



Dynamic Digestive Health Surveillance System (DDHSS): A Conceptual Framework for Longitudinal Colorectal Cancer Surveillance

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ABSTRACT

Background: Colorectal cancer (CRC) remains a leading cause of cancer-related morbidity and mortality worldwide. Although fecal immunochemical tests (FIT) and colonoscopy detect precancerous lesions and early-stage CRC, current screening strategies remain largely age-based and episodic, limiting their ability to capture longitudinal changes in individual risk. Advances in electronic health records (EHRs), longitudinal healthcare databases, and artificial intelligence (AI) provide opportunities for more adaptive CRC risk monitoring. **Objectives:** This review evaluates limitations of conventional CRC screening and the potential role of longitudinal healthcare data integration and AI-assisted risk stratification in adaptive CRC surveillance. **Methods:** A structured narrative review was conducted using PubMed, Scopus, and ScienceDirect for publications from 2016 to 2026 related to CRC screening, longitudinal surveillance, healthcare informatics, and AI. Thirty-eight eligible publications were retained for narrative synthesis. Evidence on CRC screening performance, predictive modeling, and AI-assisted surveillance was synthesized to develop a conceptual framework. **Discussion:** CRC susceptibility evolves under biological, metabolic, genetic, environmental, and screening-related influences. The reviewed evidence showed persistent residual risk after negative screening, heterogeneity in post-screening risk trajectories, and the potential value of integrating FIT results, previous endoscopic findings, clinical variables, and routinely collected healthcare data for adaptive risk monitoring. However, predictive models remain limited by incomplete prospective validation, calibration uncertainty, algorithmic bias, data interoperability constraints, and insufficient evidence of real-world clinical utility. Based on the synthesized evidence, DDHSS is proposed as a conceptual framework for longitudinal CRC risk monitoring and referral support. **Conclusion:** DDHSS provides a hypothesis-generating integrative framework that connects longitudinal healthcare data, predictive analytics, risk stratification, and surveillance feedback. It should be interpreted as a proposed surveillance architecture rather than a validated clinical system, and its incremental value over established screening, diagnostic, and surveillance pathways requires prospective evaluation.

Keywords: artificial intelligence, colorectal cancer, population surveillance, risk stratification, screening

ABSTRAK

Latar Belakang: Kanker kolorektal (CRC) tetap menjadi salah satu penyebab utama morbiditas dan mortalitas akibat kanker di seluruh dunia. Meskipun tes imunokimia feses (FIT) dan kolonoskopi efektif dalam mendeteksi lesi prakanker serta CRC stadium awal, strategi skrining saat ini masih didominasi pendekatan berbasis usia dan dilakukan secara episodik. Pendekatan tersebut belum



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sepenuhnya menangkap perubahan risiko individu dari waktu ke waktu. Kemajuan rekam medis elektronik (EHR), data kesehatan longitudinal, dan kecerdasan buatan (AI) membuka peluang pengembangan pemantauan risiko CRC yang lebih adaptif. **Tujuan:** Tinjauan ini mengevaluasi keterbatasan skrining CRC konvensional serta potensi integrasi data longitudinal dan stratifikasi risiko berbantuan AI dalam surveilans CRC adaptif. Metode: Kajian naratif terstruktur dilakukan melalui penelusuran PubMed, Scopus, dan ScienceDirect untuk publikasi tahun 2016–2026. Sebanyak 38 publikasi memenuhi kriteria dan disintesis secara naratif. **Pembahasan:** Risiko CRC bersifat dinamis dan dipengaruhi faktor biologis, metabolik, genetik, lingkungan, serta riwayat skrining. Bukti yang ditinjau menunjukkan masih adanya risiko residual setelah hasil skrining negatif, heterogenitas lintasan risiko pascaskrining, serta potensi integrasi hasil FIT, temuan endoskopi sebelumnya, variabel klinis, dan data kesehatan rutin untuk mendukung pemantauan risiko yang lebih adaptif. Namun, model prediktif yang ada masih dibatasi oleh kurangnya validasi prospektif, ketidakpastian kalibrasi, bias algoritma, keterbatasan interoperabilitas data, dan belum cukupnya bukti utilitas klinis di dunia nyata. Berdasarkan bukti yang disintesis, DDHSS diusulkan sebagai kerangka konseptual untuk pemantauan risiko CRC longitudinal dan dukungan rujukan. **Kesimpulan:** DDHSS merupakan kerangka integratif yang bersifat hipotesis-generatif dengan menghubungkan data kesehatan longitudinal, analitik prediktif, stratifikasi risiko, dan umpan balik surveilans. DDHSS perlu dipahami sebagai arsitektur surveilans konseptual, bukan sistem klinis tervalidasi, sehingga nilai tambahnya dibandingkan jalur skrining, diagnostik, dan surveilans yang telah ada masih memerlukan evaluasi prospektif.

Kata kunci: kanker kolorektal, kecerdasan buatan, surveilans populasi, skrining, stratifikasi risiko

1. Introduction

Colorectal cancer (CRC) remains a major global public health challenge and continues to contribute substantially to cancer-related morbidity and mortality worldwide. Current evidence indicates that the burden of CRC is influenced by demographic transition, lifestyle changes, obesity, metabolic disturbances, dietary patterns, smoking exposure, and other population-level risk factors. These determinants are also increasingly relevant in the context of early-onset CRC and changing CRC risk profiles across diverse populations.^[1,2]

Colorectal carcinogenesis is generally characterized by gradual progression from precursor lesions toward invasive malignancy, providing an important biological rationale for screening, surveillance, and early lesion detection.^[1] In addition to conventional adenomatous precursor lesions, serrated neoplasia represents an important alternative route of colorectal carcinogenesis. Serrated lesions have distinct histological and molecular characteristics and may present additional detection challenges because of their subtle morphology and frequent proximal location.^[3] Consequently, CRC is considered one of the most preventable malignancies when appropriate screening and follow-up strategies are effectively implemented.^[1]

Current CRC screening programs predominantly rely on fecal immunochemical tests (FIT) and colonoscopy.^[1] Although FIT provides a non-invasive and accessible screening modality, its sensitivity for advanced adenomas and some early precancerous lesions remains limited.^[4,5] Colonoscopy remains central to CRC prevention because it enables direct visualization and removal of precursor lesions; however, detection limitations may still occur, particularly for subtle, flat, proximally located, or serrated lesions.^[3,6,7] These limitations suggest that conventional screening approaches may incompletely capture the biological complexity and temporal evolution of colorectal neoplasia.

Interval cancers continue to be reported despite previous negative screening examinations, highlighting persistent limitations in conventional surveillance strategies.^[8] Longitudinal observational evidence further suggests that advanced colorectal neoplasia may develop more than ten years after an initially negative colonoscopy. Such findings suggest that CRC susceptibility may progressively evolve over time and may not be adequately reflected through single-timepoint risk assessment alone.^[8]

These observations provide the rationale for moving from a purely episodic screening perspective toward longitudinal risk monitoring. In this review, dynamic CRC risk is therefore treated as part of the background

rationale, while the subsequent results and discussion synthesize how existing screening, surveillance, prediction, and data-infrastructure evidence informed the proposed DDHSS framework.

CRC susceptibility varies substantially across individuals due to interactions among biological, metabolic, genetic, environmental, and behavioral determinants. Metabolic abnormalities, including insulin resistance and elevated triglyceride-glucose index, have been associated with increased colorectal carcinogenesis risk.^[9] Genetic susceptibility may also contribute to interindividual variation in CRC predisposition.^[10] Family history, obesity, smoking exposure, dietary patterns, and other clinical or behavioral factors may additionally contribute to variation in CRC risk profiles.^[2] Taken together, these factors indicate that CRC risk is not fixed after a single negative screening encounter, but may change over time as biological and clinical determinants accumulate.

The expanding availability of electronic health records (EHRs), longitudinal healthcare databases, and artificial intelligence (AI) technologies has created new opportunities for more responsive CRC surveillance approaches. Predictive models incorporating clinical variables, laboratory findings, and previous screening history have shown encouraging performance in identifying populations with elevated CRC risk who may benefit from intensified monitoring or earlier diagnostic evaluation.^[11,12]

The expanding availability of electronic health records (EHRs), longitudinal healthcare databases, and artificial intelligence (AI) technologies has created new opportunities for more responsive CRC surveillance approaches. Predictive models incorporating clinical variables, laboratory findings, and previous screening history have shown encouraging performance in identifying populations with elevated CRC risk who may benefit from intensified monitoring or earlier diagnostic evaluation. However, the extent to which these data sources and analytical approaches can be integrated into a clinically coherent longitudinal surveillance framework remains insufficiently clarified. Therefore, this review aimed to evaluate limitations associated with conventional CRC screening strategies and to synthesize evidence on longitudinal healthcare data integration, AI-assisted risk stratification, and adaptive CRC surveillance.

2. Method

This study was conducted as a structured narrative review rather than a systematic review. Therefore, a formal systematic review protocol was not adopted. To enhance methodological transparency, the review process incorporated a structured literature search, predefined eligibility criteria, sequential screening of retrieved publications, standardized data extraction domains, and comparative narrative synthesis. The methodological reporting of the review was informed by the principles of the Scale for the Assessment of Narrative Review Articles (SANRA).^[13]

A structured literature search was conducted in PubMed, Scopus, and ScienceDirect to identify relevant studies published between 2016 and 2026. The 10-year search period was selected to capture contemporary evidence on colorectal cancer screening and surveillance while encompassing recent developments in longitudinal healthcare data, predictive analytics, machine learning, and artificial intelligence relevant to colorectal cancer risk assessment. The three literature sources were selected to provide complementary coverage of biomedical, clinical, epidemiological, and multidisciplinary research relevant to the scope of this review. The search strategy combined controlled vocabulary, where applicable, and free-text terms using Boolean operators. Search terms included combinations of “colorectal cancer,” “colorectal neoplasia,” “colorectal cancer screening,” “fecal immunochemical test,” “colonoscopy,” “risk stratification,” “electronic health records,” “longitudinal healthcare data,” “artificial intelligence,” “machine learning,” “predictive modeling,” “early detection,” and “population surveillance.”

Search domain	Conceptual scope	Principal search terms
Colorectal neoplasia	Disease entity and neoplastic spectrum	“colorectal cancer” OR “colorectal neoplasia”
Screening and early detection	Conventional CRC screening and lesion detection approaches	“colorectal cancer screening” OR “fecal immunochemical test” OR “colonoscopy” OR “early detection”
Risk stratification	Individualized risk classification and surveillance allocation	“risk stratification”
Healthcare data infrastructure	Longitudinal clinical information and routinely collected health data	“electronic health records”
Artificial intelligence and predictive analytics	Computational approaches for risk estimation and surveillance support	“artificial intelligence” OR “machine learning”
Population surveillance	Population-level monitoring and surveillance frameworks	“population surveillance”

Table 1. Principal search domains and search terms used for literature identification.

The searches were last updated on 11 July 2026. Database-specific search syntax was adapted to each search interface. In PubMed, the search used combinations of Title/Abstract terms: (“colorectal cancer” OR “colorectal neoplasia” OR “colorectal adenoma”) AND (“colorectal cancer screening” OR “fecal immunochemical test” OR FIT OR colonoscopy OR “early detection” OR surveillance) AND (“risk stratification” OR “risk prediction” OR “predictive model” OR “electronic health records” OR “longitudinal healthcare data” OR “artificial intelligence” OR “machine learning” OR “population surveillance”). In Scopus, equivalent terms were searched using TITLE-ABS-KEY fields. In ScienceDirect, equivalent keyword combinations were searched using the platform search interface. The search was limited to publications from 2016 to 2026. Retrieved records were exported to Rayyan for screening and reference management. Duplicate records were removed using Rayyan-assisted duplicate detection followed by manual verification based on title, authorship, DOI, and overlapping database records.

Eligible literature included original research articles, systematic reviews, meta-analyses, and clinical studies discussing colorectal cancer screening performance, longitudinal surveillance, predictive modeling, healthcare data integration, or AI-assisted detection approaches in adult populations. Editorials, opinion papers, case reports, conference abstracts without sufficient methodological information, and studies focused primarily on therapeutic interventions without relevance to colorectal cancer surveillance or early detection were excluded.

Titles and abstracts were screened according to the predefined eligibility criteria, followed by full-text assessment of potentially eligible publications. Full-text exclusion was determined according to relevance to CRC screening, surveillance, risk prediction, longitudinal healthcare data, or AI-assisted risk stratification. Publications were excluded at full-text assessment when they focused primarily on therapeutic interventions without relevance to screening or surveillance, involved populations or outcomes outside the scope of this review, did not address risk prediction or longitudinal surveillance, or were publication types without sufficient methodological detail. Selection was not based on whether study findings supported the proposed DDHSS framework.

Screening and data extraction were conducted by one reviewer and subsequently checked by a second author for eligibility and extraction accuracy. Discrepancies were resolved through discussion until consensus was reached. Because initial screening was not performed independently in duplicate, residual selection error remains possible and was acknowledged as a methodological limitation of the review.

Data were extracted using a prespecified evidence-mapping form covering author and publication year, country or study setting, study design, population characteristics, sample size, data source, candidate predictors or data inputs, outcome definition, analytical approach or model type, model performance or principal quantitative findings, validation approach, methodological limitations, and relevance to the proposed DDHSS components. Extracted data were used to construct a study-level evidence table and to support comparative narrative synthesis across the predefined evidence domains.

Following title and abstract screening and full-text assessment, 38 eligible publications were retained for data extraction and narrative synthesis across the predefined evidence domains of the review. These publications were grouped according to their primary contribution to conventional CRC screening performance, interval cancer and longitudinal risk evolution, colorectal carcinogenesis pathways, risk-stratified screening, predictive modeling, longitudinal healthcare data integration, AI-assisted analytics, and implementation or governance considerations.

The extracted evidence was synthesized using a comparative narrative approach. Studies were compared according to evidence domain, intended population, data source, screening or surveillance strategy, predictor structure, analytical approach, validation status, implementation limitation, and relevance to DDHSS. Comparative synthesis was conducted across prespecified dimensions comprising clinical pathway, intended population, data inputs, temporal updating, clinical output, validation status, implementation requirements, main strengths, and major limitations. DDHSS was not assumed to be superior to existing approaches; rather, its proposed contribution was inferred only where longitudinal integration and adaptive risk updating addressed limitations repeatedly identified across the reviewed literature.

3. Discussion

3.1 Literature Identification and Evidence Mapping

The database searches identified 383 records, including 147 records from PubMed, 211 from Scopus, and 25 from ScienceDirect. After removal of 86 duplicate records, 297 titles and abstracts were screened. Of these, 54 full-text publications were assessed for eligibility, and 38 publications were retained as the primary evidence set for study-level data extraction and narrative synthesis. Sixteen full-text publications were excluded because they were not directly relevant to colorectal cancer screening or surveillance, focused primarily on therapeutic interventions, involved populations or outcomes outside the scope of this review, did not address risk prediction or longitudinal surveillance, or were publication types such as editorials, opinion articles, case reports, or conference abstracts without sufficient methodological detail.

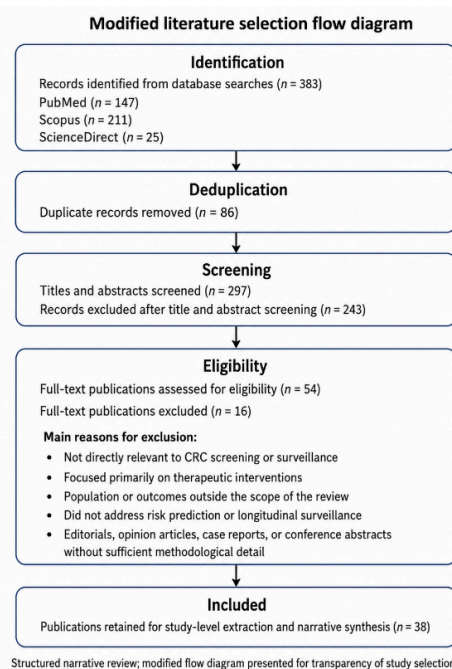


Figure 1. Modified literature selection flow diagram for the structured narrative review.

The included publications were mapped across predefined evidence domains relevant to the development of DDHSS, including conventional CRC screening performance, residual risk and interval cancer following negative screening, adenoma-carcinoma and serrated carcinogenesis pathways, FIT-based and biomarker-based screening, risk-stratified screening, predictive modeling, longitudinal healthcare data integration, AI-assisted analytics, and implementation or governance considerations. Examples include studies on residual risk after negative colonoscopy and screening-negative status,^[6,8] quantitative FIT performance,^[4,5,24] serrated and post-polypectomy risk,^[14-21] risk-stratified screening and predictive modeling,^[22-27] EHR-based or AI-assisted prediction,^[11,12,28-33] and programmatic or implementation evidence.^[34-57] The study-level characteristics of the included publications are summarized in Table 2

Author/year	Country	Study design	Population	Data source	Inputs/predictors	Outcome	Analysis/model	Main findings	Validation method	Limitations	DDHSS relevance
Mo et al., 2023 ^[56]	China / multicentre	Multicentre retrospective cohort with blinded independent validation	1,138 participants: healthy controls, advanced adenoma, and CRC; early-stage CRC enriched	Plasma cfDNA methylation sequencing, colonoscopy/pathology, survival follow-up	191 ctDNA methylation haplotype markers	CRC and advanced adenoma detection; relapse-free and overall survival	L2-penalized logistic regression classifier	Validation AUC 0.937 for CRC and 0.903 for advanced adenoma; sensitivity 86.6% for CRC and 79.0% for advanced adenoma; specificity 88.1%	Independent blinded validation cohort	Retrospective design; limited healthy controls; not a population-based screening cohort; no longitudinal EHR integration	Supports biomarker-based pre-colonoscopy triage and shows how continuous molecular risk scores could supplement clinical data inputs
Shono et al., 2020 ^[146]	Japan	Retrospective multicentre cohort with 5-year follow-up	3,115 asymptomatic adults ≥ 40 years undergoing first lifetime colonoscopy and at least one surveillance colonoscopy	Endoscopy reports, histology findings, surveillance timing	Baseline colonoscopy phenotype: no neoplasia/diminutive polyps, small adenoma, advanced adenoma, invasive cancer	Advanced colorectal neoplasia after baseline colonoscopy	Kaplan-Meier analysis and Cox proportional hazards models	Baseline advanced neoplasia phenotype stratified future advanced neoplasia risk and supported shorter surveillance intervals in high-risk groups	No external validation; internal cohort follow-up only	Retrospective design; exclusion of many without follow-up; no lifestyle variables; no colonoscopy quality indicators	Provides a rule-based backbone for converting baseline lesion phenotype into automated surveillance interval recommendations
Jodal et al., 2024 ^[21]	Norway / registry-based cohort	Nested case-control study within a national longitudinal adenoma cohort	40,848 individuals with resected adenomas; molecular analysis subset with matched metachronous CRC cases and controls	Cancer registry, death registry, medical records, histopathology, low-coverage whole-genome sequencing	Age, advanced adenoma status, DNA copy-number losses	Metachronous CRC	Conditional multivariable logistic regression	C-statistic was approximately 69.8% for age + advanced adenoma + copy-number losses; molecular features added minimal improvement over clinical variables	Nested case-control design with matched controls; no independent external validation	Restricted to single baseline adenoma; limited case count; incomplete lifestyle factors; residual confounding possible	Supports using prior lesion morphology as a core risk input and cautions against over-weighting molecular markers without incremental value
Chi et al., 2024 ^[51]	China	Retrospective cohort using electronic medical records from three tertiary hospitals	4,345 patients with serrated polyps; 1,605 had synchronous advanced adenoma	Electronic medical records, colonoscopy reports, pathology reports, BMI, smoking, alcohol history	Age, sex, BMI, smoking, alcohol exposure, serrated polyp size/type/location	Synchronous advanced adenoma in patients with serrated polyps	Multivariable logistic regression	Identified age-specific risk factors for synchronous advanced adenoma; no discrimination metrics reported	No external validation	Retrospective hospital-based data; selection bias; no longitudinal CRC incidence; no AI model	Supports structured capture of serrated polyp features and demographic/lifestyle factors for risk-gated follow-up
Winter et al., 2024 ^[47]	Australia	Multicentre prospective randomized controlled trial protocol	Elevated-risk individuals in the Southern Cooperative Program for the Prevention of Colorectal Cancer	Surveillance colonoscopy, quantitative FIT, pathology, quality-of-life surveys, cost data, preference data	Quantitative fecal hemoglobin and elevated-risk clinical history	Advanced neoplasia under on-time vs FIT-delayed surveillance colonoscopy strategy	FIT-threshold-based surveillance strategy with logistic regression and cost-utility analysis planned	Protocol only; no outcome results yet	Prospective randomized design planned; pending	Protocol-stage evidence; possible self-selection; not blinded; elevated-risk Australian population only	Shows how FIT-based dynamic gating could personalize surveillance timing and reduce unnecessary colonoscopy

Liu et al., 2025 ^[6]	China	Retrospective population-screening cohort	69,809 adults aged 40-74 years in a community CRC screening program; 527 screening-negative participants underwent colonoscopy	High-risk factor questionnaire, double FIT, colonoscopy, demographics, lifestyle, screening database	HRFQ result, FIT result, age, BMI, smoking and other classical risk factors	Colorectal neoplasia, advanced colorectal neoplasia, advanced adenoma, CRC	Binary logistic regression comparing HRFQ and FIT predictive ability	Among screening-negative colonoscopy participants, neoplasia, advanced neoplasia and CRC were detected in 26.9%, 11.2% and 1.5%, respectively	No external validation	Retrospective design; small colonoscopy subset among screening-negative individuals; self-selection bias; limited lesion-quality indicators	Demonstrates that negative screening is not zero risk and supports periodic recalibration using combined questionnaire, FIT and clinical data
Yu et al., 2024 ^[38]	China	Population-based prospective cohort within the Cancer Screening Program in Urban China	286,339 adults aged 45-74 years after exclusion; 41,315 categorized as high risk	Epidemiologic questionnaire, colonoscopy, histopathology, community-level access and socioeconomic variables	Risk score based on epidemiologic factors; healthcare access and social determinants	Colonoscopy uptake and detection of CRC, advanced adenoma and adenoma	Programmatic risk-score strategy; regression for uptake determinants	Colonoscopy uptake was 19.02%; detection rates were 0.10% for CRC and 5.38% for advanced adenoma	Prospective programmatic cohort; no formal model validation metrics	Self-reported exposures; incomplete representativeness; no long-term incidence/mortality outcomes; no predictive calibration	Supports risk-based invitation, outreach and resource-prioritization functions within a population surveillance platform
Dong et al., 2024 ^[40]	China	Multicentre population-based prospective cohort comparing RF vs RF-FIT strategies	2,467,429 screening participants aged 40-74 years in the Chinese National CRC Screening Program	Questionnaire, FIT, colonoscopy, pathology, web-based national coordinating system, program cost data	Questionnaire-based risk factors, FIT positivity, family history, prior polyps, intestinal disease	Colonoscopy referral, CRC/advanced neoplasia detection, efficiency and cost-effectiveness	Rule-based risk score combined with FIT; comparative programmatic analysis	Combining questionnaire risk assessment with FIT improved colonoscopy yield and program efficiency compared with questionnaire alone	Large real-world prospective program evaluation; no individual prediction-model validation	Non-randomized comparison; potential confounding; missing data not imputed; limited long-term outcome follow-up	Provides an operational template for combining routine risk-factor fields and FIT results into automated colonoscopy prioritization
Zhang et al., 2024 ^[52]	China	Retrospective pooled study	Patients with colorectal adenomas across pooled datasets; focus on small/diminutive adenomas with high-grade dysplasia	Colonoscopy and histopathology records	Adenoma size and dysplasia grade	High-grade dysplasia burden by adenoma size	Descriptive and comparative pathological analysis	Small and diminutive adenomas contributed a substantial absolute number of high-grade dysplasia cases despite lower per-lesion risk	No external validation; pooled retrospective analysis	Retrospective design; limited longitudinal outcome linkage; no dynamic risk model	Supports recording granular polyp size and histology because clinically important risk may not be captured by size alone
Song et al., 2023 ^[41]	International	Systematic review of noninvasive biomarkers for CRC screening	Studies evaluating stool, blood, urine or other noninvasive biomarkers for CRC detection	Published biomarker studies and diagnostic performance data	FIT, stool DNA, blood biomarkers, methylation markers, miRNA and other noninvasive biomarkers	CRC and advanced neoplasia detection	Narrative/systematic synthesis of biomarker performance	Noninvasive biomarkers have variable performance and may complement, but not replace, established FIT/colonoscopy pathways	Review-level synthesis; validation depends on included studies	Heterogeneous biomarker platforms; many studies not population-screening based; variable external validation	Supports multi-input surveillance architecture in which FIT and emerging biomarkers can be incorporated as dynamic evidence streams
Heisser et al., 2023 ^[8]	Germany	Large repeated-screening colonoscopy analysis	Approximately 120,000 repeated screening colonoscopies ≥ 10 years after negative baseline screening colonoscopy	Screening colonoscopy records and neoplasia findings	Sex and interval since negative baseline colonoscopy	Adenoma and advanced neoplasia prevalence after negative colonoscopy	Prevalence comparison across interval strata	Advanced neoplasia prevalence remained measurable 10+ years after negative colonoscopy and increased modestly over longer intervals	Large registry-based repeated-screening dataset; no model validation	Observational design; potential selection effects among repeat-screened individuals	Supports the premise that risk after negative screening evolves over time and should be periodically reassessed

He et al., 2023 ^[48]	China	Observational consecutive retrospective study	Average-risk individuals undergoing colonoscopy screening	Colonoscopy records, adenoma detection data	Patient characteristics and colonoscopy quality indicators	Adenoma detection rate	Descriptive and regression-based analysis	Adenoma detection varied across screening populations and quality parameters	Single retrospective cohort; no external validation	Retrospective single-setting evidence; limited longitudinal outcome linkage	Supports incorporating colonoscopy quality and detection history into longitudinal surveillance evaluation
Willauer et al., 2022 ^[39]	United States	Community CRC screening program analysis	Predominantly Hispanic community population in Texas	Screening program records, colonoscopy and pathology outcomes	Demographics and screening participation characteristics	Colorectal neoplasia prevalence	Programmatic prevalence analysis	Demonstrated clinically relevant neoplasia burden in an underserved screening population	Real-world program data; no predictive validation	Local population; limited generalizability; not an AI or dynamic surveillance model	Highlights the need for equity-sensitive population monitoring and subgroup performance assessment
Carballal et al., 2022 ^[49]	Spain	FIT-based screening program cohort	Participants in a FIT-based CRC screening program with adenomatous polyposis	FIT program database, colonoscopy, pathology, follow-up records	Adenomatous polyposis, colonoscopy findings, screening history	Advanced neoplasia during follow-up	Cohort follow-up analysis	Adenomatous polyposis within FIT-based screening was associated with elevated follow-up neoplasia risk	Programmatic cohort follow-up; no external validation	Specific screening-program population; observational design	Supports integrating prior colonoscopy and pathology history into adaptive surveillance intensity
Djinbajian et al., 2023 ^[14]	Canada	Matched case-cohort study	Patients with serrated lesions undergoing surveillance colonoscopy	Colonoscopy and histopathology records	Type and characteristics of serrated lesions	Total metachronous advanced neoplasia	Matched risk comparison	Serrated lesion history contributed to metachronous advanced neoplasia risk	Matched cohort design; no external validation	Observational design; residual confounding; no EHR-based dynamic prediction	Supports including serrated-lesion metadata as a structured risk input
Vithayathil et al., 2022 ^[50]	United States	Development of a large longitudinal colonoscopy-based cohort	Patients undergoing colonoscopy within a health system-based cohort	Colonoscopy database linked with longitudinal clinical data	Colonoscopy findings, demographics, clinical history, longitudinal follow-up data	Integrated research infrastructure for CRC and colonoscopy outcomes	Cohort construction and data-linkage methodology	Demonstrated feasibility of creating an integrated longitudinal colonoscopy cohort	Data infrastructure validation rather than predictive validation	Single health-system setting; dependent on data quality and linkage completeness	Provides a direct model for DDHSS data acquisition and longitudinal linkage architecture
Bjerrum et al., 2020 ^[17]	Denmark	Long-term cohort from a gFOBT-positive screening program	Screen-detected adenoma patients followed for long-term CRC risk	Screening cohort records, pathology, cancer registry follow-up	Screen-detected adenoma characteristics	Long-term CRC risk after adenoma detection	Longitudinal cohort risk estimation	Screen-detected adenomas conferred persistent long-term CRC risk	Registry-linked follow-up; no external validation	gFOBT-era cohort; may not fully translate to FIT-based programs	Supports continued longitudinal risk monitoring after initial lesion detection
Lieberman et al., 2020 ^[18]	United States	Prospective screening cohort with 10-year colonoscopy outcomes	Individuals undergoing baseline screening colonoscopy and surveillance follow-up	Baseline colonoscopy, pathology, surveillance outcomes	Baseline colonoscopy findings, adenoma features	10-year CRC and advanced neoplasia outcomes	Cohort outcome analysis by baseline lesion category	Baseline colonoscopy findings strongly stratified 10-year surveillance outcomes	Prospective cohort follow-up; no external validation model	Cohort-specific practice context; no dynamic EHR/AI updating	Supports using baseline colonoscopy phenotype as a central longitudinal risk anchor
Chen et al., 2019 ^[55]	China	Multicentre randomized trial protocol (TARGET-C)	Chinese CRC screening population planned for comparison of novel screening strategies	Questionnaire, FIT/novel screening tests, colonoscopy confirmation planned	Novel screening strategy inputs and risk-assessment variables	CRC and advanced neoplasia detection; comparative screening effectiveness	Randomized comparative screening strategy evaluation planned	Protocol only; no clinical outcome results yet	Multicentre randomized validation planned	No results available; generalizability depends on trial completion and implementation context	Supports prospective comparative testing of screening strategies before system-level adoption
Zorzi et al., 2018 ^[42]	Italy	Retrospective cohort from FIT screening programs	Participants in organized FIT-based screening programs	FIT screening records, colonoscopy, pathology, long-term follow-up	Screening round, anatomical site, FIT-based detection history	Long-term detection rates of proximal and distal advanced neoplasia	Cohort detection-rate analysis	Long-term detection rates differed between proximal and distal advanced neoplasia, indicating site-specific detection limitations	Program-level cohort follow-up; no prediction-model validation	Retrospective program data; potential quality variation	Supports site-aware surveillance and feedback monitoring of screening program performance

Selby et al., 2018 ^[4]	United States	Community-based cohort study	Large community screening population undergoing quantitative FIT	FIT results, screening registry, CRC outcomes	Quantitative FIT threshold	CRC detection sensitivity and specificity	Threshold-performance analysis	CRC sensitivity increased at lower FIT thresholds while specificity decreased, demonstrating capacity-dependent trade-offs	Community-based outcome linkage; no external model validation	Threshold findings depend on local program characteristics and follow-up completeness	Supports dynamic threshold-setting and colonoscopy-capacity-aware referral rules
Weigl et al., 2018 ^[37]	Germany / United States data components	Screening population genetic risk score study	Colorectal cancer screening participants evaluated for advanced neoplasms	Genetic data, colonoscopy findings, demographic variables	Genetic risk score and clinical risk factors	Prevalence of advanced neoplasms	Association and discrimination analysis	Genetic risk score was associated with advanced neoplasm prevalence but required integration with clinical data	Screening population analysis; no dynamic external implementation validation	Genetic risk alone has limited operational utility; ancestry/generalizability issues	Supports optional hereditary/genetic risk layer with caution regarding fairness and external validity
Liles et al., 2018 ^[5]	United States	Prospective cohort study	Screening participants undergoing quantitative FIT and colonoscopy/reference assessment	Quantitative FIT, colonoscopy and pathology results	Fecal hemoglobin concentration	Advanced colorectal neoplasia detection	Diagnostic accuracy analysis	Quantitative FIT showed measurable performance for advanced neoplasia but threshold choice affected sensitivity and specificity	Prospective cohort with reference-standard follow-up	Single program context; limited dynamic risk variables	Supports using quantitative FIT as a continuous dynamic predictor rather than only binary positive/negative status
Dube et al., 2017 ^[19]	International	Systematic review and meta-analysis	People with low-risk adenomas at baseline colonoscopy	Published cohort studies of adenoma outcomes	Low-risk adenoma status at baseline	Advanced adenoma, CRC and CRC mortality	Meta-analysis of risk estimates	Low-risk adenomas were associated with lower subsequent risk than high-risk lesions, supporting differential surveillance intensity	Review-level synthesis; quality depends on included studies	Heterogeneity in surveillance definitions and follow-up; observational evidence	Supports separate surveillance trajectories for low-risk vs high-risk post-polypectomy populations
Chen et al., 2017 ^[45]	Germany	Screening cohort laboratory stability study	CRC screening cohort with stool samples for FIT	FIT results from fresh/frozen samples, ambient temperature exposure, outcomes	Sample condition and ambient temperature	Detection of CRC and adenomas by FIT	Diagnostic performance comparison	Fresh vs frozen samples and ambient temperature had limited effect on CRC/adenoma detection by FIT	Screening cohort with colonoscopy outcome linkage	Focused on pre-analytical handling rather than longitudinal risk prediction	Supports standardization and quality assurance for FIT data streams used by DDHSS
Yu et al., 2016 ^[53]	International	Meta-analysis of observational studies	Adults evaluated in studies of type 2 diabetes mellitus and colorectal adenoma	Published observational studies	Type 2 diabetes mellitus	Colorectal adenoma risk	Meta-analysis of association estimates	Type 2 diabetes mellitus was associated with increased colorectal adenoma risk	Review-level synthesis	Observational confounding; heterogeneous diabetes and adenoma definitions	Supports metabolic comorbidity as a baseline and longitudinal risk input
Quintero et al., 2016 ^[36]	Spain	Large multicentre cross-sectional study	First-degree relatives of individuals with CRC	Clinical risk data and colonoscopy findings	Family history characteristics and age	Advanced neoplasia	Risk comparison by family-history profile	First-degree relatives had clinically relevant advanced neoplasia risk, supporting familial-risk stratification	Multicentre cross-sectional validation of risk association	Cross-sectional design; no dynamic follow-up or AI model	Supports hereditary/family history as a stable baseline risk input requiring distinct pathway handling
Bouras et al., 2023 ^[54]	International consortium	Genome-wide interaction analysis	Participants from genetic epidemiology datasets of CRC risk	Genotype data, folate-related exposure data, CRC outcome data	Genetic variants, folate exposure, gene-environment interaction terms	CRC risk	Genome-wide interaction analysis	Folate-related gene-environment interactions may contribute to CRC susceptibility	Genetic association framework; replication depends on included cohorts	Complex interpretation; ancestry and exposure-measurement limitations; not ready as clinical triage model	Supports the concept that risk evolves from interacting biological and environmental determinants

Heer et al., 2023 ^[43]	Canada	Diagnostic performance study	Individuals under age 50 evaluated with FIT for CRC/advanced neoplasia	FIT, colonoscopy/pathology outcomes	FIT result and age group	CRC and advanced neoplasia detection	Diagnostic accuracy analysis	FIT showed measurable but imperfect performance in individuals under age 50	Outcome-linked diagnostic evaluation; no external model validation	Younger population; event counts and spectrum may limit precision	Supports adaptive use of FIT within early-onset or younger-risk surveillance contexts
Patel et al., 2022 ^[34]	United States	Guideline / expert recommendations	Average-risk adults considered for CRC screening start/stop ages	Evidence review and expert consensus	Age, screening eligibility and stopping considerations	Recommended screening start and stop ages	Guideline synthesis	Updated age-based screening recommendations provide the current conventional comparator for DDHSS	Guideline methodology; not a primary validation study	Age-based framework cannot fully capture longitudinal individualized risk changes	Defines the conventional population-screening pathway that DDHSS should support, not replace
Baile-Maxia et al., 2023 ^[20]	International	Systematic review and meta-analysis	Patients after endoscopic resection of high-risk adenomas	Published follow-up studies of high-risk adenoma outcomes	High-risk adenoma features, baseline colonoscopy findings	Metachronous CRC or advanced adenoma	Meta-analysis of risk factors	High-risk adenoma features predicted subsequent metachronous advanced lesions	Review-level synthesis; QUIPS/prognostic appraisal in included evidence	Observational heterogeneity; inconsistent follow-up and outcome definitions	Supports automated risk-updating after high-risk adenoma resection and specialist surveillance coordination
Frazzoni et al., 2025 ^[34]	Italy	Predictive model study in an organized screening program	Participants in a FIT-based organized CRC screening program	Quantitative FIT and screening outcomes	Quantitative fecal hemoglobin concentration and screening variables	CRC risk stratification	Predictive model based on quantitative FIT	Quantitative FIT-based prediction stratified CRC risk within an organized screening program	Model-development/validation within screening program dataset	Requires external validation and calibration in other populations	Supports quantitative FIT as a scalable input for dynamic risk scoring and colonoscopy prioritization
Pham et al., 2024 ^[35]	International	Systematic review and meta-analysis	Patients with iron deficiency evaluated for colonoscopy triage	Published diagnostic studies of FIT in iron deficiency	FIT result in the setting of iron deficiency	CRC/advanced neoplasia detection and colonoscopy triage	Diagnostic meta-analysis	FIT may improve colonoscopy triage in iron-deficiency populations but cannot replace diagnostic evaluation when clinically indicated	Review-level synthesis	Heterogeneity in iron-deficiency definitions, thresholds and referral populations	Supports separating diagnostic-evaluation triggers from routine population surveillance pathways
van Lier et al., 2023 ^[46]	International	Systematic review and meta-analysis	Studies evaluating urinary volatile organic compounds for CRC screening	Urinary VOC platforms, colonoscopy/histopathology reference standards	Urinary VOC fingerprints or chemical markers	CRC detection	Diagnostic accuracy meta-analysis	Fingerprinting methods showed pooled sensitivity around 84% and specificity around 70%, but adenoma evidence was insufficient	Review-level synthesis using diagnostic study quality assessment	Small primary studies, heterogeneous platforms, case-control bias, limited external validation	Supports potential secondary triage biomarkers only after validation and interoperability planning
Silva-Illanes and Espinoza, 2018 ^[57]	International	Systematic review of Markov models for economic evaluation	Hypothetical CRC screening cohorts simulated in 34 models	Model inputs from registries, RCTs, colonoscopy studies and epidemiologic sources	Screening strategy, natural history assumptions, test performance, costs and utilities	Cost-effectiveness, life-years/QALYs, CRC incidence and mortality projections	Critical appraisal of Markov state-transition models	CRC screening economic results depend heavily on model structure, calibration and assumptions	Review of model calibration/validation reporting	Many models had limited transparency, calibration and validation reporting	Supports future DDHSS economic evaluation under local colonoscopy-capacity and cost constraints
Symonds et al., 2025 ^[44]	International	Systematic review and paired diagnostic meta-analysis	Adult participants in studies comparing FIT and blood-based CRC screening tests	FIT, blood biomarkers, colonoscopy/histopathology outcomes	FIT and blood-based biomarkers such as cfDNA, proteins, miRNA and SEPT9	CRC detection	Random-effects and bivariate diagnostic meta-analysis	Blood tests had lower sensitivity than FIT in pooled comparisons; high heterogeneity and bias limited interpretation	QUADAS-2 and paired diagnostic synthesis	Spectrum bias, heterogeneous thresholds, small biomarker studies, limited population-screening validity	Supports prioritizing validated FIT while allowing future incorporation of blood markers only after robust validation

Thayalasekaran et al., 2020 ^[7]	International / organized screening programs	Systematic review and meta-analysis of randomized controlled trials	3,645 FIT/FOBT-positive participants undergoing colonoscopy in organized screening programs	RCT-level endoscopy and histopathology outcomes	Endoscopic technological innovations in colonoscopy	Adenoma detection, advanced adenoma detection, cancer detection and procedure quality	Random-effects meta-analysis	Add-on endoscopic technologies did not consistently improve detection outcomes across organized screening trials	Meta-analysis restricted to RCTs; risk-of-bias assessment	Technology heterogeneity, operator blinding impossible, limited subgroup data	Supports using surveillance dashboards and quality monitoring rather than assuming technology alone improves screening performance
Baile-Maxia et al., 2024 ^[15]	International	Systematic review and meta-analysis	493,949 patients after endoscopic resection of serrated polyps	Colonoscopy/pathology data and follow-up outcomes from published studies	Serrated polyp type, size, dysplasia, number, location and synchronous adenomas	Metachronous CRC or advanced lesions	Random-effects meta-analysis with prognostic risk-of-bias assessment	Advanced serrated polyps had higher CRC incidence than non-advanced serrated polyps; serrated lesion features informed surveillance risk	Review-level synthesis; QUIPS/prognostic appraisal	Observational confounding, attrition bias, incomplete lesion metadata, variable follow-up	Supports structured capture of serrated-polyp metadata and automated post-polypectomy risk scheduling

Table note: Table 2 summarizes the 38 primary publications retained for study-level evidence extraction. The complete reference list contains 57 sources because additional methodological, ethical, reporting, and contextual references were used to support narrative interpretation, AI governance, and framework development.

Table 2. Characteristics of studies included in the narrative synthesis.

The complete reference list contains 57 sources because additional contextual and methodological references were used to support reporting quality, conceptual interpretation, and implementation considerations. These additional sources included narrative review methodology, clinical prediction model reporting and appraisal guidance, AI governance and ethics guidance, algorithmic fairness literature, and supporting background references. They were not treated as primary study-level evidence in the extraction table unless they directly contributed empirical, clinical, or model-development evidence to the DDHSS framework. This distinction was made to separate the primary evidence set used for narrative synthesis from supporting references used for methodological and governance justification.

Evidence mapping showed that existing CRC risk-management approaches remain fragmented across separate clinical functions. Population screening studies primarily addressed age-based eligibility, FIT thresholds, colonoscopy uptake, and detection performance. Post-colonoscopy and post-polypectomy studies focused on baseline lesions, metachronous neoplasia, and surveillance intervals. Risk-stratified screening studies incorporated demographic, lifestyle, family history, metabolic, FIT-based, and previous screening variables, whereas EHR-based and machine learning studies examined the feasibility of integrating routinely collected healthcare data for prediction. However, few studies combined longitudinal data acquisition, dynamic risk recalibration, clinical response pathways, and evaluative feedback into a unified surveillance architecture. This evidence gap provided the conceptual basis for DDHSS as an integrative risk-monitoring and referral-support framework rather than a validated replacement for existing CRC screening or surveillance pathways.

3.2 Conventional CRC Screening, Residual Risk, and the Need for Longitudinal Monitoring

Conventional CRC screening is commonly organized around age-based eligibility, repeated FIT-based testing, and colonoscopy referral after positive screening or clinically indicated assessment.^[1,4,5] This approach is scalable and remains central to population-level CRC prevention; however, it is inherently episodic and may incompletely capture changes in individual risk between screening rounds.

Residual risk persists after negative screening. Among individuals undergoing repeat screening colonoscopy 10 years after a negative examination, advanced neoplasia prevalence was 3.6% in women and 5.2% in men, increasing modestly to 4.9% and 6.6%, respectively, at 14 years or more after the negative baseline examination.^[8] In a community-based cohort of primary screening-negative participants who subsequently underwent colonoscopy, colorectal neoplasia, advanced colorectal neoplasia, and CRC were detected in 26.9%, 11.2%, and 1.5% of participants, respectively.^[6] FIT-based screening also demonstrates threshold-dependent performance, with programmatic CRC sensitivity ranging from 66.0% at a 30 microg/g threshold to 79.3% at a 10 microg/g threshold and specificity ranging from 87.0% to 94.7%.^[4]

These limitations do not diminish the value of conventional screening, but they indicate that screening results should be interpreted within an evolving longitudinal risk context. Figure 2 illustrates that adenoma and advanced neoplasia prevalence may increase with longer intervals following a previous negative colonoscopy.^[8] Accordingly, the rationale for DDHSS is not to replace established FIT or colonoscopy pathways, but to add an adjunctive layer of longitudinal risk monitoring, referral support, and feedback-based recalibration.

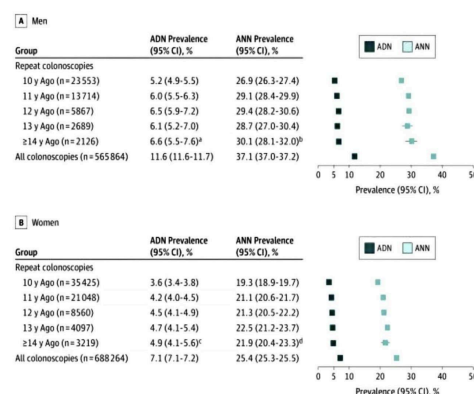


Figure 2. Prevalence of adenoma (ADN) and advanced neoplasia (ANN) according to surveillance interval following previous negative colonoscopy. Adapted from Heisser et al.^[8]

Taken together, these studies create a more coherent sequence from conventional screening methods, to their residual limitations, and finally to the conceptual need for DDHSS as an adjunctive longitudinal monitoring framework.

3.3 Adenoma-Carcinoma Sequence and Longitudinal Surveillance

The gradual progression of colorectal precursor lesions provides a fundamental biological rationale for longitudinal colorectal cancer surveillance.^[1,3] Colorectal carcinogenesis generally occurs through gradual accumulation of molecular and histological changes transforming premalignant lesions into invasive malignancy over several years. This prolonged progression pathway creates a valuable temporal window for preventive intervention, surveillance, and early lesion detection.

Importantly, the biological progression of colorectal neoplasia demonstrates substantial interindividual variability influenced by lesion morphology, molecular characteristics, metabolic factors, genetic susceptibility, and hereditary predisposition.^[3,9,10,14,15] Consequently, CRC progression cannot be adequately characterized as a uniform linear process applicable to all populations.

Post-colonoscopy and post-polypectomy studies have demonstrated that baseline colorectal findings possess substantial prognostic value for predicting future advanced neoplasia. Baseline advanced adenoma, high-risk adenoma features, serrated lesion history, and previous colonoscopy findings are associated with subsequent metachronous colorectal neoplasia and may inform surveillance intensity.^[14-21] These observations suggest that prior screening findings should not be interpreted as isolated clinical events but rather as components of continuously evolving longitudinal risk trajectories.

From a surveillance perspective, the adenoma-carcinoma sequence further highlights the limitations of single-timepoint screening strategies. Although colonoscopy remains highly effective for detection and removal of precancerous lesions, subsequent carcinogenic progression may still occur under the influence of newly emerging risk determinants or previously undetected lesions. Therefore, effective CRC surveillance may require periodic reassessment of evolving clinical risk rather than exclusive dependence on fixed post-screening intervals.

Beyond the conventional adenoma-carcinoma sequence, the serrated neoplasia pathway represents an important alternative route of colorectal carcinogenesis. Sessile serrated lesions constitute major precursor lesions within this pathway and are characterized by distinct molecular and histological features. From a surveillance perspective, serrated lesions present additional challenges because they are frequently located in the proximal colon, may exhibit subtle or flat morphological features, and tend to produce limited bleeding, which may reduce their detectability through conventional colonoscopy and FIT-based approaches. These characteristics reinforce the limitation of conceptualizing CRC development exclusively through the conventional adenoma-carcinoma sequence and further support surveillance strategies capable of integrating previous endoscopic findings, molecular and clinical risk determinants, and longitudinal changes in individual risk profiles.^[3,14,15]

The biological characteristics of colorectal carcinogenesis therefore support the need for surveillance systems capable of integrating cumulative clinical information, repeated screening outcomes, and evolving individual risk profiles over time.

3.4 Risk Stratification in Colorectal Cancer Screening

Growing recognition of interindividual variability in colorectal cancer (CRC) susceptibility has driven a gradual transition from conventional uniform screening paradigms toward more individualized surveillance strategies.^[22] Traditional age-based screening models assume relatively homogeneous population risk distribution, whereas epidemiological evidence increasingly demonstrates substantial variation in CRC predisposition across demographic, hereditary, metabolic, and lifestyle-related contexts.^[23]

Risk-oriented screening frameworks aim to tailor surveillance intensity according to multiple determinants associated with colorectal carcinogenesis, including family history, obesity, dietary behavior, smoking exposure, metabolic abnormalities, quantitative FIT findings, and previous screening results.^[2,22-25] Such observations suggest that reliance on standardized screening intervals alone may inadequately reflect interindividual variability in CRC susceptibility.

Recent predictive approaches integrating FIT values, clinical variables, laboratory parameters, and behavioral characteristics have demonstrated measurable discriminatory performance for identifying individuals with elevated probabilities of colorectal neoplasia. In a longitudinal population-based screening cohort, incorporation of FIT and lifestyle-related variables improved 10-year CRC risk prediction compared with a demographic-only model, increasing the C-index from 0.622 to 0.718.^[25] Machine learning approaches using routine clinical data have also shown potential for risk stratification; for example, a random forest model for young-onset CRC achieved AUCs of 0.859 in internal validation and 0.888 in temporal validation, with corresponding recall values of 0.840 and 0.872.^[12] However, evidence from FIT-based and other CRC risk prediction models remains heterogeneous, with limitations related to risk of bias, external validation, and readiness for routine clinical implementation.^[26] From a clinical perspective, these models may support more efficient allocation of colonoscopy resources by prioritizing diagnostic evaluation toward populations with disproportionately higher risk burdens while potentially reducing unnecessary invasive procedures among lower-risk groups.

Longitudinal cohort analyses additionally demonstrate increasing divergence in cumulative CRC incidence across different surveillance categories over time, as illustrated in Figure 3.^[25] The widening separation of risk trajectories observed throughout follow-up periods suggests that CRC susceptibility evolves unevenly across populations and may not be adequately addressed through static surveillance allocation.

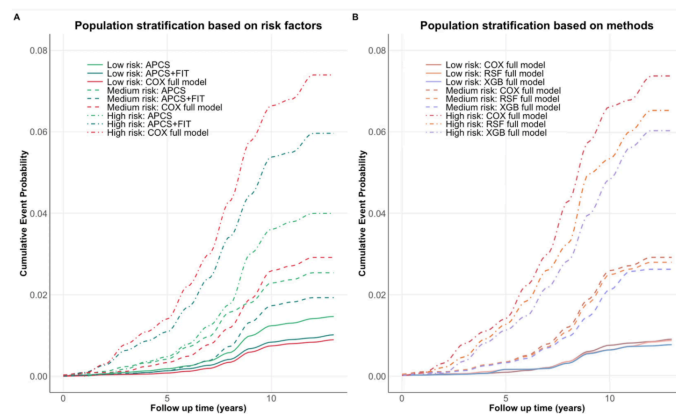


Figure 3. Cumulative probability of colorectal cancer occurrence across different risk strata within a longitudinal screening cohort. Divergence of risk trajectories over time illustrates population heterogeneity in colorectal cancer risk.^[25]

Across risk-stratified CRC screening studies, the most informative predictors appear to be context-dependent but can be grouped into several clinically relevant domains. Screening-related variables, particularly FIT results or quantitative fecal hemoglobin concentration, represent strong near-term predictors of CRC and advanced colorectal neoplasia.^[24,26] Previous colorectal findings, including baseline adenoma characteristics, advanced adenoma, serrated lesion history, and prior colonoscopy results, are also important predictors of future metachronous neoplasia.^[14–21] Demographic and clinical factors such as increasing age, male sex, family history of CRC, obesity, smoking exposure, dietary patterns, metabolic abnormalities, personal screening characteristics, and screening history contribute to baseline susceptibility and are frequently incorporated into risk-stratified screening models.^[22–23,25,27] In machine learning models using routine clinical data for young-onset CRC, explainability analysis identified inflammatory, screening, hematologic, and tumor-marker variables, including C-reactive protein, FIT, lymphocyte count, carcinoembryonic antigen, and lactate dehydrogenase, as highly informative predictors.^[12] Therefore, adaptive surveillance frameworks such as DDHSS should prioritize both stable baseline predictors, including age, sex, family history, and hereditary risk, and dynamic predictors, including FIT findings, gastrointestinal symptoms, laboratory abnormalities, metabolic changes, and previous screening outcomes.

Despite these promising developments, implementation of risk-oriented CRC screening remains associated with important methodological and operational constraints. Variability in healthcare infrastructure, inconsistency in data completeness, limited interoperability between healthcare databases, and demographic heterogeneity may substantially influence predictive reliability across clinical environments. In addition, surveillance models relying predominantly on baseline variables may insufficiently capture temporal

fluctuations in CRC susceptibility occurring throughout longitudinal follow-up.^[1,2]

These limitations highlight the importance of surveillance systems capable of integrating continuously updated clinical information to support more precise and individualized CRC screening strategies.

3.5 Integration of Longitudinal Healthcare Data and Artificial Intelligence

Rapid expansion of healthcare informatics and artificial intelligence (AI) technologies has created new opportunities for more refined approaches to colorectal cancer (CRC) surveillance and risk estimation. In the context of DDHSS, AI should not be interpreted as a single homogeneous method, but rather as a group of computational approaches that may include regression-based prediction models, survival models, tree-based machine learning algorithms, ensemble methods, deep learning architectures, and natural language processing for unstructured clinical data. This distinction is important because each model class differs in data requirements, interpretability, validation needs, and implementation feasibility.^[28-29]

Longitudinal CRC surveillance requires integration of heterogeneous data sources that are repeatedly generated across healthcare encounters. These may include structured electronic health record variables, demographic characteristics, gastrointestinal symptom profiles, laboratory findings, FIT results, colonoscopy history, histopathological findings, medication exposure, metabolic risk markers, family history, and previous screening outcomes. In addition, natural language processing and language-model-based approaches may enable extraction of clinically relevant information from unstructured or semi-structured electronic medical record data, including physician notes, referral descriptions, and endoscopy-related documentation.^[28-30] Integration of these data sources may allow risk estimation to shift from static single-timepoint classification toward continuously updated individual risk trajectories.^[11,12]

From an analytical perspective, different AI and machine learning approaches may serve different functions within CRC surveillance. Regression-based and survival models remain useful when interpretability and time-to-event estimation are prioritized. Tree-based ensemble models, including random forest and gradient boosting approaches, may capture nonlinear relationships and interactions among clinical, laboratory, and screening-related predictors. Deep learning and natural language processing approaches may be useful when large-scale imaging, endoscopy, histopathology, or unstructured textual data are incorporated. However, increased model complexity does not automatically imply clinical superiority; models intended for surveillance must demonstrate not only discrimination but also calibration, external validity, temporal stability, clinical utility, and operational feasibility.^[11-12,29,31-32]

Several methodological issues are particularly important before AI-assisted CRC surveillance can be translated into practice. First, model performance should be evaluated using discrimination metrics such as AUC or C-index, calibration metrics, decision-curve analysis, and external or temporal validation rather than internal validation alone. Second, longitudinal surveillance models require monitoring for model drift, because changes in screening uptake, population characteristics, laboratory platforms, coding practices, and healthcare access may alter predictive performance over time. Third, missing data and inconsistent EHR documentation may introduce systematic error, especially when symptoms, family history, lifestyle factors, or colonoscopy findings are incompletely recorded.^[29,31-32]

Algorithmic bias represents a major concern in AI-assisted CRC surveillance. Models trained on non-representative datasets may underperform in populations that differ by age, sex, ethnicity, socioeconomic status, healthcare access, comorbidity burden, or screening participation. This issue is particularly relevant for population-level surveillance because biased risk estimation could intensify existing inequities by preferentially directing diagnostic resources toward groups already well represented in healthcare datasets while under-identifying underserved populations. Therefore, fairness assessment, subgroup performance evaluation, transparent reporting of training data characteristics, and periodic recalibration are necessary components of responsible AI implementation.^[32-33]

Data governance is another critical requirement. Longitudinal surveillance systems depend on repeated linkage of sensitive health information across time and healthcare settings. Therefore, implementation of DDHSS would require clear policies for patient privacy, data security, consent or lawful data use, data ownership, access control, auditability, and accountability for model-driven recommendations. AI outputs should be positioned as clinical decision-support tools rather than autonomous decision-makers, with healthcare professionals retaining oversight over colonoscopy referral, intensified follow-up, or routine

screening decisions. Explainability mechanisms, such as feature-importance analysis or clinically interpretable risk summaries, may improve clinician trust and enable review of whether model outputs are biologically plausible and clinically actionable.^[29,32–33]

Accordingly, the integration of longitudinal healthcare data and AI into CRC surveillance should be understood as a multilayered implementation pathway rather than a purely technical modeling exercise. A clinically credible DDHSS would require reliable data infrastructure, interoperable health records, validated prediction models, transparent reporting, fairness assessment, explainable outputs, ethical governance, and continuous post-implementation monitoring. These requirements provide the methodological foundation for the proposed DDHSS framework and distinguish it from conventional episodic screening strategies that rely primarily on age-based eligibility and fixed screening intervals.

3.6 Conceptual Framework of Dynamic Digestive Health Surveillance System (DDHSS)

Based on the synthesized evidence, the Dynamic Digestive Health Surveillance System (DDHSS) is proposed as a conceptual population-based model integrating cumulative healthcare data, predictive analytical modeling, risk stratification, and responsive colorectal cancer (CRC) monitoring. The proposed approach is intended to address a major limitation of conventional CRC screening strategies, which predominantly rely on static age-based eligibility criteria and episodic screening intervals that inadequately reflect the evolving nature of CRC susceptibility across time.

DDHSS is intended as a longitudinal risk-monitoring and referral-support framework rather than a replacement for established CRC screening, diagnostic evaluation, post-polypectomy surveillance, or hereditary cancer surveillance pathways. Asymptomatic average-risk adults, symptomatic individuals, patients with previous colorectal neoplasia, and individuals with hereditary CRC predisposition should enter distinct clinical pathways. In this context, asymptomatic average-risk adults remain within population-based screening pathways, while individuals with positive FIT results, alarm gastrointestinal symptoms, unexplained iron-deficiency anemia, or other findings requiring diagnostic investigation should undergo guideline-concordant clinical evaluation rather than routine risk-based surveillance alone.^[1,26,34–35] Similarly, individuals with previous advanced adenomas, high-risk serrated lesions, or hereditary cancer predisposition should continue to receive established post-polypectomy or specialist surveillance, with DDHSS functioning only as an adjunctive coordination and risk-updating layer.^[14–15,18,20,22] This distinction is essential to prevent the proposed framework from being interpreted as an autonomous screening replacement or as a substitute for clinical judgment.

No fully established program identical to DDHSS was identified in the reviewed literature. However, several related programs and pilot-like components support the feasibility of individual DDHSS elements. Existing evidence includes family-history and genetic risk stratification,^[36,37] population-level screening uptake and combined FIT-questionnaire risk assessment programs,^[38–40] noninvasive biomarker streams and site-specific FIT screening evidence,^[41–46] FIT-personalized surveillance protocols, colonoscopy quality monitoring, post-polypectomy follow-up, and longitudinal colonoscopy cohort infrastructure,^[47–50] serrated-polyp and small-adenoma risk characterization,^[51,52] metabolic and gene-environment risk evidence,^[53,54] and prospective comparative screening protocols, ctDNA methylation biomarkers, and economic modeling frameworks.^[55–57] These examples should be interpreted as partial analogues rather than validation of DDHSS as an integrated clinical system.

As illustrated in Figure 4, DDHSS consists of four interconnected components: longitudinal healthcare data acquisition, AI-assisted analytical processing, risk stratification, and healthcare system response. These components operate within an evaluative feedback cycle that supports periodic reassessment of surveillance outcomes and ongoing refinement of individualized CRC risk profiles.

To clarify how the reviewed literature informed the development of DDHSS, a comparative synthesis of the principal evidence domains, existing surveillance approaches, remaining limitations, and corresponding DDHSS responses is presented in Table 3.

Existing approach / evidence domain	Clinical pathway and intended population	Main data inputs and updating pattern	Clinical output	Key limitation identified from the literature	DDHSS positioning
Age-based population screening	Screening; asymptomatic average-risk adults within eligible age ranges	Age, screening eligibility, FIT or colonoscopy protocol; fixed guideline/program intervals	Routine invitation, repeat screening, or colonoscopy after positive screening test	Episodic screening may not capture evolving individual risk between rounds	Adds longitudinal risk monitoring using repeated clinical, laboratory, screening, and historical data rather than age alone
FIT-based screening and prediction	Screening; asymptomatic screening-eligible individuals	Qualitative or quantitative FIT, sometimes with demographic or clinical variables; updated by screening round	Negative screen, repeat FIT, or colonoscopy after positive FIT	Threshold-dependent performance; limited sensitivity for some advanced adenomas, non-bleeding lesions, and heterogeneous risk profiles	Treats FIT as one dynamic input integrated with symptoms, laboratory change, colonoscopy history, and longitudinal clinical data
Diagnostic evaluation for symptomatic individuals	Diagnostic pathway; patients with alarm symptoms or clinically concerning findings	Rectal bleeding, bowel habit change, weight loss, iron-deficiency anemia, abdominal symptoms, laboratory findings, clinical assessment; updated when new triggers appear	Guideline-concordant diagnostic evaluation, including colonoscopy or other work-up when indicated	Symptomatic patients should not be managed as routine surveillance because symptoms may indicate current disease	Does not replace diagnostic evaluation; may support referral prioritization and care coordination when diagnostic triggers are present
Post-polypectomy surveillance	Surveillance; individuals with previous adenoma, serrated lesion, or colorectal precursor lesion	Baseline/follow-up colonoscopy, lesion number, size, histology, resection completeness, surveillance history; updated after endoscopy/histopathology	Shortened or extended surveillance colonoscopy interval according to guideline-based risk	Applies after lesion detection and does not monitor broader population risk before diagnosis	Incorporates prior colonoscopy and histopathology into broader longitudinal risk updating without replacing established intervals
Hereditary CRC surveillance	Specialist surveillance; suspected or confirmed hereditary CRC predisposition	Family history, genetic testing, syndrome criteria, specialist assessment; updated according to syndrome-specific guidance	Intensive colonoscopic and extracolonic surveillance according to hereditary risk	Syndrome-specific pathway should not be replaced by a general population risk score	May support documentation, coordination, and risk updating when hereditary risk information is recorded; specialist surveillance remains primary

Static clinical risk scores	Risk prediction; individuals assessed in screening or clinical settings	Baseline demographic, lifestyle, family history, metabolic, clinical, and sometimes FIT-related variables; usually infrequently updated	Estimated risk category or screening recommendation	Static estimates may become outdated when symptoms, FIT, laboratory values, or endoscopic findings change	Emphasizes repeated recalculation as new longitudinal clinical information becomes available
EHR-based and machine-learning prediction models	Predictive analytics; health record or study-derived populations	EHR variables, laboratory values, diagnoses, medications, FIT, symptoms, demographics, and prior screening history; updating depends on model design	Predicted CRC or advanced neoplasia risk, risk classification, or alert	Often retrospective; limited by missing data, coding variability, calibration, bias, explainability, and external validation	Positions AI as decision support within a monitored cycle requiring validation, calibration, fairness assessment, clinician oversight, and feedback evaluation
DDHSS conceptual framework	Adjunctive longitudinal risk-monitoring and referral-support framework across appropriate pathways	Longitudinal EHR, FIT, symptoms, laboratory change, colonoscopy/histopathology history, demographic risk factors, and prior screening outcomes; recalibrated after new events or periodic reassessment	Risk monitoring, referral support, intensified follow-up recommendation, program evaluation, and feedback-based recalibration	Conceptual framework requiring prospective validation, interoperability, governance, calibration, equity assessment, and capacity evaluation	Integrative architecture, not a replacement for established screening, diagnostic evaluation, post-polypectomy surveillance, hereditary surveillance, or clinical judgment

Table 3. Integrated comparative evidence map of existing CRC risk-management approaches and DDHSS positioning

This integrated comparison clarifies that DDHSS is not proposed as a replacement for established CRC screening, diagnostic evaluation, post-polypectomy surveillance, hereditary surveillance, or validated prediction models. Instead, DDHSS is positioned as an adjunctive longitudinal framework that may connect these pathways through repeated data acquisition, dynamic risk updating, referral support, clinical oversight, and evaluative feedback. Its proposed contribution therefore lies in coordination and integration rather than assumed superiority over existing CRC risk-management approaches. Prospective validation is required before DDHSS can be translated into clinical or public health practice.

To strengthen the practical interpretation of DDHSS, each component of the framework should be understood not only as a conceptual domain but also as an operational module requiring feasibility assessment. Longitudinal healthcare data acquisition would depend on the availability of structured electronic medical records, standardized FIT reporting, laboratory results, colonoscopy and histopathology records, demographic data, family history, and routinely documented clinical encounters.^[11,12,22] Gastrointestinal symptom profiles should therefore be operationalized through structured symptom fields rather than unstructured self-report alone. These may include clinician-verified or patient-reported information on rectal bleeding, persistent change in bowel habit, abdominal pain, unexplained weight loss, anemia-related symptoms, symptom duration, and recurrence pattern.^[26] However, the feasibility of this component would depend on completeness of documentation, interoperability between primary care and referral systems, and standardization of symptom recording.

Risk stratification within DDHSS should also be explicitly linked to clinical action. In a conceptual implementation model, low-risk individuals may continue routine population-based screening when FIT results are negative, no alarm symptoms are present, and no major hereditary or previous advanced neoplasia risk is identified. Intermediate-risk individuals may require intensified follow-up, repeated assessment, or shorter surveillance intervals when risk determinants accumulate, such as persistent gastrointestinal symptoms, metabolic abnormalities, family history, prior non-advanced adenoma, or increasing predicted risk scores. High-risk individuals may require expedited colonoscopy referral or specialist evaluation when positive FIT, alarm symptoms, iron-deficiency anemia, previous advanced adenoma, hereditary risk indicators, or substantially elevated model-predicted risk are present.^[12,22,24,26,27] These categories should not be interpreted as fixed thresholds; rather, they represent a conceptual framework that requires prospective validation, local calibration, and health-system-specific capacity assessment before implementation.

Prospective development of DDHSS would require a prespecified prediction target and time horizon, such as incident CRC, advanced colorectal neoplasia, advanced adenoma, or the need for expedited diagnostic colonoscopy within a defined follow-up period. Risk categories should be derived from calibrated predicted probabilities and decision-curve analysis under local colonoscopy-capacity constraints rather than from arbitrary cutoffs.^[28,31] Risk estimates may be recalculated following a new FIT result, colonoscopy or histopathology finding, clinically meaningful laboratory change, newly documented gastrointestinal symptom, or a prespecified periodic reassessment interval. Therefore, the low-, intermediate-, and high-risk categories proposed in DDHSS should be interpreted as operational concepts requiring prospective validation rather than fixed clinical thresholds. This requirement is particularly important because prediction targets for population screening, diagnostic evaluation, post-polypectomy surveillance, and hereditary cancer surveillance may differ and should not be collapsed into a single undifferentiated risk score.

The first component involves acquisition of healthcare information routinely generated within primary healthcare services. As presented in the framework, the collected datasets include electronic medical records, gastrointestinal symptom profiles, laboratory examination results including FIT, previous screening outcomes, and colonoscopy findings. Demographic characteristics, body mass index, family history of colorectal malignancy, and hereditary risk-related information may additionally contribute to individualized risk assessment. Rather than depending exclusively on isolated screening encounters, DDHSS conceptualizes CRC monitoring as a longitudinal process utilizing cumulative clinical information derived from routine healthcare interactions.

Following data acquisition, aggregated datasets are processed through predictive analytical modules designed to synthesize multiple clinical and screening-related variables for individualized CRC risk assessment. As shown in the “Data Integration and AI-Based Risk Prediction” component, the proposed system incorporates integrated population datasets, machine learning algorithms, and dynamic scoring mechanisms. Within DDHSS, CRC susceptibility is conceptualized as an evolving clinical trajectory rather than a fixed

single-timepoint classification. Consequently, gastrointestinal symptoms, laboratory abnormalities, FIT findings, colonoscopy results, demographic factors, and other clinical variables may progressively influence individualized CRC risk profiles throughout surveillance follow-up.

The resulting analytical outputs subsequently inform stratification into low-, intermediate-, or high-risk categories requiring different levels of clinical monitoring. As illustrated in Figure 4, lower-risk populations may continue routine screening protocols, whereas intermediate-risk individuals may undergo intensified follow-up. Higher-risk populations may require colonoscopy referral and closer surveillance. Importantly, surveillance categorization within DDHSS remains adaptable to newly acquired clinical information and changing patient risk trajectories.

The final component involves healthcare system response and implementation of surveillance strategies. Outputs generated from predictive analytical processes may support clinical warning systems, targeted screening recommendations, epidemiological monitoring, cohort analysis, trend observation, and program evaluation. Through this mechanism, DDHSS extends beyond individualized prediction models and supports a population-oriented surveillance structure integrating preventive medicine, healthcare informatics, and AI-assisted clinical decision support.

A major conceptual feature of DDHSS lies in the incorporation of an evaluative feedback loop (“Evaluative Feedback Cycle”) connecting surveillance outcomes back into the analytical process. This iterative mechanism enables periodic reassessment of surveillance effectiveness, refinement of predictive performance, recalibration of surveillance categories, and more efficient allocation of healthcare resources over time. Accordingly, the proposed system emphasizes continuous surveillance reassessment and longitudinal continuity rather than static one-time risk classification.

In contrast to conventional age-based screening strategies, DDHSS emphasizes integration of continuously updated clinical information, repeated reassessment of CRC susceptibility, and more adaptive surveillance allocation. Such an approach may facilitate earlier identification of individuals undergoing progressive risk evolution despite previous negative screening findings while simultaneously improving distribution of diagnostic resources toward populations demonstrating persistently elevated or progressively increasing CRC risk.

Nevertheless, DDHSS remains a hypothesis-generating conceptual model requiring further prospective validation before broader implementation can be considered. Future investigations should prioritize multicenter validation studies, interoperability assessment across heterogeneous healthcare systems, economic evaluation, longitudinal predictive stability analysis, and ethical governance related to privacy protection and responsible AI implementation.

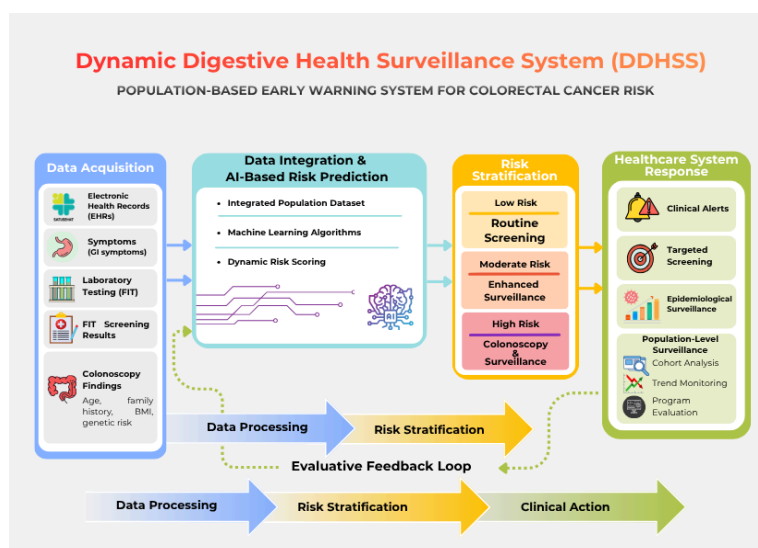


Figure 4. Conceptual framework of the Dynamic Digestive Health Surveillance System (DDHSS) integrating longitudinal clinical information, predictive risk modeling, and responsive colorectal cancer surveillance within primary healthcare settings.

3.7 Strengths, Limitations, and Bias Considerations

This review has several strengths. First, it addresses colorectal cancer surveillance from an integrative perspective by linking population screening, longitudinal risk evolution, post-screening residual risk, healthcare data infrastructure, and AI-assisted prediction within a single conceptual framework. Second, the review used a structured search strategy across multiple databases and applied predefined eligibility criteria, evidence-mapping domains, and comparative synthesis dimensions. Third, the proposed DDHSS framework was positioned cautiously as an adjunctive risk-monitoring and referral-support architecture rather than as a replacement for established screening, diagnostic evaluation, post-polypectomy surveillance, hereditary surveillance, or clinical judgment.

Several limitations should also be acknowledged. Although the literature search was structured, this review was not registered as a systematic review and did not apply a formal meta-analytic protocol. Screening was not performed independently in duplicate at the initial stage; therefore, residual selection error remains possible despite subsequent checking by a second author. The review is also susceptible to selection bias and publication bias because relevant unpublished studies, non-indexed reports, or studies outside the selected databases may not have been captured.

Heterogeneity across the included literature limited direct comparison between studies. The reviewed publications differed in population characteristics, screening settings, predictor definitions, FIT thresholds, colonoscopy outcomes, follow-up duration, analytical methods, validation strategies, and reporting quality. As a result, quantitative synthesis was not performed, and the conclusions should be interpreted as comparative narrative synthesis rather than pooled evidence of effectiveness. This heterogeneity also limits the extent to which findings from one healthcare system or screening program can be generalized to other settings.

Contextual bias and overgeneralization are additional concerns. Many studies on risk prediction, EHR-based modeling, and AI-assisted CRC prediction were developed in specific healthcare systems with particular data structures, population characteristics, referral pathways, and colonoscopy capacities. Their external validity may be limited in settings with different screening coverage, digital infrastructure, health-seeking behavior, resource availability, or burden of colorectal neoplasia. Therefore, DDHSS should not be interpreted as a universally applicable model without local calibration and implementation assessment.

The evidence supporting AI-assisted CRC prediction also remains limited by methodological and implementation challenges. Many predictive models were retrospective, incompletely reported calibration and subgroup performance, and had limited prospective or external validation. Potential algorithmic bias may arise from missing data, coding variability, unequal healthcare access, imbalanced training populations, and underrepresentation of specific demographic or clinical subgroups. These issues may affect model transportability, fairness, explainability, and clinical safety if AI outputs are implemented without clinician oversight and post-deployment monitoring.

Finally, DDHSS remains a hypothesis-generating conceptual framework. The present review does not provide direct evidence that DDHSS is superior to existing CRC screening, diagnostic, post-polypectomy, hereditary surveillance, or prediction-based approaches. Its proposed contribution is limited to conceptual integration of longitudinal data acquisition, adaptive risk updating, referral support, and evaluative feedback. Prospective validation, calibration, clinical utility assessment, equity evaluation, cost-effectiveness analysis, and real-world implementation studies are required before DDHSS can be translated into clinical or public health practice.

4. Conclusion

Conventional age-based and episodic colorectal cancer screening approaches possess substantial limitations in identifying high-risk individuals in a timely manner. Current evidence indicates that CRC susceptibility evolves progressively under the influence of biological, metabolic, genetic, and environmental determinants.

DDHSS should therefore be interpreted as a proposed integrative architecture rather than a validated clinical system. Its incremental value over established screening, diagnostic evaluation, post-polypectomy surveillance, hereditary surveillance, and prediction-based approaches remains unproven and requires prospective validation before clinical or public health implementation.

Further studies are required to evaluate clinical effectiveness, implementation feasibility, economic impact, interoperability, and external validity of the proposed framework across diverse healthcare settings.

5. Declaration of AI-Assisted Tools

The authors used AI-assisted language tools to support language editing, organization, and formatting. All scientific content, interpretation, citations, and final manuscript decisions were reviewed and approved by the authors. No AI tool was used as an autonomous source of evidence or as a substitute for authorial judgment.

6. Acknowledgements

Not applicable.

7. Conflict of Interest

The authors declare that no conflicts of interest exist regarding the publication of this review.

References

- [1] Maida M, Dahiya DS, Shah YR, Tiwari A, Gopakumar H, Vohra I, et al. Screening and surveillance of colorectal cancer: a review of the literature. *Cancers (Basel)*. 2024;16(15):2746. doi:10.3390/cancers16152746.
- [2] Hua H, Jiang Q, Sun P, Xu X. Risk factors for early-onset colorectal cancer: systematic review and meta-analysis. *Front Oncol*. 2023;13:1132306. doi:10.3389/fonc.2023.1132306.
- [3] Wang JD, Xu GS, Hu XL, Li WQ, Yao N, Han FZ, et al. The histologic features, molecular features, detection and management of serrated polyps: a review. *Front Oncol*. 2024;14:1356250. doi:10.3389/fonc.2024.1356250.
- [4] Selby K, Jensen CD, Lee JK, Doubeni CA, Schottinger JE, Zhao WK, et al. Influence of varying quantitative fecal immunochemical test positivity thresholds on colorectal cancer detection: a community-based cohort study. *Ann Intern Med*. 2018;169(7):439-447. doi:10.7326/M18-0244.
- [5] Liles EG, Perrin N, Rosales AG, Smith DH, Feldstein AC, Mosen DM, et al. Performance of a quantitative fecal immunochemical test for detecting advanced colorectal neoplasia: a prospective cohort study. *BMC Cancer*. 2018;18(1):509. doi:10.1186/s12885-018-4402-x.
- [6] Liu Y, Fang Y, Xu Y, Wang S, Wu Y, Bai K, et al. Colonoscopy outcomes of primary screening negative participants highlight the missed diagnosis problem of colorectal cancer screening: an observational study from Yuexiu district in Guangzhou, China. *Front Oncol*. 2025;15:1642326. doi:10.3389/fonc.2025.1642326.
- [7] Thayalasekaran S, Frazzoni L, Antonelli G, Fuccio L, Radaelli F, Andrealli A, et al. Endoscopic technological innovations for neoplasia detection in organized colorectal cancer screening programs: a systematic review and meta-analysis. *Gastrointest Endosc*. 2020;92(4):840-847.e9. doi:10.1016/j.gie.2020.06.046.
- [8] Heisser T, Kretschmann J, Hagen B, Niedermaier T, Hoffmeister M, Brenner H. Prevalence of colorectal neoplasia 10 or more years after a negative screening colonoscopy in 120000 repeated screening colonoscopies. *JAMA Intern Med*. 2023;183(3):183-190. doi:10.1001/jamainternmed.2022.6215.
- [9] Wang L, Lin Y, Liao Y, Shen J. Association between triglyceride-glucose index and risk of colorectal carcinogenesis: a meta-analysis of observational studies. *Front Oncol*. 2025;15:1569824. doi:10.3389/fonc.2025.1569824.
- [10] Cheraghpour M, Askari M, Tierling S, Shojae S, Sadeghi A, Ketabi Moghadam P, et al. A systematic review and meta-analysis for the association of the insulin-like growth factor-1 pathway genetic polymorphisms with colorectal cancer susceptibility. *Front Oncol*. 2023;13:1168942. doi:10.3389/fonc.2023.1168942.
- [11] Yau STY, Hung CT, Leung EYM, Chong KC, Lee A, Yeoh EK. Predicting the risk of colorectal cancer among diabetes patients using a random survival forest-guided approach. *Front Oncol*. 2024;14:1457446. doi:10.3389/fonc.2024.1457446.
- [12] Zhen J, Li J, Liao F, Zhang J, Liu C, Xie H, et al. Development and validation of machine learning models for young-onset colorectal cancer risk stratification. *NPJ Precis Oncol*. 2024;8(1):1-11. doi:10.1038/s41698-024-00719-2.
- [13] Baethge C, Goldbeck-Wood S, Mertens S. SANRA-a scale for the quality assessment of narrative review articles. *Res Integr Peer Rev*. 2019;4:5. doi:10.1186/s41073-019-0064-8.
- [14] Djinbachian R, Lafontaine ML, Anderson JC, Pohl H, Dufault T, Boivin M, et al. Risk of total metachronous advanced neoplasia at surveillance colonoscopy after detection of serrated lesions: a matched case-cohort study. *Endoscopy*. 2023;55(8):728-736. doi:10.1055/a-2020-6797.

- [15] Baile-Maxía S, Mangas-Sanjuán C, Ladabaum U, Sánchez-Ardila C, Sala-Miquel N, Hassan C, et al. Risk factors for metachronous colorectal cancer or advanced lesions after endoscopic resection of serrated polyps: a systematic review and meta-analysis. *Gastrointest Endosc.* 2024;100(4):605-615.e14. doi:10.1016/j.gie.2024.05.021.
- [16] Shono T, Oyama S, Oda Y, Yokomine K, Murakami Y, Miyamoto H, et al. Risk stratification of advanced colorectal neoplasia after baseline colonoscopy: cohort study of 17 Japanese community practices. *Dig Endosc.* 2020. doi:10.1111/den.13516.
- [17] Bjerrum A, Lindebjerg J, Andersen O, Fischer A, Lynge E. Long-term risk of colorectal cancer after screen-detected adenoma: experiences from a Danish gFOBT-positive screening cohort. *Int J Cancer.* 2020;147(4):940-947. doi:10.1002/ijc.32850.
- [18] Lieberman D, Sullivan BA, Hauser ER, Qin X, Musselwhite LW, O’Leary MC, et al. Baseline colonoscopy findings associated with 10-year outcomes in a screening cohort undergoing colonoscopy surveillance. *Gastroenterology.* 2020;158(4):862-874.e8. doi:10.1053/j.gastro.2019.07.052.
- [19] Dubé C, Yakubu M, McCurdy BR, Lischka A, Koné-Péfoyo A, Walker MJ, et al. Risk of advanced adenoma, colorectal cancer, and colorectal cancer mortality in people with low-risk adenomas at baseline colonoscopy: a systematic review and meta-analysis. *Am J Gastroenterol.* 2017;112(12):1790-1801. doi:10.1038/ajg.2017.360.
- [20] Baile-Maxía S, Mangas-Sanjuán C, Ladabaum U, Hassan C, Rutter MD, Bretthauer M, et al. Risk factors for metachronous colorectal cancer or advanced adenomas after endoscopic resection of high-risk adenomas. *Clin Gastroenterol Hepatol.* 2023;21(3):630-643. doi:10.1016/j.cgh.2022.12.005.
- [21] Jodal HC, Akwiwu EU, Lemmens M, Delis-van Diemen PM, Klotz D, Leon LG, et al. Risk prediction of metachronous colorectal cancer from molecular features of adenomas: a nested case-control study. *Cancer Res Commun.* 2024. doi:10.1158/2767-9764.CRC-23-0186.
- [22] Issaka RB, Chan AT, Gupta S. AGA clinical practice update on risk stratification for colorectal cancer screening and post-polypectomy surveillance: expert review. *Gastroenterology.* 2023;165(5):1280-1291. doi:10.1053/j.gastro.2023.06.033.
- [23] Zhang Y, Sheng C, Fan Z, Liu Y, Liu X, Duan H, et al. Risk-stratified screening and colorectal cancer incidence and mortality: a retrospective study from the Prostate, Lung, Colorectal, and Ovarian Cancer Screening Trial. *Prev Med.* 2024;187:108117. doi:10.1016/j.ypmed.2024.108117.
- [24] Frazzoni L, Pecere S, Hassan C, Fuccio L, del Vecchio LE, Fabbri C, et al. A predictive model based on quantitative fecal immunochemical test can stratify the risk of colorectal cancer in an organized screening program. *Clin Gastroenterol Hepatol.* 2025;23(7):1247-1254.e7. doi:10.1016/j.cgh.2024.09.036.
- [25] Pu J, Zhou B, Yao Y, Wu Z, Wen Y, Xu R, et al. Development and validation of a lifestyle-based 10-year risk prediction model of colorectal cancer for early stratification: evidence from a longitudinal screening cohort in China. *Nutrients.* 2025;17(11):1898. doi:10.3390/nu17111898.
- [26] Hampton JS, Kenny RPW, Rees CJ, Hamilton W, Eastaugh C, Richmond C, et al. The performance of FIT-based and other risk prediction models for colorectal neoplasia in symptomatic patients: a systematic review. *eClinicalMedicine.* 2023;63:102204. doi:10.1016/j.eclinm.2023.102204.
- [27] Vanaclocha-Espí M, Romeo-Cervera P, Castan-Cameo S, Pérez-Sanz E, Ibañez J, Llorens-Ivorra C, et al. Risk of advanced adenoma detection in colorectal cancer screening programmes according to personal characteristics and screening history. *Int J Cancer.* 2026;158(5):1272-1280. doi:10.1002/ijc.70182.
- [28] Collins GS, Moons KGM, Dhiman P, Riley RD, Beam AL, van Calster B, et al. TRIPOD+AI statement: Updated guidance for reporting clinical prediction models that use regression or machine learning methods. *BMJ.* 2024. doi:10.1136/bmj-2023-078378 PubMed PMID: 38626948.
- [29] Vasey B, Nagendran M, Campbell B, Clifton DA, Collins GS, Denaxas S, et al. Reporting guideline for the early-stage clinical evaluation of decision support systems driven by artificial intelligence: DECIDE-AI. *Nat Med.* 2022;28(5):924-933. doi:10.1038/s41591-022-01772-9.
- [30] Yang X, Xu J, Ji H, Li J, Yang B, Wang L. Early prediction of colorectal adenoma risk: leveraging large-language model for clinical electronic medical record data. *Front Oncol.* 2025;15:1508455. doi:10.3389/fonc.2025.1508455.
- [31] Moons KGM, Damen JAAG, Kaul T, Dhiman P, Collins GS, Reitsma JB, et al. PROBAST+AI: an updated quality, risk of bias, and applicability assessment tool for prediction models using regression or artificial intelligence methods. *BMJ.* 2025;388:e082505. doi:10.1136/bmj-2024-082505.
- [32] World Health Organization. Ethics and governance of artificial intelligence for health: WHO guidance. Geneva: World Health Organization; 2021.

- [33] Chen RJ, Wang JJ, Williamson DFK, Chen TY, Lipkova J, Lu MY, et al. Algorithmic fairness in artificial intelligence for medicine and healthcare. *Nat Biomed Eng.* 2023;7(6):719-742. doi:10.1038/s41551-023-01056-8.
- [34] Patel SG, May FP, Anderson JC, Burke CA, Dominitz JA, Gross SA, et al. Updates on age to start and stop colorectal cancer screening: recommendations from the U.S. Multi-Society Task Force on Colorectal Cancer. *Gastrointest Endosc.* 2022;95(1):1-15. doi:10.1016/j.gie.2021.06.012.
- [35] Pham J, Laven-Law G, Symonds EL, Wassie MM, Cock C, Winter JM. Faecal immunochemical tests can improve colonoscopy triage in patients with iron deficiency: a systematic review and meta-analysis. *Crit Rev Oncol Hematol.* 2024;201:104439. doi:10.1016/j.critrevonc.2024.104439.
- [36] Quintero E, Carrillo-Palau M, Leoz ML, Cubiella J, Gargallo Puyuelo C, Lanás A, et al. Risk of advanced neoplasia in first-degree relatives with colorectal cancer: a large multicenter cross-sectional study. *PLoS Med.* 2016;13(5):e1002008. doi:10.1371/journal.pmed.1002008.
- [37] Weigl K, Thomsen H, Balavarca Y, Hellwege JN, Shrubsole MJ, Brenner H. Genetic risk score is associated with prevalence of advanced neoplasms in a colorectal cancer screening population. *Gastroenterology.* 2018;155(1):88-98.e10. doi:10.1053/j.gastro.2018.03.030.
- [38] Yu Z, Li B, Zhao S, Du J, Zhang Y, Liu X, et al. Uptake and detection rate of colorectal cancer screening with colonoscopy in China: a population-based, prospective cohort study. *Int J Nurs Stud.* 2024;153:104728. doi:10.1016/j.ijnurstu.2024.104728.
- [39] Willauer AN, Zuckerman MJ, Alomari A, Alvarado LA, Salaiz R, Casner N, et al. Colorectal neoplasia prevalence in a predominantly Hispanic community: results from a colorectal cancer screening program in Texas. *Am J Med Sci.* 2022;364(4):394-403. doi:10.1016/j.amjms.2022.03.013.
- [40] Dong X, Du L, Luo Z, Xu Y, Wang C, Wang F, et al. Combining fecal immunochemical testing and questionnaire-based risk assessment in selecting participants for colonoscopy screening in the Chinese National Colorectal Cancer Screening Program: a population-based cohort study. *PLoS Med.* 2024;21(2):e1004340. doi:10.1371/journal.pmed.1004340.
- [41] Song D, Wang F, Ju Y, He Q, Sun T, Deng W, et al. Application and development of noninvasive biomarkers for colorectal cancer screening: a systematic review. *Int J Surg.* 2023;109(4):925-935. doi:10.1097/JS9.0000000000000260.
- [42] Zorzi M, Hassan C, Capodaglio G, Narne E, Turrin A, Baracco M, et al. Divergent long-term detection rates of proximal and distal advanced neoplasia in fecal immunochemical test screening programs: a retrospective cohort study. *Ann Intern Med.* 2018;169(9):602-609. doi:10.7326/M18-0855.
- [43] Heer E, Ruan Y, Pader J, Mah B, Ricci C, Nguyen T, et al. Performance of the fecal immunochemical test for colorectal cancer and advanced neoplasia in individuals under age 50. *Prev Med Rep.* 2023;32:102124. doi:10.1016/j.pmedr.2023.102124.
- [44] Symonds EL, Dix M, Wassie MM, Bulamu NB, Young GP, Winter JM. Is blood the new stool? Status of blood tests for CRC screening. *Best Pract Res Clin Gastroenterol.* 2025;102049. doi:10.1016/j.bpg.2025.102049.
- [45] Chen H, Werner S, Brenner H. Fresh vs frozen samples and ambient temperature have little effect on detection of colorectal cancer or adenomas by a fecal immunochemical test in a colorectal cancer screening cohort in Germany. *Clin Gastroenterol Hepatol.* 2017;15(10):1547-1556.e5. doi:10.1016/j.cgh.2016.10.018.
- [46] van Liere ELSA, van Dijk LJ, Bosch S, Vermeulen L, Heymans MW, Burchell GL, et al. Urinary volatile organic compounds for colorectal cancer screening: a systematic review and meta-analysis. *Eur J Cancer.* 2023;186:69-82. doi:10.1016/j.ejca.2023.03.002.
- [47] Winter JM, Cornthwaite KJ, Young GP, Wilson C, Chen G, Woodman R, et al. FIT for purpose: study protocol for a randomized controlled trial to personalize surveillance colonoscopy for individuals at elevated risk of colorectal cancer. *Int J Colorectal Dis.* 2024. doi:10.1007/s00384-023-04493-8.
- [48] He X, Lv X, Zhang B, Ying X, Hu C, Zhou X, et al. Adenoma detection rate in average-risk population: an observational consecutive retrospective study. *Cancer Control.* 2023;30:10732748231193243. doi:10.1177/10732748231193243.
- [49] Carballal S, Sánchez-García A, Moreira L, Cuellar-Monterrubio JE, Bernuy J, Daca M, et al. Prevalence of adenomatous polyposis in a fecal immunochemical test-based colorectal cancer screening program and risk of advanced neoplasia during follow-up. *Endoscopy.* 2022;54(7):688-697. doi:10.1055/a-1660-5353.
- [50] Vithayathil M, Smith S, Goryachev S, Naylor J, Song M. Development of a large colonoscopy-based longitudinal cohort for integrated research of colorectal cancer: Partners Colonoscopy Cohort. *Dig Dis Sci.* 2022;67(2):473-480. doi:10.1007/s10620-021-06882-x.

- [51] Chi T, Liu Y, Yang C, Jia Q, Zhao Q. Analysis of clinical characteristics and risk factors on serrated polyps with synchronous advanced adenoma in elderly and non-elderly people: a retrospective cohort study. *BMJ Open*. 2024;14:e083930. doi:10.1136/bmjopen-2024-083930.
- [52] Zhang J, Sun H, Xiong F, Lei S, Zhou G, Xiao X, et al. The absolute number of small and diminutive adenomas with high-grade dysplasia is substantially higher compared with large adenomas: a retrospective pooled study. *Front Oncol*. 2024;14:1294745. doi:10.3389/fonc.2024.1294745.
- [53] Yu F, Guo Y, Wang H, Feng J, Jin Z, Chen Q, et al. Type 2 diabetes mellitus and risk of colorectal adenoma: a meta-analysis of observational studies. *BMC Cancer*. 2016;16:642. doi:10.1186/s12885-016-2685-3.
- [54] Bouras E, Kim AE, Lin Y, Morrison J, Du M, Albanes D, et al. Genome-wide interaction analysis of folate for colorectal cancer risk. *Am J Clin Nutr*. 2023;118(5):881-891. doi:10.1016/j.ajcnut.2023.08.010.
- [55] Chen H, Li N, Shi JF, Ren J, Liu C, Zhang Y, et al. Comparative evaluation of novel screening strategies for colorectal cancer screening in China (TARGET-C): a study protocol for a multicentre randomised controlled trial. *BMJ Open*. 2019;9(4):e025935. doi:10.1136/bmjopen-2018-025935.
- [56] Mo S, Dai W, Wang H, Lan X, Ma C, Su Z, et al. Early detection and prognosis prediction for colorectal cancer by circulating tumour DNA methylation haplotypes: a multicentre cohort study. *eClinicalMedicine*. 2023;55:101717. doi:10.1016/j.eclinm.2022.101717.
- [57] Silva-Illanes N, Espinoza M. Critical analysis of Markov models used for the economic evaluation of colorectal cancer screening: a systematic review. *Value Health*. 2018;21(7):858-873. doi:10.1016/j.jval.2017.11.010.