epithelial cells. The surface of the epithelium can be elevated as a consequence of their presence, but not to the extent of the cobblestoning sometimes observed with giant papillae. For the purposes of standardizing population-based surveys to estimate the prevalence of trachoma, intensive training courses are conducted for ophthalmic health care workers.[4,5] For emergency department work, however, reference to the grading card of the World Health Organization simplified system[3] may be helpful.

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In reply:

In the Images in Emergency Medicine article titled "Young Boy With Roughening in the Inner Eyelids," we reported an 8-year-old child with conjunctival hyperemia, increased tearing, moderate itching of the right eye, and intense inflammatory papillary thickening of the upper tarsal conjunctiva of the right eye. The patient was from a city located in the Brazilian Amazon jungle and he was assessed during a national survey of trachoma prevalence in schoolchildren. We considered allergic conjunctivitis within our differential. Giant papillae (papillary hypertrophy) observed in atopic keratoconjunctivitis and vernal keratoconjunctivitis differ from the lymphoid follicles of trachoma. We considered trachoma conjunctivitis because of the intense trachomatous inflammation in addition to lymphoid follicular inflammation, which may explain the exuberant clinical feature mimicking giant papillae. In this case, there was excellent clinical response to antibiotic therapy, and no other treatment was given. Laboratory testing (microscopy of conjunctival scrapings, isolation in cell culture, direct fluorescent antibody, enzyme immunoassay, serology, nucleic acid hybridization probes, and nucleic acid amplification tests)[1] was unavailable for diagnostic confirmation, an admitted limitation of this report. Allergic keratoconjunctivitis was an important part of the differential in this case. Other possibilities included viral and bacterial infections.[2]

The occurrence of trachoma is directly related to low socioeconomic status and poor sanitation conditions, hygiene, and access to water, which favor the dissemination of *Chlamydia trachomatis*, the causal agent of the disease. Although the burden of trachoma has been reduced in Brazil, the disease continues to occur, especially affecting the poorest and most disadvantaged populations in the country.[3]

We appreciate the letter by Talero et al,[4] and we believe that their comments contribute positively to our article, particularly the recommendation of the grading card of the

World Health Organization simplified system in emergency department work.

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Fragility Measures: More Limitations Considered

To the Editor:

We commend the work by Brown et al[1] that, using the fragility index and fragility quotient, assesses the fragility of randomized controlled trials in the emergency medicine literature. Although they provide a good overview of the limitations of the 2 metrics, we would like to further question the utility of fragility measures.

In their critique of fragility measures, Carter et al[2] suggested that fragility index is a "P-value in sheep's clothing." In their article, they demonstrated the strong relationship between *P* values, fragility index, and sample size. The results of their study were based on 60,000 simulated clinical trials using a combination of 10 sample sizes (100 to 1,000), with relative risks of 1.0, 0.67, and 0.33 for intervention versus control.[2] They showed that *P* values decrease as sample size increases when the effect size is nonzero; the inverse relationship is observed when fragility index and sample size are compared. Stated another way, if the effect size is held constant and the sample size increases, the fragility index likewise increases.[2]

In their study, Brown et al noted that the overall sample size for included trials was a median of 140 (interquartile range 69.5 to 286), with the overall fragility index for primary outcomes of the 74 included studies equal to 5 (interquartile range 2 to 11.75) and a fragility quotient of 0.039 (interquartile range 0.015 to 0.081). The small median sample size in randomized controlled trials in this study could be one reason for the low fragility index, as mentioned above. Furthermore, as Carter et al[2] observed, randomized controlled trials "are designed to balance the sample size with expected efficacy. In doing so, the [fragility index] is also minimized and results will necessarily hinge on fewer events. This is unavoidable, particularly in the context of clinical equipoise and finite resources."

Although certainly fragility quotient (fragility index normalized to study size) addresses some of these concerns, relative measures of fragility have not proven to be a reliable indicator of study quality, as the authors suggested (for example, the Collaborative Study Group captopril study, which established the use of angiotensin-converting enzyme inhibitors for the prevention of worsening diabetic nephropathy).[3] The primary endpoint of Collaborative Study Group was a doubling of the baseline serum creatinine concentration. Using the methods of Brown et al, we calculated the fragility index of Collaborative Study Group's primary endpoint to be 4, with a fragility quotient of 0.009, or 1 event per 100 patients. Or consider the West of Scotland Coronary Prevention trial, the first major study to demonstrate the efficacy of statins in the primary prevention of nonfatal myocardial infarction or death from coronary artery disease in men with hypercholesterolemia.[4] The fragility index of this study was 34, with a fragility quotient of 0.005. The fragility index and fragility quotient of these studies suggest these trials are quite fragile, yet have proved clinically meaningful in daily practice.