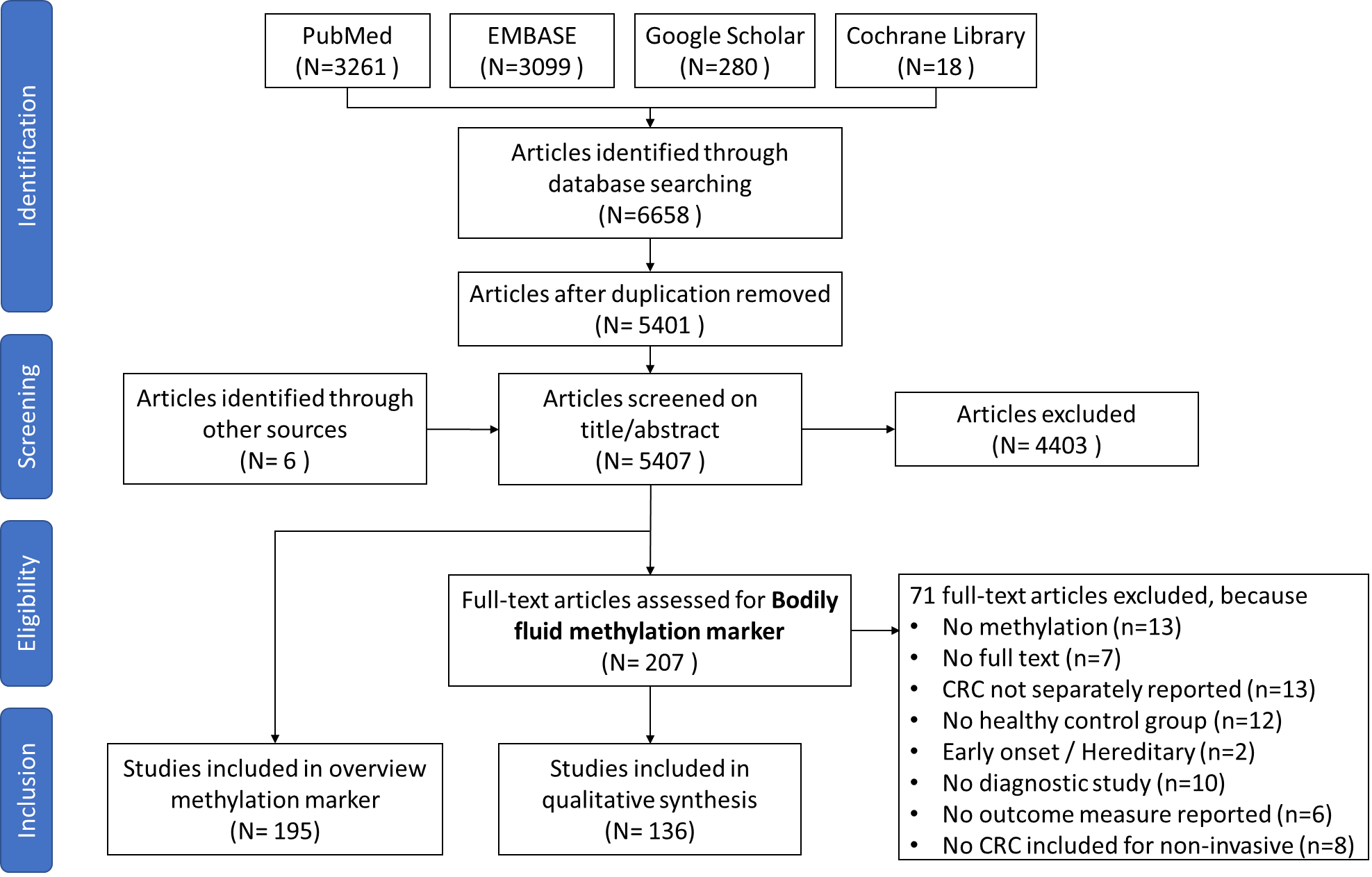
**SUPPLEMENTARY MATERIAL**

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**Supplementary Figure 1**. Flowchart of the study identification process. A total of 136 articles reporting body fluid-based colorectal cancer DNA methylation markers were selected for qualitative assessment.

b

a

**Supplementary Figure 2**. Yearly identified (1985–2020) DNA methylation biomarkers for CRC detection in tissue **(a)** and body fluid **(b)** samples; The length of bars denotes total number of biomarkers investigated across all selected studies per year. Each bar is divided into two categories, with the orange color indicating the number of biomarkers newly identified in that year and the blue color representing the number of biomarkers discovered in previous years. (a)Total number of biomarkers identified in tissue samples per year. (b)Total number of biomarkers identified in bodily fluid samples per year.

**Supplementary Table 1**. Search Strategy for diagnostic methylation markers in colorectal cancer

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Pubmed | Embase | Cochrane Library | Google Scholar |
| 1 | "methylation"[MeSH Terms] OR "methylation"[All Fields] OR hypermethylation[All Fields] OR hypomethylation[All Fields] OR promoter[All Fields] | ‘DNA methylation’ OR ‘hypermethylation’ OR ‘hypomethylation’ OR ‘methylation’ OR ‘promoter methylation’ | ‘methylation’ [MeSH Terms] | ‘DNA methylation’ |
| 2 | “colorectal neoplasms”[MeSH Terms] OR ((“colorectal”[All Fields] OR “rectal”[All Fields] OR “colon”[All Fields] OR “colonic”[All Fields] OR “sigmoid”[All Fields]) AND (“carcinoma”[All Fields] OR “cancer”[All Fields] OR “neoplasm”[All Fields] OR “tumor”[All Fields])) | ‘colorectal cancer’ OR ‘colon cancer’ OR ‘rectal cancer’ | ‘colorectal neoplasms’ [MeSH Terms] | ‘colorectal cancer’ |
| 3 | "diagnosis"[MeSH Terms] OR "diagnosis"[All Fields] OR "detection"[All Fields] | ‘diagnosis’ OR ‘detection’ | ‘diagnosis’ [MeSH Terms] | ‘diagnosis’ |
| 4 |  |  |  | ‘clinical test’ |
| Search | 1 and 2 and 3 | 1 and 2 and 3 | 1 and 2 and 3 | 1 and 2 and 3 and 4 |

**Supplementary Table 2**. Included references in the systematic review

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**Supplementary Table 3**. STARD checklist, adapted for this study

|  |  |  |  |
| --- | --- | --- | --- |
| **Section** | **No** | **Item** | **Interpretation and scoring** |
| **Title or abstract** | | | |
|  | 1 | Identification as a study of diagnostic accuracy using at least one measure of accuracy (such as sensitivity, specificity, predictive values, or AUC) |  |
| **Abstract** | | | |
|  | 2 | Structured summary of study design, methods, results, and conclusions (for specific guidance, see STARD for Abstracts) |  |
| **Introduction** | | | |
|  | 3 | Scientific and clinical background, including the intended use and clinical role of the index test | Intended use or clinical role not mentioned = 0.5 |
| 4 | Study objectives and hypotheses | Also 1.0 point if only objectives are mentioned |
| **Methods** | | | |
| Study design | 5 | Whether data collection was planned before the index test and reference standard were performed (prospective study) or after (retrospective study) | If described: 1.0 point, if you can implicitly conclude it from text: 0.5 point |
| Participants | 6 | Eligibility criteria |  |
|  | 7 | On what basis potentially eligible participants were identified (such as symptoms, results from previous tests, inclusion in registry) |  |
| 8 | Where and when potentially eligible participants were identified (setting, location, and dates) |  |
| 9 | Whether participants formed a consecutive, random, or convenience series |  |
| Test methods | 10a | Index test, in sufficient detail to allow replication | In case the article referred to another article for primer and probe sequences, 0.5 point was awarded. |
|  | 10b | Reference standard, in sufficient detail to allow replication | Excluded. |
| 11 | Rationale for choosing the reference standard (if alternatives exist) | Excluded. |
| 12a | Definition of and rationale for test positivity cut-offs or result categories of the index test, distinguishing pre-specified from exploratory | (Q-MSP should usually define cut-off) |
| 12b | Definition of and rationale for test positivity cut-offs or result categories of the reference standard, distinguishing pre-specified from exploratory | Excluded. |
| 13a | Whether clinical information and reference standard results were available to the performers or readers of the index test |  |
| 13b | Whether clinical information and index test results were available to the assessors of the reference standard | Excluded. |
| Analysis | 14 | Methods for estimating or comparing measures of diagnostic accuracy | Only frequencies = 0.5 points, if sens + spec are mentioned = 1.0 point. |
|  | 15 | How indeterminate index test or reference standard results were handled |  |
| 16 | How missing data on the index test and reference standard were handled | Excluded. |
| 17 | Any analyses of variability in diagnostic accuracy, distinguishing pre-specified from exploratory | Excluded. |
|  | 18 | Intended sample size and how it was determined |  |
| **Results** | | | |
| Participants | 19 | Flow of participants, using a diagram | Excluded. |
|  | 20 | Baseline demographic and clinical characteristics of participants | If characteristics are not summarized, thus individual patient samples are described (often in supplement) 0.5 points. |
| 21a | Distribution of severity of disease in those with the target condition |  |
| 21b | Distribution of alternative diagnoses in those without the target condition | Excluded. |
| 22 | Time interval and any clinical interventions between index test and reference standard | Excluded. |
| Test results | 23 | Cross tabulation of the index test results (or their distribution) by the results of the reference standard | Cross tabulation or distribution of methylation marker for healthy/CRC = 1.0 point |
|  | 24 | Estimates of diagnostic accuracy and their precision (such as 95% confidence intervals) | Precision for estimates of diagnostic accuracy (such as 95% confidence intervals) are reported = 1.0 point  only frequencies with CI/SD/SEM =0.5 points  no CI's = 0 |
| 25 | Any adverse events from performing the index test or the reference standard | Excluded. |
| **Discussion** | | | |
|  | 26 | Study limitations, including sources of potential bias, statistical uncertainty, and generalisability | In case only one limitation was mentioned or limitations were mentioned without explanation, 0.5 point was awarded.  No limitations mentioned = 0 point |
| 27 | Implications for practice, including the intended use and clinical role of the index test |  |
| **Other information** | | | |
|  | 28 | Registration number and name of registry | Excluded. |
| 29 | Where the full study protocol can be accessed | Excluded. |
| 30 | Sources of funding and other support; role of funders |  |

**Supplementary Table 5.** Study characteristics of the studies regarding diagnostic CRC markers in bodily fluids.

|  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study characteristics** | | | | | **Cases** | | | | | **Controls** | | | | **Diagnostic performance** | | | | | **Experimental methods** | |
|  | Design | Marker | Sample | Collection period | N | Age, mean±SD  (range) | TNM/Dukes stage | Tumor location | Methylation,% (CI) | Type | N | Age, mean±SD  (range) | Methylation %  (CI) | Se,%  (CI) | Sp,%  (CI) | AUC,%  (CI) | PPV,%  (CI) | NPV,%  (CI) | DNA isolation | Methylation method |
| Abbaszadegan 2007 [1] | P. | p16 | stool |  | 21 | 59.2 ± 13.3 (34- 83) | B1 14%,  B2 52%,  C2 24%,  UN 10% | 40% distal  60% proximal | 20 |  | 20 |  | 0 | 20 | 100 |  |  |  | Phenol / chloroform | MSP |
| Ahlquist 2012 [2] | R. | *SEPT9* | plasma |  | 52 | 69  (61-75) | I 23%,  II 23%,  III 27%,  IV 27% | 50% distal  50% proximal | 60  (41-77) | NC | 49 | 63  (52-71) | 27 | 60  (41-77) | 73  (58-85) |  |  |  | Exact Sciences | Exact Sciences |
| Naini 2018 [3] | CC | *MGMT* | serum | 2013-2014 | 30 |  | I 20%,  II 56.7%,  III 20%,  IV 3.3% |  |  | NC | 40 |  |  | 90 | 100 |  |  |  | EZ DNA  Methylation Kit | MSP |
| Ashoori 2018 [4] | CC | *BMP3* | plasma | 2011-2014 | 59 | 62.2 |  |  |  | NED | 37 | 60.6 |  | 66 | 76 |  |  |  | QIAamp DNA Blood Mini Kit | MSP |
| Babaei 2016 [5] | P | *SFRP2* | stool |  | 20 | 58 |  |  | 60 | H | 58 |  | 8 | 60 | 92 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Baek 2009 [6] | P | *MLH1* | stool | 2007-2008 | 60 | 61.4±8.1 | I-II 58.3%  III-IV 41.7% | 88.3% distal  11.7% proximal | 30 | NC | 37 | 58.8±10.7 |  | 30 |  |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
|  |  | *MGMT* |  |  |  |  |  |  | 51.7 |  |  |  |  | 51.7 |  |  |  |  |  |  |
|  |  | *VIM* |  |  |  |  |  |  | 38.3 |  |  |  |  | 38.3 |  |  |  |  |  |  |
|  |  | *MLH1, Vimentin, MGMT panel* |  |  |  |  |  |  | 75 |  |  |  | 13.5 | 75 | 86.5 |  |  |  |  |  |
| Bartak 2017 [7] | P | *PRIMA1* | plasma |  | 47 |  | A-B 57.4%  C-D 42.6% |  | 80.9 |  | 37 |  | 27 | 57.4 | 100 | 82.2  (73.8-90.7) |  |  | EZ DNA methylation kit | MethyLight |
|  |  | *SDC2* |  |  |  |  |  |  | 89.4 |  |  |  | 2.7 | 87.2 | 100 | 93  (87.1-98.8) |  |  |  |  |
|  |  | *SFRP1* |  |  |  |  |  |  | 85.1 |  |  |  | 18.9 | 80.9 | 83.8 | 86.9  (79.5-94.2) |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  | 72.3 |  |  |  | 10.8 | 63.8 | 97.3 | 86.3  (78.9-9.37) |  |  |  |  |
|  |  | *SFRP1 + SFRP2 + SDC2 + PRIMA1* |  |  |  |  |  |  |  |  |  |  |  | 91.5 | 97.3 | 97.8  (95.4-100) |  |  |  |  |
| Bedin 2017 [8] | P | *OSMR* | plasma |  | 70 | 67  (61-73) | I 16%  II 21%  III 42%  IV 21% | 70% distal  30% proximal | 44 | H | 36 | 66  (59-73) | 14 | 44.3 | 86.1 | 69 | 86.1 | 44.3 | QIAamp DNA Mini Kit | Q-PCR |
|  |  | *SFRP1* |  |  |  |  |  |  | 63 |  |  |  | 8 | 62.9 | 91.7 | 79.5 | 93.6 | 55.9 |  |  |
|  |  | *OSMR + SFRP1* |  |  |  |  |  |  | 67 |  |  |  | 19 | 67.1 | 80.6 |  | 87 | 55.8 |  |  |
| Belshaw 2004 [9] | P | *APC* | stool |  | 12 |  |  |  | 1.6 | H | 21 |  | 1.7 |  |  |  |  |  | QIAamp DNA Stool mini kit | MSP and COBRA |
|  |  | *HPP1* |  |  |  |  |  |  | 1.8 |  |  |  | 1.5 |  |  |  |  |  |  |  |
|  |  | *MGMT* |  |  |  |  |  |  | 14.1 |  |  |  | 20.4 |  |  |  |  |  |  |  |
|  |  | *MLH1* |  |  |  |  |  |  | 0.7 |  |  |  | 0.6 |  |  |  |  |  |  |  |
|  |  | *p16ink4a* |  |  |  |  |  |  | 2.1 |  |  |  | 1.1 |  |  |  |  |  |  |  |
|  |  | *ESR1 (+164)* |  |  |  |  |  |  | 44.2 |  |  |  | 42.8 |  |  |  |  |  |  |  |
|  |  | *ESR1 (+223)* |  |  |  |  |  |  | 33.6 |  |  |  | 36.8 |  |  |  |  |  |  |  |
|  |  | *ESR1 (+313)* |  |  |  |  |  |  | 39.1 |  |  |  | 38.5 |  |  |  |  |  |  |  |
| Bosch 2012 [10] |  | *GATA4* | stool |  | 21 | 69.7±8.6 | I 23%,  II 36%,  III 30%,  IV 9%,  UN 2% |  |  | H | 60 | 55.3±10.4 |  | 57 | 94 | 76  (62-90) |  |  | QIAamp DNA Stool mini kit | qMSP |
|  |  | *OSMR* |  |  |  |  |  |  |  |  |  |  |  | 29 | 94 | 60  (45-75) |  |  |  |  |
|  |  | *PHACTR3* |  |  | 22 |  |  |  |  |  | 66 |  |  | 55  (33-75) | 95  (87-98) | 78  (64-91) |  |  |  |  |
|  |  | *PHACTR3 + OSMR + GATA4* |  |  |  |  |  |  |  |  |  |  |  | 62 | 87 |  |  |  |  |  |
|  |  | *GATA4* | stool |  | 44 | 71±9.3 | I 23%,  II 36%,  III 30%,  IV 9%,  UN 2% |  |  | H | 30 | 51.8±9.9 |  | 39 | 93 |  |  |  | QIAamp DNA Stool mini kit | qMSP |
|  |  | *OSMR* |  |  |  |  |  |  |  |  |  |  |  | 43 | 90 |  |  |  |  |  |
| Bosch 2012 [10] |  | *PHACTR3* |  |  |  |  |  |  |  |  |  |  |  | 66  (50-79) | 100  (86-100) | 87  (79-95) |  |  |  |  |
|  |  | *PHACTR3 + OSMR + GATA4* |  |  |  |  |  |  |  |  |  |  |  | 68 | 83 |  |  |  |  |  |
| Cassinotti 2012 [11] | P | *CYCD2* | plasma |  | 30 | 68.3  (49-85) | I 37%,  II 63% | 73% distal,  27% proximal | 96.7 | H | 30 | 61.2  (40-80) | 63.3 | 97 | 37 |  |  |  | DNAzol BD + proteinase K | MethDet 56 |
|  |  | *HIC1* |  |  |  |  |  |  | 63.3 |  |  |  | 6.7 | 63 | 93 |  |  |  |  |  |
|  |  | *PAX5* |  |  |  |  |  |  | 86.7 |  |  |  | 56.7 | 87 | 43 |  |  |  |  |  |
|  |  | *RASSF1A* |  |  |  |  |  |  | 93.3 |  |  |  | 46.7 | 93 | 53 |  |  |  |  |  |
|  |  | *RB1* |  |  |  |  |  |  | 90 |  |  |  | 46.7 | 90 | 53 |  |  |  |  |  |
|  |  | *SRBC* |  |  |  |  |  |  | 33.3 |  |  |  | 6.7 | 33 | 93 |  |  |  |  |  |
|  |  | *CYCD2 + HIC1 + PAX5 + RASSF1A + RB1 + SRBC* |  |  |  |  |  |  |  |  |  |  |  | 83.7  (70.5-96.9) | 67.9  (51.2-84.6) |  |  |  |  |  |
| Chang 2010 [12] | P | *ITGA4* | stool | 2007 | 30 | 67.1±7.5 | I-II 47%,  III-IV 53% | 83% distal,  17% proximal | 36.7 | NC | 31 | 58.8±10.2 |  | 36.7 | 100 |  |  |  | QIAamp DNA Stool mini kit | MSP |
|  |  | *p16* |  |  |  |  |  |  | 40 |  |  |  |  | 40 | 96.8 |  |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  | 60 |  |  |  |  | 60 | 100 |  |  |  |  |  |
|  |  | *ITGA4 + SFRP2 + p16* |  |  |  |  |  |  | 70 |  |  |  |  | 70 | 96.8 |  |  |  |  |  |
| Chen 2017 [13] | P | *SEPT9* | blood | 2012-2013 | 51 |  | 0-II 45%,  III-IV 55% | 92% distal,  8% proximal |  | NC | 9 | 65.8±12.4  (total population) |  | 47 | 89 |  | 96 | 22 | Abbott mSample Preparation System DNA reagent kits | Abbott real- time PCR |
| Chen 2005 [14] | P | *VIM* | stool |  | 94 | 66±12.4 | I-II 64%,  III-IV 36% | 68% distal,  32% proximal |  | H | 198 | 65.5±7.3 |  | 46  (36-56) | 90  (85-94) |  |  |  |  | MSP |
| Church 2014 [15] | P | *SEPT9* | plasma | 2008-2010 | 53 | 67 | I-II 68%,  III-IV 32% |  | 48.2  (32.4-63.6) | H | 938 | 61 | 8.5  (6.9-10.3) | 48.2  (32.4-63.6) | 91.5  (89.7-93.1) |  | 5.2  (3.5-7.5) | 99.5  (99.2-99.6) | Epi proColon | Epi proColon |
|  |  | *SEPT9* |  |  | 51 |  |  |  |  |  |  |  |  | 63.9  (47.5-79.2) | 88.4  (86.2-90.4) |  | 4.82  (3.53-6.73) | 99.63  (99.38-99.79) |  |  |
| deVos 2009 [16] | P | *SEPT9* | plasma |  | 97 | 62.5  (37-87) | I 23%,  II 39%,  III 35%,  IV 3% |  |  |  | 172 | 60 (40-87) |  | 75  (65-83) | 87  (81-91) |  |  |  | Chemagic viral DNA/RNA kit | RT-PCR |
|  |  | *SEPT9* |  |  | 90 | 65  (41-86) | I 21%,  II 44.5%,  III 30%,  IV 4.5% |  |  |  | 155 | 54 (40-90) |  | 72 | 86 |  |  |  |  |  |
| Ebert 2006 [17] |  | *ALX4* | serum |  | 30 | 63.5  (29-81) |  |  |  |  | 30 | 54  (25-78) |  | 83.3 | 70 | 83.9  (72.1-92.1) |  |  | MagnaPure device | MS-APPCR |
|  |  | *ALX4* | serum |  |  |  |  |  |  |  |  |  |  | 90 | 53.3 |  |  |  |  |  |
| Elliott 2013 [18] | P | *APC* | stool |  | 19 | 72±9.36 |  |  |  | NC | 20 | 54.3±12.85 |  |  |  |  |  |  | QIAamp DNA Stool Mini Kit | Q-MSP |
|  |  | *CDH1* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *ESR1* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *MLH1* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *p14arf* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *HPP1 / TMEFF2* |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Frattini 2008 [19] |  | *p16 INK4a* | plasma |  | 18 | 65  (38-87) | B 36,  C 28,  D 6 | Rectum 33,  Colon 37 | 61.1 |  |  | 60.5  (40-64) |  | 61.1 |  |  |  |  | QIAamp Blood Extraction Kit | fluorescent- methylation specific PCR (F-MSP) |
| Fu 2018 [20] |  | *SEPT9* | plasma | 2015-2016 | 98 |  | 0 3 (3.1%),  I 23 (23.5%),  II 31 (31.6%),  III 31 (31.6%),  IV 8 (8.2%),  UN 2 (2%) | Colon 18.4%;  Rectum 81.6% |  | NED | 253 |  |  | 61.22  (51.33-70.27) | 98.42  (96.01-99.38) | 80.2  (74-86.4) | 93.75  (85-97.54) | 86.76  (82.35-90.2) | Epi proColon  2.0 kit | RT-PCR |
| Gao 2012 [21] | P | *total methylated DNA* | leucocyte s | cohort 1985-88 | 221 | 58  (54-61) |  |  |  | NED | 219 | 58  (54-62) |  |  |  |  |  |  |  | Illumina GoldenGate Methylation Cancer Panel 1 |
| Glockner 2009 [22] | P | *TFPI2* | stool |  | 11 | 60.7 |  |  |  | H | 12 | 54.2 |  | 73  (39-94) | 100  (74-100) |  | 100  (63-100) | 80  (52-96) | Phenol / chloroform | Q-MSP |
|  |  | *TFPI2* | stool |  | 26 | 69.3 |  |  |  | H | 45 | 55 |  | 89  (70-98) | 79  (64-90) |  | 72  (53-86) | 92  (78-98) | QIAamp DNA Stool Mini Kit |  |
|  |  | *TFPI2* | stool |  | 47 | 71.1 |  |  |  | H | 30 | 52.3 |  | 76  (60-88) | 93  (77-99) |  | 94  (80-99) | 73  (56-86) | QIAamp DNA Stool Mini Kit |  |
| Guo 2013 [23] | P | *FBN1* | stool | 2012-2013 | 75 | 58.5±12.5 | I 16%,  II 40%,  III 40%,  UN 4% | 83% distal,  17% proximal |  |  | 30 | 58.4±12.9 |  | 72 | 93.3 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| He 2014 [24] |  | *p33ING1b* | stool |  | 61 |  | AB 33,  CD 28 | Rectum 52.5%;  Colon 47.5% |  | NC | 20 | n=30 <=58 years  n=31 >58 years  (total population) |  | 73.77 | 95 |  |  |  | QIAamp DNA Stool Mini Kit | Nested MSP |
| He 2018 [25] | P | *SEPT9* | blood |  | 300 |  | 0 23 (7.7%),  I 42 (14%),  II 99 (33%),  III 124 (41.3%),  IV 12 (0.4%) |  |  | NED | 568 |  |  | 73.7 | 97 |  |  |  | Epi proColon® Plasma Quick Kit | RT-PCR |
| Hellebrekers 2009 [26] | P | *GATA4* | stool |  | 28 | 55 | I 36%,  II 28,5%,  III 28,5%,  IV 7% |  |  |  | 45 | 69 |  | 71  (55-88) | 84  (74-95) | 81  (70-89) |  |  | QIAamp DNA stool midi test kit | Q-MSP |
|  |  | *GATA4* |  |  | 47 | 52 | I 21%,  II 40%,  III 28%,  IV 9%,  UN 2% |  |  |  | 30 | 71 |  | 51  (37-65) | 93  (84-100) |  |  |  |  |  |
| Herbst 2011 [27] |  | *ALX4* | serum |  | 15 | 68  (37-91) |  |  |  |  | 32 |  |  | 46.6 | 66.3 |  |  |  | QIAamp DNA blood mini kit | qMSP |
|  |  | *NEUROG1* |  |  | 15 |  |  |  |  |  | 32 |  |  | 55.5 | 81.3 |  |  |  |  |  |
|  |  | *SEPT9* |  |  | 15 |  |  |  |  |  | 32 |  |  | 46.6 | 81.3 |  |  |  |  |  |
|  |  | *vimentin* |  |  | 15 |  |  |  | I 51.9 %,  II 64.3 % |  | 32 |  |  | 31.1 | 60 |  |  |  |  |  |
|  |  | *NEUROG1* |  |  | 97 | 64  (44-83) | I 27 (27.8%),  II 70 (72.2%) | 39.2% distal  33.0% rectal  27.8% proximal | 94.2 | H | 45 | 63  (44-81) |  | 60.8  (50.4-70.6) | 91.1 | 73.4  (64.9-81.1) |  |  | QIAamp DNA blood mini kit | qMSP |
| Huang 2007 [28] | P | *SFRP2* | stool |  | 52 |  |  |  |  | NC | 24 |  | 4.2 | 94.2 | 95.83 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Huang 2007 [29] | P | *HPP1* | stool |  | 52 | 63.5±11.8 | AB 27 (51.92%),  CD: 25 (48.08%) | 77% distal,  23% proximal |  | NC | 24 | 59.6±8.2 |  | 71.4\* | 85.4 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
|  |  | *MGMT* |  |  |  |  |  |  |  |  |  |  |  | 46\* | 93.8 |  |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  |  |  |  |  |  | 90.5\* | 83.3 |  |  |  |  |  |
| Itzkowitz 2008 [30] | P | DY | stool | 2005-2006 | 42 | 67.44±11.21 | I 11 (26.2%),  II 14 (33.3%),  III 14 (33.3%),  IV 3 (7.1%) | 66,7% distal,  33,3% proximal |  | NC | 241 | 56.9±6.33 |  | 60  (44.5-73.0) | 85  (80-89) |  |  |  |  | MSP |
|  |  | hV+DY |  |  |  |  |  |  |  |  |  |  |  | 86  (72.2-93.3) | 73  (67.1-78.2) |  |  |  |  |  |
|  |  | *vimentin* |  |  |  |  |  |  |  |  |  |  |  | 81  (66.7-90.0) | 82  (76.4-86.1) |  |  |  |  |  |
| Itzkowitz 2007 [31] | P | *vimentin* | stool | 2005 | 40 | 65.6±10.3 | I 8 (20%),  II 10 (25%),  III 17 (43%),  IV 5(12%) | 73% distal,  17% proximal |  | NC | 122 | 58.5±7.2 |  | 72.5  (57.2-83.9) | 86.9  (79.8-91.8) |  |  |  |  | MSP |
|  |  | *vimentin* + DIA / DY |  |  |  |  |  |  |  |  |  |  |  | 87.5  (73.9-94.5) | 82  (74.2-87.8) |  |  |  |  |  |
|  |  | *HLTF1* |  |  |  |  |  |  |  |  |  |  |  | 37.5  (24.2-53) | 92.6  (86.6-96.1) |  |  |  |  |  |
| Jin 2015 [32] | P | *SEPT9* | blood | 2013-2014 | 135 | 60.9±12.1 | I 18 (20%),  II 23 (25.6%),  III 44 (48.9%),  IV 5 (5.5%) | Left side 93,  Right side 42 | 74.8 | NC | 91 | 50.1±12.8 |  | 74.8  (67.0-81.6) | 87.4  (83.5-90.6) |  |  |  | Epi proColon 2.0 test | RT-PCR |
| Johnson 2014 [33] | P | *SEPT9* | stool | 2012 | 97 |  | 0 2 (2%),  I 26 (26%),  II 20 (20%),  III 23 (23%),  IV 13 (13%),  UN 17 (17%) |  |  | NED | 193 | 50-84  (total population) |  | 73.3  (63.9-80.9) | 81.5  (75.5-86.3) |  |  |  | Epi proColon test | PCR |
| Kalimutho 2011 [34] | P | *miR-34b/c* | stool |  | 28 | 66  (49-79) | 0 5 (18%),  I 2 (7%),  II 6 (21%),  III 3(11%) | 75% distal,  25%proximal |  | H | 39 | 58 (35-65) | 12.82 | 75 | 87.18 |  |  |  |  | MSP |
| Karam 2018 [35] | P | *p16* | serum / blood |  | 65 | 62.5±11.2 | AB 40 (62.6%),  CD 25 (38.4%) | Colon  26 (41%)  Rectum  39 (58%) |  | H | 70 | 61.6±12.1 |  | 55.38  (43.3-66.8) | 98.5  (92.3-99.7) |  |  |  | QIAamp DNA Blood Mini Kit | MSP |
| Kim 2009 [36] |  | *B4GALT1* | stool |  | 16 |  |  |  |  | NC | 10 |  |  | 56 | 80 | 72±10$ |  |  | Phenol / chloroform / isoamylalcoh ol | MSP |
|  |  | *OSMR* |  |  | 20 |  |  |  |  | NC | 15 |  |  | 45 | 100 | 86±7$ |  |  |  |  |
|  |  | *SFRP4* |  |  |  |  |  |  |  |  |  |  |  | 55 | 100 | 78±7$ |  |  |  |  |
|  |  | *OSMR + SFRP1* |  |  |  |  |  |  |  |  |  |  |  | 60 | 100 | 83±6$ |  |  |  |  |
|  |  | *OSMR* |  |  | 69 |  | I 18 (26%),  II 27 (39%),  III 18 (26%),  IV 6 (9%),  UN 12 (43%) |  |  | H | 81 |  |  | 38 | 95 |  |  |  |  |  |
| Kim 2015 [37] | P | *EYA4* | stool |  | 13 | 58  (42-75) | A 4,  B 4,  C 5 |  | 100 | NED | 19 |  | 5.26 | 100 | 94.74  (75-99) |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Kisiel 2018 [38] | CC | *BMP3, VAV3, ZDHHC1* | stool | cohort I: since 2009  cohort II: 1990-1994 |  |  |  |  |  | IBD |  |  |  | 92  (60-100) | 90  (86-93) | 91  (77-100) |  |  | QIAamp DNA Mini Kit | QuARTS  assays |
| Kisiel 2013 [39] | CC | *BMP3* | stool | 2009-2011 | 19 | 60  (45-72) |  | Splenic flexure = 6 |  | IBD | 35 | 60  (45-77) |  | 100 | 91 |  |  |  |  | RT-MSP |
|  |  | *NDRG4 + BMP3* |  |  |  |  |  |  |  |  |  |  |  | 100  (63-100) | 89 |  |  |  |  |  |
| Kitkumthorn 2012 [40] | P | *LINE-1* | blood |  | 36 | 59.47±9.3 |  |  |  | FOC | 144 | 48.67±12.1 |  | 52.78 | 86.81 | 75.5 |  |  | QIAamp DNA Blood Mini Kit | PCR |
| Kriegshauser 2017 [41] | P | *SFRP2* | stool |  | 18 |  | I 2 (11%),  II 16 (89%) | 83% distal,  17% proximal |  | NC | 22 | 57.4  (18-90)  (total population) |  | 61.1 | 86.3 |  |  |  |  | MSRH |
|  |  | *SFRP2* |  |  |  |  |  |  |  |  |  |  |  | 77.7 | 77.3 |  |  |  |  | MethyLight |
| Leclerc 2017 [42] | P | *PDK4* | blood |  | 40 | 59 |  |  |  |  | 40 | 58 |  |  |  |  |  |  | Gentra Puregene Blood Kit |  |
|  |  | *PDK4* |  |  | 18 | 60 |  |  |  |  | 29 | 60 |  |  |  |  |  |  |  |  |
| Lee 2009 [43] | R | *APC +*  *MGM T + RASSF2A + Wif1* | plasma | 2004-2007 | 243 | 61±11 | I 44 (18%),  II 199 (82%) | 77% distal,  23% proximal |  | H | 276 |  |  | 86.5  (81.7-90.8) | 92.1  (88.2-95.0) | 92.7 | 90.6  (86.0-94.1%) | 88.8  (84.4-92.2%) | QIAamp DNA Blood Mini Kit | MSP |
|  |  | *Wif-1* |  |  |  |  |  |  |  |  |  |  |  | 36.7  (30.6-43.7) | 90.6  (86.4-93.1) | 64.1 | 77.5  (68.6-84.7%) | 62.1  (56.9-66.1%) |  |  |
| Lenhard 2005 [44] |  | *HIC1* | stool |  | 26 |  | I 1 (4%),  II 5 (19%),  III 7 (27%),  IV 13 (50%) | 58% distal,  42% proximal |  | NC | 32 |  |  | 42  (23-63) | 100 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Leung 2004 [45] | P | *APC* | stool |  | 20 | 69  (45-90) | B 7,  C 8,  D 4 | 55% distal,  45% proximal | 20 | NC | 20 | age-matched |  |  |  |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
|  |  | *ATM* |  |  |  |  |  |  | 25 |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *HLTF* |  |  |  |  |  |  | 25 |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *hMLH1* |  |  |  |  |  |  | 20 |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *MGMT* |  |  |  |  |  |  | 20 |  |  |  |  |  |  |  |  |  |  |  |
|  |  | *ATM + APC + hMLH1 + HLTF + MGMT* |  |  |  |  |  |  |  |  |  |  |  | 70  (46-88) | 100 |  |  |  |  |  |
| Leung 2005 [46] | P | *APC* | serum |  | 49 | 57  (47-80) | I 5 (11%),  II 15 (33%),  III 17 (38%),  IV 8 (18%) | 51% distal,  45% proximal,  4% synchronous |  | NC | 41 | age-matched |  | 6.1 | 100 | 53 |  |  | QIAamp Blood Kit | Methylight |
|  |  | *HLTF* |  |  |  |  |  |  |  |  |  |  |  | 32.7 | 92.7 | 63 |  |  |  |  |
|  |  | *hMLH-1* |  |  |  |  |  |  |  |  |  |  |  | 42.9 | 97.6 | 71 |  |  |  |  |
| Leung 2007 [47] | P | *APC + ATM + hMLH1 + sFRP2 + HLTF + MGMT + GSTP1* | stool |  | 20 |  |  | 40% distal,  60% proximal |  | NC | 30 | 69  (50-70)  (total population) |  | 75  (50.9-91.3) | 90  (73.5-97.9) |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
|  |  | *COX2* |  |  |  |  |  |  |  |  |  |  |  | 50  (27.2-72.8) | 93  (77.2-99.2) |  |  |  |  |  |
| Li 2015 [48] | P | *FBN1* | stool | 2012-2014 | 89 | <50 n=24,  50-60 n=24,  60-70 n=22,  >70 n=19 | A 17,  B 36,  C 36 | Left=19,  Transverse=5,  Right=8,  Rectum=57 |  | H | 30 |  |  | 70.8 | 93.3 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
|  |  | *SNCA* |  |  |  |  |  |  |  |  |  |  |  | 70 | 100 |  |  |  |  |  |
|  |  | *SCNA + FBN1* |  |  |  |  |  |  |  |  |  |  |  | 84.3 | 93.3 |  |  |  |  |  |
| Liu 2013 [49] | P | *EYA4* | serum | 2003-2005 | 26 | 67.1  (46-83) |  |  |  | H | 26 | 67.1  (46-83) |  | 57.7 | 90 | 76.8  (63.4-90.1) |  |  |  | qPCR |
|  |  | *SEPT9* |  |  |  |  |  |  |  |  |  |  |  | 50 | 90 | 79.3  (66.6-91.9) |  |  |  |  |
|  |  | *TAC1* |  |  |  |  |  |  |  |  |  |  |  | 57.7 | 90 | 78.9  (66.4-91.4) |  |  |  |  |
|  |  | *TAC1 + EYA4* |  |  |  |  |  |  |  |  |  |  |  | 84.6 | 80.8 | 85.1  (74.2-96.1) |  |  |  |  |
|  |  | *TAC1 + SEPT9* |  |  |  |  |  |  |  |  |  |  |  | 73.1 | 92.3 | 82.1  (70.1-94) |  |  |  |  |
| Lofton-Day 2008 [50] | P | *bisDNA* | plasma |  | 133 | 65 |  | 88% distal  12% proximal |  | NC | 179 |  |  | 15 | 95 | 61 |  |  | MagNa Pure LC Total Nucleic Acid Isolation Kit | HM qPCR |
|  |  | *NGFR* |  |  |  |  |  |  |  |  |  |  |  | 33 | 95 | 70 |  |  |  |  |
|  |  | *SEPT9* |  |  |  |  |  |  |  |  |  |  |  | 52 | 95 | 80 |  |  |  |  |
|  |  | *TMEFF2* |  |  |  |  |  |  |  |  |  |  |  | 30 | 95 | 72 |  |  |  |  |
|  |  | *SEPT9 + NGFR* |  |  |  |  |  |  |  |  |  |  |  |  |  | 81 |  |  |  |  |
|  |  | *TMEFF2 + NGFR + SEPT9 + bisDNA* |  |  |  |  |  |  |  |  |  |  |  |  |  | 79 |  |  |  |  |
| Lu 2014 [51] | P | *GATA4* | stool | 2011-2012 | 56 | 60.6±12.19 | I-II 57,  III-IV 43 | 89% distal  11% proximal | 42.9  (30.77-55.86) |  | 40 |  | 5 | 42.9  (30.77-55.86) | 95  (83.5-98.62) |  |  |  | QiaAmp DNA Stool mini-kit | MSP PCR |
|  |  | *GATA5* |  |  |  |  |  |  | 83.9  (72.19-91.31) |  |  |  | 17.5 | 83.9  (72.19-91.31) | 82.5  (68.05-91.25) |  |  |  |  |  |
|  |  | *NDRG4* |  |  |  |  |  |  | 28.6  (18.42-41.48) |  |  |  | 2.5 | 28.6  (18.42-41.48) | 97.5  (87.12-99.56) |  |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  | 57.1  (44.14-  69.23) |  |  |  | 10 | 57.1  (44.14-69.23) | 90  (76.95-96.04) |  |  |  |  |  |
| Lu 2014 [51] |  | *VIM* |  |  |  |  |  |  | 41.1  (29.17-54.12) |  |  |  | 15 | 41.1  (29.17-54.12) | 85  (70.93-92.94) |  |  |  |  |  |
|  |  | *SFRP2 + GATA4 + GATA5 + NDRG4 + VIM* |  |  |  |  |  |  | 96.4  (87.88-99.02) |  |  |  | 35 | 96.4  (87.88-99.02) | 65  (49.51-77.87) |  |  |  |  |  |
| Lange 2012 [52] | P | *C9orf50* | plasma | 2008-2011 | 75 |  |  |  |  |  | 66 |  |  |  |  | 70  (64-76) |  |  | QIAamp Circulating Nucleic Acid Kit | MethyLight |
|  |  | *THBD-M* |  |  |  |  |  |  |  |  |  |  |  |  |  | 80  (74-87) |  |  |  | MethyLight |
|  |  | *THBD-M + C9orf50* |  |  |  |  |  |  |  |  |  |  |  |  |  | 80  (73-87) |  |  |  | MethyLight |
|  |  | *C9orf50* | serum | 2008-2011 | 72 |  |  |  |  |  | 6 |  |  |  |  | 69  (64-75) |  |  | QIAamp Circulating Nucleic Acid Kit | MethyLight |
|  |  | *THBD-M* |  |  |  |  |  |  |  |  |  |  |  |  |  | 82  (75-89) |  |  |  | MethyLight |
|  |  | *THBD-M + C9orf50* |  |  |  |  |  |  |  |  |  |  |  |  |  | 83  (76-89) |  |  |  | MethyLight |
| Mayor 2009 [53] | P | *EN1* | stool | 1996-1998 | 30 |  | A 7,  B 6,  C 9,  D 5,  ADE 3 | 83% distal  17% proximal | 26.7 |  | 30 |  | 3.3 | 26.7 | 96.7 |  |  |  |  | RT-PCR |
|  |  | *EN1* | serum |  |  |  |  |  | 13.6 |  |  |  | 0 | 13.6 | 100 |  |  |  |  |  |
| Melotte 2009 [54] | P | *NDRG4* | stool |  | 28 | 69.3±9 | I 35.7%,  II 28.6%,  III 28.6%,  IV 7.1% |  |  | H | 45 | 55±11.5 |  | 61  (43-79) | 93  (90-97) | 77  (66-86) |  |  |  | Q-MSP |
|  |  | *NDRG4* |  |  | 47 | 71.1±9 | I 21.3%,  II 40.4%,  III 27.7%,  IV 2.1% |  |  | H | 30 | 52.3±9.8 |  | 53  (39-67) | 100  (86-100) |  |  |  |  | Q-MSP |
| Melotte 2015 [55] | P | *FOXE1* | plasma | 2007 | 154 | <=65 n=44;  >65 n= 110 | I 28%;  II 28%,  III 30%,  IV 14% |  |  | H | 444 | <=65 n=253;  >65 n=191 |  | 46  (38-54) | 93  (91-95) | 70  (69-73) |  |  | QIAamp Circulating Nucleic Acid Test Kit | Q-MSP |
|  |  | *GATA5* |  |  |  |  |  |  |  |  |  |  |  | 18  (12-24) | 99  (98-100) | 59  (55-63) |  |  |  |  |
|  |  | *NDRG4* |  |  |  |  |  |  |  |  |  |  |  | 27  (20-34) | 95  (93-97) | 61  (57-65) |  |  |  |  |
|  |  | *SYNE1* |  |  |  |  |  |  |  |  |  |  |  | 47  (39-55) | 96  (94-98) | 72  (68-75) |  |  |  |  |
|  |  | *FOXE1 + SYNE1* |  |  |  |  |  |  |  |  |  |  |  | 56  (48-64) | 90  (87-93) |  |  |  |  |  |
|  |  | *FOXE1 + SYNE1* | plasma | 2007 | 66 | <=65 n=24;  >65 n=42 | I 41%,  II 23%,  III 30%,  IV 6% |  |  | H | 240 | <=65 n=105;  >6 5 n=93 |  | 58  (46-70) | 91  (80-100) |  |  |  | QIAamp Circulating Nucleic Acid Test Kit | Q-MSP |
| Melson 2013 [56] | R | *CYCD2* | plasma |  | 30 | 68.3  (49-85) | I 37%,  II 63%,  III 0%,  IV 0% | 73% distal,  27% proximal |  | PE | 30 | 61.2  (40-80) |  | 70 | 73 | 83 |  |  | DNAzol BD and proteinase K | MSRE-PCR |
|  |  | *HIC* |  |  |  |  |  |  |  |  |  |  |  | 77 | 83 | 86 |  |  |  |  |
|  |  | *VHL* |  |  |  |  |  |  |  |  |  |  |  | 76 | 67 | 70 |  |  |  |  |
|  |  | *CYCD2, HIC + VHL* |  |  |  |  |  |  |  |  |  |  |  | 83 | 93 | 94 |  |  |  |  |
|  |  | *CYCD2, HIC + VHL* |  |  |  | 55.9  (45-72) | II 100% | 50% distal,  50% proximal |  | PE |  | 52.6  (50-61) |  | 70 | 90 | 90 |  |  | DNAzol BD and proteinase K | MSRE-PCR |
| Miotto 2004 [57] | P | *CDH4* | plasma |  | 46 |  |  |  | 70 | H | 17 |  | 0 | 70 | 100 |  |  |  | Wizard genomic DNA purification kit | semi-nested PCR |
| Mitchell 2016 [58] | P | *FGF5* | white blood cells | 2006-2011 | 20 | 61  (32-86) | I 5%,  II 38%,  III 31%,  IV 11%,  UN 15% | 65% distal,  35% proximal | 85 | ABD | 40 | 56  (41-83) | 17.5 |  |  |  |  |  | QIAamp circulating nucleic acid kit | MSP |
|  |  | *IRF4* |  |  | 22 |  |  |  | 59.1 |  | 24 |  | 15.9 |  |  |  |  |  |  |  |
|  |  | *PDX1* |  |  | 20 |  |  |  | 45 |  | 20 |  | 30 |  |  |  |  |  |  |  |
|  |  | *SOX21* |  |  | 20 |  |  |  | 85 |  | 20 |  | 50 |  |  |  |  |  |  |  |
|  |  | *GRASP* |  |  | 44 |  |  |  | 54.5 |  | 44 |  | 6.8 |  |  |  |  |  |  |  |
|  |  | *SDC2* |  |  | 44 |  |  |  | 59.1 |  | 44 |  | 15.9 |  |  |  |  |  |  |  |
|  |  | *BCAT1* |  |  | 74 |  |  |  | 64.9 |  | 144 |  | 3.5 |  |  |  |  |  |  |  |
|  |  | *IKZF1* |  |  | 74 |  |  |  | 67.6 |  | 144 |  | 4.9 |  |  |  |  |  |  |  |
|  |  | *SEPT9* |  | 2006-2011 | 44 |  |  |  | 59.1 |  | 44 |  | 4.5 |  |  |  |  |  | QIAamp circulating nucleic acid kit | HeavyMethyl assay |
| Muller 2004 [59] | P | *CALCA* | stool | 2003-2004 | 10 | 67.5  (46-85) |  | 80% distal,  20% proximal | 40 | ABD | 13 | 46  (18-69) | 0 |  |  |  |  |  | QIAamp DNA Stool Kit | MethyLight, real-time PCR |
|  |  | *IGFBP2* |  |  |  |  |  |  | 20 |  |  |  | 0 |  |  |  |  |  |  |  |
|  |  | *PGR* |  |  |  |  |  |  | 80 |  |  |  | 31 |  |  |  |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  | 90 |  |  |  | 23 | 90  (56-100) | 77  (46-95) |  |  |  |  |  |
|  |  | *SFRP5* |  |  |  |  |  |  | 89 |  |  |  | 46 |  |  |  |  |  |  |  |
|  |  | *CALCA* |  | 2003-2004 | 13 | 63  (34-90) |  | 85% distal,  15% proximal | 31 | ABD | 13 | 47 | 0 |  |  |  |  |  | QIAamp DNA Stool Kit | MethyLight, real-time PCR |
|  |  | *IGFBP2* |  |  |  |  |  |  | 8 |  |  |  | 8 |  |  |  |  |  |  |  |
| Muller 2004 [59] |  | *PGR* |  |  |  |  |  |  | 77 |  |  |  | 31 |  |  |  |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  | 77 |  |  |  | 23 | 77  (46-95) | 77  (46-95) |  |  |  |  |  |
|  |  | *SFRP5* |  |  |  |  |  |  | 77 |  |  |  | 23 |  |  |  |  |  |  |  |
| Nagai 2017 [60] | P | *LINE-1* | plasma | 2012-2014 | 114 | 63±12.5 | I-II 50%,  III-IV 50% | 70,2% distal,  29,8% proximal |  | NED | 53 | 50.6±19.3 |  | 65.8 | 90 | 81 |  |  | Phenol / chloroform / isoamyl alcohol | AQAMA |
| Nagasaka 2009 [61] | P | *RASSF2 loc1* | stool | 2004-2007 | 84 | 65.2±11.3 | I-II 48%,  III-IV 52% | 66,7% distal,  33,3% proximal | 27.4 | NED | 113 | 66.1±12.5 | 2.7 | 27.4 | 97.3 |  |  |  | QIAmp DNA Mini Kit | High- sensitivity assay for bisulfite DNA (Hi-SA) |
|  |  | *RASSF2 loc2* |  |  |  |  |  |  | 35.7 |  |  |  | 2.7 | 35.7 | 97.3 |  |  |  |  |  |
|  |  | *SFRP2 loc1* |  |  |  |  |  |  | 57.1 |  |  |  | 3.5 | 57.1 | 96.5 |  |  |  |  |  |
|  |  | *SFRP2 loc2* |  |  |  |  |  |  | 38.1 |  |  |  | 4.4 | 38.1 | 95.6 |  |  |  |  |  |
|  |  | combination |  |  |  |  |  |  | 75 |  |  |  | 10.6 | 75 | 89.4 |  |  |  |  |  |
| Grutzmann 2008 [62] | P | *SEPT9* | blood |  | 252 | 61 | I 25%,  II 33%,  III 23%,  IV 11%,  NA 8% | 70% distal,  30% proximal | 48  (41-54) |  | 102 | 59 | 7  (3-14) | 48  (41-54) | 93  (86-97) |  |  |  | Total Nucleic Acid Large Volume DNA extraction kit | PCR |
|  |  | *SEPT9* |  |  | 126 | 67 | I 17%,  II 29%,  III 43%,  IV 9%,  NA 2% | 77% distal,  23% proximal | 58  (49-67) |  | 183 | 56 | 10  (6-15) | 58  (49-67) | 90  (85-94) |  |  |  |  |  |
|  |  | *SEPT9* |  |  |  |  |  |  | 72  (63-80) |  |  |  | 10 (6-16) | 72  (63-80) | 90  (84-94) |  |  |  |  |  |
| Nan 2013 [63] | CC | Genomic DNA methylation | leucocytes | 1989-1990 | 358 | 59 |  |  |  | NED | 661 | 59 |  |  |  |  |  |  |  | ABI PRISM 7900HT Sequence Detction System |
| Nishio 2010 [64] | P | *RUNX3* | serum |  | 344 | 63.9±12.8 | I 19.2%,  II 31.4%,  III 36%,  IV 13.4% | 67% distal,  33% proximal | 29 | H | 56 | 63.9  (38-83) | 0 |  |  |  |  |  | Dneasy Blood & Tissue Kit | RTQ-MSP (2step MSP) |
| Niu 2017 [65] | P | *SDC2* | stool | 2014-2015 | 196 | 61  (43-79) | I-II 44.4%,  III-IV 55.6% | 78,1% distal,  21,9% proximal | 81.1 | H | 179 | 56  (43-77) | 6.7 | 81.1 | 93.3 | 92  (89-95) |  |  | QIAamp DNA Mini Kit | Q-MSP |
|  |  | *SDC2* | stool |  | 19 |  | I-II 44.4%,  III-IV 55.6% |  | 84.2 | H | 20 |  | 5 | 84.2 | 95 |  |  |  |  |  |
| Nunes 2018 [66] | P | *SEPT9* | blood |  | 72 | 63  (29–93) | 0 3 (4%),  I-II 34 (47%),  III-IV 35 (49%) | 32% distal,  68% proximal |  | FA | 103 | 52  (45–65) |  | 11.1 | 98.9 |  | 100 | 61.68 | QIAamp MinElute ccfDNA | multiplex qMSP |
|  |  | *APC* |  |  |  |  |  |  |  |  |  |  |  | 20.83 | 94.17 |  | 71.43 | 62.99 |  |  |
|  |  | *FOXA1* |  |  |  |  |  |  |  |  |  |  |  | 50 | 88.35 |  | 75 | 71.65 |  |  |
|  |  | *RARβ2* |  |  |  |  |  |  |  |  |  |  |  | 16.67 | 95.15 |  | 70.59 | 62.03 |  |  |
|  |  | *RASSF1A* |  |  |  |  |  |  |  |  |  |  |  | 13.89 | 99.03 |  | 90.91 | 62.2 |  |  |
|  |  | *SCGB3A1* |  |  |  |  |  |  |  |  |  |  |  | 26.39 | 90.29 |  | 65.52 | 63.7 |  |  |
|  |  | *SOX17* |  |  |  |  |  |  |  |  |  |  |  | 23.61 | 90.29 |  | 62.96 | 62.84 |  |  |
|  |  | PanCancer panel (*APC, FOXA1, RASSF1A*) |  |  | 37 |  |  |  |  | FA | 103 |  |  | 78.4 | 69.9 |  | 48.3 | 90 |  |  |
| Oh 2013 [67] | R | *SDC2* | serum |  | 131 | 58.4  (33-84) | I 20%,  II 44%,  III 27%,  IV 9% |  |  | NED | 125 | 51  (40-61) |  | 87  (80.0-92.3) | 95.2  (89.8-98.2) | 93  (89-96) |  |  | Dynabeads silane viral NA kit | Q-MSP |
| Oh 2017 [68] | P | *SDC2* | stool |  | 50 | 61.9  (41-84) | I 24%,  II 34%,  III 20%,  IV 22% |  | 90 | H | 22 | 58.8  (36-77) | 9.1 | 90  (78.2-96.6) | 90.9  (70.8-98.6) | 93  (85-98) |  |  | Phenol / chloroform / isoanylalcoho l; QIAamp DNA Stool Mini Kit | LTE-QMSP |
| Orntoft 2015 [69] | R | *SEPT9* | plasma | 2010-2012 | 128 | <=65 58% | I 27,3%,  II 27,3%,  III 23,4%,  IV 22% | 67% distal,  33% proximal | 73  (64-80) | NC | 150 | <=65 65% | 18  (12-25) | 73  (64-80) | 82  (75-88) |  |  |  | Epi proColon Plasma Quick kit | Epi proColon Sensitive PCR kit |
| Pack 2013 [70] | P | *APC* | plasma |  | 60 | 63.4±10.1 | I 23,3%,  II 23,3%,  III 46,7%,  IV 6,7% | 54% distal,  46% proximal |  | AP, H | 60 | 61.4±9.0 |  | 57 | 86 |  | 71 |  |  | MSP–SSCP (single- strand conformation polymorphism) |
|  |  | *DAPK1* |  |  |  |  |  |  |  |  |  |  |  | 50 | 74 |  | 54 |  |  |  |
|  |  | *E-cad (CDH1)* |  |  |  |  |  |  |  |  |  |  |  | 60 | 84 |  | 69 |  |  |  |
|  |  | *FHIT* |  |  |  |  |  |  |  |  |  |  |  | 50 | 84 |  | 65 |  |  |  |
|  |  | *SMAD4* |  |  |  |  |  |  |  |  |  |  |  | 52 | 64 |  | 53 |  |  |  |
| Park 2017 [71] | P | *BMP3* | stool | 2012-2014 | 35 | 60.6±13.04 | I-II 49%,  III-IV 51% | 66% distal,  34% proximal | 40 | NC | 40 | 55.7±14.64 | 15 | 40  (23-57) | 85  (73.4-96.5) |  |  |  | QIAamp DNA stool mini kit | qMSP |
|  |  | *NDRG4* |  |  |  |  |  |  | 68.8 |  |  |  | 20 | 68.8  (52-85) | 80  (67.0-92.9) |  |  |  |  |  |
| Park 2017 [71] |  | *SFRP2* |  |  |  |  |  |  | 60 |  |  |  | 12.5 | 60  (43-77) | 87.5  (76.8-98.2) |  |  |  |  |  |
|  |  | *TFPI2* |  |  |  |  |  |  | 31.4 |  |  |  | 10 | 31.4  (15-48) | 90  (80.3-99.7) |  |  |  |  |  |
|  |  | *SFRP2 + TFPI2 + NDRG4 + BMP3* |  |  |  |  |  |  |  |  |  |  |  | 94.3  (86.2-100) | 55  (38.9-71.1) |  |  |  |  |  |
| Pedersen 2015 [72] | CC | *BCAT1* | plasma |  | 74 | 61  (32-86) | I 5%,  II 38%,  III 31%,  IV 11%,  UN 15% | 65% distal,  35% proximal |  | NC | 144 | 56  (41-83) |  | 64.9  (52.9-75.6) | 96.5  (92.1-98.9) |  |  |  | QIAamp Circulating Nucleic Acid Kit | Q-MSP, hydrolysis probe |
|  |  | *IKZF1* |  |  |  |  |  |  |  |  |  |  |  | 67.6  (55.7-78.0) | 95.1  (90.2-98.0) |  |  |  |  |  |
|  |  | *BCAT1 + IKZF1* |  |  |  |  |  |  |  |  |  |  |  | 77  (65.8-86.0) | 92.4  (86.7-96.4) |  |  |  |  |  |
| Pedersen 2014 [73] | R | *CAHM* | plasma |  | 73 | 59±11.7 | I 16%,  II 29%,  III 32%,  IV 16%,  UN 7% |  | 55 |  | 74 | 52±8.6 | 7 | 55 | 93 |  |  |  | QIAamp Circulating Nucleic Acid Kit | Q-MSP |
| Pedersen 2015 [74] | P | *BCAT1* | plasma | 2011-2014 | 129 | 69  (37-90) | I 22%,  II 33%,  III 31%,  IV 12%,  UN 2% | 50% distal,  40% proximal, | 57  (48-66) | NC | 450 | 58  (40-85) | 5  (3-7) | 57  (48-66) | 95  (93-97) |  |  |  | QIASymphony Circulating Nucleic Acid Kit | Q-MSP |
|  |  | *IKZF1* |  |  |  |  |  |  | 48  (39-57) |  |  |  | 1  (0-2) | 48  (39-57) | 99  (98-100) |  |  |  |  |  |
|  |  | *BCAT1 + IKZF1* |  |  |  |  |  |  | 66  (57-74) |  |  |  | 5  (3-8) | 66  (57-74) | 95  (92-97) |  |  |  |  |  |
| Potter 2014 [75] | R | *SEPT9* | plasma |  | 44 | 50-59 9%.  60-69 55%.  >69 36% | I 39%,  II 27%,  III 23%,  IV 11% |  | 68  (53-80) | NC | 444 | 50-59 45%.  60-69 29%.  >69 27% | 21.2  (19-23) | 68  (53-80) | 78.8  (76.7-80.8) |  | 2.5 | 99.7 | Epi proColon Plasma Quick kit | Epi pro- Colon Sensitive PCR kit |
| Rasmussen 2017 [76] | CC | *ALX4* | plasma | 2003-2005 | 193 | 67.5±11.5 |  |  | 28.5  (22.2-35.4) | RA | 102 | 64.7±14.2 | 1  (0-5.3) | 28.5  (22.2-35.4) |  |  |  |  | The easy- MagTM platform | nested PCR |
|  |  | *APC* |  |  |  |  |  |  | 42  (34.9-49.3) |  |  |  | 32.4  (23.4-42.3) | 42  (34.9-49.3) |  |  |  |  |  |  |
|  |  | *BMP3* |  |  |  |  |  |  | 28.5  (22.2-35.4) |  |  |  | 10.8  (5.5-18.5) | 28.5  (22.2-35.4) |  |  |  |  |  |  |
|  |  | *BNC1* |  |  |  |  |  |  | 11.9  (7.7-17.3) |  |  |  | 12.7  (7.0-20.8) | 11.9  (7.7-17.3) |  |  |  |  |  |  |
|  |  | *BRCA1* |  |  |  |  |  |  | 25.4  (19.4-32.1) |  |  |  | 21.6  (14.0-30.8) | 25.4  (19.4-32.1) |  |  |  |  |  |  |
|  |  | *CDKN2A* |  |  |  |  |  |  | 9.3  (5.6-14.3) |  |  |  | 3.9  (1.1-9.7) | 9.3  (5.6-14.3) |  |  |  |  |  |  |
|  |  | *HIC1* |  |  |  |  |  |  | 5.7  (2.9-10.0) |  |  |  | 1  (0-5.3) | 5.7  (2.9-10.0) |  |  |  |  |  |  |
|  |  | *HLTF* |  |  |  |  |  |  | 11.4  (7.3-16.7) |  |  |  | 3.9'  (1.1-9.7) | 11.4  (7.3-16.7) |  |  |  |  |  |  |
|  |  | *MGMT* |  |  |  |  |  |  | 5.7  (2.9-10.0) |  |  |  | 1  (0-5.3) | 5.7  (2.9-10.0) |  |  |  |  |  |  |
|  |  | *MLH1* |  |  |  |  |  |  | 45.1  (37.9-52.4) |  |  |  | 43.1  (33.4-53.3) | 45.1  (37.9-52.4) |  |  |  |  |  |  |
|  |  | *NDRG4* |  |  |  |  |  |  | 9.3  (5.6-14.3) |  |  |  | 0  (0-3.6) | 9.3  (5.6-14.3) |  |  |  |  |  |  |
|  |  | *NEUROG1* |  |  |  |  |  |  | 20.7  (15.2-27.1) |  |  |  | 19.6  (12.4-28.6) | 20.7  (15.2-27.1) |  |  |  |  |  |  |
|  |  | *NPTX2* |  |  |  |  |  |  | 69.9  (62.9-76.3) |  |  |  | 58.8  (48.6-68.5) | 69.9  (62.9-76.3) |  |  |  |  |  |  |
|  |  | *OSMR* |  |  |  |  |  |  | 11.4  (7.3-16.7) |  |  |  | 6.9  (2.8-13.6) | 11.4  (7.3-16.7) |  |  |  |  |  |  |
|  |  | *PHACTR3* |  |  |  |  |  |  | 14.5  (9.9-20.3) |  |  |  | 5.9  (2.2-12.4) | 14.5  (9.9-20.3) |  |  |  |  |  |  |
|  |  | *PPENK* |  |  |  |  |  |  | 10.4  (6.4-15.6) |  |  |  | 3.9  (1.1-9.7) | 10.4  (6.4-15.6) |  |  |  |  |  |  |
|  |  | *RARB* |  |  |  |  |  |  | 25.4  (19.4-32.1) |  |  |  | 69.6  (59.7-78.3) | 25.4  (19.4-32.1) |  |  |  |  |  |  |
|  |  | *RASSF1A* |  |  |  |  |  |  | 11.4  (7.3-16.7) |  |  |  | 15.7  (9.2-24.2) | 11.4  (7.3-16.7) |  |  |  |  |  |  |
|  |  | *SDC2* |  |  |  |  |  |  | 24.4  (18.5-31.0) |  |  |  | 5.9  (2.2-12.4) | 24.4  (18.5-31.0) |  |  |  |  |  |  |
|  |  | *SEPT9* |  |  |  |  |  |  | 24.4  (18.5-31.0) |  |  |  | 4.9  (1.6-11.1) | 24.4  (18.5-31.0) |  |  |  |  |  |  |
|  |  | *SFRP1* |  |  |  |  |  |  | 21.8  (16.2-28.3) |  |  |  | 6.9  (2.8-13.6) | 21.8  (16.2-28.3) |  |  |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  | 20.2  (14.8-26.6) |  |  |  | 17.6  (10.8-26.4) | 20.2  (14.8-26.6) |  |  |  |  |  |  |
| Rasmussen 2017 [76] |  | *SPG20* |  |  |  |  |  |  | 15.5  (10.7-21.4) |  |  |  | 11.8  (6.2-19.6) | 15.5  (10.7-21.4) |  |  |  |  |  |  |
|  |  | *SST* |  |  |  |  |  |  | 30.1  (23.7-37.1) |  |  |  | 31.4  (22.5-41.4) | 30.1  (23.7-37.1) |  |  |  |  |  |  |
|  |  | *TAC1* |  |  |  |  |  |  | 52.8  (45.6-60.1) |  |  |  | 47.1  (37.1-57.2) | 52.8  (45.6-60.1) |  |  |  |  |  |  |
|  |  | *TFPI2* |  |  |  |  |  |  | 7.3  (4.0-11.9) |  |  |  | 2  (0.2-6.9) | 7.3  (4.0-11.9) |  |  |  |  |  |  |
|  |  | *THBD* |  |  |  |  |  |  | 9.8  (6.0-14.9) |  |  |  | 1  (0-5.3) | 9.8  (6.0-14.9) |  |  |  |  |  |  |
|  |  | *VIM* |  |  |  |  |  |  | 17.6  (12.5-23.7) |  |  |  | 11.8  (6.2-19.6) | 17.6  (12.5-23.7) |  |  |  |  |  |  |
|  |  | *WIF1* |  |  |  |  |  |  | 9.8  (6.0-14.9) |  |  |  | 3.9  (1.1-9.7) | 9.8  (6.0-14.9) |  |  |  |  |  |  |
|  |  | *WNT5A* |  |  |  |  |  |  | 6.2  (3.3-10.6) |  |  |  | 4.9  (1.6-11.1) | 6.2  (3.3-10.6) |  |  |  |  |  |  |
|  |  | *ALX4, BMP3, NPTX2, RARB, SDC2, SEPT9,*  *VIM +* age + sex |  |  |  |  |  |  |  |  |  |  |  | 90.7 | 72.5 | 86 | 6 | 99.8 |  |  |
| Ravegnini 2015 [77] |  | *SEPT9* | blood | start from 2005 | 27 | 67.5±9.6 |  |  | 61.64 | FTP | 26 | 59.6±5.8 | 79.7 | 92.3 | 66.7 | 77  (64-91) |  |  | QIAamp DNA Mini Kit | Q-MSP |
| Rezvani 2017 [78] | CC | *SPG20* | plasma | 2016 | 37 | 55.97±12.63 |  | 22% distal,  65% proximal | 7.7  (median) (4.15-15.28) | NC | 37 | 55.94±11.84 | 0.59  (median) (0.14-1.12) | 81.1 | 96.9 | 98.4 |  |  | QIAamp DNA Blood Mini Kit | MethyLight |
| Roperch 2013 [79] | P | *NPY* | serum |  | 9 | 67.9±12.9 | I-II 6 (19%),  III-IV 26 (81%) |  |  | NC | 30 | 59.1±16.5 |  | 87 | 80 |  | 47 | 97 | ZR Serum DNA kit | QM-MSP |
|  |  | *PENK* |  |  | 23 |  |  |  |  | NC | 131 |  |  | 78 | 90 |  | 61 | 95 |  |  |
|  |  | *WIF1* |  |  | 32 |  |  |  |  | NC | 161 |  |  | 59 | 95 |  | 70 | 92 |  |  |
| Sabbioni 2003 [80] | P | *TPEF* | leukocyte |  | 29 |  |  |  | 86 | H | 16 |  | 0 | 86\* | 100\* |  |  |  | Phenol/chloroform, Wizard genomic DNA purification kit | MSP |
| Sakamoto 2010 [81] | P | *p16* | serum |  | 51 | 69.6±1.02 | I 39%,  II 29%,  III 12%,  IV 20% | p16 methylated tumors only: 67% distal, 33% proximal | 59 (MSP),  81 (IP-MSP) | H | 10 | 67.8±2.84 | 0 | 59 (MSP)  81 (IP-MSP) | 100 |  |  |  | QIAamp Boold Kit | MSP |
| Salehi 2015 [82] | P | *ALX4* | serum |  | 25 | 67 |  |  | 68 | NC | 25 |  | 12 | 88 | 68 |  |  |  | QIAamp blood mini kit | MSP |
| Salehi 2012 [83] | P | *SFRP1* | stool |  | 25 | 58±12.87 |  | 40% distal  60% proximal | 52 | H | 25 |  | 8 | 52 | 92 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Shirahata 2014 [84] | P | *vimentin* | serum |  | 242 | VIM positive: 67.48;  VIM negative 67.04 | 0 3%,  I 15%,  II 30%,  III 31%,  IV 20%,  UN 1% | 66% distal  34% proximal | 32.6 | H | 25 |  |  | 32.6 |  |  |  |  | Phenol | qMSP |
|  |  | *CEA + CA19-9 + VIM* |  |  |  |  |  |  |  |  |  |  |  | 55.6 |  |  |  |  |  |  |
| Song 2012 [85] | P | *VIM* | urine |  | 20 | 60.45±13.3 | I 20%,  II 35%,  III 20%,  IV 20% |  | 75 (in LMW DNA) | NC | 20 | 73.8 (7.4) | 10 |  |  |  |  |  | Wizard DNA Isolation Kit | MethyLight |
| Song 2018 [86] | P | *SEPT9* | blood |  | 465 |  | I 52 (11.2%),  II 129 (27.7%),  III 165 (35.5%),  IV 25 (5.4%),  UN 94 (20.2%) |  |  | NED | 610 |  |  | I 53.8,  II 80.6,  III 77.4,  IV 84.2 | 97.2 | 81 |  |  | Epi proColon 2.0 assay | Epi proColon  2.0 assay |
| Suehiro 2018 [87] |  | *TWIST1* | serum | 2015-2017 |  | 71  (41–91) | I 14 (77.8%),  II 1 (5.6%),  III 3 (16.7%) | Right 10 (55.6%),  Left 8 (44.4%) |  | NC |  | 55  (33–79) | 25 | 44.4  (21.5-69.3) | 92 | 65.22 |  |  | MagNA Pure Compact Nucleic Acid Isolation Kit I | combined restriction digital PCR (CORD) |
|  |  | *SEPT9* |  |  |  |  |  |  | 18 |  |  |  |  | 44.4 | 92 | 64.67 |  |  |  |  |
| Suehiro 2018 [88] | P | *TWIST1* | stool |  | 83 | 68  (44-92) | I 31.33%,  II 16.87%,  III 40.96%,  IV 7.23% |  |  | NC | 10 | 55  (41-81) | 0 | 33.7  (23.7-45.0) | 100 |  |  |  | QIAamp DNA Stool Mini Kit | Droplet digital PCR |
| Symonds 2016 [89] | P | *BCAT1 & IKZF1 (panel)* | plasma | 2011-2014 | 66 | 67.4  (42.6-85.4) | I 25.78%,  II 37.88%,  III 25.78%,  IV 10.61% | 54% distal  46% proximal | 33.7  (23.7-45.0) | NED | 1315 | 62.6  (41.1-85.4) | 8.2 | 62.1  (49.3-73.8) | 91.8  (90-93) |  |  |  | QIAsymphon y DNA kit | MSP |
| Symonds 2016 [89] |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |  |
| Takane 2014 [90] | P | *EFHD1* | blood |  | 120 | 67.7±11.4 | I 10%,  II 25%,  III 10%,  IV 55% | 66% distal  34%proximal | 62.1  (49.3-73.8) | ABD | 96 | 63±13.6 | 22 | 63 | 78 |  |  |  | QIAamp DNA Mini Kit | MSP |
|  |  | *PPP1R3C* |  |  |  |  |  |  | 62 |  |  |  | 19 | 81 | 81 |  |  |  | QIAamp DNA Mini Kit | MSP |
|  |  | *PPP1R3C, EFHD1* |  |  |  |  |  |  | 81 |  |  |  | 4 | 53 | 96 |  |  |  |  |  |
|  |  | *PPP1R3C or EFHD1* |  |  |  |  |  |  | 53 |  |  |  | 36 | 90 | 64 |  |  |  |  |  |
| Tang 2011 [91] | P | *SFRP2* | stool |  | 169 |  | I-II 82 (58%),  III-IV 60 (42%) | Methylated cases only:  70% distal  30% proximal | 90 | ABD | 63 |  | 46 | 84 | 54 |  |  |  | QIAamp DNA Stool Mini kit | MSP |
|  |  | *SFRP2* | serum |  | 169 |  | I-II 53 (47%),  III-IV 60 (53%) | Methylated cases only:  71% distal  29% proximal | 84 | ABD | 63 |  | 6 | 66.9 | 93.7 |  |  |  | QIAamp blood mini kit |  |
| Tanzer 2010 [92] | P | *ALX4* | plasma |  | 5 | 59  (27-79) | I 80%;  III 20% |  | 66.9 | H | 22 | 42.5  (25-69) | 18 (cohort 2, 2/3 exp positive),  59 (cohort 2, 1/3 exp positive) |  |  |  |  |  | MagNAPure LC Total Nucleic Acids Large Volume Extaction Kit | qRT-PCR |
|  |  | *SEPT9* |  |  | 28 | 67  (63-71) | 0 18%;  I 7.14%;  IV 50%;  UN 25% |  | 40 (cohort 2, 2/3 exp positive),  80 (cohort 2, 1/3 exp positive) | H | 12 | 60.5  (52-72) | 9 (both cohorts combined, 2/3 exp positive);  12 (both cohorts combined, 1/3 positive) |  |  |  |  |  | MagNAPure LC Total Nucleic Acids Large Volume Extaction Kit | heavy methylight |
|  |  | *SEPT9 & ALX4* panel |  |  | 33 | Cohort 1:  67  (63-71);  Cohort 2:  59  (27-79) | Cohort 1  0 5 (18%),  I 2 (7%),  IV 14 (50%),  UN 7 (25%).  Cohort 2  I 4 (80%),  III 1(20%) |  | 73 (both cohort combined, 2/3 exp positive); 82 (both cohorts combined, 1/3 exp positive) | H | 34 | Cohort 1  60.5  (52-72);  Cohort 2  42.5  (25-69) | 18 (cohort 2, 2/3 exp positive),  5 (cohort 2, 3/6 exp positive) |  |  |  |  |  | MagNAPure LC Total Nucleic Acids Large Volume Extaction Kit | qRT-PCR |
| Toth 2012 [93] | P | *SEPT9* | plasma |  | 92 | 67.8±9.8 | I 27%,  II15%,  III39%,  IV 19% | 39% distal  61% proximal, | 95.6 | NED | 92 | 62.6±9.9 | 15.2 | 95.6  (89.2-98.8) | 84.8  (75.8-91.4) |  |  |  | Epi proColon 2.0 plasma quick kit | RT-PCR |
|  |  | *SEPT9* |  |  | 23 |  |  |  | 79.3 |  | 14 |  | 1 | 79.3  (69.6-87.1) | 98.9  (94.1-100) |  |  |  |  |  |
| Toth 2014 [94] | P | *SEPT9* | plasma |  | 34 | 68.3±9.3 | I 18%,  II 32%,  III 32%,  IV15%,  UN 3% |  | 88.2 | NED | 24 | 48 ±14.9 | 8.3 |  |  |  |  |  | Epi proColon 2.0 Plasma Quick Kit | qRT-PCR |
| Wang 2008 [95] | P | *SFRP2* | stool | 2005-2007 | 69 |  | I-II: 43%,  III-IV: 57% | 70% distal  30% proximal | 87 | NC | 30 |  | 6.7 | 87 | 93.3 |  |  |  | QIAamp DNA Stool Mini Kit | MethyLight |
| Wang 2008 [96] | P | *RASSF1A* | serum | 2006-2007 | 45 |  | I 11%,  II 36%,  III 31%,  IV 22% |  | 28.9 | H | 30 |  | 0 |  |  |  |  |  | QIAamp blood mini kit | MSP |
| Warren 2011 [97] | P | *SEPT9* | plasma | 2008-2009 | 50 | 62  (42-85) | I 14%,  II 62%,  III 14%,  IV 10% | 76.6% distal,  23.4% proximal | All stages: 90;  early-stage 87 | NC | 94 | 58  (40-86) | 12 | 90  (77.4-96.3) | 88  (79.6-93.7) |  | 3.61 | 99.94 | nucleic acid extraction kit | RT-PCR |
| Wu 2016 [98] | P | *SEPT9* | plasma |  | 291 |  | 0 1%,  I 13%,  II 23%,  III 28%,  IV 11%,  UN 24% |  | 76.6  (71.3-81.4) | NC | 295 |  | 4.1  (2.1-7) | 76.6  (71.3-81.4) | 95.9 | 88.2 | 83.8 | 91.1 | BioChain plasma processing kit | MSP |
| Wu 2011 [99] | P | *DLC1* | serum | 2008-2011 | 85 |  | I-II: 46%,  III-IV: 54% | 72% distal  28% proximal | 42.4 | ABD | 45 |  | 8.9 |  |  |  |  |  | QIAamp Blood Mini Kit | MSP |
| Wu 2014 [100] | P | *miR-34a* | stool | 2012-2013 | 82 |  | I 13 (16%) |  | 76.8 | H | 40 |  | 5 | 76.8 | 93.6 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
|  |  | *miR-34b/c* |  |  |  |  |  |  | 93.6 |  |  |  | 0 | 95 | 100 |  |  |  |  |  |
| Xiao 2015 [101] | P | *NDRG4* | blood | 2010-2011 | 84 | 56  (38-73) | I-II 57.1%,  III-IV 42.9% |  |  | H | 16 | 55.6  (40-74) |  | 54.8 | 78.1 |  |  |  | TGuide Blood Genomic DNA Extraction kit | nested MSP |
|  |  | *NDRG4* | stool |  |  |  |  |  |  |  |  |  |  | 76.2 | 89.1 |  |  |  | Bioneer Stool DNA Extaction kit | nested MSP |
|  |  | *NDRG4* | urine |  |  |  |  |  |  |  |  |  |  | 72.6 | 85 |  |  |  |  | nested MSP |
|  |  | *NDRG4* | urine |  | 76 | 54  (39-71) |  |  | 72.4 | FOC | 36 |  |  |  |  |  |  |  |  |  |
| Xiao 2014 [102] | P | *SFRP2* | stool | 2011-2013 | 40 | 57.5  (41-84) | A 7,  B 19,  C 5,  D 9 | 15% distal  85%proximal | 87.5 | NC | 57 | 59  (43-75) | 9 | 87.5 | 91 |  |  |  | QIAamp DNA Stool Mini Kit | MS-HRM |
|  |  | *VIM* |  |  |  |  |  |  | 55 |  |  |  | 7 | 55 | 93 |  |  |  |  |  |
| Xiao 2014 [102] |  | *SFRP2 + VIM* |  |  |  |  |  |  | 92.5 |  |  |  | 8.8 | 92.5 | 91 |  |  |  |  |  |
| Xie 2018 [103] | P | *SEPT9* | plasma | 2016-2018 | 123 | 66.07 | I 5 (4.9%),  II 36 (35.0%),  III 58 (56.3%),  IV 4 (3.8%) | Colon 77 (62.5%),  Rectum 46 (37.5%) |  | FOC | 125 | 66.17 |  | 61.8  (53.0–69.9) | 89.6  (83.0–93.8) | 75.7  (70.1–80.7) |  |  | EZ DNA Methylation Direct™ Kit | MSP |
| Zhang 2013 [104] |  | *SPG20* | stool |  | 96 | 62.2±9.5 | I 18%,  II 32%,  III 45%,  IV: 4% | Methylated cases only:  77% distal  23% proximal | 80.2 | NC | 30 | 62.9±8.9 | 0 | 80.2 | 100 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Zhang 2012 [105] | P | *TFPI2* | stool | 2008-2009 | 60 | 63.4±4.5 | I-II 47%,  III-IV 53% | 68% distal  32% proximal | 68.3 | NC | 30 | 59.2±8.4 | 0 | 68.3 | 100 |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Zhang 2017 [106] | P | *CNRIP1* | blood | 2013-2014 | 50 | 69.35  (48-82) | I-II 54%,  III-IV 46% | 56% distal  44%proximal | 85.5 | H | 20 | 49.23  (37-75) | 63.66 |  |  |  |  |  |  | qMSP |
| Zhang 2007 [107] | P | *SFRP1* | stool |  | 19 | 66  (46-84) | I 52%,  II 17%,  III 24%,  IV 7% | 83% distal  17% proximal | 84 | H | 15 | 59  (36-87) | 14 | CRC: 84;  CRC + adenoma  89  (75-100) | 86  (65-99) |  |  |  | QIAamp DNA Stool Mini Kit | MSP |
| Zhang 2015 [108] | P | *GATA5* | plasma | 2012-2013 | 57 | 56.64±8.27 | I-II 58%,  III-IV 42% | Colon 19,  Rectum 38 | 61.4 | NC | 47 | 61.4±12.41 | 21.28 | 61.4  (47.57-74) | 78.72  (64.34-89.3) |  |  |  | QIAamp DNA Blood Mini Kit | MSP |
|  |  | *ITGA4* |  |  |  |  |  |  | 36.84 |  |  |  | 19.15 | 36.84  (24.45-50.66) | 80.85  (66.74-90.85) |  |  |  |  |  |
|  |  | *SFRP2* |  |  |  |  |  |  | 54.39 |  |  |  | 27.66 | 54.39  (40.66-67.64) | 72.34  (57.36-84.38) |  |  |  |  |  |
|  |  | *GATA5, ITGA4* |  |  |  |  |  |  |  |  |  |  |  | 6.52  (1.37-17.9) | 82.46  (70.09-91.25) |  |  |  |  |  |
|  |  | *GATA5, SFRP2* |  |  |  |  |  |  |  |  |  |  |  | 42.86  (29.71-50) | 91.49  (79.62-90) |  |  |  |  |  |
|  |  | *GATA5 or ITGA4* |  |  |  |  |  |  |  |  |  |  |  | 73.68  (60.34-84.46) | 65.96  (50.69-79.14) |  |  |  |  |  |
|  |  | *GATA5 or SFRP2* |  |  |  |  |  |  |  |  |  |  |  | 73.68  (60.34-84.46) | 65.96  (50.69-79.14) |  |  |  |  |  |
|  |  | *GATA5, SFRP2, ITGA4* |  |  |  |  |  |  |  |  |  |  |  | 15.79  (7.48-27.87) | 93.62  (82.46-98.66) |  |  |  |  |  |
|  |  | *GATA5, SFRP2 or ITGA4* |  |  |  |  |  |  |  |  |  |  |  | 80.7  (68.09-89.95) | 55.32  (40.12-69.83) |  |  |  |  |  |
|  |  | *SFRP2, ITGA4* |  |  |  |  |  |  |  |  |  |  |  | 21.05  (11.38-33.89) | 85.11  (71.69-93.80) |  |  |  |  |  |
|  |  | *SFRP2 or ITGA4* |  |  |  |  |  |  |  |  |  |  |  | 70.18  (56.60-81.57) | 61.7  (46.38-75.49) |  |  |  |  |  |
| Zhou 2017 [109] | P | *PCDH18* | plasma |  | 20 |  | I-II 29%,  III-IV 71% |  | 25.17  (0.02-100)^ |  | 20 |  | 1.655  (0-3.712)^ |  |  | 85 |  |  | QIAamp DNA Midi blood kit | Q-MSP |
| Chen 2019 [110] | R | *BMP3* | stool |  | 41 | 55.9  (28-73) |  |  |  |  | 152 | 46.2 (21-74) |  |  |  | 68.2 |  |  | polyvinylpolypyrrolidone / proteinase K (GenMagBio protocol) | Q-MSP |
|  |  | *NDRG4* |  |  |  |  |  |  |  |  |  |  |  |  |  | 80 |  |  |  |  |
|  |  | *SDC2* |  |  |  |  |  |  |  |  |  |  |  |  |  | 80 |  |  |  |  |
|  |  | *SEPT9* |  |  |  |  |  |  |  |  |  |  |  |  |  | 81.5 |  |  |  |  |
|  |  | *SEPT9, NDRG4, SDC2* |  |  |  |  |  |  |  |  |  |  |  | 90 |  | 92.4 |  |  |  |  |
| Chen 2019 [111] | CC | *SDC2* | serum |  | 111 | 61±12  (25-89) | I: 11.7%  II: 44.2%  III: 35.1%  IV: 6.3%  UN: 2.7% | 54.0% distal  42.3% proximal |  | NED | 114 | 33.2±8.3  (19-60) |  | 71.2  (61.8-79.2) | 95.6  (89.6-98.4) | 88.1  (83.5-92.8) |  |  | cfDNA extraction kit (Suzhou VersaBio Technologies Co. Ltd) | Q-MSP |
|  |  | *SEPT9* |  |  |  |  |  |  |  |  |  |  |  | 73  (63.6-80.8) | 95.6  (89.6-98.4) | 85.4  (80-90.7) |  |  |  |  |
|  |  | *SEPT9, SDC2* |  |  |  |  |  |  |  |  |  |  |  | 86.5  (78.4-92) | 92.1  (85.1-96.1) | 92.2  (88.3-96.1) |  |  |  |  |
| Jensen 2019 [112] | R | *C9orf50* | Plasma | 2014 | 113 | 70.8±9.1 | I:14%  II: 60%  III:20%  IV: 6% | 57.5% distal  42.5% proximal | 76.0 | FTP  NC | 87 | 67.2±6.6 |  | 76.0 | 91.0 | 86 |  |  | QIAamp® Circulating Nucleic Acids kit | ddPCR |
|  |  | *KCNQ5* |  |  |  |  |  |  | 83.0 |  |  |  |  | 83.0 | 95.0 | 91 |  |  |  |  |
|  |  | *CLIP4* |  |  |  |  |  |  | 77.0 |  |  |  |  | 77.0 | 99.0 | 88 |  |  |  |  |
|  |  | *C9orf50, KCNQ5, CLIP4* |  |  |  |  |  |  | 85.0 |  |  |  |  | 85.0 | 99.0 |  |  |  |  |  |
| Li 2019 [113] | CC | *SFRP2* | Serum |  | 62 |  | I:21%  II: 45%  III:27%  IV: 5% | 43.0% distal  52.0% proximal  5% UN | 69.4 | NED | 55 |  | 12.7 | 69.4  (56.2-80.1) | 87.3  (74.9-94.3) | 82.1 |  |  | cfDNA extraction kit (VersaBio Technologies Co. Ltd.) | MethylLight |
| Ma 2019 [114] | P | *SEPT9* | Plasma |  | 117 | 67.3±12.8 | I:17%  II: 40%  III:30%  IV: 3%  UN : 9% | 78.6% distal  20.4% proximal  1%synchronous | 73.2  (65.0-81.1) | NC | 70 | 63.1±11.7 | 29.0 | 73.2  (65.0-81.1) | 71.0 |  |  |  | Epi proColon 2.0 Epigenomics AG | Epi proColon 2.0 |
| Pakbaz 2019 [115] | CC | *VIM* | Stool | 2017 | 49 | 61.2 |  |  | 60.0 | NED | 30 | 58.8 | 0 | 60.0 | 100 |  | 100 | 65.2 | QIAamp DNA Stool Mini Kit | MSP |
| Pasha 2019 [116] | CC | *SFRP1* | serum |  | 85 |  | I:11%  II: 46%  III:40%  IV: 3% |  | 77.6 | NED | 40 |  | 0 | 77.7 | 70.0 |  | 84.6 | 59.8 | QIAamp DNA Stool Mini Kit | MSP |
|  |  | *RUNX3* |  |  |  |  |  |  | 60.0 |  |  |  | 0 | 60.0 | 82.5 |  | 87.9 | 49.3 |  |  |
|  |  | *SFRP1 + RUNX3* |  |  |  |  |  |  |  |  |  |  |  | 80.0 | 70.0 |  | 85.0 | 62.2 |  |  |
|  |  | *SFRP1, RUNX3 + CEA* |  |  |  |  |  |  |  |  |  |  |  | 84.7 | 67.5 |  | 84.7 | 67.5 |  |  |
| Picardo 2019 [117] | CC | *B4GALT1* | Plasma | 2008-2016 | 54 | 64  (38-93) |  | 70.4% distal  29.6% proximal | 46.0 |  | 19 |  | 0 | 50.0 | 100 | 75.0  (59.2-90.8) |  |  | phenol chloroform | Q-MSP |
| Salama 2019 [118] | CC | *P14ARF* | Blood | 2016-2018 | 60 | 48±11 | I:18%  II: 72%  III:10% | 41.6% distal  58.3% proximal | 60.0 |  | 30 | 45±9 | 13.3 | 60.0 | 86.7 |  | 90 | 52.0 | QIAamp® Spin Columns (QIAGEN Inc. CA 91355, USA) | MSP |
|  |  | *RASSF1A* |  |  |  |  |  |  | 55.0 |  |  |  | 3.3 | 55.0 | 96.7 |  | 97.1 | 51.8 |  |  |
| Sun 2019 [119] | P | *SEPT9* | Plasma |  | 63 |  |  |  | 73.0 | NED | 494 |  | 5.5 | 73.0  (60.1-83.1) | 94.5  (92.0-96.3) | 83.5  (75.8-91.3) | 63.0  (50.9-73.8) | 96.5  (94.3-97.9) | BioChain Science and Technology, Inc. (Beijing) | Epi proColon 2.0 |
| Sun 2019 [120] | CC | *BMP3* | Stool |  | 105 |  | I:15%  II: 31%  III:33%  IV: 12%  UN:8% | 75.2% distal  14.3% proximal  10.5% UN |  | NC | 102 |  |  | 37.1 | 89.8 | 62.0 |  |  | QIAamp Fast DNA Stool mini kit | MethylLight |
|  |  | *SFRP2* |  |  |  |  |  |  |  |  |  |  |  | 38.6 | 90.7 | 78.8 |  |  |  |  |
|  |  | *NDRG4* |  |  |  |  |  |  |  |  |  |  |  | 46.7 | 90.7 | 68.1 |  |  |  |  |
|  |  | *SDC2* |  |  |  |  |  |  |  |  |  |  |  | 68.6 | 91.7 | 80.0 |  |  |  |  |
| Zhao 2019 [121] | CC | *SDC2* | Plasma |  | 117 | 61.8  (28-89) | I:17%  II: 43%  III:32%  IV: 3%  UN :4% | 45.3% distal  52.1% proximal  2.6% UN | 69.2 | NC | 166 | 36.6  (21-69) | 4.2 | 69.2  (59.9-77.3) | 95.8  (91.2-98.1) | 88.6  (84.3-93.0) |  |  | cfDNA extraction kit (Suzhou VersaBio) | Q-MSP |
|  |  | *SEPT9* |  |  |  |  |  |  | 82.1 |  |  |  | 4.2 | 82.1  (73.6-88.3) | 95.8  (91.2-98.1) | 90.0 |  |  |  |  |
|  |  | *SDC2 + SEPT9* |  |  |  |  |  |  | 88.9 |  |  |  | 7.2 | 88.9  (81.4-93.7) | 92.8  (87.4-96.0) | 94.1  (90.9-97.3) |  |  |  |  |
| Bagheri 2020 [122] | CC | *TFPI2* | Blood |  | 50 | 55.8  (24-83) | I:32%  II: 38%  III:18%  IV: 12% |  | 43.9 | NC | 50 | 54.4  (30-80) | 11.6 | 88.0 | 92.0 | 94.0 |  |  | Genomic DNA Isolation kit (GeNetBio) | MethyQESD |
|  |  | *NDRG4* |  |  |  |  |  |  | 38.8 |  |  |  | 12.2 | 86.0 | 92.0 | 95.0 |  |  |  |  |
|  |  | *TFPI2 + NDRG4* |  |  |  |  |  |  |  |  |  |  |  |  |  | 96.1 |  |  |  |  |
| Bhat 2019 [123] | CC | *PARK2* | Blood |  | 200 |  | I-II: 36%  III-IV: 64% |  | 33.0 | H | 200 |  |  | 33.0 |  |  |  |  |  | MSP |
| Bi 2019 [124] | P | *CHST7* | Blood | 2004-2010 | 478 | 60±11.5 | A: 9%  B: 49%  C: 35%  D: 7% |  |  | FOC | 462 | 58±11 |  |  |  |  |  |  | QIAamp DNA Blood Mini kit | MS-HRM |
| Constancio 2019 [125] | CC | *SEPT9* | Plasma | 2015-2019 | 100 | 66  (27-93) | I-II: 39%  III-IV: 61% | 77.0% distal  23.0% proximal |  | A | 136 | 57  (45-84) |  | 8.0  (4.0-15.0) | 100 | 53.3  (45.8-60.8) |  |  | QIAmp MinElute ccfDNA (Qiagen) | Q-MSP |
|  |  | *SOX17* |  |  |  |  |  |  |  |  |  |  |  | 11.0  (6.0-19.0) | 100 | 55.0  (47.5-62.5) |  |  |  |  |
|  |  | *SEPT9 + SOX17* |  |  |  |  |  |  |  |  |  |  |  | 12.0  (6.0-20.0) | 100 |  |  |  |  |  |
| Kerachian 2020 [126] | CC | *CLDN1, INHBA + SLC30A10* | Plasma |  | 22 | 67  (44-82) |  | 41.0% distal  59.0% proximal | 41.0 |  | 20 | 56  (45-84) | 0 | 41.0 | 100 |  |  |  | QIAamp Circulating Nucleic Acid kit | MethylLight |
| Yong-Suk 2019 [127] | CC | *SFRP2* | Serum | 2008-2010 | 68 |  |  |  | 86.8 | H | 60 |  | 0 | 86.8 | 100 |  |  |  |  | MSP |
|  |  | *SFRP2* | Stool |  |  |  |  |  | 89.7 |  |  |  | 0 | 89.7 | 100 |  |  |  | phenol chloroform isoamyl alcohol |  |
| Liu 2020 [128] | P | *COL4A1* | Stool | 2014-2016 | 80 | 60  (46-78) | I-II: 54%  III-IV: 46% | 79.0% distal  21.0% proximal | 88.8 | H | 83 | 58  (45-77) | 12.0 | 88.8 | 88.0 | 96.5  (94.1-98.9) |  |  |  | Q-MSP |
|  |  | *COL4A2* |  |  |  |  |  |  | 92.5 |  |  |  | 8.4 | 92.5 | 91.6 | 96.6  (94.1-99.1) |  |  |  |  |
|  |  | *ITGA4* |  |  |  |  |  |  | 82.5 |  |  |  | 3.6 | 82.5 | 96.4 | 95.3  (92.0-98.5) |  |  |  |  |
|  |  | *TLX2* |  |  |  |  |  |  | 88.8 |  |  |  | 3.6 | 88.8 | 96.4 | 95.6  (92.3-98.9) |  |  |  |  |
|  |  | *COL4A2 + TLX2* |  |  |  |  |  |  | 91.3 |  |  |  | 2.4 | 91.3 | 97.6 | 98.3  (96.7-99.9) |  |  |  |  |
|  |  | *COL4A1* |  |  | 18 | 62  (47-77) | I-II: 33%  III-IV: 67% | 61.0% distal  39.0% proximal | 83.0 |  | 18 | 59  (48-74) | 6.0 | 83.0 | 94.0 | 95.2  (88.2-100) |  |  |  |  |
|  |  | *COL4A2* |  |  |  |  |  |  | 100.0 |  |  |  | 6.0 | 100 | 94.0 | 99.1  (96.6-100) |  |  |  |  |
|  |  | *ITGA4* |  |  |  |  |  |  | 94.0 |  |  |  | 6.0 | 94.0 | 94.0 | 94.0  (84.8-100) |  |  |  |  |
|  |  | *TLX2* |  |  |  |  |  |  | 89.0 |  |  |  | 6.0 | 89.0 | 94.0 | 94.6  (86.7-100) |  |  |  |  |
| Liu 2020 [129] | CC | *SEPT9* | Stool | 2018-2019 | 72 | 60  (35-86) | I:21%  II: 25%  III:32%  IV: 12%  UN : 10% | 45.8% distal  45.8% proximal  8.4% UN |  | NED | 76 | 45  (16-67) |  | 1/3 replicates 97,2; 2/3 replicates 88,9; 3/3 replicates 86,1; 3/3 replicates plus Ct <40 83,3 | 1/3 replicates 48,7; 2/3 replicates 69,7; 3/3 replicates 86,9; 3/3 replicates plus Ct<40 92,1 | 93.5  (89.5-97.5) |  |  | stool DNA extration kit Suzhou Versabio Tech | Q-MSP |
|  |  | *SEPT9* | Plasma |  | 90 | 61  (28-86) | I:20%  II: 30%  III:29%  IV: 11%  UN : 10% | 43.3% distal  45.6% proximal  11.1% UN |  |  | 81 | 42  (21-76) |  | 1/3 replicates: 85,6; 2/3 replicates 64,4; 3/3 replicates 53,3; 3/3 replicates plusCt<40 46,7 | 1/3 replicates 90,1; 2/3 replicates 93,8; 3/3 replicates 96,3; 3/3 replicates plus Ct<40 98,8 | 88.5  (83.2-93.8) |  |  |  |  |
| Luo 2020 [130] | R | *CG10673833* | Blood | 2015-2017 | 801 | 58  (24-85) | I:5%  II: 17%  III:26%  IV: 51%  UN : 1% |  |  | H | 1021 | 47  (19-90) |  |  |  |  |  |  | Elite health cf DNA extraction kit | ddPCR |
|  |  | *CG10673833* |  |  | 29 | (45-75) |  |  | 89.7 | NC | 1386 | (45-75) | 13.2 | 89.7  (72.7-97.8) | 86.8  (84.9-88.4) | 90.0  (88.5-94.2) | 11.8  (10.1-13.8) | 99.8  (99.3-99.9) |  |  |
| Suehiro 2020 [131] | P | *TWIST1* | Stool | 2007-2019 | 205 | 69  (33-92) | I:34%  II: 25%  III:38%  IV: 3% | 66.3% distal  33.7% proximal | 44.4 | NC | 71 | 51  (33-79) | 8.5 | 44.4  (37.4-51.5) | 91.5  (82.5-96.8) |  |  |  | QIAamp DNA Stool Mini kit (Qiagen) | CORD |
|  |  | *TWIST1 +* FIT |  |  |  | 70  (33-93) |  |  |  |  |  |  |  | 95.6  (91.8-98.0) | 80.3  (69.1-88.8) |  |  |  |  |  |
| Vega-Benedetti 2020 [132] | CC | *GRIA4* |  |  | 10 |  | 0: 10%  I:10%  II: 30%  III:30%  IV: 20% | 20.0% distal  80.0% proximal | 40.0(Q-MSP)  90.0(ddPCR) |  |  |  |  |  |  |  |  |  | QIAamp DNA Stool Mini Kit (Qiagen) | MethylLight |
|  |  | *VIPR2* | Stool |  |  |  |  |  | 70.0(Q-MSP)  90.0(ddPCR) |  |  |  |  |  |  |  |  |  |  |  |
| Yang 2020 [133] | CC | NDRG4 | Stool | 2016-2020 | 50 | 60.2±13.6 | I-III: 74%  IV: 26% | 30.0% distal  70.0% proximal |  | NC | 50 | 64.9±11 |  |  |  | 94.9 |  |  | sequence‑specific DNA captures and magnetic beads‑based oligonucleotides | Q-MSP |
|  |  | *SDC2* |  |  |  |  |  |  |  |  |  |  |  |  |  | 99.2 |  |  |  |  |
|  |  | *TFPI2* |  |  |  |  |  |  |  |  |  |  |  |  |  | 96.9 |  |  |  |  |
|  |  | *NDRG4, SDC2, TFPI2, KRAS +* β-actin |  |  |  |  |  |  |  |  |  |  |  | 90.0 | 94.0 | 94.8 |  |  |  |  |
| Zhao 2020 [134] | CC | *SFRP2* | Plasma |  | 122 | 61.8  (30-88) | I:16%  II: 31%  III:36%  IV: 7%  UN : 11% | 51.6% distal  45.1% proximal  3.3% UN |  | NED  NC | 91 | 39.3  (23-69) |  | 63.1  (53.9-71.5) | 90.1  (81.6-95.1) | 78.7  (72.9-84.6) |  |  | cfDNA extraction kit (Suzhou VersaBio) | Q-MSP |
|  |  | *SDC2* |  |  |  |  |  |  |  |  |  |  |  | 56.6  (47.3-65.4) | 95.6  (88.5-98.6) | 76.5  (70.4-82.6) |  |  |  |  |
|  |  | *SFRP2 + SDC2* |  |  |  |  |  |  |  |  |  |  |  | 76.2  (67.5-83.3) | 87.9  (79.0-93.5) | 85.6  (80.6-90.5) |  |  |  |  |
| Zhao 2020 [135] | CC | *SEPT9 (test)* | Stool | 2018-2019 | 55 | 60  (35-86) | 0: 2%  I:20%  II: 27%  III:33%  IV: 7%  UN : 11% | 44.0% distal  49.0% proximal  7% UN |  | NC | 65 | 45.2  (24-69) | 4.6 | 85.5  (72.8-93.1) | 95.4 | 89.2  (83.1-95.3) |  |  | stool DNA extraction kit (Suzhou VersaBio Technologies Co., Ltd.) | Q-MSP |
|  |  | *SDC2*  *(test)* |  |  |  |  |  |  |  |  |  |  | 6.2 | 83.6  (70.7-91.8) | 93.8 | 93.0  (87.7-98.3) |  |  |  |  |
|  |  | *SEPT9 + SDC2*  *(test)* |  |  |  |  |  |  |  |  |  |  | 9.2 | 89.1  (77.1-95.5) | 90.8  (80.3-96.2) | 95.6  (92.4-98.8) |  |  |  |  |
|  |  | *SEPT9*  *(validation)* |  |  | 39 | 59  (27-83) | I:23%  II: 20%  III:41%  IV: 8%  UN: 8% | 44.0% distal  49.0% proximal  7% UN |  |  | 59 | 47.9  (24-83) |  | 82.1  (65.9-91.9) | 96.6  (87.3-99.4) | 94.8  (90.1-99.5) |  |  |  |  |
|  |  | *SDC2*  *(validation)* |  |  |  |  |  |  |  |  |  |  |  | 87.2  (71.8-95.2) | 96.6  (87.3-99.4) | 93.7  (87.5-99.9) |  |  |  |  |
|  |  | *SEPT9 + SDC2*  *(validation)* |  |  |  |  |  |  |  |  |  |  |  | 92.3  (78.0-98.0) | 93.2  (82.7-97.8) | 97.7  (95.2-100) |  |  |  |  |
| Han 2019 [136] | CC | *SDC2* | Stool | 2017-2018 | 245 |  | 0: 1%  I:22%  II: 29%  III:39%  IV: 9% | 76.5% distal  18.0% proximal  5.5% other | 90.0 | NED  NC | 245 |  | 9.8 | 90.2  (85.8-93.6) | 90.2  (85.8-93.6) | 90.2  (87.6-92.8) |  |  | MaXtract High Density tube (Qiagen) and phenol-chloroform-isoamylalcohol | LTE-Q-MSP |

N=number of samples, Se=sensitivity, Sp=specificity, AUC=area under the curve, ROC=receiver operating characteristic curve, PPV=positive predictive value, NPV=negative predictive value, CI=confidence interval, F=forward primer, R=reverse primer, MF=methylated forward primer, MR=methylated reverse primer, UF=unmethylated forward primer, UR=unmethylated reverse primer, M=methylated probe sequence, U=unmethylated probe sequence, IM=internal primer specific for methylated alleles; IU=internal primer specific for unmethylated alleles, PCR=polymerase chain reaction, MSP=methylation specific PCR, qMSP=quantitative MSP, AQAMA=Modified absolute quantitative analysis of methylated alleles assay, qRT-PCR=quantitative real-time PCR, Hi-SA=High-sensitivity assay for bisulfite DNA, MS-APPCR=methylation-specific arbitrarily primed polymerase chain reaction, QuARTS assays=Quantitative Allele-Specific Real-Time Target and Signal Amplification Assays, P=prospective, R=retrospective, CC=case-control, NC=normal colonoscopy, NED=no evidence of disease, IBD=Inflammatory bowel disease without neoplasia; ABD=allowing benign disease; FOC=free of cancer; PE=Polyps excluded; AP=Adenomatous polyp with low-grade dysplasia; RA=Resectable adenomas included; FTP=FOBT test positive; H=healthy; (F)A=(Female) asymptomatic; Se=sensitivity, Sp=specificity

\* Sensitivity of detecting cancer and precancerous lesions (including 10 advanced adenomas and 1 unclassfied with dysplasia),

# numbers between brackets in the column indicate SD or range,

$ study provides AUC with SD,

^ study provides the methylation percentage of the corresponding gene in tumor or control samples within a range.