WEB-BASED SUPPLEMENTARY MATERIALS FOR

"AREA UNDER THE FREE-RESPONSE ROC CURVE (FROC) AND A RELATED SUMMARY INDEX"

BY

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WEB APPENDIX A. AREA UNDER THE FROC CURVE AND ITS IDEAL BOOTSTRAP VARIANCE

Here we derive the ideal bootstrap variance for the area under the empirical FROC curve (FAUC) for the data consisting of actually negative subjects and actually positive subjects with *t* abnormalities. In this case the area under the empirical FROC curve can be expressed as follows:

$$\hat{A}_{\rho\circ\pi} = \frac{1}{tS_t\left(S_t + S_0\right)}\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1 \\ l\neq j}}^{S_t}\xi_{jl} + \sum_{j=1}^{S_t}\nu_{jj} + \sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right)$$

where $\{\xi\}$, $\{\nu\}$ and $\{\eta\}$ are the random variables corresponding to the comparisons (in terms of *w* in eq. 6 of the manuscript) between sets of *FP* and *TP* marks located on different actually positive examinations (ξ), on the same actually positive examinations (ν), and on an actually negative and an actually positive examination (η).

The denominator of the FAUC estimator, $tS_t*(S_t+S_0)$ is fixed by design, and the variance of the numerator can be represented as a linear combination of 6 terms:

$$V\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1 \\ l\neq j}}^{S_t}\xi_{jl} + \sum_{j=1}^{S_t}\nu_{jj} + \sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right) = V\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1 \\ l\neq j}}^{S_t}\xi_{jl}\right) + V\left(\sum_{j=1}^{S_t}\nu_{jj}\right) + V\left(\sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right) +$$

$$+2\times\left\{C\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1 \\ l\neq j}}^{S_t}\xi_{jl}, \sum_{j=1}^{S_t}\nu_{jj}\right) + C\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1 \\ l\neq j}}^{S_t}\xi_{jl}, \sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right) + C\left(\sum_{j=1}^{S_t}\nu_{jj}, \sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right)\right\}$$

As we show below these 6 terms are in total associated with 15 potentially nonzero covariances. The first variance (of $\Sigma\xi$) is associated with six generally non-zero covariances:

$$V\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1\\l\neq j}}^{S_t}\xi_{jl}\right)=S_t\left(S_t-1\right)\times\begin{Bmatrix}V\left(\xi_{jl}\right)+\\C\left(\xi_{jl},\xi_{lj}\right)\end{Bmatrix}+S_t\left(S_t-1\right)\left(S_t-2\right)\times\begin{Bmatrix}C\left(\xi_{jl},\xi_{jl'}\right)+C\left(\xi_{jl},\xi_{j'l}\right)+\\C\left(\xi_{jl},\xi_{l'j}\right)+C\left(\xi_{jl},\xi_{lj'}\right)\end{Bmatrix}$$

In addition, there are two potentially non-zero covariances associated with *{ξ}* and *{ν}*:

$$C\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1\\l\neq j}}^{S_t}\xi_{jl},\sum_{j=1}^{S_t}\nu_{jj}\right)=S_t\left(S_t-1\right)\times\left\{C\left(\xi_{jl},\nu_{jj}\right)+C\left(\xi_{jl},\nu_{ll}\right)\right\}$$

and two potentially nonzero covariances associated with *{ξ}* and *{η}*:

$$C\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1\\l\neq j}}^{S_t}\xi_{jl},\sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right)=S_t\left(S_t-1\right)S_0\times\left\{C\left(\xi_{jl},\eta_{ij}\right)+C\left(\xi_{jl},\eta_{il}\right)\right\}$$

The second variance (of *Σν*) is associated with only a single potentially non-zero covariance:

$$V\left(\sum_{j=1}^{S_t}\nu_{jj}\right)=S_t\times V\left(\nu_{jj}\right)$$

In addition, there is a single potentially non-zero covariance of *{ν}* and *{η}*:

$$C\left(\sum_{j=1}^{S_t}\nu_{jj},\sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right)=S_0S_t\times C\left(\nu_{jj},\eta_{ij}\right)$$

Finally, the third variance (of *Ση*) is associated with three potentially nonzero covariances:

$$V\left(\sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right)=S_0S_t\times V\left(\eta_{ij}\right)+S_tS_0\left(S_0-1\right)\times C\left(\eta_{ij},\eta_{kj}\right)+S_0S_t\left(S_t-1\right)\times C\left(\eta_{ij},\eta_{il}\right)$$

We estimate the variance of the estimator of the area under the FROC curve (FAUC) as variance in the bootstrap sample space, *B*, where subjects are resampled independently within each group of subjects with the same number of abnormalities. The form of the FAUC estimator permits us to derive an *ideal* or *exact* (Efron and Tibshirani, 1993) bootstrap variance, namely the variance over the infinite number of the independent bootstrap samples.

Below, we provide the expressions for the ideal bootstrap version of the 15 previously introduced covariances. The following computation requires knowledge of the results of comparisons of all subjects, $\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0+S_t,S_t}$ (defined in eq. 6 of the manuscript and illustrated in Web Appendix C). We distinguish three structural parts of $\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0+S_t,S_t}$, namely: $w^{t,t}=\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=S_0+1,s=1}^{S_0+S_t,S_t}$, $w^{t}=\left\{w_{S_0+s,s}\right\}_{s=1}^{S_t}$, and $w^{0,t}=\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0,S_t}$. These sets describe the equally likely realizations of the random variables *ξ*, *v*, and *η*, correspondingly. Furthermore, "*" distinguishes the random index in the bootstrap space from the index in the dataset; "• "denotes summation, and "‾" denotes averaging over the dotted index.

$$V_B\left(\xi_{j^*l^*}\right)=\frac{1}{\left(S_t\right)^2}\sum_{j=1}^{S_t}\sum_{l=1}^{S_t}\left(w_{jl}^{t,t}\right)^2-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)^2 \qquad C_B\left(\xi_{j^*l^*},\xi_{l^*j^*}\right)=\frac{1}{\left(S_t\right)^2}\sum_{j=1}^{S_t}\sum_{l=1}^{S_t}w_{jl}^{t,t}\times w_{lj}^{t,t}-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)^2$$

$$C_B\left(\xi_{j^*l^*},\xi_{j^*l'^*}\right)=\frac{1}{S_t}\sum_{j=1}^{S_t}\left(\overline{w}_{j\bullet}^{t,t}\right)^2-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)^2 \qquad C_B\left(\xi_{j^*l^*},\xi_{j'^*l^*}\right)=\frac{1}{S_t}\sum_{l=1}^{S_t}\left(\overline{w}_{\bullet l}^{t,t}\right)^2-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)^2$$

$$C_B\left(\xi_{j^*l^*},\xi_{l'^*j^*}\right)=\frac{1}{S_t}\sum_{j=1}^{S_t}\overline{w}_{j\bullet}^{t,t}\times\overline{w}_{\bullet j}^{t,t}-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)^2=C_B\left(\xi_{j^*l^*},\xi_{l^*j'^*}\right)$$

$$C_B\left(\xi_{j^*l^*},\nu_{j^*j^*}\right)=\frac{1}{S_t}\sum_{j=1}^{S_t}\overline{w}_{j\bullet}^{t,t}\times w_j^t-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)\times\left(\overline{w}_{\bullet}^{t}\right) \qquad C_B\left(\xi_{j^*l^*},\nu_{l^*l^*}\right)=\frac{1}{S_t}\sum_{l=1}^{S_t}\overline{w}_{\bullet l}^{t,t}\times w_l^t-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)\times\left(\overline{w}_{\bullet}^{t}\right)$$

$$C_B\left(\xi_{j^*l^*},\eta_{i^*l^*}\right)=\frac{1}{S_t}\sum_{l=1}^{S_t}\overline{w}_{\bullet l}^{t,t}\times\overline{w}_{\bullet l}^{0,t}-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)\times\left(\overline{w}_{\bullet\bullet}^{0,t}\right) \qquad C_B\left(\xi_{j^*l^*},\eta_{i^*j^*}\right)=\frac{1}{S_t}\sum_{j=1}^{S_t}\overline{w}_{j\bullet}^{t,t}\times\overline{w}_{\bullet j}^{0,t}-\left(\overline{w}_{\bullet\bullet}^{t,t}\right)\times\left(\overline{w}_{\bullet\bullet}^{0,t}\right)$$

$$V_B\left(\nu_{j^*j^*}\right)=\frac{1}{S_t}\sum_{j=1}^{S_t}\left(w_j^t\right)^2-\left(\overline{w}_{\bullet}^{t}\right)^2$$

$$C_B\left(\nu_{j^*j^*},\eta_{i^*j^*}\right)=\frac{1}{S_t}\sum_{j=1}^{S_t}w_j^t\times\overline{w}_{\bullet j}^{0,t}-\left(\overline{w}_{\bullet}^{t}\right)\times\left(\overline{w}_{\bullet\bullet}^{0,t}\right)$$

$$V_B\left(\eta_{i^*j^*}\right)=\frac{1}{S_0S_t}\sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\left(w_{ij}^{0,t}\right)^2-\left(\overline{w}_{\bullet\bullet}^{0,t}\right)^2$$

$$C_B\left(\eta_{i^*j^*},\eta_{k^*j^*}\right)=\frac{1}{S_t}\sum_{j=1}^{S_t}\left(\overline{w}_{\bullet j}^{0,t}\right)^2-\left(\overline{w}_{\bullet\bullet}^{0,t}\right)^2 \qquad C_B\left(\eta_{i^*j^*},\eta_{i^*l^*}\right)=\frac{1}{S_0}\sum_{i=1}^{S_0}\left(\overline{w}_{i\bullet}^{0,t}\right)^2-\left(\overline{w}_{\bullet\bullet}^{0,t}\right)^2$$

WEB APPENDIX B. IDEAL BOOTSTRAP VARIANCE OF Λ

The nonparametric estimator of the proposed index *Λ* for the data where all actually positive subjects have *t* abnormalities can be expressed as follows:

$$\hat{\Lambda} = \hat{A}_{\rho\circ\pi} - \widehat{FPR}_{\pi} + \frac{\widehat{TPF}_{\pi}}{\varphi} = \frac{\sum_{j=1}^{S_t}\sum_{\substack{l=1\\l\neq j}}^{S_t}\xi_{jl} + \sum_{j=1}^{S_t}\nu_{jj} + \sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}}{tS_t\left(S_0+S_t\right)} - \frac{\sum_{i=1}^{S_0}n_i^0 + \sum_{j=1}^{S_t}n_j^t}{\left(S_0+S_t\right)} + \frac{1}{\varphi}\times\frac{\sum_{j=1}^{S_t}m_j^t}{tS_t}$$

Its variance can be partitioned in the following manner:

$$V\left(\hat{\Lambda}\right) = V\left(\hat{A}_{\rho\circ\pi}\right) + V\left(\widehat{FPR}_{\pi}\right) + \frac{V\left(\widehat{TPF}_{\pi}\right)}{\varphi^2} - $$
$$-2\times C\left(\hat{A}_{\rho\circ\pi},\widehat{FPR}_{\pi}\right) + \frac{2}{\varphi}\times C\left(\hat{A}_{\rho\circ\pi},\widehat{TPF}_{\pi}\right) - \frac{2}{\varphi}\times C\left(\widehat{FPR}_{\pi},\widehat{TPF}_{\pi}\right)$$

The variance of $\hat{A}_{\rho\circ\pi}$ was derived in Web Appendix A.

The covariances with the $\widehat{FPR}_{\pi}$ can be further reduced to the following expressions:

$$V\left(\widehat{FPR}_{\pi}\right) = V\left(\frac{\sum_{i=1}^{S_0}n_i^0 + \sum_{j=1}^{S_t}n_j^t}{S_0+S_t}\right) = \frac{S_0}{\left(S_0+S_t\right)^2}\times V\left(n_i^0\right) + \frac{S_t}{\left(S_0+S_t\right)^2}\times V\left(n_j^t\right)$$

$$C\left(\widehat{FPR}_{\pi},\hat{A}_{\rho\circ\pi}\right) = C\left\{\frac{1}{S_0+S_t}\left(\sum_{j=1}^{S_t}n_j^t + \sum_{i=1}^{S_0}n_i^0\right), \frac{1}{tS_t\left(S_0+S_t\right)}\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1\\l\neq j}}^{S_t}\xi_{jl} + \sum_{j=1}^{S_t}\nu_{jj} + \sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij}\right)\right\} =$$
$$= \frac{1}{tS_t\left(S_0+S_t\right)^2}\left\{\begin{array}{c} S_t\left(S_t-1\right)\times C\left(n_j^t,\xi_{jl}\right) + S_t\left(S_t-1\right)\times C\left(n_l^t,\xi_{jl}\right) + \\ S_t\times C\left(n_j^t,\nu_{jj}\right) + \\ S_0S_t\times C\left(n_j^t,\eta_{ij}\right) + S_0S_t\times C\left(n_i^0,\eta_{ij}\right) \end{array}\right\}$$

$$C\left(\widehat{FPR}_{\pi},\widehat{TPF}_{\pi}\right) = C\left(\frac{\sum_{j=1}^{S_t}n_j^t}{S_0+S_t},\frac{\sum_{j=1}^{S_t}m_j^t}{tS_t}\right) = \frac{S_t}{tS_t\left(S_0+S_t\right)}\times C\left(n_j^t,m_j^t\right)$$

Similarly, the covariances with the $\widehat{TPF}_{\pi}$ can be further reduced to the following expressions:

$$V\left(\widehat{TPF}_{\pi}\right) = V\left(\frac{\sum_{j=1}^{S_t}m_j^t}{tS_t}\right) = \frac{S_t}{\left(tS_t\right)^2}V\left(m_j^t\right)$$

$$C\left(\widehat{TPF}_{\pi}, \hat{A}_{\rho\circ\pi}\right) = C\left\{ \frac{1}{tS_t}\sum_{j=1}^{S_t} m_j^t, \quad \frac{1}{tS_t\left(S_0+S_t\right)}\left(\sum_{j=1}^{S_t}\sum_{\substack{l=1\\l\neq j}}^{S_t}\xi_{jl} + \sum_{j=1}^{S_t}\nu_{jj} + \sum_{i=1}^{S_0}\sum_{j=1}^{S_t}\eta_{ij} \right)\right\} =$$

$$= \frac{1}{\left(tS_t\right)^2\left(S_0+S_t\right)}\left\{ \begin{array}{c} S_t\left(S_t-1\right)\times C\left(m_j^t,\xi_{jl}\right) + S_t\left(S_t-1\right)\times C\left(m_l^t,\xi_{jl}\right) \\ +S_t\times C\left(m_j^t,\nu_{jj}\right) \\ +S_tS_0\times C\left(m_j^t,\eta_{ij}\right) \end{array} \right\}$$

The ideal bootstrap versions of variances and covariances used in the formulae above can be computed using the results of the comparisons of all subjects, $\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0+S_t,S_t}$ (defined in eq. 6 of the manuscript and illustrated in Web Appendix C). We distinguish three structural parts of $\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0+S_t,S_t}$, namely: $w^{t,t} = \left\{w_{\tilde{s}s}\right\}_{\tilde{s}=S_0+1,s=1}^{S_0+S_t,S_t}$, $w^t = \left\{w_{S_0+s,s}\right\}_{s=1}^{S_t}$, and $w^{0,t} = \left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0,S_t}$. These sets describe the equally likely realizations of the random variables *ξ, ν*, and *η,* correspondingly. Furthermore, "*" distinguishes the random index in the bootstrap space from the index in the dataset, "•" denotes summation, and "¯" denotes averaging over the dotted index.

$$V_B\left(n_{i*}^0\right) = \frac{\sum_{i=1}^{S_0}\left(n_i^0\right)^2}{S_0} - \left(\overline{n}_{\bullet}^0\right)^2 \quad V_B\left(n_{j*}^t\right) = \frac{\sum_{j=1}^{S_t}\left(n_j^t\right)^2}{S_t} - \left(\overline{n}_{\bullet}^t\right)^2$$

$$C_B\left(n_{j*}^t,\xi_{j*l*}\right) = \frac{\sum_{j=1}^{S_t} n_j^t\times\overline{w}_{j\bullet}^{t,t}}{S_t} - \left(\overline{n}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet\bullet}^{t,t}\right) \qquad C_B\left(n_{l*}^t,\xi_{j*l*}\right) = \frac{\sum_{l=1}^{S_t} n_l^t\times\overline{w}_{\bullet l}^{t,t}}{S_t} - \left(\overline{n}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet\bullet}^{t,t}\right)$$

$$C_B\left(n_{j*}^t,\nu_{j*j*}\right) = \frac{\sum_{j=1}^{S_t} n_j^t\times w_j^t}{S_t} - \left(\overline{n}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet}^t\right)$$

$$C_B\left(n_{j*}^t,\eta_{i*j*}\right) = \frac{\sum_{j=1}^{S_t} n_j^t\times\overline{w}_{\bullet j}^{0,t}}{S_t} - \left(\overline{n}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet\bullet}^{0,t}\right) \qquad C_B\left(n_{i*}^0,\eta_{i*j*}\right) = \frac{\sum_{i=1}^{S_0} n_i^0\times\overline{w}_{i\bullet}^{0,t}}{S_0} - \left(\overline{n}_{\bullet}^0\right)\times\left(\overline{w}_{\bullet\bullet}^{0,t}\right)$$

$$C_B\left(n_{j*}^t,m_{j*}^t\right) = \frac{\sum_{j=1}^{S_t} n_j^t\times m_j^t}{S_t} - \left(\overline{n}_{\bullet}^t\right)\times\left(\overline{m}_{\bullet}^t\right)$$

$$V_B\left(m_{j*}^t\right) = \frac{\sum_{j=1}^{S_t}\left(m_j^t\right)^2}{S_t} - \left(\overline{m}_{\bullet}^t\right)^2$$

$$C_B\left(m_{j*}^t,\xi_{j*l*}\right)=\frac{\sum_{j=1}^{S_t} m_j^t \times \overline{w}_{j\bullet}^{t,t}}{S_t}-\left(\overline{m}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet\bullet}^{t,t}\right) \quad C_B\left(m_{l*}^t,\xi_{j*l*}\right)=\frac{\sum_{l=1}^{S_t} m_l^t \times \overline{w}_{\bullet l}^{t,t}}{S_t}-\left(\overline{m}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet\bullet}^{t,t}\right)$$

$$C_B\left(m_{j*}^t,\nu_{j*j*}\right)=\frac{\sum_{j=1}^{S_t} m_j^t \times w_j^t}{S_t}-\left(\overline{m}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet}^t\right)$$

$$C_B\left(m_{j*}^t,\eta_{i*j*}\right)=\frac{\sum_{j=1}^{S_t} m_j^t \times \overline{w}_{\bullet j}^{0,t}}{S_t}-\left(\overline{m}_{\bullet}^t\right)\times\left(\overline{w}_{\bullet\bullet}^{0,t}\right)$$

WEB APPENDIX C. ILLUSTRATION OF COMPUTATION OF SEVERAL KEY QUANTITIES

To illustrate of the computation of several key quantities formulated in the manuscript we selected eight different subjects from the dataset we analyzed in Section 5. The observations corresponding to these subjects are summarized in Web Figure 1.

We begin by demonstrating how to compute the empirical FROC points. For this purpose we need information on the total number of subjects (S_0+S_t); the total number of the abnormalities (tS_t) and the rating and type of each of the rated marks (*{x}, {y}*). Information on which marks were associated with a specific subject can be ignored. The computations are illustrated in Web Table 1.

If in Web Table 1 we had divided by the total numbers of *TP* ($\sum_{s=1}^{S_t} m_s^t$ =2) and *FP* ($\sum_{s`=1}^{S_0} n_{s`}^0+\sum_{s=1}^{S_t} n_s^t$ =9) marks in the computation of *TPF* and *FPR* correspondingly we would have obtained estimates for the ROC curve based on the *TP* and *FP* marks. The computation of the areas (columns J, K) using these quantities would have led to an estimate of the area under such an ROC curve of 0.806≈0.453*4/2*8/9. This illustrates the equivalence shown in equation (7) of the manuscript.

Web Table 2 lists the values $\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0+S_t,S_t}$ (eq. 6 of the manuscript) that are used for the estimation of FAUC and related components of variances. For purposes of the estimation of the bootstrap moments formulated in Web Appendices A and B, we need to distinguish three structural parts of the above table namely: $w^{0,t}=\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0,S_t}$, $w^{t,t}=\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=S_0+1,s=1}^{S_0+S_t,S_t}$, and

$w^{t}=\left\{w_{S_0+s,s}\right\}_{s=1}^{S_t}$. These sets describe the equally likely realizations of the random variables η, ξ and v, correspondingly. The first set (the top half of Web Table 2) corresponds to the comparisons of actually positive and actually negative subjects:

$$w^{0,t}=\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=1,s=1}^{S_0,S_t}=\begin{pmatrix}1&2&0&0\\1&1&0&0\\1&3&0&0\\0&0&0&0\end{pmatrix}\qquad relevant\quad averages:$$

$$\left\{\overline{w}_{\bullet l}^{0,t}\right\}_{l=1}^{S_t}=\left\{\frac{\sum_{i=1}^{S_0}w_{il}^{0,t}}{S_0}\right\}_{l=1}^{S_t}=\begin{pmatrix}\frac{3}{4}&\frac{6}{4}&0&0\end{pmatrix}\quad \left\{\overline{w}_{i\bullet}^{0,t}\right\}_{i=1}^{S_0}=\left\{\frac{\sum_{l=1}^{S_t}w_{il}^{0,t}}{S_t}\right\}_{i=1}^{S_0}=\begin{pmatrix}3/4\\2/4\\4/4\\0\end{pmatrix}\quad \overline{w}_{\bullet\bullet}^{0,t}=\frac{\sum_{i=1}^{S_0}\sum_{l=1}^{S_t}w_{il}^{0,t}}{S_0S_t}=\frac{9}{16}$$

The second set (the bottom half of Web Table 2) corresponds to the comparisons within a set of actually positive subjects:

$$w^{t,t}=\left\{w_{\tilde{s}s}\right\}_{\tilde{s}=S_0+1,s=1}^{S_0+S_t,S_t}=\begin{pmatrix}0&0&0&0\\1&1&0&0\\1.5&2&0&0\\0&0&0&0\end{pmatrix}\qquad relevant\quad averages:$$

$$\left\{\overline{w}_{\bullet l}^{t,t}\right\}_{l=1}^{S_t}=\left\{\frac{\sum_{j=1}^{S_t}w_{jl}^{0,t}}{S_t}\right\}_{l=1}^{S_t}=\begin{pmatrix}\frac{2.5}{4}&\frac{3}{4}&0&0\end{pmatrix}\quad \left\{\overline{w}_{j\bullet}^{t,t}\right\}_{j=1}^{S_t}=\left\{\frac{\sum_{j=1}^{S_t}w_{jl}^{t,t}}{S_t}\right\}_{j=1}^{S_t}=\begin{pmatrix}0\\2/4\\3.5/4\\0\end{pmatrix}\quad \overline{w}_{\bullet\bullet}^{t,t}=\frac{\sum_{j=1}^{S_t}\sum_{l=1}^{S_t}w_{jl}^{t,t}}{\left(S_t\right)^2}=\frac{5.5}{16}$$

The third set (the diagonal in the bottom half of Web Table 2) corresponds to the comparisons within the same actually positive subjects:

$$w^t = diag\left(w^{t,t}\right) = \left\{w_{S_0+s,s}\right\}_{s=1}^{S_t} = \begin{pmatrix}0\\1\\0\\0\end{pmatrix} \qquad relevant \quad average: \; \overline{w}_{\bullet}^{t} = \frac{\sum_{j=1}^{S_t} w_j^t}{S_t} = \frac{1}{4}$$

Other quantities relevant for estimation of the components of the variance of Λ are: 1) The numbers of *FP* marks (realizations of random variables n^0 and n^t):

$$\left\{n_i^0\right\}_{i=1}^{S_0} = \begin{pmatrix}2\\1\\3\\0\end{pmatrix} \quad and \quad \left\{n_j^t\right\}_{j=1}^{S_t} = \begin{pmatrix}0\\1\\2\\0\end{pmatrix} \quad relevant\ averges: \; \overline{n}_{\bullet}^{0} = \frac{\sum_{i=1}^{S_0} n_i^0}{S_0} = \frac{6}{4} \quad \overline{n}_{\bullet}^{t} = \frac{\sum_{j=1}^{S_t} n_j^0}{S_t} = \frac{3}{4}$$

and, 2) The number of *TP* marks (realizations of a random variable m^t):

$$\left\{m_j^t\right\}_{j=1}^{S_t} = \begin{pmatrix}1\\1\\0\\0\end{pmatrix} \quad relevant\ averges: \; \overline{m}_{\bullet}^{t} = \frac{\sum_{j=1}^{S_t} m_j^t}{S_t} = \frac{2}{4}$$

The area under the empirical FROC curve is (using eq. 6 of the manuscript):

$$\hat{A}_{\rho\circ\pi} = \frac{1}{tS_t\left(S_0+S_t\right)} \sum_{\tilde{s}=1}^{S_0+S_t} \sum_{s=1}^{S_t} w_{\tilde{s}s} = \frac{S_0 S_t \times \overline{w}_{\bullet\bullet}^{0,t} + \left(S_t\right)^2 \times \overline{w}_{\bullet\bullet}^{t,t}}{tS_t\left(S_0+S_t\right)} = \frac{\left(9+5.5\right)}{4\times\left(4+4\right)} = \frac{14.5}{32} \approx 0.453$$

which is equal to what was computed in Web Table 1.

Since in the set of eight selected subjects there is the same fraction of the actually positive subjects and actually negative subjects as in the dataset used in Section 5 (4/4=100/100), φ (eq. 9 of the manuscript) will also be equal to that from Section 5 (i.e. $\varphi \approx 0.06$). Thus, using equation 8 from the manuscript the estimate of Λ is:

$$\hat{\Lambda} = \hat{A}_{\rho\circ\pi} - \widehat{FPR_{\pi}} + \frac{\widehat{TPF_{\pi}}}{\varphi} \approx 0.453 - 1.125 + \frac{0.5}{0.06} \approx 7.66$$

Therefore, for the selected set of eight subjects the performance improvement of the system over the "guessing" system is 46% ($\Lambda * \varphi \approx 0.46$) of the improvement achievable by a perfect system.

CAPTIONS FOR WEB FIGURES

Web Figure 1. Observations on eight subjects sampled from the dataset analyzed in Section 5.

Each row represents one out of the total of eight subjects selected from the data we analyzed in Section 5. The four subjects without an abnormality (t=0) include: one without any rated marks (#4) and three with varying numbers of FP marks (#1-3). The values of n, m, x, and y for these subjects represent the realization of the random variables n^0 , m^0 , x^0, *and* y^0, *correspondingly (eq. 1 of the manuscript). The four subjects with a single abnormality (t=1) include: one with no rated marks (#8), one with only FP marks (#7), one with both FP and TP marks (#6), and one with only TP marks (#5). The values of n, m, x, and y for these subjects represent the realization of the random variables* n^t , m^t , x^t, *and* y^t, *correspondingly (eq. 1 of the manuscript).*

Web Figure 2. The empirical FROC curve corresponding to estimates in Web Table 1.

The dots correspond to the points computed in Web Table 1.

The shaded area is FAUC - the area under the empirical FROC curve (eq. 6 in the manuscript).

CAPTIONS FOR WEB TABLES

Web Table 1. Direct computations of the empirical FROC points and areas.

**-1 is an artificial rating which is used to "select" all rated marks regardless of the actual ratings.*

The columns correspond to the following notations and formulae used in the manuscript:

$A \leftrightarrow S_0 + S_t$; $B \leftrightarrow tS_t$; $D \leftrightarrow$ either $x^0_{s`c`}$, x^t_{sc} or y^t_{sc} (eq. 1) and to ε in equation 5;

$E \leftrightarrow \sum_{s=1}^{S_t} \sum_{c=1}^{m^t_s} I\left(y^t_{sc} > \varepsilon\right)$ for ε>0 and $\sum_{s=1}^{S_t} m^t_s$ for ε=-1 (eq. 5);

$F \leftrightarrow \widehat{TPF_{\rho\circ\pi}}(\varepsilon)$ for ε>0 and $\widehat{TPF_\pi}$ for ε=-1 (eq. 5);

$G \leftrightarrow \sum_{s`=1}^{S_0} \sum_{c`=1}^{n^0_{s`}} I\left(x^0_{s`c`} > \varepsilon\right) + \sum_{s=1}^{S_t} \sum_{c=1}^{n^t_s} I\left(x^t_{sc} > \varepsilon\right)$ for ε>0 and $\sum_{s`=1}^{S_0} n^0_{s`} + \sum_{s=1}^{S_t} n^t_s$ for ε=-1 (eq.5);

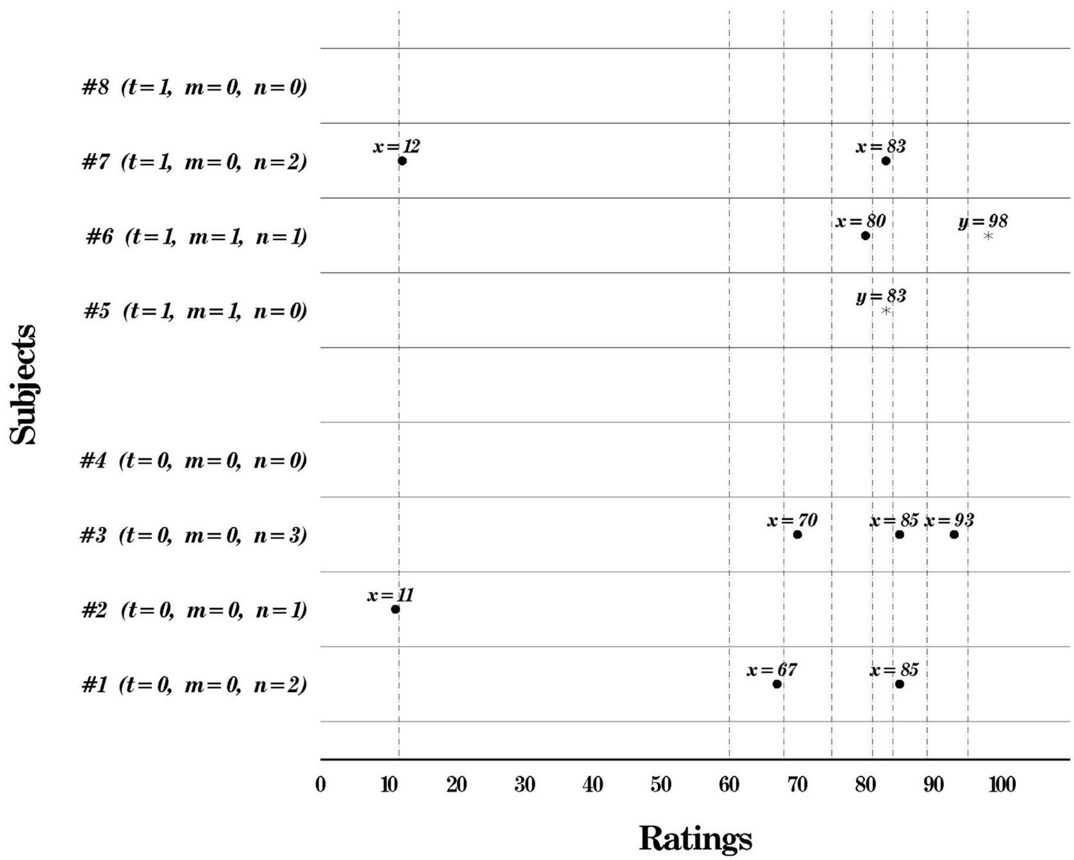
$H \leftrightarrow \widehat{FPR_{\rho\circ\pi}}(\varepsilon)$ for ε>0 and $\widehat{FPR_\pi}$ for ε=-1 (eq. 5);

K in the last row corresponds to the total area under the empirical FROC curve (FAUC)

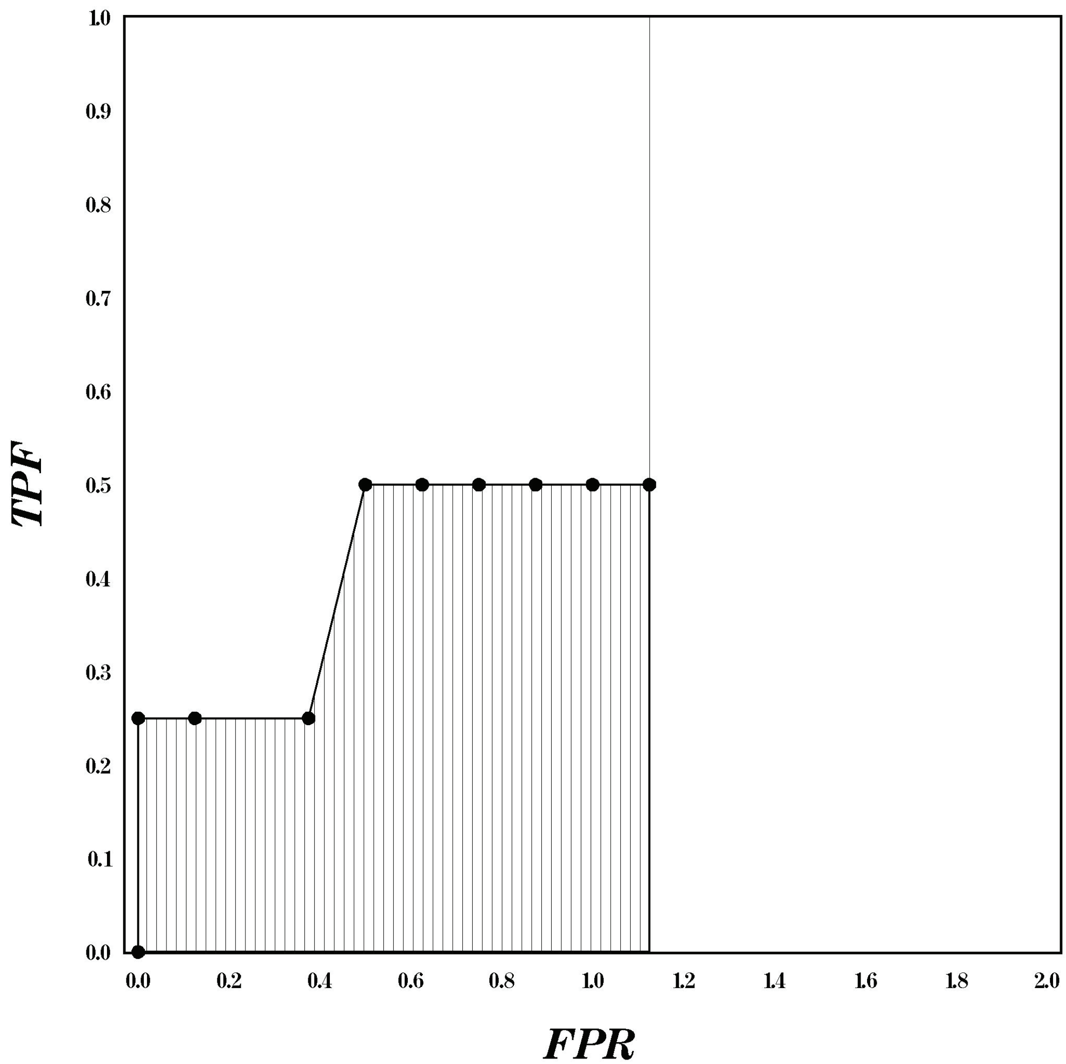
Web Table 2. Results of the comparison of subjects according to the function *w* defined in equation (6) of the manuscript.

If a subject does not have either the FP or TP marks that are needed for the comparison, the ratings for the "missing" marks are denoted with "•". According to the definition of w in equation (6) of the manuscript the comparison with "•" always results in 0.

Web Figure 1. Observations on eight subjects sampled from the dataset analyzed in Section 5.



Web Figure 2. The empirical FROC curve corresponding to estimates in Web Table 1.



WEB TABLES

Web Table 1. Direct computations of the empirical FROC points and areas.

A	B	C	D	E	**F**	G	**H**	I	J	K
Total number of subjects	Total number of abnormalities	Type of marks	Rating	Number of *TP* marks (y) rated above the rating in D	***TPF***	Number of *FP* marks (x) rated above the rating in D	***FPR***	Empirical point #	Partial area under the empirical FROC between the empirical point with # in I and the preceding point	Partial area up to the empirical point with # in I
					(=E/B)		**(=G/A)**		($=(H_I-H_{I-1})*(F_I+F_{I-1})/2$)	$(=J_I+K_{I-1})$
8	**4**	y	98	0	**0/4=0.00**	0	**0/8=0.00**	1		
		x	93	1	**1/4=0.25**	0	**0/8=0.00**	2	0.000	0.000
		x	85	1	**1/4=0.25**	1	**1/8≈0.13**	3	0.031	0.031
		x	85							
		y	83	1	**1/4=0.25**	3	**3/8≈0.38**	4	0.063	0.094
		x	83							
		x	80	2	**2/4=0.50**	4	**4/8=0.50**	5	0.047	0.141
		x	70	2	**2/4=0.50**	5	**5/8≈0.63**	6	0.063	0.203
		x	67	2	**2/4=0.50**	6	**6/8=0.75**	7	0.063	0.266
		x	12	2	**2/4=0.50**	7	**7/8≈0.88**	8	0.063	0.328
		x	11	2	**2/4=0.50**	8	**8/8=1.00**	9	0.063	0.391
			-1*	2	**2/4=0.50**	9	**9/8≈1.13**	10	0.063	**0.453**

Web Table 2. Results of the comparison of subjects according to the function *w* defined in equation (6) of the manuscript.

Subject ID = $\tilde{s}$ from eq. 6,7, A1	**s\` from eq. 1,5,7**	**s from eq. 1,5,6,7, A1**			**Subject ID (= $\tilde{s}$ from eq. 6,7, A1)**			
					5	**6**	**7**	**8**
					Index *s* from eq.1,5,6,7, A1			
					1	**2**	**3**	**4**
					Ratings for the *TP* marks for subjects with a single (t=1) abnormality (*realization of* y^t)			
					$y^1_{11}=83$	$y^1_{21}=98$	•	•
1	**1**		**Ratings for the *FP* marks for the subjects without abnormalities (*t=0*) (*realizations of* x^0)**	$x^0_{11}=67$, $x^0_{12}=85$	$\left(+\begin{matrix}1\\0\end{matrix}\right)=1$	$\left(+\begin{matrix}1\\1\end{matrix}\right)=2$	$\left(+\begin{matrix}0\\0\end{matrix}\right)=0$	$\left(+\begin{matrix}0\\0\end{matrix}\right)=0$
2	**2**			$x^0_{21}=11$	1	1	0	0
3	**3**			$x^0_{31}=70$, $x^0_{32}=85$, $x^0_{33}=93$	$\left(+\begin{matrix}1\\0\\0\end{matrix}\right)=1$	$\left(+\begin{matrix}1\\1\\1\end{matrix}\right)=3$	$\left(+\begin{matrix}0\\0\\0\end{matrix}\right)=0$	$\left(+\begin{matrix}0\\0\\0\end{matrix}\right)=0$
4	**4**			•	0	0	0	0
5		**1**	**Ratings for the *FP* marks for the subjects with a single (*t=1*) abnormality (*realizations of* x^t)**	•	0	0	0	0
6		**2**		$x^1_{21}=80$	1	1	0	0
7		**3**		$x^1_{31}=12$, $x^1_{32}=83$	$\left(+\begin{matrix}1\\0.5\end{matrix}\right)=1.5$	$\left(+\begin{matrix}1\\1\end{matrix}\right)=2$	$\left(+\begin{matrix}0\\0\end{matrix}\right)=0$	$\left(+\begin{matrix}0\\0\end{matrix}\right)=0$
8		**4**		•	0	0	0	0