Appendices

Online Supplement For

When Algorithmic Predictions Use Human-Generated Data: A Bias-Aware Classification Algorithm for Breast Cancer Diagnosis

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In Appendix A, we present a summary of notation and provide some additional results for the main analysis—the case when the mean error and the error variance are independent. Appendix B provides the additional results for the case when the mean error and the error variance are interdependent. We present the proofs for the results in Appendix C.

A. Model Notation and Additional Results

We summarize the model notation we used in the main text in Table 3.

Table 3 Summary of Notation Used in the Analysis

x_c/x_i	:	True risk due to clinical-risk information/mammogram
$\mu_{..}/\sigma_{..}$	:	mean/standard deviation of risk due to to information source (first subscript) being either *mammogram (i)* or *clinical-risk information (c)* and health status (second subscript) being either *cancer (c)* or *noncancer (n)*
Δ_i/Δ_c	:	The differences in the mean risks for the cancer and noncancer populations due to mammogram/clinical-risk information
$P(+)/P(-)$	:	The probability of the presence or absence of disease in the patient population
β	:	Bias factor
$\hat{x}_i$	:	Bias-adjusted risk score due to mammogram
$\rho_c/\rho_n = \rho$	:	The correlation coefficient between mammogram and clinical-risk information for cancer/noncancer patients
σ_0	:	Error variance (variability in error due to bias)
$\alpha(\beta,\sigma_0)/\alpha^*(\beta,\sigma_0)$	:	Weight/optimal weight assigned to clinical-risk information
r	:	Aggregate information
$k(\alpha,\beta,\sigma_0)/k^*(\beta,\sigma_0)$	:	Threshold/optimal threshold to biopsy
μ_c/μ_n	:	Mean of aggregate information for *cancer (c)*/*noncancer (n)*patients
$\sigma = \sigma_n = \sigma_c$	:	Standard deviation of aggregate information for *cancer (c)*/*noncancer (n)*patients
$I(\alpha,\beta,\sigma_0)$	:	Information content of the aggregate information
h	:	Discriminative ability of mammogram relative to that of the clinical-risk information
t	:	Relative utility of detecting cancer compared to reassuring its absence
		Outcome Variables
$FN/FP/TP/TN$	:	Classification outcomes: false negative/false positive/true positive/true negative
$P(.)$	:	Probability of various classification outcomes
$U_.$	:	Utility values associated with various classification outcomes
$U(\alpha,\beta,\sigma_0,k)/U^*(\beta,\sigma_0)$	:	Expected utility / Optimal Expected Utility
$AUC(\alpha,\beta,\sigma_0)/AUC^*(\beta,\sigma_0)$	:	Overall discriminative ability as measured by AUC / optimal AUC
$V(\beta,\sigma_0)$	:	The value of bias-aware algorithmic design

PROPOSITION 5. *The following statements characterize the optimal weight assigned to the clinical-risk information.*

i $\alpha^*(\beta,\sigma_0)$ *is decreasing in* β.

ii $\alpha^*(\beta,\sigma_0)$ *is increasing in* σ_0.

iii $\alpha^*(\beta,\sigma_0)$ *is increasing in* σ_{i}.

iv *If* $\left(h-\frac{(\sigma_{\mathrm{i}}^2+\sigma_0^2)}{\sigma_{\mathrm{i}}^2\rho}\right)^2<\frac{\left(\sigma_{\mathrm{i}}^2+\sigma_0^2\right)^2}{\sigma_{\mathrm{i}}^2\rho^2}-\frac{(\sigma_{\mathrm{i}}^2+\sigma_0^2)}{\sigma_{\mathrm{i}}^2}$, *then* $\alpha^*(\beta,\sigma_0)$ *is increasing in* σ_{c}; *otherwise, it is decreasing in* σ_{c}.

v *If* $\sigma_0^2<\sigma_{\mathrm{i}}^2(h^2-1)$, *then* $\alpha^*(\beta,\sigma_0)$ *is decreasing in* ρ; *otherwise, it is increasing in* ρ.

We highlighted parts of the above proposition in the main body. For coherence of the discussion here, we repeat some parts that were already discussed. In (*i*), the presence of bias increases the influence of the clinical-risk information and the CDSS would counteract such an increase by reducing the weight assigned to the clinical-risk information. In (*ii*), we find, somewhat surprisingly, that an increase in the variance of error increases the weight assigned to the clinical-risk information. This is because, under bias, an increase in σ_0 increases the variability of the imaging risk, which in turn reduces the precision of the imaging risk as compared to the clinical-risk information. The intuition behind (*iii*) and (*iv*) of Proposition 5 relates to both σ_{i} and σ_{c} being interpreted as the inverse of the respective source's precision, ceteris paribus. Clearly, a decrease in the precision of one piece of risk information relative to that of the other decreases the weight assigned to the former if the weight is positive. Since the imaging risk always has a positive weight regardless of the bias, a decrease in its precision decreases its weight. On the other hand, when the bias is large such that the condition stated in (*iv*) of the proposition is satisfied, the weight assigned to the clinical-risk information is negative. In this case, a decrease in precision of the clinical-risk information increases its weight towards zero. In (*v*), an increase in the correlation decreases the weight assigned to the clinical-risk information when the variance of error due to bias is low enough. Such a finding is intuitive because an increase in the correlation makes the information content of the clinical-risk information less valuable. When the variance of error is high such that the imaging risk already captures most of the information content of the clinical-risk information, the CDSS alters the negative weight of the clinical-risk information to bring it closer to zero when the correlation increases.

PROPOSITION 6. $U^*(\beta,\sigma_0)$ *is (i) independent of* β *and decreases in (ii)* σ_0, *(iii)* σ_{i}, *(iv)* σ_{c}, *and (v)* ρ.

Part (*i*) suggests that the mean error can be totally eliminated. Part (*ii*) of the above proposition (together with Proposition 1) shows that when the bias cannot be eliminated, then, under optimal classification, a reduction in the variance of error mitigates the negative effect of bias. This provides support for the value of bias-reducing efforts even when classifier design accounts for the mean bias in the input data. However, it suggests that a targeted effort on variation is useful. Parts (*iii*)–(*v*) are intuitive. Parts (*iii*) and (*iv*) reveal that an improvement in the precision, defined as the inverse of variance, of either risk source improves the optimal utility because an increase in precision increases the discriminatory ability of the risk source. An increase in the correlation between the two risks decreases utility as in part (*v*) because an increase in correlation causes more of the information content of one risk source to be embedded in the other, thus reducing the incremental value of a risk source in the presence of the other.

B. Interdependent Error Mean and Error Variance

Theorem 2 characterizes the optimal weight and the decision threshold that maximizes the performance. Since β and σ_0 are fixed, replacing σ_0 with $\beta\sigma_0$ in Theorem 1 establishes the result.

THEOREM 2. *Define the optimal weight assigned to the clinical-risk information, $\alpha^*(\beta,\sigma_0)$, and the optimal decision threshold, $k^*(\beta,\sigma_0)$, as*

$$\alpha^*(\beta,\sigma_0) := \frac{1}{1+\frac{\sigma_{\rm i}\sigma_{\rm c}(h-\rho)}{\sigma_{\rm i}^2(1-h\rho)+\beta^2\sigma_0^2-\sigma_{\rm i}\sigma_{\rm c}\beta(h-\rho)}} \tag{16}$$

$$k^*(\beta,\sigma_0) := k(\alpha^*(\beta,\sigma_0),\beta,\sigma_0). \tag{17}$$

Then, $\alpha^*(\beta,\sigma_0)$ and $k^*(\beta,\sigma_0)$ maximize the total expected utility and $\alpha^*(\beta,\sigma_0)$ maximizes the AUC.

Proposition 7 is the analog of Proposition 3 under the assumption of interdependent mean error and error variance. The proposition characterizes the conditions under which eliminating the clinical-risk information from the system is more valuable than using it despite the biases it may induce. Since both β and σ_0 are fixed, replacing σ_0 with $\beta\sigma_0$ in Proposition 3 establishes the result.

PROPOSITION 7. *If $h \geq 1$ and*

$$\frac{1}{h}-\sqrt{\frac{(h^2-1)\beta^2\sigma_0^2}{\sigma_{\rm i}^2}} < \rho,$$

then $U^*(\beta,\sigma_0) < U(0,0,0,k(\alpha^*(0,0),0,0))$; otherwise, $U^*(\beta,\sigma_0) > U(0,0,0,k(\alpha^*(0,0),0,0))$.

C. Proofs of Structural Results

Proof of Theorem 1

To prove Theorem 1, we use two preparatory lemmas. The first lemma states a closed-form formula of the optimal decision threshold, $k(\alpha,\beta,\sigma_0)$, for fixed α, β, and σ_0, that maximizes the expected utility, $E[U(\alpha,\beta,\sigma_0,k)]$. We mathematically formulate the associated optimization problem as

$$k(\alpha,\beta,\sigma_0):=\operatorname*{argmax}_k \; E[U(\alpha,\beta,\sigma_0,k)]. \tag{18}$$

Using the optimal threshold, $k(\alpha,\beta,\sigma_0)$, defined in (18), we can rewrite the utility maximization problem in (6) as

$$U^*(\beta,\sigma_0)=\max_\alpha \; E[U(\alpha,\beta,\sigma_0,\, k(\alpha,\beta,\sigma_0))]. \tag{19}$$

Hence, to calculate the optimal utility, $U^*(\beta,\sigma_0)$, we first maximize $E[U(\alpha,\beta,\sigma_0,k)]$ with respect to k for a given α and then with respect to α. The following lemma provides the closed form solution for the optimal threshold associated with optimization problem stated in (18).

Lemma 1. *Let α, β, σ_0 be given; $\mu_{\text{p}},\mu_{\text{n}},\sigma$ be defined as in* (2)*; and t defined as in* (9)*. Assuming $\mu_{\text{n}}<\mu_{\text{p}}$, the unique solution of the problem in* (18) *is given by*

$$k(\alpha,\beta,\sigma_0)=\frac{\mu_{\text{n}}+\mu_{\text{p}}}{2}-\frac{\ln(t)\sigma^2}{\mu_{\text{p}}-\mu_{\text{n}}}. \tag{20}$$

Proof of Lemma 1: To prove this lemma, we utilize the facts that a continuously differentiable function with a negative derivative is strictly decreasing and the function is strictly increasing if its derivative is positive. For any α, β, and σ_0, we can write the expected utility $E[U(\alpha,\beta,\sigma_0,k)]$ using equation (5) as

$$\begin{aligned} E[U(\alpha,\beta,\sigma_0,k)] &= (U_{\text{TP}}-U_{\text{FN}})P(TP)+(U_{\text{FP}}-U_{\text{TN}})P(FP) \\ &+ U(FN)P(+)+U(TN)P(-). \qquad (21) \\ &= (U_{\text{TP}}-U_{\text{FN}})\int_k^\infty f(r|+)P(+)dr+(U_{\text{FP}}-U_{\text{TN}})\int_k^\infty f(r|-)P(-)\mathrm{d}r \\ &+ U(FN)P(+)+U(TN)P(-), \qquad (22) \end{aligned}$$

where equation (22) follows from the definitions of $P(FP)$ and $P(FN)$ given in equations (3), and (4). To find the optimal threshold that maximizes expected utility, $E[U(\alpha,\beta,\sigma_0,k)]$, we differentiate it with respect to k and set the derivative to 0:

$$\frac{\partial E[U(\alpha,\beta,\sigma_0,k)]}{\partial k} = [(U_{\mathrm{TP}}-U_{\mathrm{FN}})P(+)f(k^*|+)]\Big|_{r=k}^{r=\infty}+[(U_{\mathrm{FP}}-U_{\mathrm{TN}})P(-)f(k^*|-)]\Big|_{r=k}^{r=\infty}, \tag{23}$$

$$= (U_{\mathrm{FN}}-U_{\mathrm{TP}})P(+)\frac{e^{-\frac{(k-\mu_{\mathrm{p}})^2}{2\sigma^2}}}{\sigma}+(U_{\mathrm{TN}}-U_{\mathrm{FP}})P(-)\frac{e^{-\frac{(k-\mu_{\mathrm{n}})^2}{2\sigma^2}}}{\sigma}. \tag{24}$$

Note that our assumptions on the ordering of utility values for true or false assessments suggest that $(U_{\mathrm{TN}}-U_{\mathrm{FP}})>0$ and $(U_{\mathrm{TP}}-U_{\mathrm{FN}})>0$ holds, which allows us to rewrite (24) as

$$\frac{\partial E[U(\alpha,\beta,\sigma_0,k)]}{\partial k} = (U_{\mathrm{TN}}-U_{\mathrm{FP}})P(-)\left[-\frac{t}{\sigma}e^{-\frac{(k-\mu_{\mathrm{p}})^2}{2\sigma^2}}+\frac{e^{-\frac{(k-\mu_{\mathrm{n}})^2}{2\sigma^2}}}{\sigma}\right] \tag{25}$$

$$= \underbrace{(U_{\mathrm{TN}}-U_{\mathrm{FP}})P(-)\frac{e^{-\frac{(k-\mu_{\mathrm{n}})^2}{2\sigma^2}}}{\sigma}}_{\geq 0}\left(-te^{\frac{\left(\mu_{\mathrm{n}}^2-\mu_{\mathrm{p}}^2\right)}{2\sigma^2}}e^{\frac{k(\mu_{\mathrm{p}}-\mu_{\mathrm{n}})}{\sigma^2}}+1\right). \tag{26}$$

Let $d(k) := \frac{\partial E[U(\alpha,\beta,\sigma_0,k)]}{\partial k}$ and $k(\alpha,\beta,\sigma_0)$ be such that $d(k(\alpha,\beta,\sigma_0))=0$. From equation (26), we observe that the sign of $d(k)$ is the same as the function $g(k)$ defined as

$$g(k) := -te^{\frac{\left(\mu_{\mathrm{n}}^2-\mu_{\mathrm{p}}^2\right)}{2\sigma^2}}e^{\frac{k(\mu_{\mathrm{p}}-\mu_{\mathrm{n}})}{\sigma^2}}+1. \tag{27}$$

By differentiating $g(k)$ with respect to k, we obtain

$$g'(k) = -t\frac{\mu_{\mathrm{p}}-\mu_{\mathrm{n}}}{\sigma^2}e^{\frac{\left(\mu_{\mathrm{n}}^2-\mu_{\mathrm{p}}^2\right)}{2\sigma^2}}e^{-\frac{k(\mu_{\mathrm{p}}-\mu_{\mathrm{n}})}{\sigma^2}}, \tag{28}$$

which is strictly negative due to the assumption that $\mu_{\mathrm{p}}-\mu_{\mathrm{n}}>0$. Therefore, $g(k)$ is strictly decreasing in k. Moreover, we can easily verify that $g(-\infty)=1>0$ and $g(\infty)=-\infty$. Hence, the following conditions hold.

i. $g(k)>0$ for $k<k(\alpha,\beta,\sigma_0)$ and

ii. $g(k)<0$ for $k>k(\alpha,\beta,\sigma_0)$,

where $k(\alpha,\beta,\sigma_0)$ is such that $g(k(\alpha,\beta,\sigma_0))=0$. Since $d(k)$ has the same sign as $g(k)$, we conclude that $d(k)>0$ for $k<k(\alpha,\beta,\sigma_0)$ and $d(k)<0$ for $k>k(\alpha,\beta,\sigma_0)$. Because $d(k)$ is the derivative of the expected utility, we conclude that the expected utility is increasing for $k\in(-\infty,k(\alpha,\beta,\sigma_0))$ and it is decreasing for $k\in(k(\alpha,\beta,\sigma_0),\infty)$. Therefore, $k(\alpha,\beta,\sigma_0)$ is the unique value that maximizes the expected utility. We obtain a closed-form formula for $k(\alpha,\beta,\sigma_0)$ by letting $g(k(\alpha,\beta,\sigma_0))=0$ as

$$k(\alpha,\beta,\sigma_0)=\frac{\mu_{\text{p}}+\mu_{\text{n}}}{2}-\frac{\ln(t)\sigma^2}{\mu_{\text{p}}-\mu_{\text{n}}}. \tag{29}$$

Note that we assumed $\mu_{\text{n}}<\mu_{\text{p}}$. However, we do not bound α to enforce $\mu_{\text{n}}<\mu_{\text{p}}$ as some α values may indicate the contrary. The case $\mu_{\text{n}}>\mu_{\text{p}}$ can be shown exactly as above by replacing μ_{p} with $-\mu_{\text{p}}$ and μ_{n} with $-\mu_{\text{n}}$. □

Lemma 2 optimizes the information content $I(\alpha,\beta,\sigma_0)$ over α for given β and σ_0. Later, we will observe that both the AUC and expected utility are increasing functions of $I(\alpha,\beta,\sigma_0)$. Recall that we defined $I(\alpha,\beta,\sigma_0)$ as

$$I(\alpha,\beta,\sigma_0):=\frac{\mu_{\text{c}}-\mu_{\text{n}}}{\sigma} \tag{30}$$

LEMMA 2. *Given $I(\alpha,\beta,\sigma_0)$ as defined in equation* (30)*, then*

$$\alpha^*(\beta,\sigma_0):=\frac{1}{1+\frac{\sigma_{\text{i}}\sigma_{\text{c}}(h-\rho)}{\sigma_{\text{i}}^2(1-h\rho)+\sigma_0^2-\sigma_{\text{i}}\sigma_{\text{c}}\beta(h-\rho)}} \tag{31}$$

maximizes the information content, $I(\alpha,\beta,\sigma_0)$. Moreover, the optimal information content $I^*(\beta,\sigma_0)$ has the following closed form.

$$I^*(\beta,\sigma_0)=I(\alpha^*(\beta,\sigma_0),\beta,\sigma_0)=\frac{\Delta_{\text{c}}}{\sigma_{\text{c}}}\sqrt{1+\frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\text{i}}^2}}}, \tag{32}$$

and

$$I^*(\beta,\sigma_0)<I^*(\beta,0)=I^*(0,0). \tag{33}$$

Proof of Lemma 2: By the definition of the information content, $I(\alpha,\beta,\sigma_0)$, we have

$$I(\alpha,\beta,\sigma_0) = \frac{\mu_c-\mu_{\text{n}}}{\sigma} \tag{34}$$

$$= \frac{(1-\alpha)\Delta_{\text{i}}+(\alpha+(1-\alpha)\beta)\Delta_{\text{c}}}{\sqrt{(1-\alpha)^2\sigma_{\text{i}}^2+(1-\alpha)^2\sigma_0^2+(\alpha+\beta(1-\alpha))^2\sigma_{\text{c}}^2+2(1-\alpha)(\alpha+\beta(1-\alpha))\rho\sigma_1\sigma_2}}, \tag{35}$$

where equation (35) follows by substituting the definitions in equation (2) into (34). Next, note that for any $\alpha\neq 1,\beta>0$ and $\sigma_0>0$, we have

$$I(\alpha,\beta,\sigma_0)<I(\alpha,\beta,0), \tag{36}$$

which proves the inequality on the left in equation (33). Moreover, for any α, β, σ_0

$$I(\alpha,0,0)=I\left(\frac{\alpha-\beta}{1+\alpha-\beta},\beta,0\right), \tag{37}$$

which proves the equality on the right of equation (33). Next we will show that optimal α is given in (31). First, note that when $\Delta_{\rm i}-\Delta_{\rm c}>0$

$$I(-\infty,\beta,\sigma_0)=\frac{\Delta_{\rm i}-(1-\beta)\Delta_{\rm c}}{\sqrt{\sigma_{\rm i}^2+\beta^2\sigma_0^2+(1-\beta)^2\sigma_{\rm c}^2-2\rho(1-\beta)\sigma_{\rm i}\sigma_{\rm c}}}=-I(\infty,\beta,\sigma_0)>0. \tag{38}$$

Therefore, (i) the information content, $I(\alpha,\beta,\sigma_0)$, is bounded in the limit as α goes to infinity or negative infinity, and (ii) the bounds are the negation of one another. We can calculate the derivative of $I(\alpha,\beta,\sigma_0)$ with respect to α, denoted as $I'(\alpha,\beta,\sigma_0)$, as

$$I'(\alpha,\beta,\sigma_0)=\frac{\Delta_{\rm c}[\alpha[(1-\beta)\sigma_{\rm i}\sigma_{\rm c}(\rho-h)-\Delta_{\rm c}\sigma_{\rm i}^2(1-h\rho)+\Delta_{\rm c}\beta\sigma_0^2]+\beta\sigma_{\rm i}\sigma_{\rm c}+\sigma_{\rm i}^2(1-h\rho)+\sigma_0^2]}{(1-\alpha)^2\sigma_{\rm i}^2+(1-\alpha)^2\sigma_0^2+(\alpha+(1-\alpha)\beta)^2\sigma_{\rm c}^2+2\rho(1-\alpha)(\alpha+(1-\alpha)\beta)\sigma_{\rm i}\sigma_{\rm c}}. \tag{39}$$

From equation (39), we observe that the denominator of $I'(\alpha,\beta,\sigma_0)$ is strictly positive and the numerator is a linear function of α. Therefore, depending on the parameters, we have either

1. $I'(\alpha,\beta,\sigma_0)$ is positive in $(-\infty,\alpha^*(\beta,\sigma_0))$ and it is negative in $(\alpha^*(\beta,\sigma_0),\infty)$ or
2. $I'(\alpha,\beta,\sigma_0)$ is negative in $(-\infty,\alpha^*(\beta,\sigma_0))$ and it is positive in $(\alpha^*(\beta,\sigma_0),\infty)$,

where $\alpha^*(\beta,\sigma_0)$ is such that

$$I(\alpha^*(\beta,\sigma_0),\beta,\sigma_0)=0 \Longrightarrow \alpha^*(\beta,\sigma_0):=\frac{-\sigma_{\rm i}\sigma_{\rm c}\beta(h-\rho)+\sigma_{\rm i}^2(1-h\rho)+\sigma_0^2}{\sigma_{\rm i}\sigma_{\rm c}(1-\beta)(h-\rho)+\sigma_{\rm i}^2(1-h\rho)\sigma_0^2}. \tag{40}$$

As a result of this we have either

1. $I(\alpha,\beta,\sigma_0)$ is increasing in $(-\infty,\alpha^*(\beta,\sigma_0))$ and it is decreasing in $(\alpha^*(\beta,\sigma_0),\infty)$ or
2. $I(\alpha,\beta,\sigma_0)$ is decreasing in $(-\infty,\alpha^*(\beta,\sigma_0))$ and it is increasing in $(\alpha^*(\beta,\sigma_0),\infty)$.

Since $I(-\infty,\beta,\sigma_0)=-I(\infty,\beta,\sigma_0)$, for fixed β and σ_0, $|I(\alpha,\beta,\sigma_0)|$ is maximum at $\alpha^*(\beta,\sigma_0)$. Finally, by substituting the closed-form formula of $\alpha^*(\beta,\sigma_0)$ into the definition of information content, we obtain the following closed form for the optimal information content

$$I^*(\beta,\sigma_0)=I(\alpha^*(\beta,\sigma_0),\beta,\sigma_0)=\frac{\Delta_{\rm c}}{\sigma_{\rm c}}\sqrt{1+\frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2}}}. \tag{41}$$

□

We are now ready to prove Theorem 1. Let α and β be fixed. Then, using the closed-form formula for optimal threshold, $k(\alpha,\beta,\sigma_0)$, obtained in Lemma 1, we get

$$\begin{aligned}\max_k E[U(\alpha,\beta,\sigma_0,k)] &= E[U(\alpha,\beta,\sigma_0,k(\alpha,\beta,\sigma_0)))] \\ &= -(U_{\text{TP}}-U_{\text{FN}})P(+)\left(1-\Phi\left(\frac{k(\alpha,\beta,\sigma_0)-\mu_{\text{p}}}{\sigma}\right)\right) \\ &- (U_{\text{FP}}-U_{\text{TN}})P(-)\left(1-\Phi\left(\frac{k(\alpha,\beta,\sigma_0)-\mu_{\text{n}}}{\sigma}\right)\right) \\ &+ P(+)U_{\text{TP}}+P(-)U_{\text{FP}}, \qquad (42) \\ &= -(U_{\text{TP}}-U_{\text{FN}})P(+)\left(1-\Phi\left(-\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)\right) \\ &- (U_{\text{FP}}-U_{\text{TN}})P(-)\left(1-\Phi\left(\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta)}\right)\right)+T, \qquad (43)\end{aligned}$$

where $T=P(+)U_{\text{TP}}+P(-)U_{\text{FP}}$ is constant. From equation (43), we observe that α and β appear in the expected utility function only through $I(\alpha,\beta,\sigma_0)$. Note that $t=\left(\frac{U_{\text{TP}}-U_{\text{FN}}}{U_{\text{TN}}-U_{\text{FP}}}\cdot\frac{P(+)}{P(-)}\right)$ is constant. We therefore can write the optimal expected utility given β and σ_0, $U^*(\beta,\sigma_0)$, as

$$\begin{aligned}U^*(\beta,\sigma_0) &= \max_\alpha\left[\max_k E[U(\alpha,\beta,\sigma_0,k)]\right], \qquad (44) \\ &= \max_\alpha\Bigg[-(U_{\text{TP}}-U_{\text{FN}})P(+)\left(1-\Phi\left(-\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)\right) \\ &\quad - (U_{\text{TN}}-U_{\text{FP}})P(-)\left(1-\Phi\left(\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)\right)+T\Bigg], \qquad (45) \\ &= \max_\alpha \underbrace{(U_{\text{TN}}-U_{\text{FP}})P(-)}_{\geq 0}\Bigg[t\left(1-\Phi\left(-\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)\right) \\ &\quad - \left(1-\Phi\left(\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)\right)\Bigg]+T, \qquad (46)\end{aligned}$$

where equation (45) follows from (43) and equation (46) follows by the rearrangement of terms. Since $(U_{\text{TN}}-U_{\text{FP}})P(-)$ is constant and positive and T is constant, it follows from equation (46) that maximizing the expected utility is equivalent to maximizing the following function

$$F(I(\alpha,\beta,\sigma_0)):=t\left[1-\Phi\left(-\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)\right]-\left[1-\Phi\left(\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)\right]. \qquad (47)$$

Differentiating $F(I(\alpha,\beta,\sigma_0))$ with respect to the information content, $I(\alpha,\beta,\sigma_0)$, we obtain

$$\frac{\mathrm{d}F(I(\alpha,\beta,\sigma_0))}{\mathrm{d}I(\alpha,\beta,\sigma_0)}=\left[te^{-\frac{\left(-\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)^2}{2}}\left(\frac{1}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)^2}\right)+e^{-\frac{\left(\frac{I(\alpha,\beta,\sigma_0)}{2}-\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)}\right)^2}{2}}\left(\frac{1}{2}+\frac{\ln(t)}{I(\alpha,\beta,\sigma_0)^2}\right)\right] \tag{48}$$

$$=e^{-\frac{\left(\frac{I(\alpha,\beta,\sigma_0)}{2}+\frac{\ln(t)^2}{I(\alpha,\beta,\sigma_0)}\right)^2}{2}}\left[t\left(\frac{1}{2}-\frac{\ln t}{I(\alpha,\beta,\sigma_0)^2}\right)+t\left(\frac{1}{2}+\frac{\ln t}{I(\alpha,\beta,\sigma_0)^2}\right)\right] \tag{49}$$

$$=te^{-\frac{\left(\frac{I(\alpha,\beta,\sigma_0)}{2}+\frac{\ln(t)^2}{I(\alpha,\beta,\sigma_0)}\right)^2}{2}}>0, \tag{50}$$

where equations (49) and (50) follow from rearrangement of terms. Equation (50) shows that the derivative of $F(\alpha,\beta,\sigma_0)$ is strictly positive. As a result, we conclude that it is a strictly increasing function of the information content, $I(\alpha,\beta,\sigma_0)$. Hence, $U^*(\beta,\sigma_0)$ is an increasing function of $I(\alpha,\beta,\sigma_0)$. This in turn implies that the value of α maximizing $I(\alpha,\beta,\sigma_0)$ also maximizes $U^*(\beta,\sigma_0)$ for fixed β, σ_0. The closed-form formulas for the optimal weight and optimal threshold in the first part of Theorem 1 follow from Lemmas 1 and 2, respectively.

For the second part of Theorem 1, we are maximizing AUC. Mathematically, we can write the maximization problem as

$$\max_{\alpha} AUC(\alpha,\beta)=\max_{\alpha}\Phi\left(\frac{\mu_{\mathrm{p}}-\mu_{\mathrm{n}}}{\sqrt{2}\sigma}\right)=\max_{\alpha} AUC\left(\frac{I(\alpha,\beta,\sigma_0)}{\sqrt{2}}\right). \tag{51}$$

Since $\Phi(\cdot)$ is a strictly increasing function, maximizing $AUC(\alpha,\beta,\sigma_0)$ is equivalent to maximizing the information content of the aggregate information. The closed-form formula for optimal α is calculated in Lemma 2. □

As we also alluded to in the main body, the remaining proofs require a technical assumption. We now formally state the assumption.

ASSUMPTION 1. *$\rho<\min(h,1/h)$.*

Proof of Proposition 1

In the proof of Theorem 1, we have shown that for fixed β and σ_0, $U^*(\beta,\sigma_0)$ is increasing in $I^*(\alpha,\beta)$. Moreover, in Lemma 2, we identified

$$I^*(\beta,\sigma_0)=I(\alpha^*(\beta,\sigma_0),\beta,\sigma_0)=\frac{\Delta_{\mathrm{c}}}{\sigma_{\mathrm{c}}}\sqrt{1+\frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\mathrm{i}}^2}}}. \tag{52}$$

From equation (52), it is clear that $I^*(\beta,\sigma_0)$ is a strictly decreasing function of σ_0 and is independent of β. Hence,

$$I^*(\beta,\sigma_0) < I^*(\beta,0) = I^*(0,0). \tag{53}$$

In the proof of Theorem 1, we showed that the expected utility is increasing in information content, from which it follows that

$$U^*(\beta_2,\sigma_0) = U^*(\beta_1,\sigma_0) < U^*(\beta_1,0) = U^*(0,0). \tag{54}$$

Note that the equality $U^*(\beta_2,\sigma_0) = U^*(\beta_1,\sigma_0)$ in (54) is due to the fact that $I^*(\beta,\sigma_0)$ is independent of β. For the second part of the proposition, from equation (51), it follows that $AUC(\alpha,\beta)$ is an increasing function of the information content. Therefore, from the same reasoning used in the expected utility case, we obtain the inequalities on AUC.

□

Proof of Proposition 2

Let $V(\beta,h,\rho,\sigma_0)$ be the value of bias-aware algorithm defined as in (13). We write

$$V(\beta,h,\rho,\sigma_0) := \frac{\Delta_{\mathrm{c}}\sqrt{\frac{(h-\rho)^2}{\frac{\sigma_0^2}{\sigma_1^2}-\rho^2+1}}}{\sigma_{\mathrm{c}}} - \frac{\Delta_{\mathrm{c}}\left(\frac{\beta\sigma_2(h-\rho)}{\sigma_1}+(h-\rho)^2-\rho^2+1\right)}{\sigma_{\mathrm{c}}\sqrt{\left(\frac{\beta\sigma_2(h-\rho)}{\sigma_1}-\rho^2+1\right)^2+(h-\rho)^2\left(-\rho^2+\frac{\sigma_0^2}{\sigma_1^2}+1\right)}}. \tag{55}$$

Taking the derivative of $V(\beta,h,\rho,\sigma_0)$ with respect to β, we get

$$\frac{\partial V}{\partial \beta} = \frac{\Delta_{\mathrm{c}}(h-\rho)^3(\beta\sigma_{\mathrm{c}}(\rho-h)\sigma_{\mathrm{i}}+\sigma_0^2)}{\sigma_{\mathrm{i}}\sqrt{\left(\frac{\beta\sigma_{\mathrm{c}}(h-\rho)}{\sigma_{\mathrm{i}}}-\rho^2+1\right)^2+(h-\rho)^2\left(\frac{s^2}{\sigma_{\mathrm{i}}^2}-\rho^2+1\right)}} \times \frac{1}{(2\beta(\rho^2-1)\sigma_{\mathrm{c}}(h-\rho)\sigma_{\mathrm{i}}-(h-\rho)^2(\beta^2\sigma_{\mathrm{c}}^2+\sigma_0^2)+(\rho^2-1)(h^2-2h\rho+1)\sigma_{\mathrm{i}}^2)}. \tag{56}$$

Notice that the denominator is always negative, due to our assumption that $\rho < h$ and the numerator is positive when $\beta < \frac{\sigma_0^2}{\sigma_{\mathrm{c}}\sigma_{\mathrm{i}}(h-\rho)}$. Hence, the value of bias-aware algorithm is decreasing when β is small enough; otherwise, it is increasing. The derivative with respect to σ_0 is given below in equation (57). As the numerical example also demonstrated, both increasing and decreasing behavior is possible depending on parameter values.

$$\frac{\partial V}{\partial \sigma_0} = \frac{\sigma_0 \Delta_c (h-\rho)^2 \left(\frac{\frac{\beta\sigma_c(h-\rho)}{\sigma_i} + h^2 - 2h\rho + 1}{\left(\left(\frac{\beta\sigma_c(h-\rho)}{\sigma_i} - \rho^2 + 1 \right)^2 + (h-\rho)^2 \left(\frac{\sigma_0^2}{\sigma_i^2} - \rho^2 + 1 \right) \right)^{3/2}} - \frac{1}{\left(\frac{\sigma_0^2}{\sigma_i^2} - \rho^2 + 1 \right)^2 \sqrt{\frac{(h-\rho)^2}{\frac{\sigma_0^2}{\sigma_i^2} - \rho^2 + 1} + 1}} \right)}{\sigma_c \sigma_i^2} \tag{57}$$

□

Proof of Proposition 3

In Lemma 2, we have shown that the optimal information content is

$$I^*(\beta,\sigma_0) = \frac{\Delta_c}{\sigma_c} \sqrt{1 + \frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_i^2}}}. \tag{58}$$

Let $I_i = \Delta_i/\sigma_i$ be the information content of the imaging. Also let $U_i = U(0,0,0,k(\alpha^*,0,0))$ denote the optimal expected utility solely based on the imaging. In the proof of Theorem 1, we have shown that the optimal expected utility $U^*(\beta,\sigma_0)$ is an increasing function of the information content, $I(\alpha,\beta,\sigma_0)$. Therefore, given β and σ_0, if $I^*(\beta,\sigma_0) < I_i$, we have

$$U^*(\beta,\sigma_0) < U_i. \tag{59}$$

Therefore, using (58), we obtain

$$I^*(\beta,\sigma_0) = \frac{\Delta_c}{\sigma_c} \sqrt{1 + \frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_i^2}}} < \frac{\Delta_i}{\sigma_i} \Longrightarrow \frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_i^2}} < h^2 - 1, \tag{60}$$

from which the first part of the proposition follows. Now, if

$$\frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_i^2}} > h^2 - 1, \tag{61}$$

then $I^*(\beta,\sigma_0) > I_i \Longrightarrow U^*(\beta,\sigma_0) > U_i$, which concludes the proof of the proposition. □

Proof of Proposition 4

Similar to Proposition 1, we calculate the optimal information content, this time under the proportional error mean and error variance, as

$$I^*(\beta,\sigma_0) = I(\alpha^*(\beta,\sigma_0),\beta,\sigma_0) = \frac{\Delta_c}{\sigma_c} \sqrt{1 + \frac{(h-\rho)^2}{1-\rho^2+\frac{\beta^2\sigma_0^2}{\sigma_i^2}}}. \tag{62}$$

In contrast to Proposition 1, the optimal information content is decreasing in β this time, which implies that both $U^*(\beta_2,\sigma_0) < U^*(\beta_1,\sigma_0)$ and $AUC^*(\beta_2,\sigma_0) < AUC^*(\beta_1,\sigma_0)$. Finally, the equalities on the right-hand side of equations (14) and (15) follow by letting $\sigma_0 = 0$, which completes the proof of the proposition. □

Proof of Proposition 5

Lemma 2 gave the optimal weight on clinical-risk information, $\alpha^*(\beta,\sigma_0)$, as

$$\alpha^*(\beta,\sigma_0) = \frac{\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}\beta(\rho-h)+\sigma_0^2}{\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(\beta-1)(\rho-h)+\sigma_0^2}. \tag{63}$$

By differentiating $\alpha^*(\beta,\sigma_0)$ with respect to β, we obtain

$$\frac{\mathrm{d}\alpha^*(\beta,\sigma_0)}{\mathrm{d}\beta} = \frac{-\sigma_{\mathrm{i}}^2\sigma_{\mathrm{c}}^2(\rho-h)^2}{\left(\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(\beta-1)(\rho-h)+\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_0^2\right)^2}, \tag{64}$$

which is always negative. As a result $\alpha^*(\beta,\sigma_0)$ is decreasing in β, which completes the proof of the first part of the proposition. For the second part of the proposition, let

$$\frac{\mathrm{d}\alpha^*(\beta,\sigma_0)}{\mathrm{d}\sigma_0} = \frac{2\sigma_0\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(h-\rho)}{\left(\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(\beta-1)(\rho-h)+\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_0^2\right)^2}, \tag{65}$$

which is increasing due to the assumption that $\rho < h$.

For the third part of the proposition,

$$\frac{\mathrm{d}\alpha^*(\beta,\sigma_0)}{\mathrm{d}\sigma_{\mathrm{i}}} = \frac{\sigma_{\mathrm{i}}^2\sigma_{\mathrm{c}}\left[-\rho-h^2\rho+2h+\rho\frac{\sigma_0^2}{\sigma_{\mathrm{i}}^2}\right]}{\left(\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(\beta-1)(\rho-h)+\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_0^2\right)^2} = \frac{\sigma_{\mathrm{i}}^2\sigma_{\mathrm{c}}\left[h-\rho+h(1-h\rho)+\rho\frac{\sigma_0^2}{\sigma_{\mathrm{i}}^2}\right]}{\left(\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(\beta-1)(\rho-h)+\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_0^2\right)^2}, \tag{66}$$

which is always positive from our assumptions that $\rho < h$ and $h\rho < 1$.

For the fourth part of the proposition,

$$\frac{\mathrm{d}\alpha^*(\beta,\sigma_0)}{\mathrm{d}\sigma_{\mathrm{c}}} = \frac{\sigma_{\mathrm{i}}^3\left[\rho(1+h^2+\frac{\sigma_0^2}{\sigma_{\mathrm{i}}^2}^2)-2h(1+\frac{\sigma_0^2}{\sigma_{\mathrm{i}}^2})\right]}{\left(\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(\beta-1)(\rho-h)+\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_0^2\right)^2}, \tag{67}$$

which can be shown to be positive if and only if

$$\left(h-\frac{(\sigma_{\mathrm{i}}^2+\sigma_0^2)}{\sigma_{\mathrm{i}}^2\rho}\right)^2 < \frac{(\sigma_{\mathrm{i}}^2+\sigma_0^2)^2}{\sigma_{\mathrm{i}}^2\rho^2} - \frac{(\sigma_{\mathrm{i}}^2+\sigma_0^2)}{\sigma_{\mathrm{i}}^2}. \tag{68}$$

For the final part of the proposition, observe that

$$\frac{\mathrm{d}\alpha^*(\beta,\sigma_0)}{\mathrm{d}\rho} = \frac{\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}[\sigma_0^2-\sigma_{\mathrm{i}}^2(h^2-1)]}{\left(\sigma_{\mathrm{i}}\sigma_{\mathrm{c}}(\beta-1)(\rho-h)+\sigma_{\mathrm{i}}^2(1-h\rho)+\sigma_0^2\right)^2}, \tag{69}$$

which is negative if $\sigma_0^2 < \sigma_{\rm i}^2(h^2-1)$, and positive otherwise. Therefore, if $\sigma_0^2 < \sigma_{\rm i}^2(h^2-1)$, then $\alpha^*(\beta,\sigma_0)$ is decreasing in ρ; otherwise, it is increasing in ρ, which completes the proof of the proposition. □

Proof of Proposition 6

From Lemma 2, we have

$$I^*(\beta,\sigma_0) = I(\alpha^*(\beta,\sigma_0),\beta,\sigma_0) = \frac{\Delta_{\rm c}}{\sigma_{\rm c}}\sqrt{1+\frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2}}}. \tag{70}$$

The first and second parts of the proposition are because

$$1+\frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2}} \tag{71}$$

does not depend on β and is decreasing in σ_0, respectively. For the third part we take the derivative of $I^*(\beta,\sigma_0)$ with respect to $\sigma_{\rm i}$ and get

$$\frac{{\rm d}I^*(\beta,\sigma_0)}{{\rm d}\sigma_{\rm i}} = \frac{\Delta_{\rm i}(\rho-h)}{\sigma_{\rm i}^2\left(1+\frac{(h-rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2}}\right)}, \tag{72}$$

which is negative if

$$\rho < h = \frac{\Delta_{\rm i}\sigma_{\rm c}}{\Delta_{\rm c}\sigma_{\rm i}},$$

and is positive otherwise. Based on Assumption 1, the optimal utility is decreasing in $\sigma_{\rm i}$.

For the fourth part, we calculate

$$\frac{{\rm d}I^*(\beta,\sigma_0)}{{\rm d}\sigma_{\rm c}} = \frac{-\Delta_{\rm c}(\frac{\sigma_0^2}{\sigma_{\rm i}^2}+1-h\rho)}{\sigma_{\rm c}^2(1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2})(1+\frac{(h-\rho)^2}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2}})} < 0, \tag{73}$$

which comes from Assumption 1, $h\rho < 1$. Hence, the optimal utility is decreasing in $\sigma_{\rm c}$.

For the final part, we calculate

$$\frac{{\rm d}I^*(\beta,\sigma_0)}{{\rm d}\rho} = \frac{\Delta_{\rm c}}{\sigma_{\rm c}}\sqrt{\frac{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2}}{1-\rho^2+\frac{\sigma_0^2}{\sigma_{\rm i}^2}+(h-\rho)^2}}(\rho-h)(\frac{\sigma_0^2}{\sigma_{\rm i}^2}+1-h\rho), \tag{74}$$

which is always negative under Assumption 1, $\rho < h < 1/\rho$. Hence, the optimal utility is decreasing in ρ. □