

CORRESPONDENCE



Antibiotics versus Appendectomy for Acute Appendicitis — Longer-Term Outcomes

TO THE EDITOR: Antibiotic treatment of appendicitis is now described as an “accepted first-line treatment” by the American College of Surgeons¹ on the basis of the results of several randomized trials.² In the Comparison of Outcomes of Antibiotic Drugs and Appendectomy (CODA) trial,³ we previously reported short-term outcomes involving 1552 patients with appendicitis (with or without an appendicolith). In that trial, we found that antibiotic treatment was noninferior to appendectomy on the basis of a measure of general health status at 30 days, with similar rates of safety events. Among the patients in the antibiotics group, 29% had undergone appendectomy by 90 days (41% with an appendicolith vs. 25% without). Here, we report our findings regarding longer-term outcomes, including the risk of recurrence of appendicitis and the rate of eventual appendectomy among the patients who were assigned to receive antibiotic therapy — outcomes that are also important for clinical decision making.

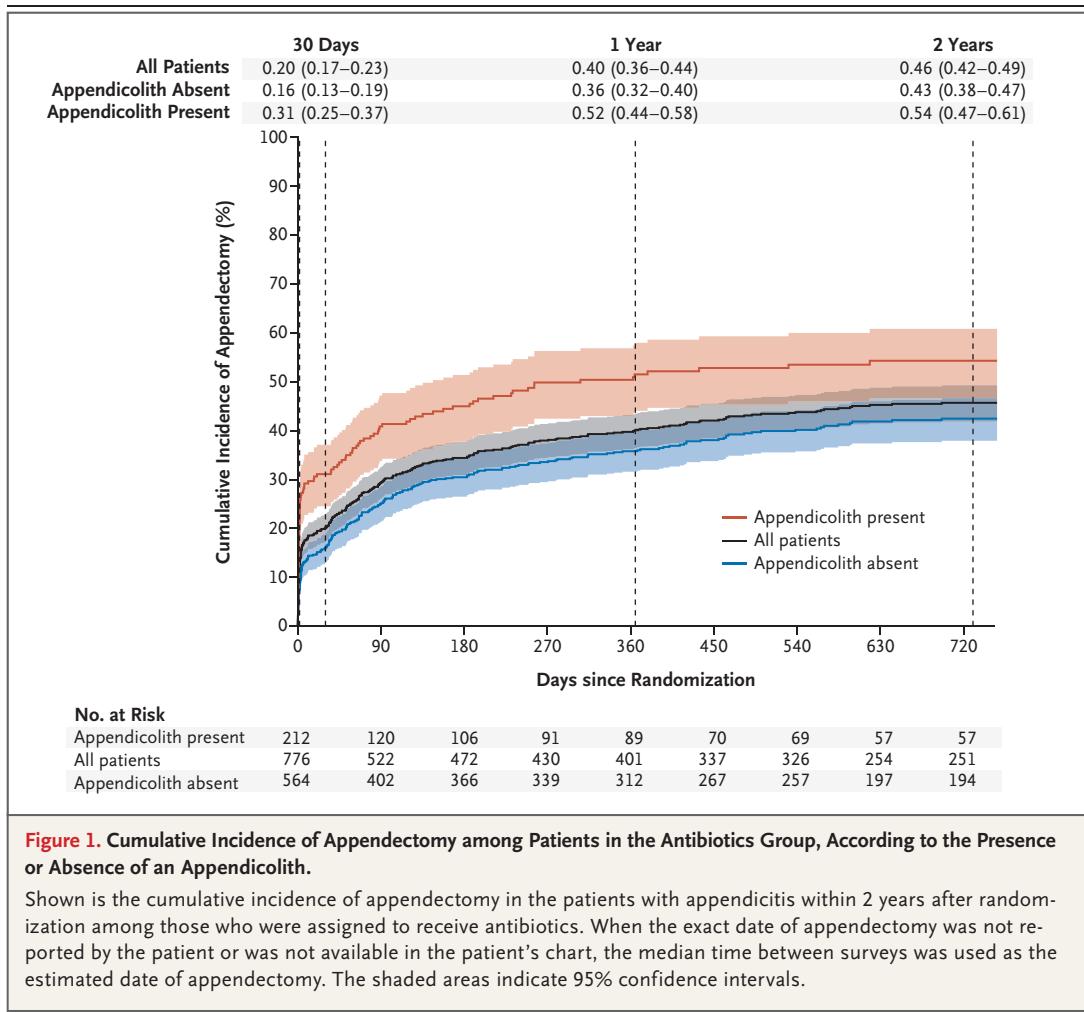
The methods that we used in this trial have been described previously⁴ and are summarized in the Supplementary Appendix, available with the full text of this letter at NEJM.org. We defined recurrence of appendicitis as the performance of appendectomy in which the primary indication for surgery was for clinical reasons occurring 31 to 365 days after randomization. Appendicitis was considered to have been confirmed on the basis of the pathological findings. Data collection ended 1 year after the final patient had been recruited, with 82% of the patients enrolled for more than 2 years, 44% for more than 3 years, and 15% for more than 4 years. Surveys in which patients were asked

about outcomes (and if they had an appendectomy, what they thought was the reason for the appendectomy) were available for 79% of the patients at 1 year, 57% at 2 years, 10% at 3 years, and 5% at 4 years (Fig. S1 in the Supplementary Appendix). Characteristics of the patients at baseline (Table S1) and 90-day outcomes³ were reported previously.

In the antibiotics groups, the percentage of patients who underwent subsequent appendectomy was 40% (95% confidence interval [CI], 36 to 44) at 1 year and 46% (95% CI, 42 to 49) at 2 years (Fig. 1); the percentages were 49% (95% CI, 44 to 53) at 3 and 4 years, according to limited longer-term follow-up (Fig. S2). At 30 days after randomization, the risk of appendectomy was 27% (95% CI, 23 to 30) through 1 year. Appendectomy was more common among patients who had an appendicolith, but this greater risk was attenuated with time. The hazard ratio for appendectomy among patients with an appendicolith as compared with those without an appendicolith was 2.9 (95% CI, 1.9 to 4.4) within 48 hours, 1.4 (95% CI, 0.8 to 2.4) from 48 hours to 30 days, and 1.1 (95% CI, 0.8 to 1.6) from 31

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days to 2 years. Of the 333 patients in the antibiotics group who underwent appendectomy after randomization, appendicitis was confirmed in 278 of 297 (94%) for whom a pathology report was available. Primary indications for appendectomy and pathological confirmation of appendicitis are shown in Table S2.

After 30 days, complications were uncommon in the two treatment groups, regardless of the presence or absence of an appendicolith (Table S3). Among patients with recurrence in the antibiotics group, perforation was reported in 20% (95% CI, 13 to 28), a percentage that was similar to that in the appendectomy group (16%; 95% CI, 13 to 19).³ Among patients with 2-year follow-up, 62 of 443 (14%) in the antibiotics group had received an additional course of antibiotics; of these patients, 66% underwent subsequent

appendectomy. Since the reporting of our initial findings, 2 additional neoplasms were identified among the patients in the antibiotics group (Table S4).

In our trial, the longer-term incidence of appendectomy in the antibiotics group was higher than pooled results from prior trials.¹ This finding is probably related to our inclusion of patients with radiographic evidence of an appendicolith or perforation, common findings in patients with appendicitis. Limitations of the trial, in addition to those described previously,³ include the absence of data beyond 1 or 2 years in a substantial percentage of patients, the lack of a widely accepted time window for defining recurrence, and the use of nonstandardized pathological reports or, in some cases, missing reports. In order to address missing data in

comparing safety events and complications, we used a weighted cohort analysis with results that were similar to those in an unweighted analysis (Table S5). Patients who were prescribed an additional course of antibiotics and who did not undergo appendectomy were not counted as recurrences because appendicitis could not be confirmed.

Although some clinicians and patients may determine that these longer-term rates of appendectomy make antibiotics a less desirable treatment than early appendectomy, substantial numbers of patients report a preference for antibiotics, even if appendectomy may ultimately be necessary.⁵ The present data will further inform shared decision making between clinicians and their patients with appendicitis, including those with an appendicolith (see videos, which are being made available with permission from the authors).

The CODA Collaborative

The members of the writing committee (Giana H. Davidson, M.D., M.P.H., David R. Flum, M.D., M.P.H., Sarah E. Monsell, M.S., Lillian S. Kao, M.D., Emily C. Voldal, B.A., Patrick J. Heagerty, Ph.D., Erin Fannon, B.A., Danielle C. Lavalley, Ph.D., Pharm.D., Bonnie Bizzell, M.Ed., Sarah O. Lawrence, M.A., Bryan A. Comstock, M.S., Anusha Krishnadasan, Ph.D., Robert J. Winchell, M.D., Wesley H. Self, M.D., M.P.H., Callie M. Thompson, M.D., Farhood Farjah, M.D., M.P.H., Pauline K. Park, M.D., Hasan B. Alam, M.D., Darin Saltzman, M.D., Ph.D., Gregory J. Moran, M.D., Amy H. Kaji, M.D., Ph.D., Daniel A. DeUgarte, M.D., Matthew Salzberg, M.D., Lisa Ferrigno, M.D., M.P.H., Katherine A. Mandell, M.D., M.P.H., Thea P. Price, M.D., Nicole Siparsky, M.D., Jacob Glaser, M.D., Patricia Ayoung-Chee, M.D., M.P.H., William Chiang, M.D., Jesse Victory, D.O., Bruce Chung, M.D., Damien W. Carter, M.D., Matthew E. Kutcher, M.D., Alan Jones, M.D., Julie Holihan, M.D., Mike K. Liang, M.D., Brett A. Faine, Pharm.D., Joseph Cuschieri, M.D., Heather L. Evans, M.D., Jeffrey Johnson, M.D., Joe H. Patton, M.D., Natasha Coleman, M.D., Katherine Fischkoff, M.D., M.P.A., F. Thurston Drake, M.D., M.P.H., Sabrina E. Sanchez, M.D., M.P.H., Charles Parsons, M.D., Stephen R. Odom, M.D., Larry G. Kessler, Sc.D., and David A. Talan, M.D.) assume responsibility for the overall content and integrity of this letter. Dr. Flum can be contacted at daveflum@uw.edu or at the Surgical Outcomes Research Center, Box 356410, University of Washington, Seattle, WA 98195.

From University of Washington Medical Center—UW Medicine (G.H.D., D.R.F., E.F., D.C.L., B.B., S.O.L., F.F., L.G.K.), University of Washington (S.E.M., E.C.V., P.J.H., B.A.C.), Swedish Medical

Center (K.A.M.), and Harborview Medical Center—UW Medicine (J.C., H.L.E.), Seattle, and Providence Regional Medical Center, Everett (J.G.) — all in Washington; McGovern Medical School, University of Texas Health Science Center (L.S.K.), Lyndon B. Johnson General Hospital, University of Texas (J.H., M.K.L.), and HCA Healthcare Kingwood, University of Houston (M.K.L.) — all in Houston; BC Academic Science Health Network, Vancouver, BC, Canada (D.C.L.); Olive View—UCLA Medical Center (A.K., D.S., G.J.M., D.A.T.), Harbor—UCLA Medical Center (A.H.K., D.A.D.), and UCLA Ronald Reagan Medical Center (D.A.T.), Los Angeles, and the University of California, San Francisco (J.C.) — all in California; Weill Cornell Medical Center (R.J.W.), Tisch Hospital, NYU Langone Medical Center (P.A.-C., W.C., J.V.), Bellevue Hospital Center, NYU School of Medicine (W.C.), and Columbia University Medical Center (N.C., K.F.) — all in New York; Vanderbilt University Medical Center, Nashville (W.H.S., C.M.T.); University of Utah, Salt Lake City (C.M.T.); University of Michigan Medical Center, Ann Arbor (P.K.P., H.B.A.), and Henry Ford Health System, Detroit (J.J., J.H.P.) — both in Michigan; UHealth, University of Colorado Hospital, Denver (M.S., L.F.); Rush University Medical Center, Chicago (T.P.P., N.S.); Morehouse School of Medicine, Atlanta (P.A.-C.); Maine Medical Center, Portland (B.C., D.W.C.); University of Mississippi Medical Center, Jackson (M.E.K., A.J.); University of Iowa Hospitals and Clinics, Iowa City (B.A.F.); Medical University of South Carolina, Charleston (H.L.E.); and Boston University Medical Center (F.T.D., S.E.S.) and Beth Israel Deaconess Medical Center (C.P., S.R.O.) — both in Boston.

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A video is available at [NEJM.org](https://www.nejm.org)