

# New insight from whole-genome sequencing of Europe's 2011 *E. coli* outbreaks

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Using whole-genome sequencing, a team led by researchers from Harvard School of Public Health (HSPH) and the Broad Institute has traced the path of the *E. coli* outbreak that sickened thousands and killed over 50 people in Germany in summer 2011 and also caused a smaller outbreak in France. It is one of the first uses of genome sequencing to study the dynamics of a food-borne outbreak and provides further evidence that genomic tools can be used to investigate future outbreaks and provide greater insight into the emergence and spread of infectious diseases.

The study, conducted in collaboration with groups at the Pasteur Institute in France, Assistance Publique-Hôpitaux de Paris, and Statens Serum Institut in Denmark, appears on February 6, 2012 in an advance online edition of *Proceedings of the National Academy of Sciences*.

"A genome contains the record of a strain's evolutionary history, so by looking at the differences between the genomes of multiple bacteria from an outbreak we can get really useful clues about what happened in the outbreak. In this way, tracking outbreaks is like detective work, and this approach will be a powerful tool in trying to understand future outbreaks," said lead author Yonatan Grad, a research fellow in the Center for Communicable Disease Dynamics, Department of Epidemiology at HSPH and infectious disease physician at Brigham and Women's Hospital in Boston.

"This work is a testament to the power of [genome sequencing](#) and

analysis to shed light on the mechanisms that drive disease outbreaks," said co-senior author Deborah Hung, a core faculty member at the Broad Institute, an assistant professor at Massachusetts General Hospital and Harvard Medical School, and an infectious disease physician at Brigham and Women's Hospital. "We can see things that we simply couldn't see before, and that holds promise for improving public health."

The outbreak in Germany, which was caused by the strain *E. coli* O104:H4, led to around 4,000 cases of bloody diarrhea, 850 cases of hemolytic uremic syndrome (HUS), which can lead to kidney failure, and over 50 deaths. The source of the outbreak was traced to sprouts from an organic farm in Germany. In France, where 15 people were sickened with bloody diarrhea that progressed to HUS in nine people, the source of the outbreak was sprouts, germinated from seeds purchased at a garden retailer, that were served at a children's community center buffet. European investigators, using traditional epidemiological methods, traced the outbreaks to a shipment of seeds from Egypt that arrived in Germany in December 2009.

The researchers, led by Grad and senior authors Hung and William Hanage, associate professor of epidemiology at HSPH, analyzed isolates of *E. coli* bacteria from both the German and French outbreaks. Based on conventional molecular epidemiological analysis, the *E. coli* strains from the outbreaks in [Germany](#) and France appear identical.

However, by harnessing the Broad's expertise in whole-genome sequencing and analysis, the researchers were able to determine that there were small, but measurable, differences among the isolates. They made two surprising findings: All the strains connected to the larger German outbreak were found to be nearly identical, while the strains in France showed greater diversity; and the German isolates appeared to be a subset of the diversity seen in the French isolates.

"If genomes have fewer differences than we expect, like the German outbreak, it suggests that the [outbreak](#) might have passed through a bottleneck. A bottleneck might be something like disinfection procedures that killed most but not all of the bugs, or maybe passage through a single infected individual," said Hanage.

Another hypothesis offered by the researchers is that there was uneven distribution of diversity in the original shipment of contaminated seeds.

As costs for genomic sequencing decline, these tools, combined with traditional epidemiological techniques, can provide greater insight into the emergence and spread of [infectious diseases](#) and will help guide preventive public health measures in the future.

**More information:** "Genomic Epidemiology of the Escherichia coli O104:H4 Outbreaks in Europe, 2011," Yonatan H. Grad, Marc Lipsitch, Michael Feldgarden, Harindra M. Arachchi, Gustavo C. Cerqueira, Michael FitzGerald, Paul Godfrey, Brian J. Haas, Cheryl Murphy, Carsetn Russ, Sean Sykes, Bruce J. Walker, Jennifer R. Wortman, Sarah Young, Qiandong Zeng, Amr Abouelleil, James Bochicchio, Sara Chauvin, Timothy DeSmet, Sharvari Gujja, Caryn McCowan, Anna Montmayeur, Scott Stellman, Jakob Frimodt-Moller, Andreas M. Petersen, Carsten Struve, Karen A. Krogfelt, Edouard Bingen, Francois-Xavier Weill, Eric S. Lander, Chad Nusbaum, Bruce W. Birren, Deborah T. Hung, William P. Hanage, *Proceedings of the National Academy of Sciences*, online February 6, 2012.

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