

Online supplementary Table S5. Studies adopting a single-gate design

A. Studies solely adopting a single-gate (reversed flow design): biomarkers reported more than once for the same tumour type and panels

Author (Year)	Cases	Controls	Cut-off point(s)	Sensitivity (% or as reported)	Specificity (% or as reported)	AUC
1. Measures of diagnostic performance available for individual biomarkers, in studies adopting a single-gate design						
Apolipoprotein AII-AT/ATQ, and CA19-9 used in combination (pancreatic cancer)						
Honda et al (2019) ¹	<ul style="list-style-type: none"> 156 PaC from EPIC cohort median age at diagnosis 60.9 (37.2-79.6), median age at blood draw 58.1 (34.9-75.7) 53% male Staging NA; 13 localised, 73 metastatic, 69 unknown Measures according to months prior to diagnosis (lag times): up to six months, >6-18, 18, >18-36 and >36-40 months 	<ul style="list-style-type: none"> 213 participants in the EPIC cohort not diagnosed with cancer (blood donors, healthy conscious, screening participants, health insurance holders) median age at blood draw 58.0 (34.5-75.4) 53% male (matched) 	<p>Individual measures, crude values only</p> <ul style="list-style-type: none"> Cut-off 1: ApoAII-AT/ATQ sensitivity at 95% specificity, 30.3 ng/ml Cut-off 2: ApoAII-AT/ATQ sensitivity at 98% specificity, 27.7 ng/ml <p>Combination with CA19-9, crude values only</p> <ul style="list-style-type: none"> CA19-9: 37 U/ml and 38 U/ml 	<ul style="list-style-type: none"> Cut off 1: up to 6 months (m) 0.21 (0.07-0.52), >6-18m 0.25 (0.11-0.47), 18m 0.24 (0.12-0.42), >18-36m 0.05 (0.01-0.19), >36-40m 0.07 (0.02-0.18). Cut-off 2: up to 6m 0.14 (0.03-0.47), >6-18m 0.21 (0.08-0.46), 18m 0.19 (0.08-0.40), >18-36m 0.05 (0.01-0.20), >36-40m 0.04 (0.01-0.15). CA19-9 (37 U/ml) and ApoAII-ATQ/AT (27.7 ng/ml): up to 6m 0.57 (0.29-0.82), >6-18m 0.39 (0.22-0.59), 18m 0.45 (0.30-0.61), >18-36m 0.09 (0.03-0.22), >36-40m 0.07 (0.02-0.16). CA19-9 (38 U/ml) and ApoAII-ATQ/AT (25 ng/ml): up to 6m 0.57 (0.29-0.82), >6-18m 0.36 (0.19-0.56), 18m 0.43 (0.28-0.59), >18-36m 0.07 (0.01-0.19), >36-40m 0.07 (0.02-0.16). 	NA	<ul style="list-style-type: none"> Logistic regression model: 0.62 (0.47-0.77) at lag times ≤6m, 0.65 (0.54-0.75) >6-18m, 0.53 (0.43-0.62) >18m and 0.52 (0.44-0.60) > 36m Combined CA19-9 and ApoA2-ATQ/AT in logistic regression model 0.78 (0.66-0.91) at lag times ≤6m, 0.74 (0.64-0.84) .6-18m, 0.63 (0.54-0.72) >18m months and 0.56 (0.48-0.64) >36m
Honda et al (2015) ²	<p>Cohort 1</p> <ul style="list-style-type: none"> 131 IDACP Mean age 68.8 (SD 9.01) 55% male Staging: most at advanced stages <p>Cohort 2</p> <ul style="list-style-type: none"> 155 IDACP Age and sex NA Staging: most advanced 	<p>Cohort 1</p> <ul style="list-style-type: none"> 131 HC Mean age 62.5 (SD 10.8) 52% male <p>Cohort 2</p> <ul style="list-style-type: none"> 57 pancreatic disease other than IDACP (2) Age and sex NA 	<ul style="list-style-type: none"> Results provided for both ELISA and mass spectrometric analysis ELISA: apoAII-ATQ/AT 46.3µg/ml and CA19-9 75 units/ml 	<p>NA</p> <p>ApoAII-ATQ/AT + CA19-9 95.4%</p>	<p>NA</p> <p>ApoAII-ATQ/AT + CA19-9 98.3%</p>	<ul style="list-style-type: none"> ApoAII-ATQ/AT (0.935 for ELISA, 0.885 for MS analysis). ApoAII-ATQ (0.427 for Elisa) and ApoAII-AT (0.856 for Elisa) ApoAII-ATQ/AT alone (0.944), IDACP patients vs HC.

Author (Year)	Cases	Controls	Cut-off point(s)	Sensitivity (% or as reported)	Specificity (% or as reported)	AUC
						<ul style="list-style-type: none"> • ApoAII-ATQ/AT alone for stage IV vs healthy controls (0.946)
	Cohort 3 <ul style="list-style-type: none"> • 98 PaC • Age and sex NA • Staging: all early stages 	Cohort 3 <ul style="list-style-type: none"> • 62 CP, 31 acute benign biliary obstruction, 61 HC • Age and sex NA 		NA	NA	<ul style="list-style-type: none"> • Linear combination of log-transformed CA19-9 and apoAII-ATQ/AT, 0.879 (0.823–0.930).
Honda et al (2012) ^{3a}	Cohort 1 <ul style="list-style-type: none"> • 103 PDAC • mean age 61.5 • 53% male • Does not meet criteria as used to calculate first measures of performance 	Cohort 1 <ul style="list-style-type: none"> • 112 HC • mean age 61.3 (SD 13.0) • 50% male • Does not meet criteria as used to calculate first measures of performance 	• NA	• Does not meet criteria	• Does not meet criteria	• Does not meet criteria
	Cohort 2 <ul style="list-style-type: none"> • 62 PaC • mean age 63.3 (8.34) • 61% male • Staging NA 	Cohort 2 <ul style="list-style-type: none"> • 41 HC (does not meet criteria) • mean 61.5 (11.2) • 56% male 	• NA	• Does not meet criteria	• Does not meet criteria	• Does not meet criteria as less than 50 controls
	Cohort 3 <ul style="list-style-type: none"> • 52 PaC • Mean age 63.1 (9.85) • 56% male • Staging NA 	Cohort 3 <ul style="list-style-type: none"> • 53 HC and 58 CP • HC mean 39.1 (15.6), CP 50.3 (8.9) • HC 59% male, CP 74% male 	• NA	• N/A	• N/A	• Cohort 3, cancer vs healthy 0.958 (0.920-0.996) (ApoAII-2)
	Cohort 4 <ul style="list-style-type: none"> • 249 PDAC and 18 other malignant tumour of the pancreas • PDAC mean age 64.4 (9.11), other 68.3 (9.74) • PDAC 59% male, other 67% male • Staging NA 	Cohort 4 <ul style="list-style-type: none"> • 128 HC, 38 benign tumour or cyst and 14 CP • HC mean 46.6 (16.8), benign tumour or cyst 63.5 (11.0), CP 60.2 (10.2) • HC 65% male, benign tumour or cyst 45% male, CP 86% male 	• NA	<ul style="list-style-type: none"> • 93.39% (ApoAII-2+CIII-0 and CA19-9) – all tumour stages • 94.20% (ApoAII-2+CIII-0 and CA19-9) – stage III only • 91.60% (ApoAII-2+CIII-0 and CA19-9) – stage IV only 	<ul style="list-style-type: none"> • 93.22% (ApoAII-2+CIII-0 and CA19-9) – all tumour stages • 93.22% (ApoAII-2+CIII-0 and CA19-9) – stage III only • 93.22% (ApoAII-2+CIII-0 and CA19-9) – stage IV only 	• Cohort 4: only available combining ApoAII-2 with ApoCIII-0 (not shown)
Pepsinogen (PGI/PGII) (gastric cancer)						
Gantuya et al (2019) ⁴	<ul style="list-style-type: none"> • 50 GC (54% H pylori prevalence) • No information on age and sex • Staging NA 	<ul style="list-style-type: none"> • 752 non-cancer patients (302 antrum limited CG and/or atrophy and 450 corpus CG and/or atrophy (77% H. pylori prevalence) • Mean age: 53.8 (SD 1, 27-78) • 31% male 	<ul style="list-style-type: none"> • PG I/II < 2.2 and PGI < 28ng/mL were the best cut-off points 	<ul style="list-style-type: none"> • PGI: 70% • PG I/II: 66% 	<ul style="list-style-type: none"> • PGI: 70% • PG I/II: 65.1% 	<ul style="list-style-type: none"> • PGI: 0.76 (0.68-0.84) • PGI/II: 0.70 (0.62-0.77)
Kang et al (2008) ⁵	<ul style="list-style-type: none"> • 380 GC (intestinal and diffuse type) 	<ul style="list-style-type: none"> • 172 BGU, 119 DU, 107 dysplasia 	<ul style="list-style-type: none"> • PG I ≤ 70 ng/mL • PG I/II ratio ≤ 3.0 	<ul style="list-style-type: none"> • PG I: intestinal type 77.7%, diffuse type 64.7%. 	<ul style="list-style-type: none"> • PG I: intestinal type 20.2%, diffuse type 20.2%. 	NA

Author (Year)	Cases	Controls	Cut-off point(s)	Sensitivity (% or as reported)	Specificity (% or as reported)	AUC
	<ul style="list-style-type: none"> Age and sex not available for cases separately No information on staging 	<ul style="list-style-type: none"> Age and sex not available for controls separately 		<ul style="list-style-type: none"> PG I/II: intestinal type 62.3%, diffuse type 55.8% 	<ul style="list-style-type: none"> PG I/II: intestinal type 61.0%, diffuse type 61.0% 	
Kikuchi et al (2011) ⁶	<ul style="list-style-type: none"> 122 GC Age: 68.2 years (41-87, SD 9.7) 74% male Staging NA 	<ul style="list-style-type: none"> 16 GU or DU, 17 superficial gastritis, 66 CAG, 79 no abnormality Age: 56.2 years (22-82, SD 14.9) 55% male 	<ul style="list-style-type: none"> Conventional PG: PG I \leq 70 ng/ml and PG I/II ratio \leq 3. Strict PG: PG I \leq 30 ng/ml and PG I/II ratio \leq 2 	<ul style="list-style-type: none"> Conventional PG: 77.9%, strict PG:41.3%, Normal and non-malignant conditions combined 	<ul style="list-style-type: none"> Conventional PG: 61.8%, strict PG:90.4% Normal and non-malignant conditions combined 	NA
Yanaoka et al (2008) ^{7b}	<ul style="list-style-type: none"> 63 GC Age: 50.3-51.8 (mean range) 100% male 86% early, 14% late stages 	<ul style="list-style-type: none"> 5146 HC Mean age: 49.2 \pm 4.7 100% male 	<ul style="list-style-type: none"> \leq70 ng/mL and PG I/II ratio of \leq3.0 (1), \leq50 ng/mL and PG I/II ratio of \leq3.0 (2), \leq30 ng/mL and PG I/II ratio of \leq2.0 (3) 	<ul style="list-style-type: none"> Cut-off 1: 58.7% (45.6-70.8%). Cut-off 2: 49.2% (36.5-62.0%) Cut-off 3: \leq2.0: 27.0% (16.9-39.9%). 	<ul style="list-style-type: none"> Cut-off 1: 73.4% (72.1-74.6%). Cut-off 2: 80.5% (79.4-81.6%) Cut-off 3: \leq2.0: 92.0% (91.3-92.8%). 	NA
2. Measures of diagnostic performance available for established biomarkers combined with novel biomarkers not shown above, in studies adopting a single-gate design						
CA19-9 (pancreatic cancer)						
O'Brien et al (2015) ⁸	<ul style="list-style-type: none"> 101 PaC Age NA for validation cohort 100% female Staging NA 	<ul style="list-style-type: none"> 184 HC Age not available for validation cohort 100% female 	<ul style="list-style-type: none"> CA19-9 $>$25 U/mL; $>$30 U/mL; $>$37 U/mL and $>$40 U/mL – in combination with CA125 $>$20 U/mL; $>$25 U/mL; $>$30 U/mL Measures reported according to time to diagnosis: 0-4 years, 0-2 years; 1-4 years Measures reported for restricted set (removing serial samples) 	<ul style="list-style-type: none"> 0-4: CA19-9 ($>$25) or CA125 ($>$20) 50.0%; CA19-9 ($>$30) or CA125 ($>$25) 39.9%; CA19-9 ($>$37) or CA125 ($>$30) 30.4%; CA19-9 ($>$40) or CA125 ($>$25) 31.9%. 0-2: CA19-9 ($>$25) or CA125 ($>$20) 53.1%; CA19-9 ($>$30) or CA125 ($>$25) 46.9%; CA19-9 ($>$37) or CA125 ($>$30) 40.6%; CA19-9 ($>$40) or CA125 ($>$25) 37.5%. 1-4: CA19-9 (cut-off$>$25) or CA125 ($>$20) 45.4%; CA19-9 ($>$30) or CA125 ($>$25) 34.3%; CA19-9 ($>$37) or CA125 ($>$30) 23.1%; CA19-9 ($>$40) or CA125 ($>$25) 25.9%. 	<ul style="list-style-type: none"> 0-4: CA19-9 ($>$25) or CA125 ($>$20) 73.8%; CA19-9 ($>$30) or CA125 ($>$25) 89.1%; CA19-9 ($>$37) or CA125 ($>$30) 91.3%; CA19-9 ($>$40) or CA125 ($>$25) 91.3%. 0-2: CA19-9 ($>$25) or CA125 ($>$20) 71.6%; CA19-9 ($>$30) or CA125 ($>$25) 89.5%; CA19-9 ($>$37) or CA125 ($>$30) 90.5%; CA19-9 ($>$40) or CA125 ($>$25) 92.6% 1-4: CA19-9 ($>$25) or CA125 ($>$20) 73.8%; CA19-9 ($>$30) or CA125 ($>$25) 89.2%; CA19-9 ($>$37) or CA125 ($>$30) 91.5%; CA19-9 ($>$40) or CA125 ($>$25) 90.8%. 	NA for validation set
Tavano et al (2018) ⁹	<ul style="list-style-type: none"> 74 PaC Median age 69 (61-76) 54% male Staging NA for validation cohort (majority late stages overall) 	<ul style="list-style-type: none"> 117 HC Median age 62 (55-70) 45% male 	<ul style="list-style-type: none"> CA 19-9 36 U/mL – in combination with miR-1290 (610 number of copies/ul) 	<ul style="list-style-type: none"> Combined: 83.8% 	<ul style="list-style-type: none"> Combined: 96.6% 	<ul style="list-style-type: none"> Combined: 0.923 (0.876-0.969)

Author (Year)	Cases	Controls	Cut-off point(s)	Sensitivity (% or as reported)	Specificity (% or as reported)	AUC
Zhou et al (2014) ¹⁰	<ul style="list-style-type: none"> • 152 PaC • Mean age 56 (SD 13.5) • 67% male • Staging: 5 IA, 12 IB, 36 IIA, 20 IIB, 40 III, 39 IV 	<ul style="list-style-type: none"> • 96 HC, 91 CP, 20 pre-malignancies • Mean age: HC 58 (7.6), CP 58 (15.0), pre-malignancies 60 (11.3) • HC 75% male; CP 57% male; pre-malignancy 75% male 	<ul style="list-style-type: none"> • CA19-9 in combination with ULBP2 and MIC • Optimum cut-offs (determined by ROC analysis): CA19-9 18.44 U/ml, ULBP2 94.08 pg/ml and MIC-1 642.83 pg/ml 	<ul style="list-style-type: none"> • NA for combination 	<ul style="list-style-type: none"> • NA for combination 	<ul style="list-style-type: none"> • PaC vs CP (PaC vs HC not available in combination): MIC-1 + ULBP2 + CA 19-9: 0.982; MIC-1 + CA 19-9: 0.932; ULBP-1 + CA 19-9: 0.953
3. Measures of diagnostic performance available for a panel only in studies adopting a single-gate design						
Different panels (pancreatic cancer) ^c						
Balaseenthil et al (2017) ¹¹	<ul style="list-style-type: none"> • 98 PaC (52 with no diabetes or pancreatitis) • Age and sex not available • Staging: 7 IA, 8 IB, 1 II, 40 IIA and 42 IIB 	<ul style="list-style-type: none"> • 62 chronic pancreatitis, 31 acute biliary obstruction, 61 healthy (50 with no diabetes or pancreatitis) • Age and sex not available 	<ul style="list-style-type: none"> • Optimal cut-offs defined by logistic regression, for the panel (TFPI+TNC-FN III-C+CA19-9) • Risk score (RS) determined using a formula • Optimal cut-off: 5.79. Panel with CA19-9 alone optimal cut-off 1.12 	<ul style="list-style-type: none"> • cancer (all stages) vs healthy controls: 0.75 (0.65-0.83) • cancer (stage I-II only) vs healthy controls: 0.73 (0.6-0.84) • cancer (all stages) vs chronic pancreatitis: 0.75 (0.65-0.83) • cancer (stage I-II only) vs chronic pancreatitis: 0.73 (0.62-0.84) • cancer (all stages) with no diabetes or pancreatitis vs healthy with no diabetes or pancreatitis: 0.81 (0.69-0.90) 	<ul style="list-style-type: none"> • cancer (all stages) vs healthy controls: 0.82 (0.71-0.90) • cancer (stage I-II only) vs healthy controls: 0.82 (0.72-0.90) • cancer (all stages) vs chronic pancreatitis: 0.71 (0.60-0.82) • cancer (stage I-II only) vs chronic pancreatitis: 0.71 (0.60-0.81) • cancer with no diabetes or pancreatitis vs healthy with no diabetes or pancreatitis: 0.84 (0.72-0.94) 	<ul style="list-style-type: none"> • cancer (all stages) vs healthy controls: 0.83 (0.76-0.89) • cancer (stage I-II only) vs healthy controls: 0.79 (0.70-0.87) • cancer (all stages) vs chronic pancreatitis: 0.78 (0.71-0.85) • cancer (stage I-II only) vs chronic pancreatitis: 0.75 (0.65-0.84) • cancer with no diabetes or pancreatitis vs healthy with no diabetes or pancreatitis: 0.89 (0.82-0.95)
Mellby et al (2018) ¹²	<ul style="list-style-type: none"> • 2 cohorts; only one for validation (US cohort) • 143 PaC • Median age only by staging; range (overall) 24-87 • 57% male • Staging: 15 I, 75 II, 15 III and 38 IV 	<ul style="list-style-type: none"> • 219 HC, 57 CP • HC median age 63.0 (24-86), CP 55.5 (32-81) • HC 53% male, CP 46% male 	<ul style="list-style-type: none"> • 29 panel signature without any established biomarkers used in combination (CA19-9 was analysed but not retained) 	<ul style="list-style-type: none"> • Panel only: 95% for stages I and II 	<ul style="list-style-type: none"> • Panel only: 93% for stages I and II 	<ul style="list-style-type: none"> • Panel only: PaC stages I and II vs HC: 0.963 (0.94 - 0.98), on the basis of the three training sets; Chronic Pancreatitis vs patients with PaC stage I and II: 0.84

^aOutcomes available by staging, but as N by staging was not available eligibility was uncertain and data were not extracted. ^bPPVs were also provided: Cut-off 1: 2.6% (1.9-3.6%); Cut-off 2: 3.0% (2.1-4.3%); cut-off 3: 4.0% (2.4-6.4%). Abbreviations: ACG: atrophic chronic gastritis; ApoAII-AT/ATQ: apolipoprotein AII-AT/ATQ; BGU: benign gastric ulcer; DU: duodenal ulcer; CG: Chronic gastritis; CP: chronic pancreatitis; EPIC: European Prospective Investigation into Cancer and Nutrition; GC: gastric cancer; GU: gastric ulcer; IDACP: invasive ductal adenocarcinoma of pancreas; MIC: macrophage-inhibitory cytokine 1; MPV: mean platelet volume; NA: not available; PaC: pancreatic cancer; PDAC: pancreatic ductal adenocarcinoma; PDW: platelet distribution width; PGI/II: serum pepsinogen I/II; TFPI: plasma tissue factor pathway inhibitor; NTC-FN III-C: tenascin-C; ULBP2: UL16 binding protein 2. ^cLeelawat et al 2010 also adopted a reversed-flow design but was not added as it was the only study investigating CA19-9 for cholangiocarcinoma.

B. Studies adopting a hybrid design with a reversed-flow design (either confirmed or likely) for at least one control, with measures: biomarkers reported more than once

Author (Year)	Cases	Controls	Cut-off point(s)	Sensitivity (% or as reported)	Specificity (%)	AUC
CA19-9 (pancreatic cancer)						
Duraker et al (2007)	<ul style="list-style-type: none"> 123 PaC (with and without obstructive jaundice) Age and sex not available Staging NA; 17 resectable, 106 unresectable 	<ul style="list-style-type: none"> 58 benign pancreatic diseases (with and without obstructive jaundice) Age and sex not available 	<ul style="list-style-type: none"> CA19-9 37 U/ml and 29 U/ml (two different kits), combined with CEA: 5 ng/ml CA 125: 35 U/ml and 26/ml (two different kits) 	<ul style="list-style-type: none"> CEA or CA 19-9 86.2; CEA or CA125 64.2; CA 19-9 or CA125 91.9; CEA + CA 19-9 34.1; CEA + CA125 30.9; CA 19-9 + CA125 46.3; CEA + CA 19-9 + CA 125 26.8 	<ul style="list-style-type: none"> CEA or CA 19-9 72.4; CEA or CA125 70.7; CA 19-9 or CA125 60.3 ; CEA + CA 19-9 94.8; CEA + CA125 98.3; CA 19-9 + CA125 93.1 ; CEA + CA 19-9 + CA 125 98.3 	<ul style="list-style-type: none"> NA
Firpo et al (2009) ¹³	<ul style="list-style-type: none"> 75 PaC Median age 69 (range 48-92) 61% male Staging: 1 IA, 3 IB, 7 IIA, 24 IIB, 17 III, 23 IV 	<ul style="list-style-type: none"> 150 HC, 32 CP, 42 benign neoplasm and periampullary lesions, and other benign periampullary lesions HC median age 66 (30-94), CP 50 (32-77), benign neoplasm and periampullary lesions 70.5 (41-91). NA other HC 61% male, CP 53% male, benign neoplasm and periampullary lesions 48% male, NA other 	<ul style="list-style-type: none"> CA19-9: 54.54 U/ml - in combination with haptoglobin 2821.5 ng/ml and SAA 68.445 ng/ml (derived from classification three algorithm that did not include healthy controls) 	<ul style="list-style-type: none"> Panel only: PaC vs benign neoplasms 81.3%; PaC vs CP 81.3%; PaC vs healthy controls 81.3%; PaC vs combined controls 81.3% 	<ul style="list-style-type: none"> Panel only: PaC vs benign neoplasms 88.1%; PaC vs CP 90.6%; PaC vs healthy controls 98.7%; PaC vs combined controls 95.5% 	<ul style="list-style-type: none"> NA for combination
Liu et al (2012) ¹⁴	<ul style="list-style-type: none"> 138 PaC patients Mean age 61.8 (SD 10.6) 64% male Staging: 27 I; 39 II; 17 III and 55 IV 	<ul style="list-style-type: none"> 107 CP, 68 HC CP mean age 48.6 (14.0), HC 60.5 (11.3) CP 66% male, HC 66% male 	<ul style="list-style-type: none"> Combination of CA19-9 (cut-off >37 U/mL) with miR-16 and miR-196a using logistic regression Formula to calculate miRNAs relative abundance - cel-miR-39 as the internal standard 	<ul style="list-style-type: none"> Combinations only (miRNA panel and CA19-9): PCa vs normal: 92.0% (87.5–96.5). PCa vs CP: 87.7% (82.2–93.2) PCa vs CP and normal: 87.7% (82.2–93.2) 	<ul style="list-style-type: none"> Combinations only (miRNA panel and CA19-9): PCa vs normal: 95.6% (90.7–100.0) PCa vs CP: 96.3% (92.7–99.9) PCa vs CP and normal: 97.7% (95.5–99.9) 	<ul style="list-style-type: none"> Combinations only (miRNA panel and CA19-9): PCa vs normal: 0.979, p < 0.000). PCa vs CP: 0.956, p < 0.000). PCa vs CP and normal: 0.952, p < 0.000).
Rychlikova et al (2016) ¹⁵	<ul style="list-style-type: none"> 64 PaC patients Age not available 58% male Staging: 10 II, 24 III and 29 IV 	<ul style="list-style-type: none"> 71 CP, 66 T2DM, 48 HC (37 CP also had DM) Age and sex not available 	<ul style="list-style-type: none"> CA 19-9 (cut-off 29 kU/L) - combined with osteopontin (cut-off 102 ng/ml) Combination: cut-off value of 3.77 	<ul style="list-style-type: none"> Combination for PaC vs CP: 83% 	<ul style="list-style-type: none"> Combination for PaC vs CP: 89% 	<ul style="list-style-type: none"> Combination for PaC vs CP: 0.88 ± 0.03
CEA (gastric cancer)						
Li et al (2018) ¹⁶	<ul style="list-style-type: none"> Model building (met eligibility) 176 GC Age and sex not available Staging: 63 early stage and 113 advanced stage) 	<ul style="list-style-type: none"> Model building (met eligibility) 117 atypical hyperplasia, 204 HC. Age and sex not available. 	<ul style="list-style-type: none"> CEA (cut-off 3.45) - in combination with CA724 (cut-off 5.80), IL-6 (cut-off 20.31), IL-8 (cut-off 1.45) and TNF-α (cut-off 7.82) 	NA	NA	<ul style="list-style-type: none"> GC vs HC 0.95 (0.93-0.97). Early-stage GC vs HC: 0.95 (0.92- 0.98). Advanced-stage GC vs HC: 0.95 (0.92- 0.97),

Author (Year)	Cases	Controls	Cut-off point(s)	Sensitivity (% or as reported)	Specificity (%)	AUC
			<ul style="list-style-type: none"> Combinations used binary logistic regression 			<ul style="list-style-type: none"> GC vs atypical hyperplasia did not include CEA in panel.
	<ul style="list-style-type: none"> Further validation (independent study) 58 GC Age and sex not available Staging: 19 early and 39 advanced 	<ul style="list-style-type: none"> Further validation (independent study) 41 atypical hyperplasia, 66 HC. Age and sex not available 		<ul style="list-style-type: none"> GC vs healthy controls 89.66%. Early-stage GC vs HC: 84.21%. Advanced-stage GC vs HC: 92.31% GC vs atypical hyperplasia did not include CEA in panel 	<ul style="list-style-type: none"> GC vs healthy controls 92.42%. Early-stage GC vs HC: 90.91%. Advanced-stage GC vs HC: 90.91% GC vs atypical hyperplasia did not have CEA in panel 	NA
Yun et al (2017) ^{17a}	<ul style="list-style-type: none"> 194 GC Mean age 54.7 (SD 9.7), range 28-77 61% male Staging: 99 I/II, 95 III/IV 	<ul style="list-style-type: none"> 185 HC, 191 GU HC mean age 54.7 (9.7), range 50-72. GU mean age 54.9 (5.2), range 35-71 HC 56% male, GU 58% male 	<ul style="list-style-type: none"> CEA in combination with MPV, PDW, CEA. Cut-off values NA 	<ul style="list-style-type: none"> GC vs HC: CEA+MPV 0.820; CEA+PDW 0.835. GC vs GU: CEA+MPV 0.851; CEA+PDW 0.990 	<ul style="list-style-type: none"> GC vs HC: CEA+MPV 0.838; CEA+PDW 0.908. GC vs GU: CEA+MPV 0.770; CEA+PDW 0.979 	<ul style="list-style-type: none"> GC vs HC: CEA+MPV 0.889 (0.854-0.919); CEA+PDW 0.939 (0.910-0.961). GC vs GU: CEA+MPV 0.876 (0.839-0.907); CEA+PDW 0.996 (0.984-1.000)

^aBoth PPVs and NPVs were also provided: PPVs: GC vs HC: CEA+MPV 0.841; CEA+PDW 0.905. GC vs GU: CEA+MPV 0.789; CEA+PDW 0.980. NPVs: NPV: GC vs HC: CEA+MPV 0.816; CEA+PDW 0.840. GC vs GU: CEA+MPV 0.835; CEA+PDW 0.989. Abbreviations: CP: chronic pancreatitis; GC: gastric cancer; GU: gastric ulcer; MPV: mean platelet volume; NA: not available. PaC: pancreatic cancer; PDW: platelet distribution width; SAA: serum amyloid A.

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