Study links overuse of antibiotics with severe COVID-19 side effects

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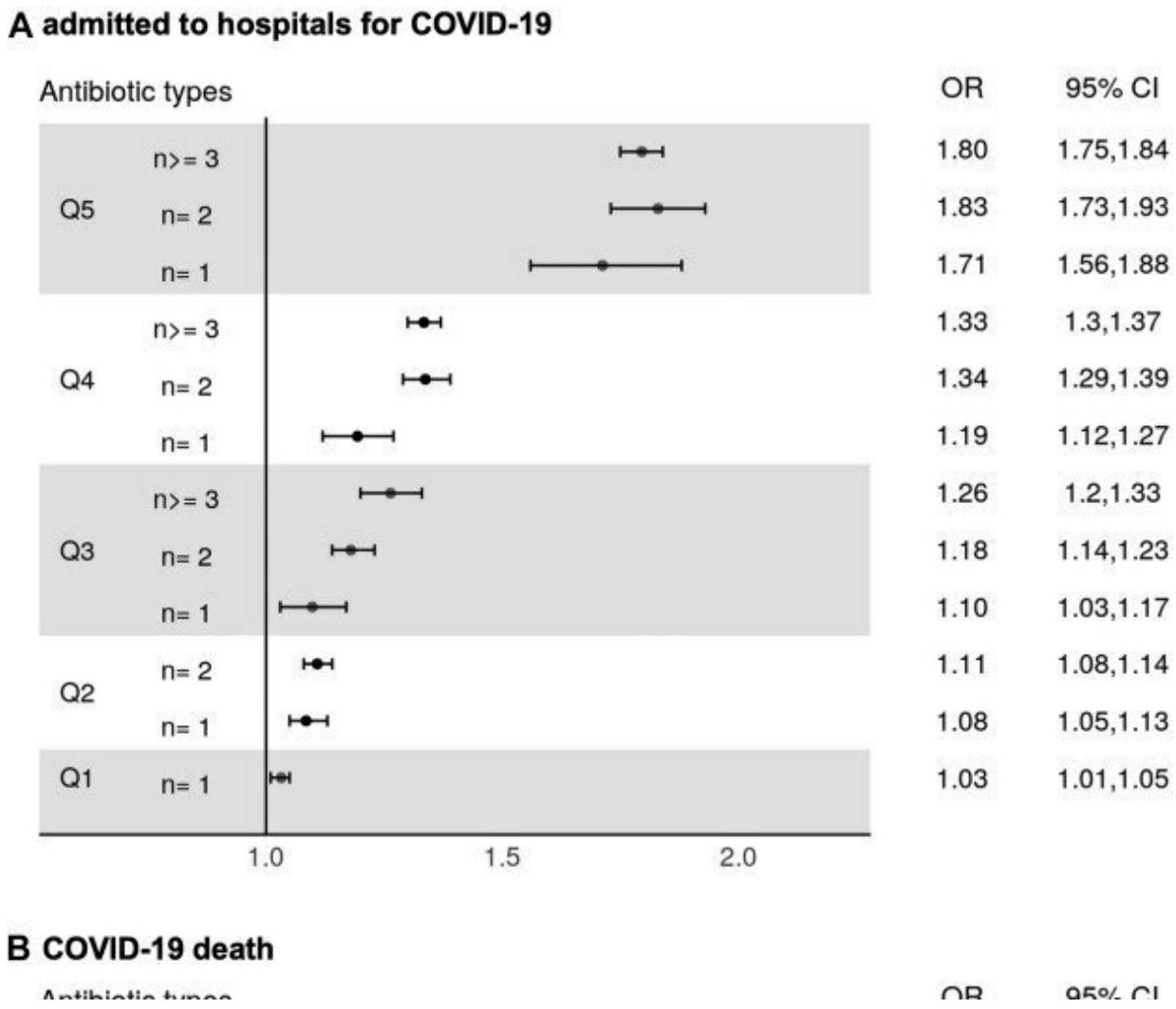

Adjusted ORs for COVID-19 outcomes (A. admitted to hospitals; B. death) stratified by number of antibiotic types in the 3 years by quintile (Q1–Q5) of total number of prior antibiotic prescription. Credit: *eClinicalMedicine* (2023).

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Frequent and diverse use of antibiotics may be associated with developing more severe outcomes after a COVID-19 infection, including death, a study led by University of Manchester scientists has shown.

The findings published in *eClinicalMedicine*, act as a warning against the overuse of antibiotics in people.

The team, which also included researchers from the Universities of Oxford and Leeds, were the first to explore how the severity of COVID-19 disease is affected by prior antibiotic use.

The research team found:

- Patients with more frequent antibiotic exposure in the past three years were at higher odds of experiencing severe COVID-19 outcomes, including hospital admission and 30-day mortality.
- Using a range of antibiotics was more likely to be associated with COVID-19 hospital admission.
- The odds for hospitalized patients dying from COVID-19 related complications in most frequent antibiotics exposure group were 1.34 higher than patients without prior antibiotic exposure.
- Larger number of prior antibiotic type was also associated with more severe COVID-19 related hospital admission
- The odds of hospitalization for patients with the highest history of prior antibiotic use and most antibiotic types were 1.8 times greater than patients without antibiotic exposure.

The NHS OpenSAFELY platform, a secure open-source software platform for analysis of electronic health records allowed the researchers

to integrate primary and secondary care, COVID-19 test, and death registration data from February 2020 to December 2021.

The sample included 0.67 million patients from an eligible 2.47 million patients with recent COVID-19 infection.

Of the 0.67 million, 98,420 patients were admitted to hospitals, 22,660 died and 55 unique antibiotics were prescribed.

Cases were identified by the researchers according to different severity of COVID-19 outcomes and they created five groups, based on the number of previous three-year antibiotic prescriptions to indicate the frequency of prior antibiotic exposure.

Each group was further split based on the number of different antibiotic types a patient was prescribed.

Co-principal investigator Professor Tjeerd van Staa from The University of Manchester said, "Our study has provided evidence that patients with high prior antibiotic use were more likely to experience severe COVID-19 outcomes, including hospital admission and even death.

"In addition, we also found an association between the number of different prior antibiotic types and COVID-19 related hospital admission .

"One potential explanation may be that frequent antibiotic use increases the likelihood of patients being infected with viruses or bacteria, leading to increased susceptibility to adverse consequences of infection.

"The literature also shows that antibiotic treatment might also alter gut microbiota, which can impact metabolic and immune function.

"While in most situations, gut microbiota will recover after stopping an antibiotic course, frequent antibiotic use may affect the resilience of gut microbiomes more seriously."

Co-principal investigator Dr. Victoria Palin from The University of Manchester said, "There is little evidence to suggest that repeated intermittent antibiotic exposure is effective in reducing infection-related complications. Indeed, there is mounting evidence that it can be unsafe.

"That is why there needs to be more awareness of the impact of long-term antibiotic exposure and its adverse outcomes. We would discourage regular and indiscriminate prescribing of these drugs for self-limiting infections.

"Common infection guidelines in England, as developed by the National Institute for Health and Care Excellence, focus on the treatment of the first infection episode .

"They do not provide guidance around repeated antibiotic use and a patient's risk of developing resistance.

"Antibiotic prescribing guidelines should also clearly outline the possible adverse consequences to a patient of using an antibiotic for self-limiting bacterial infections. Personalized patient leaflets should be provided highlighting these risks and the risks of the patient's bacteria developing resistance to antibiotics."

More information: Ya-Ting Yang et al, Repeated antibiotic exposure and risk of hospitalisation and death following COVID-19 infection (OpenSAFELY): a matched case–control study, *eClinicalMedicine* (2023). DOI: 10.1016/j.eclinm.2023.102064