# nature portfolio

**Supplementary information**

# An ensemble of neural networks provides expert-level prenatal detection of complex congenital heart disease

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**Supplementary Information**

Ensemble learning models provide expert-level prenatal detection of complex congenital heart disease

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**Supplemental Tables**

## Table S1. Training and test datasets.

| Data Source | Dataset Name | Dataset Notes | Normal Echo | CHD Echo | Normal US | CHD US | Total |
|---|---|---|---|---|---|---|---|
| UCSF – Source Data | Training | 90% of Source Data<br>Subset of studies used for:<br>- view classifier: 926<br>- diagnostic classifiers: 1,316<br>- segmentation: 1,248 | 787 | 400 | 139 | | 1,326 |
| | FETAL-125 | 10% of Source Data, by lesion | 88 | 37 | | | 125 |
| UCSF – Additional Data | OB-125 | same patients as in FETAL-125 | | | 88 | 37 | 125 |
| UCSF – Additional Data | OB-4000 | includes OB-125 | | | 4,071 | 37 | 4,108 |
| UCSF – Additional Data | TWINS-10 | 10 sets of twins, two sets with 1 normal fetus, 1 CHD fetus | 18 | 2 | | | 20 |
| Boston Children's – Additional Data | BCH-400 | | 32 | 391 | | | 423 |

CHD, congenital heart disease; Echo; fetal echocardiogram. US, fetal screening ultrasound.

**Table S2. Summary of diagnostic performance in different test cases.** CHD prevalence is again shown to aid in interpretation of predictive values; the prevalence of CHD in a typical population is 0.8-1%, and in a high-risk population is about 5%[10].

| Method | Model | Model | Model | Clinicians | Model | Model | Model | Model | Model | Model | Model |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Test set | FETAL-125* | OB-125* | OB-125† | OB-125‡ | OB-125§ | OB-4000* | OB-4000‖ | BCH-400* | Twins‖ | OB-125 NL vs. TOF* | OB-125 NL vs. HLHS* |
| CHD prevalence | 30% | 30% | 30% | 30% | 30% | 0.9% | 0.9% | 92% | 10% | 6% | 8% |
| Sensitivity | 100% (95% CI 90-100) | 95% (95% CI 84-99) | 88% (95% CI 47-100) | 86% (95% CI 82-90) | 95% (95% CI 88-96) | 95% (95% CI 84-99) | 95% (95% CI 84-99) | 98% (95% CI 96-99) | 100% (95% CI 15-100) | 71% (95% CI 29-96) | 89% (95% CI 52-100) |
| Specificity | 62% (95% CI 51-72) | 68% (95% CI 57-78) | 90% (95% CI 73-98) | 68% (95% CI 64-72) | 39% (95% CI 28-50) | 59% (95% CI 57-61) | 56% (95% CI 55-58) | 41% (95% CI 24-59) | 72% (95% CI 47-90) | 89% (95% CI 80-94) | 92% (95% CI 84-97) |
| PPV | 51% (95% CI 45-58) | 59% (95% CI 51-66) | 70% (95% CI 44-88) | 44% (95% CI 39-48) | 41% (95% CI 37-46) | 52% (95% CI 50-54) | 2% (95% CI 2) | 95% (95% CI 94-96) | 29% (95% CI 16-46) | 33% (95% CI 19-51) | 53% (95% CI 35-71) |
| NPV | 100% (95% CI 100) | 97% (95% CI 89-99) | 96% (95% CI 81-99) | 95% (95% CI 95-96) | 94% (95% CI 91-97) | 94% (95% CI 81-99) | 100% (95% CI 100) | 59% (95% CI 40-76) | 100% (95% CI 100) | 98% (95% CI 92-99) | 99% (95% CI 93-100) |
| AUC | 0.98 | 0.93 | 0.98 | — | 0.91 | 0.92 | 0.99 | 0.89 | 0.89 | 0.83 | 0.98 |

\* All possible images present
† Only 5 images present, one image per view
‡ Low-quality images (target views not chosen by human labelers)
§ 6.5 percent of views scrambled to simulate error in view classification
‖ high-confidence images (only used images with view-prediction probabilities greater the first quartile for diagnosis)
CHD = congenital heart disease, NPV= negative predictive value, PPV = positive predictive value, NL = normal, TOF = tetralogy of Fallot, HLHS = hypoplastic left heart syndrome

**Table S3. Average Jaccard similarities for labeled and predicted anatomic structures.**

| Structure | thorax | heart | RA | RV | LA | LV | spine | bkgrnd |
|---|---|---|---|---|---|---|---|---|
| Overall | 0.79 | 0.86 | 0.77 | 0.70 | 0.63 | 0.60 | 0.67 | 0.99 |
| Normal | 0.80 | 0.87 | 0.82 | 0.77 | 0.72 | 0.78 | 0.69 | 0.99 |
| TOF | 0.73 | 0.86 | 0.81 | 0.63 | 0.64 | 0.65 | 0.47 | 0.98 |
| HLHS | 0.77 | 0.82 | 0.66 | 0.59 | 0.47 | 0.29 | 0.62 | 0.99 |

TOF, tetralogy of Fallot; HLHS, hypoplastic left heart syndrome; RA, right atrium;
RV, right ventricle; LA, left atrium; LV, left ventricle.