

# Intestinal cancer and the risk for other cancer in the same person

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| <b>Submission date</b><br>11/06/2023   | <b>Recruitment status</b><br>No longer recruiting | <input type="checkbox"/> Prospectively registered<br><input type="checkbox"/> Protocol            |
| <b>Registration date</b><br>16/06/2023 | <b>Overall study status</b><br>Completed          | <input type="checkbox"/> Statistical analysis plan<br><input checked="" type="checkbox"/> Results |
| <b>Last Edited</b><br>15/06/2023       | <b>Condition category</b><br>Cancer               | <input type="checkbox"/> Individual participant data  |

## Plain English summary of protocol

### Background and study aims

Disparities between tumors arising via different carcinogenetic pathways have not been studied systematically. This study evaluated the differences in the risk for non-intestinal cancer between patients with intestinal cancer originating from different carcinogenetic statuses.

### Who can participate?

Adult patients with histologically confirmed colorectal cancer

### What does this study involve?

This is a retrospective cohort study describing the association between intestinal and not intestinal cancer among patients with different carcinogenetic backgrounds. This retrospective European multicenter cohort study included 1706 CRC patients treated between 1986 and 2019, in three different countries.

### What are the possible benefits and risks of participating?

The possible benefit is to understand the relationship between different types of cancer in the same patient. There are no risks for participants.

### Where is the study run from?

Umeå University (Sweden)

### When is the study starting and how long is it expected to run for?

January 2013 to March 2021

### Who is funding the study?

1. Faculty of Medicine at Umeå University
2. Cancer Foundation Finland
3. Cancer Research Foundation in Northern Sweden
4. Nordic Cancer Union
5. The Northern Healthcare Regional Association

Who is the main contact?

Ioannis Gkekas (Senior Consultant Surgeon), ioannis.gkekas@umu.se (Sweden)

## Contact information

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Principal investigator

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## **Additional identifiers**

### **Clinical Trials Information System (CTIS)**

Nil known

### **ClinicalTrials.gov (NCT)**

Nil known

### **Protocol serial number**

Nil known

## **Study information**

### **Scientific Title**

Sporadic deficient mismatch repair in colorectal cancer increases the risk for non-colorectal malignancy

### **Acronym**

registerMMR

### **Study objectives**

A higher association between sporadic deficient mismatch repair (dMMR) status and the risk of non-colorectal malignancy in patients with known colorectal cancer (CRC)

### **Ethics approval required**

Ethics approval required

### **Ethics approval(s)**

approved 02/12/2014, Regional Medical Review Board in Umeå, Department of Medical Strengthening (Regional etikprövningsnämnden i Umeå Avdelningen för Medicinsk Forskning) (Samverkanshuset, C/o Umeå Universitet, Umeå, 90187, Sweden; +46 (0)104750800; [registrator@etikprovning.se](mailto:registrator@etikprovning.se)), ref: 2014-371-31M

### **Study design**

Multicenter retrospective cohort study

### **Primary study design**

Observational

## Study type(s)

Screening

## Health condition(s) or problem(s) studied

Association between sporadic dMMR status and the risk of non-colorectal malignancy in patients with known colorectal cancer

## Interventions

This study is a retrospective cohort describing the association between intestinal and not intestinal cancer among patients with different carcinogenetic backgrounds. This retrospective European multicenter cohort study included 1706 CRC patients treated between 1986 and 2019, in three different countries. The proficiency (pMMR) or deficiency (dMMR) of mismatch repair was determined by immunohistochemistry. Cases were analyzed for BRAFV600E mutation, and BRAF mutation cases were further analyzed for hypermethylation status in the promotor region of MLH1 in order to distinguish between sporadic and hereditary cases. Scandinavian patients were matched against their respective National Cancer Registries. Thorough scrutiny of medical files was performed for the Czech cohort to identify any non-colorectal malignancy within 20 years prior to or after the diagnosis of CRC. Poisson regression analysis was performed to identify the incidence rate of non-colorectal malignancy. For validation purposes, standardized incidence ratios (SIR) were calculated for each cancer reported, adjusted for age, year, and sex.

## Intervention Type

Other

## Primary outcome(s)

The risk for non-colorectal malignancy before and after this diagnosis, compared to patients with different MMR tumors is measured using Incidence Rate Ratio (IRR) in both the univariable and multivariable analyses at one timepoint

## Key secondary outcome(s)

Standardized incidence ratios (SIR) are calculated for each of the cancer forms reported (patients with pMMR and dMMR separately) and adjusted for sex, year (in one-year classes), and age (in five-year classes) at one timepoint

## Completion date

02/03/2021

# Eligibility

## Key inclusion criteria

1. Histologically confirmed CRC
2. Stage confirmed and transformed to the American Joint Committee on Cancer (AJCC) TNM classification
3. Available clinical and pathological data regarding the course of the disease and demographic data

## Participant type(s)

Patient

**Healthy volunteers allowed**

No

**Age group**

Mixed

**Lower age limit**

18 years

**Upper age limit**

100 years

**Sex**

All

**Total final enrolment**

1706

**Key exclusion criteria**

1. Patients younger than 18 years
2. Inconclusive immunohistochemical analysis (IHC) or missing data

**Date of first enrolment**

29/10/2015

**Date of final enrolment**

12/01/2021

**Locations****Countries of recruitment**

Czech Republic

Finland

Sweden

**Study participating centre**

Umeå University hospital

Daniel Naezéns väg

Umeå

Sweden

907 37

**Study participating centre**

**Helsinki University Hospital Department of Surgery**  
Haartmaninkatu 8  
P.O. Box 63  
Helsinki  
Finland  
00014

**Study participating centre**  
**Masaryk Memorial Cancer Institute**  
Žlutý kopec 543/7  
Brno  
Czech Republic  
60200

## **Sponsor information**

### **Organisation**

Cancer Research Foundation in Northern Sweden (Cancerforskningsfonden i Norrland)

## **Funder(s)**

### **Funder type**

University/education

### **Funder Name**

Medicinska fakulteten, Umeå Universitet

### **Alternative Name(s)**

Faculty of Medicine at Umeå University, Faculty of Medicine, Umeå University, Faculty of Medicine, Medicinska fakulteten

### **Funding Body Type**

Private sector organisation

### **Funding Body Subtype**

Universities (academic only)

### **Location**

Sweden

**Funder Name**

Syöpäsäätiö

**Alternative Name(s)**

Cancer Foundation Finland, Cancerstiftelsen

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

Finland

**Funder Name**

Cancer Research Foundation in Northern Sweden

**Alternative Name(s)**

Northern Sweden Cancer Foundation

**Funding Body Type**

Private sector organisation

**Funding Body Subtype**

Trusts, charities, foundations (both public and private)

**Location**

Sweden

**Funder Name**

Nordic Cancer Union

**Funder Name**

Northern Healthcare Regional Association

## Results and Publications

**Individual participant data (IPD) sharing plan**

The datasets generated during and/or analysed during the current study are/will be available upon request from Ioannis Gkekas, [ioannis.gkekas@umu.se](mailto:ioannis.gkekas@umu.se). The type of data that will be shared is completely anonymization for every variable and includes sex, age, cancer stage, and type of

cancer. These data will be available immediately. Consent from participants was not required or obtained. Ethical and legal restrictions are in concordance with the ethical approval obtained.

## IPD sharing plan summary

Available on request

## Study outputs

| Output type                                   | Details                       | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|-------------------------------|--------------|------------|----------------|-----------------|
| <a href="#">Participant information sheet</a> | Participant information sheet | 11/11/2025   | 11/11/2025 | No             | Yes             |
| <a href="#">Thesis results</a>                | Doctoral thesis; study V      | 21/05/2021   | 15/06/2023 | No             | No              |