GENERIC SAS® MACRO FOR EVALUATING ACCURACY MEASURES FOR MULTIPLE DIAGNOSTIC TESTS

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Introduction

- Measures of diagnostic accuracy quantify ability of diagnostic test to detect presence/absence of disease if present/absent compared to standard.
- Common measures of diagnostic accuracy include Sensitivity, Specificity, Predictive values, AUC for ROC curves.

Gaps with available tools

- Evaluate a single diagnostic test at a time
- Analyst need to summarize data into a 2x2 contingency table before analysis
- Mostly produce inaccurate confidence interval estimation via normal distribution approximation

The *%diag_test* SAS macro

- Evaluate multiple diagnostic tests simultaneously.
- Uses patient-level data and creates a 2x2 contingency table as part of output.
- Automated to saves on analysis time, reduces transcription (copy-pasting) errors, produce publication-quality outputs.
- Easy to use as analyst specifies data, “truth” and “test” variables and cutoff values.
- Produces > 15 different measures of evaluating diagnostic accuracy and ROC curves.
- Provides several methods for computing confidence intervals.
- Generic to use with data from other settings than the laboratory.
- Provides for domain/sub-population level analysis.

The %*diag_test* macro parameters

parameter	description
data	name of input dataset
truthvar	name of reference/truth/gold standard variable e.g., abbott_plasma_vl
truthcutvalue	cutoff value to use to categorize values of test variable as having disease or not e.g., 1,000 so that if value ≥ 1,000 then presence of disease, otherwise absence of disease
testvarlist	list of diagnostic test variable(s) separated by space e.g., vdbs_vl mdbs_vl ddbs_vl
testcutvalue	cutoff value to use to categorize values of test variable as having disease or not e.g., 1,000 so that if value ≥ 1,000 then presence of disease, otherwise absence of disease
decimalpoints	(optional) number of decimal places for each estimated measure (default=1)
alpha	(optional) desired level of significance (default=0.05, for 95% confidence intervals)
missvaluelabel	(optional) value label for missing values. If missing data have a format, it should be provided, otherwise macro assumes the default format "."

The %*diag_test* macro parameters

parameter	description
varmethod	(optional) method for computing confidence intervals. included here are: "Normal" (default) for normal distribution approximations, "Wilson" (most desired) for Wilson score and "Exact" for exact binomial approximation
domain	(optional) domain variable for sub-population analysis
domainvalue	(optional) value of domain/sub-population of interest (should be numeric). Required if domain is specified
condition	(optional) any conditional statements to create and or fine-tune the final analysis dataset specified using one IF statement
surveyname	(optional) abbreviation for survey/study to be included in the output
outputdir	path for directory/folder where output is saved
tablename	short name of output table
tabletitle	title of output table
print	variable for displaying/suppressing the output table on the output window which takes the values (NO=suppress output, YES=show output)

Example use of %*diag_test* macro

- Reproduce analysis for "*Evaluation of dried blood spots (DBS) compared to plasma as an alternative for HIV-1 viral load (VL) monitoring in resource-limited settings [2]*"
- Plasma blood used as gold standard/reference test in VL monitoring
- Plasma VL reagents costly and blood must be prepared in a reference laboratory setting
- DBSs are easy to prepare in a resource-limited setting
- 3 DBSs - (1) venous blood (V-DBS), (2) microcapillary blood (M-DBS), (3) directly spotting (D-DBS) compared to Plasma all tested on Abbott m2000 platform
- Virologic failure (VF) threshold of ≥1000 copies/mL for both diagnostic and reference tests

Example use of %*diag_test* macro

Diagnostic test(s)		Reference test (Abbott Plasma VL copies/ml)			Diagnostic accuracy measures	
Test category	**Test result**	**>=1000**	**<1000**	**Total**	**Measure**	**Estimate (95 % CI)**
V-DBS VL copies/ml	>=1000	219	35	254	Sensitivity (%)	90.1 (85.7 - 93.3)
					Specificity (%)	93.1 (90.6 - 95.0)
	<1000	24	475	499	Positive Predictive Value (PPV) (%)	86.2 (81.4 - 89.9)
					Negative Predictive Value (NPV) (%)	95.2 (92.9 - 96.7)
	Total	243	510	753	Upward Misclassification (%)	6.9 (5.0 - 9.4)
					Downward Misclassification (%)	9.9 (6.7 - 14.3)
					False Omission Rate (FOR) (%)	4.8 (3.3 - 7.1)
					False Discovery Rate (FDR) (%)	13.8 (10.1 - 18.6)
					Positive Likelihood Ratio (LR+)	13.1 (9.5 - 18.1)
					Negative Likelihood Ratio (LR-)	0.1 (0.1 - 0.2)
					Diagnostic Accuracy (%)	92.2 (90.0 - 93.9)
					Disease Prevalence (%)	32.3 (29.0 - 35.7)
					Diagnostic Odds Ratio (DOR)	123.8 (71.9 - 213.3)
					Kappa Agreement	0.8 (0.8 - 0.9)
					Youden's Index	0.8 (0.8 - 0.9)
					F-score	0.9 (0.9 - 0.9)

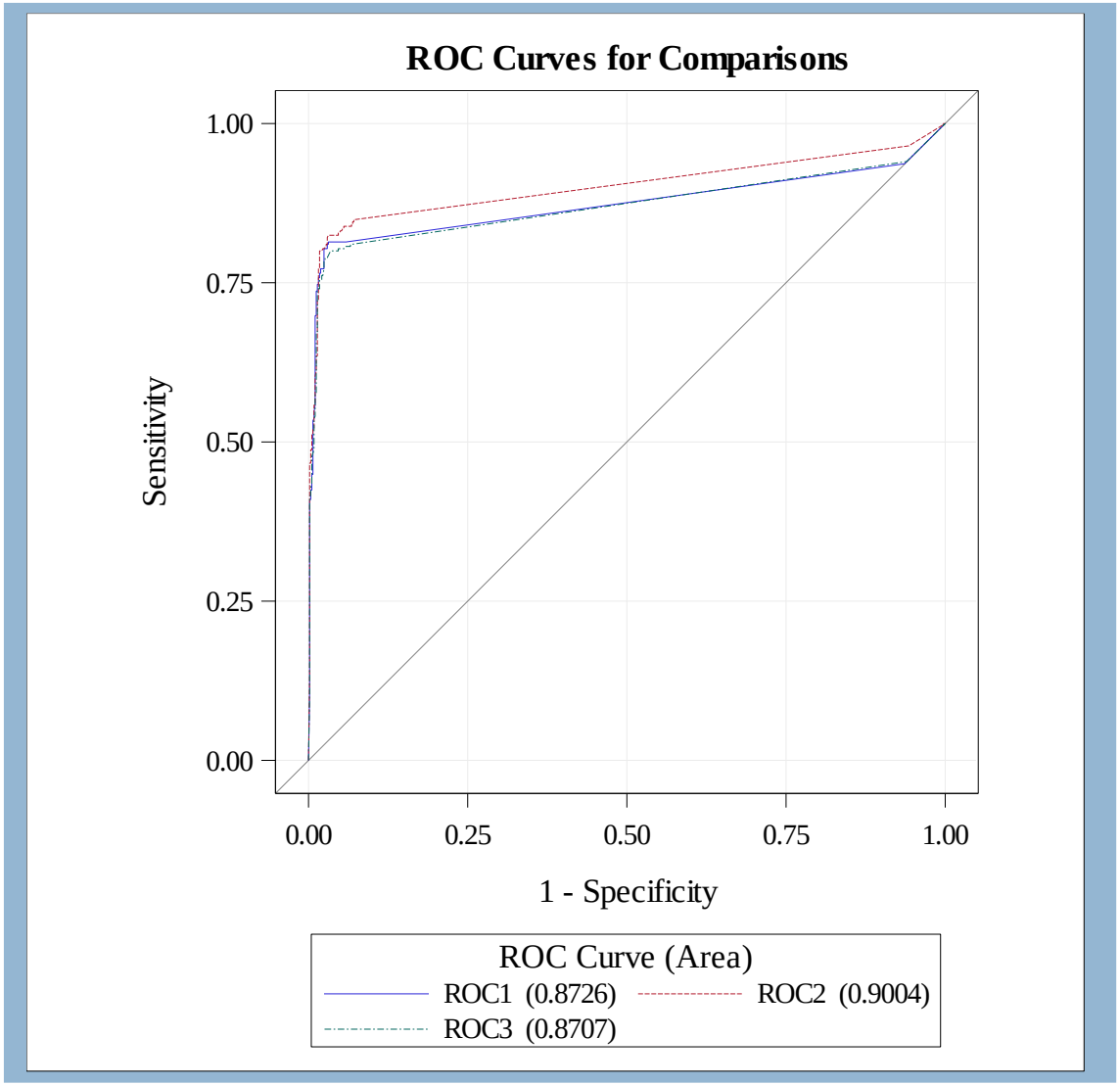
Example use of %*diag_test* macro

Diagnostic test(s)		Reference test (Abbott Plasma VL copies/ml)			Diagnostic accuracy measures	
Test category	**Test result**	**>=1000**	**<1000**	**Total**	**Measure**	**Estimate (95 % CI)**
M-DBS VL copies/ml	>=1000	213	26	239	Sensitivity (%)	90.3 (85.8 - 93.4)
					Specificity (%)	94.9 (92.6 - 96.5)
	<1000	23	480	503	Positive Predictive Value (PPV) (%)	89.1 (84.5 - 92.5)
					Negative Predictive Value (NPV) (%)	95.4 (93.2 - 96.9)
	Total	236	506	742	Upward Misclassification (%)	5.1 (3.5 - 7.4)
					Downward Misclassification (%)	9.7 (6.6 - 14.2)
					False Omission Rate (FOR) (%)	4.6 (3.1 - 6.8)
					False Discovery Rate (FDR) (%)	10.9 (7.5 - 15.5)
					Positive Likelihood Ratio (LR+)	17.6 (12.1 - 25.6)
					Negative Likelihood Ratio (LR-)	0.1 (0.1 - 0.2)
					Diagnostic Accuracy (%)	93.4 (91.4 - 95.0)
					Disease Prevalence (%)	31.8 (28.6 - 35.2)
					Diagnostic Odds Ratio (DOR)	171.0 (95.4 - 306.5)
					Kappa Agreement	0.8 (0.8 - 0.9)
					Youden's Index	0.9 (0.8 - 0.9)
					F-score	0.9 (0.9 - 0.9)

Example use of %*diag_test* macro

Diagnostic test(s)		Reference test (Abbott Plasma VL copies/ml)			Diagnostic accuracy measures	
Test category	**Test result**	**>=1000**	**<1000**	**Total**	**Measure**	**Estimate (95 % CI)**
D-DBS VL copies/ml	>=1000	208	28	236	Sensitivity (%)	88.1 (83.4 - 91.7)
					Specificity (%)	94.5 (92.1 - 96.2)
	<1000	28	480	508	Positive Predictive Value (PPV) (%)	88.1 (83.4 - 91.7)
					Negative Predictive Value (NPV) (%)	94.5 (92.1 - 96.2)
	Total	236	508	744	Upward Misclassification (%)	5.5 (3.8 - 7.9)
					Downward Misclassification (%)	11.9 (8.3 - 16.6)
					False Omission Rate (FOR) (%)	5.5 (3.8 - 7.9)
					False Discovery Rate (FDR) (%)	11.9 (8.3 - 16.6)
					Positive Likelihood Ratio (LR+)	16.0 (11.1 - 23.0)
					Negative Likelihood Ratio (LR-)	0.1 (0.1 - 0.2)
					Diagnostic Accuracy (%)	92.5 (90.4 - 94.2)
					Disease Prevalence (%)	31.7 (28.5 - 35.2)
					Diagnostic Odds Ratio (DOR)	127.3 (73.6 - 220.4)
					Kappa Agreement	0.8 (0.8 - 0.9)
					Youden's Index	0.8 (0.8 - 0.9)
					F-score	0.9 (0.9 - 0.9)

Example use of *%diag_test* macro



Conclusion

- The *%**diag_test*** macro is a powerful and more advanced analytic tool for analysis of data from diagnostic studies.
- It provides a pool of measures to choose from and compare against to make concrete decision to adopt or reject diagnostic tests.
- The *%**diag_test*** macro adds to pool of tools developed by the authors to automate data analysis techniques.
- Code is easy to modify to include other diagnostic measures and variance estimation methods.
- For results interpretation, user should consult subject matter as importance of diagnostic measures depend on disease prevalence or disease spectrum or both.

References

- The *%diag_test* SAS macro source code: https://github.com/kmuthusi/diagnostic-testing-macro

IMPLEMENTATION SCIENCE

Field Evaluation of Dried Blood Spots for HIV-1 Viral Load Monitoring in Adults and Children Receiving Antiretroviral Treatment in Kenya: Implications for Scale-up in Resource-Limited Settings

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Source: *JAIDS*. 2016, 74(4):399-406. doi: 10.1097/QAI.0000000000001275

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