

| First author (year)       | Title   |
|---------------------------|---|
| Karl (2008)               | Improved Diagnosis of Colorectal Cancer Using a Combination of Fecal Occult       |
| Omata (2011)              | Diagnostic performance of quantitative fecal immunochemical test and multivar     |
| Bosch (2012)              | DNA Methylation of Phosphatase and Actin Regulator 3 Detects Colorectal Car       |
| Ahlquist (2012)           | Next-Generation Stool DNA Test Accurately Detects Colorectal Cancer and Lai       |
| Ahlquist (2012)           | The Stool DNA Test Is More Accurate Than the Plasma Septin 9 Test in Detect       |
| Lidgard (2013)            | Clinical Performance of an Automated Stool DNA Assay for Detection of Colore      |
| Stegeman (2014)           | Combining risk factors with faecal immunochemical test outcome for selecting      |
| Imperiale (2014)          | Multitarget Stool DNA Testing for Colorectal-Cancer Screening                     |
| Auge (2014)               | Risk stratification for advanced colorectal neoplasia according to fecal hemogl   |
| Kim (2014) (development)  | Predictive Model Combining Fecal Calgranulin B and Fecal Occult Blood Tests       |
| Kim (2014) (validation)   | Predictive Model Combining Fecal Calgranulin B and Fecal Occult Blood Tests       |
| Redwood (2016)            | Stool DNA Testing for Screening Detection of Colorectal Neoplasia in Alaska N     |
| Baxter (2016)             | Microbiota-based model improves the sensitivity of fecal immunochemical test      |
| Wong (2017) (development) | Quantitation of faecal Fusobacterium improves faecal immunochemical test in       |
| Wong (2017) (validation)  | Quantitation of faecal Fusobacterium improves faecal immunochemical test in       |
| Xie (2017) (development)  | Fecal Clostridium symbiosum for noninvasive detection of early and advanced       |
| Xie (2017) (validation)   | Fecal Clostridium symbiosum for noninvasive detection of early and advanced       |
| Cooper (2018)             | Risk-adjusted colorectal cancer screening using the FIT and routine screening     |
| Van de Veerdonk (2018)    | Risk stratification for colorectal neoplasia                                      |
| Bosch (2019)              | Multitarget Stool DNA Test Performance in an Average-Risk Colorectal Cancer       |
| Liang (2019)              | A novel faecal Lachnoclostridium marker for the non-invasive diagnosis of colo    |
| Park (2019)               | Usefulness of risk stratification models for colorectal cancer based on fecal her |
| Duran-Sanchon (2020)      | Identification and Validation of MicroRNA Profiles in Fecal Samples for Detectio  |
| Duran-Sanchon (2021)      | Fecal MicroRNA-Based Algorithm Increases Effectiveness                            |
| De Klaver (2021)          | Clinical Validation of a Multitarget Fecal Immunochemical Test forColorectal Ca   |
| Kortlever (2021)          | Individualized faecal immunochemical test cut-off                                 |
| Mo (2021)                 | Fecal Multidimensional Assay  |
| Soonklang (2021)          | Comparison of multiple statistical models for the development of clinical predict |
| Zhang (2021)              | Leveraging Fecal Microbial Markers to Improve the Diagnostic Accuracy of the      |

| First author (year)       | DOMAIN 1 |     |         |         |
|---------------------------|----------|-----|---------|---------|
|                           | 1.1      | 1.2 | A       | B       |
| Karl (2008)               | N        | N   | High    | High    |
| Omata (2011)              | Y        | N   | High    | High    |
| Bosch (2012)              | PN       | N   | High    | High    |
| Ahlquist (2012)           | N        | N   | High    | High    |
| Ahlquist (2012)           | N        | N   | High    | High    |
| Lidgard (2013)            | N        | N   | High    | High    |
| Stegeman (2014)           | Y        | Y   | Low     | Low     |
| Imperiale (2014)          | Y        | Y   | Low     | Low     |
| Auge (2014)               | Y        | N   | High    | High    |
| Kim (2014) (development)  | N        | NI  | High    | High    |
| Kim (2014) (validation)   | N        | NI  | High    | High    |
| Redwood (2016)            | Y        | N   | High    | High    |
| Baxter (2016)             | NI       | N   | High    | High    |
| Wong (2017) (development) | NI       | N   | High    | High    |
| Wong (2017) (validation)  | NI       | N   | High    | High    |
| Xie (2017) (development)  | NI       | NI  | Unclear | Unclear |
| Xie (2017) (validation)   | NI       | NI  | Unclear | Unclear |
| Cooper (2018)             | Y        | N   | High    | High    |
| Van de Veerdonk (2018)    | Y        | N   | High    | High    |
| Bosch (2019)              | Y        | Y   | Low     | Low     |
| Liang (2019)              | N        | N   | High    | High    |
| Park (2019)               | Y        | N   | High    | High    |
| Duran-Sanchon (2020)      | Y        | N   | High    | High    |
| Duran-Sanchon (2021)      | Y        | N   | High    | High    |
| De Klaver (2021)          | Y        | N   | High    | High    |
| Kortlever (2021)          | Y        | Y   | Low     | Low     |
| Mo (2021)                 | N        | N   | High    | High    |
| Soonklang (2021)          | Y        | Y   | Low     | Low     |
| Zhang (2021)              | Y        | N   | High    | High    |

| First author (year)       | DOMAIN 2 |     |     |      |     |
|---------------------------|----------|-----|-----|------|-----|
|                           | 2.1      | 2.2 | 2.3 | A    | B   |
| Karl (2008)               | Y        | PY  | Y   | Low  | Low |
| Omata (2011)              | Y        | Y   | Y   | Low  | Low |
| Bosch (2012)              | Y        | PY  | Y   | Low  | Low |
| Ahlquist (2012)           | PY       | Y   | Y   | Low  | Low |
| Ahlquist (2012)           | PY       | Y   | Y   | Low  | Low |
| Lidgard (2013)            | Y        | Y   | Y   | Low  | Low |
| Stegeman (2014)           | Y        | PY  | Y   | Low  | Low |
| Imperiale (2014)          | Y        | Y   | Y   | Low  | Low |
| Auge (2014)               | Y        | Y   | Y   | Low  | Low |
| Kim (2014) (development)  | Y        | PY  | Y   | Low  | Low |
| Kim (2014) (validation)   | Y        | PY  | Y   | Low  | Low |
| Redwood (2016)            | Y        | PY  | Y   | Low  | Low |
| Baxter (2016)             | Y        | PY  | Y   | Low  | Low |
| Wong (2017) (development) | Y        | Y   | Y   | Low  | Low |
| Wong (2017) (validation)  | Y        | Y   | Y   | Low  | Low |
| Xie (2017) (development)  | Y        | PY  | Y   | Low  | Low |
| Xie (2017) (validation)   | Y        | PY  | Y   | Low  | Low |
| Cooper (2018)             | Y        | Y   | Y   | Low  | Low |
| Van de Veerdonk (2018)    | Y        | NI  | Y   | Low  | Low |
| Bosch (2019)              | Y        | Y   | Y   | Low  | Low |
| Liang (2019)              | Y        | Y   | Y   | Low  | Low |
| Park (2019)               | Y        | Y   | Y   | Low  | Low |
| Duran-Sanchon (2020)      | Y        | PY  | Y   | Low  | Low |
| Duran-Sanchon (2021)      | Y        | PY  | Y   | Low  | Low |
| De Klaver (2021)          | Y        | PY  | Y   | Low  | Low |
| Kortlever (2021)          | Y        | PY  | Y   | Low  | Low |
| Mo (2021)                 | N        | PY  | Y   | High | Low |
| Soonklang (2021)          | Y        | PY  | Y   | Low  | Low |
| Zhang (2021)              | Y        | Y   | Y   | Low  | Low |

| First author (year)       | DOMAIN 3 |     |     |     |     |     |
|---------------------------|----------|-----|-----|-----|-----|-----|
|                           | 3.1      | 3.2 | 3.3 | 3.4 | 3.5 | 3.6 |
| Karl (2008)               | Y        | Y   | Y   | Y   | NI  | N   |
| Omata (2011)              | Y        | Y   | Y   | Y   | NI  | Y   |
| Bosch (2012)              | Y        | Y   | Y   | Y   | Y   | Y   |
| Ahlquist (2012)           | Y        | Y   | Y   | Y   | NI  | N   |
| Ahlquist (2012)           | Y        | Y   | Y   | Y   | NI  | N   |
| Lidgard (2013)            | Y        | Y   | Y   | Y   | Y   | N   |
| Stegeman (2014)           | Y        | Y   | Y   | Y   | NI  | Y   |
| Imperiale (2014)          | Y        | Y   | Y   | Y   | NI  | Y   |
| Auge (2014)               | Y        | Y   | Y   | Y   | NI  | Y   |
| Kim (2014) (development)  | Y        | Y   | Y   | Y   | NI  | Y   |
| Kim (2014) (validation)   | Y        | Y   | Y   | Y   | NI  | Y   |
| Redwood (2016)            | Y        | Y   | Y   | Y   | Y   | Y   |
| Baxter (2016)             | Y        | Y   | Y   | Y   | NI  | N   |
| Wong (2017) (development) | Y        | Y   | Y   | Y   | Y   | Y   |
| Wong (2017) (validation)  | Y        | Y   | Y   | Y   | Y   | Y   |
| Xie (2017) (development)  | Y        | Y   | Y   | Y   | Y   | Y   |
| Xie (2017) (validation)   | Y        | Y   | Y   | Y   | Y   | Y   |
| Cooper (2018)             | Y        | Y   | Y   | Y   | Y   | Y   |
| Van de Veerdonk (2018)    | Y        | Y   | Y   | Y   | Y   | Y   |
| Bosch (2019)              | Y        | Y   | Y   | Y   | Y   | Y   |
| Liang (2019)              | Y        | N   | Y   | Y   | NI  | Y   |
| Park (2019)               | Y        | Y   | Y   | Y   | NI  | Y   |
| Duran-Sanchon (2020)      | Y        | Y   | Y   | Y   | NI  | NI  |
| Duran-Sanchon (2021)      | Y        | Y   | Y   | Y   | NI  | NI  |
| De Klaver (2021)          | Y        | Y   | Y   | Y   | Y   | PY  |
| Kortlever (2021)          | Y        | Y   | Y   | Y   | NI  | Y   |
| Mo (2021)                 | Y        | Y   | Y   | Y   | Y   | NI  |
| Soonklang (2021)          | Y        | Y   | Y   | Y   | NI  | NI  |
| Zhang (2021)              | Y        | Y   | Y   | Y   | NI  | Y   |

| First author (year)       | DOMAIN 3 |     |
|---------------------------|----------|-----|
|                           | A        | B   |
| Karl (2008)               | High     | Low |
| Omata (2011)              | Low      | Low |
| Bosch (2012)              | Low      | Low |
| Ahlquist (2012)           | High     | Low |
| Ahlquist (2012)           | High     | Low |
| Lidgard (2013)            | High     | Low |
| Stegeman (2014)           | Low      | Low |
| Imperiale (2014)          | Low      | Low |
| Auge (2014)               | Low      | Low |
| Kim (2014) (development)  | Low      | Low |
| Kim (2014) (validation)   | Low      | Low |
| Redwood (2016)            | Low      | Low |
| Baxter (2016)             | High     | Low |
| Wong (2017) (development) | Low      | Low |
| Wong (2017) (validation)  | Low      | Low |
| Xie (2017) (development)  | Low      | Low |
| Xie (2017) (validation)   | Low      | Low |
| Cooper (2018)             | Low      | Low |
| Van de Veerdonk (2018)    | Low      | Low |
| Bosch (2019)              | Low      | Low |
| Liang (2019)              | High     | Low |
| Park (2019)               | Low      | Low |
| Duran-Sanchon (2020)      | Unclear  | Low |
| Duran-Sanchon (2021)      | Unclear  | Low |
| De Klaver (2021)          | Low      | Low |
| Kortlever (2021)          | Low      | Low |
| Mo (2021)                 | Unclear  | Low |
| Soonklang (2021)          | Unclear  | Low |
| Zhang (2021)              | Low      | Low |

| First author (year)       | DOMAIN 4 |     |     |     |     |     |
|---------------------------|----------|-----|-----|-----|-----|-----|
|                           | 4.1      | 4.2 | 4.3 | 4.4 | 4.5 | 4.6 |
| Karl (2008)               | Y        | Y   | Y   | NI  | Y   | N   |
| Omata (2011)              | Y        | Y   | PY  | N   | Y   | Y   |
| Bosch (2012)              | Y        | NI  | Y   | Y   | NI  | N   |
| Ahlquist (2012)           | PY       | Y   | PY  | N   | Y   | N   |
| Ahlquist (2012)           | N        | Y   | PY  | NI  | Y   | N   |
| Lidgard (2013)            | Y        | Y   | Y   | NI  | Y   | N   |
| Stegeman (2014)           | PY       | Y   | N   | Y   | Y   | Y   |
| Imperiale (2014)          | Y        | Y   | PY  | N   | NA  | Y   |
| Auge (2014)               | Y        | PY  | Y   | NI  | Y   | Y   |
| Kim (2014) (development)  | Y        | N   | Y   | NI  | Y   | N   |
| Kim (2014) (validation)   | N        | N   | Y   | NI  | NA  | N   |
| Redwood (2016)            | N        | Y   | N   | N   | NA  | Y   |
| Baxter (2016)             | PY       | Y   | NI  | NI  | Y   | NI  |
| Wong (2017) (development) | Y        | N   | Y   | NI  | Y   | N   |
| Wong (2017) (validation)  | N        | N   | Y   | NI  | NA  | N   |
| Xie (2017) (development)  | Y        | N   | PY  | N   | N   | NI  |
| Xie (2017) (validation)   | Y        | N   | PY  | N   | NA  | NI  |
| Cooper (2018)             | Y        | Y   | N   | N   | Y   | Y   |
| Van de Veerdonk (2018)    | Y        | Y   | N   | N   | Y   | Y   |
| Bosch (2019)              | N        | Y   | N   | N   | NA  | Y   |
| Liang (2019)              | Y        | Y   | N   | N   | Y   | N   |
| Park (2019)               | Y        | Y   | N   | N   | N   | Y   |
| Duran-Sanchon (2020)      | Y        | Y   | NI  | NI  | Y   | Y   |
| Duran-Sanchon (2021)      | Y        | Y   | NI  | NI  | NA  | Y   |
| De Klaver (2021)          | Y        | Y   | N   | N   | Y   | Y   |
| Kortlever (2021)          | Y        | Y   | N   | N   | Y   | Y   |
| Mo (2021)                 | PY       | Y   | Y   | NI  | Y   | N   |
| Soonklang (2021)          | N        | N   | PY  | N   | N   | Y   |
| Zhang (2021)              | PY       | N   | N   | N   | Y   | N   |

| First author (year)       | DOMAIN 4 |     |     |         |
|---------------------------|----------|-----|-----|---------|
|                           | 4.7      | 4.8 | 4.9 | A       |
| Karl (2008)               | N        | Y   | NI  | High    |
| Omata (2011)              | N        | Y   | Y   | High    |
| Bosch (2012)              | N        | N   | NI  | High    |
| Ahlquist (2012)           | N        | N   | NI  | High    |
| Ahlquist (2012)           | N        | N   | NI  | High    |
| Lidgard (2013)            | N        | Y   | NI  | High    |
| Stegeman (2014)           | Y        | Y   | Y   | High    |
| Imperiale (2014)          | N        | NA  | NA  | High    |
| Auge (2014)               | N        | N   | Y   | High    |
| Kim (2014) (development)  | N        | Y   | Y   | High    |
| Kim (2014) (validation)   | N        | NA  | NA  | High    |
| Redwood (2016)            | N        | NA  | NA  | High    |
| Baxter (2016)             | N        | Y   | NI  | High    |
| Wong (2017) (development) | N        | Y   | NI  | High    |
| Wong (2017) (validation)  | N        | NA  | NA  | High    |
| Xie (2017) (development)  | N        | N   | Y   | High    |
| Xie (2017) (validation)   | N        | NA  | NA  | High    |
| Cooper (2018)             | Y        | Y   | Y   | High    |
| Van de Veerdonk (2018)    | N        | N   | Y   | High    |
| Bosch (2019)              | N        | NA  | NA  | High    |
| Liang (2019)              | N        | N   | NI  | High    |
| Park (2019)               | N        | N   | PY  | High    |
| Duran-Sanchon (2020)      | Y        | Y   | NI  | Unclear |
| Duran-Sanchon (2021)      | N        | NA  | NA  | High    |
| De Klaver (2021)          | N        | Y   | Y   | High    |
| Kortlever (2021)          | N        | Y   | Y   | High    |
| Mo (2021)                 | N        | N   | NI  | High    |
| Soonklang (2021)          | Y        | Y   | Y   | High    |
| Zhang (2021)              | N        | Y   | NI  | High    |

| Legend   |  |
|----------|--|
| Domain 1 | Participants   |
| Domain 2 | Predictors   |
| Domain 3 | Outcome  |
| Domain 4 | Analysis   |
| A        | Risk of bias assessment                                  |
| B        | Concerns regarding applicability                         |
| Y        | Yes (item present, low risk of bias)                     |
| PY       | Probably yes (item likely present, low risk of bias)     |
| N        | No (item not present, high risk of bias)                 |
| PY       | Probably no (item likely not present, high risk of bias) |
| NI       | No information   |
| NA       | Not applicable (in case of validation studies)           |