between the 2 comparisons. Concerns about the small sample size have been expressed by Mazurek et al. [1], as well, in their comments on precision. Nevertheless, eliminating indeterminate results would be at odds with true comparative performance. Therefore, in such situations, a researcher could perform sensitivity analyses according to intention-to-treat analysis principles.

When the statistical significance is set at .05, P values of .06 are not statistically significant. Furthermore, when analyses with and without the indeterminate values are used, the P values should be adjusted. However, as suggested by Altman et al. [3], a P value of .05 is a convenient cutoff point, and P values of .04 and .06, which are not greatly different, should lead to similar interpretations rather than to radically different ones. This also underlines the importance of planned experiments, adequate power for important clinical differences, and decisions based on clinical findings rather than purely on statistical findings.

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References


Reply to Tamhane

To the Editor—We appreciate other researchers’ interest in refining the statistical approaches for evaluating new tests for Mycobacterium tuberculosis infection, which for the most part are not yet standardized. We concur with Dr. Tamhane’s [1] position regarding the use of McNemar’s test for correlated proportions to compare the sensitivity of the Quantiferon-TB Gold In-Tube assay (Cellestis) with the sensitivity of the tuberculin skin test. McNemar’s test could also be used to statistically compare the specificities of 2 tests in a cohort of people without infection. However, we do not know whether the subjects without tuberculosis included in our study [2] were infected with M. tuberculosis. Although the subjects did not receive diagnoses of tuberculosis, the majority of these subjects had substantial risk of being infected with M. tuberculosis.

IFN-γ release assays are promising alternatives to the tuberculin skin test. We strongly encourage efforts to develop and implement tests such as these. Many questions remain to be answered, especially with regard to the predictive value of IFN-γ release assays. Larger studies with long-term follow-up are needed to determine the value of IFN-γ release assays in predicting the risk of active tuberculosis disease.

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Traveler’s Diarrhea Chemoprophylaxis: An Alternative Recommendation

To the Editor—The article by Hill et al. [1] effectively details guidelines proposed by the Infectious Diseases Society of America for the treatment and prevention of illnesses in travelers to foreign countries. However, the discussion of traveler’s diarrhea chemoprophylaxis deserves further comment. The investigators recommend fluoroquinolones as standard preventive therapy for traveler’s diarrhea. Unfortunately, the authors neglect to discuss the correlation of fluoroquinolone administration with recent epidemic outbreaks of Clostridium difficile–associated diarrhea (CDAD) in North America. In addition, the authors only briefly refer to postinfectious irritable bowel syndrome (IBS) as a potential consequence of traveler’s diarrhea and do not give proper emphasis to the importance of preventing this postinfectious sequela.

Several clinical studies have reported increased incidence, severity, and frequency of CDAD in North America [2–6]. Epidemic outbreaks of CDAD are associated with a predominant strain of C. difficile (North American PFGE type 1/ribotype 027) that produces levels of toxins A and B that are 16–23 times higher than the levels of toxins A and B in control strains [6]. Such C. difficile isolates were uncommon prior to 2000, and their widespread emergence is thought to be a result of in-

References


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increasing antibiotic resistance to the fluoroquinolone antibiotics [4, 5]. Because fluoroquinolone administration is a primary risk factor for acquiring CDAD, control of antibiotic prescribing is a crucial preventative measure for precluding the spread of this serious illness. Thus, the association of quinolone antibiotics with the increasing incidence and severity of CDAD should serve as rationale for their exclusion from guidelines for traveler’s diarrhea chemoprophylaxis, except perhaps in rare circumstances—a position contrary to the recommendations of Hill et al [1].

An additional point of concern regarding the article by Hill et al. [1] is the lack of discussion on the critical role that traveler’s diarrhea prophylaxis may play in preventing the serious potential sequelae of postinfectious IBS. Postinfectious IBS is characterized by the onset of IBS symptoms following an episode of acute gastroenteritis (e.g., traveler’s diarrhea) in the presence of previously normal bowel function [7]. Given the accumulating evidence validating its pathophysiology, postinfectious IBS is an emerging topic of clinical importance in gastroenterology. Based on clinical studies, the incidence of postinfectious IBS is substantial, with 7%–30% of individuals receiving a diagnosis of postinfectious IBS after an enteric infection [7–9]. In addition, the impact of postinfectious IBS on quality of life can last for several months or years. Because traveler’s diarrhea is a primary risk factor for developing postinfectious IBS, antibiotic chemoprophylaxis may provide an opportunity to prevent this potentially serious illness. In this regard, the nonabsorbed antibiotic rifaximin has demonstrated clinical efficacy in preventing traveler’s diarrhea in US students traveling to Mexico and may provide a safer option for traveler’s diarrhea chemoprevention [10].

The travel medicine guidelines proposed by Hill et al. [1] are valuable; however, additional factors influencing traveler’s diarrhea chemoprevention should be emphasized, including the serious risks associated with fluoroquinolone administration (e.g., CDAD) and the importance of preventing postinfectious sequelae (e.g., postinfectious IBS).

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References


Reply to Connor

To the Editor—Dr. Connor [1] raises important issues about the use of antibiotics to treat traveler’s diarrhea (TD). He highlights the association of fluoroquinolones with the increasing problem of Clostridium difficile–associated diarrhea and its associated morbidity and mortality. He then proposes an alternative approach to the prevention of TD by prescribing prophylactic rifaximin for travelers, with the goal of decreasing the risk of TD and preventing a potential long-term sequela of TD, postinfectious irritable bowel syndrome.

Dr. Connor’s letter [1] may be read to imply that the Infectious Diseases Society of America guidelines [2] recommend widespread use of antibiotic prophylaxis with a fluoroquinolone to prevent TD. The guidelines clearly do not endorse this approach. They state that, based on currently available data, antibiotic prophylaxis with any antimicrobial against TD is not recommended for most travelers and should only be prescribed after a careful risk-benefit assessment for an individual traveler [2]. Instead, the guidelines endorse targeted short-course treatment of travelers with TD using antibiotics with demonstrated efficacy for the treatment of a subgroup of individuals.

Dr. Connor [1] also raises the specific concern of whether fluoroquinolones—as opposed to rifaximin—should be used for treatment because of the association of fluoroquinolones in certain contexts with C. difficile–associated diarrhea. The Infectious Diseases Society of America guidelines are in agreement that inappropriate use of all antibiotics should be avoided to reduce the risk of C. difficile–associated diarrhea and other adverse events. The literature regarding the treatment of TD...