

Supplementary Data

Table S1 Clinico-pathological data associated with malignant and benign cases

	Early stage (n=20)	Late stage (n=20)	Benign (n=20)
Primary site			
Caecum	3 (15%)	4 (20%)	1 (5%)
Ascending colon	6 (30%)	2 (10%)	0 (0%)
Transverse colon	0 (0%)	3 (15%)	3 (15%)
Splenic flexure	1 (5%)	0 (0%)	0 (0%)
Descending colon	1 (5%)	0 (0%)	2 (10%)
Sigmoid colon	5 (25%)	5 (25%)	8 (40%)
Rectosigmoid	0 (0%)	0 (0%)	1 (5%)
Rectum	3 (15%)	6 (30%)	2 (10%)
Undetermined	1 (5%)	0 (0%)	3 (15%)
Standardised stage			
A	7 (35%)	0 (0%)	NA
B	13 (65%)	0 (0%)	NA
C	0 (0%)	14 (70%)	NA
D	0 (0%)	6 (30%)	NA
Grade			
I	1 (5%)	2 (10%)	NA
II	12 (60%)	12 (60%)	NA
III	3 (15%)	2 (10%)	NA
Unknown	4 (20%)	4 (20%)	
Morphology			
Adenocarcinoma	20 (100%)	20 (100%)	NA

Table S2 Study group sample sizes for CEA, CYFRA21-1 and CA125 determinations.

Years to diagnosis	CEA and CYFRA21-1/CA125				
	Early control	Early case	Benign	Late control	Late case
0-1	20/24	20/23	18/20	20/30	20/29
1-2	19/24	18/23	20/20	18/21	19/22
2-3	20/20	19/23	18/24	17/22	17/20
3-4	20/20	18/20	20/22	20/22	20/27

Table S3 Tumour marker performance according to different cut-off thresholds (ng/mL) and pre-diagnosis time group. 'CEA or CYFRA' refers to a combined panel where an elevated level of either marker is considered positive. (A) Cancer cases versus non-cancer controls + benigns; (B) Cancer cases versus benign only. Green shading for sensitivity and red shading for specificity is scaled from highest to lowest value in each table.

(A)

Time group	Number/Parameter	CEA	CYFRA	CEA or	CEA	CYFRA	CEA or	CEA	CYFRA	CEA or	CEA	CYFRA	CEA or
		>5 ng/mL	>3.3 ng/mL	CYFRA	>3 ng/mL	>2 ng/mL	CYFRA	>2.5 ng/mL	>1.5 ng/mL	CYFRA	>2.5 ng/mL	>3.3 ng/mL	CYFRA
0-1 yr	Case positive (n)	10	4	12	16	11	20	23	20	31	23	4	24
	Case negative (n)	30	36	28	24	29	20	17	20	9	17	36	16
	Control positive (n)	3	2	5	8	9	17	11	21	30	11	2	13
	Control negative (n)	55	56	53	50	49	41	47	37	28	47	56	45
	Sensitivity (%)	25.0	10.0	30.0	40.0	27.5	50.0	57.5	50.0	77.5	57.5	10.0	60.0
	Specificity (%)	94.8	96.6	91.4	86.2	84.5	70.7	81.0	63.8	48.3	81.0	96.6	77.6
1-2 yr	Case positive (n)	5	1	5	11	5	13	14	10	20	14	1	14
	Case negative (n)	32	36	32	26	32	24	23	27	17	23	36	23
	Control positive (n)	4	2	6	6	4	10	11	9	18	11	2	13
	Control negative (n)	90	92	87	87	87	79	80	75	63	80	92	77
	Sensitivity (%)	13.5	2.7	13.5	29.7	13.5	35.1	37.8	27.0	54.1	37.8	2.7	37.8
	Specificity (%)	95.7	97.9	93.5	93.5	95.6	88.8	87.9	89.3	77.8	87.9	97.9	85.6
2-3 yr	Case positive (n)	4	0	4	9	3	10	11	11	18	11	0	11
	Case negative (n)	32	36	32	27	33	26	25	25	18	25	36	25
	Control positive (n)	2	1	3	4	4	8	9	12	19	9	1	10
	Control negative (n)	53	54	52	51	51	47	46	43	36	46	54	45
	Sensitivity (%)	11.1	0.0	11.1	25.0	8.3	27.8	30.6	30.6	50.0	30.6	0.0	30.6
	Specificity (%)	96.4	98.2	94.5	92.7	92.7	85.5	83.6	78.2	65.5	83.6	98.2	81.8
3-4 yr	Case positive (n)	1	0	1	9	3	11	10	10	16	10	0	10
	Case negative (n)	37	38	37	29	35	27	28	28	22	28	38	28
	Control positive (n)	4	1	5	4	6	10	7	13	20	7	1	8
	Control negative (n)	56	59	55	56	54	50	53	47	40	53	59	52
	Sensitivity (%)	2.6	0.0	2.6	23.7	7.9	28.9	26.3	26.3	42.1	26.3	0.0	26.3
	Specificity (%)	93.3	98.3	91.7	93.3	90.0	83.3	88.3	78.3	66.7	88.3	98.3	86.7
1-4 yr	Case positive (n)	10	1	10	29	11	34	35	31	54	35	1	35
	Case negative (n)	101	110	101	82	100	77	76	80	57	76	110	76
	Control positive (n)	10	4	14	14	14	28	27	34	57	27	4	31
	Control negative (n)	162	168	158	158	158	144	145	138	115	145	168	141
	Sensitivity (%)	9.0	0.9	9.0	26.1	9.9	30.6	31.5	27.9	48.6	31.5	0.9	31.5
	Specificity (%)	94.2	97.7	91.9	91.9	91.9	83.7	84.3	80.2	66.9	84.3	97.7	82.0
0-4 yr	Case positive (n)	20	5	22	45	22	54	58	51	85	58	5	59
	Case negative (n)	131	146	129	106	129	97	93	100	66	93	146	92
	Control positive (n)	13	6	19	22	23	45	38	55	87	38	6	44
	Control negative (n)	217	224	211	208	207	185	192	175	143	192	224	186
	Sensitivity (%)	13.2	3.3	14.6	29.8	14.6	35.8	38.4	33.8	56.3	38.4	3.3	39.1
	Specificity (%)	94.3	97.4	91.7	90.4	90.0	80.4	83.5	76.1	62.2	83.5	97.4	80.9

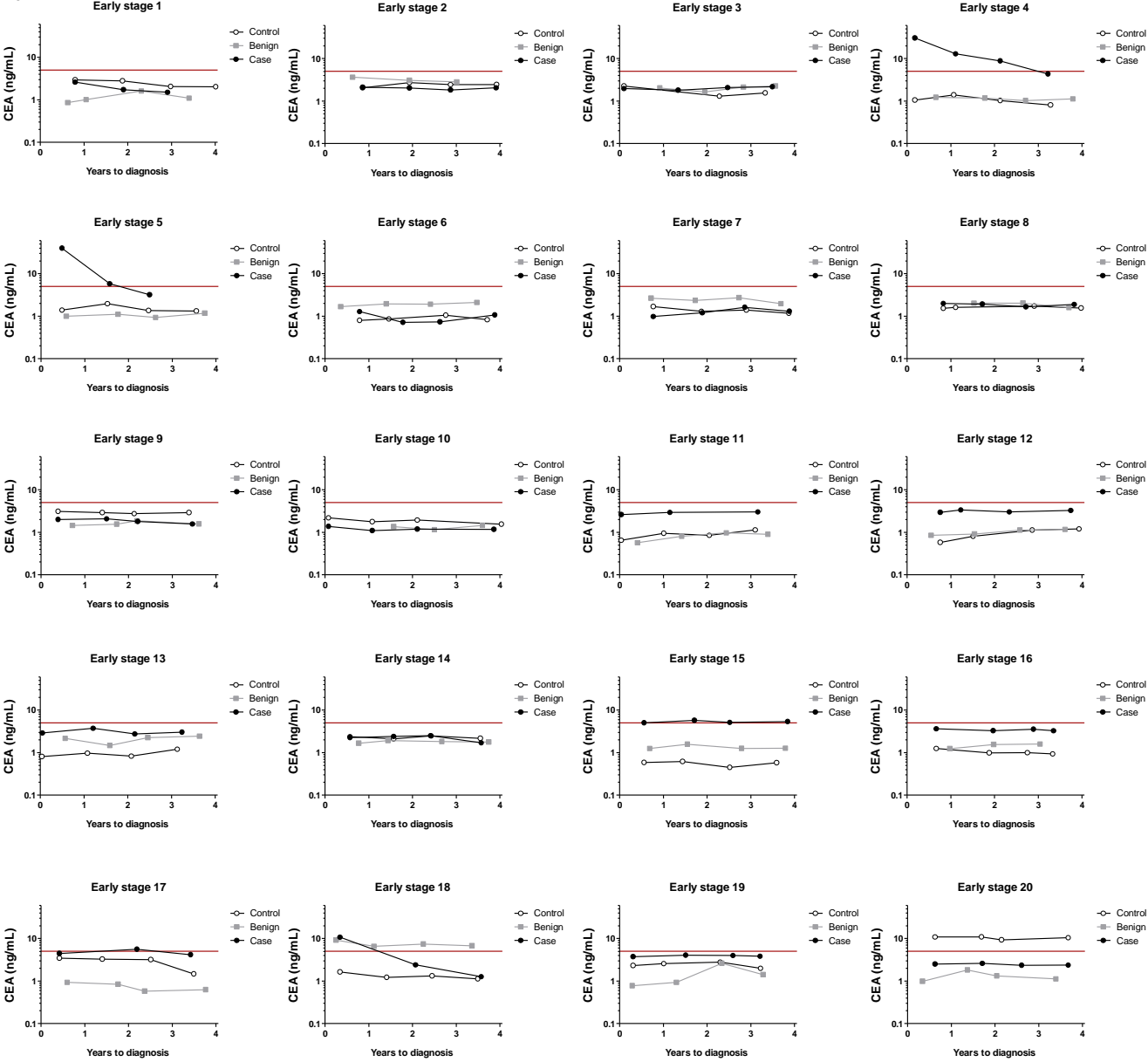
(B)

Time group	Number/Parameter	CEA	CYFRA	CEA or	CEA	CYFRA	CEA or	CEA	CYFRA	CEA or	CEA	CYFRA	CEA or
		>5 ng/mL	>3.3 ng/mL	CYFRA	>3 ng/mL	>2 ng/mL	CYFRA	>2.5 ng/mL	>1.5 ng/mL	CYFRA	>2.5 ng/mL	>3.3 ng/mL	CYFRA
0-1 yr	Case positive (n)	10	4	12	16	11	20	23	20	31	23	4	24
	Case negative (n)	30	36	28	24	29	20	17	20	9	17	36	16
	Control positive (n)	1	0	1	2	2	4	3	6	8	3	0	3
	Control negative (n)	17	18	17	16	16	14	15	12	10	15	18	15
	Sensitivity (%)	25.0	10.0	30.0	40.0	27.5	50.0	57.5	50.0	77.5	57.5	10.0	60.0
	Specificity (%)	94.4	100.0	94.4	88.9	88.9	77.8	83.3	66.7	55.6	83.3	100.0	83.3
1-2 yr	Case positive (n)	5	1	5	11	5	13	14	10	20	14	1	14
	Case negative (n)	32	36	32	26	32	24	23	27	17	23	36	23
	Control positive (n)	1	0	1	2	1	3	2	2	4	2	0	2
	Control negative (n)	19	20	19	18	19	17	18	18	16	18	20	18
	Sensitivity (%)	13.5	2.7	13.5	29.7	13.5	35.1	37.8	27.0	54.1	37.8	2.7	37.8
	Specificity (%)	95.0	100.0	95.0	90.0	95.0	85.0	90.0	90.0	80.0	90.0	100.0	90.0
2-3 yr	Case positive (n)	4	0	4	9	3	10	11	11	18	11	0	11
	Case negative (n)	32	36	32	27	33	26	25	25	18	25	36	25
	Control positive (n)	1	0	1	1	0	1	3	1	3	3	0	3
	Control negative (n)	17	18	17	17	18	17	15	17	15	15	18	15
	Sensitivity (%)	11.1	0.0	11.1	25.0	8.3	27.8	30.6	30.6	50.0	30.6	0.0	30.6
	Specificity (%)	94.4	100.0	94.4	94.4	100.0	94.4	83.3	94.4	83.3	83.3	100.0	83.3
3-4 yr	Case positive (n)	1	0	1	9	3	11	10	10	16	10	0	10
	Case negative (n)	37	38	37	29	35	27	28	28	22	28	38	28
	Control positive (n)	1	0	1	1	3	4	2	3	5	2	0	2
	Control negative (n)	19	20	19	19	17	16	18	17	15	18	20	18
	Sensitivity (%)	2.6	0.0	2.6	23.7	7.9	28.9	26.3	26.3	42.1	26.3	0.0	26.3
	Specificity (%)	95.0	100.0	95.0	95.0	85.0	80.0	90.0	85.0	75.0	90.0	100.0	90.0
1-4 yr	Case positive (n)	10	1	10	29	11	34	35	31	54	35	1	35
	Case negative (n)	101	110	101	82	100	77	76	80	57	76	110	76
	Control positive (n)	3	0	3	4	4	8	7	6	12	7	0	7
	Control negative (n)	55	58	55	54	54	50	51	52	46	51	58	51
	Sensitivity (%)	9.0	0.9	9.0	26.1	9.9	30.6	31.5	27.9	48.6	31.5	0.9	31.5
	Specificity (%)	94.8	100.0	94.8	93.1	93.1	86.2	87.9	89.7	79.3	87.9	100.0	87.9
0-4 yr	Case positive (n)	20	5	22	45	22	54	58	51	85	58	5	59
	Case negative (n)	131	146	129	106	129	97	93	100	66	93	146	92
	Control positive (n)	4	0	4	6	6	12	10	12	20	10	0	10
	Control negative (n)	72	76	72	70	70	64	66	64	56	66	76	66
	Sensitivity (%)	13.2	3.3	14.6	29.8	14.6	35.8	38.4	33.8	56.3	38.4	3.3	39.1
	Specificity (%)	94.7	100.0	94.7	92.1	92.1	84.2	86.8	84.2	73.7	86.8	100.0	86.8

All Cases vs. Benign

Figure S1 Serum CEA longitudinal profiles in individual case control samples. (A) Early stage cases; (B) Late stage cases. Horizontal line represents 5 ng/mL CEA.

(A)



(B)

