Supplemental Material

Cell-free Nucleic Acid as Promising Diagnostic Biomarkers for Gastric Cancer: a Systematic Review

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Contents:

Table S1. Protocols of blood RNA detection.

Reference	Author	Year	Specimen	Centrifugation	Extraction	Normalization
1	Aalami AH	2020	Serum	1500rpm for 10min, 12000rpm for 2min	Plasma/Serum RNA Purification Mini RNA Kit	snord47
2	Bai SY	2019	Serum	NA	TRIzol reagent	miR-16
3	Cai CC	2019	Serum	3000g for 10 min	HiPure Exosome kits	β-actin
4	Chen JL	2020	Plasma	1520g for 5 min	Blood MicroRNAExtraction and Purification kit	miR-16
5	Chen JL	2019	Plasma	3000 rpm for 5min	NA	miR-16
6	Chen SJ	2017	Plasma	NA	TRIzol LS Reagent	GAPDH
7	Chen X	2020	Serum	1000g for 10 min, 15000g for 5 min	TRIzol LS isolation kit	miR-39
8	Dong ZG	2019	Serum	3000g for 10 min	exoRNeasy Serum/Plasma Midi Kit	GAPDH
9	Elsayed ET	2018	Plasma	1200g for 10 min, 12000g for 10 min	miRNeasy Mini Kit	GAPDH
10	Emami SS	2019	Plasma	1500g for 15 min, 10000g for 5 min	Qiagen miRNeasy Serum/Plasma Kit	miR-39
11	Fu ZC	2014	Plasma	1200g for 10 min, 12000g for 10 min	mirVana PARIS kit	U6 snRNA
12	Gong Y	2018	Serum	3500rpm for 10 min	MiRcute miRNA extraction kit	NA
13	Gu XL	2021	Serum	NA	Total RNA Pure and Isolation Kit with Spin Column	U6 snRNA
14	Guo YT	2020	Serum	3000g for 15 min	TRIzol reagent	U6 snRNA
15	Han WW	2021	Serum	3500rpm for 10 min	Serum microRNA rapid extraction kit	U6 snRNA
16	Hou X	2015	Plasma	2000g for 10 min, 12000g for 10 min	Trizol kit	U6 snRNA
17	Huang SK	2016	Serum	820g for 10 min, 16000g for 10 min	Trizol LS Reagent	miR-16
18	Huang YJ	2021	Serum	NA	Total RNA Pure and Isolation Kit with Spin Column	U6 snRNA
19	Ji B	2019	Plasma	1500g for 10 min, 12000g for 10 min	TRIzol reagent	U6 snRNA
20	Kong S	2019	Plasma	NA	TRIzol reagent	GAPDH
21	Kong Y	2019	Plasma	1500rpm for 30 min, 3000rpm for 5 min, 4500rpm for 5 min	NA	U6 snRNA
22	Li BH	2017	Plasma	1500rpm for 10 min	TRIzol reagent	U6 snRNA
23	Li C	2013	Plasma	1000rpm for 10 min, 15000rpm for 10 min	mirVanaTM PARISTM Kit	U6 snRNA
24	Li C	2013	Plasma	1000rpm for 10 min, 15000rpm for 10 min	mirVanaTM PARISTM Kit	U6 snRNA
25	Li FX	2017	plasma	2000g for 30 min, 4000g for 5 min, 8000g for 5 min	NA	U6 snRNA
26	Li Y	2019	Serum	NA	miRcute Serum/Plasma miRNA Isolation Kits	U6 snRNA
27	Liu H	2017	Plasma	3000rpm for 10 min	QIAGEN miRNeasy Mini Kit	U6 snRNA
28	Liu HF	2017	Serum	3000g for 15 min	NA	NA
29	Liu HS	2012	Serum	820g for 10 min, 16000g for 10 min	mirVana miRNA isolation kit	U6 snRNA
30	Liu WW	2020	Serum	3000g for 10 min	Ambion mirVana PARIS kit	18S rRNA
31	Liu Y	2019	Serum	1200g for 10 min, 10000g for 10 min	Qiagen miRNeasy Serum/Plasma Kit	GAPDH
32	Park JL	2015	Plasma	2000g for 10 min	Ambion PARIS Kit	U6 snRNA
33	Qin SY	2021	Serum	NA	serum extraction kit	18S rRNA
34	Roy S	2022	Serum	NA	NA	β-actin
35	Saliminejad K	2022	Plasma	3000g for 10 min	RiboExTM LS reagent	U6 snRNA
36	Shan LC	2019	Serum	3500g for 10 min, 16000g for 10 min	Trizol LS Reagent	GAPDH

Table S1. Cont.

Reference	Author	Year	Specimen	Centrifugation	Extraction	Normalization
37	Shao YF	2022	Plasma	NA	NA	GAPDH
38	Shen Y	2020	Serum	3000rpm for 10 min	NA	NA
39	Shen YJ	2021	Plasma	NA	TRIzol LS	U6 snRNA
40	So JBY	2021	Serum	3000rpm for 10 min	miRNeasy serum/plasma miRNA isolation kit	NA
41	Sun XY	2022	Plasma	3000rpm for 10 min	RNA reagent kits	18S rRNA
42	Tian WY	2022	Serum	NA	TRIzol LS	U6 snRNA
43	Wu DY	2017	Serum	3000rpm for 30 min	BioTeKe miRNA extraction kit	U6 snRNA
44	Wu JH	2015	Serum	1000g for 10 min	SYBR Premix Ex Taq kit	U6 snRNA
45	Wu JH	2015	Serum	800g for 30 min	Trizol reagent	U6 snRNA
46	Xiao K	2021	Serum	3000g for 10 min	exoRNeasy Serum/Plasma Midi kit	GAPDH
47	Yan JN	2022	plasma	NA	TRIzol LS reagents	GAPDH
48	Yin G	2020	Serum	3500rpm for 10 min	RNAVzol LS	GAPDH
49	Yuan RS	2016	Plasma	3000rpm for 10 min	Trizol reagent	U6 snRNA
50	Zeng QH	2014	Serum	2000rpm for 10 min, 3000rpm for 5 min, 4500rpm for 5 min	RNA extraction kit	NA
51	Zeng WW	2020	Serum	1500rpm for 30 min, 3000rpm for 5 min, 4500rpm for 5 min	mirVana PARIS kit	U6 snRNA
52	Zhang WW	2021	Serum	NA	TRIzol LS reagent	GAPDH
53	Zhang Y	2022	Serum	NA	RNA purifcation kit	U6 snRNA
54	Zhao QF	2018	Plasma	NA	TRIzol LS Reagent	GAPDH
55	Zheng GD	2021	Serum	3000rpm for 10 min	Total Exosome RNA and Protein Isolation Kit	miR-39
56	Zhou XY	2015	Plasma	1500rpm for 30 min, 3000rpm for 5 min, 4500rpm for 5 min	Trizol Reagent	GAPDH
57	Zhou XY	2015	Plasma	NA	miRNeasy Mini kits	U6 snRNA
58	Zong W	2019	Serum	NA	serum extract Kit	18S rRNA

NA: not available

Table S2. Protocols of blood DNA detection.

Reference	Author	Year	Specimen	Centrifugation	Extraction
59	Anderson BW	2018	Plasma	NA	NA
60	Ioanna B	2013	Serum	3000rpm for 10min	High Pure Viral Nucleic Acid Kit
61	Ioanna B	2015	Serum	3000rpm for 10min	High Pure Viral Nucleic Acid Kit
62	Cao CQ	2020	Plasma	NA	plasma processing kit by BioChain
63	Chen L	2012	Serum	NA	QIAamp Circulating Nucleic Acid Kit
64	Han J	2014	Serum	1500rpm for 10min	QIAamp Circulating Nucleic Acid Kit
65	Hideura E	2020	Serum	NA	MagNA Pure Compact Nucleic Acid Isolation Kit
66	Lee HS	2013	Plasma	1500rpm for 10min, 1500g for 10min	Abbott m2000sp Sample Preparation System
67	Li H	2022	Plasma	NA	DNeasy Blood & Tissue Kit
68	Li WH	2016	Serum	NA	TIANamp Blood DNA Kit
69	Lin ZH	2017	Plasma	2500rpm for 15min	QIAamp DNA Blood Mini Kit
70	Ling ZQ	2013	Serum	NA	AxyPrep Mag Blood gDNA kit
71	Miao J	2020	Plasma	NA	DNeasy Blood & Tissue Kit
72	Pimson C	2016	Plasma	2000g for 15min	Genomic DNA Mini Kit
73	Saliminejad K	2020	Plasma	3000g for 10min	QIAamp Circulating Nucleic Acid Kit
74	Xu JB	2021	Plasma	NA	QIAamp Circulating Nucleic Acid Kit
75	Yang QF	2013	Plasma	1600g for 10min, 16000g for 10min	phenol/chloroform method
76	Yu JL	2014	Serum	1500rpm for 10min	QIAamp DNA Blood Mini Kit
77	Zhang H	2014	Plasma	NA	TIANamp Blood DNA Kit
78	Zhang X	2014	Plasma	1000g for 10min	QIAamp DNA Blood mini kit
79	Zhao LY	2022	Plasma	1350±150rpm for 10min (twice)	nucleic acid extraction kit

NA: not available

Table S3. Summary of studies reporting diagnostic performance of miRNAs for gastric cancer (only miRNAs that have been reported in >=2 studies are shown).

Study	miR-421	miR-21	miR-222	miR-106a	miR-25	miR-199a-3p	miR-93
Chen, 2019[5]	△↑						
Emami, 2019[10]		△↑	△↑				
Fu, 2014[11]			△↑				
Hou, 2015[16]				△↑			
Huang, 2016[17]		○↑					
Kong, 2019[21]					△↑		
Li, 2013[23]						△↑	
Li, 2013[24]						△↑	
Li, 2017[25]					△↑		△↑
Saliminejad, 2022[35]		○↑					
So, 2021[40]		○↑					○↑
Wu,2015[44]	△↑						
Wu,2015[45]		△↑					
Yuan,2016[49]				△↑			
Number Of Studies	2	5	2	2	2	2	2

○ represents miRNAs which are part of a panel; △ represents miRNAs which have only been analyzed individually and not as a part of a miRNA panel; ↑ represents up-regulation.

Table S4. Summary of studies reporting diagnostic performance of miRNAs for gastric cancer (only miRNAs that have been reported in >=2 studies are shown).

Study	RASSF1A	SEPT9	RUNX3	SFRP2	RNF180
Ioanna, 2015[61]	△				
Cao, 2020[62]		○			
Hideura, 2020[65]			△		
Lee, 2013[66]		△			
Lin, 2017[69]			○		
Miao, 2020[71]				△	
Pimson, 2016[72]	△				
Saliminejad, 2020[73]	△				
Xu, 2021[74]		△			△
Zhang, 2014[78]				○	○
Zhao,2022[79]		△			
Number Of Studies	3	4	2	2	2

○ represents DNAs which are part of a panel; △ represents DNAs which have only been analyzed individually and not as a part of a miRNA panel.

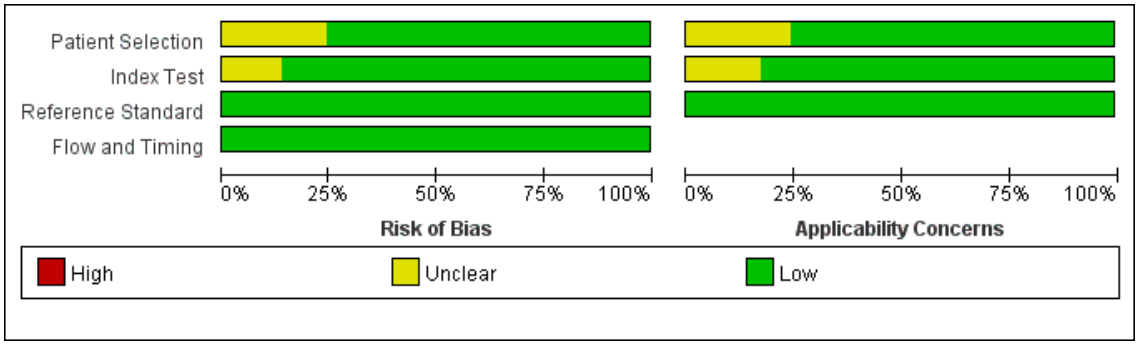

Figure S1: Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies. (cfRNA markers)

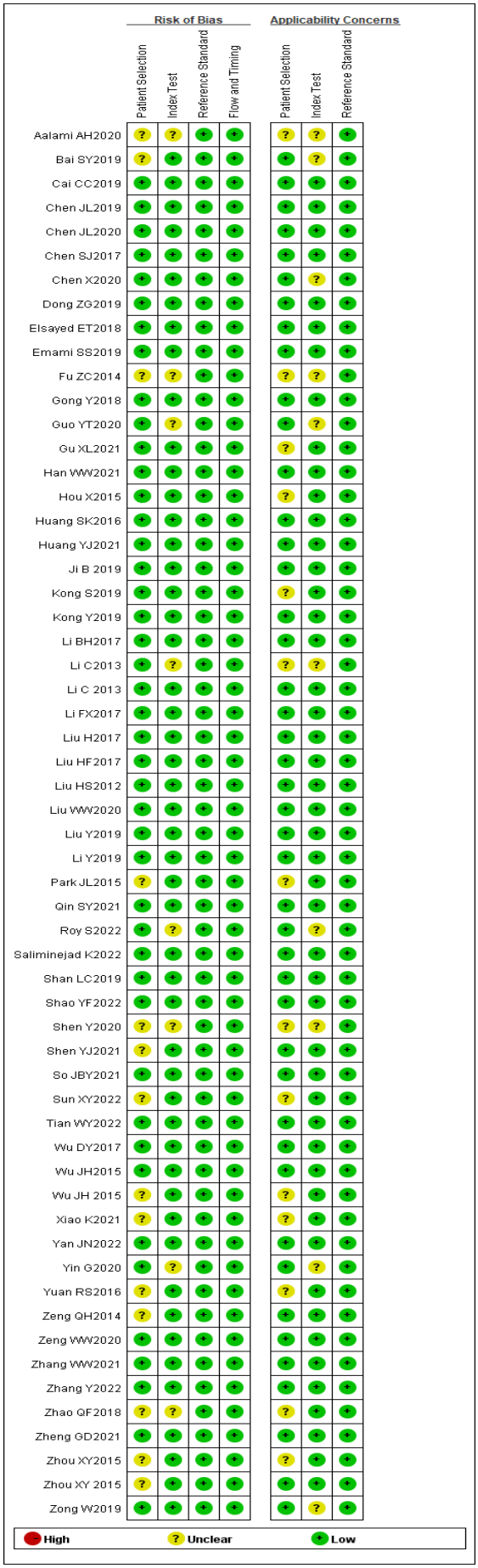

Figure S2: Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study. (cfRNA markers)

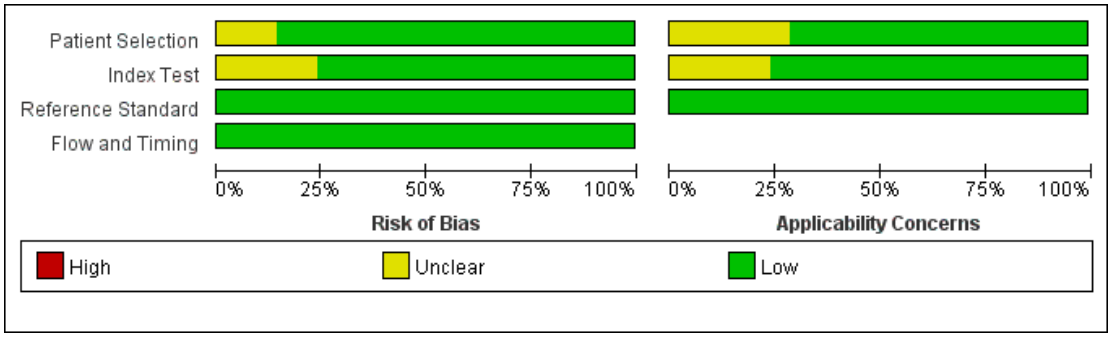

Figure S3: Risk of bias and applicability concerns graph: review authors' judgements about each domain presented as percentages across included studies. (cfDNA markers)

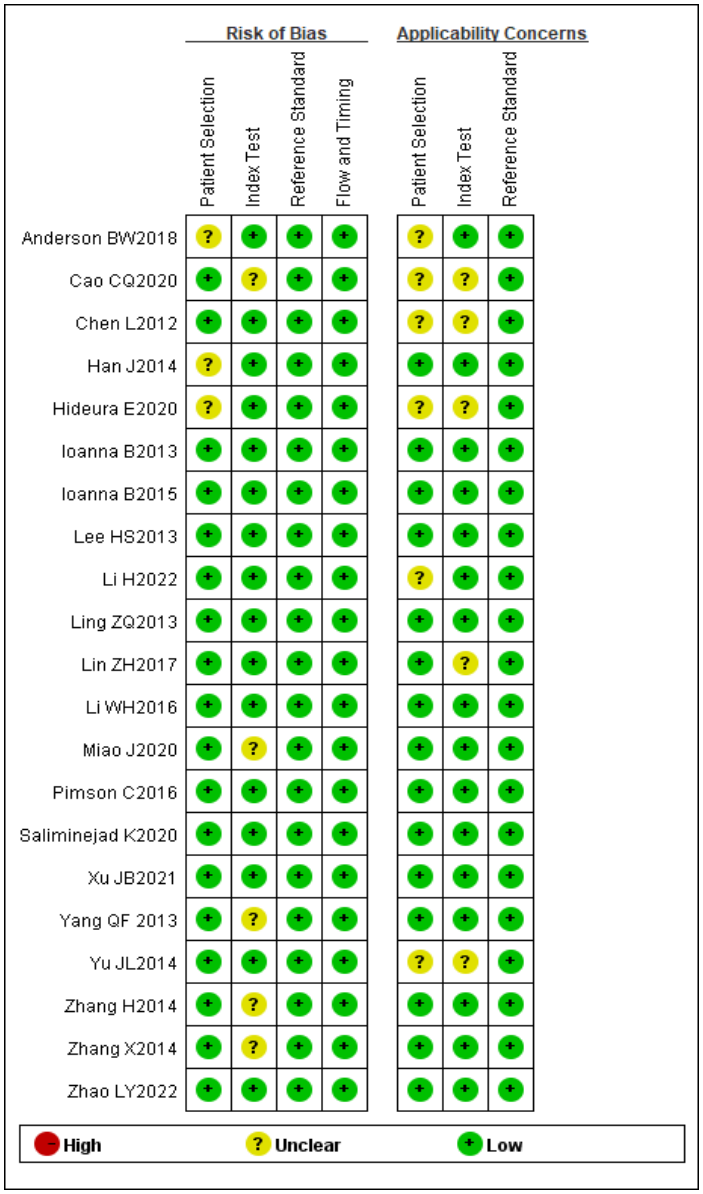

Figure S4: Risk of bias and applicability concerns summary: review authors' judgements about each domain for each included study. (cfDNA markers)

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