

# Genetic and non-genetic risk modelling in colorectal cancer

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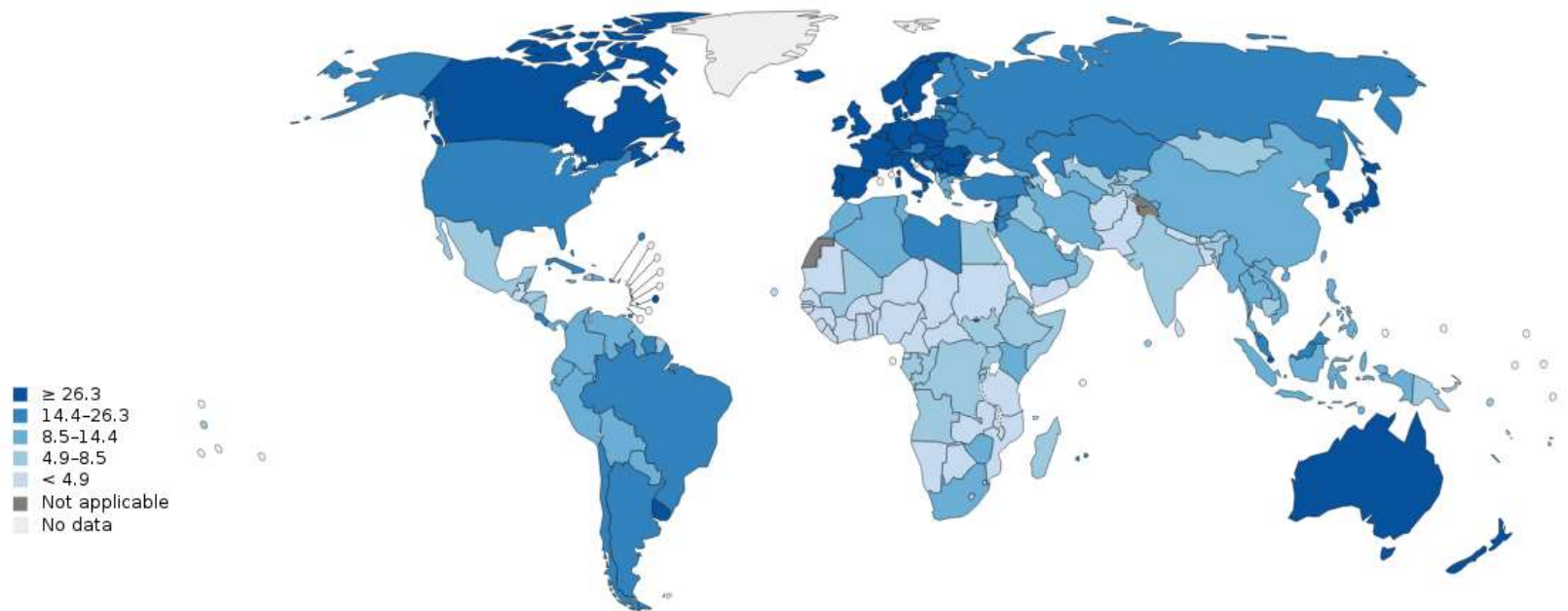
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UK Biobank conference – June 2018

# Introduction

## Colorectal cancer

Estimated age-standardized rates (World) of incident cases, both sexes, colorectal cancer, worldwide in 20



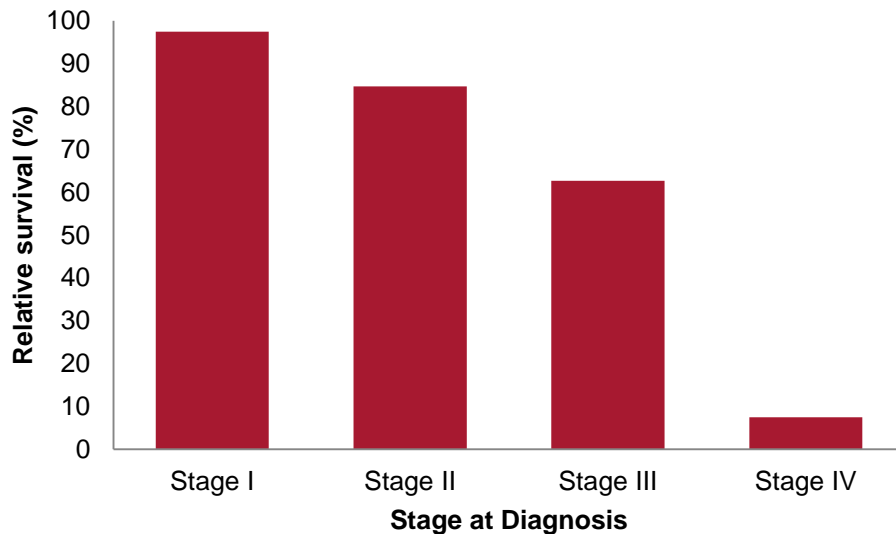
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Data source: GLOBOCAN 2012  
Map production: IARC  
(<http://gco.iarc.fr/today>)  
World Health Organization

# Introduction

## Colorectal cancer screening

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

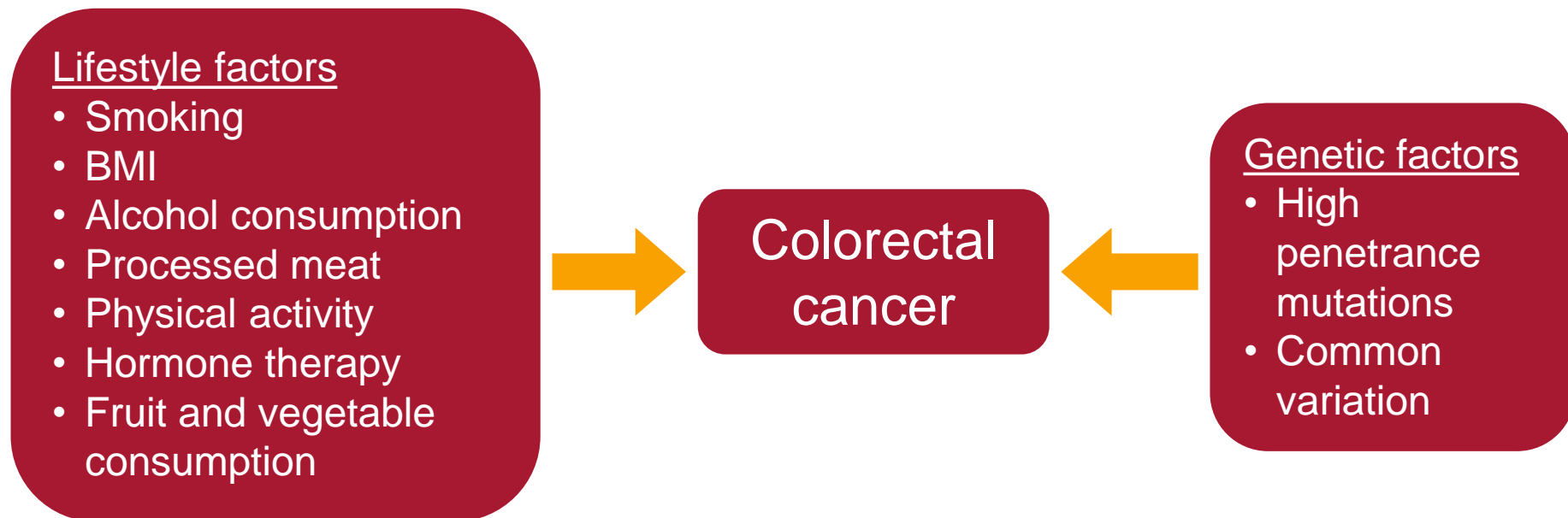


- Faecal occult blood test (FOBT)
- Faecal immunochemical test (FIT)
- Bowel scope screening
- Typically age based (>60)



# Introduction

## Colorectal cancer



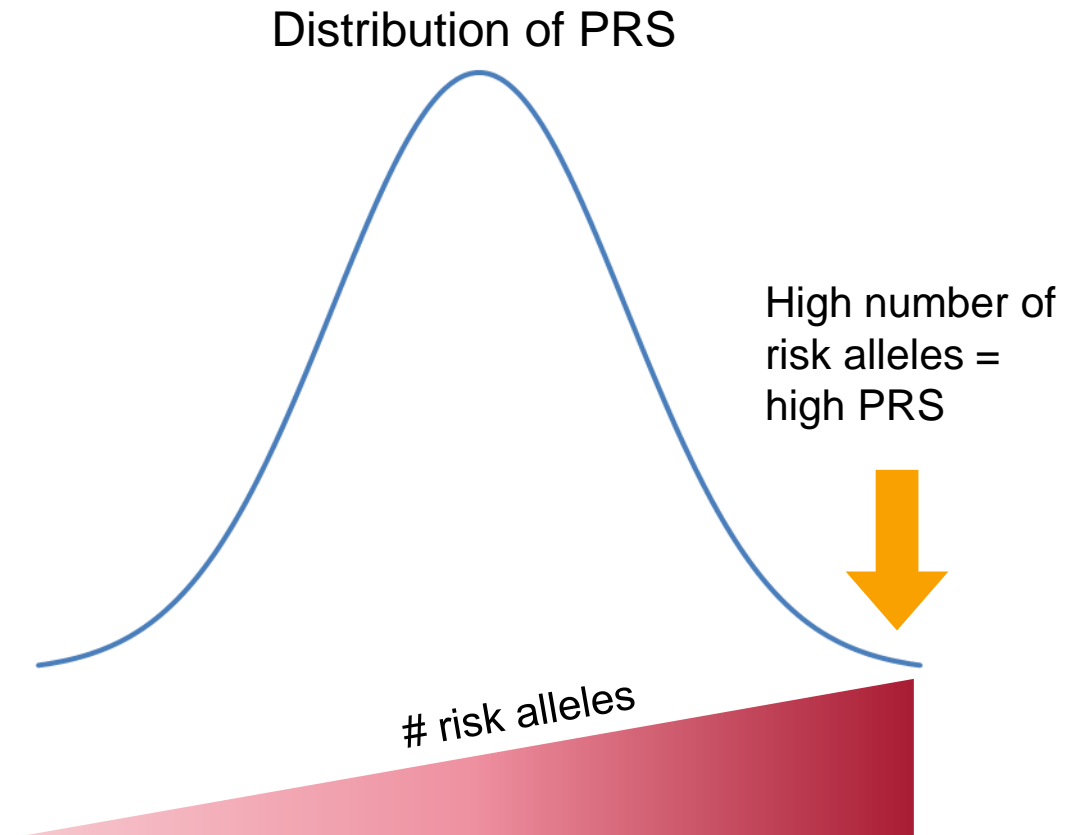
Johnson *et al.* (2013) *Cancer Causes Control*  
Botteri *et al.* (2008) *JAMA*

Chubb *et al.* (2015) *J Clin Oncol.*  
Orlando *et al.* (2016) *HMG*

# Methods

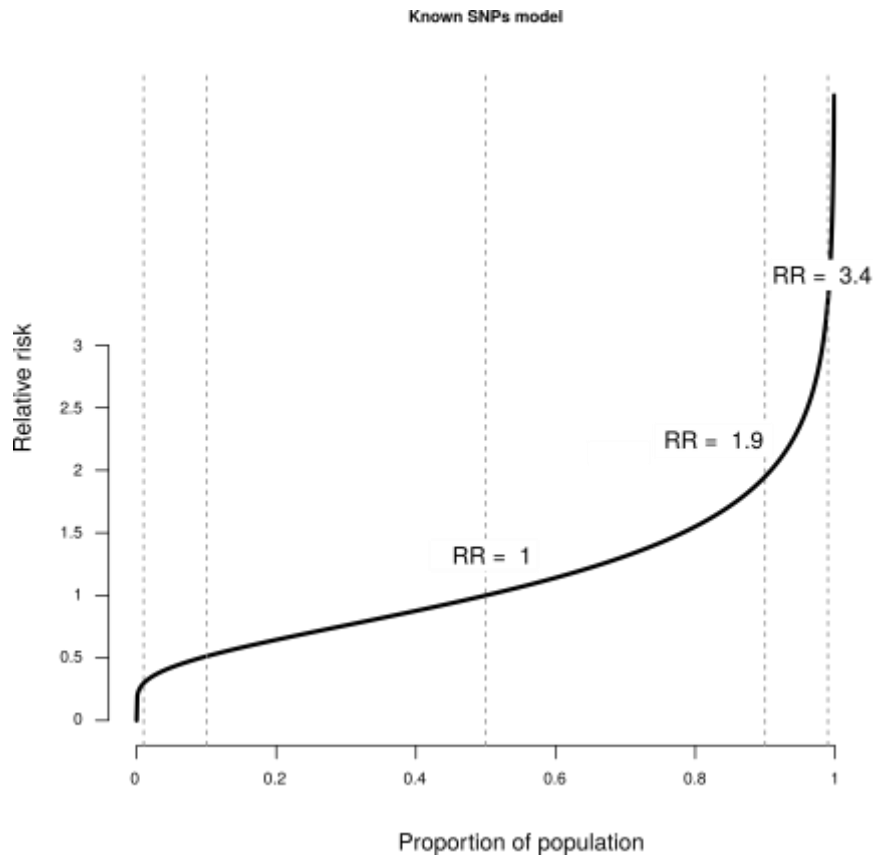
## Polygenic Risk Scores

$$PRS_j = \sum_{i=1}^N \beta_i g_{ij}$$



# 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

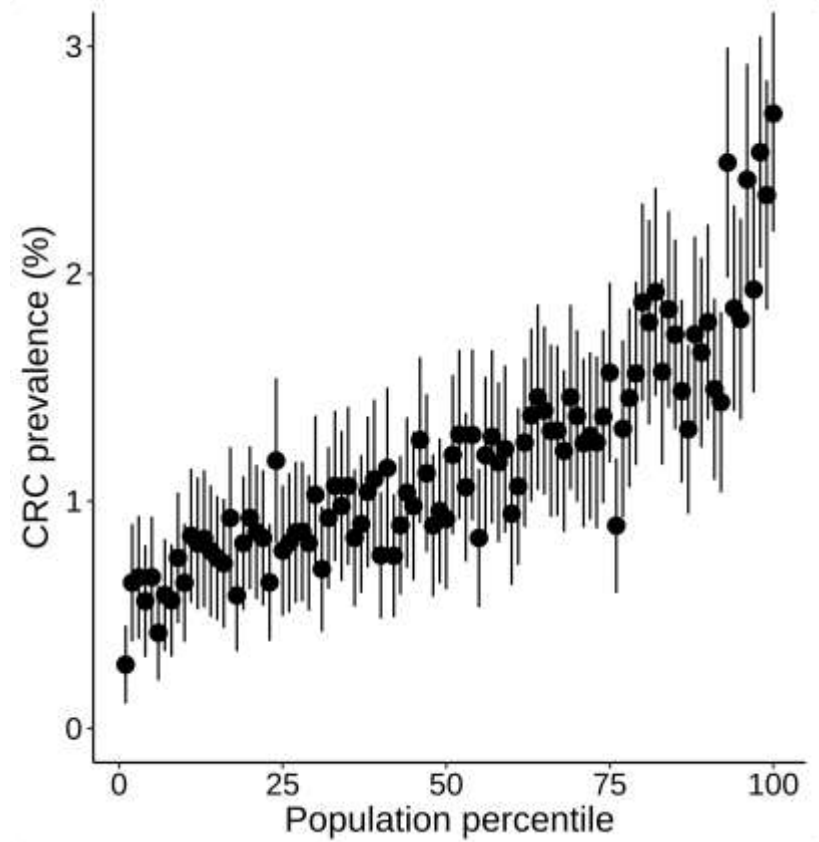
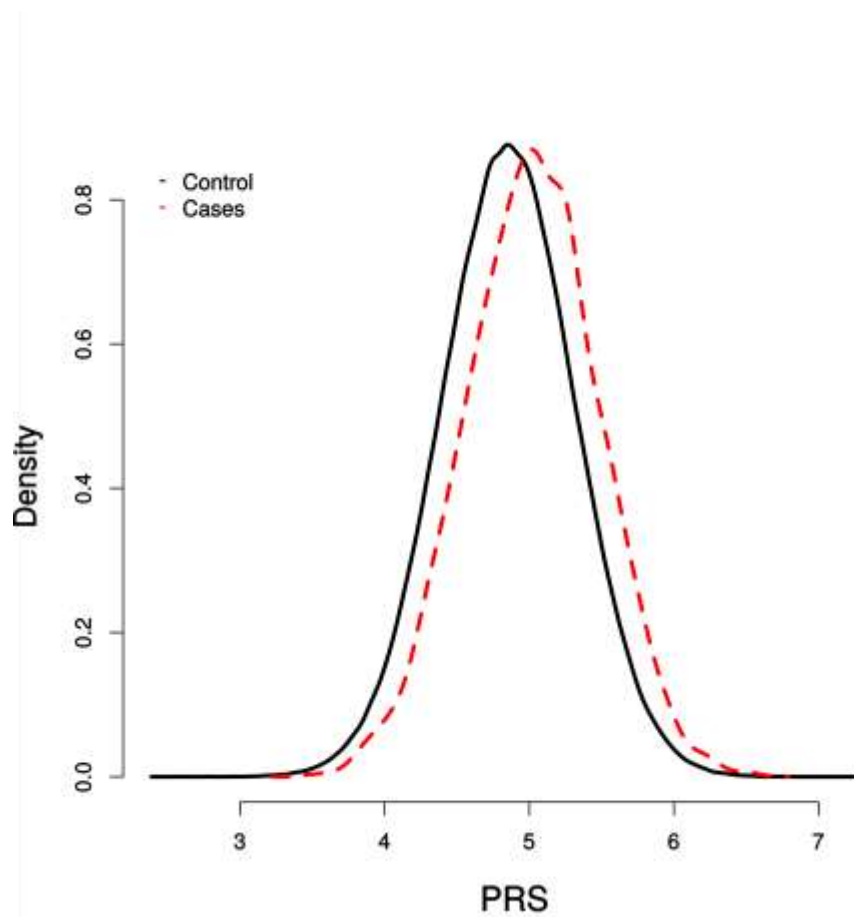
# Results

## 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

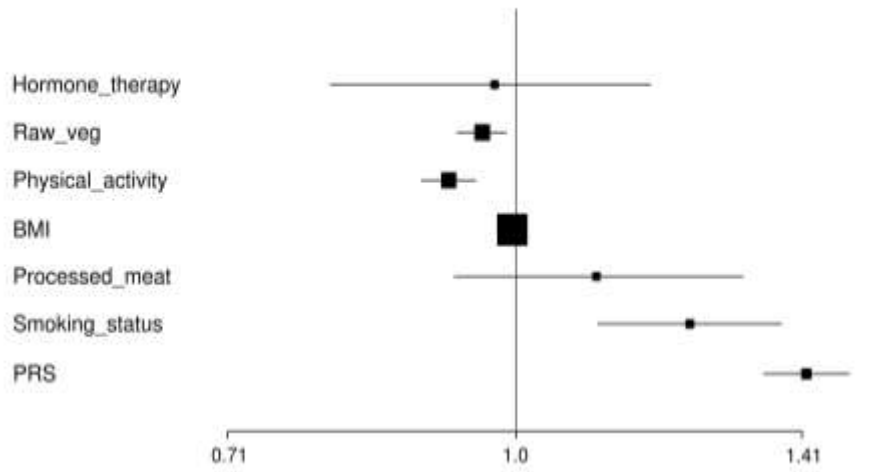




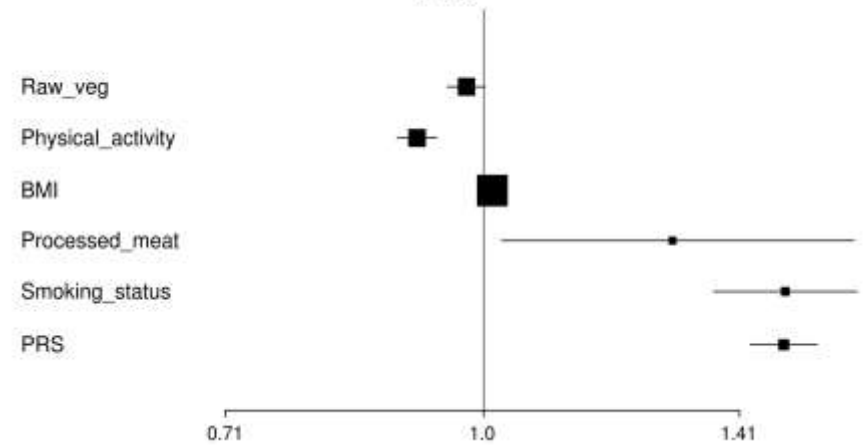
# Results

## Non-genetic factors

Female



Male



# 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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