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Pseudomonas aeruginosa Outbreak in a Neonatal Intensive Care Unit Attributed to Hospital Tap Water: Methodological and Statistical Issues to Avoid Misinterpretation

To the Editor—We were interested to read the May 2017 article by Bicking Kinsey et al.[1] The authors investigated an outbreak of *Pseudomonas aeruginosa* infections. They found that compared with controls, case patients had higher odds of being in a room without a point-of-use filter (odds ratio [OR], 37.55; 95% confidence interval [CI], 7.16–∞).[1]

Although these results are interesting, some methodological and statistical issues should be considered. The estimated effect size for some risk factors such as unfiltered water is biased due to sparse data bias. In other words, the data are inadequate to estimate a valid and precise OR. The main indicators of sparse data bias are a huge effect-size estimate and a remarkably wide and even infinite confidence interval limit.[2] The most common strategy to adjust sparse data bias is a correction of one-half, a conventional method in which one-half is added to each level of exposure–outcome combination prior to statistical analysis.[2] The problem with the conventional method is that it can lead to implausible ratio estimates.[2] Greenland and Mansournia proposed an advanced method, namely, penalization via data augmentation to adjust and minimize sparse data bias.[2,3] In this method, the effect-size estimate is assumed to falls in an acceptable and possible range, such 1/40 to 40. Using penalization, the effect-size estimates are reduced to the range specified.[2] We analyzed the presented data in the study conducted by Bicking Kinsey using the penalization method to test how the results can be influenced by sparse data bias. We found that the unfiltered water in univariable model had an estimated OR of 17.23 (95% CI, 3.56–83.19). Thus, we think the true and valid estimated OR for unfiltered water is different than 37.55 (95% CI, 7.16, ∞) as reported in the article.

The take-home message for readers is that sparse data bias is a common bias in biomedical research[4–7]; however, it is rarely addressed in analyses. Furthermore, sparse data bias can be minimized using efficient statistical methods.

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Long-Term Care Facility (LTCF) Residents Colonized With Multidrug-Resistant (MDR) *Klebsiella pneumoniae* Lineages Frequently Causing Infections in Portuguese Clinical Institutions

To the Editor—The recent increase of extended-spectrum β-lactamase (ESBL)–producing *Klebsiella pneumoniae* (*Kp*) and the emergence of carbapenemase-producing *Kp* in Portuguese clinical settings parallels epidemiological trends described in other countries.[1–4] Moreover, *Kp* isolates causing hospital infection often correspond to the patient's own colonizing strains, stressing the need to survey fecal carriage of multidrug-resistant (MDR) *Kp* in patients from different clinical settings.[5] Long-term care facilities (LTCFs) are fundamental institutions in contemporary healthcare services, mainly assisting elderly people who, due to frequent hospitalizations, recurrent antibiotic consumption, and communal living, are at a high risk of infection by MDR bacteria.[6] Different studies among European LTCFs residents have reported high rates of colonization by CTX-M-15-producing *Escherichia coli* (*Ec*) B2-ST131, but little is known regarding the prevalence and diversity of other MDR *Enterobacteriaceae* species (and particularly *Kp*) colonizing LTCFs residents.[6,7] The aim of this study was to assess the fecal carriage rate and epidemiological features of non-*Ec Enterobacteriaceae* isolates resistant to extended-spectrum β-lactams among Portuguese LTCF residents.

Fecal samples from residents (n = 47) at LTCF 1 (25 beds; n = 25 samples) and LTCF 2 (40 beds; n = 22 samples) in northern Portugal were collected during July 2015 and January 2016, respectively. Demographic and clinical characteristics of the residents are summarized in Online Supplemental Table S1. Rectal swabs were suspended in 2 mL saline solution, and 0.2 mL were seeded on chromID ESBL (bioMèrieux, Marcy-l'Étoile, France) and chromID Carba SMART plates (bioMèrieux, Marcy-l'Étoile, France) directly and after a preenrichment step in 10 mL of trypticase soy broth containing a 10-μg meropenem disk, and incubation at 37°C for 18 hours for the screening of ESBL and/or plasmid-mediated AmpC and carbapenemase producers at 37°C for 24–48 hours, respectively.[8,9] All presumptive non-*Ec Enterobacteriaceae* (representative morphotypes per plate) were selected for further characterization. ESBL/plasmid–mediated AmpC or carbapenemase production was confirmed by phenotypic or Blue-Carba tests, respectively, polymerase chain reaction (PCR), and sequencing.[9] Susceptibility testing to non-β-lactams antibiotics was performed by the disk diffusion[10] and bacterial identification was confirmed by species-specific PCR, and/or matrix-assisted laser-desorption/ionization–time-of-flight mass spectroscopy. Clonal relatedness among *Kp* isolates was evaluated by Fourier transform infrared (FTIR) spectroscopy, multilocus sequence typing (MLST), and *wzi* capsular typing.[11–13]

Air samples (250 L) from different common indoor (3 from LTCF 1 and 1 from LTCF 2) and outdoor spaces were also collected using an MAS100 (Merck Millipore, Germany) air sampler to assess microbiological air quality. The different culture medium plates (ie, plate count agar [PCA], chromID ESBL, and chromID Carba SMART) used were incubated at 25°C for 72 hours (PCA, for fungi quantification) or at 37°C for 48 hours (PCA and selective medium, for bacteria quantification). Microbiological air quality (expressed in CFU/m^3) was categorized according to the Portuguese law.[14]

A high proportion of fecal samples (19 of 47; 40.4%) was positive for non-*Ec Enterobacteriaceae* producing ESBL (29.8%) or plasmid-mediated AmpC (10.6%). Despite some epidemiological differences, similar colonization rates were observed in both institutions: 44% in LTCF 1 and 36% in LTCF 2 (Table 1). Notably, in 53% of the samples, we also identified ESBL-producing *Ec,* leading to an overall rate of fecal carriage with ESBL producers of 81% (data not shown). ESBL carriage was significantly associated with the gender, length of stay, and residents of shared rooms, whereas plasmid-mediated AmpC carriage was only significantly associated with consumption of β-lactams in the previous 3 months (Online Supplemental Table S1). Air quality was within the established standards only at LTCF 1, although in both institutions no growth was detected on selective media. The colonization rates by ESBL-producing non-*Ec Enterobacteriaceae* (29.8%) were significantly higher than those observed in these species among LTCFs and nursing home residents years ago in Portugal in 2008–2012 (~6%) or in LTCFs in other European countries in 2012–2013 (~8%).[6] Despite the low sample size, this extraordinary increase (~5-fold) is worrisome in this at-risk population; it is probably influenced by the recent global expansion of MDR *Kp* isolates in Portuguese clinical institutions.[4] Carbapenemase-producing *Enterobacteriaceae* were not

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