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Food Indwelling *Clostridium difficile* in Naturally Contaminated Household Meals: Data for Expanded Risk Mathematical Predictions

To the Editor—We read with interest the study "An Evaluation of Food as a Potential Source for *Clostridium difficile* Acquisition in Hospitalized Patients," in which Kwon et al[1] made mathematical predictions on the risk of *C. difficile* infection (CDI) acquisition due to consumption of *C. difficile* (CD)–contaminated foods in one hospital setting (presumably from a single kitchen source). Although the authors tested many small-sized, mixed-meal samples (n = 910) consumed by 149 patients (median length of hospital stay, 4 days), their mathematical predictions were based on prevalence data obtained using, apparently, nonenrichment culture methods (previously tested for fecal swabs), which are suboptimal for culturing CD and foodborne pathogens from food. Furthermore, the study used a nonstandard heat-shock treatment (80°C, 10 minutes) prior to culture, which introduces a negative bias because this heat treatment has been shown recently to kill up to 75% of CD isolates in liquid media.[2] Hence, not surprisingly, Kwon et al reported a low prevalence of CD in the tested meals (0.22%). This observed prevalence was then used for mathematical modeling. With low-prevalence data, their prediction regarding causal connections between food contamination and the incidence of CDI was, reasonably, that food is an unlikely risk for CDI (<1 colonization per 1,000 admissions) in their study.

Although the study makes an important contribution to the controversial topic of whether CDIs are foodborne, their conclusion seems biased due to suboptimal CD culture methodology. Distinctive methodological imperfections, without critical interpretation, may set us back to the first studies in the 1980s, when CD was not found in hospital meals using nonenrichment methods. After decades of believing CDI was strictly nosocomial,[3] there is now solid evidence based on whole-genome sequencing of CD isolates in hospitals that less than one-third of CDIs are nosocomial, whereas most sources of exposure that result in CDIs remain unknown.[4] With such genomic hospital discoveries, and with the persistence of CDI despite immense efforts to prevent nosocomial transmission, it is not advisable to discard the most plausible source of toxigenenic CD spores (ie, food), even if some studies report negative results. Many more unbiased reports have shown that food can be a real source of CD spores of virulent or multidrug-resistant CD strains,[5] including studies of hospital meals showing 17% and 27% prevalence on cooked and uncooked meats, respectively.[6,7] Even Kwon et al reported important CD strains in food: specifically, CD spores of toxigenic PCR-ribotypes 001 in gelatin dessert and 027 in 'vegetable/bread/grain.'

Food-dwelling CD became evident as a natural source of exposure to humans in 2005 when emerging hypervirulent CD strains causing severe disease in humans in Canada and United Kingdom were unexpectedly found in food animals[8] and retail foods.[3,9] To date, no studies have addressed kitchens as complex food environments where cross contamination and cooking practices may influence the prevalence of CD at the consumer level. Here, we would like to contribute to the external validity of the Kwon study on hospital-cooked meals by reporting, for the first time, CD data for household-cooked meals. Although we did not study colonization in humans, we blindly quantified CD in household meals, and we investigated the potential for environment–food cross contamination after visiting 35 rural and urban households in Ohio (2.3 ± 1.2 visits/each; over four months). In total, 467 samples of food (collected from 188 kitchen pots or refrigerators) and 279 samples from the household environment were processed using validated food-enrichment protocols.[9] Meals, cooked, uncooked, or processed, were sampled, homogenized, centrifuged, and stored as sediments at −80°C until processing.[9] Environmental swabs (8 cm × 4 cm × 1 cm) from kitchen countertops (n = 32), sinks (n = 56), refrigerator shelves (n = 59), gloves (n = 23), shoes (n = 56), and washing machines (n = 52) were taken using sponges premoistened with buffered peptone water (5 mL, Hydrasponge, Biotrace, London, UK).[10] Thawed samples were enriched anaerobically in CD broth for 15 days

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(37°C) and were then homogenized and ethanol shocked (not heated) prior to their inoculation and incubation onto CD agar for 5 days at 37°C. Strain identification, PCR-ribotyping, and antimicrobial resistance analyses were performed as previously described.[9]

Our methodology detected 2 CD-positive food items in 2 urban households, yielding an overall CD prevalence of 1.06% (2 of 188 meals, binomial exact 95% CI, 0.129–3.789), which is 5-fold higher than the 0.22% reported by Kwon et al (for which we computed a 95% CI, 0.026–0.792; difference > 0 was 0.84%, $P = .081$; probability $Z > z = 0.04$; binomial exact $P = .06$). CD positivity was not attributed to environmental cross contamination because 279 environmental swabs were CD negative (0%, one-sided 97.5% CI, 0–1.32). Control fecal samples from 54 farm animals yielded CD in 3 animals from farm households that did not contribute to contaminated foods. The CD isolates were toxigenic, moxifloxacin- and clindamycin-resistant PCR-ribotype 078, representing 2.15% of uncooked and commercially processed food (10-fold greater than Kwon's prevalence; 2 of 93 for vegetable and bologna; 95% CI, 0.26–7.55). All 88 household-cooked meals were CD negative, supporting the evidence that heat decreases the probability of recovering CD (0%; 1-sided 97.5% CI, 0–4.1; difference > 0; $P = .083$). Our statistical comparisons highlight that study methodologies and sampling approaches yield different results that will impact mathematical predictions.

Mathematical modeling is an important asset in estimating hypothetical population dynamics, but ultimately, practitioners and patients will benefit from estimates made using unbiased, externally valid parameters. Relevant to hospital epidemiology, we have provided estimates from a larger sample of (household) kitchens that may benefit mathematical estimations. *Clostridium difficile* has been found in recreational waters, animals, soils, and foods, but the most common exposure source everywhere (in both hospitals and the community) is food, especially commercially and/or minimally processed foods, which carry higher exposure risks. Preventive education campaigns targeting susceptible individuals during periods of maximum vulnerability using, for instance, updated peer-reviewed fact sheets relevant to CD ecology could be an affordable measure to reduce exposure risks (eg, during antibiotic or immusuppresant therapies in cancer or inflammatory bowel disease patients). To improve external validity, future studies could focus on meals more likely to carry CD, using food-validated protocols, and on increasing technical replicates to produce less biased data to expand existing risk-based mathematical predictions.

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Alexander Rodriguez-Palacios, DVSc PhD;[1]
Sanja Ilic, PhD;[2]
Jeffrey T. LeJeune, DVM PhD[3]

Affiliations: 1. Division of Gastroenterology and Liver Disease, Digestive Health Research Institute, Department of Medicine, Case Western Reserve University School of Medicine, Cleveland, Ohio; 2. Department of Human Sciences, Human Nutrition, College of Education and Human Ecology, The Ohio State University, Columbus, Ohio; 3. Food Animal Health Research Program, Ohio Agricultural Research and Development Center, The Ohio State University, Wooster, Ohio.

Address correspondence to Alexander Rodriguez-Palacios, DVSc PhD, Digestive Health Research Institute, Case Western Reserve University School of Medicine, Biomedical Research Building Room 525, 10900 Euclid Ave, Cleveland, OH 44106 (axr503@case.edu).

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