QBIO490 Literature Presentation

COLORECTAL CANCER

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RESEARCH PAPER A Colorectal cancer detected by liquid biopsy 2 years prior to clinical diagnosis in the HUNT study

REVIEW PAPER A Review of Colorectal Cancer in Terms of Epidemiology, Risk Factors, Development, Symptoms and Diagnosis

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A Review of Colorectal Cancer in Terms of Epidemiology, Risk Factors, Development, Symptoms and Diagnosis

Tomasz Sawicki, Monika Ruszkowska, Anna Danielewicz, Ewa Niedźwiedzka, Tomasz Arlukowicz, and Katarzyna E. Pryzylowicz

Published in *Cancers* by MDPI on 22 April 2021

Paper Aims to Provide an Update on Colorectal Cancer to Encourage Future Findings

01

Systematize available literature & data on epidemiology, diagnosis, type, nature of symptoms and disease stages

02

Inform strategies in controlling the disease's burden through population-based preventative initiatives

03

Update individuals about current patterns & temporal trends of colorectal cancer from a global perspective

04

Encourage the development of future strategies in prevention & treatment programs to reduce disease incidence

There Exists a Correlation b/n HDI & Colorectal Incidence

POLAND

INDIA

CRC incidence & mortality occurs in medium-high HDI countries

Developed countries are at the highest risk of colon cancer

METHODOLOGY

Promising Research Is Ongoing to Mitigate Occurrence and Improve Prognosis

Studying lifestyle may aid researchers

MORE INFO NEEDED

Despite having promising results in reducing the burden of colon cancer, current evidence is still insufficient

Correlation between sedentary lifestyle, smoking, obesity, etc.

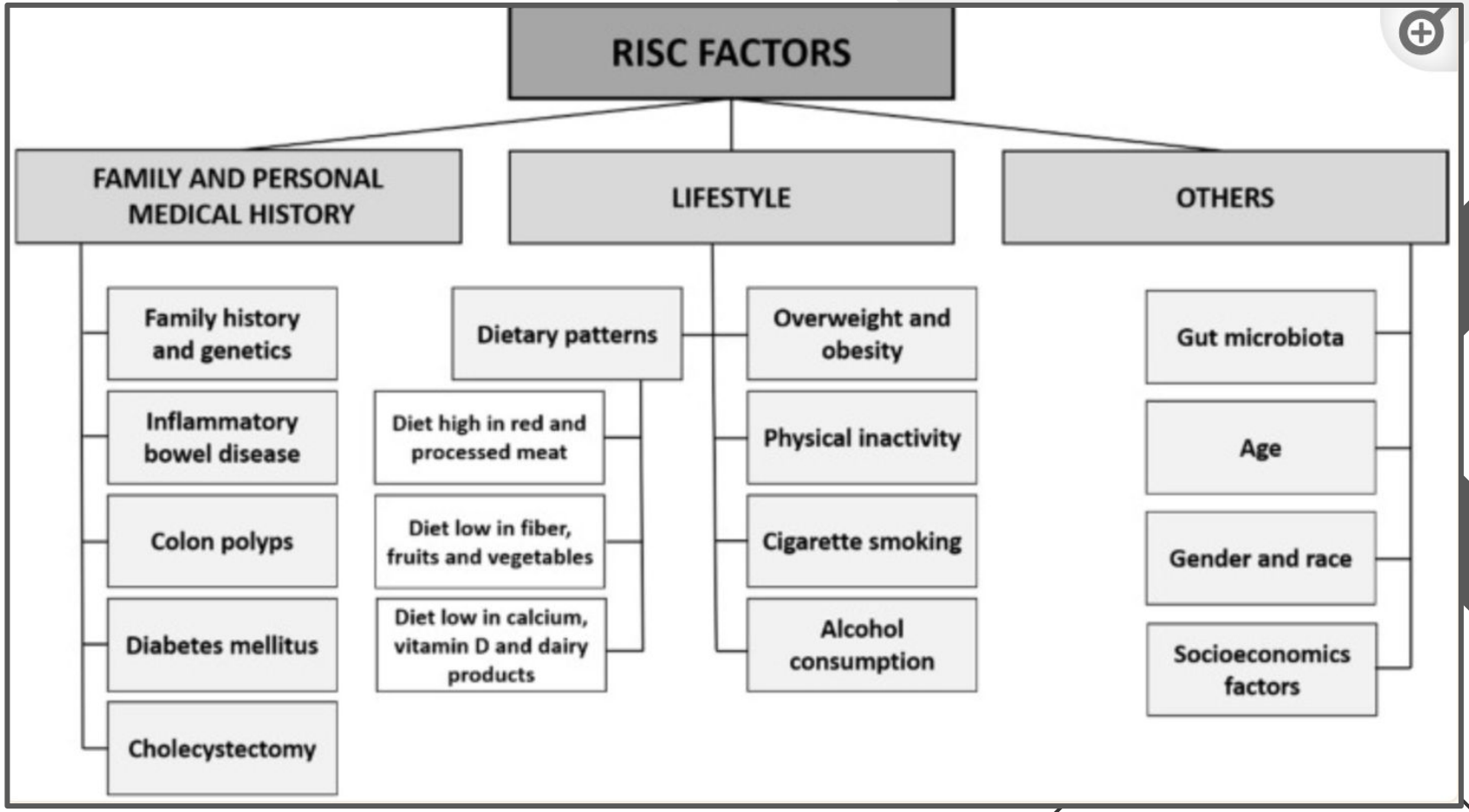
RISK FACTORS

Lifestyle, hereditary, ecological factors contribute to colorectal cancer

GI symptoms may suggest colorectal cancer

DIAGNOSIS

Screening diagnostic methods include FIT, gFOBT, colonoscopy, sigmoidoscopy, and digital rectal exam


RISC FACTORS
FAMILY AND PERSONAL MEDICAL HISTORY
LIFESTYLE
OTHERS
Family history and genetics
Inflammatory bowel disease
Colon polyps
Diabetes mellitus
Cholecystectomy
Dietary patterns
Diet high in red and processed meat
Diet low in fiber, fruits and vegetables
Diet low in calcium, vitamin D and dairy products
Overweight and obesity
Physical inactivity
Cigarette smoking
Alcohol consumption
Gut microbiota
Age
Gender and race
Socioeconomics factors

RESEARCH PAPER

A Colorectal cancer detected by liquid biopsy 2 years prior to clinical diagnosis in the HUNT study

Siv S. Brenne, Poul Henning Madsen, Inge Søkilde Pedersen, Kristian Hveem, Frank Skorpen, Henrik Bygum Krarup, Guro F. Giskeødegård, and Eivor A. Laugsand

Published in *British Journal of Cancer by Nature* on 12 July 2023

Hypothesis Claims Early Diagnosis w/ Liquid Biopsy

- The authors hypothesize that a circulating tumor DNA (ctDNA) test, also termed liquid biopsy, can diagnose colorectal cancer (CRC) earlier than current clinical screening methods
    - The expectation is to establish a possible diagnosis by ctDNA up to 2 years before standard screening

Methodology Is Enabled by a Large Population Study

Retrospective study drawing from blood samples collected during a population health panel in Nord- Trøndelag county, Norway

Selected 106 samples diagnosed with CRC within 2 years of collection

Performed ctDNA testing on the cancer-diagnosed samples plus 106 controls

Extracted DNA with a commercial method, qualified tumor DNA by analyzing promoter gene methylation

- Searched for 20 different genes present in early diagnosis of CRC
- Based on combined sensitivity and specificity, 8 genes of interest were selected and analyzed

Key Findings Result in a Genomics-based Diagnostic Panel

Identified most sensitive colorectal cancer gene markers: NDRG4 and WNT5A

Identified most specific colorectal cancer gene markers: AGBL4, BMP3, FLI1, IKZF1, NPTX2, SFRP1, SFRP2, SDC2, SLC8A1 and VIM

Developed diagnostic panel of 8 significant ctDNA markers. 2 out of 8 found means CRC positive

Key Findings Demonstrate Curative Benefits from ctDNA

Confirmed the hypothesis that screening with ctDNA test diagnosed colorectal cancer up to 2 years before other established methods

Study reached a positive predictive value of 75.4%

Research is highly clinically relevant if ctDNA testing becomes a standard screening tool that can detect earlier and improve prognosis

FIGURE 1 RESULTS

Receiver operating characteristic curve

Plot of true positive vs. false positive rate

AUC > 0.5, predictive power

p<.001, strong evidence against null hypothesis

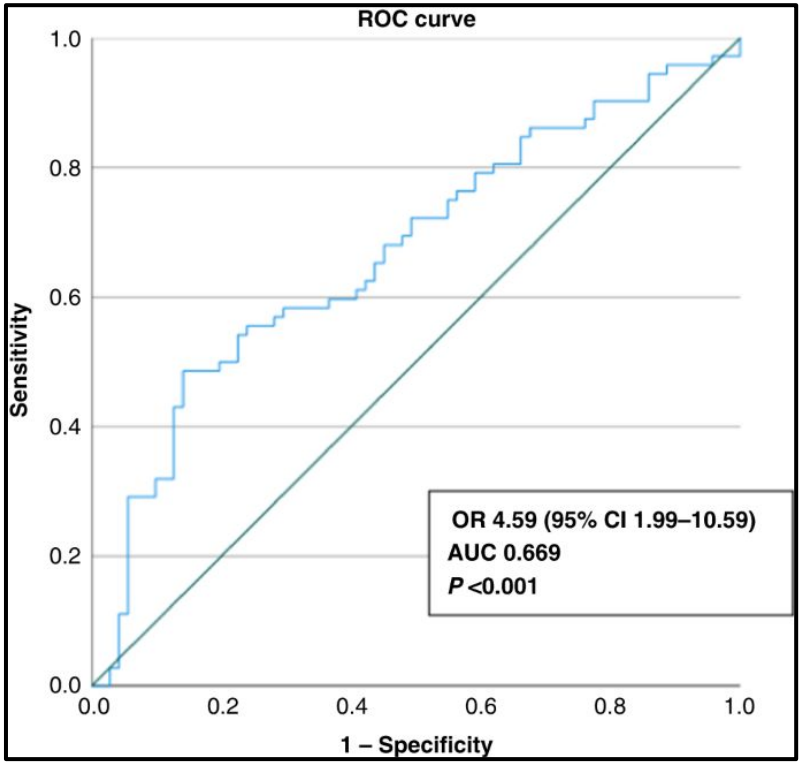
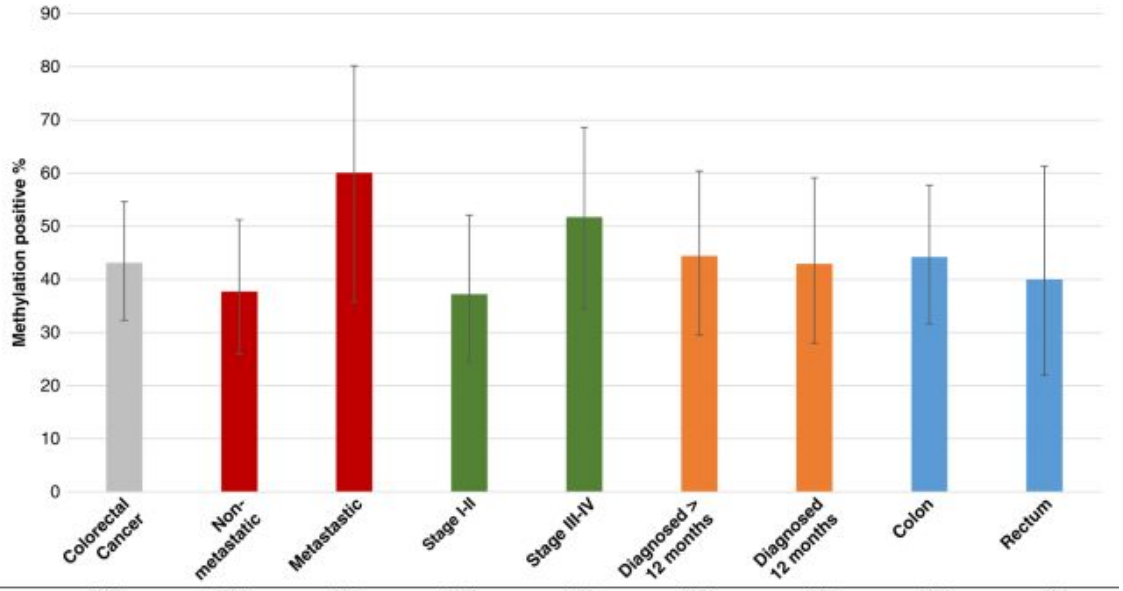


FIGURE 2 RESULTS



n/N	31/72	20/53	9/15	16/43	15/29	16/36	15/35	23/52	8/20
% (95% CI)	43.1 (32.3–54.6)	37.7 (25.9–51.2)	60.0 (35.7–80.2)	37.2 (24.4–52.1)	51.7 (34.4–68.6)	44.4 (29.5–60.4)	42.9 (28.0–59.1)	44.2 (31.6–57.7)	40.0 (21.9–61.3)
OR (95% CI	4.59 (1.99–10.59)	3.68 (1.56–8.67)	5.76 (1.64–20.21)	3.79 (1.49–9.63)	6.04 (2.19–16.64)	4.13 (1.57–10.87)	5.13 (1.95–13.44)	4.51 (1.86–10.94)	4.76 (1.49–15.25)
P value	**< 0.001**	**0.003**	**0.006**	**0.005**	**< 0.001**	**0.004**	**< 0.001**	**< 0.001**	**0.009**

- DNA methylation regulates gene expression
  - DNA sequence unaltered
- Specimen positive if ≥ 2 markers were positive
- All p-values significant
- 95% confidence interval

Future Research QUESTIONS & Directions

Validation & differentiated 1:1 comparisons of new liquid biopsies w/ standard tools (i.e., ctDNA vs. colonoscopy by CRC stage)

What new gene, protein and miRNA tumor markers will help diagnose colorectal cancer in primary & secondary care?

Why are studies on the relationship b/n SES & CRC incidence inconsistent & what can we do to improve our understanding of this relationship?

COMPARING & CONTRASTING

REVIEW PAPER	SIMILARITIES	RESEARCH PAPER
• Risk factor focus	• Colorectal Cancer	• Provides results from a clinical study
• Insufficient evidence	• Recommend further studies	• Methylation markers in plasma
• Inconclusive	• High Clinical Relevance	• Original CRC Research
• Genomics, Proteomics, and Transcriptomics	• Up-to-date information	• Genomics
• Literature focus		• Conclusion supports hypothesis
• Focus on “why” rather than “how”		• Data focus

THANK YOU FOR LISTENING :)