

## EDITORIALS



## Antibiotics for Appendicitis — Proceed with Caution

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More than 30 years ago, while I was in training, the best diagnostician I have ever met said — much to my surprise — that some patients who had uncomplicated appendicitis could be successfully treated nonoperatively. He had drawn that conclusion from his practical experiences in the medical corps, well before the advent of modern diagnostic imaging and other technologies. His opinion clearly ran counter to standard teaching at that time in the United States. However, since then, the question of the relative efficacy of antibiotic therapy for the treatment of appendicitis has remained highly controversial. On the basis of findings from randomized trials that had relatively limited inclusion criteria and excluded patients with an appendicolith, some experts have opined that the choice between medical and surgical management should reflect a relative determination of value and preference and involve shared decision making.<sup>1,2</sup>

In a report now published in the *Journal*, Flum and colleagues<sup>3</sup> make an important contribution to the existing literature. They report short-term results of a nonblinded, noninferiority, randomized trial comparing antibiotic therapy (which was not rigidly standardized) with appendectomy (with most procedures performed laparoscopically) in 1552 adults who were treated at academic health centers across the United States. The trial included patients with an appendicolith, as well as patients with more severe disease than those included in other trials. Given the concern that the rate of adverse outcomes could be higher among patients with an appendicolith, the trial protocol included a plan to analyze their outcomes separately. The primary outcome

was health status as assessed with the European Quality of Life–5 Dimensions (EQ-5D) questionnaire, a widely used self-assessment of quality of life. At 30 days, antibiotics were noninferior to appendectomy according to results of this measure of health status.

At least two key questions should be asked when evaluating these results.<sup>4</sup> First, what other factors relevant to medical care and treatment should be considered in comparing these treatment options? Second, would patients and their providers accept an alternative to appendectomy, depending on the circumstances?

With respect to the first point, the current trial was designed with input from patients to identify outcomes that they thought were most important. Included among secondary outcomes were the rate of appendectomy in the antibiotics group, short-term clinical improvement, and National Surgical Quality Improvement Program (NSQIP)–defined complications and other complications, as well as time to recovery. By 90 days of follow-up, approximately one third of the patients assigned to receive antibiotics had undergone appendectomy. Moreover, in the antibiotics group, the rate of NSQIP-defined complications was twice as high as the rate in the appendectomy group, the number of emergency department visits was nearly three times as high, and more time was spent in the hospital. The presence of an appendicolith was found to be the primary driver of adverse outcomes, as well as the primary driver but not the sole determinant of subsequent appendectomy. There were fewer missed work days for participants and caregivers in the antibiotics group than in the appendec-

tomy group, but it is possible that this difference was driven, at least in part, by postoperative instructions.

In practical terms, because patients may appropriately prioritize different outcomes, the pros and cons of all treatment options should be presented and discussed. Considering that laparoscopic appendectomy is a highly effective therapy — rapidly resolving pain and allowing patients to return to normal activities while avoiding the subsequent risks of recurrent appendicitis and hospitalization — I believe that most providers would recommend surgical treatment for uncomplicated appendicitis if that option is available. I know I would.

However, as the authors suggest, circumstances do matter, and advantages of antibiotic treatment relative to surgery may be greater during the Covid-19 pandemic or other public health emergencies in which operating room capacity and other resources are severely constrained. The American College of Surgeons has recently released guidance on triage for nonemergency surgical procedures during the Covid-19 pandemic, suggesting that hospitals and surgical centers should consider, among other factors, the needs and informed preferences of patients, medical risks that might be incurred by delaying operation, resource availability, capacity, and safety.<sup>5</sup>

In addition to affecting the provision of surgical and medical care, the pandemic has highlighted ongoing, dreadful health care disparities in the United States and the adverse impact of social determinants, as well as structural bias and racism, on health and health outcomes. It will be important to ensure that some people, in particular vulnerable populations, are not offered antibiotic therapy preferentially or without adequate education regarding the longer-term implications. Flum and colleagues highlight the

importance of “individual characteristics, preferences, and circumstances” in making decisions based on their findings. Included among these considerations should be the effects of race or ethnic group, location, insurance status, and socioeconomic status,<sup>6-9</sup> which may affect quality of life<sup>10,11</sup> and lead to poorer outcomes for some people.

Disclosure forms provided by the author are available with the full text of this editorial at NEJM.org.

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## The Covid-19 Vaccine-Development Multiverse

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Leaving in its wake more than 12 million infections, over 550,000 deaths, and an economic toll in the trillions of dollars to date,<sup>1</sup> the SARS-CoV-2

pandemic has devastated the most vulnerable in our society — adults 65 years of age or older, persons with underlying conditions, and the ec-