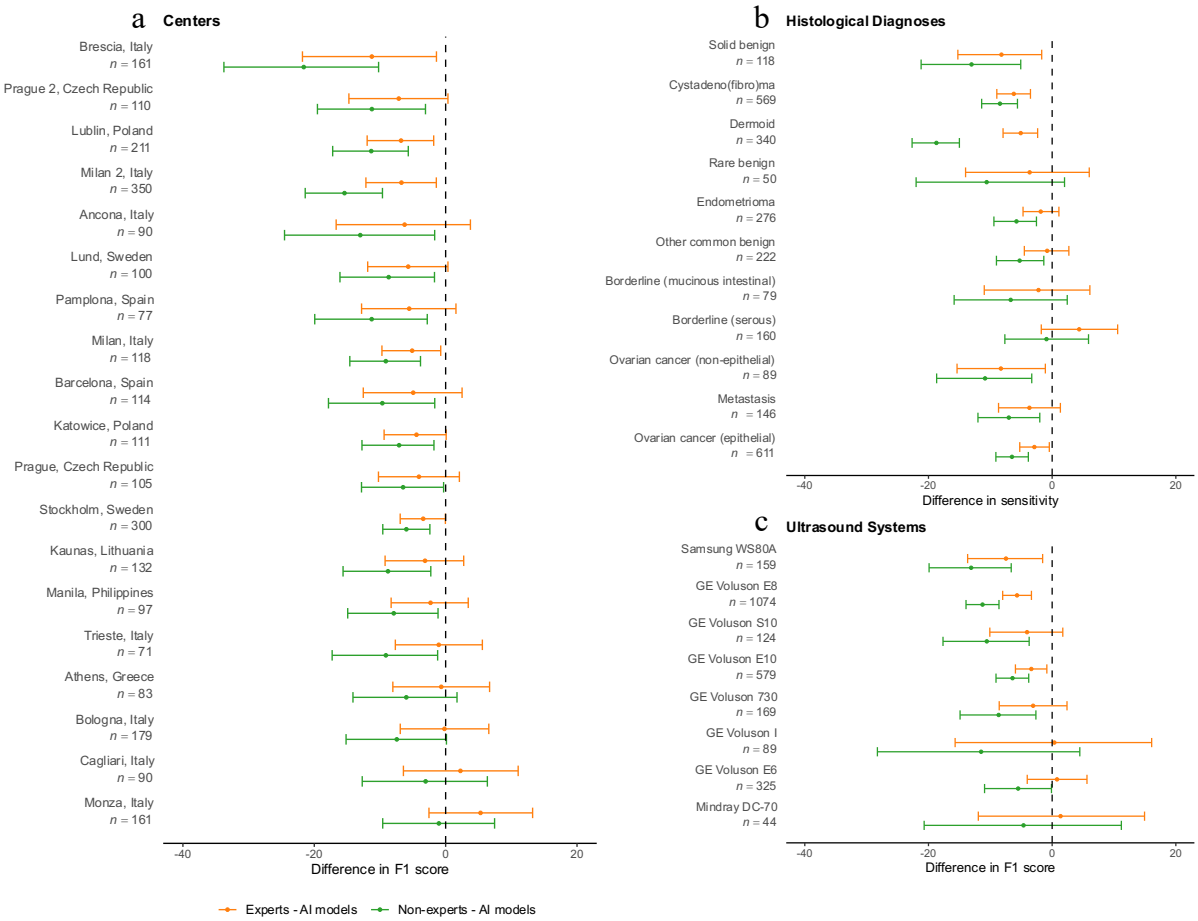
nature medicine

Supplementary information

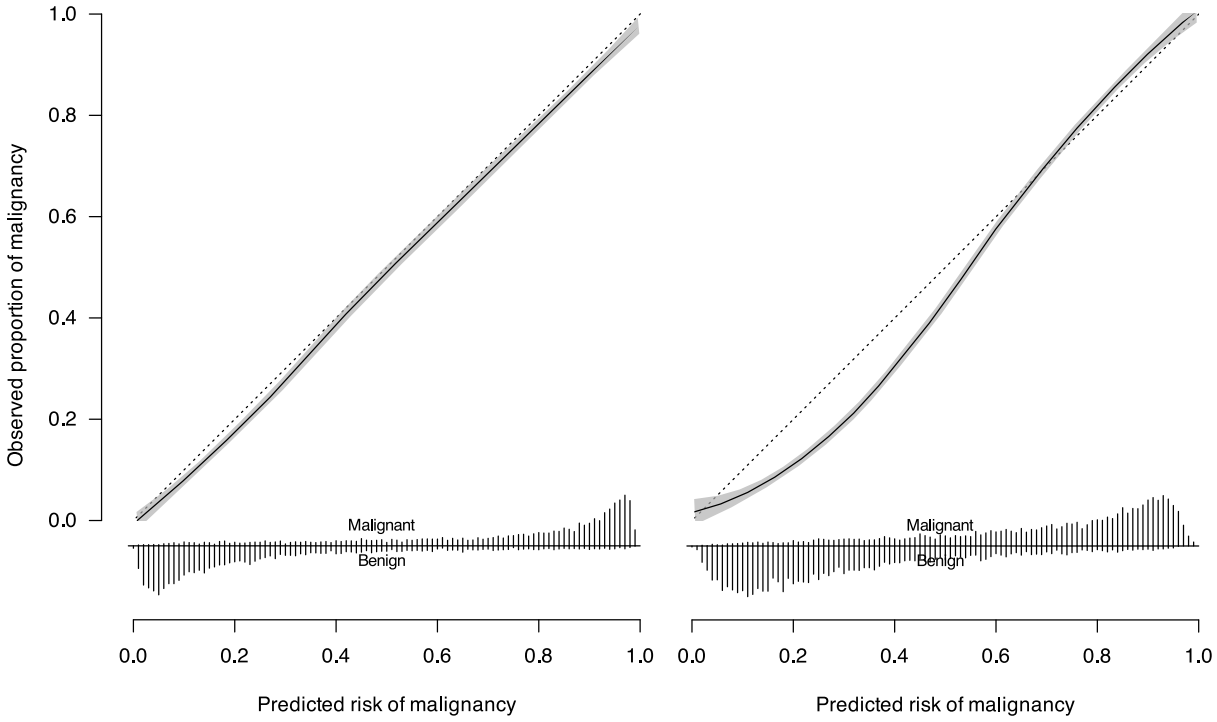
https://doi.org/10.1038/s41591-024-03329-4

International multicenter validation of AI-driven ultrasound detection of ovarian cancer

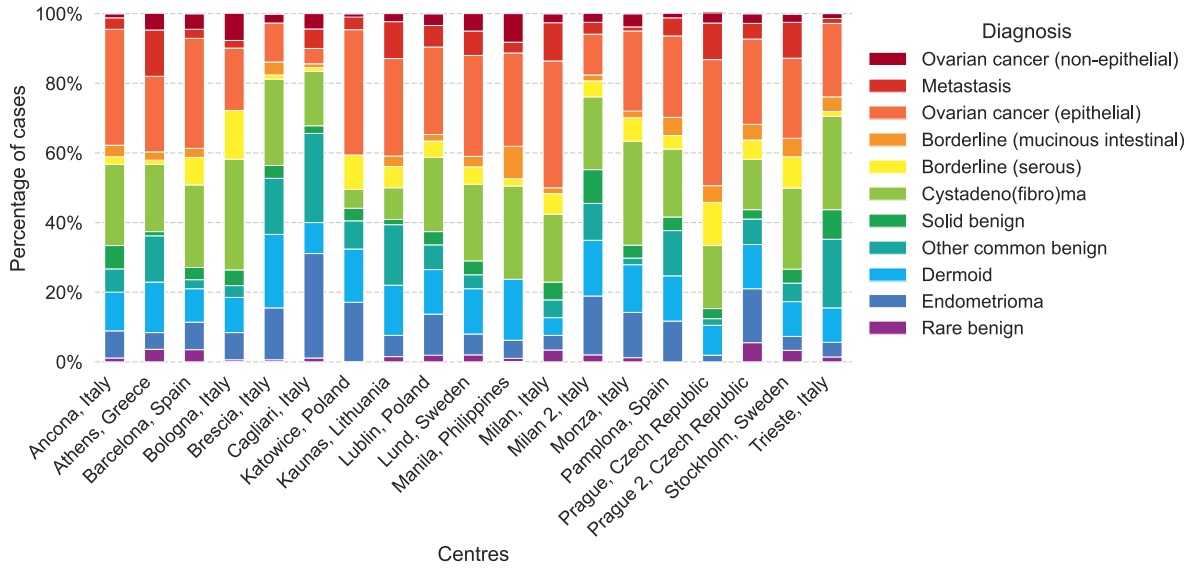
In the format provided by the authors and unedited



Supplementary Fig. 1 | Difference in performance between AI models and human examiners on various sub-groups. Differences in F1 scores between the AI models and the human examiners, by centers (**a**), ultrasound systems (**b**) and histological diagnoses (**c**). Error bars are 95% CIs through bootstrapping.



Supplementary Fig. 2 | Calibration curves of the transformer and CNN models. Calibration curves of (**a**) our transformer-based models (DeiT) and (**b**) convolutional neural network (CNN)-based models (ConvNeXt), respectively. The calibration curves are shown in solid black with 95% confidence bands in gray, depicting the relationship between the predicted risk of malignancy and the actual observed proportion of malignancy. The dotted lines represent the ideal scenario of perfect calibration, where the predicted risks precisely match the observed outcomes. The histograms at the bottom depict the distributions of predicted risks of malignancy, for malignant and benign tumors, above and below the horizontal line, respectively. The calibration curves and confidence bands are based on local regression (loess)[1], and is based on 12,673 image-level predictions. While not depicted in the figure, a linear logistic calibration curve was also fitted for each of the models, yielding (**a**) an intercept of -0.19 (95% CI, -0.24–(-)0.14) and a slope of 1.00 (95% CI, 0.96–1.03) for our transformer-based models, and (**b**) an intercept of -0.24 (95% CI, -0.29–(-)0.20) and a slope of 1.27 (95% CI, 1.23–1.32) for the CNN-based models.



Supplementary Fig. 3 | Breakdown of histological diagnoses by center

Supplementary Table 1 | Hypothesis testing: AI models vs. expert and non-expert examiners

	W	z	p	Location parameter (Hodges-Lehmann estimate)	Effect size (Rank-biserial correlation)
AI models vs. expert examiners	561	5.012	2.328×10^{-10}	3.984	1.000
AI models vs. non-expert examiners	561	5.012	2.328×10^{-10}	8.979	1.000

Results of two-sided non-parametric Wilcoxon signed-rank tests comparing the diagnostic performance of the AI models with that of expert and non-expert examiners.

Supplementary Table 2 | Performance of examiners and AI models on matching case sets

Examiner	Cases	F1 score		Sensitivity		Specificity		Accuracy		Kappa		MCC	
		Examiner	AI models	Examiner	AI models	Examiner	AI models	Examiner	AI models	Examiner	AI models	Examiner	AI models
Expert 1	932	85.04%	85.16%	83.65%	84.47%	91.50%	90.97%	88.41%	88.41%	0.756	0.757	0.756	0.757
Expert 2	676	84.37%	85.30%	81.75%	85.77%	91.79%	89.55%	87.72%	88.02%	0.743	0.752	0.744	0.752
Expert 3	2,499	82.26%	83.67%	86.16%	85.21%	82.96%	86.50%	84.31%	85.95%	0.683	0.714	0.685	0.714
Expert 4	971	82.24%	83.27%	90.72%	85.31%	80.10%	86.96%	84.35%	86.30%	0.685	0.717	0.694	0.717
Expert 5	615	82.20%	84.05%	88.19%	85.04%	81.44%	87.81%	84.23%	86.67%	0.682	0.726	0.687	0.726
Expert 6	689	81.84%	86.42%	77.54%	88.77%	92.01%	88.86%	86.21%	88.82%	0.708	0.769	0.711	0.770
Expert 7	765	81.14%	84.75%	76.42%	86.27%	90.70%	86.51%	84.44%	86.41%	0.680	0.725	0.684	0.725
Expert 8	611	81.02%	86.27%	74.80%	87.80%	93.00%	88.80%	85.43%	88.38%	0.693	0.762	0.700	0.762
Expert 9	793	81.00%	86.06%	80.75%	87.27%	87.26%	89.38%	84.62%	88.52%	0.681	0.763	0.681	0.763
Expert 10	679	80.80%	84.43%	84.67%	86.21%	84.45%	88.76%	84.54%	87.78%	0.680	0.744	0.681	0.744
Expert 11	696	80.80%	82.48%	80.07%	84.42%	88.10%	86.67%	84.91%	85.78%	0.685	0.705	0.684	0.706
Expert 12	606	80.70%	83.46%	79.01%	82.82%	87.21%	88.08%	83.66%	85.81%	0.666	0.710	0.666	0.710
Expert 13	606	80.63%	84.73%	78.63%	84.73%	87.50%	88.37%	83.66%	86.80%	0.665	0.731	0.666	0.731
Expert 14	598	80.54%	82.54%	84.15%	84.55%	82.67%	85.80%	83.28%	85.28%	0.659	0.698	0.661	0.699
Expert 15	693	80.45%	83.79%	85.27%	83.22%	80.55%	88.78%	82.54%	86.44%	0.648	0.721	0.651	0.721
Expert 16	870	80.43%	83.12%	84.27%	83.71%	82.49%	87.74%	83.22%	86.09%	0.658	0.713	0.660	0.713
Expert 17	1,313	80.10%	82.34%	87.93%	83.52%	79.14%	87.23%	82.64%	85.76%	0.649	0.704	0.657	0.704
Expert 18	644	80.07%	84.62%	88.76%	86.52%	76.66%	87.27%	81.68%	86.96%	0.634	0.733	0.645	0.734
Expert 19	738	79.87%	83.73%	83.33%	85.76%	83.78%	87.78%	83.60%	86.99%	0.661	0.729	0.662	0.730
Expert 20	1,428	79.65%	84.08%	88.02%	85.24%	77.70%	88.15%	81.86%	86.97%	0.636	0.731	0.645	0.731
Non-expert 1	572	79.57%	85.78%	87.38%	88.79%	80.73%	89.11%	83.22%	88.99%	0.655	0.768	0.663	0.769
Non-expert 2	2,555	79.51%	83.19%	83.94%	84.83%	82.08%	87.40%	82.82%	86.38%	0.648	0.718	0.651	0.718
Non-expert 3	736	79.45%	82.99%	78.23%	82.99%	87.56%	88.69%	83.83%	86.41%	0.661	0.717	0.662	0.717
Expert 21	690	79.35%	82.57%	83.59%	85.88%	83.41%	86.45%	83.48%	86.23%	0.656	0.712	0.659	0.714
Expert 22	1,120	79.33%	84.42%	79.92%	84.78%	84.23%	88.25%	82.41%	86.79%	0.640	0.730	0.640	0.730
Expert 23	722	79.08%	82.37%	92.11%	84.59%	74.27%	86.91%	81.16%	86.01%	0.626	0.708	0.647	0.709
Expert 24	628	78.28%	82.47%	86.36%	85.54%	78.50%	86.27%	81.53%	85.99%	0.625	0.708	0.633	0.710
Expert 25	585	78.10%	85.29%	92.13%	86.89%	63.21%	85.85%	76.41%	86.32%	0.538	0.725	0.568	0.726
Non-expert 4	628	77.95%	85.18%	80.08%	88.67%	82.53%	86.56%	81.53%	87.42%	0.621	0.743	0.621	0.745
Expert 26	913	77.70%	85.06%	74.81%	86.38%	86.83%	87.60%	81.71%	87.08%	0.622	0.737	0.624	0.737
Non-expert 5	564	77.54%	81.93%	79.22%	80.00%	79.29%	87.38%	79.26%	84.04%	0.583	0.677	0.583	0.677
Expert 27	619	77.41%	79.58%	77.73%	79.41%	85.56%	87.40%	82.55%	84.33%	0.632	0.669	0.632	0.669
Non-expert 6	610	77.38%	82.62%	82.63%	85.59%	80.48%	86.36%	81.31%	86.07%	0.616	0.710	0.619	0.711
Expert 28	865	76.92%	83.17%	85.29%	86.47%	76.38%	86.10%	79.88%	86.24%	0.594	0.716	0.603	0.717
Non-expert 7	644	76.82%	84.39%	83.15%	85.02%	76.39%	88.33%	79.19%	86.96%	0.581	0.732	0.587	0.732
Non-expert 8	603	76.39%	83.27%	79.28%	85.26%	79.83%	86.08%	79.60%	85.74%	0.585	0.709	0.586	0.709
Non-expert 9	622	76.25%	82.00%	72.08%	83.40%	87.39%	85.15%	80.87%	84.41%	0.603	0.683	0.606	0.683
Expert 29	723	76.19%	82.67%	81.08%	83.78%	77.99%	86.89%	79.25%	85.62%	0.579	0.704	0.583	0.704
Expert 30	597	76.05%	81.67%	89.27%	84.12%	70.88%	85.99%	78.06%	85.26%	0.566	0.694	0.588	0.694
Non-expert 10	586	75.78%	82.23%	83.98%	83.12%	75.49%	87.61%	78.84%	85.84%	0.573	0.705	0.582	0.705
Non-expert 11	594	75.74%	84.03%	70.17%	84.03%	89.89%	89.33%	81.99%	87.21%	0.616	0.734	0.621	0.734
Non-expert 12	606	75.70%	83.04%	81.27%	84.86%	76.34%	86.20%	78.38%	85.64%	0.564	0.706	0.568	0.707
Non-expert 13	703	75.45%	82.54%	89.77%	83.50%	63.50%	85.75%	74.82%	84.78%	0.509	0.691	0.537	0.691
Non-expert 14	580	75.25%	85.12%	78.24%	86.19%	79.18%	88.56%	78.79%	87.59%	0.568	0.745	0.569	0.745
Non-expert 15	1,149	75.13%	83.30%	78.08%	85.91%	81.05%	87.04%	79.90%	86.60%	0.583	0.721	0.584	0.722
Non-expert 16	655	74.96%	83.68%	84.23%	86.38%	69.95%	85.11%	76.03%	85.65%	0.525	0.709	0.537	0.710
Non-expert 17	622	74.78%	85.50%	95.45%	87.12%	55.87%	87.71%	72.67%	87.46%	0.479	0.745	0.535	0.745
Expert 31	892	74.52%	82.67%	71.88%	86.08%	86.30%	85.56%	80.61%	85.76%	0.589	0.706	0.590	0.708
Expert 32	886	74.43%	82.27%	64.79%	83.66%	93.79%	86.82%	82.17%	85.55%	0.612	0.701	0.628	0.701
Non-expert 18	649	74.25%	80.89%	87.08%	83.75%	72.13%	86.31%	77.66%	85.36%	0.553	0.691	0.572	0.692
Non-expert 19	770	74.19%	81.93%	83.76%	83.76%	71.05%	85.75%	76.23%	84.94%	0.527	0.690	0.539	0.691
Non-expert 20	583	74.04%	84.73%	92.86%	87.39%	60.00%	86.96%	73.41%	87.14%	0.490	0.736	0.534	0.737
Non-expert 21	574	73.98%	82.15%	78.45%	82.33%	77.19%	87.72%	77.70%	85.54%	0.546	0.700	0.549	0.700
Expert 33	682	73.29%	84.08%	79.51%	85.87%	73.43%	86.97%	75.95%	86.51%	0.517	0.724	0.522	0.724
Non-expert 22	598	73.16%	86.58%	75.09%	86.42%	75.98%	89.49%	75.59%	88.13%	0.508	0.759	0.509	0.759
Non-expert 23	673	73.08%	83.42%	71.43%	83.28%	82.12%	87.82%	77.56%	85.88%	0.539	0.711	0.539	0.711
Non-expert 24	694	72.73%	82.17%	89.36%	83.33%	61.41%	86.65%	72.77%	85.30%	0.474	0.697	0.507	0.697
Non-expert 25	628	72.42%	84.40%	87.35%	86.12%	65.54%	88.51%	74.04%	87.58%	0.492	0.741	0.519	0.741
Non-expert 26	607	71.91%	82.22%	75.89%	84.98%	74.86%	84.46%	75.29%	84.68%	0.500	0.688	0.502	0.689
Non-expert 27	609	71.86%	82.47%	70.64%	85.11%	83.69%	86.63%	78.65%	86.04%	0.547	0.709	0.547	0.710
Non-expert 28	612	70.18%	82.44%	66.28%	82.76%	83.19%	86.61%	75.98%	84.97%	0.502	0.693	0.504	0.693
Non-expert 29	583	69.55%	80.93%	85.78%	84.89%	61.73%	84.36%	71.01%	84.56%	0.437	0.680	0.467	0.682
Non-expert 30	568	67.96%	84.68%	69.30%	87.28%	76.76%	87.35%	73.77%	87.32%	0.458	0.739	0.458	0.740
Non-expert 31	579	67.82%	84.43%	56.61%	85.12%	92.58%	88.13%	77.55%	86.87%	0.516	0.731	0.541	0.731
Non-expert 32	1,501	63.52%	84.43%	51.97%	85.20%	92.05%	88.69%	75.82%	87.28%	0.467	0.737	0.494	0.737
Non-expert 33	578	60.30%	83.29%	56.60%	83.49%	81.97%	90.16%	72.66%	87.72%	0.396	0.736	0.398	0.736

Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient.

Supplementary Table 3 | Performance of AI models and human examiners by center

Centre	Cases		F1 score	Sensitivity	Specificity	Accuracy	Kappa	MCC	AUC	Brier score
Ancona, Italy	90 (51 benign, 39 malignant)	AI models	80.00% (68.35–89.16)	71.79% (56.76–85.37)	94.12% (86.79–100.00)	84.44% (76.67–91.11)	0.675 (0.509–0.817)	0.687 (0.530–0.824)	0.945 (0.891–0.986)	0.105 (0.075–0.139)
		Experts	73.53% (60.60–84.51)	64.10% (50.00–80.00)	92.16% (82.76–98.08)	90.00% (71.11–87.78)	0.580 (0.398–0.743)	0.597 (0.418–0.752)		
		Non-experts	66.67% (52.94–78.57)	61.54% (44.68–75.68)	84.31% (74.51–94.12)	74.44% (64.44–83.33)	0.465 (0.270–0.640)	0.475 (0.279–0.649)		
Athens, Greece	83 (47 benign, 36 malignant)	AI models	86.49% (76.92–93.98)	88.89% (77.50–97.44)	87.23% (76.92–95.83)	87.95% (80.72–93.98)	0.756 (0.604–0.880)	0.757 (0.608–0.885)	0.931 (0.862–0.981)	0.098 (0.064–0.138)
		Experts	86.11% (76.06–93.75)	83.33% (70.59–94.59)	91.49% (82.50–98.04)	87.95% (80.72–95.18)	0.755 (0.601–0.880)	0.755 (0.606–0.886)		
		Non-experts	81.08% (68.97–89.55)	80.56% (67.50–93.02)	85.11% (73.81–94.00)	83.13% (74.70–90.36)	0.659 (0.479–0.807)	0.660 (0.483–0.808)		
Barcelona, Spain	114 (58 benign, 56 malignant)	AI models	84.11% (75.79–90.91)	80.36% (69.81–90.16)	89.66% (81.03–96.67)	85.09% (78.07–91.23)	0.701 (0.561–0.824)	0.704 (0.567–0.825)	0.899 (0.837–0.951)	0.128 (0.098–0.160)
		Experts	79.63% (69.90–86.96)	78.57% (65.45–87.69)	82.76% (72.73–92.06)	80.70% (72.81–86.84)	0.613 (0.443–0.738)	0.614 (0.448–0.746)		
		Non-experts	74.29% (64.65–82.88)	73.21% (60.71–84.31)	77.59% (66.67–88.33)	75.44% (67.54–83.33)	0.508 (0.346–0.661)	0.509 (0.348–0.664)		
Bologna, Italy	179 (104 benign, 75 malignant)	AI models	73.53% (64.57–81.20)	66.67% (56.06–77.27)	89.42% (82.95–95.00)	79.89% (73.74–85.47)	0.576 (0.452–0.692)	0.584 (0.461–0.699)	0.855 (0.794–0.909)	0.151 (0.122–0.182)
		Experts	72.97% (64.79–80.77)	73.33% (62.86–82.90)	81.73% (73.33–88.29)	77.65% (71.51–83.80)	0.538 (0.416–0.662)	0.538 (0.417–0.664)		
		Non-experts	66.23% (56.72–74.53)	66.67% (55.55–77.14)	75.00% (66.39–83.18)	72.07% (64.80–78.21)	0.426 (0.276–0.547)	0.426 (0.276–0.548)		
Brescia, Italy	161 (131 benign, 30 malignant)	AI models	77.19% (63.16–88.14)	73.33% (56.52–88.89)	96.18% (92.59–99.22)	91.93% (87.58–95.65)	0.723 (0.561–0.854)	0.725 (0.566–0.855)	0.921 (0.853–0.970)	0.086 (0.063–0.112)
		Experts	64.41% (50.79–78.69)	63.33% (47.37–81.48)	93.13% (87.90–96.95)	86.96% (81.99–92.55)	0.568 (0.408–0.737)	0.570 (0.412–0.738)		
		Non-experts	55.38% (40.00–69.23)	60.00% (42.31–78.57)	87.02% (80.83–92.31)	81.99% (75.78–88.20)	0.442 (0.266–0.610)	0.444 (0.268–0.616)		
Cagliari, Italy	90 (75 benign, 15 malignant)	AI models	75.00% (54.55–90.00)	80.00% (57.14–100.00)	93.33% (87.18–98.63)	91.11% (84.44–96.67)	0.686 (0.468–0.877)	0.698 (0.472–0.879)	.922 (0.767– 0.997)	0.074 (0.050–0.104)
		Experts	75.86% (55.56–90.00)	80.00% (60.00–100.00)	92.00% (86.25–97.47)	91.11% (84.44–96.67)	0.711 (0.475–0.877)	0.713 (0.492–0.877)		
		Non-experts	62.50% (41.38–80.00)	73.33% (50.00–94.12)	88.00% (80.26–94.67)	85.56% (77.78–92.22)	0.541 (0.308–0.752)	0.546 (0.322–0.758)		
Katowice, Poland	111 (55 benign, 56 malignant)	AI models	95.58% (91.09–99.08)	96.43% (90.74–100.00)	94.55% (87.72–100.00)	95.50% (90.99–99.10)	0.910 (0.820–0.982)	0.910 (0.822–0.982)	0.977 (0.947–0.997)	0.067 (0.047–0.091)
		Experts	91.07% (84.96–96.00)	91.07% (82.35–97.96)	92.73% (83.64–98.21)	90.99% (85.59–96.40)	0.820 (0.710–0.925)	0.820 (0.711–0.925)		
		Non-experts	89.09% (81.63–94.21)	89.29% (79.99–96.36)	89.09% (78.95–96.08)	89.19% (81.98–93.69)	0.784 (0.639–0.874)	0.784 (0.640–0.875)		
Kaunas, Lithuania	132 (66 benign, 66 malignant)	AI models	86.61% (79.66–92.31)	83.33% (73.85–91.89)	90.91% (83.33–97.06)	87.12% (81.06–92.42)	0.742 (0.621–0.848)	0.745 (0.624–0.849)	0.952 (0.915–0.981)	0.098 (0.075–0.124)
		Experts	83.33% (75.97–89.92)	81.82% (72.88–91.53)	84.85% (75.38–92.75)	83.33% (77.27–90.15)	0.667 (0.543–0.797)	0.668 (0.543–0.798)		
		Non-experts	78.12% (69.35–84.89)	78.79% (68.63–88.24)	77.27% (65.57–86.11)	78.03% (70.45–84.09)	0.561 (0.405–0.682)	0.561 (0.406–0.685)		
Lublin, Poland	211 (124 benign, 87 malignant)	AI models	80.87% (74.12–86.86)	85.06% (77.01–92.22)	82.26% (75.57–88.79)	83.41% (78.20–88.63)	0.663 (0.558–0.762)	0.665 (0.562–0.765)	0.897 (0.852–0.937)	0.130 (0.103–0.158)
		Experts	73.80% (66.67–80.85)	79.31% (70.59–87.78)	74.19% (67.46–82.71)	76.78% (71.09–82.46)	0.534 (0.420–0.649)	0.538 (0.427–0.652)		
		Non-experts	69.84% (61.80–76.70)	75.86% (66.67–85.06)	70.16% (62.07–78.05)	72.51% (66.35–78.67)	0.452 (0.329–0.566)	0.460 (0.335–0.573)		
Lund, Sweden	100 (51 benign, 49 malignant)	AI models	85.15% (76.92–91.84)	87.76% (78.00–96.00)	82.35% (70.83–92.00)	85.00% (78.00–92.00)	0.700 (0.552–0.835)	0.702 (0.556–0.835)	0.895 (0.827–0.951)	0.136 (0.106–0.169)
		Experts	79.61% (70.10–87.27)	83.67% (73.47–93.88)	72.55% (60.38–84.62)	79.00% (70.00–86.00)	0.581 (0.408–0.721)	0.587 (0.417–0.731)		
		Non-experts	75.73% (66.67–84.91)	79.59% (69.39–91.30)	70.59% (57.41–82.76)	75.00% (67.00–84.00)	0.501 (0.340–0.678)	0.503 (0.343–0.680)		
Manila, Philippines	97 (49 benign, 48 malignant)	AI models	83.81% (75.51–90.91)	91.67% (82.98–98.08)	73.47% (60.87–85.71)	82.47% (75.26–89.69)	0.650 (0.497–0.794)	0.662 (0.514–0.800)	0.944 (0.896–0.980)	0.110 (0.078–0.145)
		Experts	81.63% (72.50–89.11)	83.33% (72.55–93.48)	79.59% (66.67–89.80)	81.44% (73.20–88.66)	0.629 (0.464–0.773)	0.630 (0.465–0.774)		
		Non-experts	77.42% (65.78–84.68)	79.17% (65.38–88.68)	75.51% (61.11–85.71)	77.32% (67.01–83.51)	0.547 (0.340–0.672)	0.548 (0.342–0.680)		
Milan, Italy	118 (50 benign, 68 malignant)	AI models	89.66% (84.00–94.34)	95.59% (90.14–100.00)	76.00% (63.64–87.27)	87.29% (81.36–93.22)	0.733 (0.599–0.851)	0.743 (0.619–0.855)	0.935 (0.883–0.976)	0.101 (0.074–0.131)
		Experts	84.77% (77.86–90.32)	91.18% (83.58–97.10)	66.00% (53.85–80.00)	81.36% (73.73–87.29)	0.601 (0.446–0.737)	0.616 (0.459–0.745)		
		Non-experts	80.56% (72.87–87.01)	85.29% (76.56–93.42)	64.00% (50.00–77.08)	76.27% (68.64–83.90)	0.504 (0.339–0.656)	0.509 (0.347–0.662)		
Milan 2, Italy	350 (266 benign, 84 malignant)	AI models	78.31% (71.51–84.42)	88.10% (80.68–94.57)	88.35% (84.29–92.11)	88.29% (84.86–91.43)	0.704 (0.618–0.785)	0.712 (0.629–0.790)	0.944 (0.919–0.966)	0.098 (0.081–0.116)
		Experts	71.20% (64.00–78.39)	80.95% (71.25–88.46)	86.09% (81.89–90.16)	84.57% (80.86–88.29)	0.606 (0.518–0.702)	0.615 (0.526–0.708)		
		Non-experts	62.69% (54.78–70.29)	75.00% (64.63–83.56)	80.45% (75.48–84.94)	78.86% (74.57–83.14)	0.482 (0.386–0.583)	0.495 (0.397–0.593)		
Monza, Italy	161 (102 benign, 59 malignant)	AI models	78.50% (68.89–86.49)	71.19% (59.26–82.76)	94.12% (89.11–98.10)	85.71% (80.12–90.68)	0.680 (0.550–0.795)	0.688 (0.563–0.801)	0.960 (0.931–0.983)	0.095 (0.075–0.118)
		Experts	83.48% (75.81–90.23)	83.05% (73.53–92.31)	91.18% (84.76–96.08)	88.20% (82.61–92.55)	0.741 (0.628–0.844)	0.743 (0.629–0.845)		
		Non-experts	77.59% (68.04–85.11)	76.27% (65.52–87.10)	87.25% (80.65–93.48)	83.85% (77.64–88.82)	0.650 (0.513–0.761)	0.652 (0.515–0.762)		
Pamplona, Spain	77 (47 benign, 30 malignant)	AI models	89.66% (80.00–96.77)	86.67% (73.33–96.97)	95.74% (89.19–100.00)	92.21% (85.71–97.40)	0.834 (0.695–0.946)	0.835 (0.699–0.947)	0.962 (0.910–0.996)	0.072 (0.043–0.106)
		Experts	82.76% (69.38–91.80)	76.67% (61.54–91.67)	93.62% (84.44–100.00)	87.01% (79.22–93.51)	0.724 (0.541–0.866)	0.725 (0.548–0.869)		
		Non-experts	75.47% (61.54–86.96)	70.00% (54.29–87.10)	89.36% (79.55–97.62)	81.82% (74.03–90.91)	0.618 (0.423–0.787)	0.620 (0.430–0.791)		
Prague, Czech Republic	105 (35 benign, 70 malignant)	AI models	88.24% (81.97–93.43)	85.71% (76.92–93.42)	82.86% (69.23–94.29)	84.76% (77.14–91.43)	0.667 (0.511–0.806)	0.669 (0.517–0.809)	0.946 (0.898–0.982)	0.103 (0.079–0.131)
		Experts	84.56% (77.27–90.12)	88.57% (79.69–95.08)	57.14% (41.67–75.00)	78.10% (69.52–85.71)	0.481 (0.288–0.658)	0.487 (0.296–0.664)		
		Non-experts	82.12% (74.29–88.05)	87.14% (77.94–94.29)	51.43% (33.33–66.67)	74.29% (65.71–82.86)	0.391 (0.190–0.566)	0.396 (0.195–0.577)		
Prague 2, Czech Republic	110 (64 benign, 46 malignant)	AI models	82.11% (72.92–89.80)	84.78% (73.33–94.74)	84.38% (75.00–92.65)	84.55% (77.27–90.91)	0.685 (0.542–0.816)	0.686 (0.545–0.818)	0.921 (0.864–0.967)	0.118 (0.090–0.150)
		Experts	75.00% (64.44–84.21)	78.26% (66.00–90.00)	78.12% (67.19–87.69)	78.18% (70.00–85.45)	0.557 (0.397–0.709)	0.559 (0.400–0.713)		
		Non-experts	71.29% (59.70–80.67)	76.09% (63.04–88.10)	71.88% (60.87–82.81)	73.64% (65.45–81.82)	0.473 (0.307–0.636)	0.479 (0.311–0.638)		
Stockholm, Sweden	300 (150 benign, 150 malignant)	AI models	84.83% (80.40–88.77)	91.33% (86.52–95.54)	76.00% (68.87–82.67)	83.67% (79.33–87.67)	0.673 (0.587–0.753)	0.681 (0.597–0.759)	0.921 (0.889–0.948)	0.121 (0.102–0.142)
		Experts	81.66% (76.57–85.80)	89.33% (84.21–94.16)	69.33% (62.18–76.81)	79.67% (75.00–84.00)	0.593 (0.499–0.679)	0.608 (0.513–0.689)		
		Non-experts	79.04% (73.82–83.47)	89.33% (83.67–93.71)	63.33% (55.40–70.70)	76.33% (71.33–80.67)	0.527 (0.428–0.612)	0.545 (0.448–0.627)		
Trieste, Italy	71 (50 benign, 21 malignant)	AI models	79.17% (64.28–90.48)	90.48% (76.00–100.00)	84.00% (72.92–93.75)	85.92% (77.46–92.96)	0.688 (0.498–0.852)	0.700 (0.519–0.857)	0.950 (0.895–0.989)	0.099 (0.066–0.137)
		Experts	73.91% (57.89–86.96)	85.71% (69.22–100.00)	82.00% (70.00–91.67)	83.10% (73.24–91.55)	0.616 (0.412–0.795)	0.621 (0.433–0.804)		
		Non-experts	64.00% (46.15–77.42)	80.95% (60.00–95.00)	70.00% (58.00–83.02)	73.24% (63.38–83.10)	0.433 (0.226–0.639)	0.466 (0.247–0.656)		

Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient.

Supplementary Table 4 | Performance of AI models and human examiners by ultrasound system

Ultrasound System	Cases		F1 score	Sensitivity	Specificity	Accuracy	Kappa	MCC	AUC	Brier score
GE Voluson E6	325 (200 benign, 125 malignant)	AI models	79.15% (73.15–84.43)	74.40% (66.42–81.91)	91.50% (87.44–95.15)	84.92% (80.92–88.62)	0.674 (0.588–0.752)	0.678 (0.593–0.756)	0.911 (0.875–0.943)	0.114 (0.096–0.134)
		Experts	80.00% (74.29–85.14)	79.20% (72.00–86.32)	88.00% (83.41–92.31)	84.62% (80.62–88.31)	0.676 (0.590–0.755)	0.676 (0.591–0.755)		
		Non-experts	73.75% (66.95–79.53)	73.60% (65.08–80.74)	84.00% (78.72–88.78)	80.00% (75.38–84.00)	0.578 (0.477–0.662)	0.579 (0.477–0.663)		
GE Voluson E8	1,074 (685 benign, 389 malignant)	AI models	82.81% (79.89–85.43)	84.83% (81.28–88.29)	88.61% (86.21–90.91)	87.24% (85.20–89.20)	0.727 (0.684–0.767)	0.727 (0.684–0.768)	0.925 (0.908–0.941)	0.106 (0.096–0.117)
		Experts	77.09% (73.67–79.95)	79.69% (75.41–83.38)	84.53% (81.92–87.28)	82.87% (80.45–84.92)	0.633 (0.583–0.677)	0.635 (0.585–0.678)		
		Non-experts	71.20% (67.41–74.51)	75.32% (70.57–79.34)	79.56% (76.49–82.56)	77.93% (75.42–80.35)	0.534 (0.480–0.584)	0.536 (0.483–0.586)		
GE Voluson E10	579 (287 benign, 292 malignant)	AI models	85.57% (82.51–88.40)	89.38% (85.71–92.86)	80.14% (75.34–84.56)	84.80% (81.87–87.56)	0.696 (0.636–0.751)	0.699 (0.640–0.754)	0.926 (0.905– 0.945)	0.116 (0.103–0.129)
		Experts	81.59% (77.99–84.56)	88.01% (84.05–91.55)	71.78% (66.10–76.67)	79.97% (76.51–82.90)	0.599 (0.529–0.658)	0.606 (0.537–0.664)		
		Non-experts	78.07% (74.50–81.54)	86.30% (82.27–90.12)	64.81% (59.18–70.29)	75.65% (72.19–79.10)	0.512 (0.443–0.578)	0.523 (0.455–0.590)		
GE Voluson I	89 (74 benign, 15 malignant)	AI models	75.00% (54.55–89.47)	80.00% (57.14–100.00)	93.24% (86.96–98.63)	91.01% (84.27–96.63)	0.695 (0.468–0.869)	0.697 (0.482–0.870)	0.922 (0.770–0.997)	0.074 (0.050–0.104)
		Experts	75.86% (54.55–89.66)	80.00% (60.00–100.00)	91.89% (86.08–97.50)	91.01% (84.27–96.63)	0.710 (0.468–0.871)	0.712 (0.482–0.875)		
		Non-experts	62.50% (42.09–80.00)	73.33% (50.00–94.44)	87.84% (80.28–94.67)	85.39% (78.65–92.13)	0.540 (0.313–0.751)	0.545 (0.325–0.758)		
GE Voluson S10	124 (72 benign, 52 malignant)	AI models	83.48% (75.27–90.27)	92.31% (84.31–98.28)	79.17% (69.23–88.16)	84.68% (78.23–91.13)	0.694 (0.563–0.817)	0.705 (0.581–0.821)	0.954 (0.915–0.983)	0.105 (0.078–0.134)
		Experts	79.28% (70.37–87.18)	82.69% (72.34–92.45)	80.56% (71.83–89.71)	81.45% (75.00–88.71)	0.626 (0.494–0.767)	0.630 (0.497–0.769)		
		Non-experts	73.87% (62.92–81.55)	76.92% (65.52–88.46)	76.39% (64.79–84.72)	77.42% (68.55–83.06)	0.536 (0.359–0.661)	0.536 (0.364–0.666)		
GE Voluson 730	169 (89 benign, 90 malignant)	AI models	88.31% (82.35–93.33)	85.00% (76.62–92.41)	93.26% (87.63–97.89)	89.35% (84.62–94.08)	0.786 (0.687–0.876)	0.788 (0.691–0.877)	0.956 (0.926–0.981)	0.093 (0.073–0.115)
		Experts	85.71% (78.83–90.70)	83.75% (75.31–91.67)	88.76% (81.25–94.74)	86.98% (81.07–91.12)	0.738 (0.611–0.822)	0.739 (0.615–0.823)		
		Non-experts	70.00% (72.05–86.02)	81.25% (71.21–88.64)	80.90% (71.76–88.37)	80.07% (73.96–86.39)	0.619 (0.480–0.727)	0.620 (0.482–0.727)		
Mindray DC-70	44 (17 benign, 27 malignant)	AI models	72.73% (55.81–86.21)	59.26% (40.62–77.78)	94.12% (80.00–100.00)	72.73% (59.09–86.36)	0.481 (0.255–0.715)	0.534 (0.309–0.728)	0.919 (0.826–0.987)	0.148 (0.094–0.210)
		Experts	74.42% (57.89–87.27)	59.26% (41.67–78.57)	100.00% (86.67–100.00)	75.00% (61.36–86.36)	0.520 (0.298–0.732)	0.571 (0.375–0.760)		
		Non-experts	69.57% (50.00–82.61)	55.56% (35.71–73.91)	88.24% (73.33–100.00)	68.18% (54.55–81.82)	0.395 (0.169–0.642)	0.442 (0.208–0.667)		
Samsung WS80A	159 (104 benign, 55 malignant)	AI models	86.67% (79.28–92.68)	94.55% (87.72–100.00)	87.50% (80.73–93.52)	89.94% (84.91–94.34)	0.787 (0.681–0.881)	0.794 (0.694–0.885)	0.958 (0.926–0.983)	0.089 (0.067–0.114)
		Experts	79.67% (70.67–86.36)	89.09% (80.33–96.43)	81.73% (73.12–88.24)	84.28% (77.99–89.31)	0.671 (0.541–0.773)	0.681 (0.556–0.780)		
		Non-experts	73.77% (64.29–81.63)	87.27% (76.92–94.83)	74.04% (66.00–82.52)	79.25% (71.70–84.91)	0.568 (0.432–0.685)	0.584 (0.454–0.698)		

Data in parentheses are 95% CIs through bootstrapping. The table is limited to the eight most common ultrasound systems in the OMLC-RS dataset. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient.

Supplementary Table 5 | Performance of AI models and human examiners by level of confidence in examiners' assessments

Confidence		F1 score	Sensitivity	Specificity	Accuracy	Kappa	MCC	AUC	Brier score
Certain ***n*** **= 10,079**	AI models	87.08% (86.28–87.88)	88.98% (87.96–89.94)	90.77% (90.04–91.46)	90.10% (89.50–90.68)	0.791 (0.778–0.803)	0.791 (0.779–0.803)	0.952 (0.948–0.957)	0.084 (0.081–0.087)
	Non-expert	84.24% (83.36–85.09)	87.26% (86.17–88.31)	88.04% (87.23–88.85)	87.75% (87.10–88.38)	0.742 (0.729–0.756)	0.744 (0.730–0.757)		
Probable ***n*** **= 10,951**	AI models	81.19% (80.35–82.03)	82.44% (81.36–83.51)	84.80% (83.93–85.68)	83.80% (83.12–84.49)	0.670 (0.656–0.684)	0.670 (0.656–0.684)	0.909 (0.904–0.914)	0.124 (0.120–0.127)
	Non-experts	70.14% (69.11–71.15)	75.25% (74.01–76.50)	71.04% (69.92–72.16)	72.82% (71.98–73.66)	0.454 (0.438–0.471)	0.458 (0.441–0.474)		
Uncertain ***n*** **= 2,805**	AI models	80.63% (78.95–82.27)	81.66% (79.52–83.76)	82.96% (81.07–84.79)	82.38% (80.93–83.74)	0.645 (0.616–0.672)	0.645 (0.616–0.673)	0.899 (0.887–0.910)	0.131 (0.125–0.137)
	Non-experts	59.83% (57.63–61.97)	64.62% (61.90–67.28)	58.09% (55.58–60.61)	61.03% (59.18–62.85)	0.224 (0.187–0.260)	0.226 (0.190–0.262)		
Certain ***n*** **= 16,209**	AI models	88.69% (88.11–89.25)	90.25% (89.50–90.96)	91.42% (90.87–91.98)	90.96% (90.52–91.40)	0.812 (0.803–0.821)	0.812 (0.803–0.821)	0.957 (0.954–0.960)	0.079 (0.077–0.082)
	Experts	88.21% (87.62–88.78)	90.58% (89.87–91.29)	90.43% (89.85–91.00)	90.49% (90.04–90.94)	0.802 (0.793–0.812)	0.803 (0.794–0.812)		
Probable ***n*** **= 9,516**	AI models	77.83% (76.83–78.82)	79.20% (77.94–80.45)	82.31% (81.27–83.32)	81.00% (80.21–81.79)	0.612 (0.596–0.628)	0.612 (0.596–0.629)	0.880 (0.873–0.887)	0.142 (0.138–0.145)
	Experts	70.40% (69.29–71.49)	74.15% (72.80–75.50)	73.43% (72.27–74.58)	73.73% (72.86–74.60)	0.469 (0.451–0.486)	0.471 (0.453–0.489)		
Uncertain ***n*** **= 1,619**	AI models	75.33% (72.87–77.70)	76.05% (72.89–79.04)	77.99% (75.20–80.68)	77.10% (75.05–79.06)	0.539 (0.498–0.579)	0.540 (0.498–0.579)	0.844 (0.825–0.862)	0.162 (0.153–0.171)
	Experts	59.77% (56.85–62.61)	61.46% (57.99–64.93)	62.38% (59.19–65.58)	61.96% (59.67–64.30)	0.237 (0.191–0.285)	0.238 (0.191–0.285)		

Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient.

Supplementary Table 6 | Performance of AI models and human examiners by patient age group

Age group	Cases		F1 score	Sensitivity	Specificity	Accuracy	Kappa	MCC	AUC	Brier score
≤ 29	315 (243 benign, 72 malignant)	AI models	67.10% (57.97–75.34)	72.22% (61.43–82.35)	87.24% (82.92–91.29)	83.81% (79.68–87.94)	0.564 (0.454–0.669)	0.567 (0.458–0.672)	0.888 (0.845–0.927)	0.119 (0.100–0.139)
		Experts	65.41% (55.70–72.63)	75.00% (64.06–84.21)	83.54% (78.51–87.97)	81.59% (77.14–85.71)	0.531 (0.416–0.626)	0.543 (0.426–0.632)		
		Non-experts	57.29% (47.90–65.33)	72.22% (62.16–82.86)	76.13% (70.20–81.05)	75.24% (70.16–79.68)	0.408 (0.299–0.510)	0.428 (0.318–0.529)		
30–39	447 (348 benign, 99 malignant)	AI models	78.14% (71.56–83.87)	84.85% (77.45–91.67)	90.80% (87.64–93.71)	89.49% (86.58–92.17)	0.713 (0.632–0.786)	0.717 (0.638–0.789)	0.939 (0.911–0.963)	0.091 (0.078–0.106)
		Experts	71.80% (64.11–77.39)	81.82% (75.23–90.00)	85.63% (81.98–89.36)	85.01% (81.66–88.37)	0.610 (0.529–0.693)	0.620 (0.543–0.702)		
		Non-experts	60.41% (52.94–67.19)	75.76% (67.39–84.16)	78.16% (73.95–82.70)	77.85% (74.05–81.66)	0.460 (0.372–0.546)	0.480 (0.391–0.565)		
40–49	526 (317 benign, 209 malignant)	AI models	84.04% (80.09–87.58)	85.65% (80.75–90.32)	88.01% (84.30–91.44)	87.07% (84.22–89.92)	0.732 (0.670–0.789)	0.732 (0.671–0.790)	0.924 (0.899–0.945)	0.110 (0.096–0.125)
		Experts	80.47% (76.12–84.21)	83.25% (77.78–88.12)	84.23% (80.06–88.13)	83.84% (80.61–86.88)	0.668 (0.599–0.729)	0.670 (0.601–0.730)		
		Non-experts	75.06% (70.67–79.57)	79.90% (74.02–84.89)	78.86% (74.27–83.33)	79.09% (75.67–82.51)	0.572 (0.502–0.643)	0.574 (0.505–0.645)		
50–59	470 (266 benign, 204 malignant)	AI models	85.51% (81.82–88.99)	88.24% (83.70–92.49)	86.09% (81.89–90.16)	87.02% (84.04–90.00)	0.738 (0.675–0.799)	0.739 (0.678–0.799)	0.931 (0.907–0.954)	0.107 (0.093–0.122)
		Experts	79.34% (74.76–83.33)	82.35% (76.92–87.50)	80.45% (75.66–85.09)	81.28% (77.66–84.68)	0.624 (0.550–0.692)	0.626 (0.552–0.693)		
		Non-experts	73.66% (69.06–78.24)	78.92% (72.77–83.92)	74.06% (68.54–79.25)	75.53% (71.91–79.79)	0.512 (0.438–0.592)	0.516 (0.442–0.595)		
60–69	401 (180 benign, 221 malignant)	AI models	84.45% (81.09–88.31)	82.35% (77.29–87.14)	85.56% (80.23–90.52)	83.79% (80.05–87.28)	0.675 (0.600–0.745)	0.676 (0.603–0.746)	0.908 (0.878–0.935)	0.122 (0.104–0.141)
		Experts	80.82% (76.61–84.62)	80.09% (74.65–85.17)	77.78% (71.68–83.89)	79.05% (75.06–83.04)	0.577 (0.496–0.656)	0.577 (0.497–0.657)		
		Non-experts	77.88% (73.43–82.02)	77.38% (71.37–82.41)	74.44% (68.10–80.85)	75.81% (71.82–80.05)	0.510 (0.430–0.599)	0.510 (0.430–0.599)		
70 ≤	292 (113 benign, 179 malignant)	AI models	88.51% (84.78–91.88)	86.03% (80.85–90.96)	86.73% (80.19–92.62)	86.30% (82.19–90.07)	0.716 (0.630–0.795)	0.718 (0.633–0.797)	0.947 (0.921–0.970)	0.098 (0.081–0.115)
		Experts	86.59% (82.70–90.16)	86.03% (80.81–90.91)	79.65% (72.12–87.04)	83.56% (79.45–87.67)	0.657 (0.558–0.735)	0.658 (0.559–0.736)		
		Non-experts	84.21% (80.12–88.39)	81.56% (75.84–87.08)	82.30% (74.07–88.39)	81.16% (77.05–85.96)	0.612 (0.518–0.702)	0.615 (0.522–0.704)		

Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient. Information on patient age was missing for 125 patients.

Supplementary Table 7 | Performance of AI models and human examiners by year of examination

Year of examination	Cases		F1 score	Sensitivity	Specificity	Accuracy	Kappa	MCC	AUC	Brier score
2006–2014	493 (301 benign, 192 malignant)	AI models	84.24% (80.10–87.94)	84.90% (79.69–89.78)	89.37% (85.71–92.71)	87.63% (84.58–90.47)	0.741 (0.677–0.799)	0.741 (0.677–0.799)	0.935 (0.910–0.956)	0.101 (0.088–0.116)
		Experts	80.00% (75.54–84.24)	80.21% (75.00–86.14)	86.71% (82.71–90.37)	84.38% (81.14–87.63)	0.672 (0.604–0.738)	0.672 (0.604–0.738)		
		Non-experts	74.75% (69.85–79.41)	77.60% (71.43–83.33)	81.06% (76.56–85.47)	79.51% (76.06–83.16)	0.577 (0.503–0.650)	0.578 (0.505–0.652)		
2015–2017	556 (349 benign, 207 malignant)	AI models	82.78% (78.70–86.55)	83.57% (78.39–88.63)	89.11% (85.75–92.33)	87.05% (84.17–89.75)	0.724 (0.663–0.782)	0.724 (0.664–0.782)	0.919 (0.894–0.942)	0.109 (0.094–0.124)
		Experts	77.52% (72.86–81.58)	80.19% (74.34–85.34)	83.95% (80.24–87.89)	82.55% (79.50–85.61)	0.634 (0.566–0.696)	0.635 (0.567–0.697)		
		Non-experts	70.37% (65.43–75.11)	73.91% (67.89–79.80)	78.51% (74.25–82.91)	76.80% (73.38–80.40)	0.515 (0.442–0.586)	0.517 (0.444–0.588)		
2018	405 (233 benign, 172 malignant)	AI models	82.87% (78.49–86.84)	87.21% (81.98–92.03)	82.83% (77.83–87.50)	84.69% (81.23–88.15)	0.691 (0.619–0.758)	0.694 (0.624–0.761)	0.919 (0.890–0.943)	0.118 (0.101–0.136)
		Experts	80.22% (75.74–84.47)	86.05% (80.33–90.80)	79.40% (74.37–84.58)	81.98% (78.52–85.68)	0.639 (0.568–0.712)	0.644 (0.573–0.716)		
		Non-experts	74.48% (69.54–79.43)	81.98% (75.90–87.50)	72.96% (66.53–78.17)	76.05% (72.34–80.49)	0.524 (0.446–0.611)	0.533 (0.455–0.617)		
2019	478 (260 benign, 218 malignant)	AI models	84.06% (80.20–87.68)	83.49% (78.38–88.29)	87.31% (83.21–91.24)	85.56% (82.43–88.70)	0.709 (0.643–0.771)	0.709 (0.644–0.772)	0.927 (0.902–0.948)	0.109 (0.094–0.125)
		Experts	79.91% (76.04–84.10)	80.28% (75.34–85.71)	82.69% (78.26–87.45)	81.59% (78.45–85.15)	0.629 (0.564–0.702)	0.629 (0.565–0.703)		
		Non-experts	75.85% (71.39–80.35)	77.06% (71.36–82.67)	78.85% (73.31–83.27)	77.82% (74.06–81.59)	0.553 (0.477–0.628)	0.553 (0.478–0.628)		
2020–2021	728 (432 benign, 296 malignant)	AI models	83.50% (80.20–86.62)	85.47% (81.29–89.38)	86.81% (83.56–89.93)	86.26% (83.79–88.74)	0.717 (0.666–0.768)	0.718 (0.667–0.769)	0.939 (0.923–0.955)	0.104 (0.094–0.116)
		Experts	79.17% (75.66–82.64)	84.12% (79.81–88.22)	80.79% (76.84–84.31)	82.01% (79.26–84.89)	0.634 (0.579–0.692)	0.637 (0.583–0.695)		
		Non-experts	74.33% (70.48–78.01)	80.74% (76.37–85.46)	74.31% (70.52–78.77)	77.20% (74.18–80.22)	0.541 (0.480–0.602)	0.548 (0.487–0.607)		

Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient.

Supplementary Table 8 | Performance of AI model on a separate cohort of cases from the Stockholm center

	Remaining cases (*n* = 644)	Main analysis (*n* = 300)
F1 score	84.73% (81.59–87.64)	84.83% (80.40–88.77)
Sensitivity	92.81% (89.66–95.67)	91.33% (86.52–95.54)
Specificity	80.05% (75.85–84.06)	76.00% (68.87–82.67)
Accuracy	85.56% (82.76–88.20)	83.67% (79.33–87.67)
AUC	0.954 (0.939–0.968)	0.921 (0.889–0.948)
Kappa	0.712 (0.658–0.765)	0.673 (0.587–0.753)
MCC	0.722 (0.671–0.772)	0.681 (0.597–0.759)
Brier score	0.102 (0.090–0.115)	0.121 (0.102–0.142)
DOR	51.78 (32.51–94.76)	33.37 (17.91–75.02)
J	72.86% (67.71–77.84)	67.33% (58.84–75.23)
LR+	4.65 (3.84–5.84)	3.81 (2.92–5.28)
LR-	0.090 (0.054–0.129)	0.114 (0.059–0.180)
PPV	77.95% (73.46–82.32)	79.19% (73.02–85.06)
NPV	93.61% (90.71–96.17)	89.76% (84.14–94.66)

Performance of the AI model on the cohort of 644 patients with a post-surgical histological diagnosis (366 benign, 278 malignant) from the Stockholm center that were not included in the main analysis as they were not assessed by human examiners. Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient. DOR = diagnostic odds ratio. J = Youden's J statistic. LR+ = Positive likelihood ratio. LR– = Negative likelihood ratio. PPV = Positive predictive value. NPV = Negative predictive value.

Supplementary Table 9 | Impact of label granularity on AI model performance

	2 classes	10 classes	18 classes
F1 score	82.22% (80.39–83.91)	83.50% (81.76–85.14)	82.70% (80.93–84.36)
Sensitivity	81.38% (79.00–83.58)	84.88% (82.73–86.96)	83.50% (81.26–85.65)
Specificity	88.57% (86.99–90.13)	87.30% (85.66–88.94)	87.30% (85.63–88.92)
Accuracy	85.64% (84.29–86.95)	86.32% (85.00–87.59)	85.75% (84.44–87.07)
AUC	0.928 (0.918–0.937)	0.929 (0.919–0.939)	0.930 (0.920–0.939)
Kappa	0.702 (0.674–0.729)	0.718 (0.691–0.745)	0.706 (0.678–0.733)
MCC	0.702 (0.674–0.729)	0.718 (0.691–0.745)	0.706 (0.679–0.733)
Brier score	0.137 (0.133–0.142)	0.108 (0.101–0.114)	0.106 (0.100–0.113)
DOR	33.88 (27.46–42.37)	38.61 (31.16–48.74)	34.80 (28.23–43.73)
J	69.95% (67.07–72.66)	72.19% (69.46–74.86)	70.80% (68.04–73.52)
LR+	7.12 (6.22–8.27)	6.68 (5.90–7.69)	6.58 (5.80–7.56)
LR-	0.210 (0.185–0.237)	0.173 (0.149–0.198)	0.189 (0.164–0.215)
PPV	83.07% (80.83–85.26)	82.16% (79.93–84.38)	81.92% (79.63–84.18)
NPV	87.35% (85.68–88.92)	89.34% (87.77–90.84)	88.478% (86.85–90.04)

AI models were trained using two, ten, or 18 classes. At test-time, the model makes a binary prediction by averaging all the benign and malignant scores, as described in the main paper. Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient. DOR = diagnostic odds ratio. J = Youden's J statistic. LR+ = Positive likelihood ratio. LR– = Negative likelihood ratio. PPV = Positive predictive value. NPV = Negative predictive value.

Supplementary Table 10 | Impact of image cropping on AI model performance

	Cropped and artifacts removed	Cropped only	Auto-cropped with YOLO[2]	Uncropped
F1 score	83.50% (81.76–85.14)	82.88% (81.12–84.52)	82.78% (81.04–84.41)	81.85% (80.09–83.53)
Sensitivity	84.88% (82.73–86.96)	85.44% (83.29–87.46)	85.71% (83.58–87.73)	84.61% (82.46–86.69)
Specificity	87.30% (85.66–88.94)	85.71% (84.02–87.44)	85.27% (83.55–87.02)	84.76% (82.98–86.52)
Accuracy	86.32% (85.00–87.59)	85.60% (84.25–86.92)	85.45% (84.10–86.80)	84.70% (83.31–86.05)
AUC	0.929 (0.919–0.939)	0.926 (0.915–0.936)	0.926 (0.916–0.936)	0.918 (0.907–0.928)
Kappa	0.718 (0.691–0.745)	0.705 (0.677–0.731)	0.702 (0.674–0.729)	0.687 (0.658–0.714)
MCC	0.718 (0.691–0.745)	0.706 (0.678–0.732)	0.703 (0.676–0.731)	0.688 (0.660–0.715)
Brier score	0.108 (0.101–0.114)	0.111 (0.104–0.117)	0.111 (0.104–0.117)	0.119 (0.112–0.125)
DOR	38.61 (31.16–48.74)	35.20 (28.38–44.22)	34.73 (28.14–43.69)	30.58 (24.88–38.22)
J	72.19% (69.46–74.86)	71.15% (68.37–73.82)	70.98% (68.25–73.69)	69.37% (66.57–72.12)
LR+	6.68 (5.90–7.69)	5.98 (5.32–6.81)	5.82 (5.19–6.62)	5.55 (4.96–6.30)
LR-	0.173 (0.149–0.198)	0.170 (0.146–0.195)	0.168 (0.144–0.193)	0.182 (0.157–0.207)
PPV	82.16% (79.93–84.38)	80.47% (78.18–82.74)	80.03% (77.73–82.30)	79.27% (76.92–81.59)
NPV	89.34% (87.77–90.84)	89.52% (87.93–91.02)	89.65% (88.09–91.16)	88.88% (87.25–90.45)

Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient. DOR = diagnostic odds ratio. J = Youden's J statistic. LR+ = Positive likelihood ratio. LR– = Negative likelihood ratio. PPV = Positive predictive value. NPV = Negative predictive value.

Supplementary Table 11 | Impact of domain shift on AI model performance

	In-domain	Domain-shifted	△(in-domain - domain-shifted)	p-value
F1 score	74.54% (69.71–78.97)	70.34% (65.46–74.85)	4.20 (0.85–7.65)	0.0132
Sensitivity	90.45% (85.89–94.55)	93.26% (89.33–96.67)	-2.81 (-6.41–0.61)	0.1626
Specificity	80.58% (77.04–84.08)	73.28% (69.26–77.18)	7.31 (3.70–11.07)	$<$ 0.0001
Accuracy	83.26% (80.37–86.00)	78.69% (75.49–81.74)	4.57 (1.83–7.46)	0.0020
AUC	0.944 (0.923–0.963)	0.932 (0.909–0.953)	0.012 (-0.004–0.030)	0.1450
Kappa	0.626 (0.564–0.687)	0.552 (0.491–0.613)	0.074 (0.022–0.127)	0.0068
MCC	0.648 (0.591–0.704)	0.595 (0.540–0.649)	0.054 (0.005–0.103)	0.0314
Brier score	0.115 (0.102–0.128)	0.153 (0.141–0.166)	-0.038 (-0.047–(-)0.029)	$<$ 0.0001
DOR	39.31 (24.23–75.24)	37.93 (22.12–81.69)	1.37 (-30.29–26.44)	0.8938
J	71.03% (65.43–76.54)	66.54% (61.03–71.85)	4.50 (-0.57–9.70)	0.0808
LR+	4.66 (3.91–5.71)	3.49 (3.02–4.10)	1.17 (0.50–2.04)	0.0006
LR-	0.119 (0.067–0.175)	0.092 (0.045–0.146)	0.027 (-0.020–0.073)	0.2690
PPV	63.39% (57.44–69.26)	56.46% (50.81–62.06)	6.92 (3.07–11.01)	0.0006
NPV	95.78% (93.72–97.63)	96.69% (94.77–98.37)	-0.91 (-2.52–0.69)	0.2692

Performance of an AI model on data from a center included during training (in-domain), vs. the performance of an AI model trained on data from other centers (domain-shifted). Both models were evaluated on the same set of 657 cases from the Stockholm center. One of the models was trained on images from 500 cases from the Stockholm center (in-domain), while the other model was trained on images from 500 cases sampled from the other 19 centers (domain-shifted). Data are % (95% CI) or percentage points (95% CI) through bootstrapping, and p-values are based on two-sided non-parametric confidence interval tests. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient. DOR = diagnostic odds ratio. J = Youden's J statistic. LR+ = Positive likelihood ratio. LR– = Negative likelihood ratio. PPV = Positive predictive value. NPV = Negative predictive value.

Supplementary Table 12 | Performance of CNN-based model

	Transformer (DeiT)	CNN (ConvNeXt)
F1 score	83.50% (81.76–85.14)	82.83% (81.11–84.53)
Sensitivity	84.88% (82.73–86.96)	85.16% (82.97–87.24)
Specificity	87.30% (85.66–88.94)	85.90% (84.19–87.61)
Accuracy	86.32% (85.00–87.59)	85.60% (84.29–86.92)
AUC	0.929 (0.919–0.939)	0.925 (0.914–0.935)
Kappa	0.718 (0.691–0.745)	0.704 (0.677–0.732)
MCC	0.718 (0.691–0.745)	0.705 (0.678–0.733)
Brier score	0.108 (0.101–0.114)	0.118 (0.112–0.124)
DOR	38.61 (31.16–48.74)	34.98 (28.37–44.12)
J	72.19% (69.46–74.86)	71.07% (68.33–73.79)
LR+	6.68 (5.90–7.69)	6.04 (5.37–6.89)
LR-	0.173 (0.149–0.198)	0.173 (0.149–0.198)
PPV	82.16% (79.93–84.38)	80.63% (78.34–82.91)
NPV	89.34% (87.77–90.84)	89.37% (87.78–90.88)

Data in parentheses are 95% CIs through bootstrapping. Kappa = Cohen's kappa coefficient. MCC = Matthew's correlation coefficient. DOR = diagnostic odds ratio. J = Youden's J statistic. LR+ = Positive likelihood ratio. LR– = Negative likelihood ratio. PPV = Positive predictive value. NPV = Negative predictive value.

Supplementary Table 13 | Distribution of manufacturers and ultrasound systems

Ultrasound system	Cases
GE	3,353 (91.8%)
Voluson E8	1,607 (44.0%)
Voluson E10	1,006 (27.5%)
Voluson E6	325 (8.9%)
Voluson 730	171 (4.7%)
Voluson S10	132 (3.6%)
Voluson I	89 (2.4%)
Voluson S8	18 (0.5%)
Voluson P8	4 (0.1%)
Voluson S6	1 (0.0%)
Samsung	175 (4.8%)
WS80A	159 (4.4%)
HS70A	8 (0.2%)
Hera W10	7 (0.2%)
Accuvix A30	1 (0.0%)
Other	124 (3.4%)
Philips EPIQ	51 (1.4%)
Mindray DC-70	44 (1.2%)
Toshiba Aplio XG	15 (0.4%)
Esaote MyLab	10 (0.3%)
Mindray M9	1 (0.0%)
Aloka Prosound SSD-5000	1 (0.0%)
Canon Aplio i800	1 (0.0%)
Hitachi (unknown model)	1 (0.0%)

Counts are given with their percentage rate.

Supplementary Table 14 | Breakdown of histological diagnoses at different levels of granularity

2 classes	n	10 classes	n	18 classes	n	Histological	n
Benign	2,224 (60.9%)	Endometrioma	336 (9.2%)	Endometrioma	336 (9.2%)	Endometrioma	336 (9.2%)
		Dermoid	431 (11.8%)	Dermoid	431 (11.8%)	Dermoid	431 (11.8%)
		Other common benign	298 (8.2%)	Simple, Inclusion cyst	106 (2.9%)	Simple cyst	102 (2.8%)
						Inclusion cyst	4 (0.1%)
				Paraovarian cyst	47 (1.3%)	Paraovarian cyst	47 (1.3%)
				Functional cyst	54 (1.5%)	Functional cyst	54 (1.5%)
				Hydrosalpinx, Pyosalpinx, Tubo-ovarian abscess, Peritoneal cyst	91 (2.5%)	Hydrosalpinx	43 (1.2%)
						Pyosalpinx, Tubo-ovarian abscess	32 (0.9%)
						Peritoneal cyst	16 (0.4%)
		Solid benign	153 (4.2%)	Solid benign	153 (4.2%)	Fibroma	114 (3.1%)
						Thecoma	26 (0.7%)
						Myoma	13 (0.4%)
		Cystadeno(fibro)ma	707 (19.4%)	Cystadenoma (serous)	251 (6.9%)	Cystadenoma (serous)	251 (6.9%)
				Cystadenoma (mucinous)	283 (7.7%)	Cystadenoma (mucinous)	283 (7.7%)
				Cystadenofibroma	173 (4.7%)	Cystadenofibroma (serous)	151 (4.1%)
						Cystadenofibroma (mucinous)	22 (0.6%)
		*Rare benign**	66 (1.8%)	*Rare benign**	66 (1.8%)	Struma ovarii	23 (0.6%)
						Brenner tumor	15 (0.4%)
						Endometrioma (decidualized)	13 (0.4%)
						Schwannoma	4 (0.1%)
						Leydig cell tumor	3 (0.1%)
						Other rare benign	8 (0.2%)
		*Ultrasound follow-up**	233 (6.4%)	*Ultrasound follow-up**	233 (6.4%)	*Ultrasound follow-up**	233 (6.4%)
Malignant	1,428 (39.1%)	Borderline (serous)	207 (5.7%)	Borderline (serous)	207 (5.7%)	Borderline (serous)	207 (5.7%)
		Borderline (mucinous intestinal)	100 (2.7%)	Borderline (mucinous intestinal)	100 (2.7%)	Borderline (mucinous intestinal)	100 (2.7%)
		Ovarian cancer (epithelial)	804 (22.0%)	Ovarian cancer (serous), Carcinosarcoma, Tubal cancer	556 (15.2%)	Ovarian cancer (serous)	487 (13.3%)
						Tubal cancer	47 (1.3%)
						Carcinosarcoma	15 (0.4%)
						Other malignancy (epithelial)	7 (0.2%)
				Ovarian cancer (mucinous)	53 (1.5%)	Ovarian cancer (mucinous)	53 (1.5%)
				Ovarian cancer (endometrioid, clear-cell)	195 (5.3%)	Ovarian cancer (endometrioid)	132 (3.6%)
						Ovarian cancer (clear-cell)	63 (1.7%)
		Ovarian cancer (non-epithelial)	116 (3.2%)	Ovarian cancer (non-epithelial)	116 (3.2%)	Granulosa cell tumor	49 (1.3%)
						Yolc sac tumor	11 (0.3%)
						Dysgerminoma	10 (0.3%)
						Sertoli-Leydig cell tumor	10 (0.3%)
						Mixed Germcell tumor	8 (0.2%)
						Other malignancy (non-epithelial)	28 (0.8%)
		Metastasis	201 (5.5%)	Metastasis (colorectal, pancreas)	74 (2.0%)	Metastasis (colorectal)	66 (1.8%)
						Metastasis (pancreas)	8 (0.2%)
				Metastasis (other)	127 (3.5%)	Metastasis (gastric)	41 (1.1%)
						Metastasis (breast)	24 (0.7%)
						Metastasis (endometrial)	7 (0.2%)
						Metastasis (lymphoma)	4 (0.1%)
						Metastasis (other)	51 (1.4%)

Counts are given with their percentage rate. Histological diagnoses were grouped into ten and 18 categories based on histological diagnosis from surgery and sonographic characteristics. *For training, rare benign and ultrasound follow-up cases were, where possible, assigned to one of the other benign histological classes, based on the sonographic characteristics (as assessed by one expert examiner [E.E.]).

Supplementary Table 15 | Center-wise summary of test dataset characteristics, separately for benign and malignant cases

Center	Images per case		Year of examination		Age	
	Benign	Malignant	Benign	Malignant	Benign	Malignant
Ancona, Italy	3 (3–4)	4 (3–5)	2020 (2020–2020)	2019 (2019–2020)	49 (38–60)	55 (44–70)
Athens, Greece	5 (3–6)	7 (4–10)	2019 (2018–2020)	2019 (2019–2020)	40 (32–49)	46 (33–61)
Barcelona, Spain	4 (4–5)	4 (4–5)	2015 (2012–2019)	2014 (2012–2019)	42 (32–47)	49 (40–62)
Bologna, Italy	4 (3–6)	6 (4–7)	2018 (2017–2019)	2018 (2016–2019)	44 (33–57)	45 (34–56)
Brescia, Italy	4 (3–6)	5 (3–8)	2017 (2016–2019)	2018 (2016–2020)	45 (34–54)	61 (52–67)
Cagliari, Italy	4 (3–5)	4 (3–6)	2010 (2010–2011)	2010 (2010–2011)	42 (34–48)	53 (32–62)
Katowice, Poland	3 (2–3)	4 (3–6)	2017 (2015–2019)	2017 (2014–2018)	38 (32–42)	51 (45–62)
Kaunas, Lithuania	6 (4–8)	6 (4–10)	2020 (2018–2020)	2019 (2018–2020)	41 (31–59)	54 (43–68)
Lublin, Poland	4 (3–5)	4 (3–6)	2017 (2016–2020)	2016 (2016–2020)	42 (32–54)	55 (42–64)
Lund, Sweden	2 (2–3)	3 (2–4)	2020 (2019–2020)	2020 (2019–2020)	47 (34–64)	62 (47–73)
Manila, Philippines	5 (4–7)	4 (3–5)	2019 (2019–2020)	2019 (2019–2019)	32 (24–44)	51 (38–57)
Milan, Italy	4 (3–4)	4 (3–6)	2017 (2016–2018)	2017 (2016–2018)	50 (36–55)	52 (45–62)
Milan 2, Italy	4 (3–4)	3 (2–4)	2016 (2013–2019)	2016 (2012–2018)	44 (35–59)	55 (47–65)
Monza, Italy	3 (3–4)	5 (4–6)	2018 (2018–2019)	2018 (2017–2019)	44 (35–54)	58 (48–69)
Pamplona, Spain	3 (2–3)	3 (2–3)	2010 (2009–2011)	2010 (2009–2011)	39 (27–50)	52 (41–67)
Prague, Czech Republic	6 (4–6)	4 (4–6)	2020 (2020–2020)	2020 (2019–2020)	56 (39–68)	58 (46–68)
Prague 2, Czech Republic	5 (3–5)	5 (4–7)	2014 (2012–2015)	2014 (2012–2014)	36 (31–48)	51 (41–62)
Stockholm, Sweden	5 (3–8)	7 (4–9)	2019 (2018–2020)	2019 (2018–2020)	49 (35–59)	58 (44–72)
Trieste, Italy	5 (4–7)	8 (6–10)	2020 (2020–2020)	2020 (2019–2020)	52 (40–59)	56 (51–60)
OVERALL	**4 (3–5)**	**4 (3–6)**	**2018 (2016–2020)**	**2018 (2016–2020)**	**43 (33–55)**	**55 (44–65)**

Data are median (IQR).

References

[1] Van Calster, B. et al. A calibration hierarchy for risk models was defined: from utopia to empirical data. *J. Clin. Epidemiol.* **74**, 167–176 (2016).

[2] Redmon, J., Divvala, S., Girshick, R. & Farhadi, A. You only look once: unified, real-time object detection. *Proceedings of the IEEE Conference on Computer Vision and Pattern Recognition*, 779–788 (2016).