QT-prolonging medications (57%, globally considered), and anti-Ro/Sjogren's syndrome-related antigen A antibodies (52%) (3).

In this cohort, we found that 2 patients (5%) were receiving CFX+LSZ when TdP developed. Notably, this percentage was identical to that observed with levofloxacin, clarithromycin, or promazine (5% each) and was higher than that seen with ciprofloxacin, sotalol, or haloperidol (2%), which all represent well-recognized QT-prolonging medications (4). Only amiodarone (27%) and citalopram, fluconazole, or sertraline (7%) were more frequently administered.

Although follow-up studies are required to confirm the findings of Lorberbaum et al. (1), our observations seem to be in agreement with the view that CFX+LSZ may represent a currently overlooked contributing factor that increases the TdP risk, via specific (not class-related) QT-prolonging effects exerted by these 2 molecules when combined.

The potential harmfulness of this association should be carefully kept in mind, particularly in the presence of other recognized QT-prolonging factors. Both drugs are used worldwide, but they are presently considered as having neutral effects on ventricular repolarization.

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REPLY: Combination Therapy With Ceftriaxone and Lansoprazole, Acquired Long QT Syndrome and Torsades de Pointes Risk

We thank Dr. Lazzerini and colleagues for sharing their clinical observations supporting the drug–drug interaction (DDI) findings in our recent paper (1). In isolation, their observations could be dismissed as idiosyncratic by skeptics, but data science—the application of rigorous analytical methods to large datasets—provides the context needed to explain these effects across large patient populations. The integration of adverse event report mining, electronic health record corroboration, electrophysiology experiments, and now these case studies paints a clear picture of a DDI that could not have been identified using traditional surveillance approaches (2).

We have further capitalized on the promise of health data science by participating in Observational Health Data Sciences and Informatics (OHDSI), an international network of >140 researchers in >20 countries performing large-scale analyses on distributed databases that in total comprise >600 million patients (3). Each participating site converts their patient data to a common data model that enables analyses created at one location to be replicated across the entire network while maintaining patient privacy. This open and international collaboration has developed open source software tools for data exploration and evidence generation, conducted multivariate analyses to predict drug side effects, and improved definition of the heterogeneity in treatment pathways (4,5). The latter study was performed on an underlying population of >250 million patients from 11 data sources in 4 countries and took 20 days from conception to results from 7 sources, highlighting the efficiency with which these analyses can be performed at scale.

In the case of ceftriaxone and lansoprazole, we used a combination of public and private clinical data to identify the interaction. Through collaborations like OHDSI, these data are available to all researchers with interests in large-scale retrospective studies. We hope that the current study motivates others to participate in these new data science initiatives.

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Vitamin E May Protect Against Contrast-Induced Acute Kidney Injury

McCullough et al. (1) reviewed the pathophysiology and treatment options for contrast-induced acute kidney injury (CI-AKI). They stated that no effective adjunctive pharmaceutical had been demonstrated that either prevented or treated CI-AKI. However, they also suggested that of the agents being investigated, statins were the most promising. We would like to point out that strong evidence has also emerged regarding the effect of vitamin E against CI-AKI, which was not mentioned in their review.

Three randomized placebo-controlled trials found that vitamin E significantly prevented CI-AKI, with point estimates ranging from 52% to 75% for the decrease in the incidence of CI-AKI (2–4). All participants had chronic kidney disease and had been subjected to coronary catheterization or angiography. The latest trial reported CI-AKI cases in 14.1% of the placebo group, but in only 6.7% of the vitamin E group, which corresponded to 7.4% of participants benefitting from the vitamin, with a number needed to treat (NNT) of 13.5 (4). The 2 earlier studies found NNTs of 5.8 (2) and 10.6 (3). In each study, approximately one-half of the patients were on statin therapy; therefore, the effects of vitamin E might have also been beneficial in addition to statins.

Two of the vitamin E trials were carried out in Thailand (2,3), and 1 was carried out in Iran (4). Thus, it is not known whether the findings can be directly generalized to Western countries. Even if the positive findings might only be applicable to less developed countries, the findings are important for the populations of such countries.

Vitamin E is an essential nutrient, and therefore, its potential benefit in preventing CI-AKI is interesting. Furthermore, vitamins E and C may interact. Vitamin E decreased total mortality in male smokers aged older than 65 years if their dietary vitamin C intake level was high, but not if their vitamin C intake was low (5). Thus, a large factorial trial seems warranted to examine the effect of statins and vitamins E and C, and their combinations to discover the optimal protocol to prevent CI-AKI.

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REPLY: Vitamin E May Protect Against Contrast-Induced Acute Kidney Injury

We appreciate the comments from Drs. Hemilä and Rezaei concerning small randomized trials of short-term vitamin E for the prevention of contrast-induced acute kidney injury (CI-AKI). In the trial