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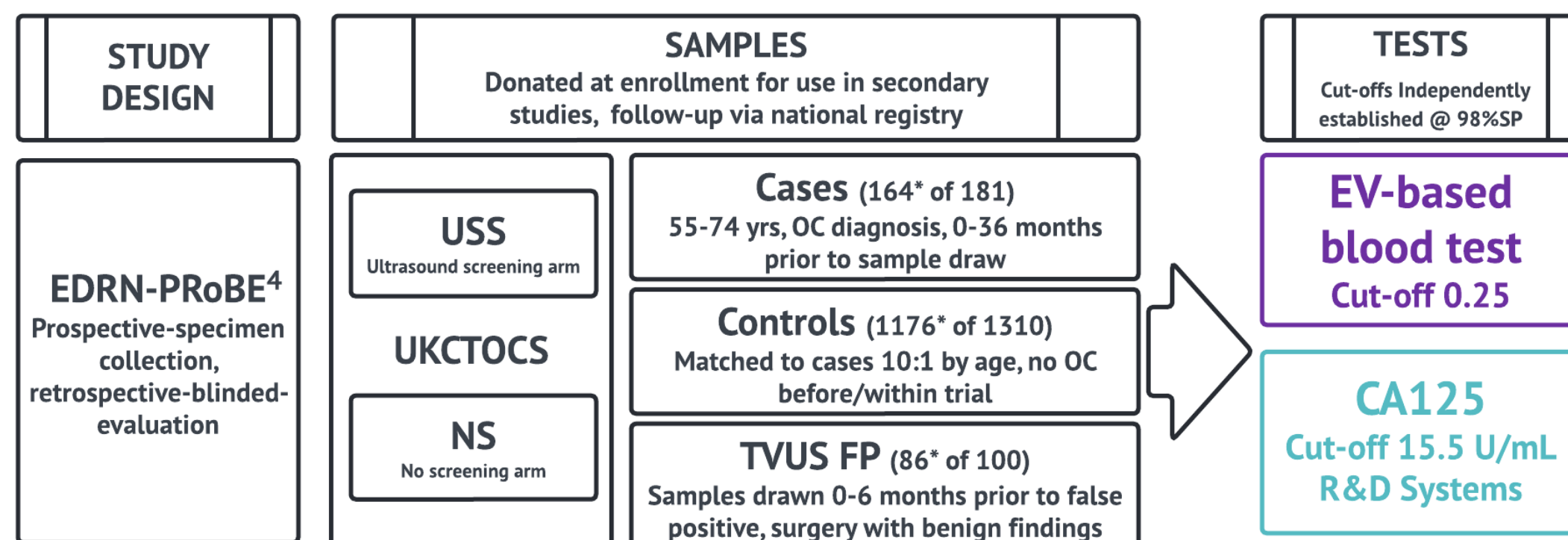
Introduction

- Screening for ovarian cancer (OC) that relies on CA125 and imaging lacks early-stage sensitivity and specificity.
- In the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) there was a significant decrease (10%) in late-stage high grade serous ovarian cancer (HGSC) but no decrease in deaths. The authors concluded that to achieve mortality reduction, novel methods are required that detect more women with HGSC, earlier in the course of the disease.^{1,2,3}
- Extracellular vesicles (EVs) in blood offer increased sensitivity due to their abundance and specificity through the detection of multiple colocalized cancer-related biomarkers.
- The Mercy Halo EV-based blood test was locked (biomarkers, classifier, cut-off) following a training study, after which we observed consistent assay performance in an independent cohort.
- Here we report on the performance of the EV-based blood test in a retrospective-blinded-evaluation nested within the United Kingdom Collaborative Trial of Ovarian Cancer Screening (UKCTOCS) which represents the intended target population for clinical application of this test.

Conclusions

- The EV-based blood test is capable of highly sensitive and specific detection of early-stage HGSC in asymptomatic postmenopausal women with superior sensitivity and specificity compared to CA125 (cut-off 15.5 U/mL).
- The rigor of the PRoBE design and use of the best possible cut-off for the CA125 comparison supports the conclusion that the EV-based blood test may be suitable for ovarian cancer screening.
- Future research will focus on the evaluation of the EV-based blood test in samples from ovarian cancer screening trials with longitudinal data.

Methods



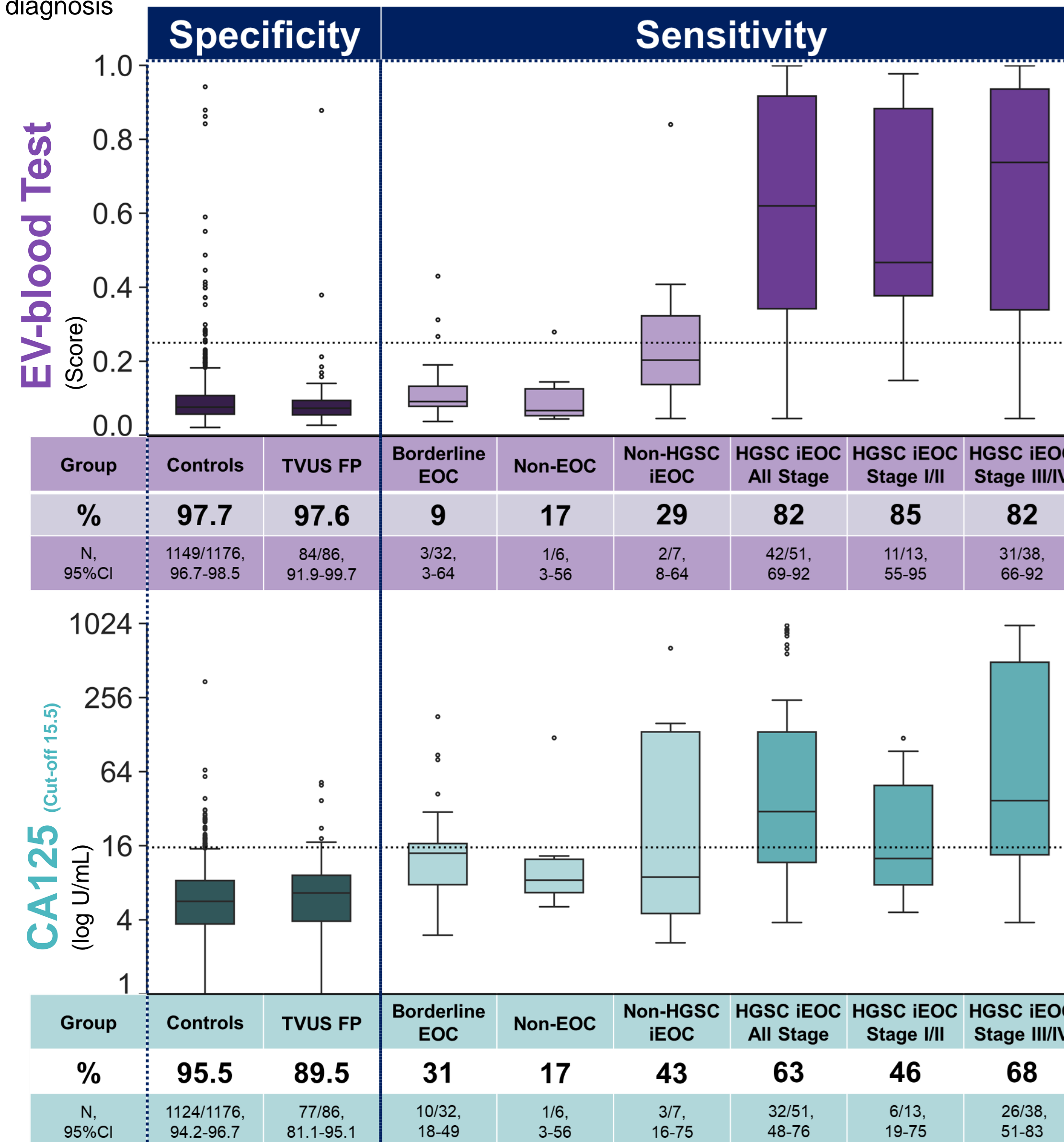
References

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Key Takeaways

- The **EV-based blood test** has significantly **higher sensitivity and specificity** over CA125 (Cut-off 15.5 U/mL) in **asymptomatic women**
- The EV-blood test may be **suitable for ovarian cancer screening**.

Fig 1 . EV-based blood test and CA125 sensitivity and specificity by group, 0-12 month prior to diagnosis



*EOC = Epithelial ovarian cancer, iEOC = Invasive epithelial ovarian cancer

Results

- The **sensitivity** 0-12 months prior to diagnosis of HGSC of the **EV-based blood test was 82% (85% Stage I/II)** and CA125 at a cut-off of 15.5 U/mL was 63% (46% Stage I/II), P = 0.011 McNemar test. (Fig 1)
- The **specificity** in controls, of the **EV-based blood test was 97.7%**, and of CA125 was 95.5%, P = 0.005 McNemar test. (Fig 1)
- The **AUC** 0-12 months prior to diagnosis of the **EV-based blood test was 0.94 (0.98 Stage I/II)** and **0.87 (0.80 Stage I/II)** for CA125. (Fig 2)
- The EV-based blood test was able to detect HGSC up to **3 years prior to diagnosis**. (Table 1)
- In samples from women with a **false positive transvaginal ultrasound (TVUS FP)** who underwent trial surgery in the USS arm and had benign pathology, **the specificity of the EV-Blood Test was 97.6%** and of CA125 was 89.5%. (Fig 1)

Fig 2. ROC Curves for EV-based blood test and CA125 for HGSC for samples drawn 0-12 months prior to diagnosis. (*P < 0.05 Delong's Test)

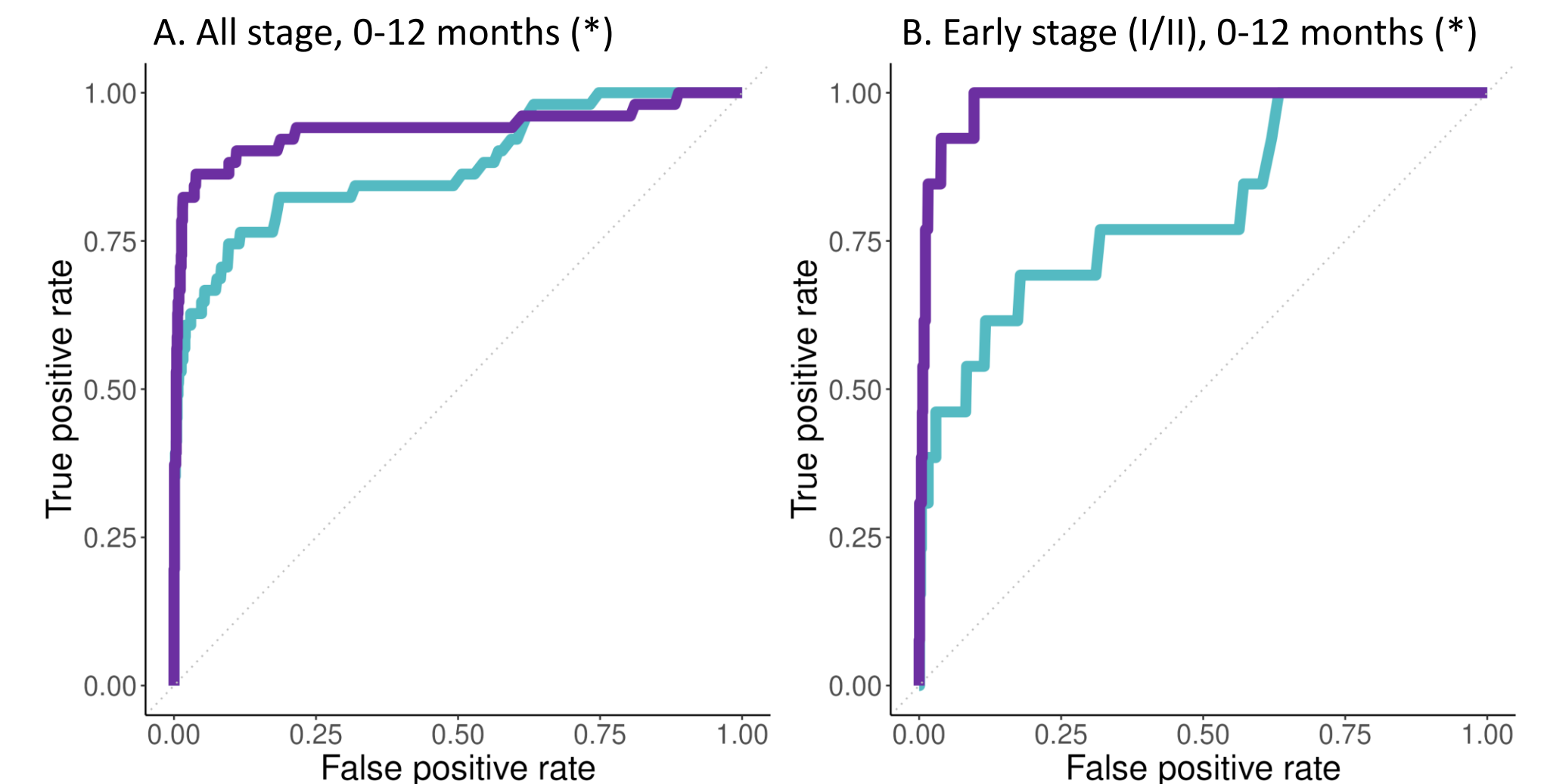


Table 1. EV-based blood test and CA125 sensitivity for 13-24, and 25-36 months prior to diagnosis by stage

HGSC iEOC		EV based blood test % (N, 95% CI)	CA125 % (N, 95% CI)
13-24 Months	All Stage	25 (7/28, 11-45)	25 (7/28, 11-45)
	Stage I/II	0 (0/6, 0-39)	33 (2/6, 4-78)
	Stage III/IV	32 (7/22, 14-55)	23 (5/22, 8-45)
25-36 Months	All Stage	15 (6/40, 6-30)	5 (2/40, 1-17)
	Stage I/II	50 (3/6, 12-88)	17 (1/6, 0-64)
	Stage III/IV	9 (3/34, 2-24)	3 (1/34, 0-15)