Supplementary Tables

Development and external validation of prediction algorithms to improve early diagnosis of cancer

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Supplementary Table 1. Numbers of men and women meeting the inclusion and exclusion criteria for the derivation cohort and each validation cohort.

	QResearch derivation	*QResearch validation*	*CPRD validation*	*QResearch derivation*	*QResearch validation*	*CPRD validation*
	Women (col %)	**Women (col %)**	**Women (col %)**	**Men(col%)**	**Men (col%)**	**Women (col %)**
total number of practices	1,071	357	398	1,071	357	398
total population aged 18-84	5,984,513 (100)	2,149,197 (100)	1,910,399	5,752,370 (100)	2,067,128 (100)	1,815,127
Exclusions						
no Townsend recorded	101,465 (1.7)	35,018 (1.6)	n/a	79,745 (1.4)	27,334 (1.3)	n/a
at least one red flag symptom in 12 months before cohort entry	382,174 (6.4)	135,133 (6.3)	120,522 (6.3)	235,354 (4.1)	81,951 (4.0)	74,491 (4.10)
Less than 2 years follow-up	1,878,085 (31.4)	702,031 (32.7)	416,871 (21.8)	1,595,553 (27.7)	597,674 (28.9)	376,916 (20.8)
Included						
Target group after exclusions	3,622,789 (60.5)	1,277,015 (59.4)	1,373,006 (71.9)	3,841,718 (66.8)	1,360,169 (65.8)	1,363,720 (75.1)
Total incident cancers during 2 years' follow-up	64,233	22,105	16,590	65,482	22,879	15,738

Supplementary Table 2: Baseline characteristics of men and women aged 18-84 years in the English QResearch derivation and validation cohorts. Values are numbers (column%) unless indicated otherwise.

	QResearch derivation women	*QResearch* validation women	*CPRD* validation women	*QResearch* derivation men	*QResearch* validation men	*CPRD* validation men
total	3622789	1277015	1373006	3841718	1360169	1363720
mean age (SD)	44.9 (17.9)	44.6 (18.0)	48.5 (18.0)	44.3 (17.1)	44.1 (17.2)	47.5 (17.4)
mean Townsend (SD)	0.5 (3.1)	0.5 (3.2)	0.0 (0.0)	0.6 (3.1)	0.6 (3.2)	0.0 (0.0)
mean BMI (SD)	26.9 (6.2)	26.8 (6.2)	133.1 (12.1)	27.3 (5.2)	27.3 (5.2)	147.6 (14.2)
mean HB (SD)	131.5 (12.4)	131.5 (12.4)	8.9 (5.0)	146.9 (14.1)	146.8 (14.1)	11.4 (6.5)
mean bilirubin (SD)	8.9 (5.1)	9.0 (5.1)	275.0 (70.4)	11.4 (6.4)	11.4 (6.4)	244.8 (66.8)
mean platelet (SD)	269.5 (69.8)	268.2 (69.6)	42.0 (4.3)	241.1 (65.7)	240.2 (65.7)	42.8 (4.4)
mean neutrophil (SD)	4.2 (1.9)	4.2 (1.9)	4.3 (1.9)	4.2 (1.9)	4.2 (1.9)	4.3 (1.8)
mean lymphocyte (SD)	2.1 (0.9)	2.1 (0.9)	2.1 (0.8)	2.1 (1.1)	2.1 (1.1)	2.1 (1.0)
mean albumin (SD)	42.2 (4.1)	42.3 (4.1)	79.3 (33.0)	43.0 (4.2)	43.1 (4.2)	79.3 (33.4)
mean alkaline phosphophatase (SD)	79.0 (35.1)	78.6 (34.0)	27.5 (5.6)	80.2 (35.8)	79.8 (35.0)	28.1 (4.9)
Ethnicity						
White	1909660(52.7)	670729 (52.5)	431376 (31.4)	1870458(48.7)	655747 (48.2)	414206 (30.4)
Indian	112558 (3.1)	35353 (2.8)	3725 (0.3)	129706 (3.4)	42315 (3.1)	5136 (0.4)
Pakistani	70054 (1.9)	18703 (1.5)	3208 (0.2)	84342 (2.2)	22961 (1.7)	4077 (0.3)
Bangladeshi	38716 (1.1)	15124 (1.2)	967 (0.1)	47999 (1.2)	18688 (1.4)	1399 (0.1)
Other Asian	82110 (2.3)	26737 (2.1)	3165 (0.2)	84431 (2.2)	25905 (1.9)	2675 (0.2)
Caribbean	40903 (1.1)	15444 (1.2)	377 (0.0)	37762 (1.0)	14381 (1.1)	345 (0.0)
Black African	95415 (2.6)	39923 (3.1)	3048 (0.2)	98852 (2.6)	41359 (3.0)	3739 (0.3)
Chinese	53693 (1.5)	14264 (1.1)	3448 (0.3)	43876 (1.1)	11804 (0.9)	3097 (0.2)
Other	162493 (4.5)	59412 (4.7)	7397 (0.5)	162376 (4.2)	60764 (4.5)	7674 (0.6)
not recorded	1057187(29.2)	381326 (29.9)	916295 (66.7)	1281916(33.4)	466245 (34.3)	921372 (67.6)
Smoking status						
nonsmoker	2190621(60.5)	784168 (61.4)	618077 (45.0)	1881690(49.0)	674289 (49.6)	547614 (40.2)
ex-smoker	639178 (17.6)	220803 (17.3)	254369 (18.5)	788647 (20.5)	275302 (20.2)	278308 (20.4)
light smoker	418867 (11.6)	146106 (11.4)	63426 (4.6)	598051 (15.6)	209634 (15.4)	56158 (4.1)
moderate smoker	95114 (2.6)	32254 (2.5)	95306 (6.9)	137925 (3.6)	47414 (3.5)	116788 (8.6)
heavy smoker	32890 (0.9)	11237 (0.9)	35058 (2.6)	73493 (1.9)	25450 (1.9)	60379 (4.4)
not recorded	246119 (6.8)	82447 (6.5)	306770 (22.3)	361912 (9.4)	128080 (9.4)	304473 (22.3)
Alcohol status						
non drinker	1812244(50.0)	642391 (50.3)	227544 (16.6)	1627240(42.4)	574725 (42.3)	154012 (11.3)
Trivial <1u/day	628130 (17.3)	227435 (17.8)	393461 (28.7)	511950 (13.3)	186273 (13.7)	258007 (18.9)
Light 1-2u/day	238654 (6.6)	79429 (6.2)	227204 (16.5)	287031 (7.5)	100298 (7.4)	279840 (20.5)
Moderate 3-6u/day	112466 (3.1)	38098 (3.0)	24979 (1.8)	283221 (7.4)	99093 (7.3)	89435 (6.6)
Heavy 7-9u/day	5354 (0.1)	1957 (0.2)	2587 (0.2)	26550 (0.7)	9092 (0.7)	11699 (0.9)
Very Heavy >9u/day	9242 (0.3)	2526 (0.2)	4379 (0.3)	24652 (0.6)	7483 (0.6)	15481 (1.1)
not recorded	816699 (22.5)	285179 (22.3)	492852 (35.9)	1081074(28.1)	383205 (28.2)	555246 (40.7)

Values recorded						
BMI	1728424(47.7)	615409 (48.2)	420387 (30.6)	1415516(36.8)	507034 (37.3)	308094 (22.6)
HB	1559943(43.1)	545269 (42.7)	467740 (34.1)	1147505(29.9)	397329 (29.2)	395410 (29.0)
bilirubin	1378849(38.1)	478996 (37.5)	503207 (36.7)	1180911(30.7)	408916 (30.1)	368430 (27.0)
platelet	1563327(43.2)	545445 (42.7)	433269 (31.6)	1151720(30.0)	398168 (29.3)	363284 (26.6)
neutrophil	1558858 43.0)	543198 (42.5)	490879 (35.8)	1147694(29.9)	396617 (29.2)	358476 (26.3)
lymphocyte	1557563(43.0)	541656 (42.4)	487243 (35.5)	1146078(29.8)	395205 (29.1)	355864 (26.1)
albumin	1363228(37.6)	478613 (37.5)	472673 (34.4)	1149327(29.9)	402155 (29.6)	397471 (29.1)
alkaline phosphatase	1403482(38.7)	487839 (38.2)	507475 (37.0)	1187780(30.9)	411274 (30.2)	416817 (30.6)
Family history (FH)						
FH breast cancer	205540 (5.7)	72004 (5.6)	35 (0.0)	48558 (1.3)	16109 (1.2)	22 (0.0)
FH bowel cancer	82357 (2.3)	28745 (2.3)	29769 (2.2)	60183 (1.6)	20422 (1.5)	4406 (0.3)
FH ovarian cancer	14239 (0.4)	4751 (0.4)	12021 (0.9)	2287 (0.1)	747 (0.1)	8170 (0.6)
FH prostate cancer	11242 (0.3)	3611 (0.3)	2624 (0.2)	28924 (0.8)	10069 (0.7)	299 (0.0)
FH lung cancer	33414 (0.9)	9836 (0.8)	710 (0.1)	26579 (0.7)	7760 (0.6)	2853 (0.2)
FH blood cancer	997 (0.0)	388 (0.0)	3437 (0.3)	1176 (0.0)	395 (0.0)	2469 (0.2)
Comorbidity						
chronic pancreatitis	1810 (0.0)	619 (0.0)	720 (0.1)	3438 (0.1)	1186 (0.1)	1350 (0.1)
COPD	61712 (1.7)	21110 (1.7)	26881 (2.0)	70917 (1.8)	24450 (1.8)	27148 (2.0)
type 2 diabetes	151045 (4.2)	52392 (4.1)	48910 (3.6)	211853 (5.5)	73549 (5.4)	67971 (5.0)
endometrial hyperplasia/polyp	21394 (0.6)	7593 (0.6)	5271 (0.4)	n/a	n/a	n/a
liver cirrhosis	5420 (0.1)	1948 (0.2)	2256 (0.2)	6230 (0.2)	2214 (0.2)	2325 (0.2)
Hepatitis C	4957 (0.1)	1615 (0.1)	1177 (0.1)	10303 (0.3)	3233 (0.2)	2288 (0.2)
Hepatitis B	8822 (0.2)	3161 (0.2)	1193 (0.1)	9456 (0.2)	3346 (0.2)	1667 (0.1)
HIV/AIDs	4113 (0.1)	1607 (0.1)	424 (0.0)	9662 (0.3)	3528 (0.3)	1310 (0.1)
General symptoms						
erectile dysfunction	n/a	n/a	n/a	51896 (1.4)	18423 (1.4)	17725 (1.3)
constipation	41432 (1.1)	14299 (1.1)	11603 (0.8)	26850 (0.7)	9391 (0.7)	7340 (0.5)
cough	204061 (5.6)	71164 (5.6)	84119 (6.1)	159332 (4.1)	55426 (4.1)	63623 (4.7)
urinary frequency	31505 (0.9)	10915 (0.9)	6359 (0.5)	16014 (0.4)	5519 (0.4)	4498 (0.3)
urinary retention	1432 (0.0)	480 (0.0)	253 (0.0)	5651 (0.1)	1983 (0.1)	1409 (0.1)
nocturia	3568 (0.1)	1674 (0.1)	811 (0.1)	7780 (0.2)	2684 (0.2)	2518 (0.2)
itching	15094 (0.4)	5268 (0.4)	5878 (0.4)	8995 (0.2)	3219 (0.2)	3392 (0.2)
change in bowels	10068 (0.3)	3500 (0.3)	2556 (0.2)	8586 (0.2)	3058 (0.2)	2042 (0.1)
bruising	6121 (0.2)	2105 (0.2)	1667 (0.1)	2259 (0.1)	786 (0.1)	651 (0.0)
back pain	219420 (6.1)	75651 (5.9)	63642 (4.6)	172518 (4.5)	59356 (4.4)	50547 (3.7)
hoarseness	8514 (0.2)	3048 (0.2)	2274 (0.2)	4661 (0.1)	1651 (0.1)	1139 (0.1)
flatulence	40048 (1.1)	13802 (1.1)	8739 (0.6)	16601 (0.4)	5580 (0.4)	3267 (0.2)
abdominal mass	5133 (0.1)	1633 (0.1)	779 (0.1)	4503 (0.1)	1382 (0.1)	713 (0.1)
dark urine	2580 (0.1)	887 (0.1)	33 (0.0)	1979 (0.1)	713 (0.1)	49 (0.0)
Alarm symptoms						
appetite loss	20711 (0.6)	6405 (0.5)	2293 (0.2)	14990 (0.4)	4719 (0.3)	1909 (0.1)
weight loss	32900 (0.9)	11146 (0.9)	7156 (0.5)	34045 (0.9)	11466 (0.8)	7345 (0.5)

abdominal distension	41502 (1.1)	14373 (1.1)	9695 (0.7)	17050 (0.4)	5836 (0.4)	3529 (0.3)
abdominal pain	242159 (6.7)	84176 (6.6)	63193 (4.6)	181651 (4.7)	62791 (4.6)	51031 (3.7)
dysphagia	20830 (0.6)	7489 (0.6)	5199 (0.4)	20679 (0.5)	7225 (0.5)	5244 (0.4)
heartburn	94113 (2.6)	32380 (2.5)	30847 (2.2)	82720 (2.2)	28730 (2.1)	26711 (2.0)
indigestion	62435 (1.7)	20477 (1.6)	16476 (1.2)	52857 (1.4)	17627 (1.3)	13898 (1.0)
haematemesis	7096 (0.2)	2497 (0.2)	2428 (0.2)	10345 (0.3)	3622 (0.3)	3542 (0.3)
rectal bleeding	56450 (1.6)	19768 (1.5)	14315 (1.0)	68190 (1.8)	23974 (1.8)	17341 (1.3)
haematuria	41837 (1.2)	14628 (1.1)	8404 (0.6)	49099 (1.3)	17345 (1.3)	12060 (0.9)
haemoptysis	8727 (0.2)	3020 (0.2)	2466 (0.2)	13677 (0.4)	4637 (0.3)	3749 (0.3)
lump in the neck	23604 (0.7)	8394 (0.7)	5352 (0.4)	16007 (0.4)	5624 (0.4)	3598 (0.3)
thrombosis	27075 (0.7)	9429 (0.7)	7832 (0.6)	26804 (0.7)	9450 (0.7)	8495 (0.6)
night sweats	13369 (0.4)	4815 (0.4)	2801 (0.2)	7910 (0.2)	2653 (0.2)	1651 (0.1)
breast lump	134892 (3.7)	47018 (3.7)	31434 (2.3)	n/a	n/a	n/a
breast pain	71647 (2.0)	25315 (2.0)	18035 (1.3)	n/a	n/a	n/a
breast skin/nipple changes	19519 (0.5)	6682 (0.5)	4235 (0.3)	n/a	n/a	n/a
inter-menstrual bleeding	43002 (1.2)	14467 (1.1)	10548 (0.8)	n/a	n/a	n/a
postmenopausal bleeding	30907 (0.9)	10724 (0.8)	9725 (0.7)	n/a	n/a	n/a
post coital bleeding	22471 (0.6)	7892 (0.6)	5888 (0.4)	n/a	n/a	n/a
testicular pain	n/a	n/a	n/a	34134 (0.9)	12191 (0.9)	5671 (0.4)
testicular lump	n/a	n/a	n/a	45667 (1.2)	16117 (1.2)	11477 (0.8)

Supplementary Table 3. Crude incidence rate of each cancer type per 1000 person years (95% CI) in the QResearch derivation cohort by data source. Percent of data on GP record only is the number of cases identified on the GP record as a proportion of all the cases identified on any of the linked data sources.

outcome		*GP record*	*GP or Mortality record*	*GP, hospital or mortality record*	*GP, hospital or mortality or cancer registry record*	*% cases recorded on GP data*
Lung	female	0.60 (0.58 to 0.62)	0.66 (0.65 to 0.68)	0.76 (0.74 to 0.78)	0.77 (0.75 to 0.78)	78
	male	0.71 (0.69 to 0.73)	0.82 (0.80 to 0.83)	0.90 (0.88 to 0.92)	0.91 (0.89 to 0.93)	78
	total	0.65 (0.64 to 0.67)	0.74 (0.73 to 0.75)	0.83 (0.82 to 0.85)	0.84 (0.83 to 0.85)	78
Colorectal	female	0.54 (0.53 to 0.56)	0.29 (0.28 to 0.30)	0.68 (0.67 to 0.70)	0.70 (0.68 to 0.72)	77
	male	0.70 (0.69 to 0.72)	0.39 (0.38 to 0.41)	0.86 (0.84 to 0.88)	0.88 (0.86 to 0.90)	80
	total	0.62 (0.61 to 0.63)	0.34 (0.33 to 0.35)	0.77 (0.76 to 0.79)	0.79 (0.78 to 0.80)	79
Gastro-oesophageal	female	0.17 (0.16 to 0.18)	0.17 (0.16 to 0.18)	0.21 (0.20 to 0.22)	0.22 (0.21 to 0.23)	77
	male	0.42 (0.41 to 0.43)	0.41 (0.40 to 0.43)	0.48 (0.47 to 0.50)	0.49 (0.47 to 0.50)	86
	total	0.30 (0.29 to 0.30)	0.29 (0.28 to 0.30)	0.35 (0.34 to 0.36)	0.36 (0.35 to 0.36)	83
Pancreas	female	0.16 (0.15 to 0.17)	0.21 (0.20 to 0.22)	0.22 (0.21 to 0.23)	0.22 (0.21 to 0.23)	72
	male	0.19 (0.18 to 0.20)	0.24 (0.23 to 0.26)	0.26 (0.25 to 0.27)	0.26 (0.25 to 0.27)	73
	total	0.18 (0.17 to 0.18)	0.23 (0.22 to 0.23)	0.24 (0.23 to 0.25)	0.24 (0.23 to 0.25)	73
Ovarian	female	0.24 (0.23 to 0.25)	0.18 (0.17 to 0.19)	0.32 (0.31 to 0.34)	0.35 (0.34 to 0.36)	69
Renal	female	0.29 (0.27 to 0.30)	0.15 (0.14 to 0.15)	0.39 (0.38 to 0.40)	0.40 (0.39 to 0.41)	71
	male	0.76 (0.74 to 0.78)	0.32 (0.31 to 0.33)	1.01 (0.99 to 1.03)	1.03 (1.01 to 1.05)	74
	total	0.53 (0.52 to 0.54)	0.23 (0.23 to 0.24)	0.70 (0.69 to 0.72)	0.72 (0.71 to 0.73)	73
Breast	female	2.24 (2.21 to 2.27)	0.49 (0.48 to 0.51)	2.42 (2.38 to 2.45)	2.39 (2.35 to 2.42)	94
Prostate	male	1.38 (1.36 to 1.41)	0.48 (0.47 to 0.50)	1.52 (1.49 to 1.54)	1.55 (1.52 to 1.57)	89
Blood	female	0.55 (0.53 to 0.56)	0.24 (0.23 to 0.25)	0.59 (0.57 to 0.61)	0.59 (0.58 to 0.61)	92
	male	0.78 (0.76 to 0.80)	0.36 (0.34 to 0.37)	0.84 (0.82 to 0.86)	0.84 (0.82 to 0.86)	92
	total	0.66 (0.65 to 0.68)	0.30 (0.29 to 0.31)	0.72 (0.70 to 0.73)	0.72 (0.71 to 0.73)	92
Uterine	female	0.40 (0.38 to 0.41)	0.13 (0.12 to 0.14)	0.54 (0.52 to 0.55)	0.54 (0.53 to 0.56)	73
Cervical	female	0.11 (0.11 to 0.12)	0.05 (0.05 to 0.05)	0.15 (0.14 to 0.15)	0.16 (0.15 to 0.16)	73
Oral	female	0.07 (0.06 to 0.07)	0.05 (0.04 to 0.05)	0.12 (0.11 to 0.13)	0.12 (0.12 to 0.13)	52
	male	0.16 (0.15 to 0.17)	0.12 (0.11 to 0.12)	0.27 (0.26 to 0.28)	0.28 (0.26 to 0.29)	59
	total	0.11 (0.11 to 0.12)	0.08 (0.08 to 0.09)	0.20 (0.19 to 0.20)	0.20 (0.19 to 0.21)	57
Testis	male	0.12 (0.11 to 0.12)	0.00 (0.00 to 0.01)	0.15 (0.14 to 0.16)	0.15 (0.15 to 0.16)	75
Liver	female	0.02 (0.02 to 0.03)	0.10 (0.09 to 0.10)	0.11 (0.11 to 0.12)	0.12 (0.11 to 0.12)	21
	male	0.08 (0.08 to 0.09)	0.17 (0.17 to 0.18)	0.19 (0.18 to 0.20)	0.19 (0.18 to 0.20)	42
	total	0.05 (0.05 to 0.06)	0.14 (0.13 to 0.14)	0.15 (0.15 to 0.16)	0.15 (0.15 to 0.16)	34
Any cancer	female	5.63 (5.58 to 5.68)	3.00 (2.97 to 3.04)	7.16 (7.11 to 7.22)	7.52 (7.46 to 7.57)	76
	male	5.56 (5.51 to 5.61)	3.72 (3.68 to 3.76)	7.14 (7.08 to 7.20)	7.49 (7.43 to 7.55)	76
	total	5.59 (5.56 to 5.63)	3.36 (3.34 to 3.39)	7.15 (7.11 to 7.19)	7.50 (7.46 to 7.54)	76

Supplementary Table 4. Crude incidence rates of cancer types per 1000 person years (95% CI) in QResearch and CPRD based on GP data only (as linked data unavailable for CPRD).

outcome		*QResearch GP record only*	*CPRD GP record only*
Lung	female	0.60 (0.58 to 0.62)	0.68 (0.65 to 0.71)
	male	0.71 (0.69 to 0.73)	0.77 (0.74 to 0.80)
	total	0.65 (0.64 to 0.67)	0.72 (0.70 to 0.75)
Colorectal	female	0.54 (0.53 to 0.56)	0.60 (0.58 to 0.63)
	male	0.70 (0.69 to 0.72)	0.75 (0.72 to 0.79)
	total	0.62 (0.61 to 0.63)	0.68 (0.66 to 0.70)
Gastro-oesophageal	female	0.17 (0.16 to 0.18)	0.20 (0.18 to 0.22)
	male	0.42 (0.41 to 0.43)	0.47 (0.45 to 0.50)
	total	0.30 (0.29 to 0.30)	0.34 (0.32 to 0.35)
Pancreas	female	0.16 (0.15 to 0.17)	0.16 (0.15 to 0.18)
	male	0.19 (0.18 to 0.20)	0.17 (0.16 to 0.19)
	total	0.18 (0.17 to 0.18)	0.17 (0.15 to 0.18)
Ovarian	female	0.24 (0.23 to 0.25)	0.26 (0.24 to 0.28)
Renal	female	0.29 (0.27 to 0.30)	0.26 (0.24 to 0.28)
	male	0.76 (0.74 to 0.78)	0.65 (0.62 to 0.68)
	total	0.53 (0.52 to 0.54)	0.46 (0.44 to 0.47)
Breast	female	2.24 (2.21 to 2.27)	2.17 (2.12 to 2.23)
Prostate	male	1.38 (1.36 to 1.41)	1.29 (1.24 to 1.33)
Blood	female	0.55 (0.53 to 0.56)	0.54 (0.51 to 0.56)
	male	0.78 (0.76 to 0.80)	0.76 (0.73 to 0.79)
	total	0.66 (0.65 to 0.68)	0.65 (0.63 to 0.67)
Uterine	female	0.40 (0.38 to 0.41)	0.42 (0.40 to 0.44)
Cervical	female	0.11 (0.11 to 0.12)	0.13 (0.12 to 0.15)
Oral	female	0.07 (0.06 to 0.07)	0.09 (0.08 to 0.10)
	male	0.16 (0.15 to 0.17)	0.20 (0.18 to 0.22)
	total	0.11 (0.11 to 0.12)	0.14 (0.13 to 0.15)
Testis	male	0.12 (0.11 to 0.12)	0.11 (0.10 to 0.13)
Liver	female	0.02 (0.02 to 0.03)	0.03 (0.02 to 0.03)
	male	0.08 (0.08 to 0.09)	0.09 (0.08 to 0.10)
	total	0.05 (0.05 to 0.06)	0.06 (0.05 to 0.06)
Any cancer	**female**	**5.63 (5.58 to 5.68)**	**5.71 (5.62 to 5.81)**
	male	**5.56 (5.51 to 5.61)**	**5.36 (5.27 to 5.45)**
	total	**5.59 (5.56 to 5.63)**	**5.54 (5.47 to 5.60)**

Supplementary Table 5 Candidate predictor variables evaluated for inclusion in new models compared with existing predictors in QCancer.

	Predictors included in final models A or B		**Not included in final models A or B**
	Existing predictors included in existing QCancer models	***New candidate predictors tested and included in final models***	***New candidate predictors tested but not included in final models***
Factors on or prior to cohort entry	Age, body mass index, smoking status, alcohol use, Townsend deprivation score. Chronic obstructive pulmonary disease, chronic pancreatitis, type 2 diabetes	Liver cirrhosis, hepatitis C, hepatitis B, HIV/AIDS.	Endometriosis, polycystic ovarian disease, rheumatoid arthritis, systemic lupus erythematosus, primary biliary cirrhosis, inflammatory bowel disease, benign breast disease
Family History recorded prior to cohort entry	breast cancer gastro-intestinal cancer prostate cancer ovarian cancer	lung cancer blood cancer	n/a
Red Flag symptoms	Thrombosis, abdominal distension, abdominal pain, appetite loss, heartburn, indigestion, dysphagia, haematemesis, rectal bleeding, haematuria, haemoptysis, neck lump, weight loss, night sweats, breast lump, breast pain, nipple discharge or breast skin changes, inter-menstrual bleeding, post-menopausal bleeding, post-coital bleeding, testicular lump, testicular pain.	No new ones tested.	n/a
Non-specific or vague symptoms in the 12 months prior to cohort entry	Change in bowel habit, bruising, cough, urinary retention, nocturia, urinary frequency	back pain, hoarseness, flatulence, abdominal mass, dark urine	Itching, bruising, Nausea, flushes, thirst, diarrhoea, pelvic pain, shoulder pain, tiredness, vaginal discharge, headache (jaundice and steatorrhea not included as too few events)
Most recent blood tests in the two years prior to cohort entry	Haemoglobin as a binary variable (<110 g/L).	Haemoglobin, platelets, bilirubin, neutrophil, lymphocytes, albumin, alkaline phosphatase.	Glycosylated haemoglobin, alanine transaminase, HBA1c random blood glucose, creatinine, alanine transaminase.

Supplementary Table 6 Summary of associations between probability of cancer and individual blood test results. Decreased means there is an increased probability of cancer associated with lower values; increased means there is an increased probability of cancer associated with higher values; no association means no association was found between cancer probability and the value

		Haemoglobin	***Neutrophils***	***Lymphocytes***	***Platelets***	***Albumin***	***Alkaline Phosphatase***	***Bilirubin***
Men	Lung	Decreased	Increased	Decreased	Increased	Decreased	Increased	No association
	Colorectal	Decreased	Increased	Decreased	Increased	Decreased	Increased	No association
	Prostate	Increased	Decreased	Increased	Increased	Increased	No association	No association
	Blood	Decreased	Decreased	Increased	No association	Decreased	Increased	Increased
	Renal	No association	Increased	Decreased	Increased	Increased	No association	No association
	Gastro-oesophageal	Decreased	Increased	Decreased	Increased	No association	Increased	No association
	Pancreas	No association	Increased	Decreased	No association	No association	Increased	Increased
	Testicular	No association	No association	Decreased	No association	No association	No association	No association
	Oral	No association	Increased	No association	No association	No association	No association	No association
	liver	No association	Decreased	Decreased	No association	Decreased	Increased	Increased
	Other	No association	No association	Decreased	Increased	No association	No association	No association
Women	Lung	No association	Increased	No association	Increased	Decreased	Increased	No association
	Colorectal	Decreased	Increased	Decreased	Increased	Decreased	Increased	Decreased
	Breast	No association	Increased	No association	No association	No association	Decreased	Increased
	Blood	Decreased	Decreased	Increased	Increased	Decreased	Increased	Increased
	Ovarian	No association	Increased	Decreased	Increased	Decreased	No association	No association
	Renal	No association	Increased	Decreased	Increased	No association	No association	No association
	Gastro-oesophageal	Decreased	Increased	No association	No association	Decreased	No association	No association
	Uterine	No association	Increased	No association	Increased	No association	No association	No association
	Pancreas	No association	Increased	No association	No association	No association	Increased	Increased
	Cervical	No association	Increased	No association	Increased	Decreased	No association	No association
	Oral	No association	No association	No association	No association	No association	Increased	No association
	Liver	Decreased	No association	Decreased	No association	Decreased	Increased	Increased
	Other	No association	No association	Decreased	Increased	No association	Increased	Increased

Supplementary Table 7: Cancer stage at diagnosis in the QResearch English validation cohort restricted to 2015-2020 due to availability of linked cancer registry data. Stages 1 and 2 considered 'early' whilst stages 3 and 4 considered late.

		Stage 1		*Stage 2*		*Stage 3*		*Stage 4*		*Not recorded*		Total	Stage1 or 2	
		Count	**Row %**	**Count**	**Row %**	**Count**	**Row %**	**Count**	**Row %**	**Count**	**Row %**	**Count**	**count**	**Row %**
Women	lung	240	16.0	88	5.9	253	16.9	763	51.0	152	10.2	**1,496**	328	21.9
	colorectal	208	15.1	319	23.1	357	25.9	363	26.3	131	9.5	**1,378**	527	38.2
	breast	1,675	34.7	1,990	41.2	485	10.0	224	4.6	457	9.5	**4,831**	3665	75.9
	blood	93	8.9	104	9.9	139	13.3	201	19.2	511	48.8	**1,048**	197	18.8
	ovarian	154	26.4	40	6.8	146	25.0	111	19.0	133	22.8	**584**	194	33.2
	renal	207	35.2	81	13.8	81	13.8	112	19.0	107	18.2	**588**	288	49.0
	gastric	48	10.2	47	10.0	122	25.9	164	34.8	90	19.1	**471**	95	20.2
	uterine	633	62.2	68	6.7	121	11.9	80	7.9	115	11.3	**1,017**	701	68.9
	pancreatic	23	4.9	62	13.3	47	10.1	241	51.6	94	20.1	**467**	85	18.2
	cervical	147	50.0	46	15.6	25	8.5	36	12.2	40	13.6	**294**	193	65.6
	oral	48	21.5	26	11.7	36	16.1	90	40.4	23	10.3	**223**	74	33.2
	liver	11	6.3	12	6.8	10	5.7	73	41.5	70	39.8	**176**	23	13.1
	other	567	37.2	196	12.9	123	8.1	137	9.0	501	32.9	**1,524**	763	50.1
	Total	***4,054***	***28.8***	***3,079***	***21.8***	***1,945***	***13.8***	***2,595***	***18.4***	***2,424***	***17.2***	**14,097**	7133	50.6
Men	lung	219	11.7	132	7.1	364	19.5	946	50.6	208	11.1	**1,869**	351	18.8
	colorectal	318	16.8	372	19.6	549	28.9	466	24.6	192	10.1	**1,897**	690	36.4
	prostate	1,089	33.4	507	15.5	640	19.6	638	19.6	387	11.9	**3,261**	1596	48.9
	blood	131	9.3	112	7.9	147	10.4	304	21.6	716	50.8	**1,410**	243	17.2
	renal	592	40.8	223	15.4	198	13.6	237	16.3	202	13.9	**1,452**	815	56.1
	gastric	75	6.8	121	11.0	294	26.8	447	40.7	162	14.7	**1,099**	196	17.8
	pancreatic	24	4.8	50	10.0	49	9.8	278	55.6	99	19.8	**500**	74	14.8
	oral	77	14.3	69	12.8	68	12.6	283	52.4	43	8.0	**540**	146	27.0
	testicular	232	67.6	18	5.2	21	6.1	5	1.5	67	19.5	**343**	250	72.9
	liver	34	9.0	43	11.4	33	8.7	94	24.9	174	46.0	**378**	77	20.4
	other	513	32.0	218	13.6	141	8.8	151	9.4	582	36.3	**1,605**	731	45.5
	Total	***3,304***	***23.0***	***1,865***	***13.0***	***2,504***	***17.4***	***3,849***	***26.8***	***2,832***	***19.7***	**14,354**	5169	36.0

Supplementary Table 8. Discrimination using c statistic values (95% CI) for early cancer diagnoses (stage 1 and 2) using models A and B (in people aged 18-84) and QCancer (in people aged 25-84) in the QResearch English validation cohort. Analyses restricted from 2015-2020 to match period for which cancer stage data was recorded.

	Women Model A	*Women Model B*	*Women QCancer*	*Men Model A*	*Men Model B*	*Men QCancer*
any cancer	0.837 (0.832 to 0.841)	0.837 (0.833 to 0.842)	0.849 (0.844 to 0.853)	0.864 (0.860 to 0.868)	0.865 (0.860 to 0.869)	0.816 (0.811 to 0.821)
lung	0.940 (0.930 to 0.950)	0.943 (0.933 to 0.952)	0.938 (0.927 to 0.949)	0.943 (0.932 to 0.954)	0.945 (0.934 to 0.956)	0.926 (0.915 to 0.938)
colorectal	0.893 (0.881 to 0.905)	0.896 (0.883 to 0.909)	0.893 (0.883 to 0.903)	0.906 (0.897 to 0.914)	0.910 (0.901 to 0.919)	0.873 (0.860 to 0.887)
breast	0.878 (0.873 to 0.884)	0.880 (0.875 to 0.885)	n/a	n/a	n/a	0.850 (0.843 to 0.856)
prostate	n/a	n/a	0.858 (0.852 to 0.865)	0.884 (0.879 to 0.889)	0.885 (0.879 to 0.890)	n/a
blood	0.762 (0.725 to 0.798)	0.766 (0.730 to 0.803)	0.796 (0.766 to 0.827)	0.820 (0.791 to 0.848)	0.824 (0.795 to 0.854)	0.739 (0.704 to 0.774)
ovarian	0.751 (0.712 to 0.789)	0.767 (0.730 to 0.805)	n/a	n/a	n/a	0.756 (0.718 to 0.793)
renal	0.869 (0.846 to 0.892)	0.868 (0.843 to 0.892)	0.910 (0.899 to 0.921)	0.930 (0.921 to 0.940)	0.929 (0.919 to 0.939)	0.826 (0.798 to 0.853)
gastro	0.909 (0.873 to 0.946)	0.912 (0.876 to 0.947)	0.925 (0.905 to 0.945)	0.933 (0.915 to 0.951)	0.934 (0.915 to 0.952)	0.898 (0.857 to 0.939)
uterine	0.919 (0.906 to 0.932)	0.918 (0.905 to 0.931)	n/a	n/a	n/a	0.884 (0.867 to 0.900)
pancreatic	0.884 (0.847 to 0.920)	0.890 (0.853 to 0.928)	0.865 (0.822 to 0.908)	0.884 (0.845 to 0.924)	0.877 (0.833 to 0.920)	0.852 (0.807 to 0.897)
cervical	0.627 (0.590 to 0.663)	0.635 (0.597 to 0.674)	n/a	n/a	n/a	0.611 (0.578 to 0.645)
oral	0.698 (0.636 to 0.760)	0.701 (0.634 to 0.768)	n/a	0.809 (0.770 to 0.847)	0.812 (0.776 to 0.847)	n/a
testicular	n/a	n/a	0.850 (0.820 to 0.879)	0.847 (0.819 to 0.876)	0.846 (0.817 to 0.874)	n/a
liver	0.799 (0.696 to 0.902)	0.862 (0.762 to 0.963)	n/a	0.911 (0.879 to 0.943)	0.924 (0.890 to 0.958)	n/a
other	0.700 (0.681 to 0.718)	0.695 (0.677 to 0.714)	0.747 (0.731 to 0.763)	0.777 (0.762 to 0.792)	0.778 (0.763 to 0.793)	0.674 (0.655 to 0.692)

Supplementary Table 9. Discrimination using c statistic values (95% CI) by cancer type using QCancer in patients aged 25-84 years in the QResearch English validation cohort and CPRD cohorts.

	QResearch cohort		*CPRD cohort*	
	QCancer Women	**QCancer Men**	**QCancer Women**	**QCancer Men**
Any cancer	0.819 (0.817 to 0.822)	0.859 (0.857 to 0.861)	0.817 (0.814 to 0.820)	0.852 (0.849 to 0.854)
Lung	0.908 (0.901 to 0.914)	0.919 (0.914 to 0.923)	0.912 (0.906 to 0.918)	0.916 (0.911 to 0.921)
Colorectal	0.856 (0.848 to 0.864)	0.874 (0.867 to 0.880)	0.845 (0.836 to 0.855)	0.862 (0.854 to 0.869)
Breast	0.842 (0.838 to 0.847)	n/a	0.823 (0.817 to 0.829)	
Prostate	n/a	0.872 (0.869 to 0.876)		0.860 (0.855 to 0.864)
Blood	0.768 (0.757 to 0.779)	0.792 (0.783 to 0.801)	0.759 (0.746 to 0.772)	0.793 (0.784 to 0.802)
Ovarian	0.791 (0.776 to 0.807)	n/a	0.807 (0.789 to 0.824)	
Renal	0.858 (0.845 to 0.870)	0.912 (0.906 to 0.917)	0.832 (0.815 to 0.849)	0.891 (0.882 to 0.899)
Gastro-oesophageal	0.882 (0.867 to 0.897)	0.921 (0.914 to 0.928)	0.873 (0.856 to 0.889)	0.915 (0.907 to 0.923)
Uterine	0.858 (0.847 to 0.870)	n/a	0.867 (0.852 to 0.881)	
Pancreas	0.843 (0.827 to 0.860)	0.873 (0.859 to 0.887)	0.847 (0.826 to 0.867)	0.872 (0.854 to 0.889)
Cervical	0.667 (0.644 to 0.691)	n/a	0.672 (0.646 to 0.698)	
Testicular	n/a	0.834 (0.812 to 0.856)		0.783 (0.754 to 0.813)
Other	0.699 (0.689 to 0.709)	0.754 (0.746 to 0.763)	0.721 (0.710 to 0.733)	0.767 (0.757 to 0.777)

Supplementary Table 10. Discrimination using polytomous discrimination index (PDI) estimates overall and by cancer type using Model A and B in men and women aged 18-84 years in the QResearch English validation cohort and CPRD cohorts.

		QResearch	*QResearch*	*CPRD*	*CPRD*
		Model A	**Model B**	**Model A**	**Model B**
Women		**PDI**	**PDI**	**PDI**	**PDI**
	Overall	0.257	0.266	0.258	0.272
	Any cancer	0.387	0.392	0.377	0.382
	Lung	0.279	0.275	0.277	0.274
	Colorectal	0.232	0.242	0.227	0.245
	Breast	0.428	0.429	0.422	0.423
	Blood	0.129	0.151	0.102	0.139
	Ovarian	0.149	0.163	0.162	0.194
	Renal tract	0.397	0.396	0.362	0.365
	Gastro	0.355	0.357	0.356	0.352
	Uterine	0.440	0.439	0.443	0.442
	Pancreatic	0.192	0.205	0.2	0.226
	Cervical	0.159	0.159	0.167	0.179
	Oral	0.221	0.220	0.227	0.226
	Liver	0.171	0.242	0.228	0.298
Men	Overall	0.308	0.323	0.295	0.31
	Any cancer	0.464	0.467	0.437	0.442
	Lung	0.292	0.301	0.276	0.283
	Colorectal	0.261	0.275	0.239	0.249
	Prostate	0.115	0.125	0.115	0.128
	Blood	0.129	0.159	0.104	0.136
	Renal tract	0.5	0.503	0.466	0.47
	Gastro	0.421	0.422	0.422	0.424
	Pancreatic	0.248	0.25	0.274	0.269
	Testicular	0.641	0.64	0.541	0.538
	Oral	0.331	0.331	0.277	0.277
	Liver	0.239	0.345	0.319	0.426

Supplementary Table 11. Calibration intercept (CITL) and calibration slope estimates (95% CI) by cancer type for Models A and B in patients aged 25-84 years in the CPRD external cohort.

	Model A women	*Model B women*	*Model A men*	*Model B men*
CITL				
Lung	-0.64 (-0.69 to -0.59)	-0.62 (-0.67 to -0.57)	-0.60 (-0.64 to -0.55)	-0.58 (-0.62 to -0.53)
Colorectal	-0.40 (-0.45 to -0.35)	-0.40 (-0.45 to -0.35)	-0.37 (-0.42 to -0.33)	-0.33 (-0.38 to -0.29)
Breast	0.32 (0.25 to 0.38)	0.31 (0.24 to 0.37)	n/a	n/a
Blood	-0.39 (-0.44 to -0.33)	-0.37 (-0.42 to -0.32)	-0.35 (-0.39 to -0.31)	-0.31 (-0.35 to -0.27)
Ovarian	-0.41 (-0.49 to -0.34)	-0.41 (-0.49 to -0.33)	n/a	n/a
Renal	-0.63 (-0.71 to -0.56)	-0.63 (-0.71 to -0.56)	-0.65 (-0.70 to -0.60)	-0.66 (-0.71 to -0.61)
Gastric	-0.37 (-0.46 to -0.28)	-0.37 (-0.45 to -0.28)	-0.23 (-0.29 to -0.18)	-0.22 (-0.27 to -0.16)
Uterine	-0.44 (-0.50 to -0.38)	-0.45 (-0.51 to -0.39)	n/a	n/a
Pancreatic	-0.60 (-0.69 to -0.50)	-0.54 (-0.63 to -0.44)	-0.62 (-0.71 to -0.53)	-0.57 (-0.67 to -0.48)
Cervical	-0.43 (-0.54 to -0.33)	-0.45 (-0.55 to -0.34)	n/a	n/a
Oral	-0.74 (-0.86 to -0.61)	-0.72 (-0.84 to -0.59)	-0.57 (-0.65 to -0.48)	-0.57 (-0.65 to -0.48)
Other	-0.55 (-0.59 to -0.50)	-0.54 (-0.59 to -0.50)	-0.56 (-0.61 to -0.52)	-0.56 (-0.60 to -0.52)
Liver	-1.77 (-2.00 to -1.54)	-1.67 (-1.90 to -1.44)	-1.00 (-1.13 to -0.88)	-0.92 (-1.04 to -0.79)
Prostate	n/a	n/a	-0.52 (-0.56 to -0.49)	-0.58 (-0.61 to -0.54)
Testicular	n/a	n/a	-0.23 (-0.34 to -0.11)	-0.21 (-0.32 to -0.09)
Slope				
Lung	1.08 (1.04 to 1.11)	1.07 (1.03 to 1.10)	1.08 (1.04 to 1.11)	1.08 (1.05 to 1.11)
Colorectal	1.06 (1.03 to 1.10)	1.06 (1.03 to 1.09)	1.06 (1.03 to 1.09)	1.06 (1.04 to 1.09)
Breast	1.13 (1.12 to 1.15)	1.13 (1.12 to 1.15)	n/a	n/a
Blood	1.05 (1.00 to 1.09)	1.07 (1.03 to 1.12)	1.09 (1.05 to 1.12)	1.08 (1.05 to 1.12)
Ovarian	1.17 (1.12 to 1.23)	1.16 (1.11 to 1.21)	n/a	n/a
Renal	1.10 (1.06 to 1.13)	1.10 (1.06 to 1.13)	1.05 (1.03 to 1.07)	1.05 (1.03 to 1.07)
Gastric	1.11 (1.07 to 1.16)	1.11 (1.06 to 1.15)	1.10 (1.07 to 1.13)	1.10 (1.07 to 1.13)
Uterine	1.09 (1.06 to 1.11)	1.09 (1.06 to 1.11)	n/a	n/a
Pancreatic	1.14 (1.08 to 1.21)	1.13 (1.08 to 1.19)	1.09 (1.04 to 1.15)	1.05 (1.00 to 1.11)
Cervical	0.97 (0.91 to 1.03)	0.97 (0.91 to 1.03)	n/a	n/a
Oral	1.06 (0.99 to 1.13)	1.06 (0.98 to 1.13)	1.02 (0.98 to 1.07)	1.02 (0.98 to 1.06)
Other	1.14 (1.08 to 1.19)	1.18 (1.13 to 1.23)	1.15 (1.10 to 1.20)	1.16 (1.11 to 1.21)
Liver	1.11 (0.97 to 1.25)	1.03 (0.92 to 1.14)	1.20 (1.13 to 1.27)	1.11 (1.05 to 1.16)
Prostate	n/a	n/a	1.20 (1.16 to 1.24)	1.20 (1.16 to 1.24)
Testicular	n/a	n/a	1.01 (0.97 to 1.06)	1.02 (0.97 to 1.07)

Supplementary Table 12. Calibration intercept (CITL) and calibration slope estimates (95% CI) by cancer type for QCancer in patients aged 25-84 years in the QResearch English validation cohort and CPRD external cohort.

	QResearch cohort		*CPRD cohort*	
	QCancer Women	**QCancer Men**	**QCancer Women**	**QCancer Men**
CITL				
Lung	0.41 (0.36 to 0.45)	0.06 (0.02 to 0.10)	-0.17 (-0.22 to -0.12)	-0.50 (-0.55 to -0.46)
Colorectal	0.25 (0.20 to 0.29)	0.13 (0.09 to 0.17)	-0.17 (-0.22 to -0.12)	-0.35 (-0.40 to -0.31)
Breast	-0.39 (-0.44 to -0.34)	n/a	-0.18 (-0.25 to -0.12)	n/a
Blood	0.46 (0.41 to 0.50)	0.57 (0.53 to 0.61)	0.09 (0.03 to 0.14)	0.24 (0.19 to 0.28)
Ovarian	-0.16 (-0.22 to -0.09)	n/a	-0.54 (-0.62 to -0.46)	n/a
Renal	0.61 (0.55 to 0.67)	0.67 (0.64 to 0.71)	0.10 (0.02 to 0.17)	0.02 (-0.03 to 0.07)
Gastric	-0.02 (-0.10 to 0.05)	-0.24 (-0.29 to -0.19)	-0.36 (-0.45 to -0.27)	-0.46 (-0.52 to -0.41)
Uterine	0.74 (0.69 to 0.79)	n/a	0.34 (0.28 to 0.40)	n/a
Pancreas	0.48 (0.40 to 0.55)	0.38 (0.31 to 0.45)	-0.10 (-0.20 to -0.01)	-0.23 (-0.32 to -0.14)
Cervical	0.19 (0.10 to 0.28)	n/a	-0.26 (-0.37 to -0.16)	n/a
Other	0.40 (0.37 to 0.43)	0.34 (0.31 to 0.37)	-0.24 (-0.28 to -0.20)	-0.27 (-0.31 to -0.24)
Prostate	n/a	0.15 (0.12 to 0.18)	n/a	-0.33 (-0.36 to -0.30)
Testis	n/a	-0.51 (-0.61 to -0.41)	n/a	-0.54 (-0.66 to -0.41)
Slope				
Lung	0.95 (0.92 to 0.97)	0.99 (0.96 to 1.01)	1.03 (1.00 to 1.05)	1.07 (1.04 to 1.10)
Colorectal	0.93 (0.91 to 0.96)	0.90 (0.88 to 0.92)	1.04 (1.00 to 1.07)	0.97 (0.94 to 1.00)
Breast	0.87 (0.86 to 0.88)	n/a	0.99 (0.97 to 1.00)	n/a
Blood	0.91 (0.88 to 0.95)	0.94 (0.91 to 0.97)	1.06 (1.02 to 1.10)	1.09 (1.05 to 1.13)
Ovarian	0.82 (0.78 to 0.87)	n/a	1.02 (0.96 to 1.07)	n/a
Renal	0.92 (0.89 to 0.94)	0.97 (0.96 to 0.99)	0.99 (0.96 to 1.03)	1.02 (1.00 to 1.04)
Gastric	0.92 (0.89 to 0.95)	0.96 (0.93 to 0.98)	1.04 (1.00 to 1.08)	1.06 (1.04 to 1.09)
Uterine	0.94 (0.92 to 0.96)	n/a	1.03 (1.01 to 1.06)	n/a
Pancreas	0.95 (0.90 to 1.00)	1.02 (0.97 to 1.06)	1.12 (1.05 to 1.18)	1.15 (1.10 to 1.21)
Cervical	0.85 (0.80 to 0.91)	n/a	0.78 (0.72 to 0.83)	n/a
Other	0.80 (0.77 to 0.83)	0.90 (0.87 to 0.92)	0.96 (0.92 to 1.00)	1.03 (1.00 to 1.07)
Prostate	n/a	0.83 (0.80 to 0.85)	n/a	0.97 (0.94 to 1.01)
Testis	n/a	0.84 (0.81 to 0.87)	n/a	0.87 (0.83 to 0.91)

Supplementary Table 13. Sensitivity of Model A, Model B and QCancer for identifying cases of cancer by type and stage at diagnosis in men and women in QResearch validation cohort at the 3% threshold. Analyses for early-stage diagnosis were restricted to 2015-2020.

		Women		*Men*	
		all stages 2015-2023	**early stage 2015-2020**	**all stages 2015-2023**	**early stage 2015-2020**
Any cancer	Total	22105	7133	22879	5169
	QCancer	14582 (66.0)	4509 (63.2)	17878 (78.1)	3948 (76.4)
	Model A	17110 (77.4)	5361 (75.2)	18903 (82.6)	4201 (81.3)
	Model B	17024 (77.0)	5304 (74.4)	18891 (82.6)	4180 (80.9)
Lung cancer	Total	2091	328	2661	351
	QCancer	387 (18.5)	58 (17.7)	785 (29.5)	121 (34.5)
	Model A	697 (33.3)	110 (33.5)	980 (36.8)	149 (42.5)
	Model B	727 (34.8)	114 (34.8)	1035 (38.9)	155 (44.2)
Colorectal cancer	Total	2003	527	2667	690
	QCancer	369 (18.4)	102 (19.4)	678 (25.4)	194 (28.1)
	Model A	413 (20.6)	112 (21.3)	725 (27.2)	210 (30.4)
	Model B	515 (25.7)	143 (27.1)	814 (30.5)	220 (31.9)
Breast cancer	Total	7158	3665	n/a	n/a
	QCancer	3544 (49.5)	1817 (49.6)	n/a	n/a
	Model A	3594 (50.2)	1840 (50.2)	n/a	n/a
	Model B	3592 (50.2)	1842 (50.3)	n/a	n/a
Blood cancer	Total	1801	197	2593	243
	QCancer	101 (5.6)	19 (9.6)	209 (8.1)	31 (12.8)
	Model A	149 (8.3)	24 (12.2)	289 (11.1)	42 (17.3)
	Model B	171 (9.5)	27 (13.7)	405 (15.6)	47 (19.3)
Ovarian cancer	Total	872	194	n/a	n/a
	QCancer	55 (6.3)	8 (4.1)	n/a	n/a
	Model A	48 (5.5)	7 (3.6)	n/a	n/a
	Model B	66 (7.6)	9 (4.6)	n/a	n/a
Renal cancer	Total	1190	288	3189	815
	QCancer	465 (39.1)	104 (36.1)	1727 (54.2)	441 (54.1)
	Model A	487 (40.9)	106 (36.8)	1780 (55.8)	460 (56.4)
	Model B	488 (41.0)	106 (36.8)	1779 (55.8)	460 (56.4)
Gastro-oesophageal	Total	683	95	1536	196
	QCancer	179 (26.2)	30 (31.6)	620 (40.4)	70 (35.7)
	Model A	174 (25.5)	30 (31.6)	606 (39.5)	66 (33.7)
	Model B	174 (25.5)	29 (30.5)	609 (39.6)	67 (34.2)
Uterine cancer	Total	1541	701	n/a	n/a
	QCancer	670 (43.5)	356 (50.8)	n/a	n/a

	Model A	695 (45.1)	368 (52.5)	n/a	n/a
	Model B	693 (45.0)	365 (52.1)	n/a	n/a
Pancreatic cancer	Total	675	85	774	74
	QCancer	19 (2.8)	*	33 (4.3)	*
	Model A	43 (6.4)	*	73 (9.4)	*
	Model B	66 (9.8)	*	115 (14.9)	*
Cervical cancer	Total	459	193	n/a	n/a
	QCancer	8 (1.7)	*	n/a	n/a
	Model A	*	*	n/a	n/a
	Model B	*	*	n/a	n/a
Oral cancer	Total	373	74	886	146
	Model A	27 (7.2)	*	243 (27.4)	28 (19.2)
	Model B	30 (8.0)	*	245 (27.7)	28 (19.2)
Liver cancer	Total	364	23	601	77
	Model A	12 (3.3)	*	45 (7.5)	4 (5.2)
	Model B	34 (9.3)	*	116 (19.3)	16 (20.8)
Other cancer	Total	2895	763	2990	731
	QCancer	97 (3.4)	18 (2.4)	174 (5.8)	26 (3.6)
	Model A	91 (3.1)	27 (3.5)	101 (3.4)	22 (3.0)
	Model B	104 (3.6)	27 (3.5)	97 (3.2)	18 (2.5)
Prostate cancer	Total	n/a	n/a	4500	1596
	QCancer	n/a	n/a	848 (18.8)	237 (14.8)
	Model A	n/a	n/a	1113 (24.7)	328 (20.6)
	Model B	n/a	n/a	1214 (27.0)	361 (22.6)
Testicular cancer	Total	n/a	n/a	482	250
	QCancer	n/a	n/a	247 (51.2)	137 (54.8)
	Model A	n/a	n/a	165 (34.2)	93 (37.2)
	Model B	n/a	n/a	147 (30.5)	79 (31.6)

*counts suppressed as < 10 events

Supplementary Table 14. Demographic characteristics of patients reclassified by Model A compared with QCancer in the English validation cohort at the 3% probability threshold. Numbers are counts and column percents.

	Women	Women	Women	Women	Men	Men	Men	Men
category	**low on both**	**high QCancer, low model A**	**low QCancer high model A**	**high on both**	**low on both**	**high QCancer, low model A**	**low QCancer high model A**	**high on both**
	no change	**classified down**	**classified up**	**high on both**	**no change**	**classified down**	**classified up**	**high on both**
Total	1071198	3736	87446	114635	1111192	8311	59103	181563
<40 years	577139 (53.9)	524 (14.0)	1049 (1.2)	3656 (3.2)	615526 (55.4)	4178 (50.3)	1258 (2.1)	598 (0.3)
40-49 years	188744 (17.6)	504 (13.5)	2630 (3.0)	11729 (10.2)	234422 (21.1)	2441 (29.4)	2255 (3.8)	1725 (1.0)
50-59 years	161481 (15.1)	586 (15.7)	12049 (13.8)	18075 (15.8)	192307 (17.3)	1204 (14.5)	7005 (11.9)	12418 (6.8)
60-69 years	103142 (9.6)	1147 (30.7)	16446 (18.8)	26644 (23.2)	68937 (6.2)	488 (5.9)	36656 (62.0)	44041 (24.3)
70+ years	40692 (3.8)	975 (26.1)	55272 (63.2)	54531 (47.6)			11929 (20.2)	122781 (67.6)
White	548430 (51.2)	1618 (43.3)	51637 (59.1)	69044 (60.2)	510171 (45.9)	4527 (54.5)	34507 (58.4)	106542 (58.7)
Indian	32094 (3.0)	243 (6.5)	1192 (1.4)	1824 (1.6)	37943 (3.4)	129 (1.6)	1204 (2.0)	3039 (1.7)
Pakistani	17066 (1.6)	145 (3.9)	540 (0.6)	952 (0.8)	20810 (1.9)	73 (0.9)	565 (1.0)	1513 (0.8)
Bangladeshi	13873 (1.3)	109 (2.9)	374 (0.4)	768 (0.7)	17368 (1.6)	56 (0.7)	326 (0.6)	938 (0.5)
Other Asian	24722 (2.3)	110 (2.9)	785 (0.9)	1120 (1.0)	23370 (2.1)	82 (1.0)	743 (1.3)	1710 (0.9)
Caribbean	12673 (1.2)	126 (3.4)	1145 (1.3)	1500 (1.3)	11539 (1.0)	92 (1.1)	566 (1.0)	2184 (1.2)
Black African	37313 (3.5)	194 (5.2)	963 (1.1)	1453 (1.3)	38637 (3.5)	156 (1.9)	926 (1.6)	1640 (0.9)
Chinese	13526 (1.3)	20 (0.5)	290 (0.3)	428 (0.4)	10969 (1.0)	26 (0.3)	278 (0.5)	531 (0.3)
Other	55042 (5.1)	168 (4.5)	1668 (1.9)	2534 (2.2)	56214 (5.1)	272 (3.3)	1359 (2.3)	2919 (1.6)
Ethnicity missing	316459 (29.5)	1003 (26.8)	28852 (33.0)	35012 (30.5)	384171 (34.6)	2898 (34.9)	18629 (31.5)	60547 (33.3)

Supplementary Table 15. Summary of SNOMED-CT and ICD-10 Clinical code groups used to identify 15 types of cancer. The contents of each group are published at https://www.qresearch.org/data/qcode-group-library/

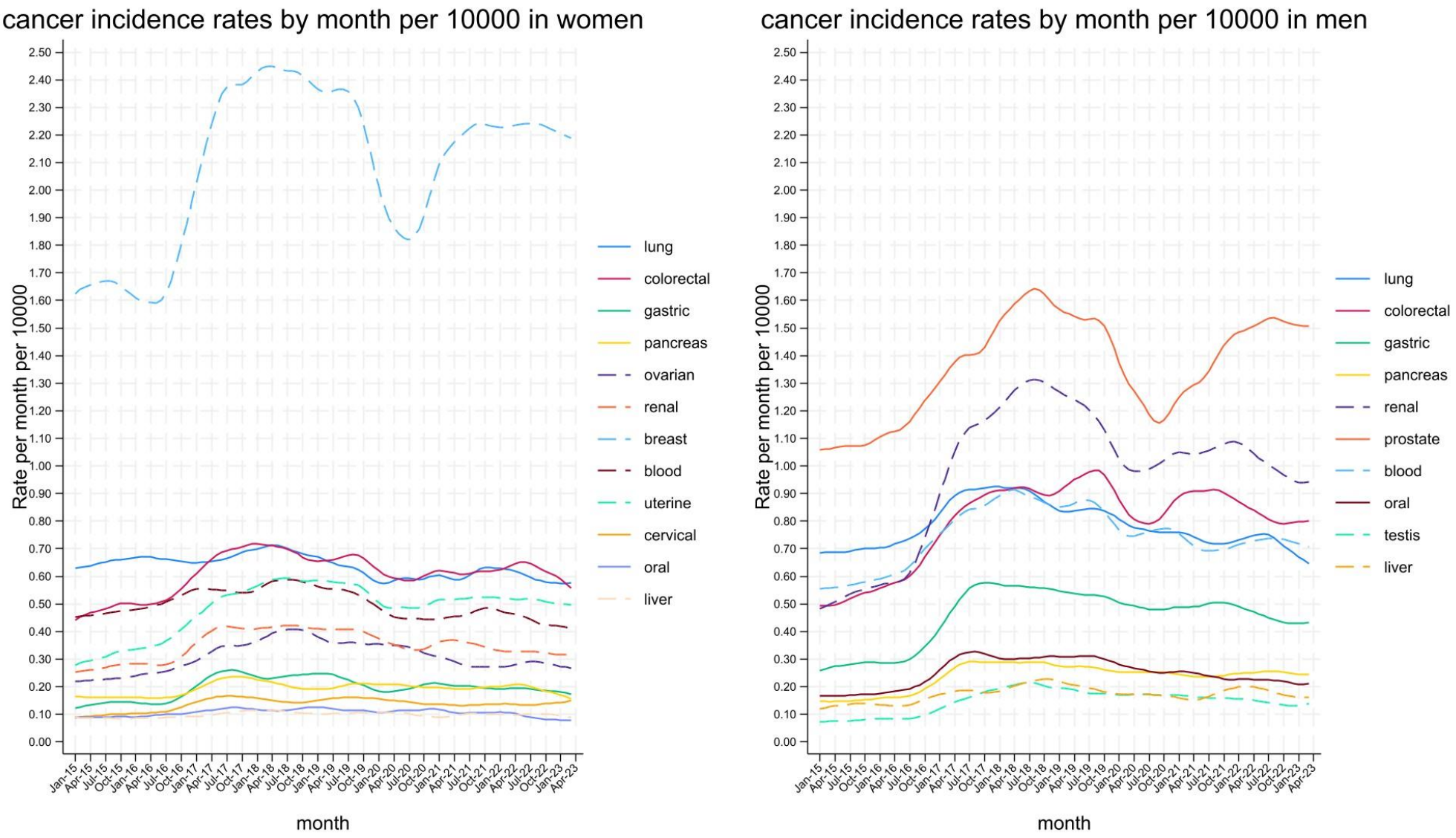
	SNOMED-CT code group ID	*ICD-10 code group ID*
Lung	51	2021
Colorectal	2009	2007
Invasive breast	52	1925
Prostate	56	2020
Blood	58	2004
Ovarian	32	2015
Renal tract	57	2027
Gastro-oesophageal	2013	2012
Uterine	54	2016
Pancreatic	216	2014
Cervical	55	2017
Oral, lip, pharyngeal	222	2023
Testicular	219	2018
Liver	2522	2753

Supplementary Table 16 Characteristics of patients with complete data for BMI, alcohol and smoking compared with those with incomplete data for these variables.

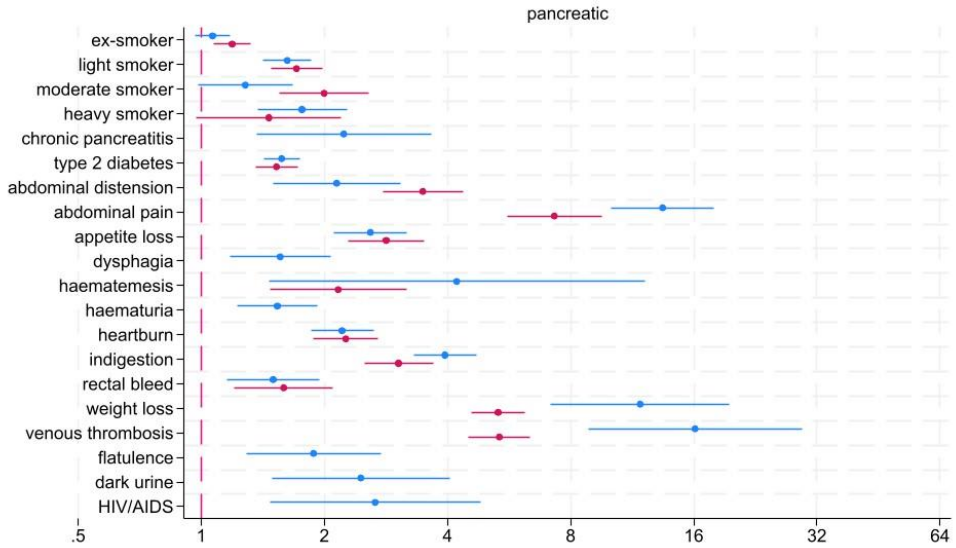
	Incomplete data	*Complete data*
Total	4707481	2757026
men	2590342 (55.0)	1251376 (45.4)
mean age (SD)	41.8 (16.6)	49.3 (17.9)
mean Townsend (SD)	0.5 (3.1)	0.5 (3.1)
White	2234514 (47.5)	1545604 (56.1)
Indian	146199 (3.1)	96065 (3.5)
Pakistani	91776 (1.9)	62620 (2.3)
Bangladeshi	47189 (1.0)	39526 (1.4)
Other Asian	105440 (2.2)	61101 (2.2)
Caribbean	42348 (0.9)	36317 (1.3)
Black African	118105 (2.5)	76162 (2.8)
Chinese	72427 (1.5)	25142 (0.9)
Other	209835 (4.5)	115034 (4.2)
Ethnicity not recorded	1639648 (34.8)	699455 (25.4)
FH breast cancer	130609 (2.8)	123489 (4.5)
FH bowel cancer	71723 (1.5)	70817 (2.6)
FH ovarian cancer	8349 (0.2)	8177 (0.3)
FH prostate cancer	21158 (0.4)	19008 (0.7)
FH lung cancer	28882 (0.6)	31111 (1.1)
FH blood cancer	950 (0.0)	1223 (0.0)
chronic pancreatitis	2048 (0.0)	3200 (0.1)
COPD	32418 (0.7)	100211 (3.6)
type 2 diabetes	60729 (1.3)	302169 (11.0)
endometrial hyperplasia or polyp	10446 (0.2)	10976 (0.4)
liver cirrhosis	4953 (0.1)	6697 (0.2)
Hepatitis C	8211 (0.2)	7049 (0.3)
Hepatitis B	10039 (0.2)	8239 (0.3)
HIV/AIDs	8144 (0.2)	5631 (0.2)
erectile dysfunction	14429 (0.3)	37497 (1.4)
constipation	28305 (0.6)	39977 (1.5)
cough	159178 (3.4)	204215 (7.4)
urinary frequency	21527 (0.5)	25992 (0.9)
urinary retention	2893 (0.1)	4190 (0.2)
nocturia	4530 (0.1)	6818 (0.2)
itching	10187 (0.2)	13902 (0.5)
change in bowels	7642 (0.2)	11012 (0.4)
bruising	3539 (0.1)	4841 (0.2)
back pain	193851 (4.1)	198087 (7.2)
hoarseness	5618 (0.1)	7557 (0.3)
flatulence	27074 (0.6)	29575 (1.1)
abdominal mass	4646 (0.1)	4990 (0.2)
dark urine	2000 (0.0)	2559 (0.1)
appetite loss	14810 (0.3)	20891 (0.8)
weight loss	22863 (0.5)	44082 (1.6)
abdominal distension	28297 (0.6)	30255 (1.1)
abdominal pain	229683 (4.9)	194127 (7.0)

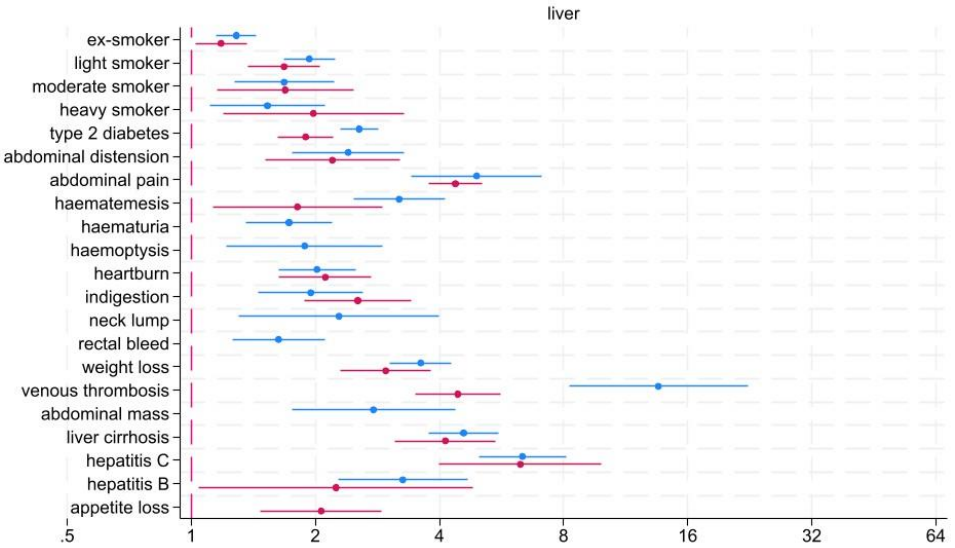
dysphagia	17870 (0.4)	23639 (0.9)
heartburn	86784 (1.8)	90049 (3.3)
indigestion	56980 (1.2)	58312 (2.1)
haematemesis	8430 (0.2)	9011 (0.3)
rectal bleeding	66142 (1.4)	58498 (2.1)
haematuria	41816 (0.9)	49120 (1.8)
haemoptysis	10350 (0.2)	12054 (0.4)
lump in the neck	21545 (0.5)	18066 (0.7)
thrombosis	24700 (0.5)	29179 (1.1)
night sweats	9573 (0.2)	11706 (0.4)
breast lump	98707 (2.1)	79715 (2.9)
breast pain	38302 (0.8)	34769 (1.3)
breast skin/nipple changes	11166 (0.2)	10645 (0.4)
inter-menstrual bleeding	22210 (0.5)	20799 (0.8)
postmenopausal bleeding	14673 (0.3)	16237 (0.6)
post coital bleeding	12087 (0.3)	10400 (0.4)
testicular pain	22259 (0.5)	11886 (0.4)
testicular lump	29075 (0.6)	16902 (0.6)
mean BMI (SD)	25.4 (5.5)	27.3 (5.8)
mean haemoglobin (SD)	138.3 (15.2)	137.8 (15.2)
mean bilirubin (SD)	10.2 (6.1)	10.0 (5.7)
mean platelet (SD)	257.7 (68.7)	257.3 (70.2)
mean neutrophil (SD)	4.2 (1.9)	4.3 (1.9)
mean lymphocyte (SD)	2.1 (0.9)	2.1 (1.0)
mean albumin (SD)	42.8 (4.2)	42.4 (4.1)
mean alkaline phosphatase (SD)	78.5 (35.6)	80.3 (35.3)

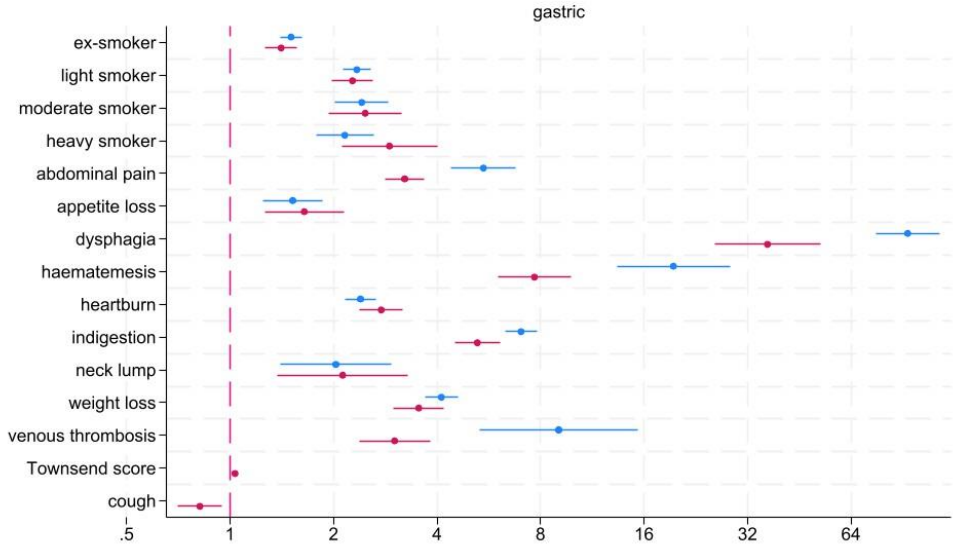
Supplementary Figure 1 Smoothed crude incidence rates of different types of cancer per 10,000 per month 2015-2023 in men and women.

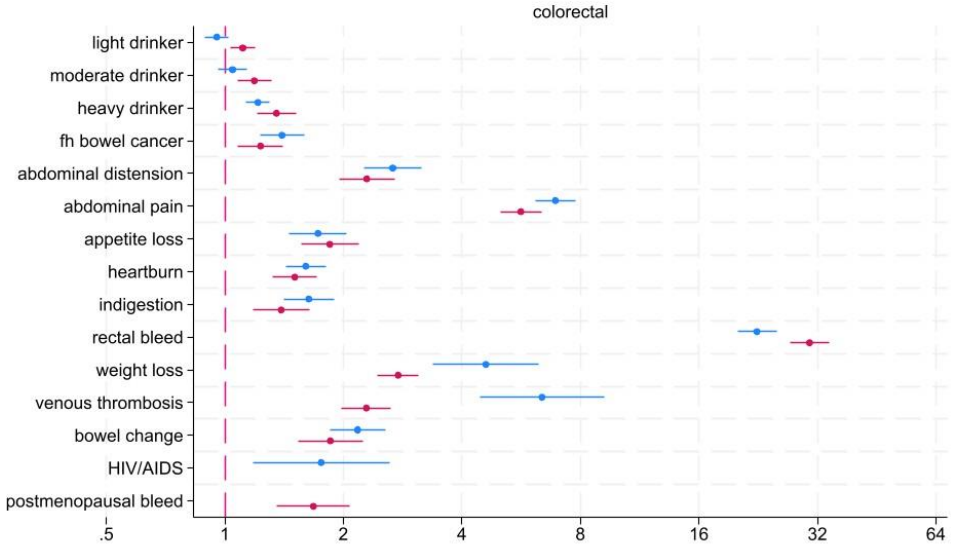


Supplementary Figure 2. Adjusted Odds ratios (95% CI) for probability of pancreatic, liver, gastro-oesophageal and colorectal cancer for final model B in the QResearch Derivation Cohort (women=red, men=blue). Odds ratios are adjusted for continuous variables (age, BMI, deprivation, blood test results)

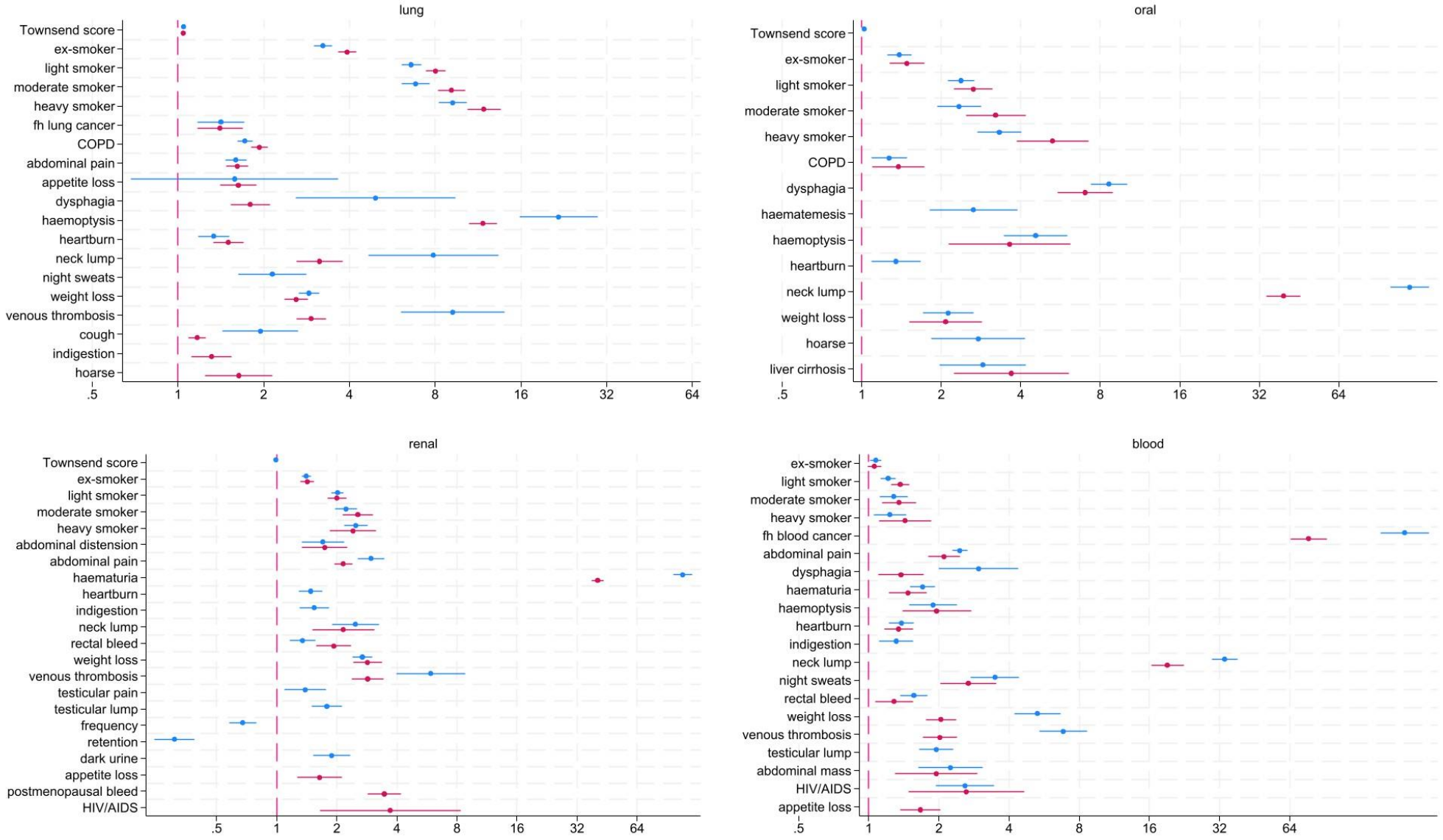




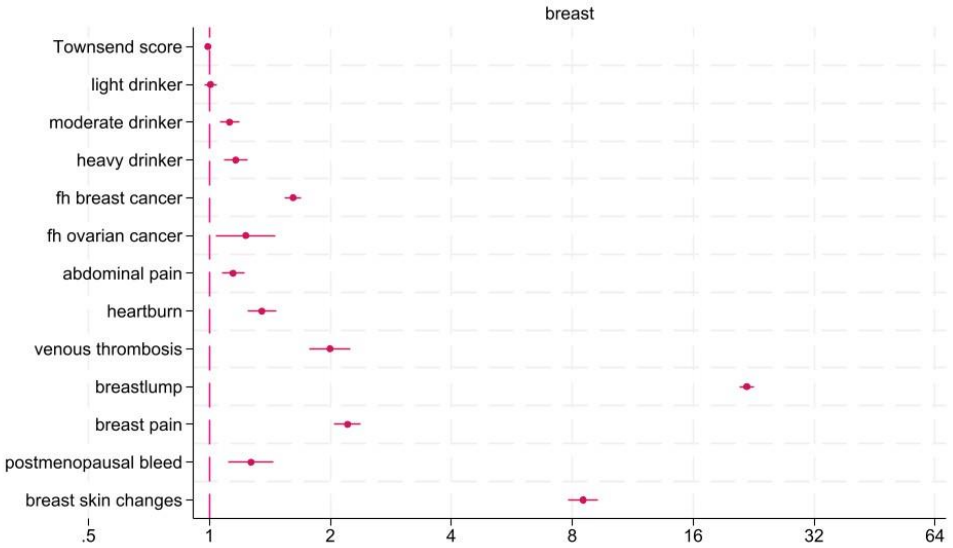


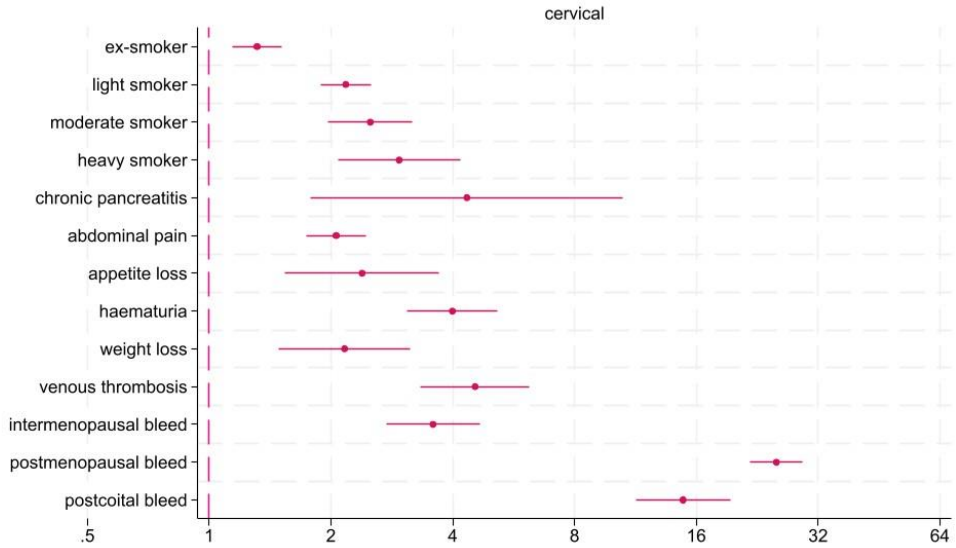


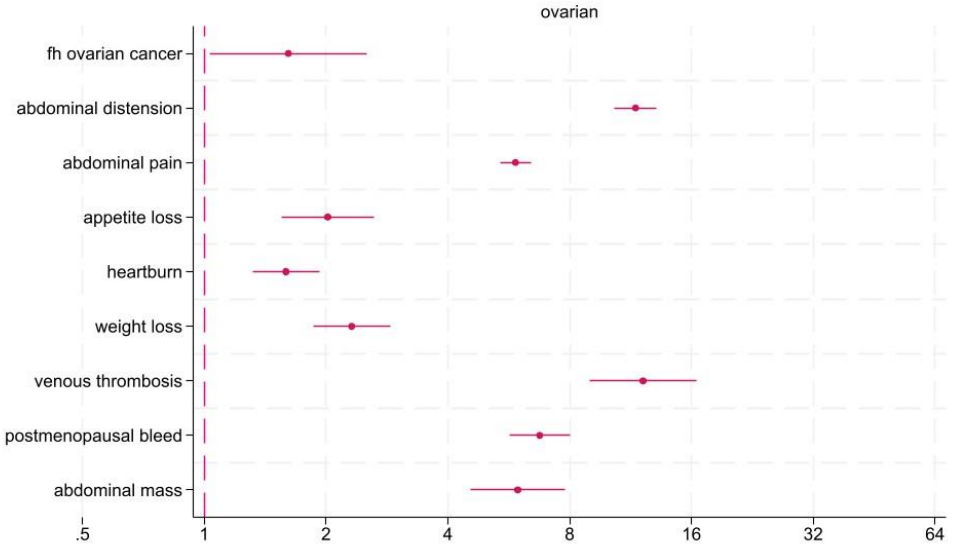
Supplementary Figure 3. Adjusted Odds ratios (95% CI) for probability of lung, oral, renal and blood cancers for final model B in the Derivation Cohort (women=red, men=blue). Odds ratios are also adjusted for continuous variables (age, BMI, deprivation, blood test results)

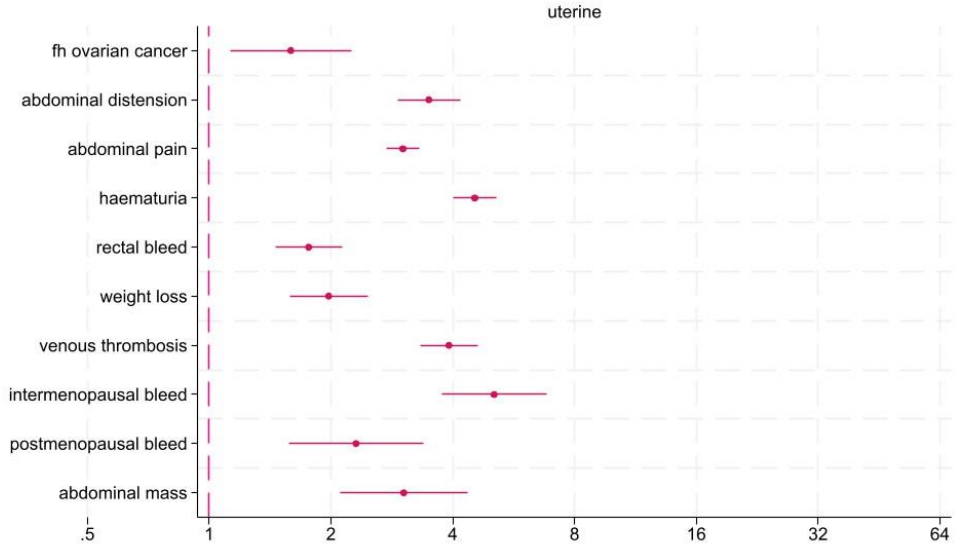


Supplementary Figure 4. Adjusted Odds ratios (95% CI) for probability for breast, cervical, ovarian, uterine cancers in women for final model B in the Derivation Cohort. Odds ratios are also adjusted for continuous variables (age, BMI, deprivation, blood test results)

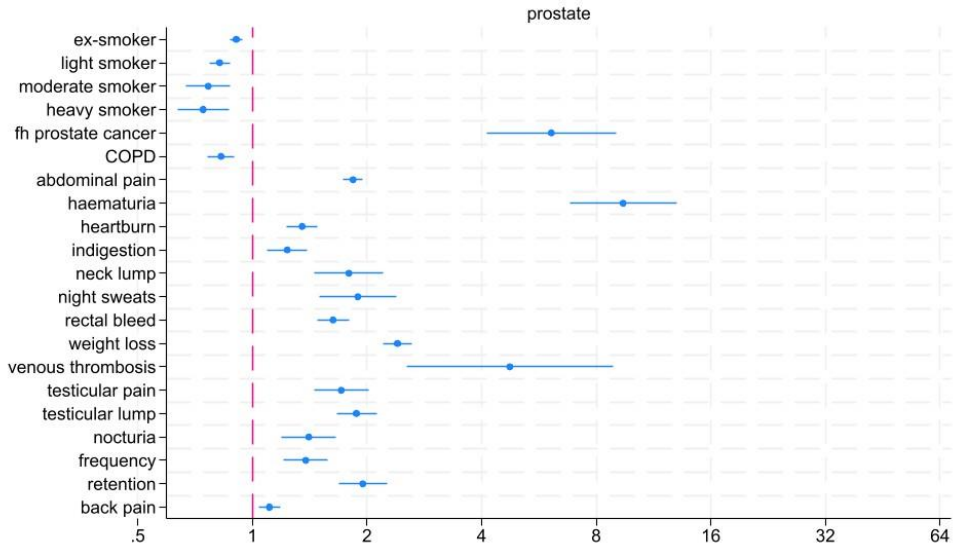


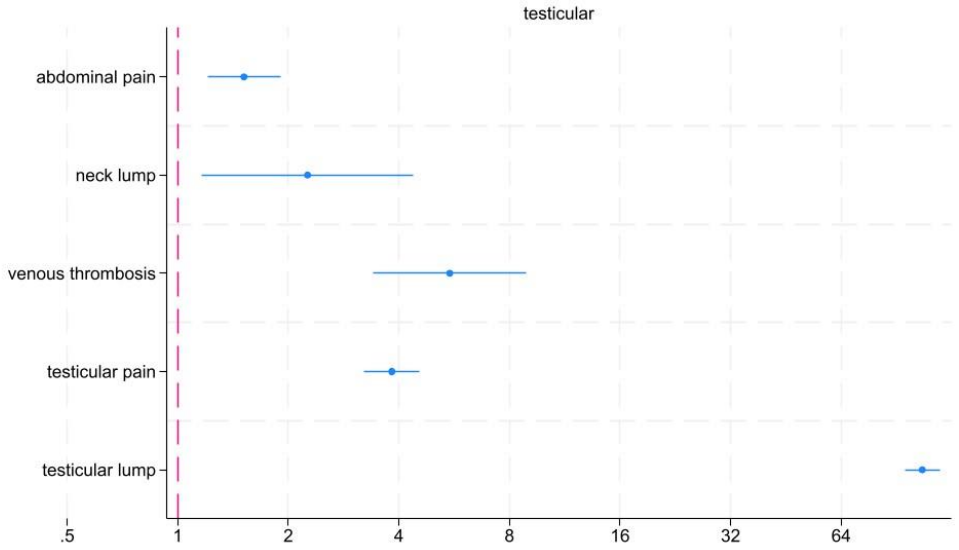


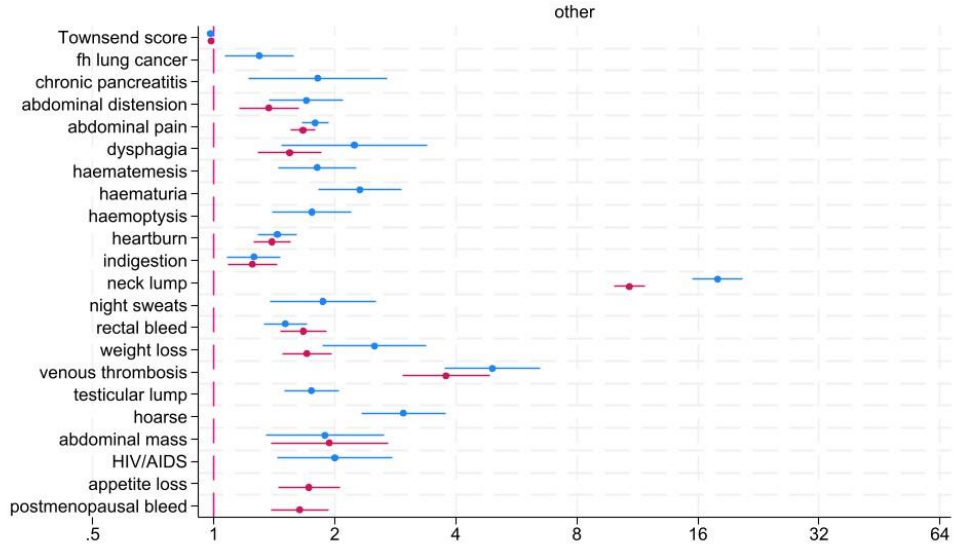




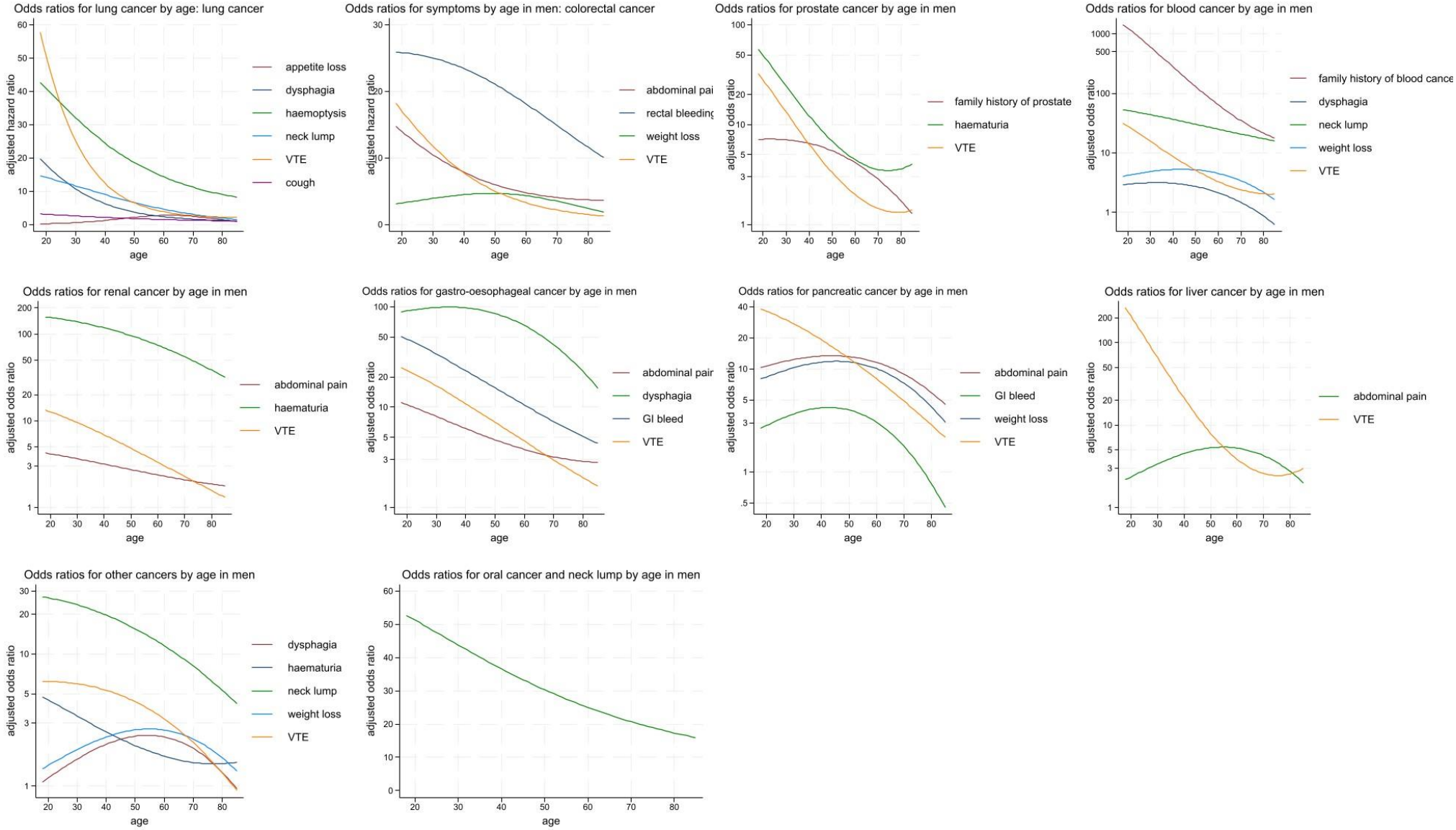
Supplementary Figure 5. Adjusted Odds ratios (95% CI) for probability of prostate, testicular and other cancers for final model B in the Derivation Cohort (women=red, men=blue)



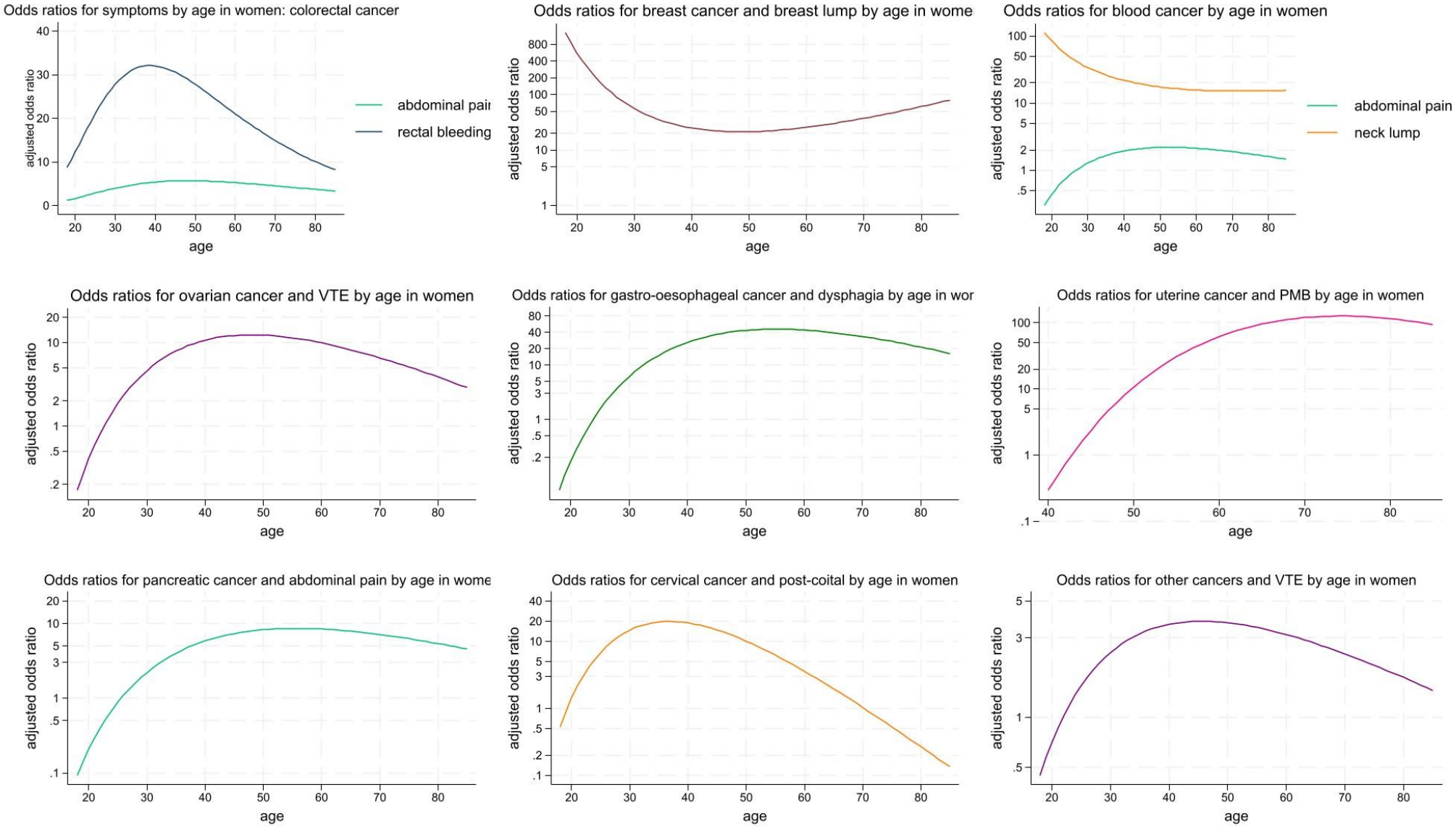




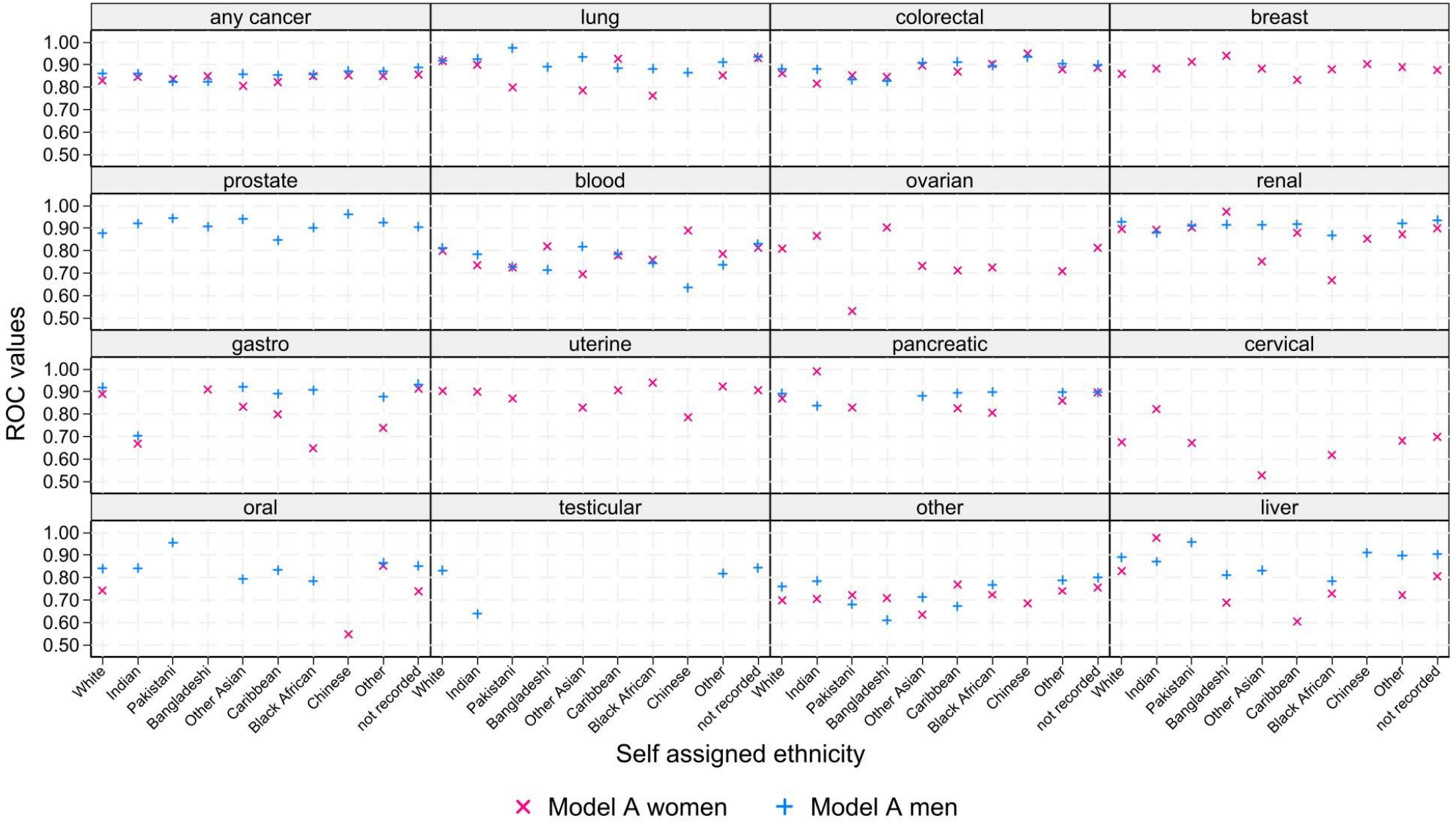
Supplementary Figure 6. Adjusted odds ratios for probability of each cancer type for symptoms by age in men.



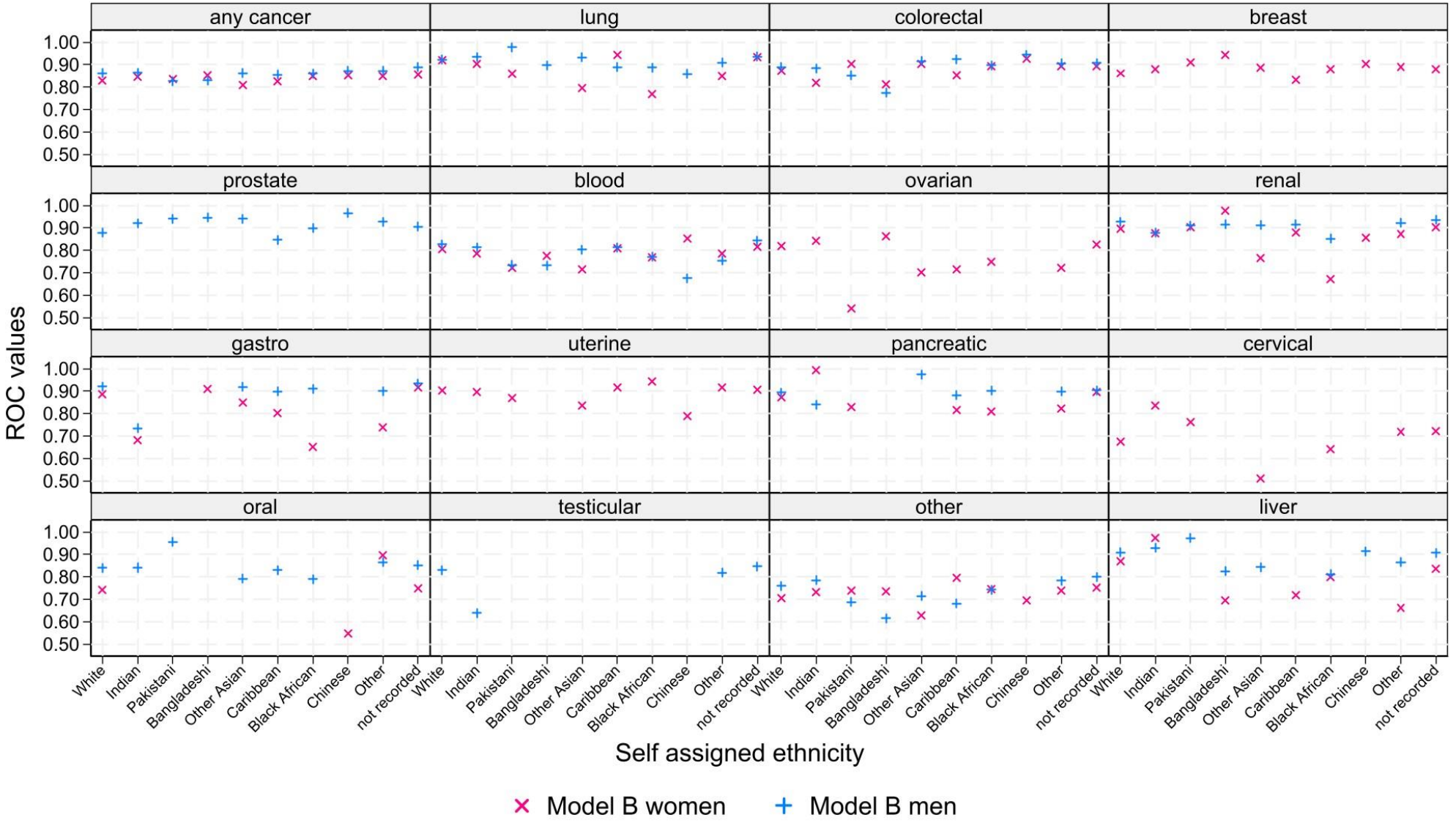
Supplementary Figure 7. Adjusted odds ratios for probability of each cancer type for symptoms by age in women.



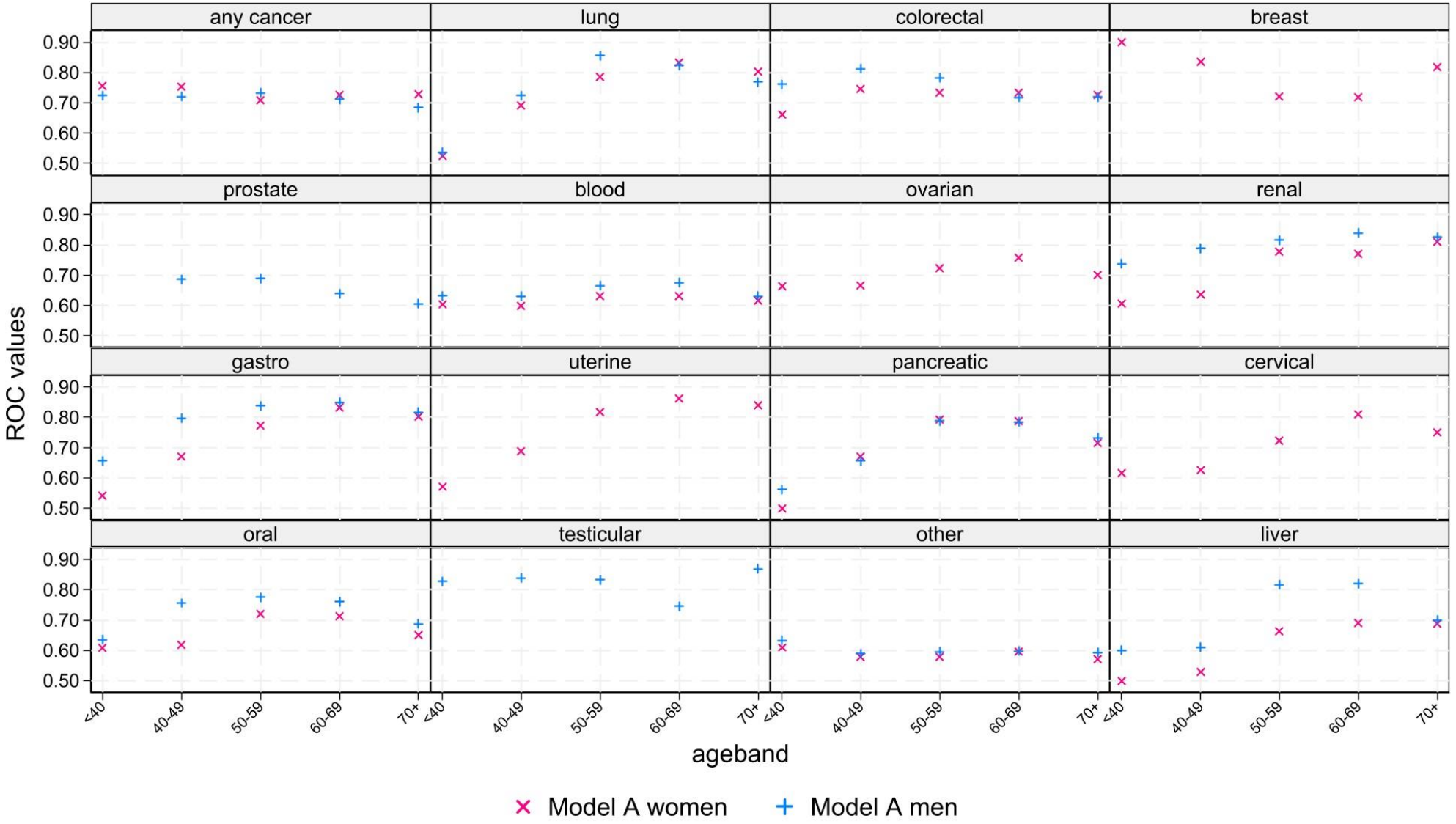
Supplementary Figure 8. Discrimination values (c statistics) for final model A (without blood tests) in men and women in the QResearch English validation cohort by ethnic group (cells with less than 5 events suppressed).



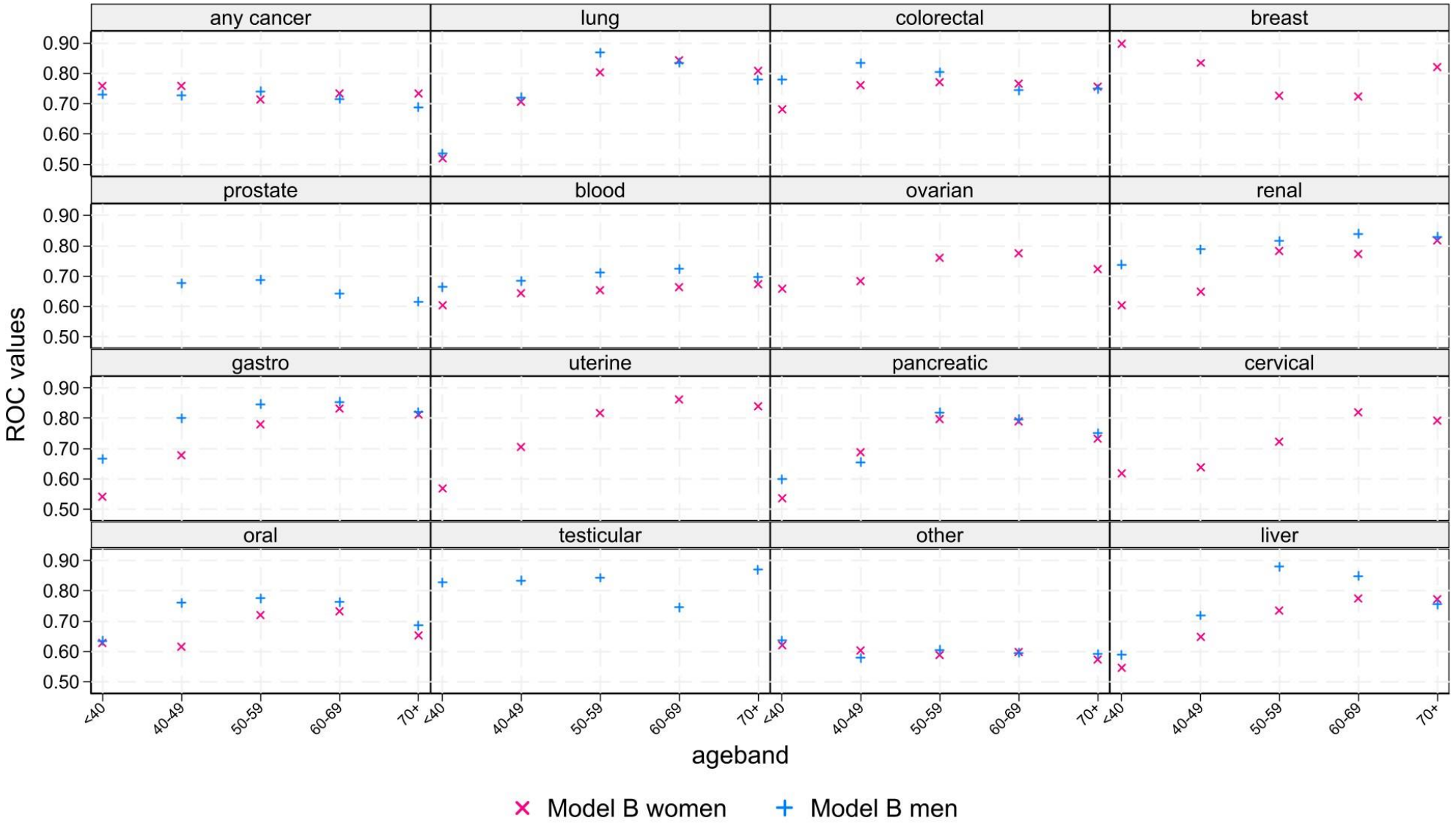
Supplementary Figure 9. Discrimination values (c statistic) for final model B (with blood tests) in men and women in the QResearch English validation cohort by ethnic group (cells with less than 5 events suppressed).



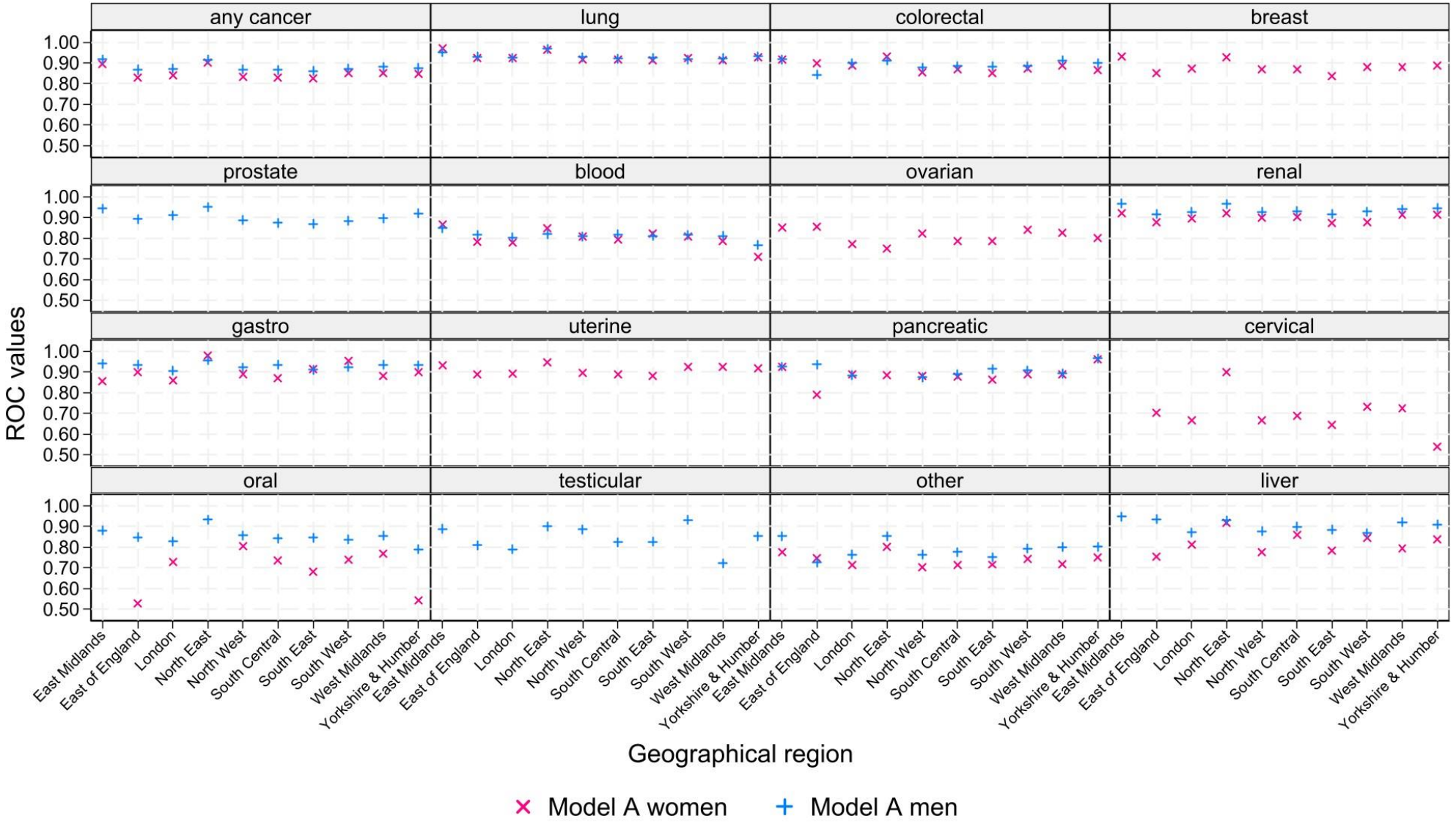
Supplementary Figure 10. Discrimination values (c statistic) for final model A (without blood test) in men and women in the QResearch English validation cohort by age group (cells with less than 5 events suppressed).



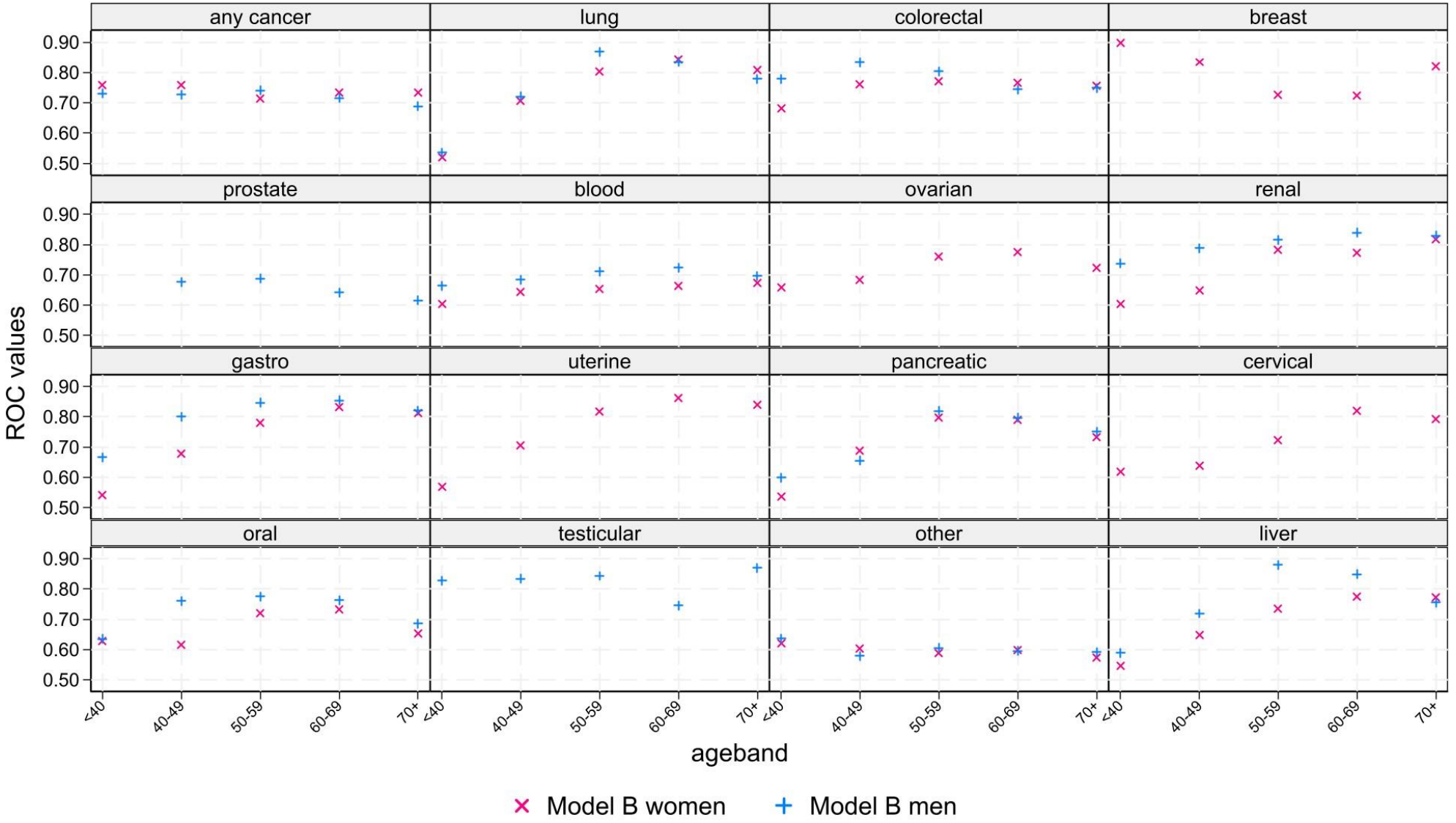
Supplementary Figure 11. Discrimination for final model B (with blood test) in men and women in the QResearch English validation cohort by age (cells with less than 5 events suppressed).



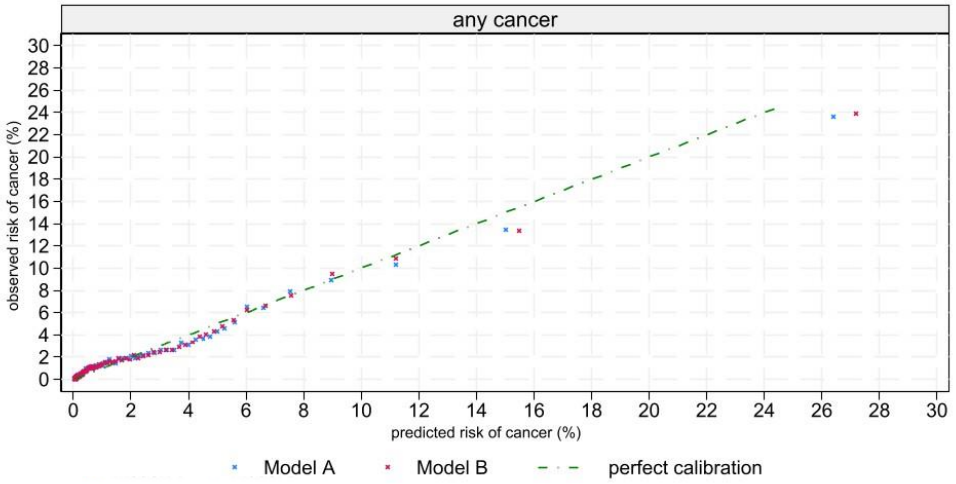
Supplementary Figure 12. Discrimination for final model A (without blood test) in men and women in the QResearch English validation cohort by geographical region (cells with less than 5 events suppressed).



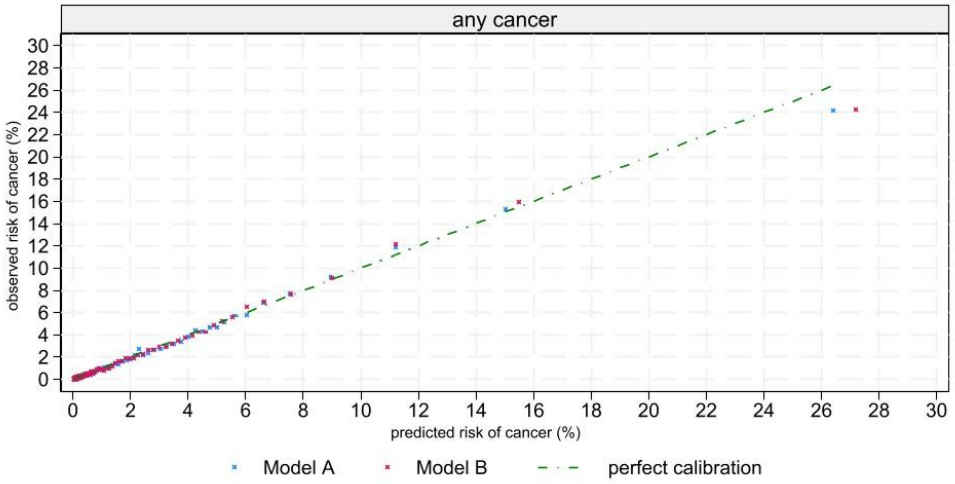
Supplementary Figure 13. Discrimination for final model B (with blood test) in men and women in the QResearch English validation cohort by geographical region (cells with less than 5 events suppressed).



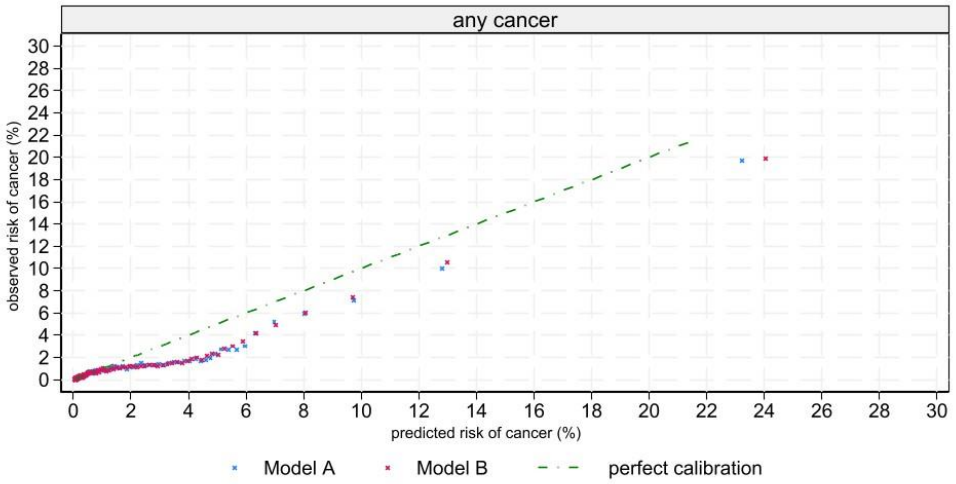
Supplementary Figure 14. Predicted to observed probability for cancer overall in men and women comparing models A and B in people aged 18-84 in the QResearch English validation cohort and CPRD cohort from the devolved administrations.



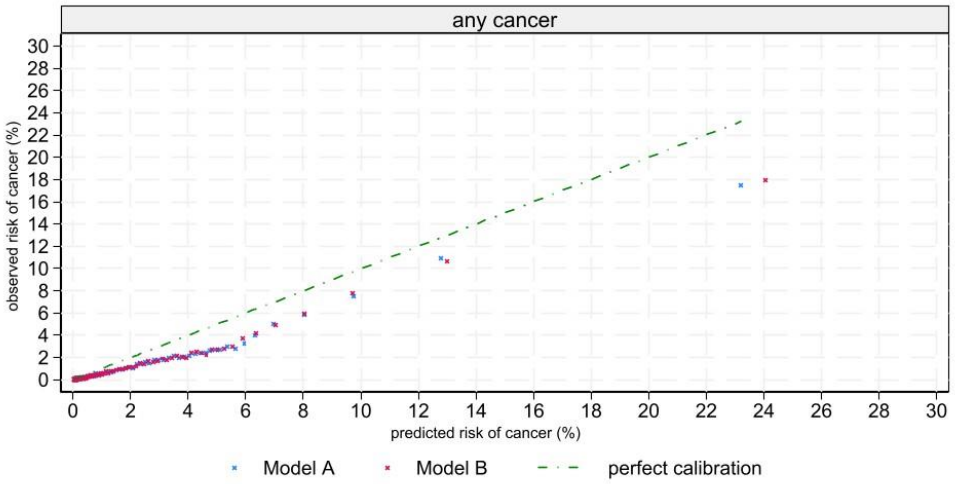
Calibration in women in England



Calibration in men in England

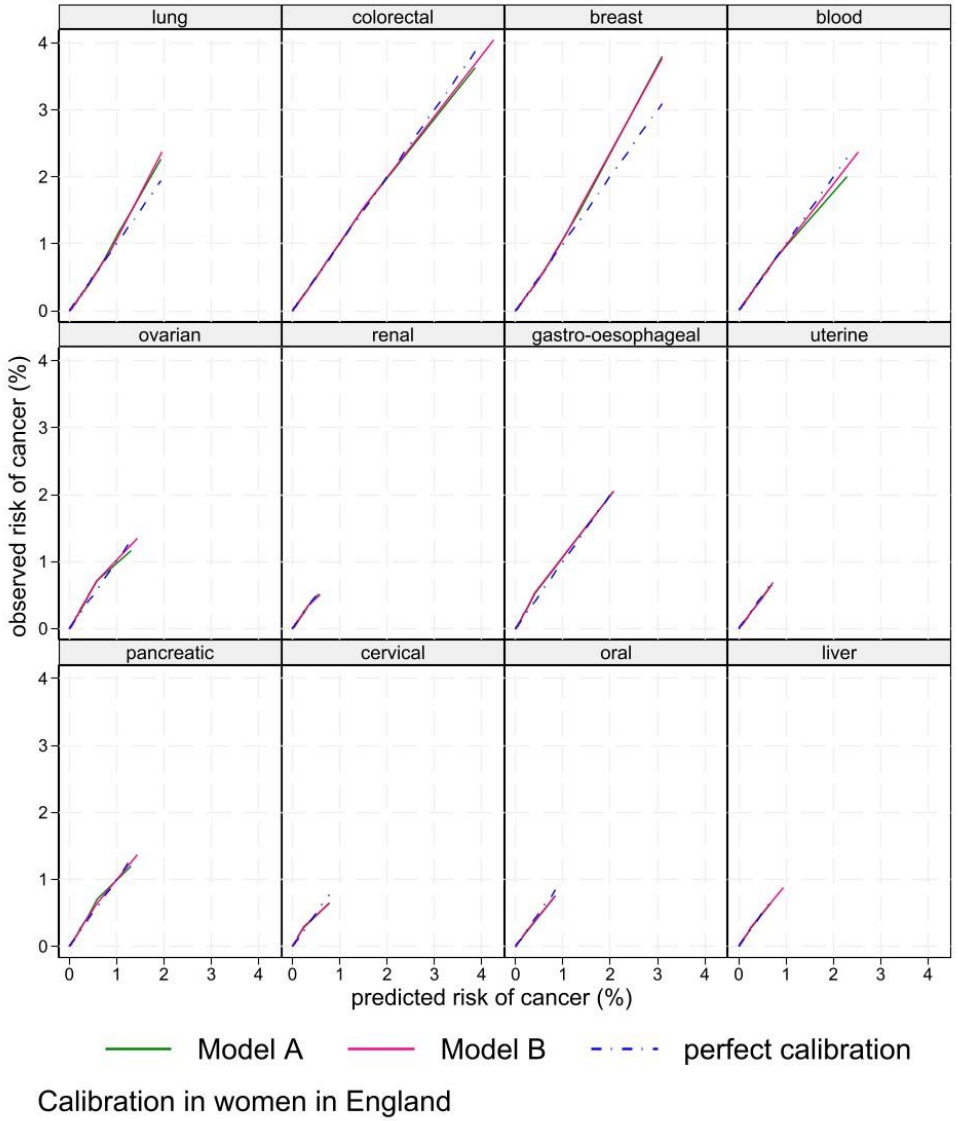


Calibration in women in devolved administrations

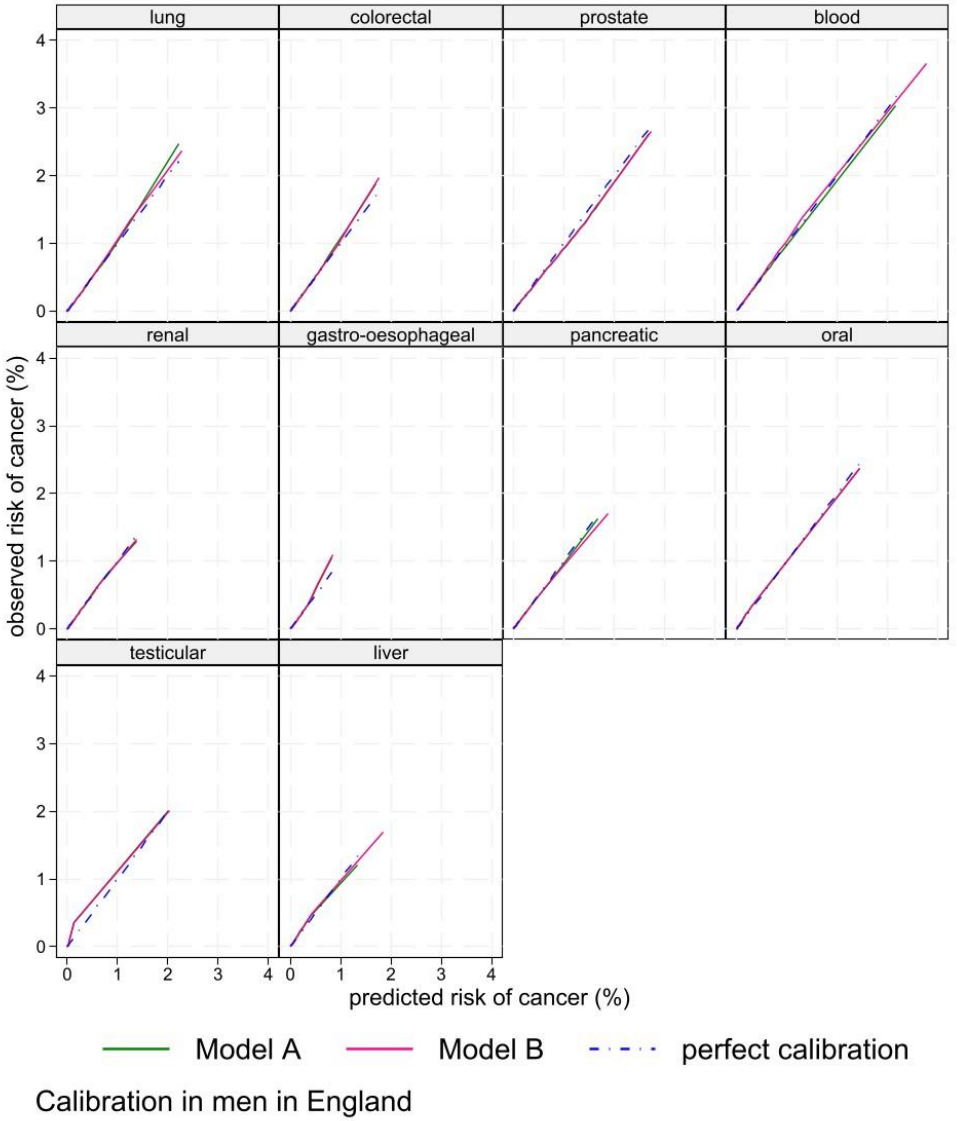


Calibration in men in devolved administrations

Supplementary Figure 15. Predicted to observed probability for each cancer type in men and women comparing models A and B in people aged 18-84 in the English validation cohort.

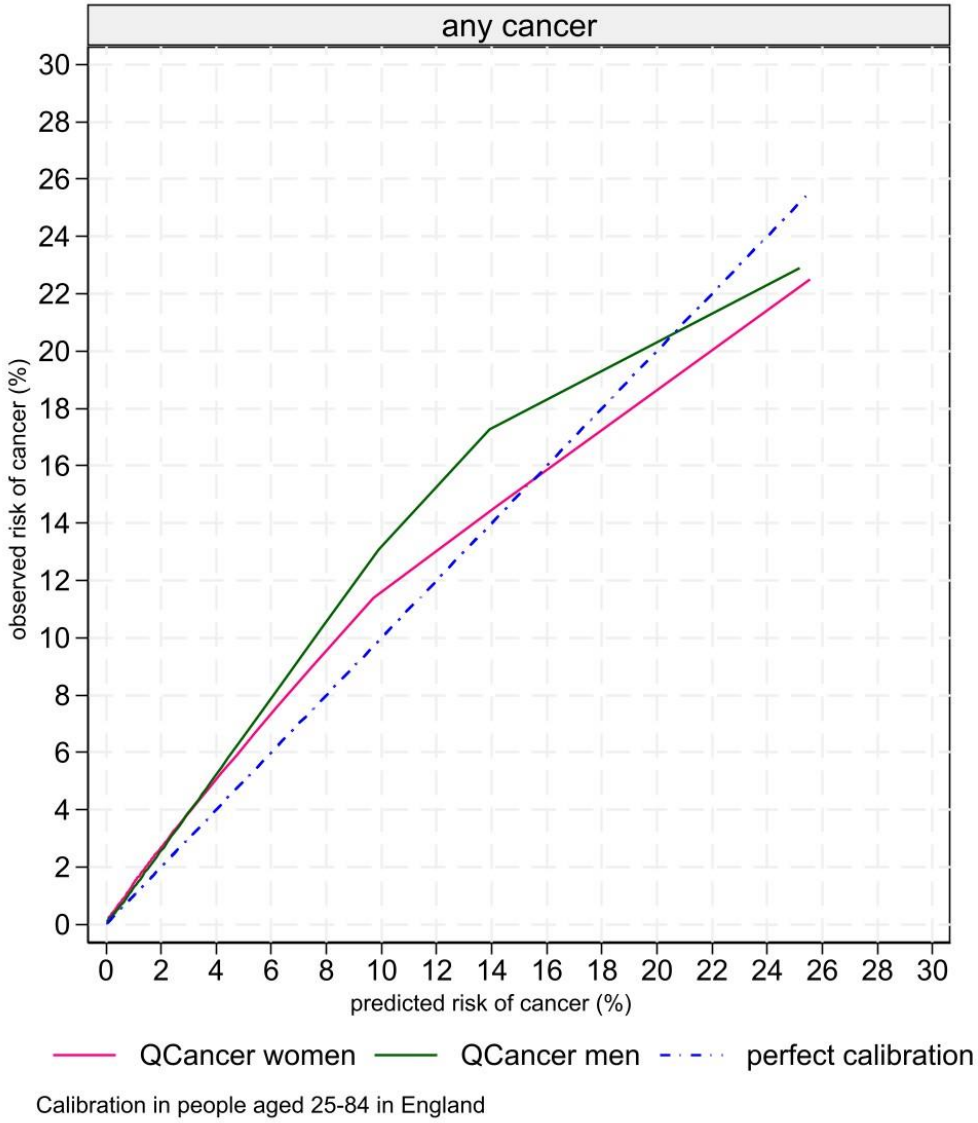


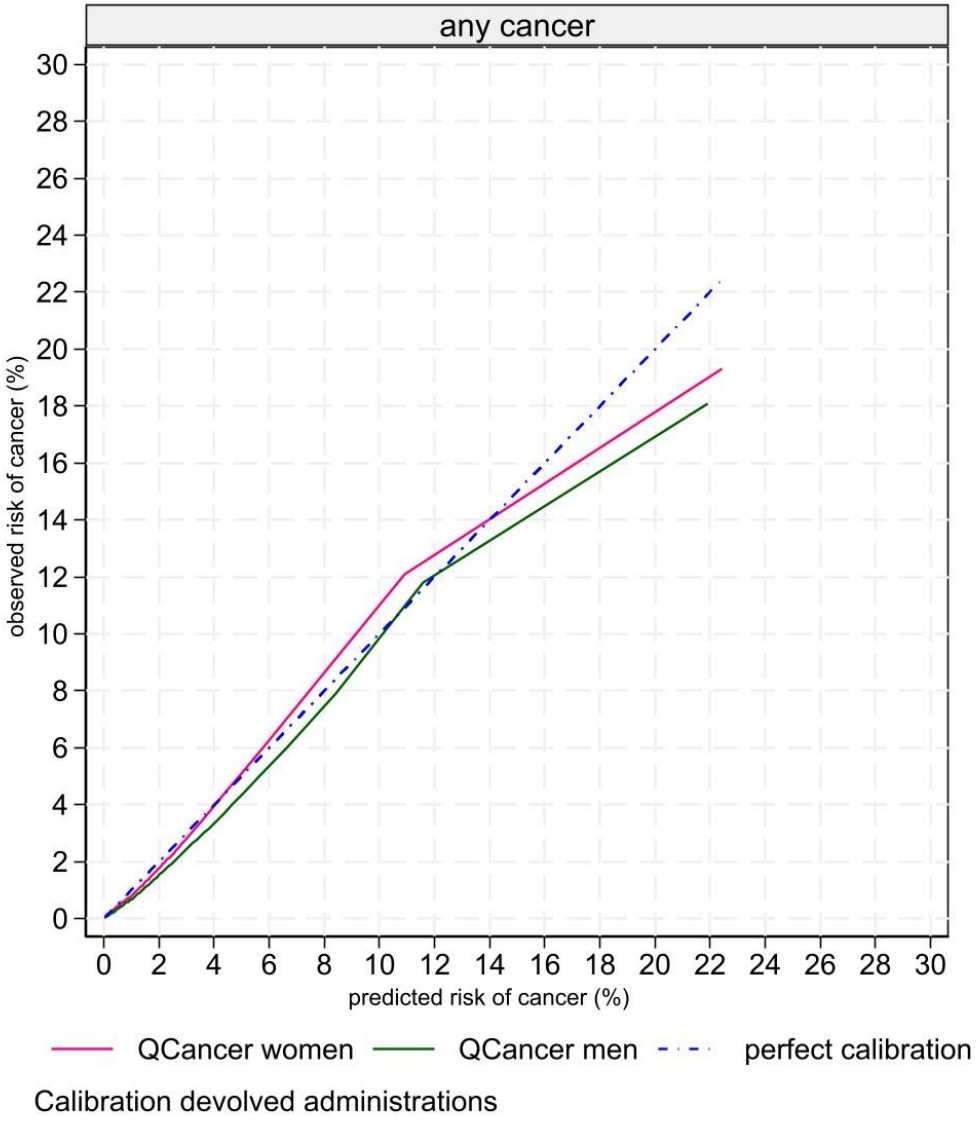
Calibration in women in England



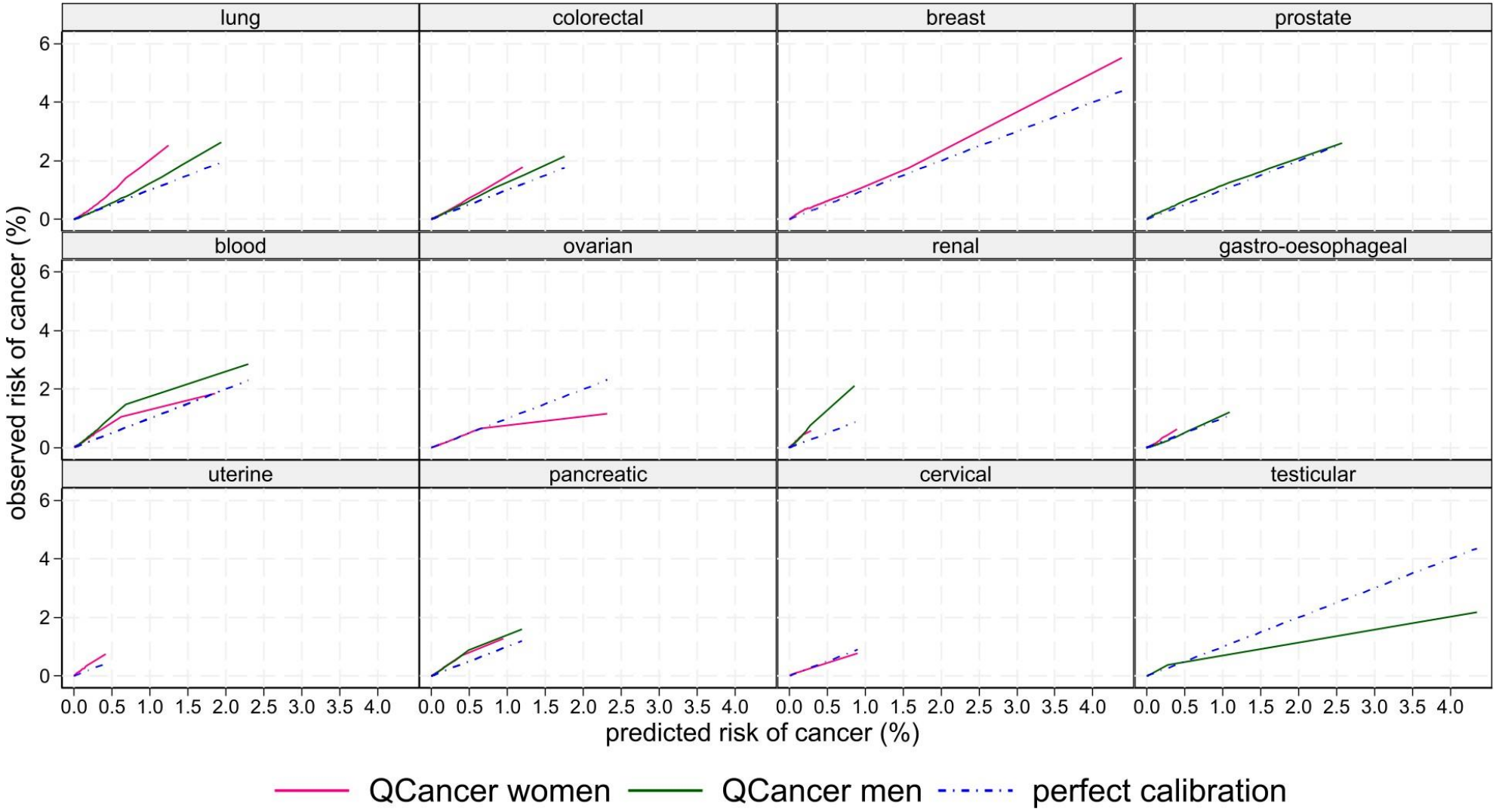
Calibration in men in England

Supplementary Figure 16 calibration plot showing predicted and observed probabilities for any cancer using QCancer in men and women aged 25-84 years in the QResearch English validation cohort and CPRD validation cohort in the devolved administrations.

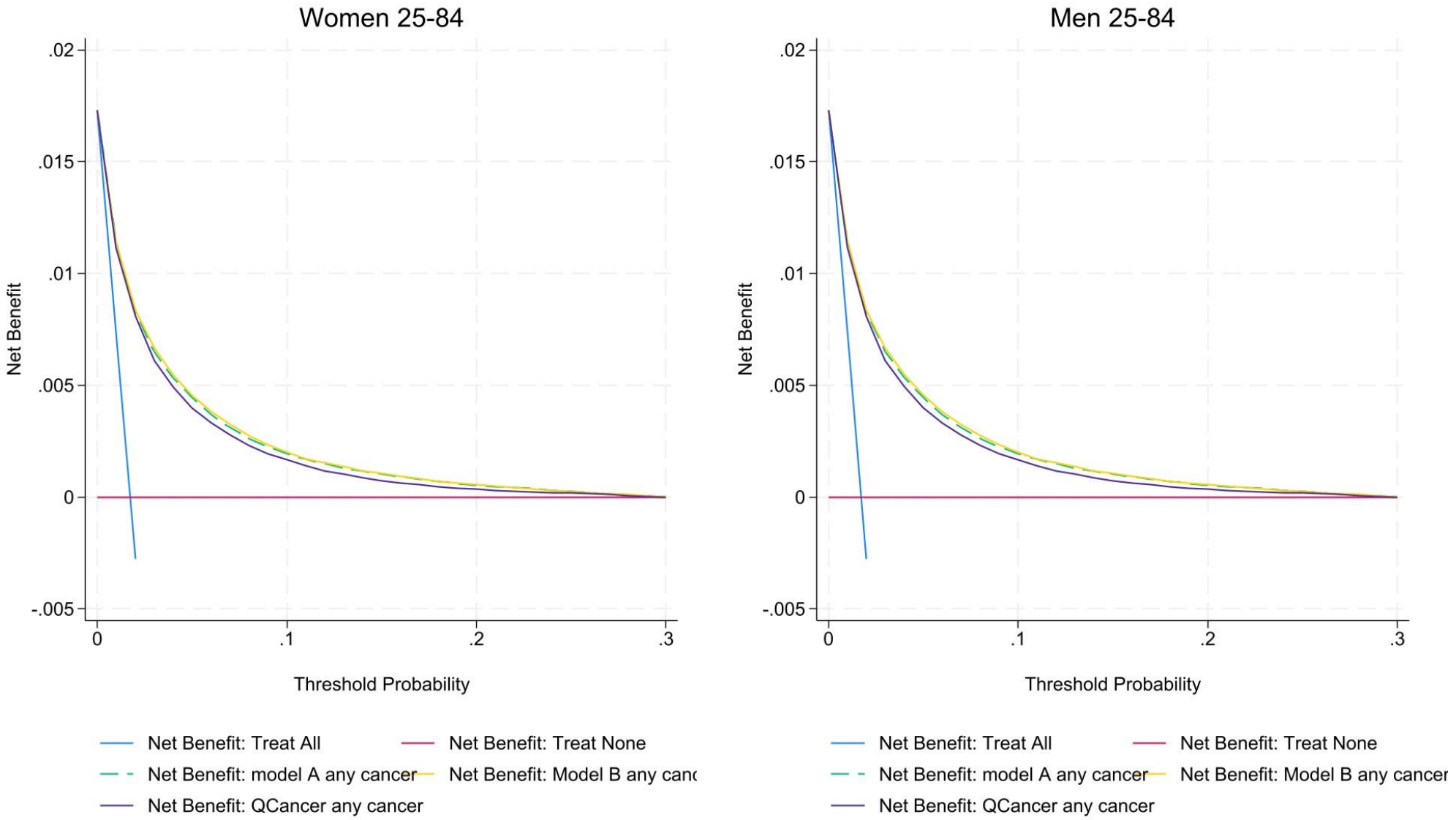




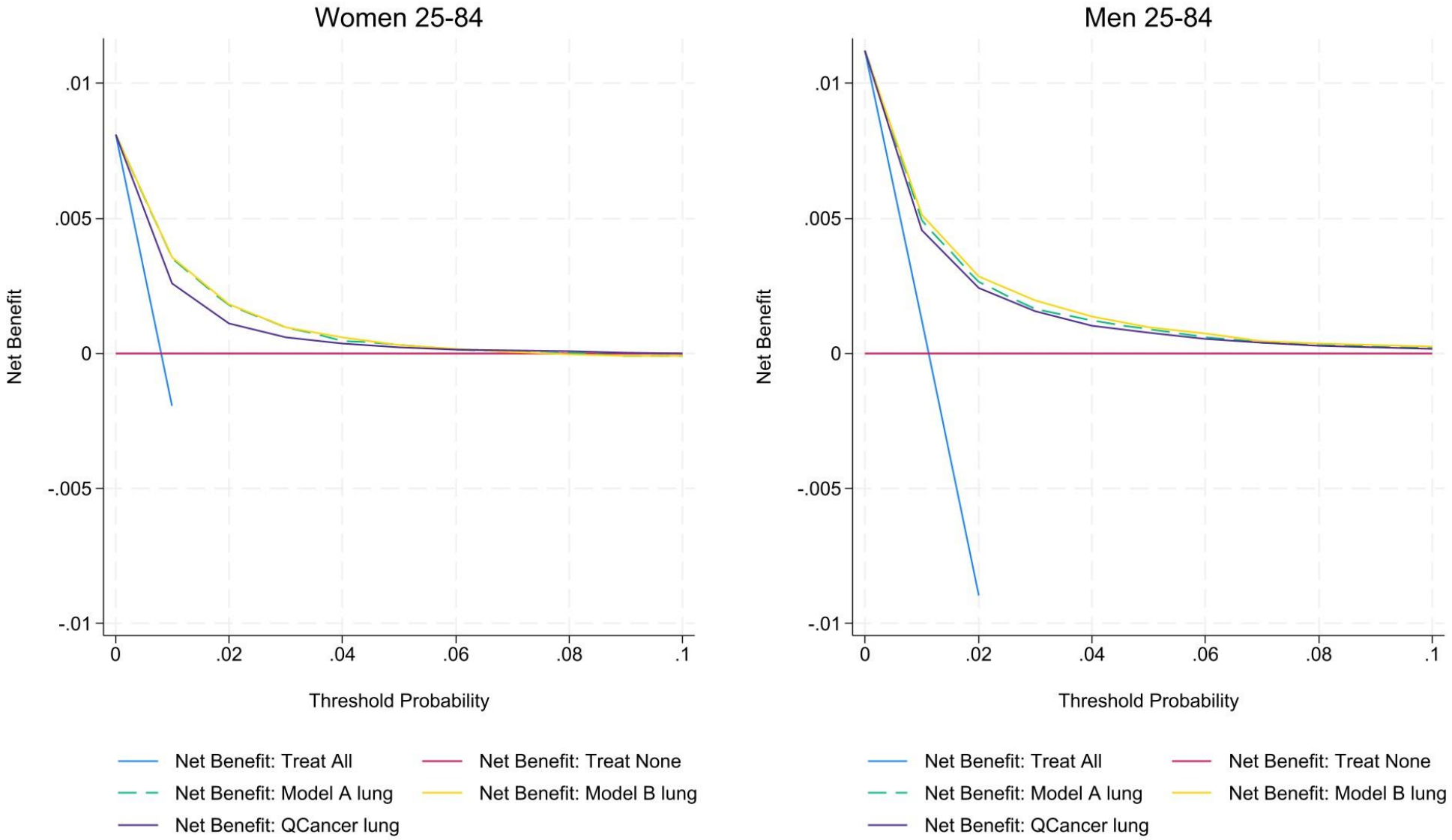
Supplementary Figure 17 calibration plot showing predicted and observed probabilities by cancer type using QCancer in men and women aged 25-84 years in the QResearch English validation cohort.



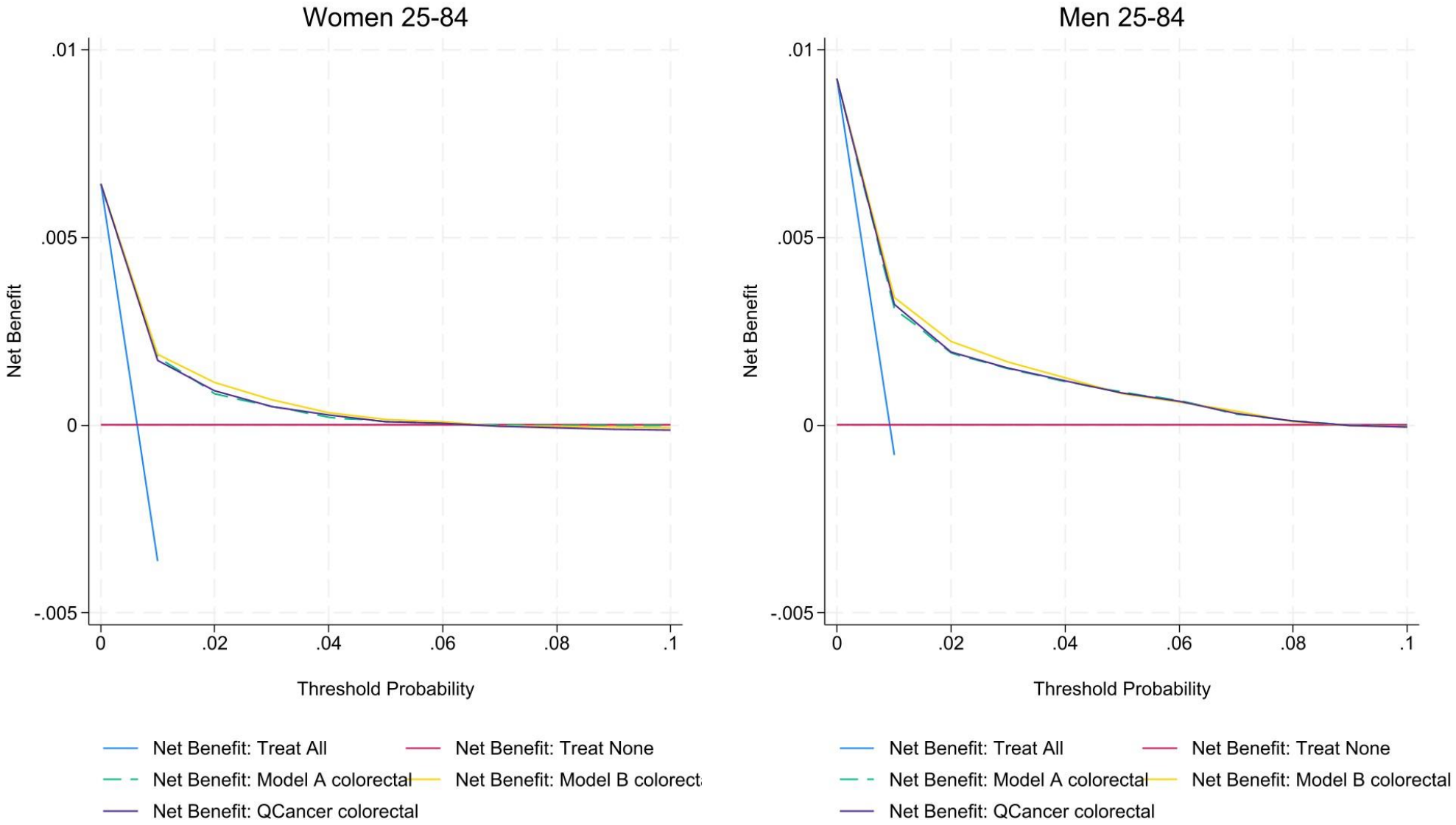
Supplementary Figure 18 Decision analysis curves in patients aged 25-84 in the English validation cohort for any cancer vs no cancer using three models (QCancer, Model A, Model B).



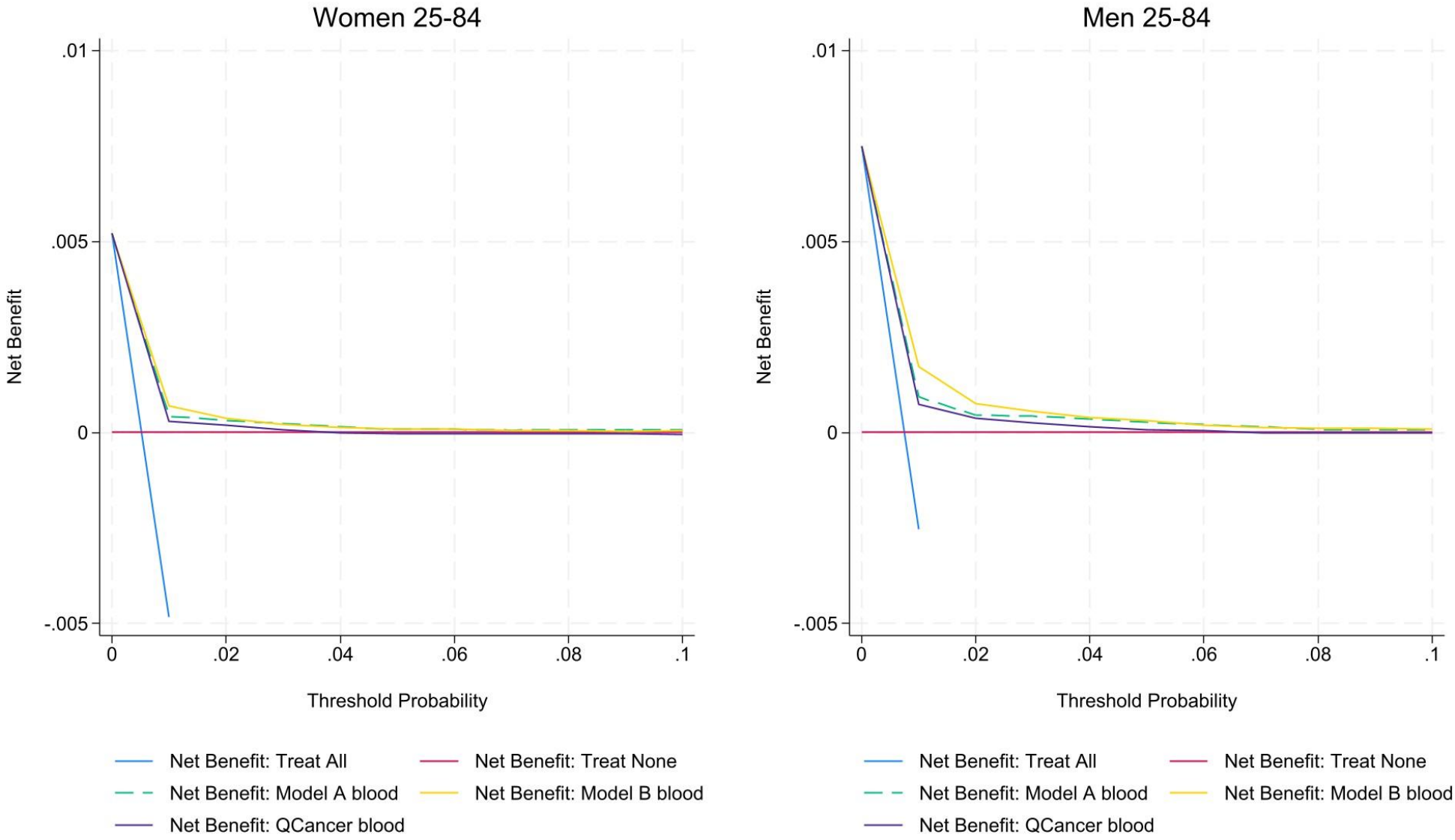
Supplementary Figure 19 Decision analysis curves in patients aged 25-84 in the English validation cohort for lung cancer



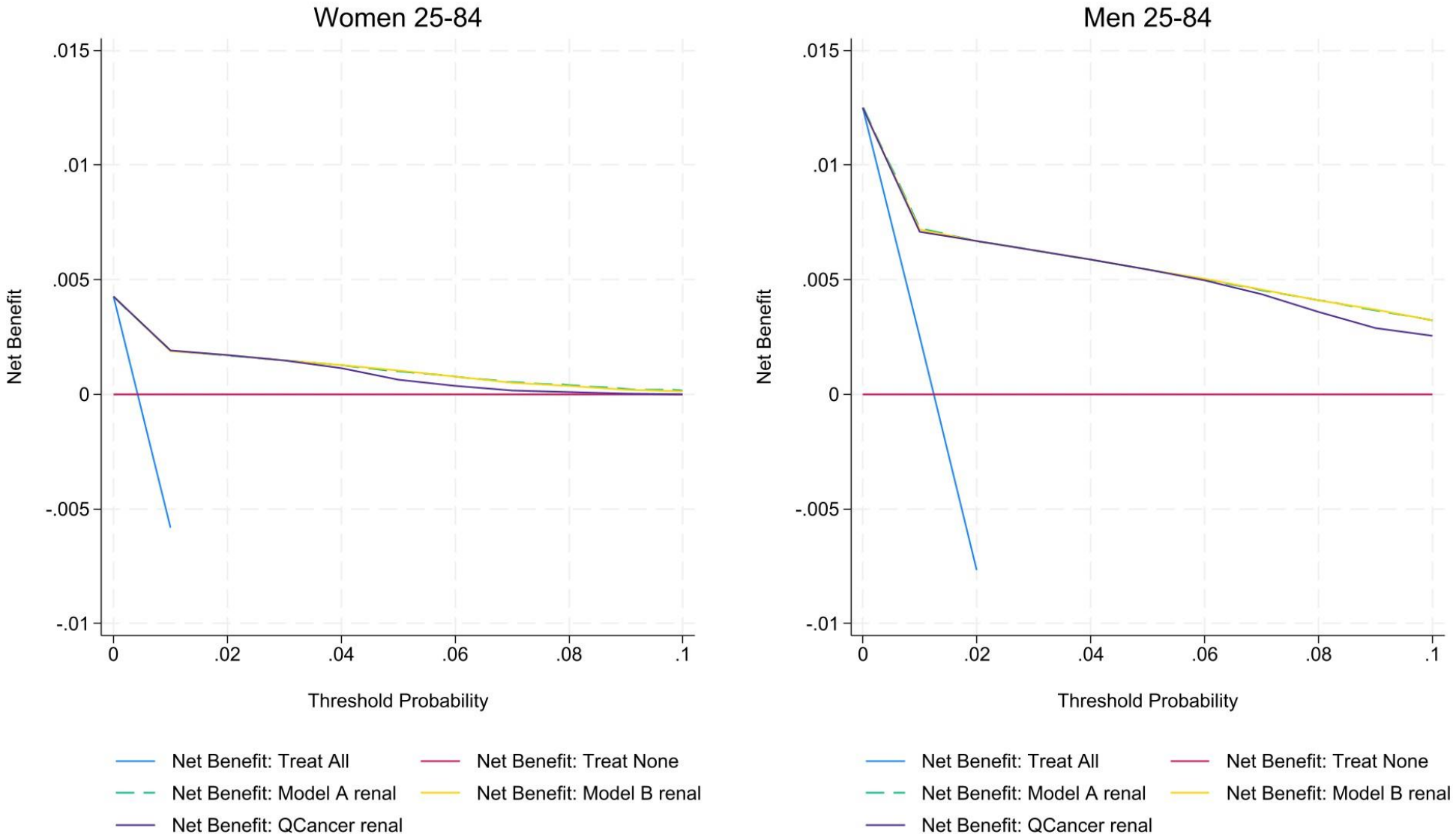
Supplementary Figure 20 Decision analysis curves in patients aged 25-84 in the English validation cohort for colorectal cancer



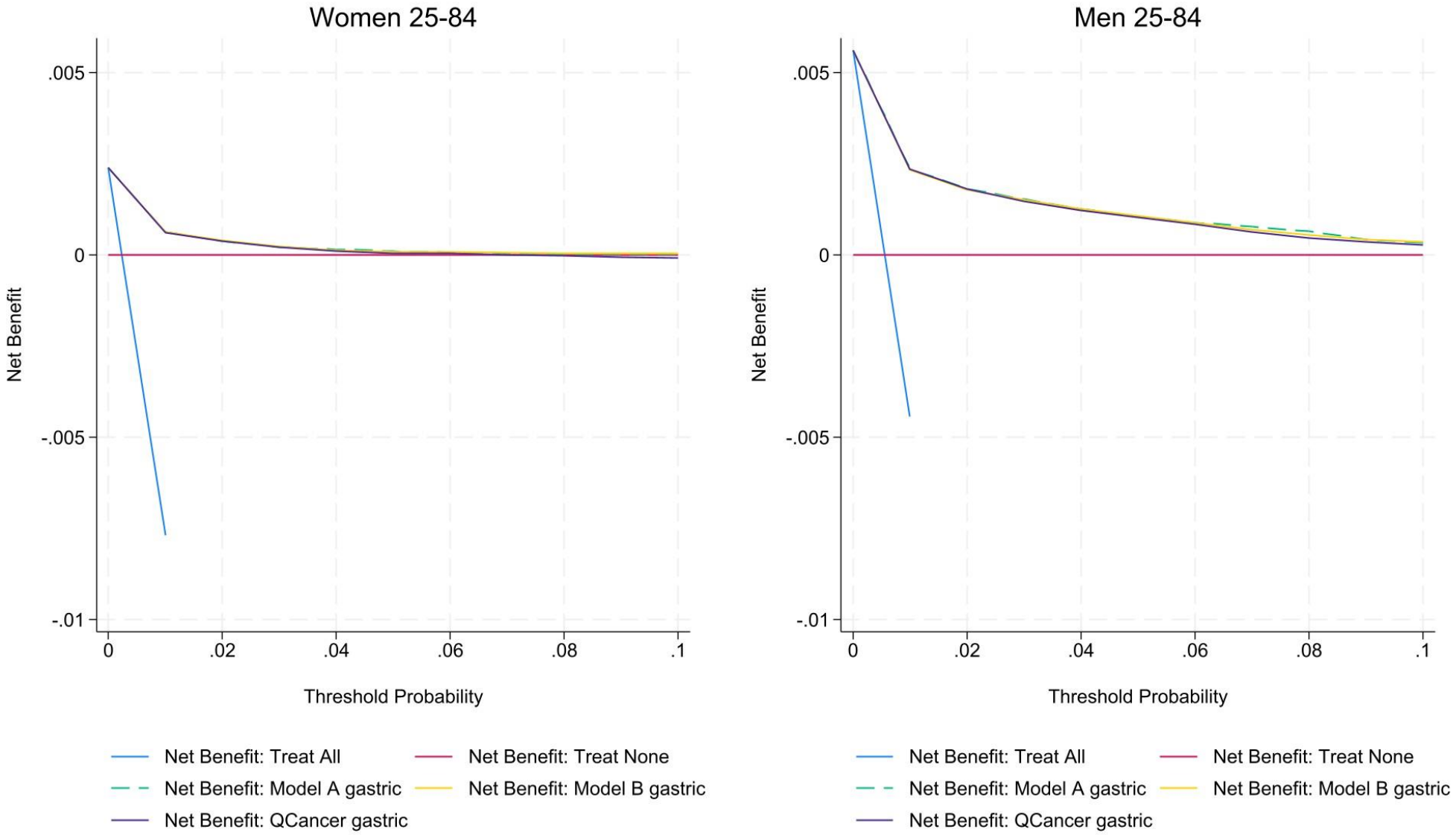
Supplementary Figure 21 Decision analysis curves in patients aged 25-84 in the English validation cohort for blood cancer



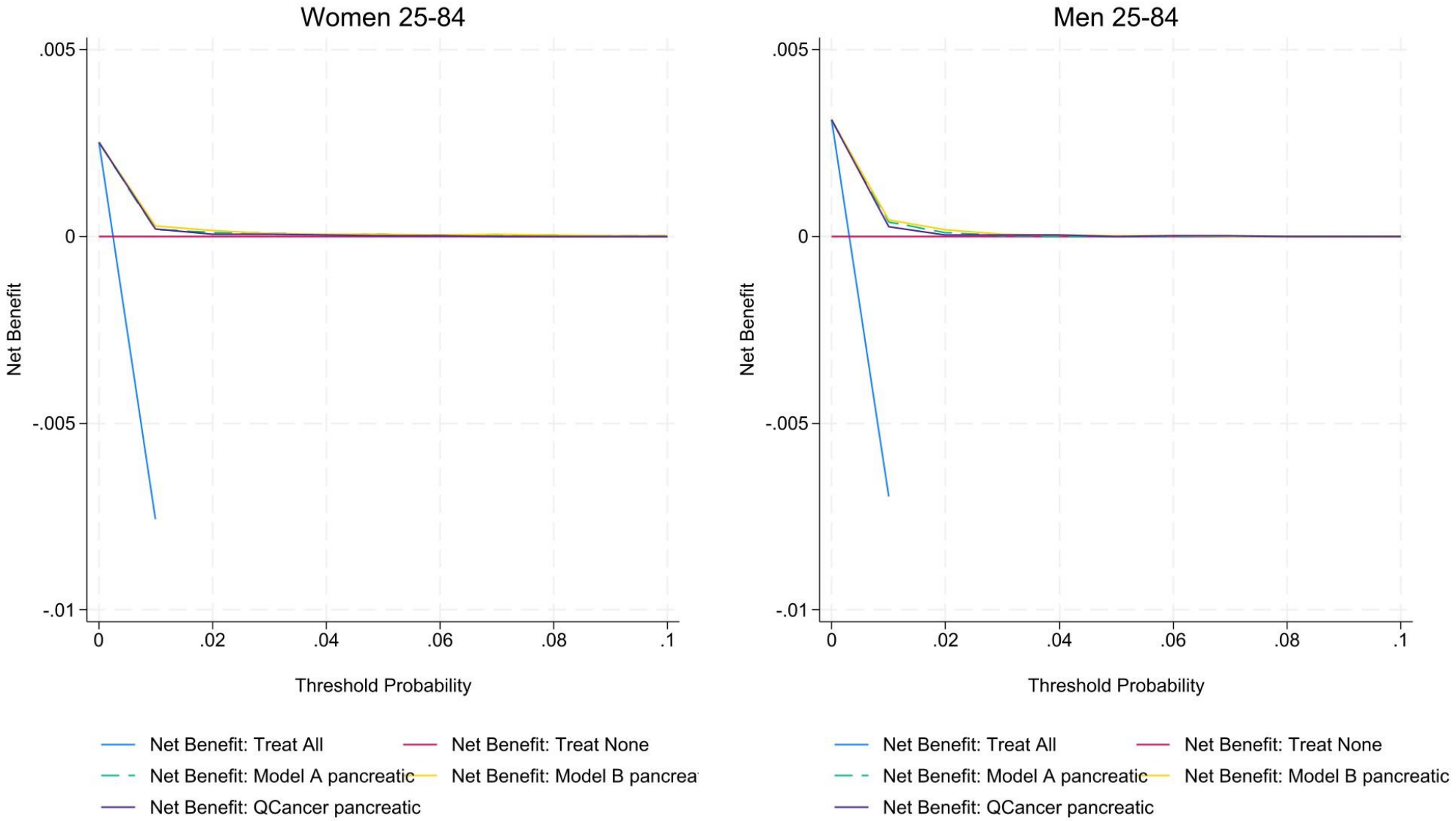
Supplementary Figure 22 Decision analysis curves in patients aged 25-84 in the English validation cohort for renal cancer



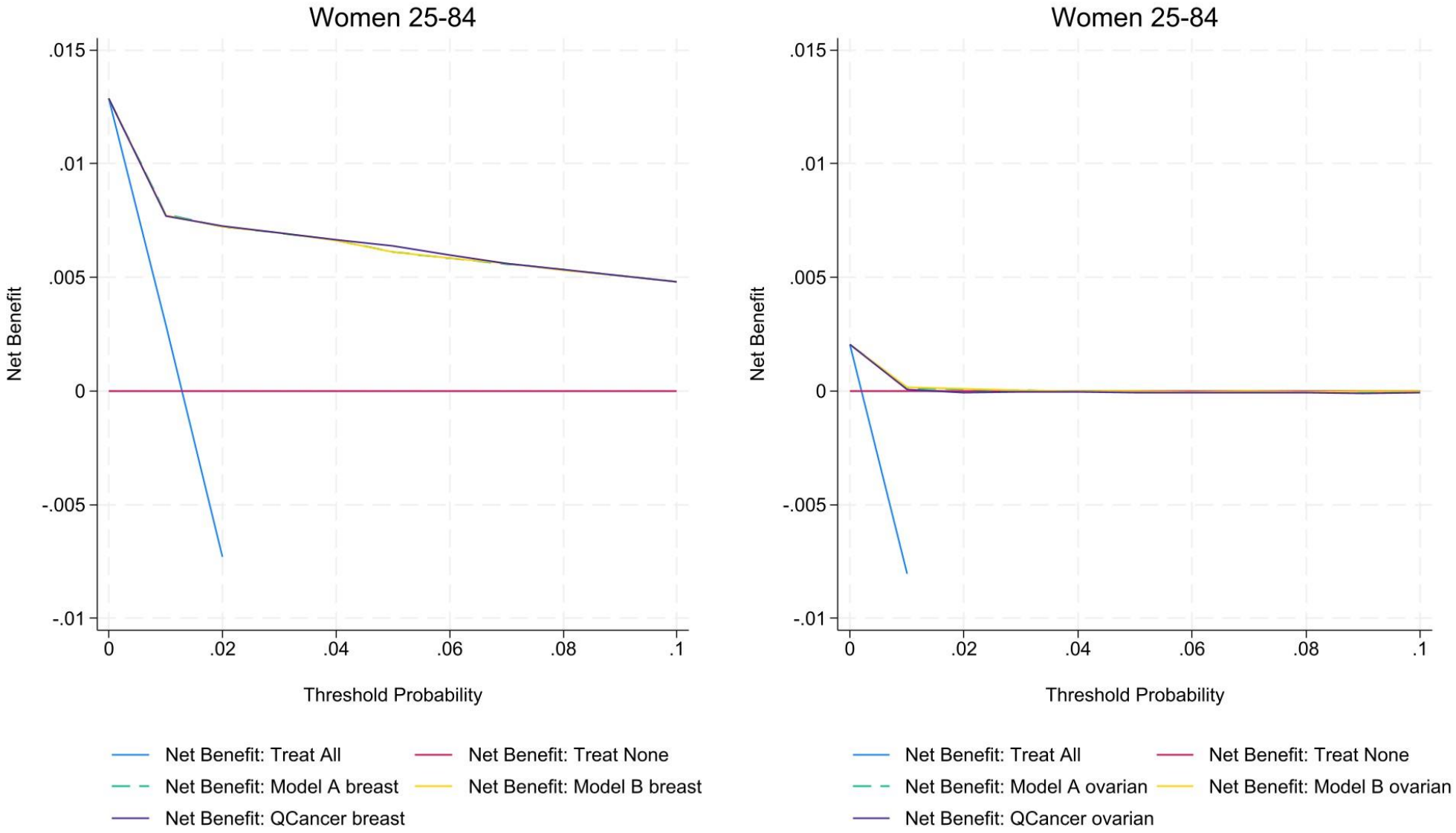
Supplementary Figure 23 Decision analysis curves in patients aged 25-84 in the English validation cohort for gastro-oesophageal cancer



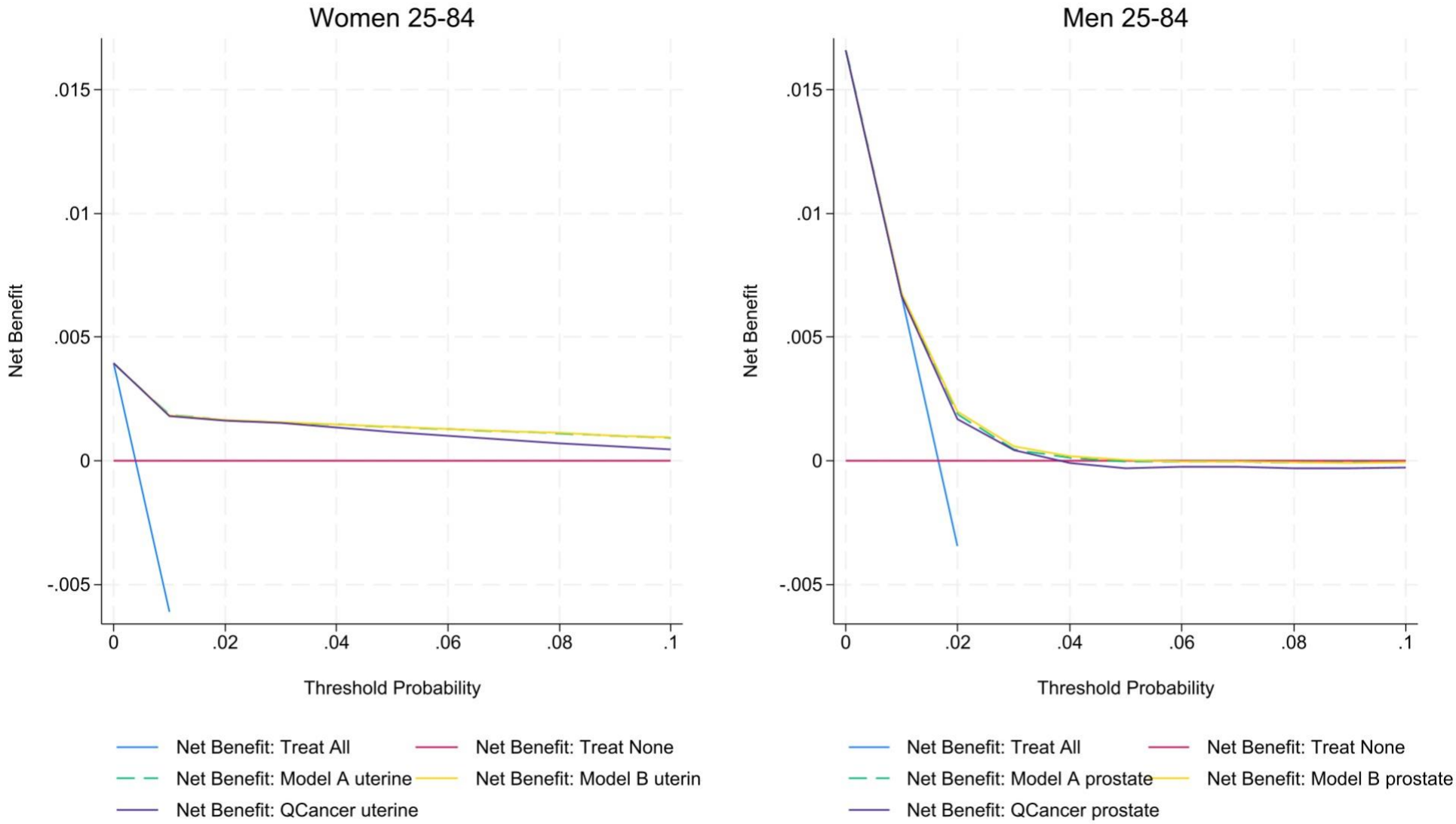
Supplementary Figure 24 Decision analysis curves in patients aged 25-84 in the English validation cohort for pancreatic cancer



Supplementary Figure 25 Decision analysis curves in women aged 25-84 in the English validation cohort for breast and ovarian cancer



Supplementary Figure 26 Decision analysis curves in aged 25-84 in the English validation cohort for uterine and prostate cancer.



Information on sample size calculations

1. Model derivation sample size

The sample size of the derivation cohort was 3,622,789 for women, and 3,841,718 for men.

Using the sample size criteria for developing a multinomial prediction model in Pate et al[1], we determined the minimum sample size required based on a maximum of 100 predictor variables and the proportions with each type of cancer. For criterion 1, based on a target shrinkage value, we specified a shrinkage factor of 0.9. For criterion 2, targeting a difference in apparent and adjusted R^2 values, we used a maximum Cox-Snell apparent R^2 value of 0.22 (derived from equation 28) and a difference of 0.01, and for criterion 3 based on obtaining a precise estimate of overall probability, we used a margin of error value of 0.01.

For criterion 1 the minimum sample size required in women ranged from 88,764 to 1,159,042 for pairwise comparisons of individual cancer types with no cancer. For pairwise comparisons between cancer types the minimum sample sizes required for some of the more rare cancer pairs exceeded the sample size available, but following suggestions in the paper by Pate el al[1], by reducing shrinkage to 0.8 and the number of predictor variables to 60 for the two rarest cancers (oral and liver) the sample size required was 3,382,393. It should be noted that only a subset of the predictor variables were considered for inclusion in the model for some cancers with fewer relevant symptoms.

Similarly in men the minimum sample size required ranged from 134,076 to 926,911 for pairwise comparisons with no cancer. For pairwise comparisons between cancer types, for the two rarest cancers (testicular and liver), the sample size required was 3,227,602 for a shrinkage of 0.8 with 80 predictor variables.

For criterion 2 the minimum sample size required was 112,679 for women, and 115,859 for men.

For criterion 3 the minimum sample size required was 1479 for women, and 1422 for men.

Across these criteria the sample size of the available data met the required minimum sample sizes of 3,382,393 in women and 3,227,602 in men for the specified criteria, allowing for a reduced shrinkage target for the rare cancer pairs where there may be some overfitting.

2. Validation sample size

The sample size of the QResearch validation dataset was 1,277,015 for women, and 1,360,169 for men. The corresponding figures for CPRD were 1,373,006 for women and 1,363,720 for men.

We calculated the minimum sample size required for the validation analyses using the criteria in Riley et al[2] for validation of a prediction model with a binary outcome, as currently there are no specific criteria published for validation of multinomial prediction models. We calculated the minimum sample size required for comparisons of each cancer type against no cancer, and selected the highest of these.

We used the pmvalsampsize command in Stata[3], with target 95% confidence interval widths of 0.2 for the calibration in the large measure O/E (criterion 1), 0.2 for the calibration slope, and 0.1 for the C statistic based on a value of 0.8.

For criterion 1 the required sample size ranged from 68,271 for breast cancer to 1,281,174 for oral and liver cancer in women, and 116,121 for prostate cancer to 960,785 for testicular cancer in men.

For criterion 2 the required sample size ranged from 11,685 for breast cancer to 471,971 for oral cancer in women, and from 12,649 for prostate cancer to 303,678 for testicular cancer in men.

For criterion 3 the required sample size ranged from 13,492 for breast cancer to 250,492 for oral and liver cancer in women, and from 22,842 for prostate cancer to 187,888 for testicular cancer in men.

Across these criteria a sample size of 1,281,174 is required in women and 960,785 in men. The number in women slightly exceeded the number available in the cohort, based on criterion 1 for oral and liver cancers meaning the confidence interval for O/E will be expected to be slightly larger than 0.2 for these cancers.

References

1. Pate, A.*, et al.* Minimum sample size for developing a multivariable prediction model using multinomial logistic regression. *Stat Methods Med Res*, 9622802231151220 (2023).
2. Riley, R.D.*, et al.* Minimum sample size calculations for external validation of a clinical prediction model with a time-to-event outcome. *Statistics in medicine* (2021).
3. Joie, E. PMSAMPSIZE: Stata module to calculate the minimum sample size required for developing a multivariable prediction model. (Boston College Department of Economics, 2018).