the hepatic confluence and when the surrounding bile duct diameter is large enough to accommodate the device. In the trial, patients whose unaffected bile duct was less than 6 mm were excluded to avoid secondary duct injuries and higher rates of spontaneous stent migration. Additional comparative safety data for self-expandable metallic stents are needed for patients who have not undergone a cholecystectomy, which predominantly applies to those having bile duct strictures in the setting of chronic pancreatitis. These limitations may spur development of expandable stents designed to address these subgroups while minimizing the need for multiple interventions.

The study's generalizability is greater than suggested by Costamagna. Patients who have undergone orthotopic liver transplantation have the highest risk of a bile duct stricture, with an annual incidence of 20% among 6500 US patients undergoing transplant, or approximately 1300 cases.[1] Approximately 30 000 individuals are diagnosed with chronic pancreatitis each year in the United States,[2] and at least 5% (1500 individuals) are expected to develop a bile duct stricture during their illness. These statistics compare with postlaparoscopic cholecystectomy, for which the risk of a postoperative bile duct stricture is approximately 0.05% of 500 000 cases each year, or 2500 incident cases.[3]

As Costamagna suggests, many postcholecystectomy strictures occur too close to the hepatic confluence to accommodate current self-expandable metallic stent models. Furthermore, some postcholecystectomy strictures result in intrahepatic or extrahepatic duct transection, which precludes endoscopic therapy altogether.[4]

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Early Antibiotic Exposure and Childhood Weight Gain

To the Editor Dr Gerber and colleagues assessed the association between antibiotic exposure during the first 6 months of life and childhood weight gain and concluded that there was no association.[1] However, there was a significant difference in weight gain in children exposed to any antibiotic in the first 24 months of life (P = .001). The subanalyses showed that this difference was significant in children who received only 1 antibiotic course (P = .01) but was greater in those who received 2 courses (P = .02) and even greater in those exposed to 3 or more courses (P = .002). Can the authors comment on these findings and explain why they did not consider these significant differences in their discussion?

A number of studies have shown that antibiotic treatment can cause dysbiosis[2] and that its effect on weight gain seems to be particularly strong in the first 2 years of life, when gut microbiota is still developing. A recent study of antibiotic exposure before age 2 years showed that it was associated with an increased risk of obesity by age 4 years (odds ratio, 1.21 [95% CI, 1.07-1.38]) and that the odds ratio increased with repeated exposure.[3] The results are similar to those of Gerber and colleagues,[1] but the authors concluded that the administration of 3 or more courses of antibiotics before age 2 years was associated with an increased risk of early childhood obesity.[3]

Gerber and colleagues also observed significant differences between antibiotic exposure to different drug categories in the first 2 years of life, but these were greatest in the case of broad-spectrum antibiotics (P = .004) and macrolides (P = .004).[1] Use of drugs that are effective against both aerobic and anaerobic bacteria, such as macrolides, has the greatest effect on increased body weight,[4] supporting the findings that changes in antibiotic-related gut microbiota cause dysbiosis and are associated with overweight. How do Gerber and colleagues explain the greater difference in the rate of weight gain in children exposed to broad-spectrum antibiotics?

I agree that the primary reasons for limiting antibiotic exposure in young, healthy children include the need to avoid development of bacterial resistance and antibiotic-related adverse events.[5] However, the relationships among antibiotic use, nutritional parameters, and the characteristics of the microbiota are still unclear and require further study.

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In Reply As Dr Esposito points out, growth trajectories did not differ between children exposed vs unexposed to antibiotics in the first 6 months of life in our study. This primary exposure window was developed a priori based on the biological mechanism through which antibiotics have been shown to influence adiposity in animal models. However, because of previous reports cited by Esposito[1,2] (and others), we also examined a secondary antibiotic exposure window (24 months) and found a statistically significant but, in our opinion, clinically meaningless increase in growth—approximately 150 g over 3 years, the equivalent of a small cup of water. Even if the finding of this secondary analysis were real, there is no evidence that 150 g of weight has any untoward health effects for any one individual and thus should not be considered a larger public health threat for the population of children exposed to antibiotics. Furthermore, no increase in growth was found in the preplanned study of twins discordant for antibiotic exposure at 24 months, and subanalyses revealed no clinically meaningful differences between antibiotic spectrum (antianaerobic or macrolides) or exposure dose response (1, 2, or ≥3 courses).

With respect to Esposito's comment, conclusions should not be based solely on *P* values but instead on point estimates and confidence intervals.[3] Large samples (such as this analysis of 40 000 patients) can lead to small *P* values that are not clinically meaningful[4] (such as 150 g of weight over 3 years' time). For the results by antibiotic spectrum and number of courses, the confidence intervals of the various point estimates all overlapped, suggesting that there were no true differences across groups.

Esposito also highlights an important distinction between our study and prior efforts to address this question: the outcome definition. Scott and colleagues,[1] Saari and colleagues,[2] and others have reported associations between early-life antibiotic use and body mass index using dichotomous outcome definitions to assess obesity over time. The practice of dichotomizing continuous data has long been condemned by statisticians.[5] In this case, dichotomizing obesity suggests that it is an all-or-nothing event and overly simplifies the characterization of growth over time. For instance, assessing whether a child ever reached the 95th percentile of body mass index would classify children that moved from the 94th percentile to the 95th percentile as moving from not obese to obese (1) without following the trajectory of this growth (eg, assessing if the child subsequently reverted to the 94th percentile) and (2) ignoring potentially significant weight gains or losses that are not proximal to this threshold, such as an increase from the 50th percentile to the 75th percentile. In contrast, the analysis of the association between antibiotic exposures and the rate of growth in all children during the first 8 years of life provides a more comprehensive and accurate assessment of antibiotic use and weight gain.

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Laboratory Testing in the Setting of Diabetic Scleredema

To the Editor Dr Chatterjee, in his case presentation of a patient with diabetic scleredema,[1] did not explain the rationale for ordering a serum immunofixation. Presumably, it was ordered to evaluate the patient for the possibility of multiple myeloma. However, based on the patient's presentation and absence of anemia, renal insufficiency, hyperproteinemia, hypercalcemia, or osteolytic lesions, plasma cell disorders should not have been high on the list of possible diagnoses.[2,3] In addition, if a plasma cell disorder was suspected, a serum protein electrophoresis study with serum free light chain testing would have been more appropriate,[4,5] as those tests in combination have a sensitivity of 100%, specificity of 97%, positive predictive value of 60%, and a negative predictive value of 100% for the diagnosis of plasma cell disorder.

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