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PARES & NONES Un break científico

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Hierarchical Modeling for Diagnostic Test Accuracy

PROBLEM

Models implemented in statistical software for the precision analysis of diagnostic tests include random-effects modeling (bivariate model) and hierarchical regression (hierarchical summary receiver operating characteristic). However, these models do not provide an overall mean, but calculate the mean of a central study when the random effect is equal to zero; hence, it is difficult to calculate the covariance between sensitivity and specificity when the number of studies in the meta-analysis is small.

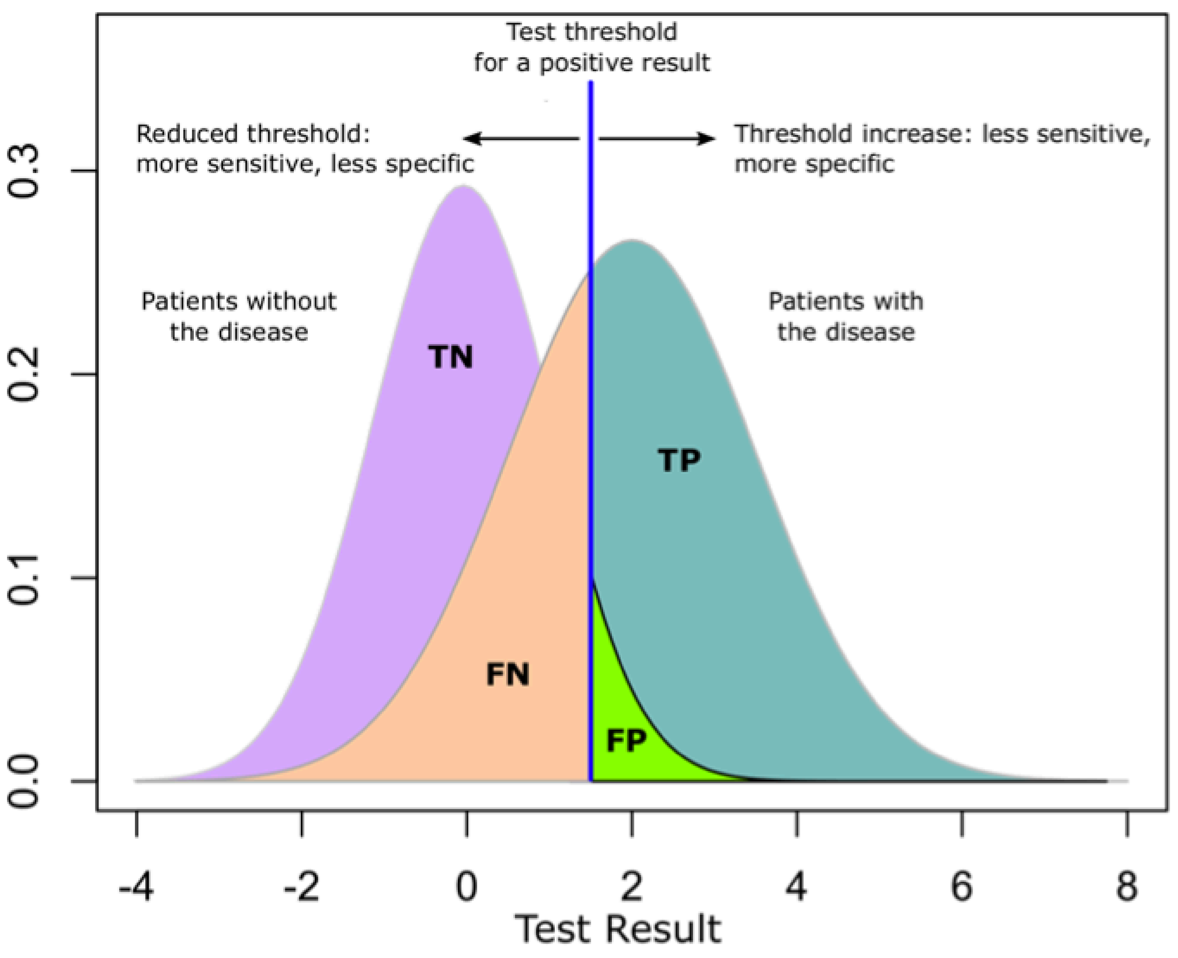
METHOD

Using simulations, we investigated the performance of four copula models **(Gauss, C90-Clayton 90; C270-Clayton 270; FGM-Farlie–Gumbel–Morgenstern)** that incorporate scenarios designed to replicate realistic situations for meta-analyses of diagnostic accuracy of the tests. Copulas permit the representation of the structure of functional dependence between sensitivity and specificity in a natural manner through multivariate distributions. The models' performances were evaluated based on p-values using the Cramér–von Mises goodness-of-fit test.

CONTRIBUTIONS

Here we used copulas as an alternative to capture the dependence between sensitivity and specificity. The posterior values were estimated using methods comprised of a class of algorithms for sampling from a probability distribution, and estimates were compared with the results of the bivariate model, which assumes statistical independence in the test results. To illustrate the applicability of the models and their respective comparisons, data from 14 published studies reporting estimates of the accuracy of the Alcohol Use Disorder Identification Test were used.

Our results indicated that copula models are valid when the assumptions of the bivariate model are not fulfilled.



RESULTS

HSROC Model

$$\begin{cases} TP \sim Binomial\left(TP_i + FN_i, Se_i\right) \\ FP \sim Binomial\left(FP_i + TN_i, Sp_i\right) \\ logit\left(Se_i\right) = \left(\theta_i + \frac{\alpha_i}{2}\right)^{-\beta/2} \\ logit\left(1 - Sp_i\right) = \left(\theta_i - \frac{\alpha_i}{2}\right)^{\beta/2} \\ \theta_i|\Theta, \gamma, Z_i, \sigma_\theta^2 \sim N\left(\Theta + \gamma Z_i, \sigma_\theta^2\right) \\ \alpha_i|\Lambda, \lambda, Z_i, \sigma_\alpha^2 \sim N\left(\Lambda + \lambda Z_i, \sigma_\alpha^2\right) \end{cases}$$

Copula Definition

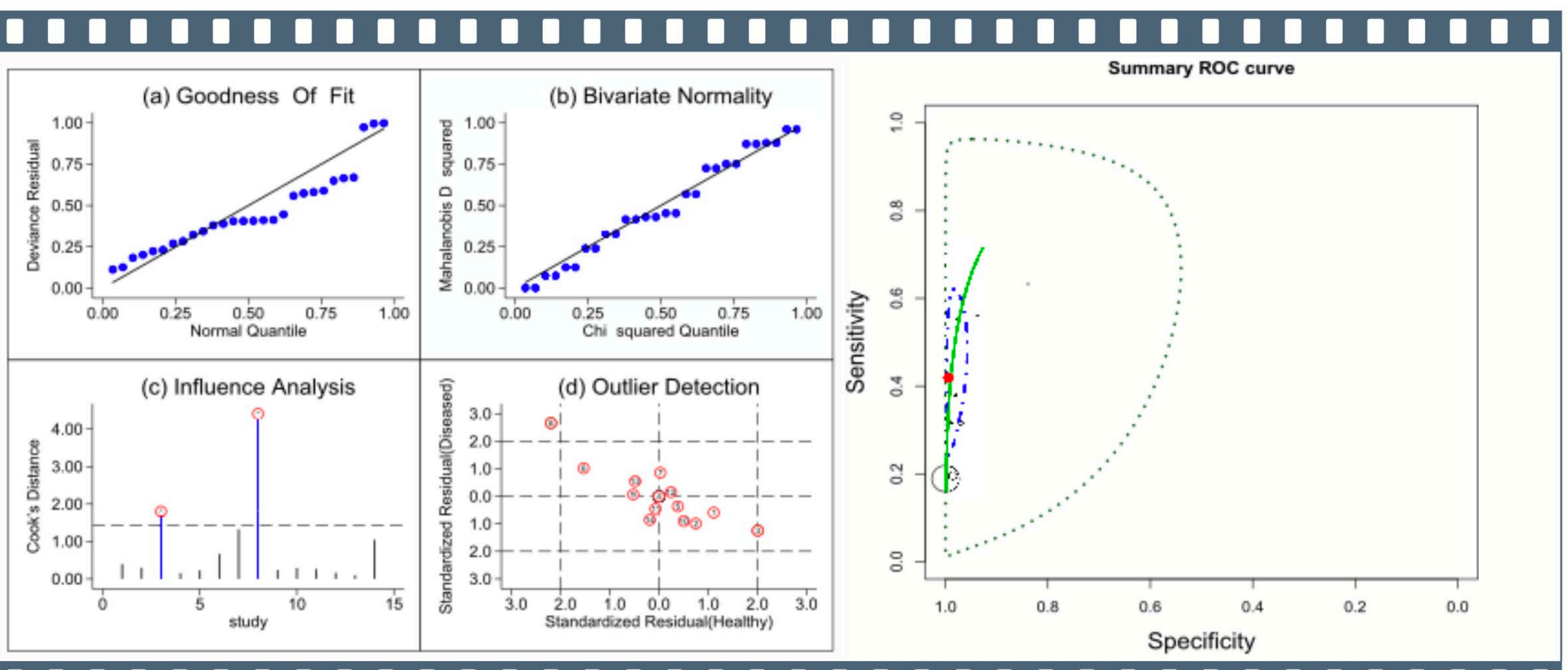
$$\begin{cases} H\left(x_1, x_2\right) = C\left(f\left(x_1\right), f\left(x_2\right)\right) = C\left(u_1, u_2\right) \\ C\left(u, 0\right) = 0 \\ C\left(0, v\right) = 0 \\ C\left(u, 1\right) = u \\ C\left(1, v\right) = v \end{cases}$$

The Hierarchical Copula Model

$$\begin{cases} TP_i \sim Binomial\left(TP_i + FN_i, Se_i\right) \\ TN_i \sim Binomial\left(TN_i + FP_i, Sp_i\right) \\ Se_i \sim Beta\left(\alpha_{Se}, \beta_{Se}\right) \\ Sp_i \sim Beta\left(\alpha_{Sp}, \beta_{Sp}\right) \\ f\left(u\right) = \frac{\Gamma\left(\alpha_{Se} + \beta_{Se}\right) u^{\alpha_{Se}-1}\left(1-u\right)^{\beta_{Se}-1}}{\Gamma\left(\alpha_{Se}\right)\Gamma\left(\alpha_{Se}\right)} \end{cases}$$

Selection of a Model Copula

$$\begin{cases} H_0 : C \in C_0 \\ vs. \\ H_1 : C \notin C_0 \end{cases}$$



Copulas	Parameter	Mean	Lower	Upper
Gauss	Se	0.862	0.766	0.920
	Sp	0.755	0.6898	0.811
	Correlation	−0.570	−0.799	−0.289
C90	Se	0.865	0.777	0.922
	Sp	0.760	0.695	0.813
	Correlation	−0.466	−0.801	−0.0005
C270	Se	0.854	0.743	0.920
	Sp	0.752	0.680	0.810
	Correlation	−0.324	−0.758	-2.219×10^{-17}
FGM	Se	0.871	0.780	0.932
	Sp	0.756	0.692	0.812
	Correlation	−0.214	−0.222	−0.121
Frank	Se	0.858	0.754	0.929
	Sp	0.751	0.773	0.808
	Correlation	−0.600	−0.767	1.000

Abbreviations: C90, Clayton 90; C270, Clayton 270; FGM, Farlie–Gumbel–Morgenstern; Se, sensitivity; Sp, specificity.

		Number of Studies in the Meta-Analysis				
Copula	Parameter	5–10	11–16	17–22	23–38	29–35
Gauss	Statistic	0.11823	0.06988	0.050 97	0.04320	0.03739
	SE	0.00252	0.00113	0.00064	0.00069	0.00061
	p-value	0.50309	0.49000	0.47070	0.44991	0.49072
Clayton	Statistic	0.16819	0.16851	0.13742	0.11023	0.03460
	SE	0.03237	0.05993	0.06356	0.07039	0.00061
	p-value	0.52656	0.52146	0.52786	0.48326	0.49891
FGM	Statistic	0.06490	0.050 25	0.04871	0.06154	0.06717
	SE	0.00293	0.00159	0.00152	0.00032	0.00416
	p-value	0.71763	0.62812	0.48737	0.34574	0.30307
Frank	Statistic	0.11127	0.06867	0.05102	0.04355	0.03735
	SE	0.00361	0.00123	0.00075	0.00078	0.00067
	p-value	0.43157	0.48938	0.46523	0.43418	0.46655

Abbreviations: FGM, Farlie–Gumbel–Morgenstern.

CONCLUSION

- The use of copulas allows the study of dependencies with structures that are not necessarily linear, which is possible in diagnostic situations in which the results are obtained after dichotomization.
- Our simulations and application to motivating examples support and extend the empirical evidence suggesting that copula methods generate reliable results in the study of diagnostic test meta-analyses. Simulation results show that the choice of analysis method strongly affects the accuracy of the diagnostic test.

REMARKS

- We have demonstrated that hierarchical copulas offer a straightforward method in the study of meta-analysis of diagnostic tests, where the accuracy of the tests depends on thresholds, while also taking into account the stochastic relationship of sensitivity and specificity.

REFERENCES

J. J. Pambabay-Calero, S. A. Bauz-Olvera and et al.
Hierarchical Modeling for Diagnostic Test Accuracy Using Multivariate Probability Distribution Functions. Mathematics 9(11), 1310, 2021.
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