

Additional data, file 2 Theoretical simulation of receiver operating characteristic (ROC) curves from crude odds ratio (OR; A) and from combinations of adjusted OR (B)

Theoretical estimation of the area under the curve from crude OR
Pathologic ST-T segment on resting ECG: 0.6534
Angina according to patient: 0.6700

Chest pain on exertion 0.6804

Theoretical estimation of the area under the curve from combinations of adjusted OR

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\text { Pathologic ST-T + Chest pain on exertion: } 0.7622
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Angina according to patient+ Chest pain on exertion: 0.7233

Pathologic ST-T + Angina according to patient + Chest pain on exertion: 0.8225

## Simulation of ROC curve and estimation of the area under the curve

An ROC curve with the corresponding area under the curve can be simulated by using the relations in a standard four-way table (Additional Table 1) for dichotomous evaluation of a marker compared to a clinical outcome. Using Table 1, the OR is estimated as $\frac{\mathrm{a} * \mathrm{~d}}{\mathrm{~b} * \mathrm{c}}$.

Additional Table 1 Standard presentation of the outcome from a marker compared to clinical outcome


Using the sensitivity, $\frac{\mathrm{a}}{\mathrm{a}+\mathrm{b}}$, and the specificity, $\frac{\mathrm{d}}{\mathrm{c}+\mathrm{d}}$, the OR can also be expressed as $O R=\frac{\text { Sens } /(1-\text { Sens })}{(1-\text { Spec }) / \text { Spec }}$ To simplify the equation, let $y=$ sensitivity, $x=$ specificity, and $\mu=O R$. The relation between OR and sensitivity and specificity can then be expressed as $\frac{y /(1-y)}{(1-x) / x}=\mu$, which yields $\frac{y}{1-y}=\frac{x}{1-x} * \mu$.

The sensitivity, y , can now be expressed as $\mathrm{y}=\frac{\mu \mathrm{x}}{\mu \mathrm{x}-\mathrm{x}+1}$ or as

Sens $=\frac{\mathrm{OR} * \text { Spec }}{\mathrm{OR} * \text { Spec }- \text { Spec }+1}$.

This implies that for a fixed OR, the sensitivity can be estimated for any given value of the specificity, which means that a ROC curve can be constructed.

The area under the curve (AUC) can be estimated by integrating the expression above, given that $\ln (O R)>0$ :
$A \cup C=\int_{0}^{1} \mathrm{ydx}=\int_{0}^{1} \frac{\mu \mathrm{x}}{\mu \mathrm{x}-\mathrm{x}+1} \mathrm{dx}=\ldots=\frac{\mu(\mu-1-\ln (\mu))}{(\mu-1)^{2}}$
if $\ln (\mathrm{OR}) \sim 0$ => AUC ~0.5.

