CORRESPONDENCE

Antipsychotics for Preventing Delirium in Hospitalized Adults

TO THE EDITOR: We read Oh and colleagues' (1) systematic review and meta-analysis on the benefits and harms of antipsychotics for preventing delirium in a cohort of surgical and critical care patients with interest. Their findings, including the results of 14 randomized controlled trials (RCTs), did not support the routine use of haloperidol or second-generation antipsychotics for this purpose.

The fragility index (FI), an intuitive measure of the robustness of RCTs, was introduced for use in critical care medicine (2). Studies with higher FI scores have more robust findings than those with low scores. The FI was recently applied to different meta-analyses in order to evaluate the results when only studies with an FI greater than 0 were included (3, 4). Although Oh and colleagues performed an excellent statistical analysis in their review, we are concerned about the fragility of the included RCTs.

We evaluated the FI of the RCTs included in Oh and colleagues' meta-analysis using a 2 × 2 contingency table and a single *P* value produced by the Fisher exact test (2). We were surprised that only 4 of the 14 included RCTs had an FI score greater than 0 for their primary outcome; the FI scores of these studies were as follows: Hakim and associates (reference 31 in Oh and colleagues' review), 1 ($P = 0.034$); Kaneko and associates (reference 41 in Oh and colleagues' review), 3 ($P = 0.003$); Prakanrattana and Prapaitrakool (reference 39 in Oh and colleagues' review), 3 ($P = 0.008$); and Wang and associates (reference 37 in Oh and colleagues' review), 2 ($P = 0.033$) (1). We then performed the meta-analysis on the delirium incidence using the DerSimonian–Laird random-effects models including only these 4 RCTs. We found no effect on delirium incidence between haloperidol and placebo (relative risk, 0.546 [95% CI, 0.296 to 1.005]) but did find a statistically significant effect between second-generation antipsychotics and placebo (relative risk, 0.376 [CI, 0.215 to 0.656]). These results show that even an analysis of robust trials confirms that second-generation antipsychotics may decrease the delirium

incidence in surgical patients but that haloperidol had no effect on this outcome.

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=L19-0754.

doi:10.7326/L19-0754

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IN RESPONSE: We understand the FI to be a measure of the statistical robustness of study results. Dr. Vargas and colleagues conclude that "analysis from robust trials confirms that second-generation antipsychotics may decrease the delirium incidence in surgical patients but that haloperidol had no effect on this outcome." This is similar to the findings reported in our systematic review and our more comprehensive report that included subgroup analysis specifically for postoperative patients (1). Our systematic review included all studies that met the eligibility criteria regardless of sample size or the statistical significance of their findings. We graded the strength of evidence according to the Agency for Healthcare Research and Quality's guide (2). With this approach, the strength of evidence is determined not solely on a threshold of statistical significance (for example, $P < 0.05$) but on many relevant domains, including consistency, indirectness, precision, and reporting bias across all studies forming the body of evidence under evaluation. We hope that this explanation helps clarify the process that we used to evaluate the strength of evidence in our systematic review.

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M19-1859.

doi:10.7326/L19-0755

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Vibrio vulnificus Infections From a Previously Nonendemic Area

TO THE EDITOR: King and colleagues (1) describe 5 patients affected by *Vibrio vulnificus* infection leading to substantial morbidity and mortality. This series is notable in that the exposures occurred within the Delaware Bay region, north of the historical range of *V vulnificus*. These 5 cases were clustered during the summers of 2017 and 2018, whereas only 1 case had been seen at the authors' hospital in the preceding 8 years. King and colleagues cite work done by Martinez-Urtaza and associates (2), who found that warming in the Gulf of Mexico since 1998 expanded the at-risk season for *V vulnificus* infection. Vezzulli and coworkers (3) similarly reported an unprecedented occurrence of human *Vibrio* infections in the coastal North Atlantic associated with increasing sea surface temperature.

Many articles have described a northward expansion of vectors of other infectious pathogens in addition to *Vibrio* species. For example, Sonenshine (4) published a review describing range expansion of various tick species in North America. Many other authors, including Ryan and colleagues (5), published predictive models on the global expansion of regions at risk for mosquito-borne diseases.

These articles and others show the shifting distribution and intensity of many infectious diseases due to changing climate conditions. It is reasonable to expect that many other infectious organisms will respond to warming global temperatures. However, most medical students and trainees currently receive no education on climate change or its influence on health variables. This leaves them unprepared to recognize or predict illness that no longer adheres to the distribution or seasonal timing of previous centuries.

We commend the American Medical Association for recently passing a resolution recommending integration of climate change education across the medical education continuum. Educating future physicians is necessary to prepare them to care for patients in a world where a wide range of

disease conditions are shifting in response to anthropogenic climate change.

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=L19-0756.

doi:10.7326/L19-0756

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TO THE EDITOR: We read King and colleagues' case report involving 5 cases affected by *V vulnificus* with interest and were curious about the opportunities for exposure to this pathogen in patients 2 through 5. Although patient 1 denied exposure to crabs or the Delaware Bay, he had the potential for multiple exposures to these pathogenic bacteria in his daily job at a seafood restaurant. Patients 2 through 5 did have exposure to crabs and the Delaware Bay, but whether these were 1-time opportunities or they had potentially repeated exposures in their daily life is unclear.

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=L19-0757.

doi:10.7326/L19-0757

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IN RESPONSE: We agree with Drs. Wai and Ahdoot that climate change will affect the epidemiology of infectious diseases and that physicians must be aware of this change in order to ensure proper diagnosis. Indeed, Cooper Medical School of Rowan University recently held a grand rounds discussion titled "Climate Change and Healthcare." As we have described, climate change has clearly affected the geographic range of infectious diseases; in addition, it will continue to profoundly affect the epidemiology of noncommunicable diseases through the direct effects of such catastrophic events as flooding and increased risks for exposure to such hazards as air pollutants and other environmental threats (1). We strongly support integrating education about the effect of climate change on both communicable and noncommunicable diseases into the medical curriculum.

Patient 2 stated that he routinely wore protective gloves while cleaning crabs; he thus at least had previous exposure to crabs while cleaning them, but he did not do so on a daily basis. Patient 5's records do not mention whether he had previous exposure to crabs from either catching or consuming them. Crabbing is a common hobby in our area during the summer months, and participants make multiple crabbing trips during the season. However, in addition to crab exposure, patients 3 and 5 had sustained cutaneous injuries during water exposure while crabbing immediately before they presented with necrotizing fasciitis. Of note, the patients in our series had predisposing risk factors for severe *V vulnificus* infection.

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=L19-0133.

doi:10.7326/L19-0758

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Firearm-Related Injury and Death in the United States

TO THE EDITOR: I read McLean and colleagues' article (1) with interest. It was wonderful and appropriate to see the President of the American College of Physicians continuing to lead our profession by proposing evidence-based interventions to reduce gun violence in the United States. The current collaborative, multiorganizational approach is clearly a great strategy to achieve results. I suggest the following further recommendations.

First, a nationally enforced waiting period for gun ownership should be enacted. Currently available evidence (2) shows that this strategy substantially reduces suicides by firearms, which are currently the cause of most gun deaths in the United States (1). This intervention may even reduce gun homicide rates (3). I hope that more data on this subject will be obtained soon.

Second, a national gun registry for semiautomatic handguns and rifles (such as AR-15s and AK-47s) should be created. This registry could exempt hunting rifles, antique guns, and such nonautomatic handguns as revolvers to blunt any concerns about Second Amendment rights. The evidence from Australia suggests that this approach alone substantially reduces the total number of gun-related deaths (4).

Finally, physicians should receive more education about guns and gun violence nationally and locally. The need to provide such education is pressing (5). Knowledgeable physicians—especially former military members and gun owners—are a great untapped resource. A speaker's roster could be developed for giving presentations to medical students and housestaff and at grand rounds and national and hospital staff meetings.

Unfortunately, eliminating this epidemic is a marathon and not a one-and-done sprint. Fortunately, the American College of Physicians is clearly up to the challenge.

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Disclosures: The author has disclosed no conflicts of interest. The form can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=L19-0743.

doi:10.7326/L19-0743

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IN RESPONSE: In August 2019, the American College of Physicians joined with 6 other physician and public health professional organizations in publishing a call to action regarding firearm injury and death as a major public health problem in the United States. We advocated for measures and impactful legislation that would reduce firearm injuries and deaths and protect patients and the communities that physicians serve. We have subsequently invited a wide variety of organizations to endorse the article. In addition to the organizations represented by the authors of the article, the following organizations are also officially endorsing the article and its recommendations:

Alliance for Academic Internal Medicine
American Academy of Allergy, Asthma, and Immunology
American Academy of Neurology
American Academy of Ophthalmology
American Academy of Physical Medicine and Rehab
American Association of Clinical Endocrinologists
American College of Cardiology
American College of Chest Physicians
American College of Obstetricians & Gynecologists
American College of Preventive Medicine
American Geriatrics Society
American Medical Group Association
American Medical Women's Association
American Psychological Association
American Society of Hematology
American Society of Nephrology
American Thoracic Society
Association of American Medical Colleges
C. Everett Koop Institute at Dartmouth
Doctors for America
Everytown for Gun Safety
Giffords
Institute for Patient- and Family-Centered Care
Manhattan District Attorney's Office
National Council of Asian Pacific Islander Physicians
National Hispanic Medical Association
National Partnership for Women & Families
Newtown Action Alliance
Prevention Institute
Renal Physicians Association
Scrubs Addressing the Firearms Epidemic
Society for Adolescent Health and Medicine
Society of Critical Care Medicine
Society of General Internal Medicine
Society of Interventional Radiology
States United to Prevent Gun Violence

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Disclosures: Disclosures can be viewed at www.acponline.org/authors/icmje/ConflictOfInterestForms.do?msNum=M19-2441.

doi:10.7326/L19-0744