

Supplement 10: Additional diagnostic accuracy metrics

Table S10.1. Diagnostic of accuracy of using CA125 thresholds equating to ~1% and ~3% risk of invasive ovarian cancer, compared to standard practice (CA125 $\geq$ 35U/ml)

Sub-group (invasive ovarian cancer incidence)	CA125 threshold	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
All ages 18-89 years	$\geq$ 35	84.9 (83.8; 86.4)	93.6 (93.5; 93.6)	7.7 (7.3; 8.0)	99.9 (99.9; 99.9)
	Applied by age category	87.7 (86.2; 89.1)	91.6 (91.5; 91.7)	6.1 (5.8; 6.3)	99.9 (99.9; 99.9)
		78.0 (76.1; 79.7)	97.6 (97.6; 97.6)	16.8 (16.1; 17.6)	99.9 (99.8; 99.9)
Age 18-49 years (0.21%)	$\geq$ 35	75.3 (70.0; 80.0)	92.5 (92.3; 92.6)	2.0 (1.8; 2.3)	99.9 (99.9; 100)
	$\geq$ 46	67.9 (62.3; 73.2)	95.8 (95.7; 95.9)	3.2 (2.8; 3.7)	99.9 (99.9; 99.9)
	$\geq$ 123	48.8 (43.0; 54.6)	99.1 (99.1; 99.2)	10.7 (9.1; 12.5)	99.9 (99.9; 99.9)
All ages 50-89 years (0.92%)	$\geq$ 35	86.2 (84.6; 87.8)	94.6 (94.5; 94.7)	12.8 (12.2; 13.4)	99.9 (99.8; 99.9)
	Applied by age category	91.0 (89.6; 92.3)	88.5 (88.3; 88.6)	6.8 (6.5; 7.1)	99.9 (99.9; 99.9)
		82.8 (81.0; 84.6)	96.5 (96.4; 96.6)	17.8 (17.0; 18.7)	99.8 (99.8; 99.9)
Age 50-59 years (0.52%)	$\geq$ 35	80.5 (76.3; 84.3)	95.7 (76.3; 84.3)	8.8 (7.9; 9.7)	99.9 (99.9; 99.9)
	$\geq$ 26	84.8 (80.9; 88.2)	91.6 (91.4; 91.8)	5.0 (4.5; 5.5)	99.9 (99.9; 99.9)
	$\geq$ 57	72.3 (67.7; 76.6)	98.1 (98.0; 98.2)	16.7 (14.9; 18.5)	99.9 (99.8; 99.9)
Age 60-69 years (1.05%)	$\geq$ 35	86.9 (83.9; 89.5)	95.9 (95.8; 96.1)	18.5 (17.1; 19.9)	99.9 (99.8; 99.9)
	$\geq$ 22	92.4 (90.0; 94.4)	89.3 (89.0; 89.5)	8.4 (7.7; 9.1)	99.9 (99.8; 99.9)
	$\geq$ 37	86.6 (83.6; 89.2)	96.2 (96.1; 96.4)	19.7 (18.2; 21.3)	99.9 (99.8; 99.9)
Age 70-79 years (1.32%)	$\geq$ 35	87.7 (84.6; 90.3)	93.6 (93.4; 93.8)	15.5 (14.2; 16.8)	99.8 (99.8; 99.9)
	$\geq$ 22	93.5 (91.0; 95.4)	84.7 (84.4; 85.1)	7.6 (6.9; 8.2)	99.9 (99.9; 99.9)
	$\geq$ 41	86.4 (83.2; 89.2)	94.9 (94.6; 95.1)	18.3 (16.8; 19.9)	99.8 (99.8; 99.8)
Age 80-89 years (1.26%)	$\geq$ 35	90.6 (88.6; 93.9)	88.6 (88.1; 89.0)	9.2 (8.1; 10.4)	99.9 (99.8; 99.9)
	$\geq$ 26	92.2 (88.1; 95.1)	81.8 (81.2; 82.3)	6.1 (5.3; 6.9)	99.9 (99.8; 99.9)
	$\geq$ 58	83.1 (78.0; 87.5)	94.0 (93.6; 94.3)	15.0 (13.2; 16.9)	99.8 (99.7; 99.8)
CA125 = cancer antigen 125, CI = confidence interval; NPV = negative predictive value; PPV = positive predictive value					

Table S10.2: The diagnostic accuracy of Ovatoools at >1% and >3% risk by early and late-stage cancer, compared to using CA125 >35U/ml

Outcome (incidence)	CA125/Ovatoools threshold	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
Early-stage invasive OC (n=580, 0.17%)	CA125 $\geq$ 35U/mL	66.7 (62.7; 70.6)	93.6 (93.5; 93.7)	1.8 (1.6; 1.9)	99.9 (99.9; 99.9)
	$\geq$ 1%	70.7 (66.8; 74.4)	92.5 (92.4; 92.5)	1.6 (1.4; 1.7)	99.9 (99.9; 100)
	$\geq$ 3%	51.7 (47.6; 55.9)	97.8 (97.7; 97.8)	3.8 (3.4; 4.2)	99.9 (99.9; 99.9)
Late-stage invasive OC (n=1247, 0.37%)	CA125 $\geq$ 35U/mL	93.3 (91.8; 94.7)	93.6 (93.5; 93.7)	5.1 (4.8; 5.4)	100 (100; 100)
	$\geq$ 1%	94.6 (93.2; 95.8)	92.5 (92.4; 92.5)	4.4 (4.2; 4.7)	100 (100; 100)
	$\geq$ 3%	89.6 (87.7; 91.2)	97.8 (97.7; 97.8)	12.8 (12.1; 13.5)	100 (100; 100)

Table S10.3: The diagnostic accuracy of Ovatoools at $\geq 1\%$ and $\geq 3\%$ risk to detect any ovarian cancer including borderline tumours, compared to using CA125 $\geq 35\text{U/ml}$

Sub-group (ovarian cancer incidence %)	CA125/Ovatoools threshold	Sensitivity, % (95% CI)	Specificity, % (95% CI)	PPV, % (95% CI)	NPV, % (95% CI)
All women (0.78)	CA125 $\geq 35\text{U/mL}$	78.6 (77.0;80.2)	93.6 (93.5;93.7)	8.8 (8.4;9.2)	99.8 (99.8;99.8)
	$\geq 1\%$	81.1 (79.5; 82.5)	92.5 (92.4;92.5)	7.7 (7.4; 8.1)	99.9 (99.8;99.9)
	$\geq 3\%$	69.3 (67.5; 71.1)	97.8 (97.7; 97.8)	19.5 (18.7; 20.3)	99.8 (99.7; 99.8)
	$\geq 1\%$	88.0 (86.5; 89.3)	89.2 (89.0; 89.3)	8.1 (7.8; 8.5)	99.9 (99.8; 99.9)
	$\geq 3\%$	77.8 (76.0; 79.5)	96.6 (96.5; 96.7)	19.9 (19.1; 20.8)	99.7 (99.7; 99.8)