# Global rise in early-onset colorectal cancer: An association with antibiotic consumption?

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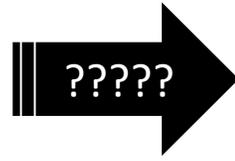[3]School of Pharmacy, Queen's University, Belfast
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30 JUNE – 3 JULY 2021

# BACKGROUND

↑ global antibiotic consumption[1] → ????? ↑ colorectal cancer (CRC) in adults aged <50 years[2,3]
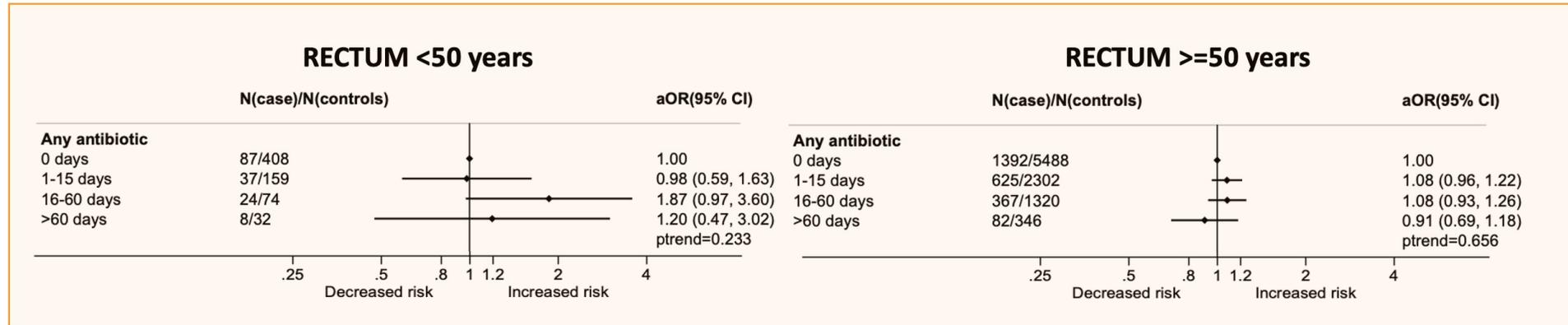
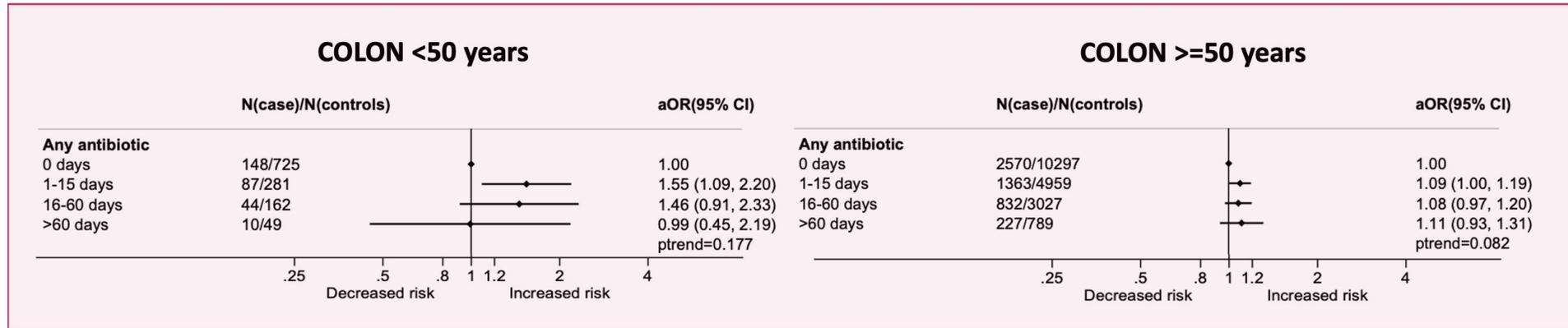- Significantly altering gut microbiome structure and diversity with antibiotic therapy has previously been shown to influence CRC genesis in older adults[4-8]

- No study before has investigated antibiotic usage in early-onset CRC

- This study will investigate the association between exposure to antibiotics and risk of EOCRC predisposition, and also evaluate antibiotic usage in older adults with CRC for comparison.

# METHODS

- Nested case-control study using Scottish primary care data

- CRC cases, diagnosed between 1999 to 2011, were identified from GP records and matched with up to 5 controls.

- Analysis were conducted separately in EOCRC cases (diagnosed <50 years) and later-onset cases (diagnosed >=50 years).

- Prescriptions for oral antibiotics (by drug class and by anaerobic/non-anaerobic effect) were extracted and total antibiotic exposure period determined for each participant.

- Cases and controls were described and conditional logistic regression used to calculate odds ratios (OR) and 95% confidence intervals (CI) for the associations between each exposure and CRC (by tumour location), adjusting for comorbidities. Test for trend was used to evaluate any exposure-response relationship.

# RESULTS

7,903 CRC (5,281 colon, 2,622 rectal) cases and 30,418 controls were identified

### COLON <50 years

| Any antibiotic | N(case)/N(controls) | | aOR(95% CI) |
|---|---|---|---|
| 0 days | 148/725 | | 1.00 |
| 1-15 days | 87/281 | | 1.55 (1.09, 2.20) |
| 16-60 days | 44/162 | | 1.46 (0.91, 2.33) |
| >60 days | 10/49 | | 0.99 (0.45, 2.19) |
| | | | ptrend=0.177 |

.25  .5  .8  1 1.2  2  4
Decreased risk — Increased risk

### COLON >=50 years

| Any antibiotic | N(case)/N(controls) | | aOR(95% CI) |
|---|---|---|---|
| 0 days | 2570/10297 | | 1.00 |
| 1-15 days | 1363/4959 | | 1.09 (1.00, 1.19) |
| 16-60 days | 832/3027 | | 1.08 (0.97, 1.20) |
| >60 days | 227/789 | | 1.11 (0.93, 1.31) |
| | | | ptrend=0.082 |

.25  .5  .8  1 1.2  2  4
Decreased risk — Increased risk

### RECTUM <50 years

| Any antibiotic | N(case)/N(controls) | | aOR(95% CI) |
|---|---|---|---|
| 0 days | 87/408 | | 1.00 |
| 1-15 days | 37/159 | | 0.98 (0.59, 1.63) |
| 16-60 days | 24/74 | | 1.87 (0.97, 3.60) |
| >60 days | 8/32 | | 1.20 (0.47, 3.02) |
| | | | ptrend=0.233 |

.25  .5  .8  1 1.2  2  4
Decreased risk — Increased risk

### RECTUM >=50 years

| Any antibiotic | N(case)/N(controls) | | aOR(95% CI) |
|---|---|---|---|
| 0 days | 1392/5488 | | 1.00 |
| 1-15 days | 625/2302 | | 1.08 (0.96, 1.22) |
| 16-60 days | 367/1320 | | 1.08 (0.93, 1.26) |
| >60 days | 82/346 | | 0.91 (0.69, 1.18) |
| | | | ptrend=0.656 |

.25  .5  .8  1 1.2  2  4
Decreased risk — Increased risk

**Forest plots for associations between any antibiotic use and risk of colorectal cancer**

Abbreviations: aOR: adjusted Odds Ratio; N: Number

Analyses adjusted for diabetes, myocardial infarction, coronary heart disease, heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic obstructive pulmonary disease, osteoporosis, renal disease, liver disease, hemiplegia/paraplegia, gallstones, acromegaly, low dose aspirin and NSAIDs

| Analyses for any antibiotic use | | <50 years | | | | >=50 years | | | | Interaction test *P*-value |
|---|---|---|---|---|---|---|---|---|---|---|
| | | Cases *N* (%) | Controls *N* (%) | Adjusted ‡OR (95%CI) | Adjusted *P*-value | Cases *N* (%) | Controls *N* (%) | Adjusted ‡OR (95%CI) | Adjusted *P*-value | |
| Colon | | 141 (49%) | 492 (40%) | **1·49 (1·07,2·07)** | 0·018 | 2,422 (49%) | 8,775 (46%) | **1·09 (1·01,1·18)** | 0·029 | 0·071 |
| Rectal | | 69 (44%) | 69 (44%) | **1·17 (0·75,1·84)** | 0·493 | 1,074 (44%) | 3,968 (42%) | **1·07 (0·96,1·19)** | 0·238 | 0·698 |
| Subgroup analyses | Proximal colon | 31 (62%) | 87 (41%) | **3·78 (1·60,8·92)** | 0·002 | 272 (43%) | 1,048 (43%) | **0·92 (0·74,1·13)** | 0·315 | 0·001 |
| | Distal colon | 20 (56%) | 60 (40%) | **3·39 (1·02,11·28)** | 0·047 | 245 (48%) | 896 (44%) | **1·14 (0·90,1·44)** | 0·289 | 0·083 |

**Associations between any antibiotic use and colon cancer and rectal cancer, including subgroup analyses of proximal and distal colon cancer**

Abbreviations: OR: odds ratio, CI confidence interval; ‡ adjusted for diabetes, myocardial infarction, coronary heart disease, heart failure, peripheral vascular disease, dementia, cerebrovascular disease, chronic obstructive pulmonary disease, osteoporosis, renal disease, liver disease, hemiplegia/paraplegia, gallstones, acromegaly, low dose aspirin and NSAIDs·

# CONCLUSION

- Antibiotic exposure may have a role in colon tumour formation across all age groups, particularly in those aged less than 50 years.

- It is possible that exposure to antibiotics could be contributing to the observed increases in EOCRC

- More studies needed to evaluate role of antibiotics

- If confirmed, our study will provide further reasons to reduce, where possible, frequent and unnecessary antibiotic prescribing.

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