Genetic and non-genetic risk modelling in colorectal cancer

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Introduction

Colorectal cancer
Introduction

Colorectal cancer screening

- Faecal occult blood test (FOBT)
- Faecal immunochemical test (FIT)
- Bowel scope screening
- Typically age based (>60)

CRC 5-year relative survival, Former Anglia Cancer Network, 2002-2006
Introduction
Colorectal cancer

Lifestyle factors
- Smoking
- BMI
- Alcohol consumption
- Processed meat
- Physical activity
- Hormone therapy
- Fruit and vegetable consumption

Genetic factors
- High penetrance mutations
- Common variation

Johnson et al. (2013) Cancer Causes Control
Botteri et al. (2008) JAMA

Orlando et al. (2016) HMG
Methods
Polygenic Risk Scores

High number of risk alleles = high PRS

\[ PRS_j = \sum_{i=1}^{N} \beta_i g_{ij} \]
Results

Colorectal cancer screening

Previously investigated a PRS based screening approach for CRC, as compared to standard age-based screening:

- Individuals in the top 1% with genetic risk have a 3-fold increased CRC risk over the population median.
- 26% fewer individuals requiring screening, at the cost of 6% fewer screen-detected cases.

Frampton et al., 2016, Ann Oncol, 27(3):429
Results
UK Biobank colorectal cancer

- Individuals with primary diagnosis of colon or rectal cancer
  - ICD-9: 153, 154
  - ICD-10: C18.9, C19, C20, D01
  - 4,225 cases

- Controls – individuals not diagnosed with cancer
  - ICD-9: 140-239
  - ICD-10: C00-D48
  - 353,225 controls

- Lifestyle information
Results

PRS distribution
Results
Non-genetic factors
Work in progress

Model genetic risk variants together with lifestyle information

• Machine learning strategy
• Feature selection to identify significant risk factors

Validation with data from National Bowel Cancer Hubs and the Breast Cancer Now Generations Study

Potential to optimise population screening for CRC, and define those individuals most likely to benefit from chemopreventative agents
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