Appendix

Model for $M \geq 3$ tests

Appendix Table 1 sets notation for true probabilities and Appendix Table 2 for observed data. The model for two tests is extended to 3 or more tests by modifying equations (11) through (24) in the obvious way.

Appendix Table 1. Notation for the number of patients and the population proportion for combinations of results from *M* tests in those with disease

Test 1	...	Test m	...	Test M	Probability
–	...	–	...	–	$\pi^{D}_{k,0\cdots0\cdots0}$
+	...	–	...	–	$\pi^{D}_{k,1\cdots0\cdots0}$
...	...	...	...	...	$\cdots$
+	...	+	...	+	$\pi^{D}_{k,1\cdots1\cdots1}$

The notation for those without disease replaces D with $\bar{D}$.

Appendix Table 2. Notation for the observed counts of combinations of results from *M* tests in those with disease

Test 1	...	Test m	...	Test M	Observed counts	Estimated probability
–	...	–	...	–	$x^{D}_{k,0\cdots0\cdots0}$	$\pi^{D}_{k,0\cdots0\cdots0}$
+	...	–	...	–	$x^{D}_{k,1\cdots0\cdots0}$	$\pi^{D}_{k,1\cdots0\cdots0}$
...	...	...	...	...	$\cdots$	$\cdots$
+	...	+	...	+	$x^{D}_{k,1\cdots1\cdots1}$	$\pi^{D}_{k,1\cdots1\cdots1}$

The notation for those without disease replaces D with $\bar{D}$.

Formulas for within study covariance matrices

Variances for logit-transformed sensitivities and false positive rates for bivariate meta-analysis (single test)

See Table 2 in the main report for notation. The within-study covariance Σ_k in study *k* has zero off-diagonal elements, because sensitivity and specificity are calculated in independent groups.

$$\Sigma_k = \begin{pmatrix} \sigma^2_{k\eta} & 0 \\ & \sigma^2_{k\xi} \end{pmatrix}, \qquad \text{(A.1)}$$

with

$$\sigma^2_{k\eta} = \frac{1}{N^D_k p^D_{k1}(1-p^D_{k1})}, \tag{A.2}$$

and

$$\sigma^2_{k\xi} = \frac{1}{N^{\bar{D}}_k p^{\bar{D}}_{k1}(1-p^{\bar{D}}_{k1})}, \tag{A.3}$$

Variances for logit-transformed sensitivities and false positive rates for the joint multivariate meta-analysis of $M \geq 2$ tests

The within-study covariance $\mathbf{\Sigma}_k$ in study *k* is

$$\mathbf{\Sigma}_k = \left[\begin{array}{c|c} \mathbf{\Sigma}_{k\eta} & \mathbf{0} \\ \hline & \mathbf{\Sigma}_{k\xi} \end{array}\right] = \left[\begin{array}{ccc|ccc} \sigma^2_{k\eta 1} & \cdots & \sigma_{k\eta 1M} & & & \\ & \ddots & \vdots & & \mathbf{0} & \\ & & \sigma^2_{k\eta M} & & & \\ \hline & & & \sigma^2_{k\xi 1} & \cdots & \sigma_{k\xi 1M} \\ & & & & \ddots & \vdots \\ & & & & & \sigma^2_{k\xi M} \end{array}\right], \tag{A.4}$$

Application of the multivariate delta method yields the following formulas. (The notation [*m*:1] indicates the sum over all patterns in which the outcome on test *m* is 1).

Variance of logit sensitivity in study *k* for test *m*:

$$\sigma^2_{k\eta m} = \frac{1}{N^D_k p^D_{k[m:1]}(1-p^D_{k[m:1]})} \tag{A.5}$$

Variance for logit false positive rate in study *k* for test *m*:

$$\sigma^2_{k\xi m} = \frac{1}{N^{\bar{D}}_k p^{\bar{D}}_{k[m:1]}(1-p^{\bar{D}}_{k[m:1]})} \tag{A.6}$$

Covariance between logit sensitivities of tests *m* and *t* in study *k*:

$$\sigma_{k\eta mt} = \frac{p^D_{k[m:1,t:1]} - p^D_{k[m:1]}p^D_{k[t:1]}}{N^D_k p^D_{k[m:1]}(1-p^D_{k[m:1]})p^D_{k[t:1]}(1-p^D_{k[t:1]})} \tag{A.7}$$

Covariance between logit false positive rates of tests *m* and *t* in study *k*:

$$\sigma_{k\xi mt} = \frac{p^{\bar{D}}_{k[m:1,t:1]} - p^{\bar{D}}_{k[m:1]}p^{\bar{D}}_{k[t:1]}}{N^D_k p^D_{k[m:1]}(1-p^D_{k[m:1]})p^D_{k[t:1]}(1-p^D_{k[t:1]})} \tag{A.8}$$

Formulas for calculating 1.96-standard-error volumes

Let $t_1, \ldots, t_M$ be the lengths of the half axes of an ellipsoid of dimension *M* that corresponds to the contour surface of one standard error. The volume V_M included in this one-standard-error surface is calculated by integration. We calculated the first three integrals. (In the following three formulas $\pi = 3.14159\ldots$)

$$V_2 = \pi t_1 t_2$$

$$V_3 = \frac{4}{3}\pi t_1 t_2 t_3$$

$$V_4 = \frac{1}{2}\pi^2 t_1 t_2 t_3 t_4$$

For a covariance matrix $\mathbf{C}$ we have to calculate the lengths of the half axes for the one-standard-error contour ellipsoid. Rotation to an orthonormal basis automatically provides the lengths of the half axes; these are the square roots of the eigenvalues $\lambda_1, \ldots, \lambda_M$ of $\mathbf{C}$. So set $t_m = \sqrt{\lambda_m}$ in the formulas above. The 1.96-standard-error volume uncorrected for multiple comparisons is

$$(z_{0.025})^M V_M,$$

With $z_{\alpha/2} = 1.96$ denoting the upper $\alpha/2$ percentile of the standard normal distribution. For example in the main report, Table 11 the volumes in rows (b) and (c) pertain to four-dimensional models and were calculated using the formula above, for $M = 4$. The confidence volume in row (a) corresponds to two independent bivariate models. It is calculated as the product of the confidence volumes of dimension 2, one for each bivariate model.

Additional results

Appendix Table 3. Point estimates and 95% confidence intervals with alternative meta-analysis methods

	logit TPR Shortened humerus	*logit TPR Shortened femur*	*logit FPR Shortened humerus*	*logit FPR Shortened femur*
Separate analyses of the two tests				
a. Bivariate, random effects (REML)	-0.458 (-0.838, -0.077)	-0.577 (-1.046, -0.107)	-2.934 (-3.310, -2.558)	-2.503 (-2.839, -2.167)
Joint analyses of the two tests				
b. Random effects, variant $\mathbf{T}_A$	-0.473 (-0.858, -0.088)	-0.507 (-0.958, -0.057)	-2.942 (-3.314, -2.569)	-2.489 (-2.815, -2.162)
c. Random effects, variant $\mathbf{T}_B$	-0.445 (-0.873, -0.018)	-0.543 (-0.969, -0.117)	-2.930 (-3.279, -2.581)	-2.506 (-2.846, -2.167)

FPR: False positive rate (1–specificity); REML: Restricted maximum likelihood; TPR: True positive rate (sensitivity). See text for the specification of variants $\mathbf{T}_A$ and $\mathbf{T}_B$.