234	99	31	5.9	81	333	greater	0.61728395
#> 52	Study 13	40	256	77	41	6.0	81	333	greater	0.49382716
#> 53	Study 14	285	155	1532	10	4.8	295	1687	greater	0.96610169
#> 54	Study 14	262	412	1275	33	5.1	295	1687	greater	0.88813559
#> 55	Study 14	253	516	1171	42	5.2	295	1687	greater	0.85762712
#> 56	Study 14	234	680	1007	61	5.3	295	1687	greater	0.79322034
#> 57	Study 14	195	969	718	100	5.5	295	1687	greater	0.66101695
#> 58	Study 14	169	1099	588	126	5.6	295	1687	greater	0.57288136
#> 59	Study 14	138	1211	476	157	5.7	295	1687	greater	0.46779661
#> 60	Study 14	91	1409	278	204	5.9	295	1687	greater	0.30847458
#> 61	Study 15	108	626	4190	6	5.0	114	4816	greater	0.94736842
#> 62	Study 15	91	2745	2071	23	5.5	114	4816	greater	0.79824561
#> 63	Study 15	74	3660	1156	40	5.7	114	4816	greater	0.64912281
#> 64	Study 15	48	4479	337	66	6.0	114	4816	greater	0.42105263
#> 65	Study 15	7	4816	0	107	6.4	114	4816	greater	0.06140351
#> 66	Study 16	184	181	5645	2	5.0	186	5826	greater	0.98924731
#> 67	Study 16	164	3437	2389	22	5.5	186	5826	greater	0.88172043
#> 68	Study 16	145	4719	1107	41	5.7	186	5826	greater	0.77956989
#> 69	Study 16	84	5593	233	102	6.0	186	5826	greater	0.45161290
#> 70	Study 16	4	5826	0	182	6.4	186	5826	greater	0.02150538
#> 71	Study 17	88	480	3212	4	5.0	92	3692	greater	0.95652174
#> 72	Study 17	74	2252	1440	18	5.5	92	3692	greater	0.80434783
#> 73	Study 17	61	2954	738	31	5.7	92	3692	greater	0.66304348
#> 74	Study 17	35	3507	185	57	6.0	92	3692	greater	0.38043478
#> 75	Study 17	4	3692	0	88	6.4	92	3692	greater	0.04347826
#> 76	Study 18	21	284	36	43	5.7	64	320	greater	0.32812500

#> 77	Study	19	49	691	441	8	5.1	57	1132	greater	0.85964912
#> 78	Study	19	42	814	318	15	5.2	57	1132	greater	0.73684211
#> 79	Study	19	32	994	138	25	5.3	57	1132	greater	0.56140351
#> 80	Study	19	26	1045	87	31	5.4	57	1132	greater	0.45614035
#> 82	Study	20	596	2062	4083	63	5.0	659	6145	greater	0.90440061
#> 81	Study	20	392	5015	1130	267	5.5	659	6145	greater	0.59484067
#> 83	Study	20	137	5999	146	522	6.0	659	6145	greater	0.20789074
#> 84	Study	21	187	8562	1112	181	5.5	368	9674	greater	0.50815217
#> 85	Study	22	9	395	37	8	5.8	17	432	greater	0.52941176
#> 86	Study	23	122	215	89	42	5.5	164	304	greater	0.74390244
#> 87	Study	23	88	265	39	76	5.7	164	304	greater	0.53658537
#> 88	Study	24	22	129	35	22	6.1	44	164	greater	0.50000000
#> 89	Study	25	79	217	665	1	6.6	80	882	greater	0.98750000
#> 90	Study	26	114	203	20	64	6.9	178	223	greater	0.64044944
#> 91	Study	26	90	219	4	88	7.4	178	223	greater	0.50561798
#> 92	Study	26	73	223	0	105	7.6	178	223	greater	0.41011236
#> 93	Study	27	135	592	96	43	5.9	178	688	greater	0.75842697
#> 94	Study	27	87	674	14	91	6.5	178	688	greater	0.48876404
#> 95	Study	28	575	980	1270	52	5.5	627	2250	greater	0.91706539
#> 96	Study	28	486	1773	477	141	6.1	627	2250	greater	0.77511962
#> 97	Study	29	23	109	5	7	6.1	30	114	greater	0.76666667
#> 98	Study	30	424	2112	121	192	6.0	616	2233	greater	0.68831169
#> 99	Study	31	338	4060	2376	29	5.7	367	6436	greater	0.92098093
#> 100	Study	32	57	32	12	7	6.0	64	44	greater	0.89062500
#> 101	Study	32	50	40	4	14	6.4	64	44	greater	0.78125000
#> 102	Study	32	47	41	3	17	6.5	64	44	greater	0.73437500
#> 103	Study	32	40	43	1	24	7.0	64	44	greater	0.62500000
#> 104	Study	33	52	79	37	13	5.6	65	116	greater	0.80000000
#> 105	Study	34	111	83	406	1	5.0	112	489	greater	0.99107143
#> 106	Study	34	110	225	264	2	5.5	112	489	greater	0.98214286
#> 107	Study	34	100	381	108	12	6.0	112	489	greater	0.89285714
#> 108	Study	34	78	465	24	34	6.5	112	489	greater	0.69642857
#> 109	Study	34	60	479	10	52	7.0	112	489	greater	0.53571429
#> 110	Study	35	20	60	30	1	5.9	21	90	greater	0.95238095
#> 111	Study	35	19	62	28	2	6.0	21	90	greater	0.90476190
#> 112	Study	35	17	76	14	4	6.1	21	90	greater	0.80952381
#> 113	Study	35	17	79	11	4	6.2	21	90	greater	0.80952381
#> 114	Study	35	17	79	11	4	6.3	21	90	greater	0.80952381
#> 115	Study	35	16	81	9	5	6.4	21	90	greater	0.76190476
#> 116	Study	35	13	81	9	8	6.5	21	90	greater	0.61904762
#> 117	Study	35	12	86	4	9	6.6	21	90	greater	0.57142857
#> 118	Study	35	11	87	3	10	6.7	21	90	greater	0.52380952

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#> 119 Study 35 11 87 3 10 6.8 21 90 greater 0.52380952
#> 120 Study 35 11 88 2 10 6.9 21 90 greater 0.52380952
#> 121 Study 35 10 88 2 11 7.0 21 90 greater 0.47619048
#> 122 Study 36 25 243 45 2 5.9 27 288 greater 0.92592593
#> 123 Study 37 12 268 25 2 5.9 14 293 greater 0.85714286
#> 124 Study 38 13 260 35 6 5.9 19 295 greater 0.68421053
#> spec fpr
#> 1 0.670690488 0.329309512
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#> 109 0.979550102 0.020449898
#> 110 0.666666667 0.333333333
#> 111 0.688888889 0.311111111
#> 112 0.844444444 0.155555556
#> 113 0.877777778 0.122222222
#> 114 0.877777778 0.122222222
#> 115 0.900000000 0.100000000
#> 116 0.900000000 0.100000000
#> 117 0.955555556 0.044444444
#> 118 0.966666667 0.033333333
#> 119 0.966666667 0.033333333
```

```
#> 120 0.977777778 0.022222222
#> 121 0.977777778 0.022222222
#> 122 0.843750000 0.156250000
#> 123 0.914675768 0.085324232
#> 124 0.881355932 0.118644068
```

Step 2: How do we get initial values?

```
init <- initHoyerAFT(res$restructured,
                     dist="loglogistic")
init
#>
#>          beta0_init lambda0_init beta1_init lambda1_init su0_init
#> Initial value   1.681153    0.04964348   1.815414    0.08091965 0.1552818
#>
#>          su1_init coru0u1_init distcode
#> Initial value 0.1284618    0.3948626      3
```

Step 3: How do we fit the model?

```
hoyerAFT <- fitHoyerAFT(data=res,
                        init=init,
                        eval_threshold=c(5.0,5.5,6.0,6.5,7.0,7.5))
```

```
hoyerAFT
#>
#> Hoyer Model
#> -----
#>
#> Number of studies : 38
#> Optimizer          : Converged
#> Hessian            : Positive definite
#> Max |grad|         : 0.03070981
#> -2 log likelihood : 209322 ( df = 7 )
#> AIC                : 209336
#> BIC                : 209347.4
#>
#> Distribution       : Loglogistic
#> Test direction     : greater
#>
```

```
#> Use summary() for parameter estimates.
summary(hoyerAFT)
#>
#> Summary: Hoyer Model
#> -----
#>
#> Parameter estimates
#> -----
#>
#>           Estimate      Std. Error
#> beta0      1.7056911000 0.00956301460
#> lambda0    0.0395020040 0.00018572655
#> su0        0.0586486790 0.00677848700
#> beta1      1.8253371000 0.01456524000
#> lambda1    0.0563984790 0.00092447216
#> su1        0.0883206310 0.01095646100
#> rho        0.8630325700 0.04544108800
#> covu0u1    0.0044704124 0.00114172000
#> logitSurv1 3.8281031000 0.26350352000
#> logitSurv1 2.1381608000 0.25933476000
#> logitSurv1 0.5953642400 0.25807906000
#> logitSurv1 -0.8238709800 0.25910740000
#> logitSurv1 -2.1378776000 0.26190467000
#> logitSurv1 -3.3611884000 0.26605427000
#> logitSurv0 2.4366671000 0.24260400000
#> logitSurv0 0.0238736250 0.24209177000
#> logitSurv0 -2.1788343000 0.24208781000
#> logitSurv0 -4.2051291000 0.24247511000
#> logitSurv0 -6.0811851000 0.24316614000
#> logitSurv0 -7.8277515000 0.24409438000
#>
#> Sensitivity / specificity
#> -----
#>   threshold  conflevel      Sens SensCI_Lower SensCI_Upper      Spec
#> 1         5.0        0.95 0.97871219 0.964826170 0.987189040 0.080419039
#> 2         5.5        0.95 0.89455725 0.836152370 0.933791700 0.494031880
#> 3         6.0        0.95 0.64459500 0.522369700 0.750482990 0.898332650
#> 4         6.5        0.95 0.30494258 0.208876300 0.421643620 0.985300440
#> 5         7.0        0.95 0.10546947 0.065915008 0.164577800 0.997719740
#> 6         7.5        0.95 0.03353069 0.020180626 0.055214536 0.999601640
#>   SpecCI_Lower SpecCI_Upper
#> 1 0.051555604 0.12334026
#> 2 0.377925030 0.61078605
```

```
#> 3 0.846102130 0.93421518
#> 4 0.976566740 0.99080968
#> 5 0.996332560 0.99858298
#> 6 0.999357390 0.99975307
```

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