Meta-Analytic Depiction Of Ordered Categorical Diagnostic Test Accuracy In ROC Space

No Thresholds Left Behind

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Outline

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Objectives

1. Review underlying concepts of medical diagnostic test evaluation
2. Provide illustrated overview of current methods for meta-analysis of diagnostic test accuracy studies with discrete outcomes
3. Describe a robust and flexible parametric algorithm for meta-analysis of ordered categorical data
4. Demonstrate implementation with Stata using two data sets, one with studies reporting same set of categories and the other with disparately categorized outcomes

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Medical Diagnostic Test

Any measurement aiming to identify individuals who could potentially benefit from preventative or therapeutic intervention

This includes:

1. Elements of medical history e.g. Retrosternal chest pain
2. Physical examination e.g. Systolic blood pressure
3. Imaging procedures e.g. Chest xray
4. Laboratory investigations. e.g. Fasting blood sugar
5. Clinical prediction rules e.g. Geneva Score for Venous Thromboembolim

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Diagnostic Test Types/Scales

1. **Dichotomous** using single implicit or explicit threshold
   eg. Presence or absence of a specific DNA sequence in blood serum
   eg. Fasting blood glucose $\geq$ 126 mg/ml diagnostic of diabetes mellitus
2. **Ordered Categorical** with multiple implicit or explicit thresholds
   eg. the BIRADS scale for mammograms: 1 'Benign'; 2 'Possibly benign'; 3 'Unclear'; 4 'Possibly malignant'; 5 'Malignant'
   eg. Clinical symptoms classified as 1 'not present', 2 'mild', 3 'moderate', or 4 'severe'
3. **Continuous**
   eg. biochemical tests such as serum levels of creatinine, bilirubin or calcium

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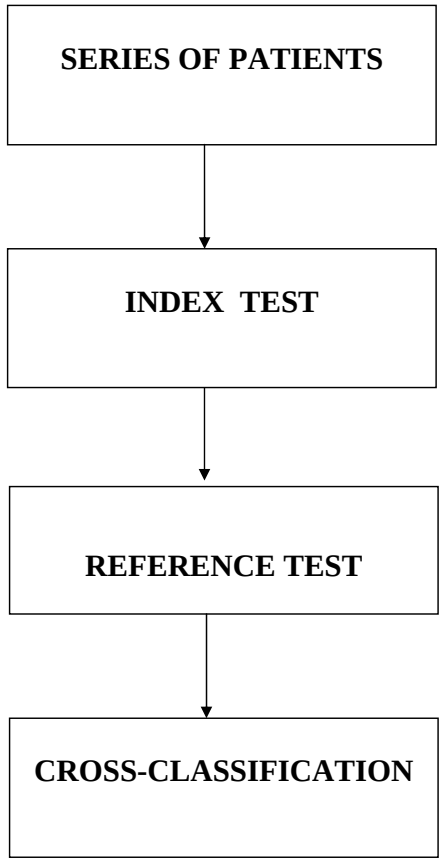
Diagnostic Accuracy Studies

Figure: Basic Study Design



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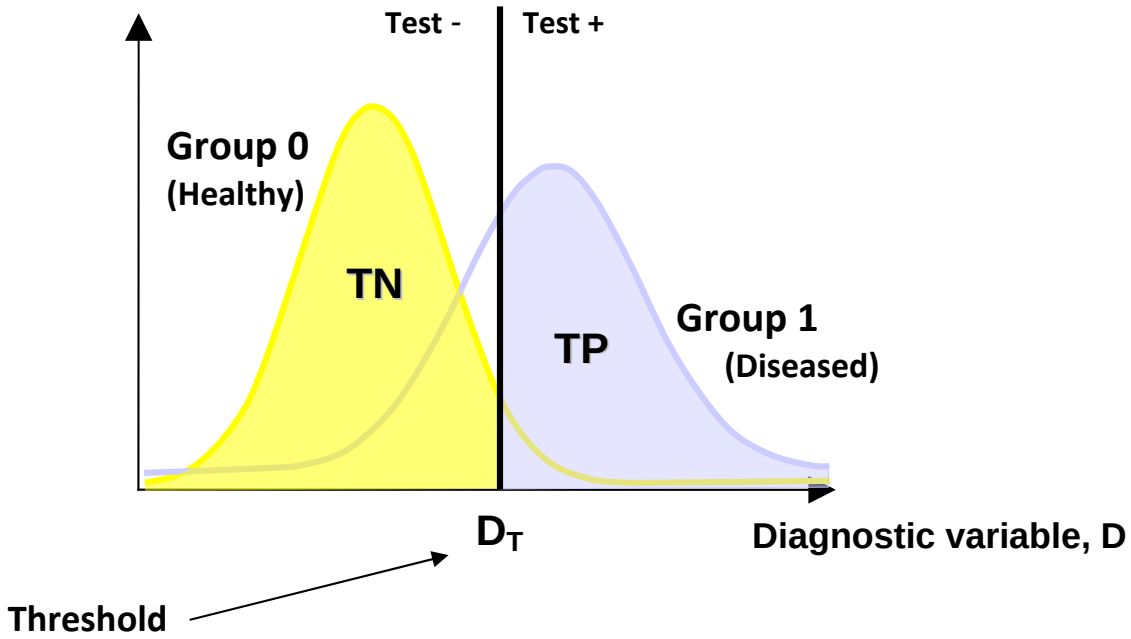
Diagnostic Accuracy Studies

Figure: Distributions of test result for diseased and non-diseased populations defined by threshold (DT)



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Binary Test Accuracy

Data Structure

Data often reported as 2×2 matrix

	Reference Test (Diseased)	Reference Test (Healthy)
Test Positive	True Positive (a)	False Positive (b)
Test Negative	False Negative (c)	True Negative (d)

1. The chosen threshold may vary between studies of the same test due to inter-laboratory or inter-observer variation

2. The higher the cut-off value, the higher the specificity and the lower the sensitivity

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Binary Test Accuracy

Measures of Test Performance

Sensitivity (true positive rate)	The proportion of subjects with disease who are correctly identified as such by test (a/a+c)
Specificity (true negative rate)	The proportion of subjects without disease who are correctly identified as such by test (d/b+d)
Positive predictive value	The proportion of test positive subjects who truly have disease (a/a+b)
Negative predictive value	The proportion of test negative subjects who truly do not have disease (d/c+d)

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Binary Test Accuracy

Measures of Test Performance

Likelihood ratios (LR) The ratio of the probability of a positive (or negative) test result in the patients with disease to the probability of the same test result in the patients without the disease (sensitivity/1-specificity) or (1-Sensitivity/specificity)

Diagnostic odds ratio The ratio of the odds of a positive test result in patients with disease compared to the odds of the same test result in patients without disease (LRP/LRN)

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Non-binary Test Accuracy

ROC Curve Analysis

The accuracy of continuously or ordinally scaled tests is best summarized by ROC curve, a plot of all pairs of (1-specificity, sensitivity) as positivity threshold varies:

1. Provides complete description of potential performance
2. Facilitates comparison and combination of information across studies of the same test
3. Guides the choice of thresholds in applications
4. Provides a mechanism for relevant comparisons between different non-binary tests

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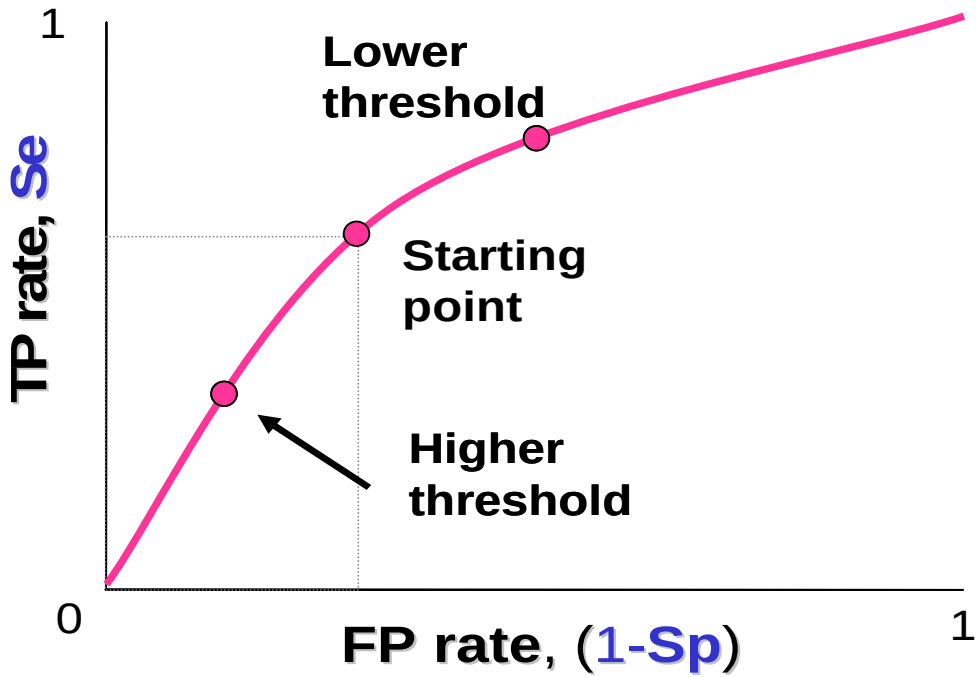
Non-binary Test Accuracy

ROC Curve Analysis

Figure: ROC curve derived from changing test threshold



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Non-binary Test Accuracy

ROC Curve Analysis

Table: **Summary Indices for ROC Curves**

Index Name	**Notation**	**Definition**	**Interpretations**
Area under Curve	AUC	Integrate ROC over range(0-1)	Average TPF across all possible FPF
Specific ROC point	ROC(t_0)	ROC(t_0)	P[$Y_D >$ q]
Partial Area under curve	pAUC(t_0)	Integrate ROC over range(0-t_0)	Average TPF across FPF $\in$ (0-t_0)
Symmetry Point	Sym	ROC(Sym)=Sym	Sensitivity=Specificity

Y_D: Test result for diseased
q=1-t_0 quantile for Y_D

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Ordinal Test Accuracy

Data Structure

1. Test result for each individual Y falls into one of J categories ("ratings")
2. These categories are ordered in terms of increasing likelihood of disease
3. Data often reported as $2 \times j$ matrix

Category	Diseased	Healthy	Total
C_1	n_{d1}	n_{h1}	n_1
.	.	.	.
.	.	.	.
.	.	.	.
C_j	n_{dj}	n_{hj}	n_j
Total	n_d	n_h	N

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Ordinal Data Analysis

Example Data

117 consecutive patients older than age 50 admitted to a Veterans Affairs (VA) nursing home (NH).

Screened for alcohol dependence using CAGE questionnaire as index test.

DSM-III-R criteria were used as Reference standard.

Forty-nine percent of study participants had lifetime alcohol abuse or dependence.

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Ordinal Data Analysis

CAGE Scores for Alcoholism Screening

CAGE is an acronym for each of four questions:

1. Have you ever felt you should cut down on your drinking?
2. Have people annoyed you by criticizing your drinking?
3. Have you ever felt bad or guilty about your drinking?
4. Have you ever had a drink in the morning to get rid of a hangover?

Each question is scored 1 or 0 for YES or NO answers respectively

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Ordinal Data Analysis

Example Data

Table: Single Study CAGE Scores

Score	0	1	2	3	4
Normal	45	9	4	2	0
Abnormal	1	9	17	7	23

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Ordinal Data Analysis

Approaches

1. Dichotomization at single threshold and analysis as binary data
2. Empirical ROC plot of sensitivity and 1-specificity at different thresholds
3. Binormal ROC analysis
4. ROC analysis via Ordinal regression

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Ordinal Data Analysis

Dichotomized Data

Recommended Positivity Threshold: Cage Score >= 2

	DSM-IIIR (Abnormal)	DSM-IIIR (Normal)	total
CAGE >= 2	47	6	53
CAGE < 2	10	54	64
Total	57	60	117

Sensitivity (percent): (47/57)*100 = 82

Specificity (percent): (54/60)*100 = 90

Positive Predictive Value (percent): (47/53)*100 = 90

Negative Predictive Value (percent): (54/64)*100 = 84

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Ordinal Data Analysis

Empirical ROC Analysis

Based on sensitivity/specificity pairs at multiple thresholds: The higher the cut-off value, the higher the specificity and the lower the sensitivity

Sensitivity (TPR) at each threshold: Number of diseased diagnosed positive/Number of diseased

Specificity (TNR) at each threshold: Number of non-diseased diagnosed negative/Number of non-diseased

cutpoint	Sensitivity	Specificity
$>= 0$	100	0
$>= 1$	98	75
$>= 2$	82	90
$>= 3$	52	96
$>= 4$	40	100
> 4	0	100

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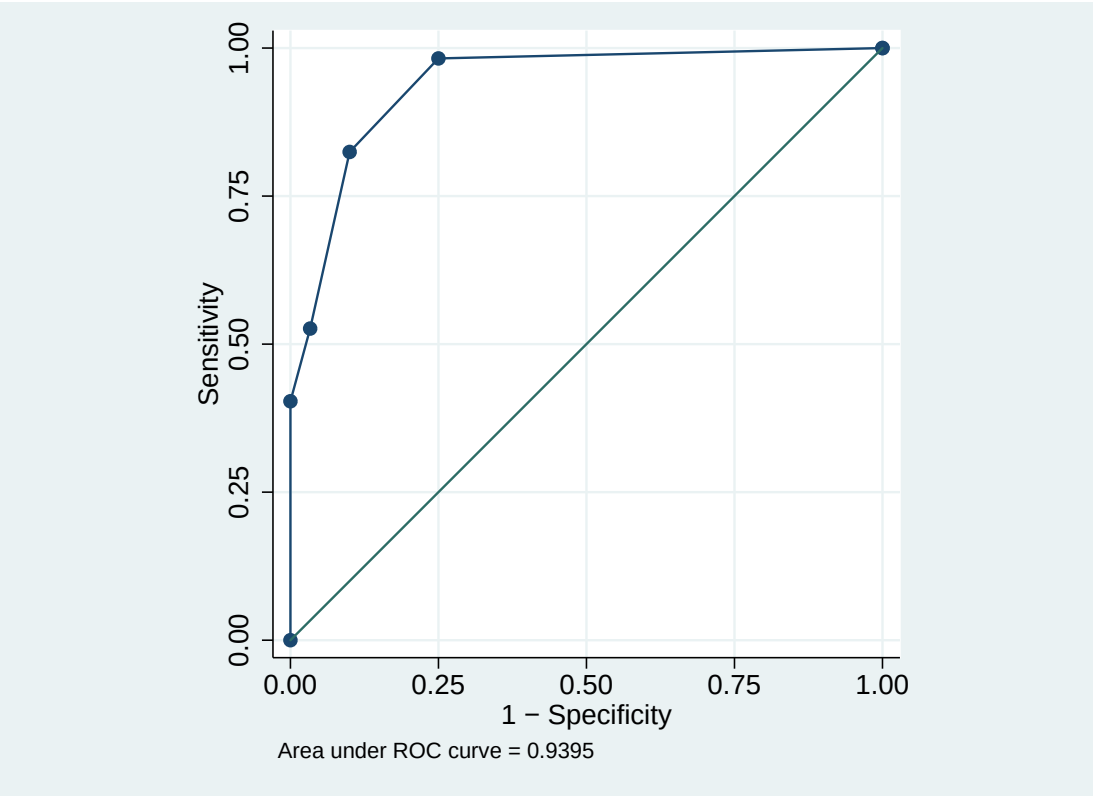
Ordinal Data Analysis

Empirical ROC Analysis with **roctab**

```
. roctab dtruth score [fw=dis], graph aspect(1)
```



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Ordinal Data Analysis

Binormal ROC Analysis

Test results of diseased and healthy subjects follow normal distributions with respective means μ_1, μ_0 and standard deviations σ_1 and σ_0

1. Scaled mean difference, a $= (\mu_1$ - $\mu_0)/\sigma_1$
2. Scale coefficient, b $= \sigma_0 \, /\sigma_1$
3. The binormal ROC curve: TPR$=$ a $+$ bΦ(FPR) $(0 \leq$ FPR $\leq 1)$
4. The area under curve, AUROC $= \Phi\left(\frac{a}{\sqrt{1+b^2}}\right)$
5. The symmetry point index, Sym $= \Phi\left(\frac{a}{1+b}\right)$

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Ordinal Data Analysis

Binormal ROC Analysis using **rocfit**

```
. rocfit dtruth score [fw=dis]
```

```
Binormal model of dtruth on score               Number of obs   =       117
Goodness-of-fit chi2(2) =       2.88
Prob > chi2             =     0.2373
Log likelihood          =  -126.31934
------------------------------------------------------------------------------
             |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
   intercept |   2.919589   0.648216     4.50   0.000     1.649110    4.190068
   slope (*) |   1.443559   0.444514     1.00   0.318     0.572328    2.314789
-------------+----------------------------------------------------------------
       /cut1 |   0.663779   0.175958     3.77   0.000     0.318907    1.008651
       /cut2 |   1.355698   0.207460     6.53   0.000     0.949083    1.762312
       /cut3 |   1.950510   0.296180     6.59   0.000     1.370009    2.531011
       /cut4 |   2.207473   0.358501     6.16   0.000     1.504824    2.910122
------------------------------------------------------------------------------
------------------------------------------------------------------------------
             |                    Indices from binormal fit
       Index |   Estimate   Std. Err.                      [95% Conf. Interval]
-------------+----------------------------------------------------------------
    ROC area |   0.951799   0.018976                      0.914606    0.988991
    delta(m) |   2.022495   0.328053                      1.379522    2.665467
        d(e) |   2.389621   0.270268                      1.859906    2.919336
        d(a) |   2.351199   0.267932                      1.826062    2.876336
------------------------------------------------------------------------------
```

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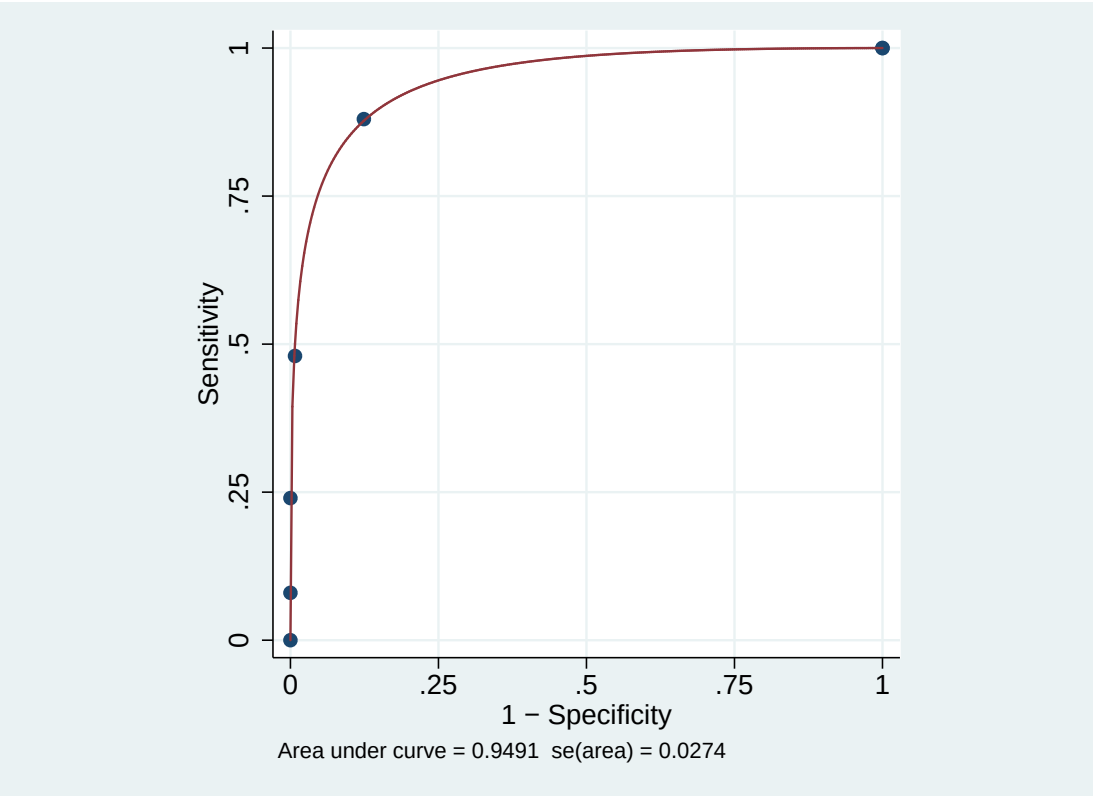
Ordinal Data Analysis

Binormal ROC Curve using **rocplot**

```
. rocplot, norefline aspect(1)
```



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Ordinal Data Analysis

ROC Analysis via Heteroskedastic Ordinal Regression

Suppose, the test result Y falls into one of J categories ("ratings")
The probability of Y falling in a given category j or lower may be modeled as a non-linear function using the ordinal regression equation:

$$g[Pr(Y \leq j \mid D)] = \frac{\theta_j - \alpha D}{exp(\beta D)}$$

g: Cumulative link function

D is a variable indicative of disease status

$\theta_j ....\theta_{j-1}$: Cut-off values on an underlying latent scale

α: Location parameter (measure of diagnostic accuracy)

β: Scale parameter (spread of responses across subjects)

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Ordinal Data Analysis

Choice of Link Functions for Ordinal Regression

1. **Probit** This is the inverse standard normal cumulative distribution function. More suitable when a dependent variable is normally distributed.
2. **Logit** $f(x) = log(x/(1-x))$. This is usually used when the dependent ordinal variable has equal category.
3. **Log-log** $f(x) = -log(-log(x))$. Recommended when the probability of the lower category is high.
4. **Complementary log-log** $f(x) = log(-log(1-x))$. Recommended when the probability of higher category is high.
5. **Cauchit** $f(x) = tan(p(x-0.5))$. This is used when extreme values are present in the data.

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Ordinal Data Analysis

Ordinal Probit ROC Analysis with **oglm**

```
. oglm score dtruth [fw=dis], link(probit) ls het(dtruth)
```

```
Heteroskedastic Ordered Probit Regression          Number of obs   =        117
                                                   LR chi2(2)      =      93.77
                                                   Prob > chi2     =     0.0000
Log likelihood = -126.31934                        Pseudo R2       =     0.2707

------------------------------------------------------------------------------
       score |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
location     |
      dtruth |   2.022494   .3280529     6.17   0.000     1.379522    2.665466
-------------+----------------------------------------------------------------
scale        |
      dtruth |  -.3671114    .307929    -1.19   0.233    -.9706412    .2364184
-------------+----------------------------------------------------------------
       /cut1 |   .6637788   .1759585     3.77   0.000     .3189066    1.008651
       /cut2 |   1.355697   .2074599     6.53   0.000     .9490835    1.762311
       /cut3 |    1.95051   .2961795     6.59   0.000     1.370009    2.531011
       /cut4 |   2.207472   .3585009     6.16   0.000     1.504824    2.910121
------------------------------------------------------------------------------
```

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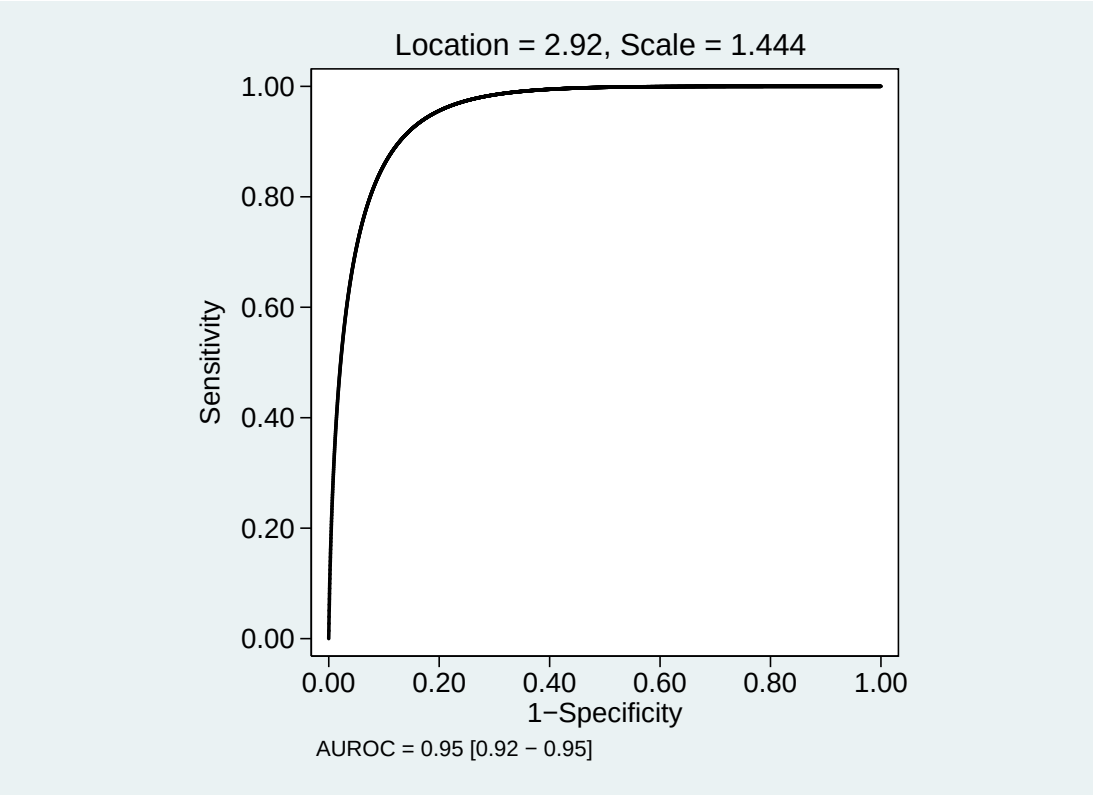
Ordinal Data Analysis

Ordinal Probit ROC Curve with **roccat**

```
. roccat,  avar('avar') avarlo('avarlo') avarhi('avarhi') bvar('bvar') ///
  bvarlo('bvarlo') bvarhi('bvarhi') np(5000)
```



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Diagnostic Meta-analysis

Critical review and statistical combination of previous research

Rationale

1. Too few patients in a single study
2. Too selected a population in a single study
3. No consensus regarding accuracy, impact, reproducibility of test(s)
4. Data often scattered across several journals
5. Explanation of variability in test accuracy
6. etc.

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Diagnostic Meta-analysis

Scope

1. Identification of the number, quality and scope of primary studies
2. Quantification of overall classification performance (sensitivity and specificity), discriminatory power (diagnostic odds ratios) and informational value (diagnostic likelihood ratios)
3. Assessment of the impact of technological evolution (by cumulative meta-analysis based on publication year), technical characteristics of test, methodological quality of primary studies and publication selection bias on estimates of diagnostic accuracy
4. Highlighting of potential issues that require further research

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Diagnostic Meta-analysis

Methodological Concepts

1. Meta-analysis of diagnostic accuracy studies may be performed to provide summary estimates of test performance based on a collection of studies and their reported empirical or estimated smooth ROC curves

2. Statistical methodology for meta-analysis of diagnostic accuracy studies focused on studies reporting estimates of test sensitivity and specificity or two by two data

3. Both fixed and random-effects meta-analytic models have been developed to combine information from such studies

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Diagnostic Meta-analysis

Methodological Concepts

1. To meta-analyze studies with results in more than two categories, results are often dichotomized in order to employ one of the binary methods

2. It is more efficient and informative to take all thresholds into account

3. Existing methods require the same number and set of thresholds, are computationally intensive adapations of the binary methods or are based on hierarchical ordinal probit regression implementable using Bayesian inference

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Example Dataset 1

10 studies on CAGE for alcohol dependence screening (5 listed in table) using Similar Thresholds

Table: Observed Data

Idnum	Author	Setting	Score	dis0	dis1	tdis0	tdis1
1	Saitz	PC	0	99	6	134	76
			1	26	9	134	76
			2	6	19	134	76
			3	2	21	134	76
			4	1	21	134	76
2	McQuade	PC	0	197	7	247	53
			1	31	11	247	53
			2	17	12	247	53
			3	2	13	247	53
			4	0	10	247	53
4	Chan	PC	0	38	2	56	48
			1	9	4	56	48
			2	7	15	56	48
			3	2	10	56	48
			4	0	17	56	48
8	Bradley	AMP	0	69	32	117	110
			1	33	20	117	110
			2	13	28	117	110
			3	1	20	117	110
			4	1	10	117	110
10	Indran	AMP	0	179	0	483	52
			1	120	4	483	52
			2	126	24	483	52
			3	53	19	483	52
			4	5	5	483	52

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Example Dataset 2

19 studies evaluating EBCT for diagnosis of coronary artery disease (15 listed in table)

Table: Disparate Thresholds

Author	Abnormal	Normal	Categories
Budoff	427	283	2
Seese	87	20	2
Yao	45	19	2
Chen	74	42	4
Hosoi	202	80	5
Budoff	983	868	5
Almeda	160	86	4
Knez	1255	860	4
Wong	28	900	5
Shaw	249	10128	5
Greenland	84	945	4
Arad	129	4484	4
Taylor	14	1611	4
Vliengenhart	50	1745	4
La Monte	287	10459	4

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Methodological Overview

1. Dichotomization At Single Threshold And Meta-Analysis As Binary Data
2. Proportional Odds Ordinal Regression Modeling
3. Bivariate Random-Effects Meta-Analysis of Slope And Intercept from Study-Specific Logit-Threshold Linear Regression
4. Bayesian Hierarchical Location-Scale Ordinal Regression Modeling

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Methods for Dichotomized Data

Examples

1. Meta-analysis of sensitivity and specificity separately by direct pooling or modeling using fixed-effects or random-effects approaches

2. Meta-analysis of positive and negative likelihood ratios separately using fixed-effects or random-efffects approaches as applied to risk ratios in meta-analysis of therapeutic trials

3. Meta-analysis of diagnostic odds ratios using fixed-effects or random-efffects approaches as applied to meta-analysis of odds ratios in clinical treatment trials

4. Summary ROC Meta-analysis using fixed-effects or random-efffects approaches

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Methods for Dichotomized Data

Example Dataset: CAGE

Table: Positivity Threshold: Score >= 2

Author	**TP**	**FP**	**FN**	**TN**
Saitz	60	9	15	125
McQuade	35	20	18	227
Brown	44	9	19	52
Chan	42	9	6	47
Aertgeerts	80	90	95	1705
Buchsbaum	215	47	79	480
Joseph	48	6	10	54
Bradley	58	15	52	102
Jones	12	1	13	128
Indran	48	184	4	299

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Methods for Dichotomized Data

Summary ROC Meta-analysis

The most commonly used and easy to implement method
It is a fixed-effects model

1. Linear regression analysis of the relationship
   D = **a** + **b**S where :
   D = (logit TPR) - (logit FPR) = ln DOR
   S = (logit TPR) + (logit FPR) = proxy for the threshold

2. **a** and **b** may be estimated by weighted or un-weighted least squares or robust regression, back-transformed and plotted in ROC space

3. Differences between tests or subgroups may examined by adding covariates to model

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Methods for Dichotomized Data

Summary ROC Meta-analysis

```
. sroc tp fn fp tn


Weighted Regression of D on S:
   Slope =  0.088, Intercept =  3.152, n = 10
       t =   0.63, prob >|t| =  0.545

   Homogeneous: thus ln(OR) =  3.152 and OR = 23.380

   AUC and Q*:
   AUC = 0.898, se(AUC) = 0.020, 95% CI = (0.858, 0.937) (homogenous)
   AUC = 0.896, se(AUC) = 0.019, 95% CI = (0.858, 0.934) (heterogenous)

   Q* = (0.829, 0.171), se(Q*) = 0.021, 95% CI = ({0.787, 0.870},{0.130, 0.213})

Correlation Test:
   Spearman correlation (rho) =  0.709, p(rho=0) = 0.022

   High correlation: use the summary ROC curve; do not use the summary TPR and FPR.
```

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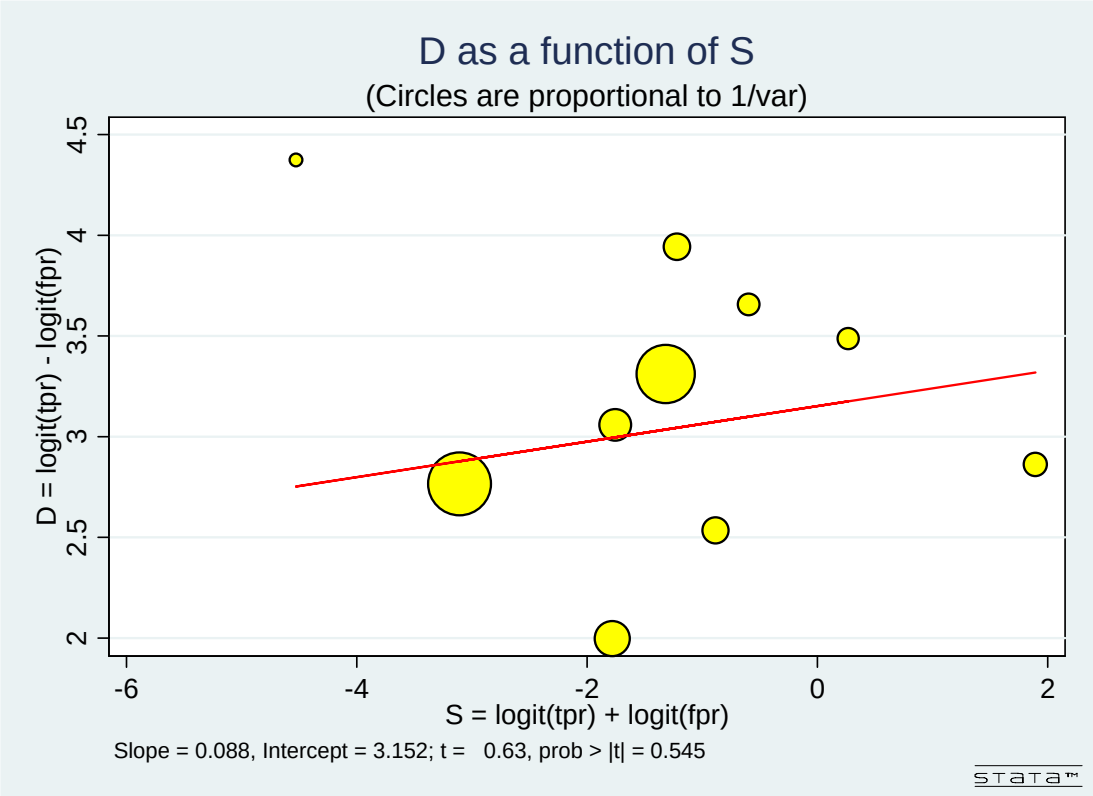
Methods for Dichotomized Data

Summary ROC Meta-analysis

```
. sroc tp fn fp tn
```

```
Weighted Regression of D on S:
Slope =  0.088, Intercept =  3.152, n = 10
t =   0.63, prob >|t| =  0.545
```



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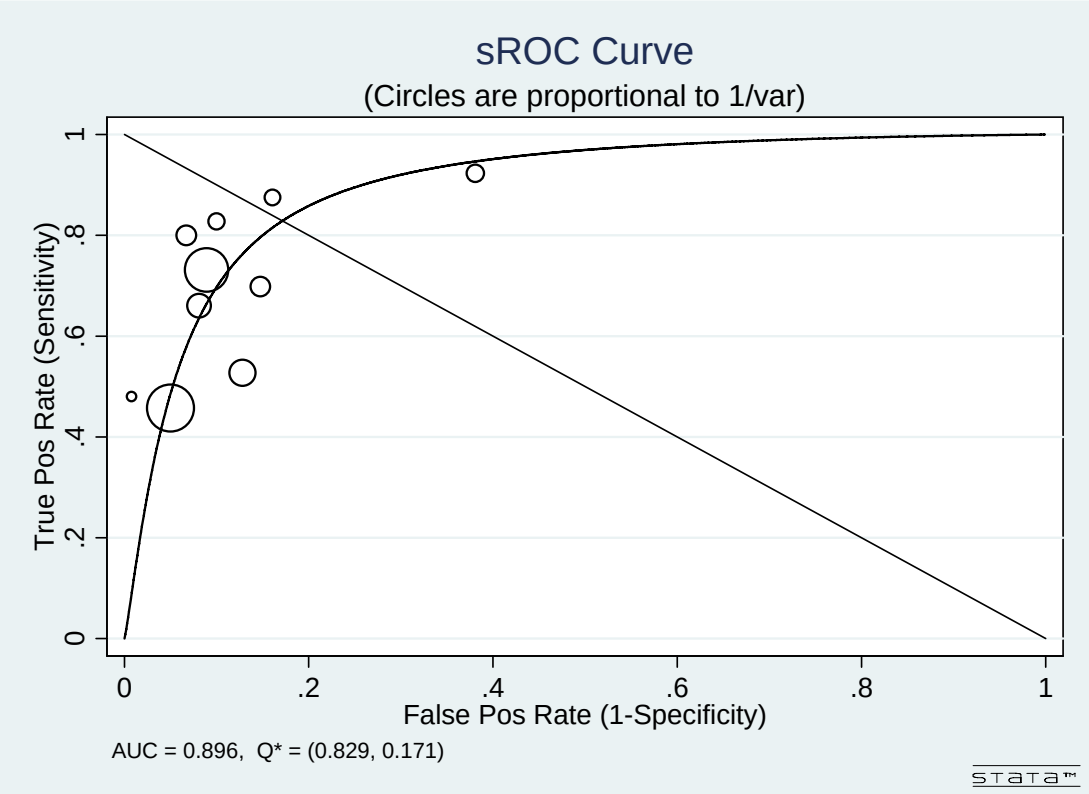
Methods for Dichotomized Data

Summary ROC Meta-analysis

```
. sroc tp fn fp tn
```



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Methods for Dichotomized Data

Mixed Effects Hierarchical Models

Mathematically equivalent models for estimating underlying SROC and average operating point and/or exploring heterogeneity

Hierarchical Summary ROC(HSROC) Model

1. Focused on inferences about the SROC curve, or comparing SROC curves but summary operating point(s) can be derived from the model parameters

Bivariate Mixed Effects Models

1. Focused on inferences about sensitivity and specificity but SROC curve(s) can be derived from the model parameters
2. Generalization of the commonly used DerSimonian and Laird random effects model

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Methods for Dichotomized Data

Hierarchical Summary ROC Regression

Level 1: Within-study variability

$$y_{ij} \sim Bin\left(n_{ij}, \pi_{ij}\right)$$

$$\texttt{logit}\left(\pi_{ij}\right) = \left(\theta_i + \alpha_i X_{ij}\right) \exp\left(-\beta X_{ij}\right)$$

θ_i and α_i Study-specific threshold and accuracy parameters

y_{ij} Number testing positive assumed to be binomially distributed

π_{ij} Probability that a patient in study i with disease status j has a positive test result

X_{ij} True disease status(coded -0.5 for those without disease and 0.5 for those with the disease)

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Methods for Dichotomized Data

Hierarchical Summary ROC Regression

Level 2: Between-study variability

$$\theta_i \sim N\left(\Theta, \sigma_\theta^2\right)$$

$$\alpha_i \sim N\left(\mathrm{A}, \sigma_\alpha^2\right)$$

- Θ and A Means of the normally distributed threshold and accuracy parameters
- σ_θ^2 and σ_α^2 Variances of mean threshold and accuracy
- β Shape parameter which models any asymmetry in the SROC curve

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Methods for Dichotomized Data

Hierarchical Summary ROC Regression of CAGE Data

```
. metandi tp fp fn tn
```

Log likelihood = -74.385097 Number of studies = 10

	Coef.	Std. Err.	z	P>|z|	[95% Conf.	Interval]
HSROC						
Lambda	2.998289	.25168			2.505006	3.491573
Theta	-.6057828	.2987906			-1.191402	-.0201641
beta	.0472602	.2613612	0.18	0.857	-.4649984	.5595187
s2alpha	.1874206	.1608058			.0348731	1.007265
s2theta	.536654	.264404			.2043224	1.409525
Summary pt.						
Se	.7052654	.0527992			.5925838	.7974353
Sp	.8961592	.0246019			.8371398	.9354399
DOR	20.65089	3.888347			14.27797	29.86834
LR+	6.791796	1.281433			4.692295	9.83069
LR-	.3288864	.0526198			.2403582	.4500212
1/LR-	3.040564	.4864715			2.222118	4.160458

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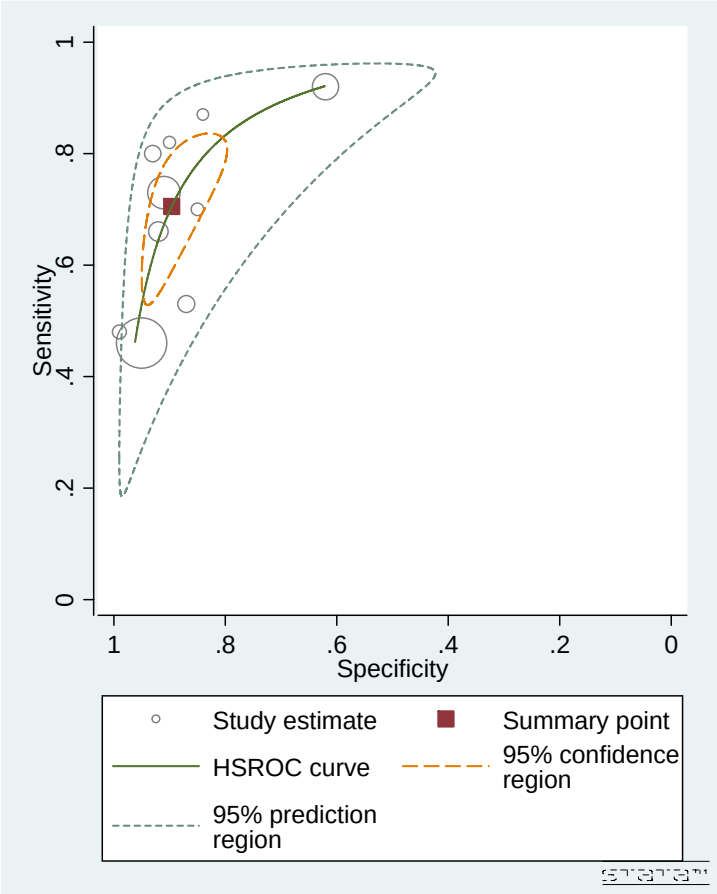
Methods for Dichotomized Data

Hierarchical Summary ROC Meta-analysis of CAGE Data

```
. metandi tp fp fn tn, plot
```



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Methods for Dichotomized Data

Bivariate Mixed Model

Level 1: Within-study variability: Approximate Normal Approach

$$\begin{pmatrix} \texttt{logit}(p_{Ai}) \\ \texttt{logit}(p_{Bi}) \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_{Ai} \\ \mu_{Bi} \end{pmatrix}, C_i \right)$$

$$C_i = \begin{pmatrix} s^2_{Ai} & 0 \\ 0 & s^2_{Bi} \end{pmatrix}$$

p_{Ai} and p_{Bi} Sensitivity and specificity of the ith study

μ_{Ai} and μ_{Bi} Logit-transforms of sensitivity and specificity of the ith study

C_i Within-study variance matrix

s^2_{Ai} and s^2_{Bi} variances of logit-transforms of sensitivity and specificity

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Methods for Dichotomized Data

Bivariate Mixed Model

Level 1: Within-study variability: Exact Binomial Approach

$$y_{Ai} \sim Bin\left(n_{Ai}, p_{Ai}\right)$$

$$y_{Bi} \sim Bin\left(n_{Bi}, p_{Bi}\right)$$

n_{Ai} and n_{Bi} Number of diseased and non-diseased

y_{Ai} and y_{Bi} Number of diseased and non-diseased with true test results

p_{Ai} and p_{Bi} Sensitivity and specificity of the ith study

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Methods for Dichotomized Data

Bivariate Mixed Model

Level 2: Between-study variability

$$\begin{pmatrix} \mu_{Ai} \\ \mu_{Bi} \end{pmatrix} \sim N\left(\begin{pmatrix} M_A \\ M_B \end{pmatrix}, \Sigma_{AB}\right)$$

$$\Sigma_{AB} = \begin{pmatrix} \sigma_A^2 & \sigma_{AB} \\ \sigma_{AB} & \sigma_B^2 \end{pmatrix}$$

μ_{Ai} and μ_{Bi} Logit-transforms of sensitivity and specificity of the ith study

M_A and M_B Means of the normally distributed logit-transforms

Σ_{AB} Between-study variances and covariance matrix

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Methods for Dichotomized Data

Bivariate Mixed Binary Regression of CAGE Data

```
. midas tp fp fn tn, res(all)

SUMMARY DATA AND PERFORMANCE ESTIMATES

Number of studies =  10
Reference-positive Units =  953
Reference-negative Units = 3609
Pretest Prob of Disease = 0.21


Correlation (Mixed Model)= -0.84
Proportion of heterogeneity likely due to threshold effect = 0.71
Interstudy variation in Sensitivity: ICC_SEN =  0.17, 95% CI = [ 0.02- 0.32]
Interstudy variation in Specificity: ICC_SPE =  0.17, 95% CI = [ 0.03- 0.31]
Heterogeneity (Chi-square): LRT_Q = 178.971, df =2.00, LRT_p =0.000
Inconsistency (I-square): LRT_I2 =  99, 95% CI = [ 98- 99]


Parameter                    Estimate          95% CI
Sensitivity                   0.72 [    0.60,    0.81]
Specificity                   0.90 [    0.84,    0.94]
Positive Likelihood Ratio      7.3 [     4.9,    10.7]
Negative Likelihood Ratio     0.31 [    0.22,    0.44]
Diagnostic Odds Ratio           23 [      16,      34]
```

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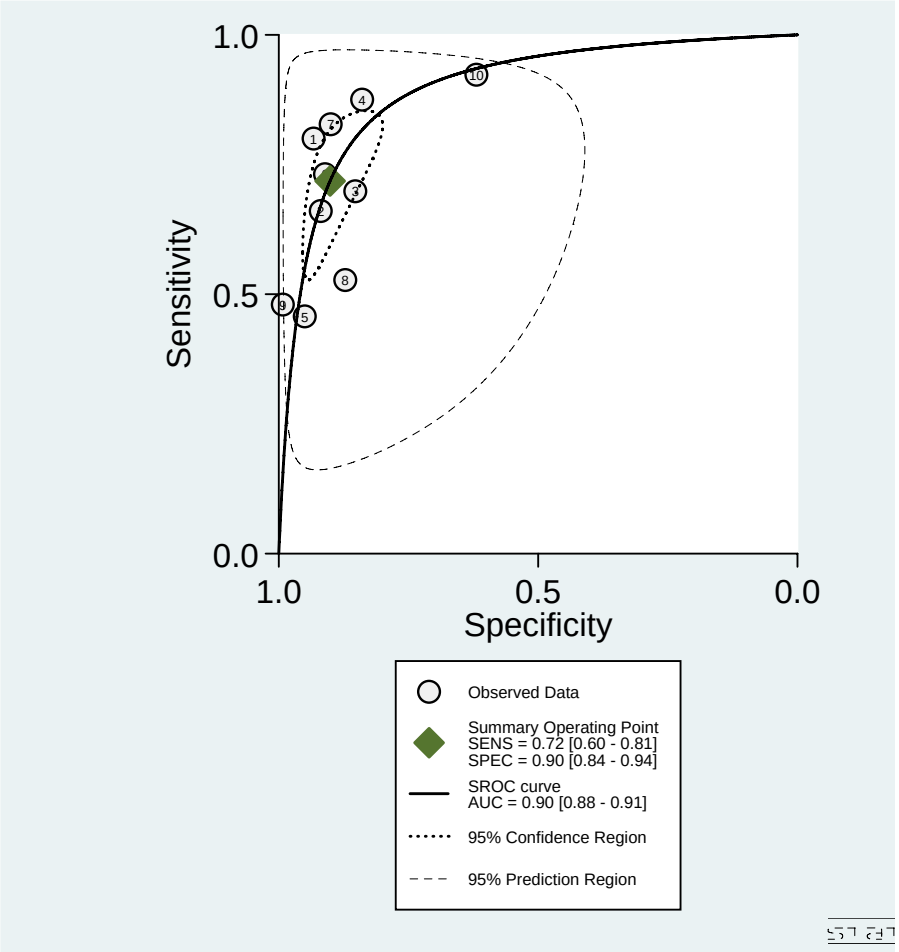
Methods for Dichotomized Data

Bivariate Summary ROC Meta-analysis of CAGE data

```
. midas tp fp fn tn, sroc(curve mean data conf pred) level(95)
```



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Proportional Odds Regression(POR) Framework

Suppose, the test result Y falls into one of J categories ("ratings")
The probability of Y falling in a given category j or lower may be modeled using the ordinal regression equation:

$$logit[Pr(Y \leq j \mid D)] = \theta_j - \alpha D$$

D is a variable indicative of disease status

$\theta_j ....\theta_{j-1}$: Cut-off values on an underlying latent scale

α: Location parameter (measure of diagnostic accuracy=log-odds ratio)

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Proportional Odds Regression(POR) Framework

Alternative Fixed- or Random-effects Approaches

1. Single POR and log-odds ratio of pooled data
2. Single POR and log-odds ratio with adjustment for study using dummy variables
3. Study-specific POR and log-odds ratios

All ROC curves are symmetric because of the assumption of a constant odds ratio for test accuracy

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Proportional Odds Regression Model

Fixed-effects POR of Pooled Data (FEPOR)

```
. oglm score resp [fw=dis], link(logit)

Ordered Logistic Regression                     Number of obs   =       4562
                                                LR chi2(1)      =    1490.31
                                                Prob > chi2     =     0.0000
Log likelihood = -4337.5234                     Pseudo R2       =     0.1466
------------------------------------------------------------------------------
score |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
------+-----------------------------------------------------------------------
resp  |    2.88352   .0794469    36.29   0.000     2.727807    3.039233
------------+-----------------------------------------------------------------
/cut1 |   1.208429   .0393556    30.71   0.000     1.131293    1.285564
/cut2 |     2.0914   .0496541    42.12   0.000      1.99408     2.18872
/cut3 |   3.280551   .0676223    48.51   0.000     3.148014    3.413088
/cut4 |   4.480682   .0913089    49.07   0.000      4.30172    4.659645
------------------------------------------------------------------------------
```

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Proportional Odds Regression Model

Random-effects POR of Pooled Data (REPOR)

```
. gllamm score resp, i(study) weight(wgt) link(ologit) eq(resp) adapt


number of level 1 units = 4562
number of level 2 units = 10
Condition Number = 9.5321335
log likelihood = -4296.7662
------------------------------------------------------------------------------
score        |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
resp         |   3.046648   .2144375    14.21   0.000     2.626358    3.466938
-------------+----------------------------------------------------------------
_cut11       |   1.204772   .0393759    30.60   0.000     1.127596    1.281947
-------------+----------------------------------------------------------------
_cut12       |   2.106683   .0501227    42.03   0.000     2.008444    2.204922
-------------+----------------------------------------------------------------
_cut13       |   3.349023   .0699056    47.91   0.000     3.212011    3.486036
-------------+----------------------------------------------------------------
_cut14       |   4.601222   .0950536    48.41   0.000      4.41492    4.787523
------------------------------------------------------------------------------
Variances and covariances of random effects
------------------------------------------------------------------------------
***level 2 (study) var(1): .37787108 (.18985077)
------------------------------------------------------------------------------
```

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Proportional Odds Regression Model

Fixed-effects POR with Studies as Dummy Variables (FEPORD)

```
. oglm score resp std2-std10 [fw=dis], link(logit)

Ordered Logistic Regression                       Number of obs   =       4562
                                                  LR chi2(10)     =    2042.14
                                                  Prob > chi2     =     0.0000
Log likelihood = -4061.6084                       Pseudo R2       =     0.2009
------------------------------------------------------------------------------
score  |      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
-------------+----------------------------------------------------------------
 resp  |   2.948556   .0861223    34.24   0.000     2.779759    3.117352
  std2 |  -.4815434   .1887587    -2.55   0.011    -.8515037   -.1115832
  std3 |  -.1028179   .2302515    -0.45   0.655    -.5541025    .3484667
  std4 |   .3582957   .2305584     1.55   0.120    -.0935903    .8101818
  std5 |  -1.132683   .1516207    -7.47   0.000    -1.429854   -.8355117
  std6 |  -.3640983   .1543584    -2.36   0.018    -.6666352   -.0615615
  std7 |   .2108051   .2254389     0.94   0.350     -.231047    .6526571
  std8 |  -.4197682   .1926105    -2.18   0.029    -.7972779   -.0422585
  std9 |  -1.088437   .2458275    -4.43   0.000     -1.57025   -.6066241
 std10 |   1.158538   .1589892     7.29   0.000     .8469249    1.470151
-------------+----------------------------------------------------------------
 /cut1 |   .8164335   .1402567     5.82   0.000     .5415355    1.091332
 /cut2 |   1.809484   .1437148    12.59   0.000     1.527808     2.09116
 /cut3 |    3.08217   .1503633    20.50   0.000     2.787464    3.376877
 /cut4 |   4.319102   .1617342    26.70   0.000     4.002108    4.636095
------------------------------------------------------------------------------
```

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Proportional Odds Regression Model

Random-effects POR with Studies as Dummy Variables (REPORD)

```
. gllamm score resp std2-std10, i(study) weight(wgt) link(ologit) eq(resp) adapt

log likelihood = -4036.4392
------------------------------------------------------------------------------
       score|      Coef.   Std. Err.      z    P>|z|     [95% Conf. Interval]
------------+-----------------------------------------------------------------
       resp |   3.025969   .2373911    12.75   0.000     2.560691    3.491247
       std2 |  -.3181025    .239889    -1.33   0.185    -.7882763    .1520714
       std3 |  -.0341522    .332904    -0.10   0.918    -.6866321    .6183278
       std4 |   .3846226   .3178453     1.21   0.226    -.2383428    1.007588
       std5 |   -.837714   .1986386    -4.22   0.000    -1.227038   -.4483895
       std6 |  -.3871265    .214832    -1.80   0.072    -.8081894    .0339365
       std7 |   .0709539   .3247724     0.22   0.827    -.5655882     .707496
       std8 |   .4799914   .2608486     1.84   0.066    -.0312623    .9912452
       std9 |  -.9218658   .3100239    -2.97   0.003    -1.529502     -.31423
      std10|   1.527305    .204173     7.48   0.000     1.127134    1.927477
------------+-----------------------------------------------------------------
_cut11      |    1.05694   .1861227     5.68   0.000     .6921464    1.421734
------------+-----------------------------------------------------------------
_cut12      |   2.069719   .1893604    10.93   0.000      1.69858    2.440859
------------+-----------------------------------------------------------------
_cut13      |   3.363219   .1957788    17.18   0.000       2.9795    3.746939
------------+-----------------------------------------------------------------
_cut14      |   4.619745   .2060105    22.42   0.000     4.215972    5.023518
------------------------------------------------------------------------------
Variances and covariances of random effects
------------------------------------------------------------------------------
                    ***level 2 (study) var(1): .45376459 (.23616602)
------------------------------------------------------------------------------
```

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Proportional Odds Regression Model

Study-specific POR

```
levelsof author, local(levels)

postutil clear

nois postfile porfile str30 Study ldor ldorse ldorlo ldorhi ///
using porresults, replace

foreach l of local levels{

local study "`l'"
nois oglm score dtruth [fw=dis] if author == "`l'", link(logit)
nlcom (avar: _b[dtruth]),  post

local ldor= _b[avar]
local ldorse=_se[avar]
local ldorlo=_b[avar]-invnorm(1-$alph)*_se[avar]
local ldorhi=_b[avar]+invnorm(1-$alph)*_se[avar]

nois post porfile ("`study'") (`ldor') (`ldorse') (`ldorlo') (`ldorhi')
        }

nois postclose porfile
```

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Proportional Odds Regression Model

Study-specific Log-odds Ratios

```
. use porresults, clear
. nois list Study  ldor ldorse ldorlo ldorhi, ///
sep(0) div ab(32) abs noo compress
```

Study	ldor	ldorse	ldorlo	ldorhi
Aertgeerts	2.543996	.1625985	2.225309	2.862683
Bradley	1.627137	.263943	1.109819	2.144456
Brown	2.655694	.4095413	1.853008	3.45838
Buchsbaum	3.492826	.1832168	3.133728	3.851925
Chan	3.679464	.5191509	2.661947	4.696981
Indran	2.17833	.2748064	1.63972	2.716941
Jones	4.223248	.6260694	2.996175	5.450322
Joseph	4.090933	.52996	3.05223	5.129636
McQuade	3.407526	.3518678	2.717878	4.097174
Saitz	3.832313	.3883162	3.071227	4.593399

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Proportional Odds Regression Model

Meta-analysis of Study-specific Log-odds Ratios

```
. mvmeta ldor ldorvar, (fixed|ml|mm|reml) vars(ldor1)
```

Model	ldor	Std. Err.	z	P>|z|	[95% Conf.	Interval]
FESSPOR	2.865804	.0891923	32.13	0.000	2.69099	3.040618
RESSPOR ML	3.087069	.2629351	11.74	0.000	2.571725	3.602412
RESSPOR MM	3.0881	.2624814	11.77	0.000	2.573646	3.602554
RESSPOR REML	3.094911	.2771367	11.17	0.000	2.551733	3.638089

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Proportional Odds Regression Model

Summary AUROCs

Approach	AUROC	CI	CIW
FEPOR	0.88	0.87-0.89	0.02
REPOR	0.89	0.86-0.92	0.06
FEPORD	0.88	0.87-0.90	0.03
REPORD	0.89	0.85-0.92	0.07
FESSPOR	0.88	0.86-0.89	0.03
RESSPOR	0.89	0.85-0.93	0.08

CI: Confidence Interval CIW: Confidence Interval weidth

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Proportional Odds Regression Model

Summary Log-odds Ratios

Approach	Logor	CI	CIW
FEPOR	2.844	2.728-3.039	0.311
REPOR	3.047	2.626-3.467	0.841
FEPORD	2.949	2.780-3.117	0.337
REPORD	3.026	2.561-3.491	0.930
FESSPOR	2.866	2.691-3.041	0.350
RESSPOR	3.095	2.552-3.638	1.086

CI: Confidence Interval CIW: Confidence Interval weidth

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Logit-Threshold/Bivariate Meta-Regression Model

This consists of:

1. Study-specific Logit-Threshold Linear Regression (Moses-Shapiro-Littenberg)
2. Bivariate Mixed Modeling Of Study-Specific Intercepts And Slopes
3. Parametric Estimation Of Summary ROC And Indices Using Mean Intercept And Slope Estimates

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Logit-Threshold/Bivariate Meta-Regression

Study-specific Logit-Threshold Linear Regression

For the *jth* threshold of the *ith* study,

$$D_{ij} = \alpha_i + \beta_i S_{ij} \text{ where:}$$

$$D_{ij} = logit(TPR_{ij}) - logit(FPR_{ij})$$

$$S_{ij} = logit(TPR_{ij}) + logit(FPR_{ij})$$

TPR = True Positive Rate; FPR = False Positive Rate

α_i = Study-specific Intercept

β_i = Study-specific Slope

α_i and β_i estimated by maximum likelihood

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Logit-Threshold/Bivariate Meta-Regression

Bivariate Meta-Regression: Within-study Variability

$$\begin{pmatrix} \alpha_i \\ \beta_i \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_{\alpha i} \\ \mu_{\beta i} \end{pmatrix}, \Sigma_W\right)$$

$$\Sigma_W = \begin{pmatrix} \sigma^2_{\alpha i} & \rho_i \sigma_{\alpha i} \sigma_{\beta i} \\ \rho_i \sigma_{\alpha i} \sigma_{\beta i} & \sigma^2_{\beta i} \end{pmatrix}$$

α_i and β_i Estimated intercept and slope estimates of the ith study

$\mu_{\alpha i}$ and $\mu_{\beta i}$ True intercept and slope estimates of the ith study

Σ_W Within-study correlation (ρ_i) variances ($\sigma^2_{\alpha i}$ and $\sigma^2_{\beta i}$) and covariance ($\rho_i \sigma_{\alpha i} \sigma_{\beta i}$) matrix

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Logit-Threshold/Bivariate Meta-Regression

Bivariate Meta-Regression: Between-study Variability

$$\begin{pmatrix} \mu_{\alpha i} \\ \mu_{\beta i} \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_{\alpha} \\ \mu_{\beta} \end{pmatrix}, \Sigma_B\right)$$

$$\Sigma_B = \begin{pmatrix} \tau_{\alpha}^2 & \kappa\tau_{\alpha}\tau_{\beta} \\ \kappa\tau_{\alpha}\tau_{\beta} & \tau_{\beta}^2 \end{pmatrix}$$

μ_{ai} and μ_{bi} True intercept and slope estimates of the ith study

μ_a and μ_b Overall intercept and slope estimates

Σ_B Between-study correlation (κ) variances (τ_a^2 and τ_2^2) and covariance ($\kappa\tau_{\alpha}\tau_{\beta}$) matrix

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Logit-Threshold/Bivariate Meta-Regression

Example data: CAGE

Author	Thresh	TPR	FPR	Author	Thresh	TPR	FPR
Saitz	1	0.92	0.27	Buchsbaum	1	0.89	0.19
Saitz	2	0.80	0.07	Buchsbaum	2	0.73	0.09
Saitz	3	0.55	0.02	Buchsbaum	3	0.44	0.02
Saitz	4	0.27	0.01	Buchsbaum	4	0.19	0.01
McQuade	1	0.87	0.20	Joseph	1	0.98	0.25
McQuade	2	0.66	0.08	Joseph	2	0.82	0.10
McQuade	3	0.43	0.01	Joseph	3	0.53	0.03
McQuade	4	0.19	0.01	Joseph	4	0.40	0.01
Brown	1	0.79	0.23	Bradley	1	0.71	0.41
Brown	2	0.70	0.15	Bradley	2	0.53	0.13
Brown	3	0.52	0.05	Bradley	3	0.27	0.02
Brown	4	0.27	0.02	Bradley	4	0.09	0.01
Chan	1	0.96	0.32	Jones	1	0.88	0.12
Chan	2	0.87	0.16	Jones	2	0.48	0.01
Chan	3	0.56	0.04	Jones	3	0.24	0.01
Chan	4	0.34	0.01	Jones	4	0.08	0.01
Aertgeerts	1	0.61	0.13	Indran	1	0.99	0.63
Aertgeerts	2	0.46	0.05	Indran	2	0.92	0.38
Aertgeerts	3	0.24	0.02	Indran	3	0.46	0.12
Aertgeerts	4	0.11	0.01	Indran	4	0.10	0.01

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Logit-Threshold/Bivariate Meta-Regression

Study-specific Linear Regression Intercepts and Slopes

Author	α	**SE(α)**	β	**SE(β)**	**Corr**
Aertgeerts	2.498	0.277	-0.024	0.061	0.900
Bradley	1.587	0.391	-0.162	0.090	0.753
Brown	2.571	0.126	-0.088	0.044	0.743
Buchsbaum	3.498	0.185	0.032	0.049	0.727
Chan	3.718	0.177	0.006	0.054	0.425
Indran	2.874	0.363	0.144	0.081	0.104
Jones	4.372	0.966	0.194	0.189	0.854
Joseph	4.308	0.337	0.119	0.101	0.468
McQuade	3.270	0.512	-0.063	0.128	0.763
Saitz	3.702	0.235	-0.033	0.067	0.649

Logit-Threshold/Bivariate Meta-Regression

Mean Intercepts and Slopes by Bivariate Mixed Modeling

Method	α	**Se(α)**	β	**Se(β)**
fixed	3.098	0.072	0.019	0.020
reml	3.199	0.252	-0.006	0.027
ml	3.198	0.239	-0.006	0.026
mm	3.199	0.237	-0.005	0.027

REML: Restricted maximum likelihood

ML: Full maximum likelihood

MM: Method of moments

Intercept(α) : Average accuracy/discriminatory power of test

Slope(β) : Measures symmetry of ROC Curve

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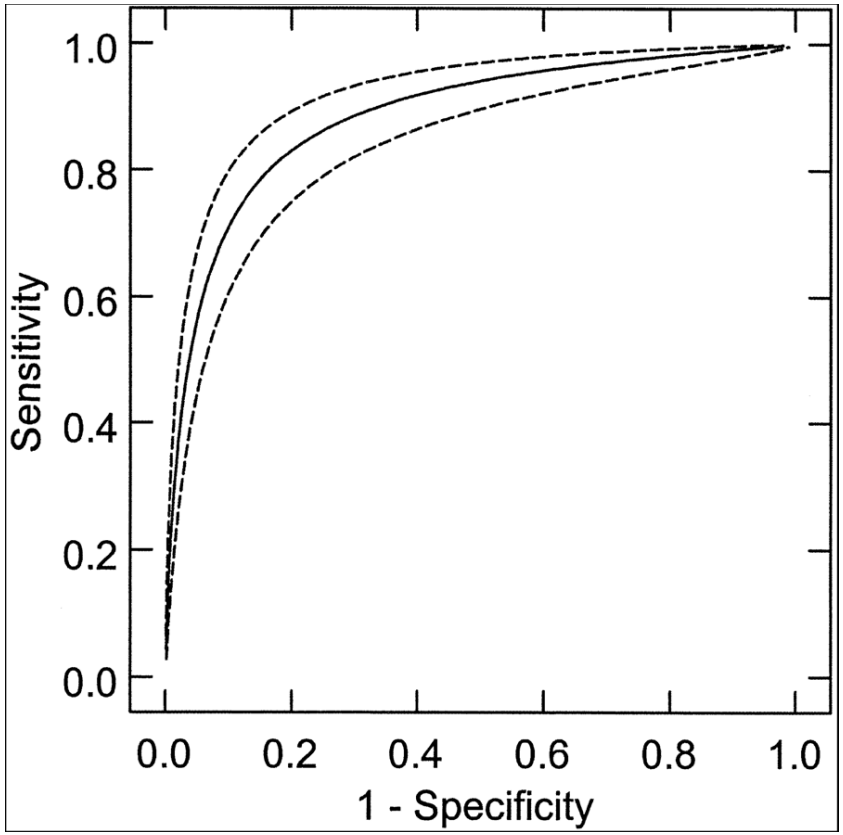
Logit-Threshold/Bivariate Meta-Regression

Summary ROC Curve



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Bayesian Hierarchical Ordinal Regression Model

Conceptual Framework

1. Random-effects formulation of meta-analysis of studies with an unequal number of nonnested categories
2. Employs a hierarchical ordinal regression model, accounting for heterogeneity of studies within-study correlation
3. Assumes that each study estimates a study-specific ROC curve that can be viewed as a random sample from a population of all ROC curves of such studies
4. Accounts for different sources of variation in the data, through study-specific location and scale parameters
5. There are several ways to construct summary ROC curves and their credible bands

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Bayesian Hierarchical Ordinal Regression Model

Model Specification

Level I (Within study variability)

$$M_{ik} \mid D_{ik}, \alpha_k, \beta_k \sim \begin{cases} \mathcal{N}(0,\ 1), & \text{if } D_{ik} = 0 \\ \mathcal{N}(\beta_k, \exp(2\alpha_k)), & \text{if } D_{ik} = 1 \end{cases}$$

$$Y_{ik} = j \ \text{ when } \ \theta_{j-1,k} \leq M_{ik} < \theta_{j,k}$$

Level II (Between study variability)

$$\alpha_k \sim \mathcal{N}(\boldsymbol{\Gamma}'\mathbf{V}_k,\ \sigma_\alpha^2)$$
$$\beta_k \sim \mathcal{N}(\boldsymbol{\Lambda}'\mathbf{W}_k,\ \sigma_\beta^2)$$

$$\theta_{0,k} \sim \mathcal{N}(0, 100), \quad \theta_{j,k} = \sum_{i=0}^{j-1} \theta_{i,k} + Exp(1), \qquad \text{for j} > 0\text{:}$$

Level III (Hyperpriors)

$$\Gamma_{l_1}, \Lambda_{l_2} \sim \mathcal{N}(0,\ 10^6), \quad \sigma_\alpha^2, \sigma_\beta^2 \sim \mathcal{IG}(0.001, 0.001)$$

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Bayesian Hierarchical Ordinal Regression Model

Specification

1. The model explicitly uses latent variables **M** that give rise to the data **Y** via a discretization process depending on thresholds θ
2. D_{ik} indicate the true disease status of the patient i in study k with $D_{ik} = 1$ if disease is present and $D_{ik} = 0$ if not
3. β_k is the location parameter and α_k the scale parameter for the ROC curve of study k.
4. V_k and W_k are study-level covariate vectors of dimensions v1 and v2 , respectively

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Bayesian Hierarchical Ordinal Regression Model

Parameter Estimation

1. Markov Chain Monte Carlo Simulation using Gibbs Sampling
2. Estimation via poster means and medians
3. Every simulated pair (β_k, α_k) defines an ROC curve
4. The sensitivity of the posterior estimates to choice of priors may be examined using several different priors for the variances of study location and scale parameters

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Bayesian Hierarchical Ordinal Regression Model

Summary ROCs, Functionals and Variability

1. Summary ROC Curves
   1. Mean SROC
   2. Pointwise SROC
   3. Loess SROC
   4. Mean Qstar and AUROC
2. Variability
   1. Envelope Bands for ROC Curves
   2. Pointwise Bands for ROC Curves
   3. Credible intervals for TPR at fixed FPR

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Bayesian Hierarchical Ordinal Regression Model

Methodology and Application

See Dukic and Gatsonis (2003) for application to data from a recently published meta-analysis evaluating accuracy of a single serum progesterone test for diagnosing pregnancy failure.

1. They meta-analyzed 20 out of 27 eligible studies, published from 1980 to 1996.
2. Among the selected studies, seven had 2 categories, four had 4, eight had 5, and one had 7.
3. Thirteen of the studies were prospective and 7 retrospective.

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Multi-stage SROC Modeling Algorithm

This consists of:

1. Estimation Of Study-Specific ROC Parameters From Observed 2 By J Data By Heteroskedastic Ordinal Regression

2. Estimation Of Mean Location And Scale From Study-Specific Estimates By Bivariate Linear Mixed Modeling

3. Estimation Of Summary ROC And Indices Using Mean Location And Scale Estimates

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Estimation Of Study-Specific ROC Parameters

Heteroskedastic Ordinal Regression Model

Suppose, the test result Y_{ik} for *ith* patient from *kth* study falls into one of J categories ("ratings"). The probability of Y_{ik} falling in a given category j or lower may be modeled as a non-linear function using the ordinal regression equation:

$$g[Pr(Y_{ik} \leq j \mid D_{ik})] = \frac{\theta_{jk} - \alpha D_{ik}}{exp(\beta D_{ik})}$$

g: Cumulative link function

D_{ik}: a variable indicative of disease status

$\theta_j ....\theta_{j-1}$: Cut-off values on an underlying latent scale

α: Location parameter (measure of diagnostic accuracy)

β: Scale parameter (spread of responses across subjects)

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Bivariate Random-effects Estimation of Mean parameters

Within-study Variability (Level 1) model

$$\begin{pmatrix} y_{1i} \\ y_{2i} \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_{1i} \\ \mu_{2i} \end{pmatrix}, \Sigma_W\right)$$

$$\Sigma_W = \begin{pmatrix} \sigma_{1i}^2 & \rho_i\sigma_{1i}\sigma_{2i} \\ \rho_i\sigma_{1i}\sigma_{2i} & \sigma_{2i}^2 \end{pmatrix}$$

y_{1i} and y_{2i} Estimated location and scale effects of the ith study

μ_{1i} and μ_{2i} True location and scale effect of the ith study

Σ_W Within-study correlation (ρ_i) variances (σ_{1i}^2 and σ_{2i}^2) and covariance ($\rho_i\sigma_{1i}\sigma_{2i}$) matrix

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Bivariate Random-effects Estimation of Mean parameters

Between-study Variability (Level 2) model

$$\begin{pmatrix} \mu_{1i} \\ \mu_{2i} \end{pmatrix} \sim N\left(\begin{pmatrix} \mu_1 \\ \mu_2 \end{pmatrix}, \Sigma_B\right)$$

$$\Sigma_B = \begin{pmatrix} \tau_1^2 & \kappa\tau_1\tau_2 \\ \kappa\tau_1\tau_2 & \tau_2^2 \end{pmatrix}$$

μ_{1i} and μ_{2i} True location and scale effects of the ith study

μ_1 and μ_2 Overall location and scale effects

Σ_B Between-study correlation (κ) variances (τ_1^2 and τ_2^2) and covariance ($\kappa\tau_1\tau_2$) matrix

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Bivariate Random-effects Estimation of Mean parameters

Estimation Methods

1. Maximum Likelihood (ML)
2. Restricted Maximum Likelihood (REML)
3. DerSimonian and Laird Method Of Moments (MM)

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Estimation of Summary ROC and Functionals

Binormal ROC Analysis

1. TPR= a + bΦ(FPR) $(0 \leq \text{FPR} \leq 1)$
2. a = meta-analytic location parameter
3. b = meta-analytic scale parameter
4. AUROC = Area under curve = $\Phi\left(\frac{a}{\sqrt{1+b^2}}\right)$
5. Sym = Symmetry point index = $\Phi\left(\frac{a}{1+b}\right)$

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Estimation of Summary ROC and Functionals

Bilogistic ROC Analysis

1. TPR= invlogit(a + b*logit(FPR)) ($0 \leq$ FPR ≤ 1)
2. a = meta-analytic location parameter
3. b = meta-analytic scale parameter
4. Area under curve (AUROC) and Symmetry point index (Sym) derived from integration of TPR= invlogit(a + b*logit(FPR))

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Example Dataset 1

Similar Thresholds

Table: Study-specific Estimates by Ordinal Probit

Study	**Location (Se)**	**Scale (Se)**	**Corr**
Aertgeerts	1.37 (0.19)	0.96 (0.11)	-0.14
Bradley	0.74 (0.16)	0.67 (0.11)	0.22
Brown	1.53 (0.38)	0.95 (0.28)	0.54
Buchsbaum	2.21 (0.20)	1.14 (0.13)	0.63
Chan	2.17 (0.44)	1.04 (0.31)	0.73
Indran	1.79 (0.28)	1.47 (0.20)	0.20
Jones	2.22 (0.64)	0.92 (0.34)	0.66
Joseph	2.92 (0.65)	1.44 (0.44)	0.72
McQuade	1.73 (0.33)	0.83 (0.19)	0.55
Saitz	2.16 (.34)	0.99 (0.21)	0.68

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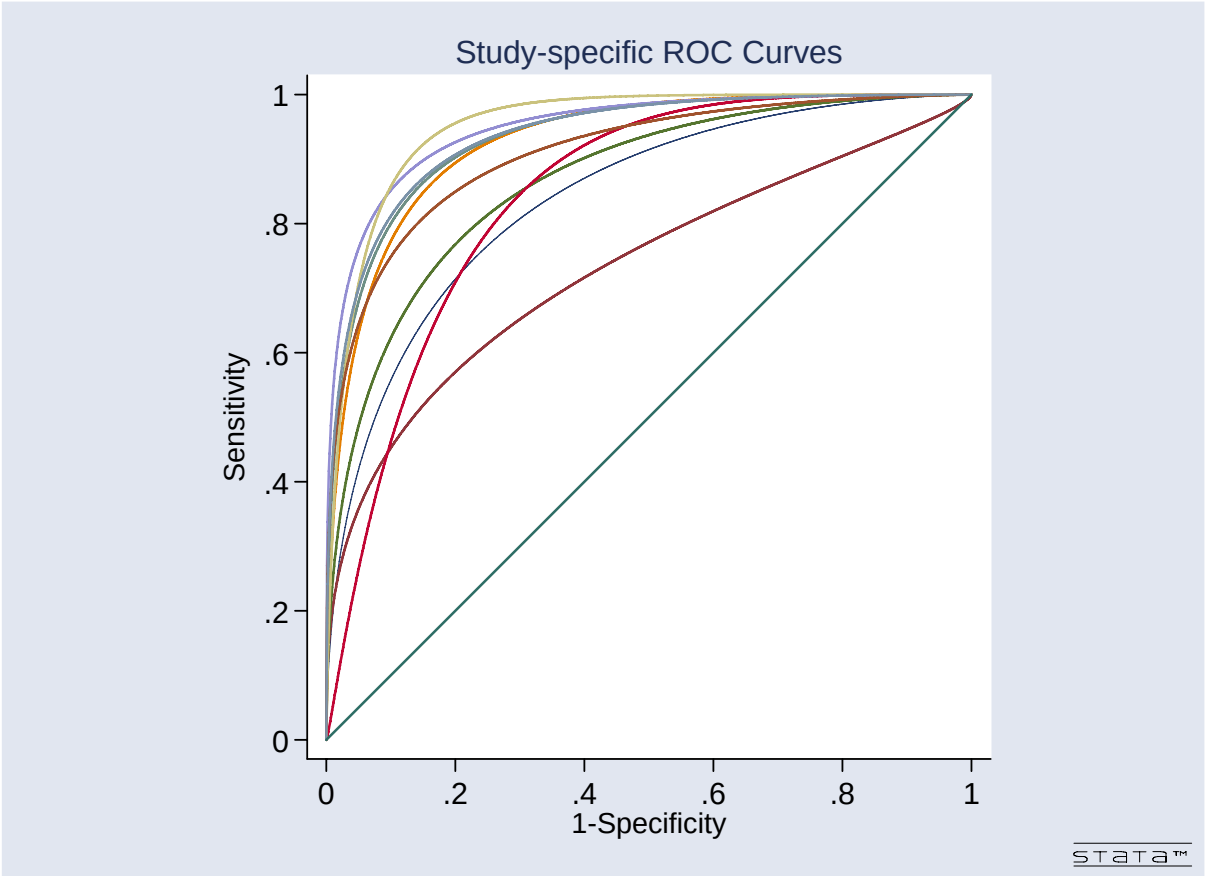
Example Dataset 1

Similar Thresholds



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Example Dataset 1

Similar Thresholds

Table: Summary performance indices by estimation method

Method	Location	Scale	Area	Sympoint
reml	1.82 (1.43-2.20)	1.00 (0.85-1.16)	0.90 (0.86-0.94)	0.82 (0.78-0.86)
ml	1.81 (1.44-2.17)	1.00 (0.85-1.15)	0.90 (0.86-0.94)	0.82 (0.78-0.85)
mm	1.83 (1.41-2.25)	1.01 (0.85-1.16)	0.90 (0.86-0.95)	0.82 (0.78-0.86)

REML: Restricted maximum likelihood

ML: Full maximum likelihood

MM: Method of moments

Location: Measure of accuracy/discriminatory power of test

Scale: Measures symmetry of ROC curve

Sympoint: Symmetry point(sensitivity=specificity)

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Example Dataset 1

Similar Thresholds

Table: Estimated between-studies SDs and correlation

Method	**SD(Location)**	**SD(Scale)**	**Corr**
REML	0.510	0.151	1.00
ML	0.473	0.140	1.00
MM	0.583	0.166	1.00

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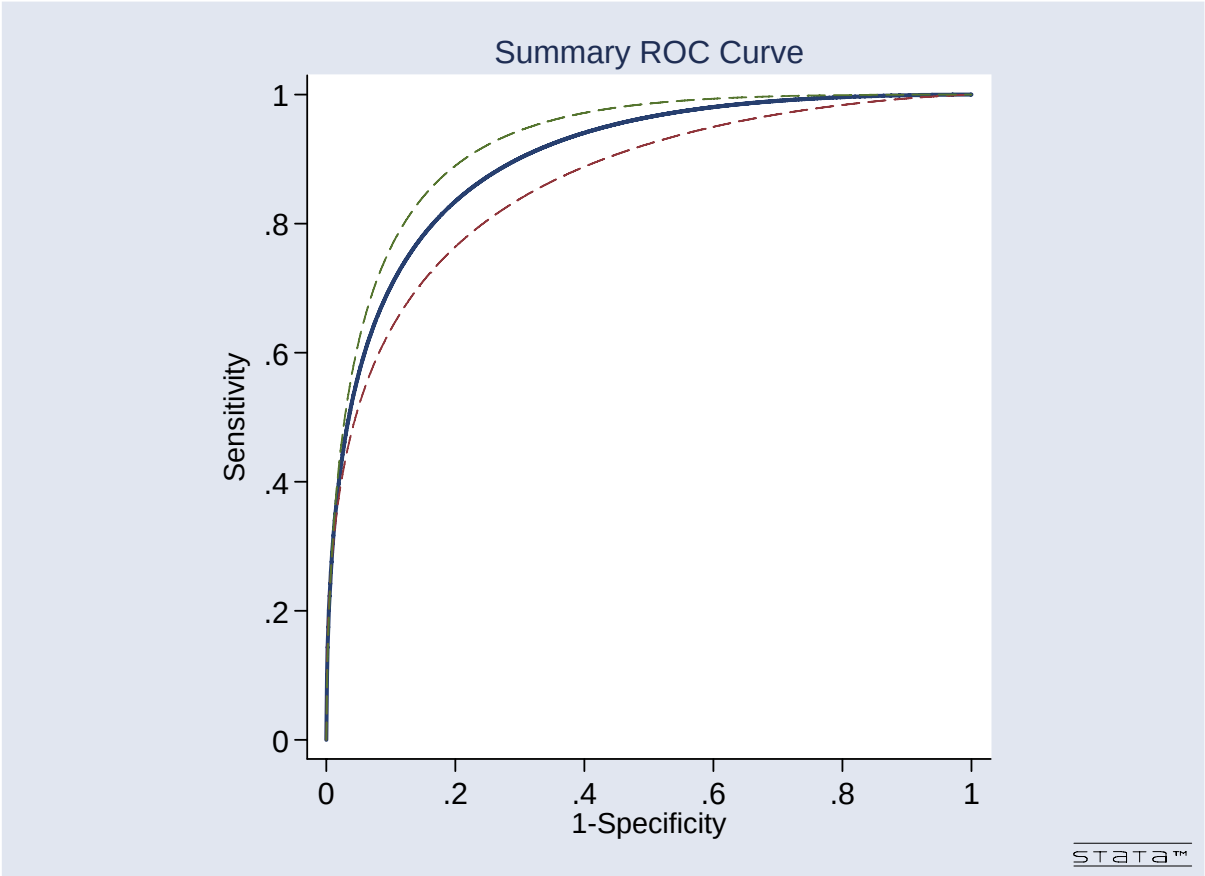
Example Dataset 1

Similar Thresholds: Using summary data from REML



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Example Dataset 2

Disparate Thresholds

Table: Study-specific Estimates by Ordinal Probit

Study	Cutpoints	Location (Se)	Scale (Se)	Corr
Almeda	4	1.32 (0.18)	1.09 0.19)	0.72
Arad	4	1.32 (0.14)	0.96 (0.11)	0.42
Bielak	6	1.86 (0.23)	1.02 (0.18)	0.70
Budoff	7	1.24 (0.06)	1.44 (0.08)	0.54
Chen	4	2.17 (0.38)	1.15 (0.31)	0.77
Greenland	4	0.54 (0.13)	0.92 (0.13)	0.27
Hosoi	5	1.34 (0.16)	0.93 (0.14)	0.67
Knez	4	1.90 (0.09)	1.35 (0.11)	0.82
LaMonte	4	1.75 (0.13)	1.27 (0.12)	0.68
Nixdorff	2	0.72 (4.01)	0.20 (3.99)	1.00
Raggi	4	1.61 (0.37)	1.62 (0.32)	0.08
Schepis	5	1.54 (0.36)	1.19 (0.31)	0.57
Seese	2	5.61 (300.45)	3.06 (234.45)	1.00
Shaw	5	0.87 (0.09)	0.97 (0.07)	-0.06
Taylor	4	0.42 (0.50)	0.53 (0.35)	-0.33
Vliengenthart	4	1.10 (0.22)	1.21 (0.20)	0.20
Wong	5	1.00 (0.27)	1.12 (0.26)	0.28
Yao	2	3.22 (78.35)	3.14 (97.37)	1.00

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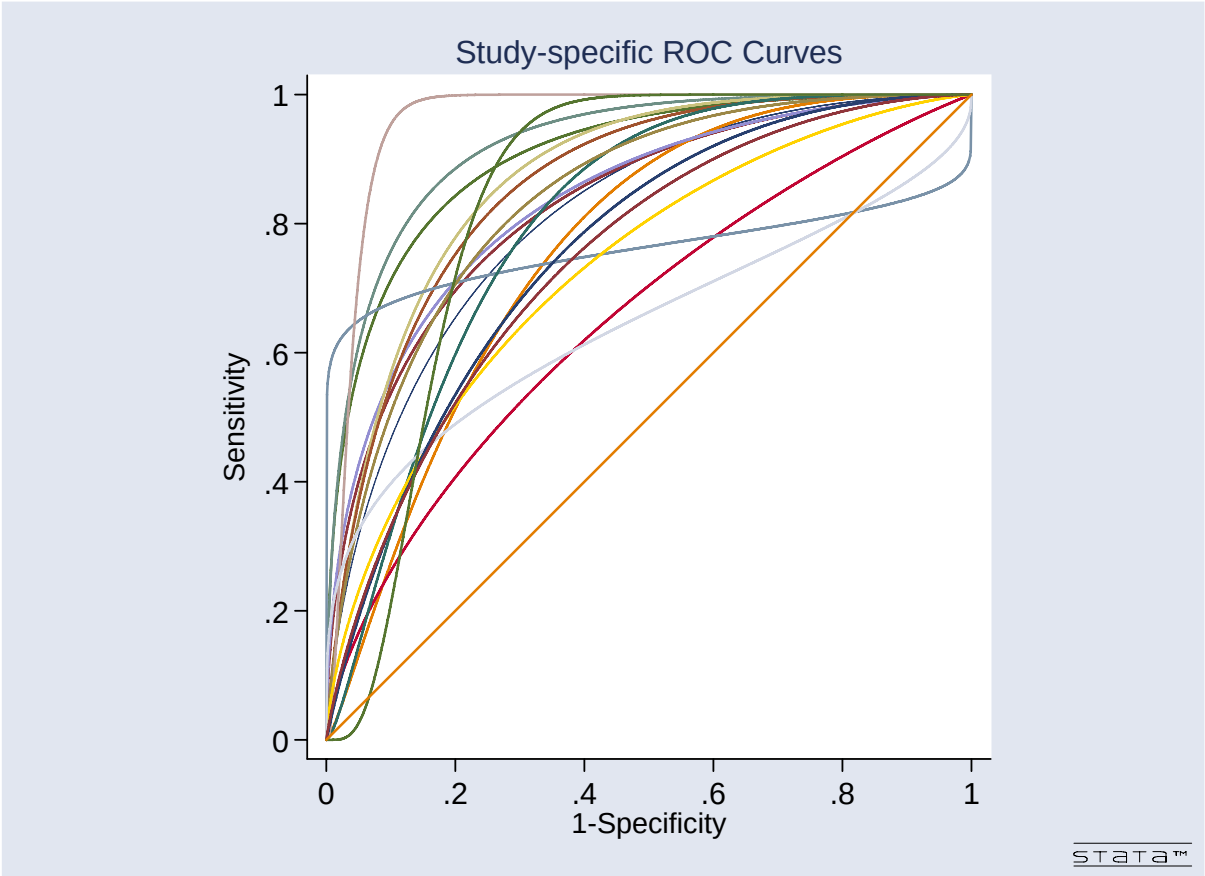
Example Dataset 2

Disparate Thresholds



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Example Dataset 2

Disparate Thresholds

Table: Summary performance indices by estimation method

Method	Location	Scale	Area	Sympoint
reml	1.36 (1.12-1.60)	1.11 (0.98-1.24)	0.83 (0.79-0.87)	0.74 (0.71-0.77)
ml	1.36 (1.13-1.60)	1.11 (0.98-1.23)	0.83 (0.79-0.86)	0.74 (0.71-0.77)
mm	1.36 (1.13-1.59)	1.11 (0.99-1.23)	0.83 (0.79-0.86)	0.74 (0.71-0.77)

REML: Restricted maximum likelihood

ML: Full maximum likelihood

MM: Method of moments

Location: Measure of accuracy/discriminatory power of test

Scale: Measures symmetry of ROC curve

Sympoint: Symmetry point(sensitivity=specificity)

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Example Dataset 2

Disparate Thresholds

Table: Estimated between-studies SDs and correlation

Method	SD(Location)	SD(Scale)	Corr
REML	0.441	0.183	0.563
ML	0.423	0.74	0.563
MM	0.420	0.174	0.562

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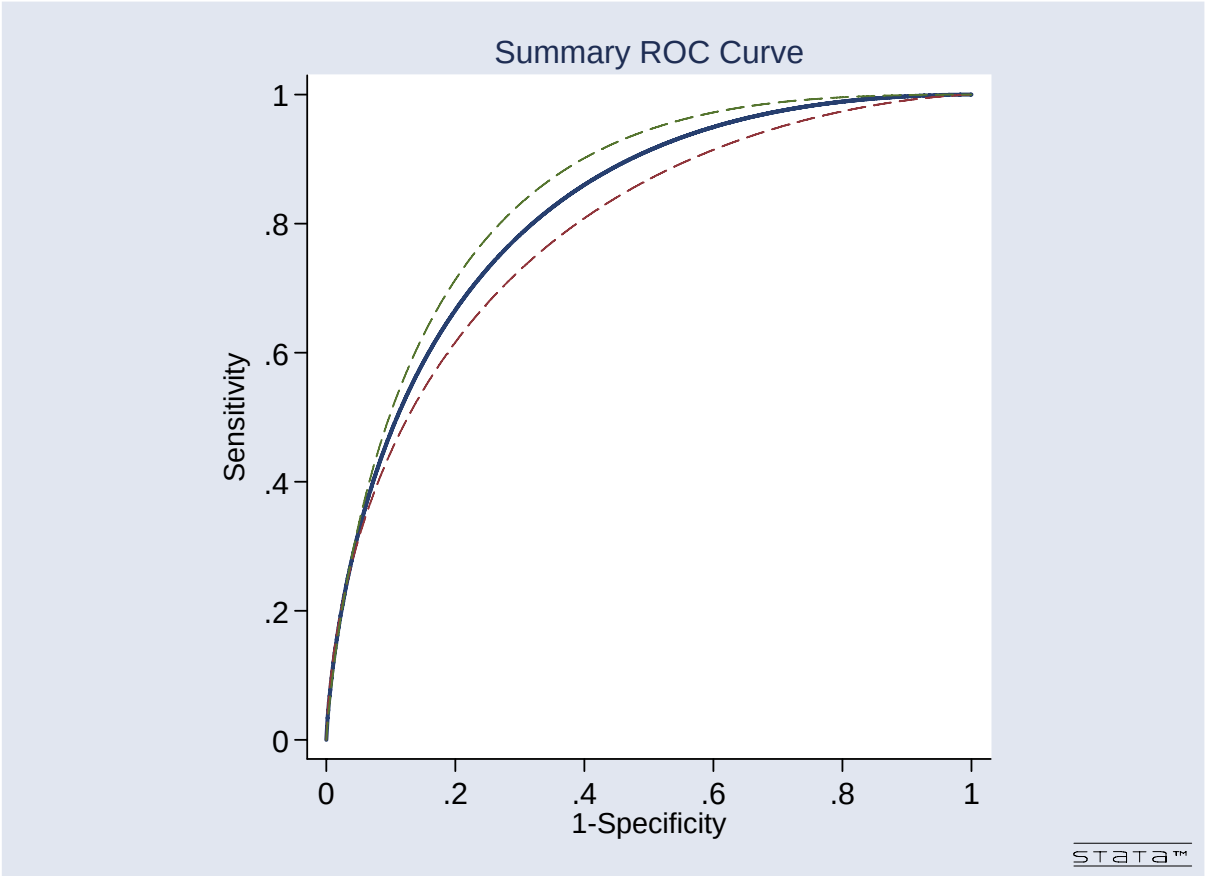
Example Dataset 2

Disparate Thresholds: Using summary results from REML



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Conclusions

1. Dichotomization of ordinal data is simple with abundance of meta-analytical methods and software programs but inefficient with loss of information
2. The "no thresholds left behind" proposed algorithm is very robust, flexible, informative and efficient
3. It is invariant to the number/set of thresholds, link function or estimation procedure

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Conclusions

1. Easily extended for covariate meta-regression and covariate-adjusted SROC analysis
2. Easily implemented in Stata using Stata-native and User-written commands
3. **midacat** module for automated implementation will be available shortly
4. Datasets, do-files and unpublished ado-files available from author on request

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