



## Important New Evidence Service In Partnership with The Centre for Medicines Optimisation at Keele University

ScriptSwitch<sup>™</sup> Rapid Update 3 – May 2017

### Antibiotic prescribing: long-term use of antibiotics and risk of colorectal adenoma

A US cohort study found that women who had previously taken antibiotics for a total of 2 months or more were at an increased risk of being diagnosed with colorectal adenoma after the age of 60. Although better evidence is required before firm recommendations can be made, this study is a reminder of the need for robust antimicrobial stewardship, as discussed in the [NICE guideline](#).

**Reference:** Cao Y, Wu K, Mehta R et al [Long-term use of antibiotics and risk of colorectal adenoma](#). Gut. Published Online First: [April 2017] doi:10.1136/gutjnl-2016-313413

#### What do we know already?

- Recent studies have suggested an association between antibiotic use and colorectal cancer. A 2015 nested case-control study using the UK's [The Health Improvement Network \(THIN\) database](#) found that past exposure to penicillins was related to a modest increase in colorectal cancer risk, possibly through effects on the colonic microbiota ([Boursi et al. 2015](#)).
- Colorectal adenomas are a precursor of the majority of colorectal cancers.
- Antibiotic consumption in England was on the rise, increasing by 6.5% between 2011 and 2014 ([Public Health England - Health matters: antimicrobial resistance](#)). However, encouragingly, a decline in has been seen more recently, with the [latest surveillance report for England](#) finding a 4.3% decrease in total antibiotic consumption between 2014 and 2015. Initiatives, such as the CCG [Quality Premium](#) for 2017-19, aim to sustain these reductions.
- The NICE guideline on [antimicrobial stewardship](#) recommends that when prescribing antimicrobials, prescribers should follow local or national guidelines on prescribing the shortest effective dose.

#### What does this evidence add?

- A large cohort study found long-term use of antibiotics between the ages of 20 and 59 years was associated with increased risk of colorectal adenoma after the age of 60. More recent antibiotic use (within the past 4 years) was not associated with an increased risk of adenoma.
- The study has a number of limitations. The observational design means causation cannot be proven. Detailed information on which antibiotics were used was not available, so the effect of different classes of antibiotics on adenoma diagnosis is not known. Participants were required to remember antibiotic use from earlier in their life, hence recall bias is likely.

## Study details

### Participants:

- Women aged 60 years or more who were enrolled on the [Nurses' Health Study](#) (n=16,642). The Nurses' Health Study is an ongoing prospective cohort study involving 121,700 female nurses in the US who were aged between 30 and 55 years at enrolment in 1976. Originally set-up to investigate the long-term effects of oral contraceptives, the Nurses' Health Study collects information every 2 years using questionnaires that cover demographics, lifestyle factors, medical history and disease outcomes. Dietary data are collected every 4 years.
- The investigators analysed data from women who were aged 60 years or more in 2004, who reported their history of antibiotic use up to age 59 and reported having at least colonoscopy between 2004 and 2010.
- Common indications for antibiotic use were respiratory infection, urinary tract infection, acne/rosacea, chronic bronchitis and dental infections.

### Intervention and comparison:

- In each questionnaire participants were asked whether they had undergone a colonoscopy, for what indications and whether colon or rectal polyps had been diagnosed. For all participants with a diagnosis, blinded study investigators extracted data on histological type, anatomic location, size and number of polyps.
- Cases of adenoma were grouped according to their features and likelihood of developing future advanced neoplasia:
  - High risk: at least 1 adenoma  $\geq 1$  cm diameter or more, or with advanced histology, or  $\geq 3$  adenomas (regardless of size or histology)
  - Low risk: all other types of adenomas
- Participants who underwent a colonoscopy but did not have a diagnosis of adenoma were used as controls.

### Outcomes and results:

- There were 1,195 newly diagnosed adenoma identified between 2004 and 2010.
- Increased total exposure to antibiotics was associated with an increased risk of adenoma. Women who used antibiotics for 2 months or more between the ages of 20 and 39 had a significantly higher risk of adenomas compared with non-users (multivariable [odds ratio \[OR\]](#) 1.36, 95% [confidence interval \[CI\]](#) 1.03 to 1.79,  $p_{\text{trend}}=0.002$ ). Similar results were observed in women aged 40 to 59 years, with women treated with antibiotics for 2 months or more at a higher risk of adenoma compared with non-users (multivariable OR 1.69, 95% CI 1.24 to 2.31,  $p_{\text{trend}}=0.001$ ). The association was similar for low-risk versus high-risk adenomas, although the association appeared stronger for proximal adenomas compared with distal adenoma.
- Antibiotic use for 15 days or more between 20-39 and 40-59 years was also associated with an increased risk of adenoma detection.
- Recent antibiotic use, occurring in the last 4 years, was not associated with an increased risk of adenoma ( $p_{\text{trend}}=0.44$ ). None of the indications for antibiotics appeared to be significantly associated with risk of adenoma.

### Level of evidence:

Level 3 (other evidence) according to the [SORT criteria](#)

### Study funding:

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