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Dr. Doi was a researcher at the Japan National Institute of Infectious Diseases in Tokyo during this work. His research interests focus on the mechanisms underlying emergence of drug-resistant viruses.

References

1. Sasaki M, Tabata K, Kishimoto M, Itakura Y, Kobayashi H, Ariizumi T, et al. S-217622, a SARS-CoV-2 main protease inhibitor, decreases viral load and ameliorates COVID-19 severity in hamsters. *Sci Transl Med*. 2023;15:eabq4064. <https://doi.org/10.1126/scitranslmed.abq4064>
2. Kuroda T, Nobori H, Fukao K, Baba K, Matsumoto K, Yoshida S, et al. Efficacy comparison of 3CL protease inhibitors ensitrelvir and nirmatrelvir against SARS-CoV-2 in vitro and in vivo. *J Antimicrob Chemother*. 2023;78:946–52. <https://doi.org/10.1093/jac/dkad027>
3. Noske GD, de Souza Silva E, de Godoy MO, Dolci I, Fernandes RS, Guido RVC, et al. Structural basis of nirmatrelvir and ensitrelvir activity against naturally occurring polymorphisms of the SARS-CoV-2 main protease. *J Biol Chem*. 2023;299:103004. <https://doi.org/10.1016/j.jbc.2023.103004>
4. Japan Ministry of Health, Labour and Welfare. Usage of drugs for the treatment of novel coronavirus infections [cited 2023 Dec 31]. https://www.mhlw.go.jp/stf/seisakunitsuite/bunya/0000121431_00324.html
5. Kiso M, Yamayoshi S, Iida S, Furusawa Y, Hirata Y, Uraki R, et al. In vitro and in vivo characterization of SARS-CoV-2 resistance to ensitrelvir. *Nat Commun*. 2023;14:4231. <https://doi.org/10.1038/s41467-023-40018-1>
6. Moghadasi SA, Heilmann E, Khalil AM, Nnabuife C, Kearns FL, Ye C, et al. Transmissible SARS-CoV-2 variants with resistance to clinical protease inhibitors. *Sci Adv*. 2023;9:eade8778. <https://doi.org/10.1126/sciadv.ade8778>
7. Jochmans D, Liu C, Donckers K, Stoycheva A, Boland S, Stevens SK, et al. The substitutions L50F, E166A, and L167F in SARS-CoV-2 3CLpro are selected by a protease inhibitor in vitro and confer resistance to nirmatrelvir. *mBio*. 2023;14:e0281522. PubMed <https://doi.org/10.1128/mbio.02815-22>
8. Flynn JM, Huang QYJ, Zvornicanin SN, Schneider-Nachum G, Shaqra AM, Yilmaz NK, et al. Systematic analyses of the resistance potential of drugs targeting SARS-CoV-2 main protease. *ACS Infect Dis*. 2023;9:1372–86. <https://doi.org/10.1021/acsinfectdis.3c00125>
9. Doi A, Tomita Y, Okura H, Matsuyama S. Frequent occurrence of mutations in nsp3 and nsp4 of SARS-CoV-2, presumably caused by the inhaled asthma drug ciclesonide. *PNAS Nexus*. 2022;1:pgac197. PubMed <https://doi.org/10.1093/pnasnexus/pgac197>
10. Japan National Institute of Infectious Diseases. Amino acid substitutions due to viral genomic mutations that may affect the efficacy of therapeutic drugs against the new coronavirus (SARS-CoV-2) (4th edition) [cited 2023 Dec 31]. <https://www.niid.go.jp/niid/ja/2019-ncov/2624-flu/12170-sars-cov-2-mutation-v4.html>

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Foodborne Disease Outbreaks Linked to Foods Eligible for Irradiation, United States, 2009–2020

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Food irradiation can reduce foodborne illnesses but is rarely used in the United States. We determined whether outbreaks related to *Campylobacter*, *Salmonella*, *Escherichia coli*, and *Listeria monocytogenes* were linked to irradiation-eligible foods. Of 482 outbreaks, 155 (32.2%) were linked to an irradiation-eligible food, none of which were known to be irradiated.

Food irradiation has been studied globally for decades and is a safe, effective means of reducing foodborne illness-causing pathogens, sterilizing insects, delaying ripening or sprouting, and extending shelf life (1,2). The US Food and Drug Administration has approved various foods for irradiation, including meat, poultry, fresh shell eggs, and spices (2) (Appendix Table, <https://wwwnc.cdc.gov/EID/article/30/6/23-0922-App1.pdf>). However, irradiation has not been widely adopted in the United States because of large fixed costs and the perception of consumer unwillingness to purchase irradiated food (3). Estimates of the amount of irradiated food available in the United States are scarce, but as of 2010, approximately one third of spices consumed and <0.1% of imported fruit, vegetables, and meats were irradiated (3).

Campylobacter, *Salmonella*, *Escherichia coli*, and *Listeria monocytogenes* are among the most common bacterial foodborne pathogens causing illnesses, hospitalizations, and death in the United States (4) and can be neutralized by irradiation at sufficient doses (5). We identified outbreaks caused by these pathogens and linked to irradiation-eligible foods; then, we determined whether any of the foods had been irradiated.

In the United States, the Foodborne Disease Outbreak Surveillance System (FDOSS) collects information from state, local, and territorial health departments about foodborne disease outbreaks. The National Outbreak Reporting System, launched in

2009, reports information gathered by FDOSS, including food processing methods such as shredding, pasteurizing, or irradiation. We searched for foodborne disease outbreaks reported and finalized through FDOSS and the National Outbreak Reporting System as of February 4, 2022, for which the date of first illness onset occurred during 2009–2020 and a confirmed pathogen was *Campylobacter*, *Salmonella*, *E. coli*, or *Listeria monocytogenes*. A foodborne disease outbreak was defined as ≥ 2 illnesses linked to a common exposure with evidence suggesting a food source. FDOSS variables we examined included method of processing, food vehicle, Interagency Food Safety Analytics Collaboration (IFSAC) food category, and the number of estimated primary illnesses, hospitalizations, and deaths. We grouped outbreaks by IFSAC category and irradiation approval status (eligible, some foods eligible, not yet eligible, or undetermined) (Appendix Table). We conducted a literature review to identify outbreaks not captured through FDOSS. We obtained foods approved for irradiation for pathogen reduction and approval years from the Code of Federal Regulations 21 Part 179 (Appendix Table).

In FDOSS, we identified 2,153 foodborne outbreaks during 2009–2020 caused by *Campylobacter*, *Salmonella*, *E. coli*, or *Listeria monocytogenes*. Of those, 482 (22.4%) included information regarding processing methods other than unknown or a missing value; none had irradiation listed as a processing method. Of the 482 outbreaks, 155 (32.2%) were linked to a food eligible for irradiation when the onset of the first reported illness occurred; those outbreaks resulted in 3,512 illnesses, 463 hospitalizations, and 10 deaths (Appendix Table). The most common sources were chicken (52 outbreaks), beef (31), and eggs (29), comprising 72% (112/155) of outbreaks linked to irradiation-eligible foods.

During our literature search, we identified 1 outbreak linked to food that might have included an irradiated ingredient. During 2009–2010, *Salmonella enterica* serotype Montevideo was found in imported pepper used in ready-to-eat salami (6). Some of the manufacturer's pepper was reportedly irradiated, but some was not. Whether the implicated product contained irradiated pepper is unclear. Irradiation was not reported as a processing method for the outbreak in FDOSS. After consultation with the Centers for Disease Control and Prevention outbreak investigation team, we determined there was insufficient evidence to link that outbreak to irradiated pepper.

The illnesses, hospitalizations, and deaths associated with outbreaks linked to irradiation-eligible foods might have been prevented or reduced had

these foods been irradiated. Irradiation has repeatedly been proposed as a strategy to reduce foodborne disease outbreaks (5,7,8). Irradiation typically eliminates a large proportion of pathogenic microorganisms. The efficacy of irradiation depends on factors like temperature and water content (9). Food may become contaminated after irradiation. Irradiation can be a useful tool in improving food safety complementary to existing food safety practices. Consumer demand for irradiated foods may be increased through education (10).

The first limitation of our study is that IFSAC food categories do not always correspond to food groups approved for irradiation by the US Food and Drug Administration (Appendix Table); therefore, misclassification of irradiation approval status might have occurred for some foods. Reporting of outbreaks to FDOSS is voluntary, and processing method information was frequently missing, so irradiation might have been underreported or unrecognized by public health partners because of limited knowledge of irradiation or unfamiliarity with labeling. For outbreaks with multiple etiologies including a pathogen other than the 4 of interest, irradiation might not have reduced those pathogens.

We identified 155 *Campylobacter*, *Salmonella*, *E. coli*, or *Listeria monocytogenes* outbreaks with a known method of processing that were linked to irradiation-eligible foods during 2009–2020; none of the implicated foods were reported as irradiated. These results suggest that some outbreaks could be prevented or mitigated through irradiation. Prioritizing food irradiation efforts, particularly for chicken, beef, and eggs, could substantially reduce outbreaks and illnesses.

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References

1. High-dose irradiation: wholesomeness of food irradiated with doses above 10 kGy. Report of a joint FAO/IAEA/WHO study group. World Health Organ Tech Rep Ser. 1999;890:i-vi, 1-197.
2. Food and Drug Administration. Food irradiation: what you need to know. 2022 [cited 2022 Jun 23]. <https://www.fda.gov/food/buy-store-serve-safe-food/food-irradiation-what-you-need-know>
3. Ferrier P. Irradiation of produce imports: small inroads, big obstacles. 2011 [cited 2022 June 27]. <https://www.ers.usda.gov/amber-waves/2011/june/irradiation-of-produce-imports>
4. Scallan E, Hoekstra RM, Angulo FJ, Tauxe RV, Widdowson MA, Roy SL, et al. Foodborne illness acquired in the United States—major pathogens. *Emerg Infect Dis*. 2011;17:7-15. <https://doi.org/10.3201/eid1701.P11101>
5. Tauxe RV. Food safety and irradiation: protecting the public from foodborne infections. *Emerg Infect Dis*. 2001;7(Suppl):516-21. <https://doi.org/10.3201/eid0707.017706>
6. Gieraltowski L, Julian E, Pringle J, Macdonald K, Quilliam D, Marsden-Haug N, et al. Nationwide outbreak of *Salmonella* Montevideo infections associated with contaminated imported black and red pepper: warehouse membership cards provide critical clues to identify the source. *Epidemiol Infect*. 2013;141:1244-52. <https://doi.org/10.1017/S0950268812001859>
7. Osterholm MT, Norgan AP. The role of irradiation in food safety. *N Engl J Med*. 2004;350:1898-901. <https://doi.org/10.1056/NEJMs032657>
8. Gunther NW IV, Abdul-Wakeel A, Scullen OJ, Sommers C. The evaluation of gamma irradiation and cold storage for the reduction of *Campylobacter jejuni* in chicken livers. *Food Microbiol*. 2019;82:249-53. <https://doi.org/10.1016/j.fm.2019.02.014>
9. World Health Organization. Safety and nutritional adequacy of irradiated food. Geneva: World Health Organization; 1994 [cited 2022 Nov 16]. <https://iris.who.int/handle/10665/39463>
10. Ablan M, Low MSF, Marshall KE, Devchand R, Koehler L, Hume H, et al. Focus groups exploring U.S. adults' knowledge, attitudes, and practices related to irradiation as a food safety intervention, 2021. *Food Prot Trends*. 2023;43:448-56.

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Effect of Myxoma Virus Species Jump on Iberian Hare Populations

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The myxoma virus species jump from European rabbits (*Oryctolagus cuniculus*) to Iberian hares (*Lepus granatensis*) has raised concerns. We assess the decline suffered by Iberian hare populations on the Iberian Peninsula and discuss the association between the effect of myxomatosis and the average abundance index, which we estimated by using hunting bags.

In July 2018, after 60 years of endemic circulation in European wild rabbits (*Oryctolagus cuniculus*), myxoma virus (MYXV) jumped to the Iberian hare (*Lepus granatensis*) (1). This species jump resulted from the emergence of a recombinant strain of MYXV, named ha-MYXV, containing a 2.8-kb insertion derived from an unknown poxvirus (2,3). Outbreak notifications rapidly spread across the Iberian Peninsula, resulting in an estimated mean mortality rate of 55.4% (median 70%) in hares (4). Concerns were raised about the effect of myxomatosis on the Iberian hare populations (4). We investigated those concerns and determined how myxomatosis affected Iberian hares by evaluating hare abundance indexes before and after the emergence of ha-MYXV.

We used hunting bag data to approximate population abundance (5). We collected information on hunting yields from hunting grounds in Portugal and the most affected regions of Spain, Andalusia, and Castilla-La Mancha during the hunting seasons (October–February) spanning from 2007–08 to 2020–21. Our study period includes 11 seasons before ha-MYXV emergence (premyxomatosis), from 2007–08 to 2017–18,