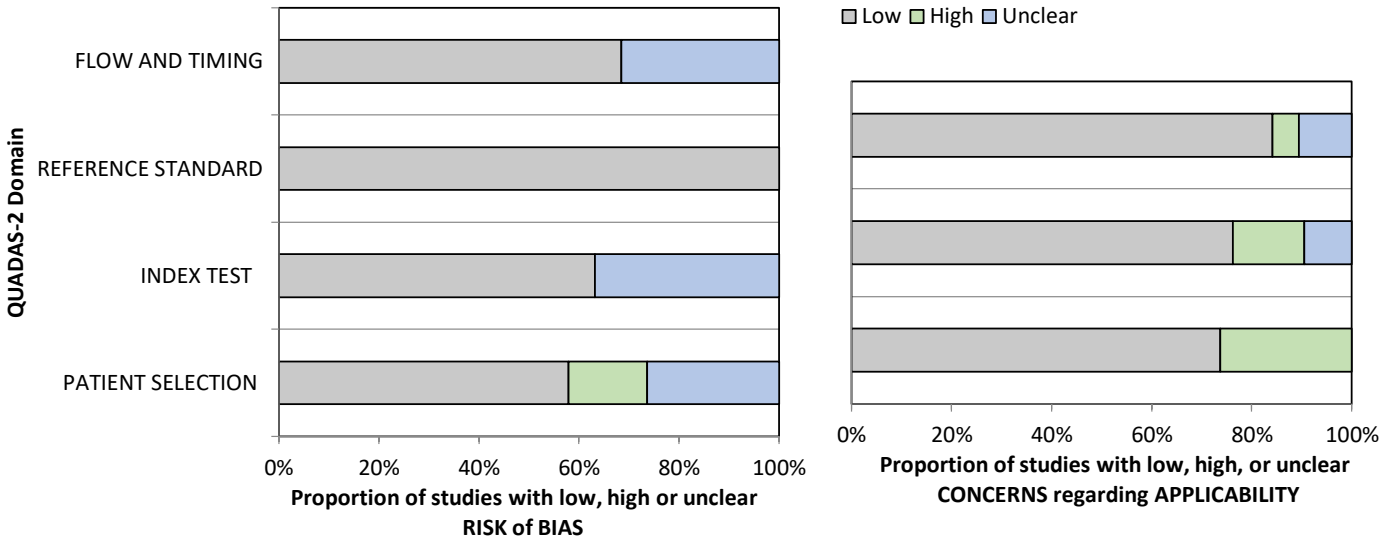
Supplementary Section

Supplementary Tables and Legends



	Risk of Bias				Applicability Concerns		
	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD	F- AND TIMING	PATIENT SELECTION	INDEX TEST	REFERENCE STANDARD
Grutzmann et al.	-	-	-	-	-	-	-
Lofton-Day et al.	?	?	-	-	+	-	-
deVos et al.	-	-	-	-	-	-	-
Tanzer et al.	?	?	-	-	-	-	-
Ahlquist et al.	+	-	-	?	-	-	-
Toth et al.	?	-	-	-	-	-	-
Lee et al.	?	?	-	-	+	-	-
Liu et al.	+	?	-	-	-	-	-
Chruch et al.	-	-	-	-	-	-	-
Johnson et al	-	?	-	-	-	-	-
Potter et al.	-	-	-	-	-	-	-
Su et al	-	?	-	?	+	+	-
Toth et al.	?	?	-	?	+	+	+
Jin et al	-	-	-	-	-	-	-
Orntoft et al.	+	-	-	-	+	-	?
Wu et al.	-	-	-	-	-	-	-
Song et al.	-	-	-	?	-	+	-
Song et al.	-	-	-	?	-	-	-
Chen et. al	-	-	-	?	-	-	?
(+) High (?) Unclear (-) Low							

Supplementary Table 1/Figure 1: Results of quality assessment of studies (QUADAS)

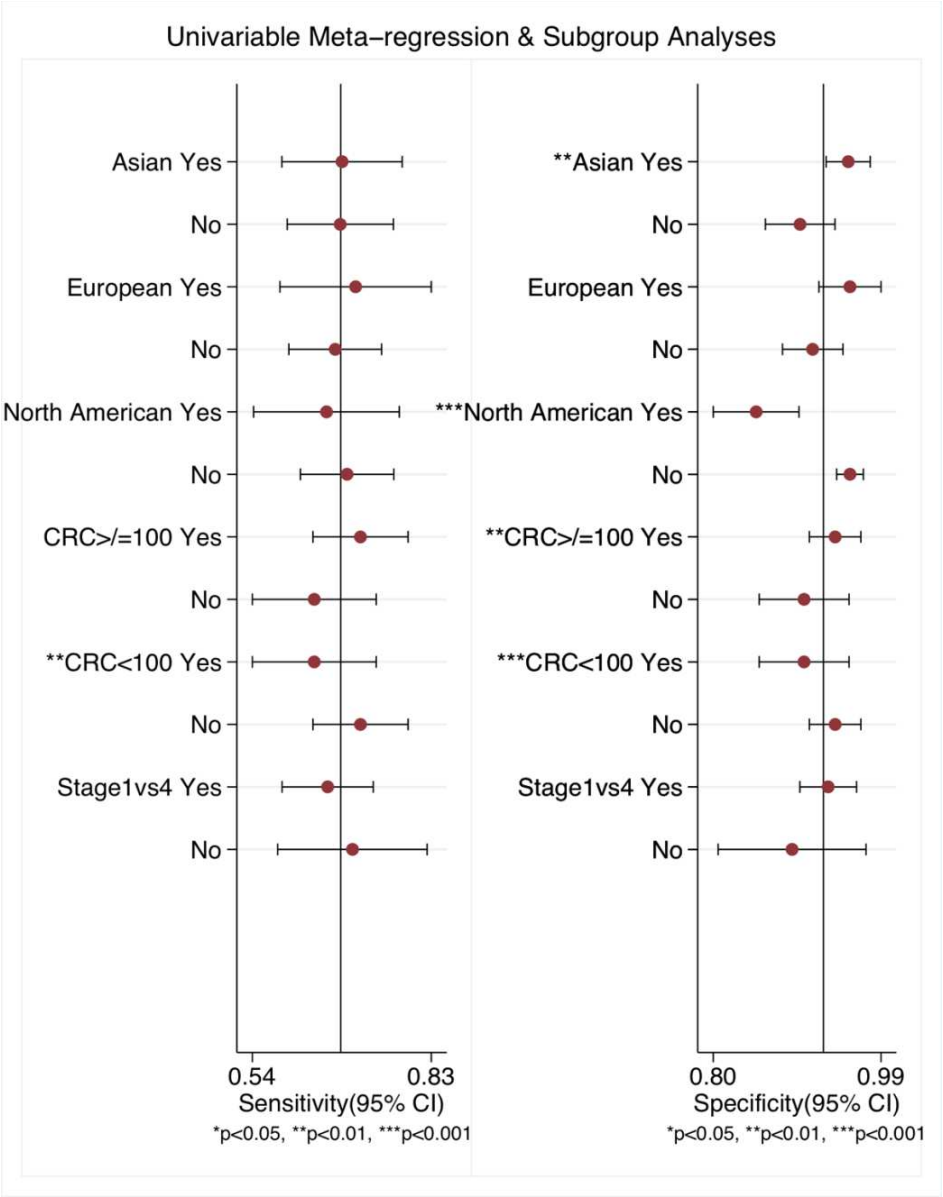
	Spearman coefficient	p-value	Threshold Effects	Non-threshold effects
Overall	0.192	0.4	No	Yes
Region of recruitment				
Asia	0.793	0.02	Yes	No
Europe	-0.47	0.42	No	Yes
North America	-0.08	0.9	No	Yes
Sample Size				
<100	0.21	0.6	No	Yes
>100	0.11	0.8	No	Yes
Threshold Level				
1/3 algorithm	0.08	0.83	No	Yes
2/3 algorithm	0.50	0.21	No	Yes

Supplementary Table 2: Spearman Correlation co-efficient of sources of heterogeneity (I^2) in meta-analysis results.

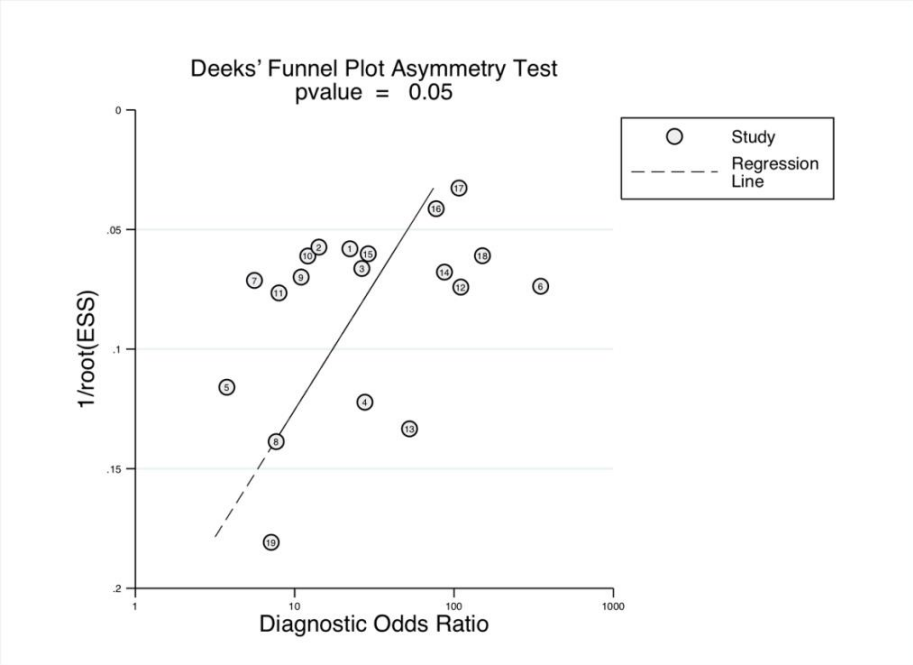
Co-variate	Category	Number of Studies	Sensitivity (95% CI)	p-value	Specificity (95% CI)	p-values
Asian	Yes	8	0.69 [0.59 - 0.79]	0.08	0.95 [0.93 - 0.98]	<0.001
	No	11	0.69 [0.60 - 0.77]		0.90[0.86 - 0.94]	
European	Yes	5	0.71 [0.59 - 0.83]	0.22	0.96 [0.92 - 0.99]	0.07
	No	14	0.68 [0.60 - 0.75]		0.91 [0.88 - 0.95]	
North American	Yes	6	0.66 [0.55 – 0.78]	0.06	0.85 [0.80 – 0.90]	<0.001
	No	13	0.70 [0.64 – 0.80]		0.96 [0.94- 0.97]	
Sample Size	<100	9	0.64 [0.54 – 0.74]	0.01	0.90 [0.85 – 0.95]	<0.001
	100+	10	0.72 [0.64 – 0.80]		0.94 [0.91 – 0.97]	
Stage	I	12	0.67 [0.59 – 0.74]	0.06	0.93 [0.90 – 0.96]	0.13
	IV	4	0.71 [0.58 – 0.83]		0.89 [0.80 – 0.97]	

Supplementary Table 3: Results of Subgroup meta-regression with country of recruitment, CRC case sample size, and recruiting more Stage 1 over Stage 4 as covariates. Significant p-values represent the effect of covariate on the pooled sensitivity and specificity.

Supplementary Figures

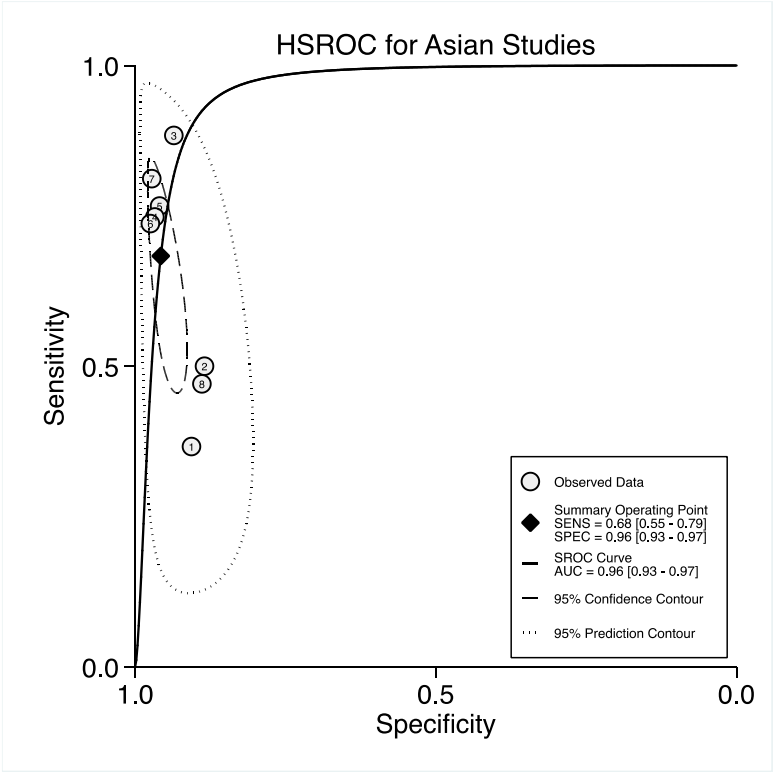


Supplementary Figure 2: Subgroup meta-regression forest plot with confidence intervals.

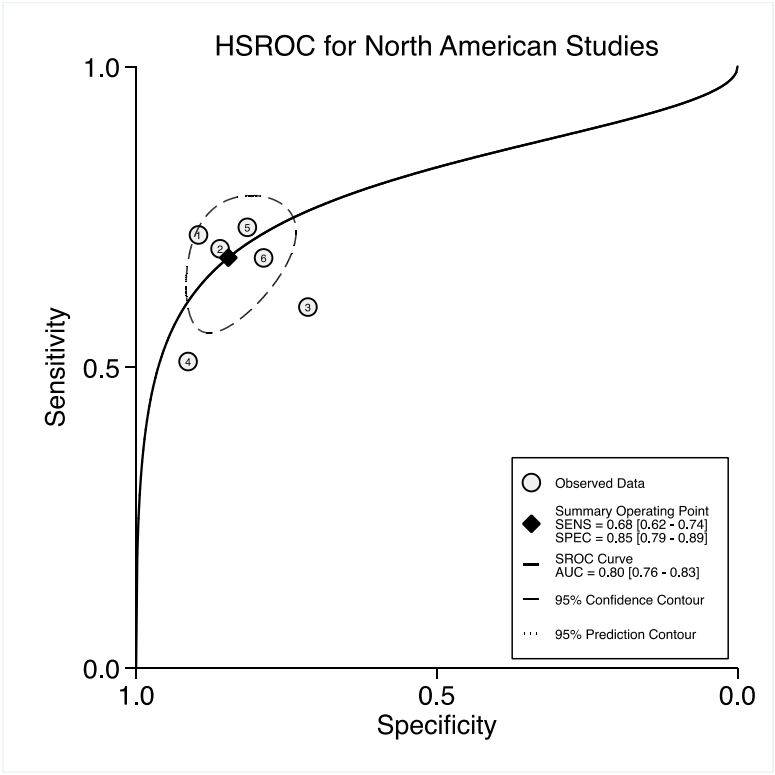


Supplementary Figure 3: Deek's Funnel Plot - Study points and regression line generated by Deek's asymmetry test to assess publication bias.

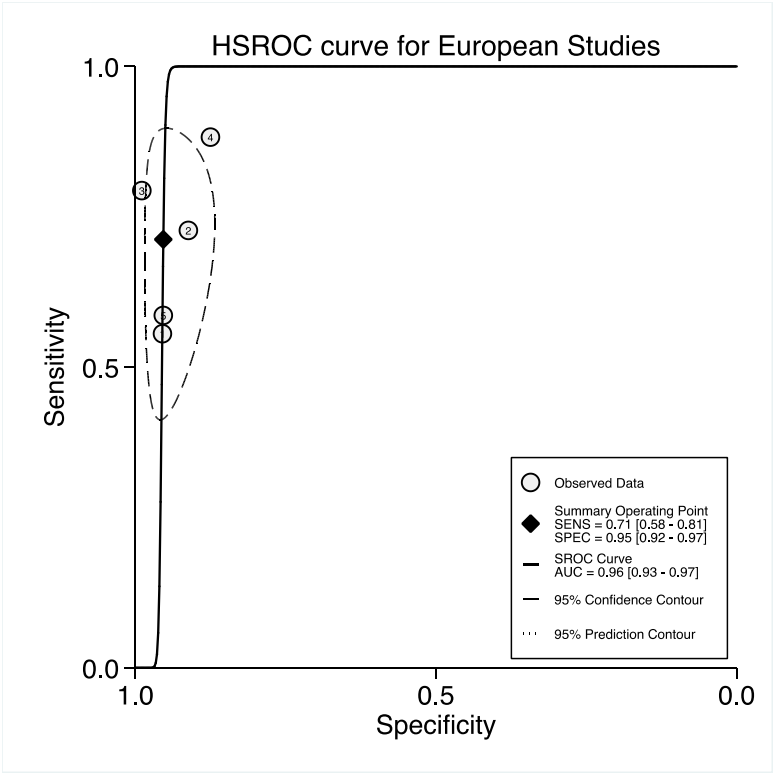
Supplementary Figure 4:



4a)



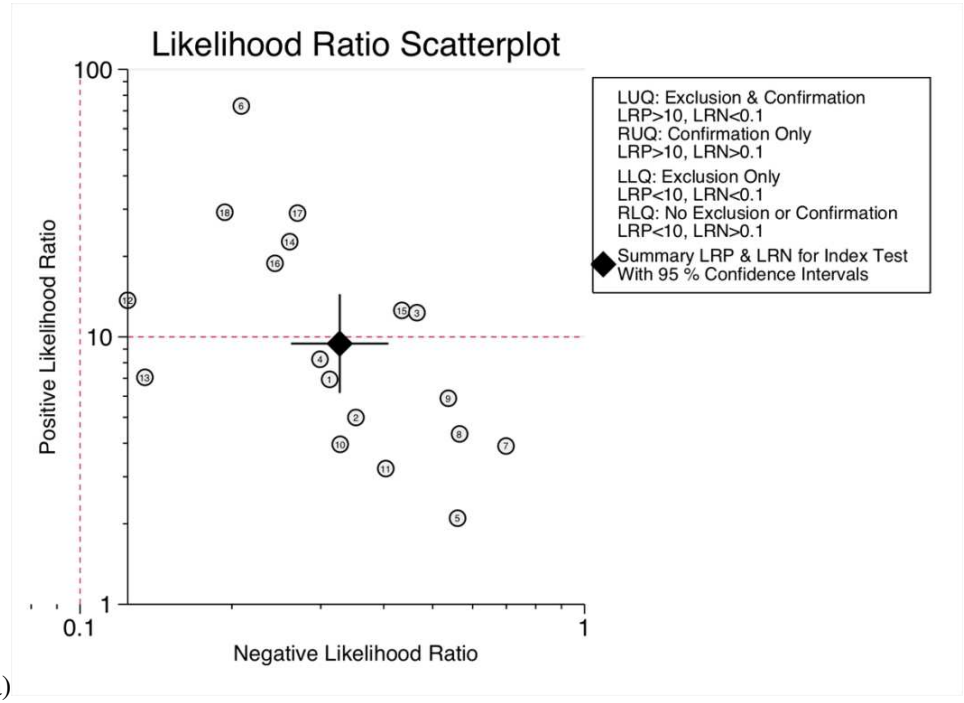
4b)



4c)

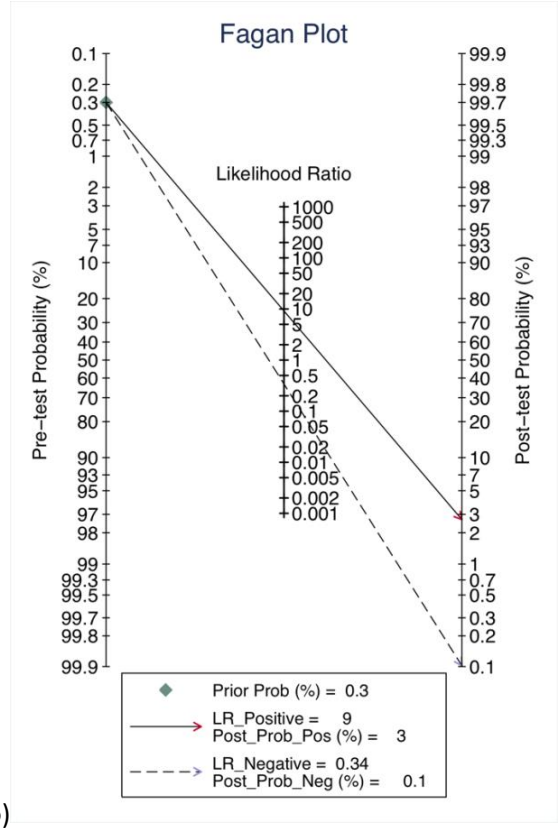
Supplementary Figure 4: a)HSROC plot for Asian studies b)HSROC plot for North American studies c) HSROC plot for European studies.

Supplementary Figure 5:



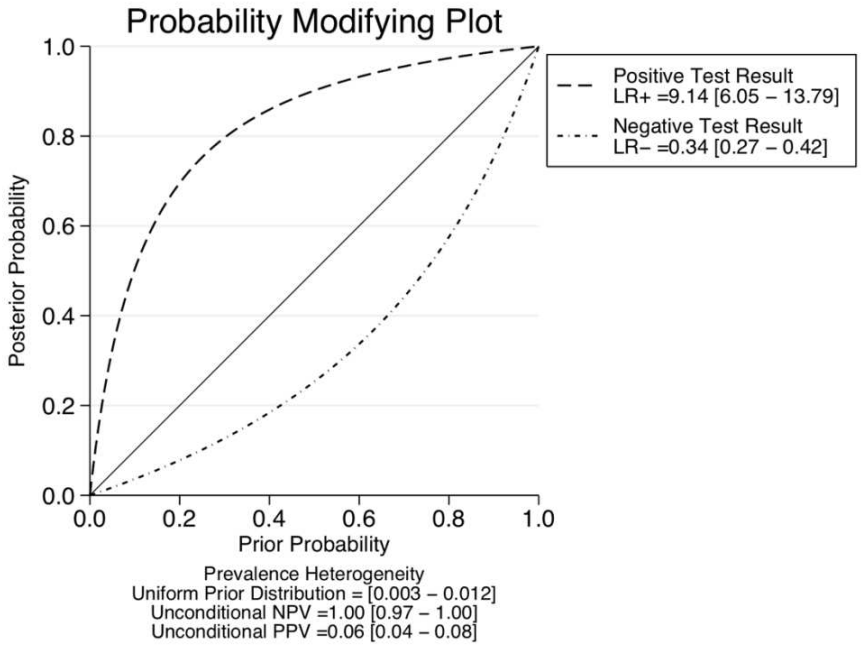
5a)

Supplementary Figure 5a: Likelihood scattergram, individual points are studies, with the summary point and 95% confidence intervals.



5b)

Supplementary Figure 5b: Fagan's plot for pre-test and post-probabilities with likelihood ratios. This example uses a pre-test probability of 0.3% (Average CRC risk) to illustrate the test efficiency. This plot visually summarises the effect of the pre-test probability and likelihood ratio to the post-test probability. For a test to be clinically valid, the dotted line must always lie below the solid line on the right side.



5c)

Supplementary Figure 5c: Probability modifying graph which takes into account CRC prevalence depicting change in post-test probability for a range of pre-test probabilities from 0.3% (Average CRC risk) to 1.2% (Elevated CRC risk).