Impact of whole genome sequencing on the investigation of outbreaks of STEC O157:H7

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Impact of whole genome sequencing on the investigation of food-borne outbreaks of Shiga toxin-producing *Escherichia coli* serogroup O157:H7, England, 2013 to 2017

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We aim to provide insight and guidance on the utility of whole genome sequencing (WGS) data for investigating food-borne outbreaks of Shiga toxin-producing *Escherichia coli* (STEC) O157:H7 in England between 2013 and 2017. Analysis of WGS data delivered an unprecedented level of strain discrimination when compared with multilocus variable number tandem repeat analysis. The robustness of the WGS method ensured confidence in the microbiological identification of linked cases, even when epidemiological links were obscured. There was evidence that phylogeny

been identified by epidemiological links, although from 2012 prospective typing using MLVA was also in use [4,5]. PHE implemented whole genome sequencing (WGS) as the molecular typing method of choice for all isolates of STEC O157:H7 in June 2015 [6]. The aim of this perspective is to summarise the evaluation and share experiences on the utility of whole genome sequencing (WGS) data for investigating food-borne outbreaks of STEC O157:H7 in England and discuss the impact of this approach on informing risk assessment and risk management of this clinically important food-

Phylogenetic relationships

SNPs

0

250

High level of strain discrimination – unparalleled sensitivity for outbreak detection

High level of accuracy - robust case definition improves case ascertainment

Epidemiological data linked to isolates closely related to the outbreak strain provides context and information on likely routes of transmission

Genome wide association of all available data may provide evidence of the geographical origin of the outbreak strain and be able to track transmission on a global scale

Shiga toxin-producing (STEC) *E. coli* O157

- Gastrointestinal pathogen that causes severe bloody diarrhoea and Haemolytic Uraemic Syndrome. HUS is associated with long-term renal, cardiac and neurological complications

- Treatment options are limited as antibiotics contraindicated

- Zoonotic – animal reservoir is mainly cattle, sheep and goats, but almost all animals can be transiently colonised and act as secondary transmission vectors

- Transmission can be food or waterborne or via direct contact with animals or their environment

Two siblings die after suffering E coli infection

Neil Johnston Midlands Correspondent

Two children from the same family have died after contracting *E. coli*.

Public Health England (PHE) said last night that the two youngsters, from Charnwood, Leicestershire, had been treated in the past two weeks, but it

with farm animals and infected water," she said. "PHE are working with partners to investigate further to try to determine a source of infection."

Most food poisoning cases of *E. coli* are caused by a strain known as O157 which is often passed on through raw and undercooked meat. Typically there
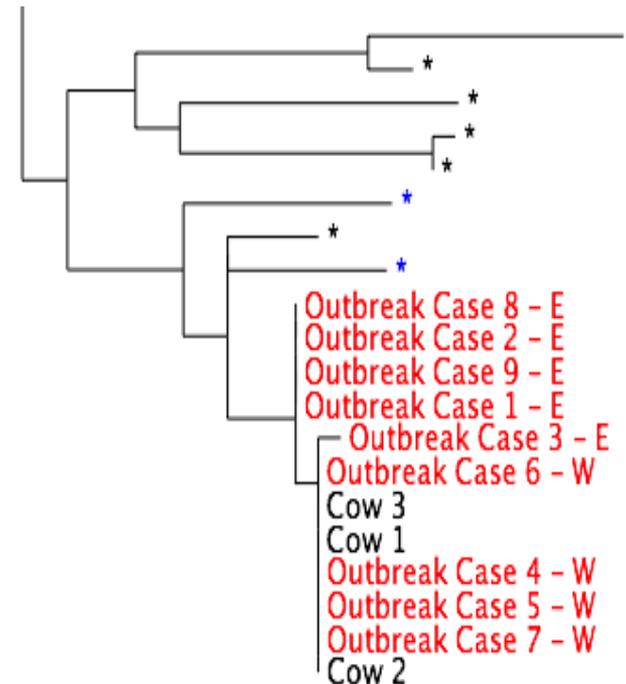
Robust case definition for case ascertainment

Whole genome sequencing improved case ascertainment in an outbreak of Shiga toxin-producing *Escherichia coli* O157 associated with raw drinking milk

H. BUTCHER[1]†, R. ELSON[2]†, M. A. CHATTAWAY[3], C. A. FEATHERSTONE[4], C. WILLIS[5], F. JORGENSEN[5], T. J. DALLMAN[3], C. JENKINS[3]*, J. McLAUCHLIN[5,6], C. R. BECK[7] AND S. HARRISON[1]

• September 2014 - five cases of STEC O157:H7 reporting recent consumption of raw drinking milk purchased from the same farm

• Farmer was advised to suspend sale of RDM and conduct product recall. Supply lines identified and distribution terminated.

• No STEC detected in RDM but outbreak strain was isolated from cattle on the implicated farm

• WGS identified four additional cases – initially none reported consumption of RDM

• Following a second interview 3 of the 4 admitted buying RDM from the implicated farm

Whole genome sequencing improved case ascertainment in an outbreak of Shiga toxin-producing *Escherichia coli* O157 associated with raw drinking milk

Public Health England
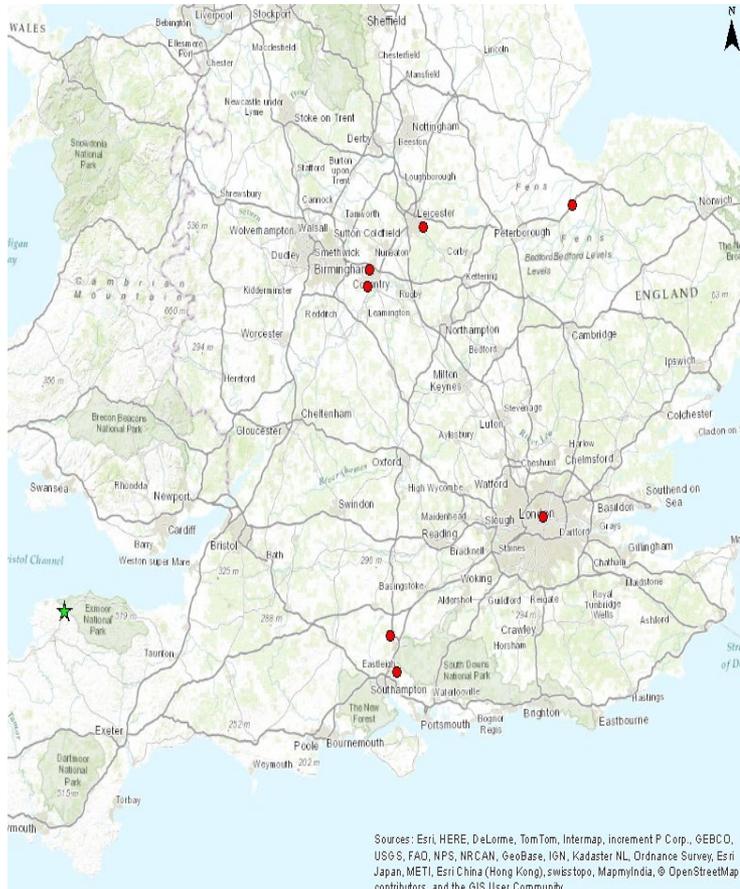
- In England, farmers can only sell RDM at the "farm gate" – not via a secondary retailer

- Attempt to keep RDM outbreaks localised

- Internet sales are a loop hole – farmers can sell direct to customers at a "virtual farm gate"

- RDM delivered by the driver of this inconspicuous van

Linking sporadic and outbreak cases to a common source

Public Health
England

An outbreak of Shiga toxin-producing *Escherichia coli* O157: H7 associated with contaminated salad leaves: epidemiological, genomic and food trace back investigations[‡]

A. F. W. MIKHAIL[1], C. JENKINS[1]*, T. J. DALLMAN[1], T. INNS[2,3], A. DOUGLAS[1], A. I. C. MARTÍN[4], A. FOX[1], P. CLEARY[2,3], R. ELSON[1] AND J. HAWKER[2,3]

An outbreak of Shiga toxin-producing *Escherichia coli* O157: H7 associated with contaminated salad leaves: epidemiological, genomic and food trace back investigations[‡]
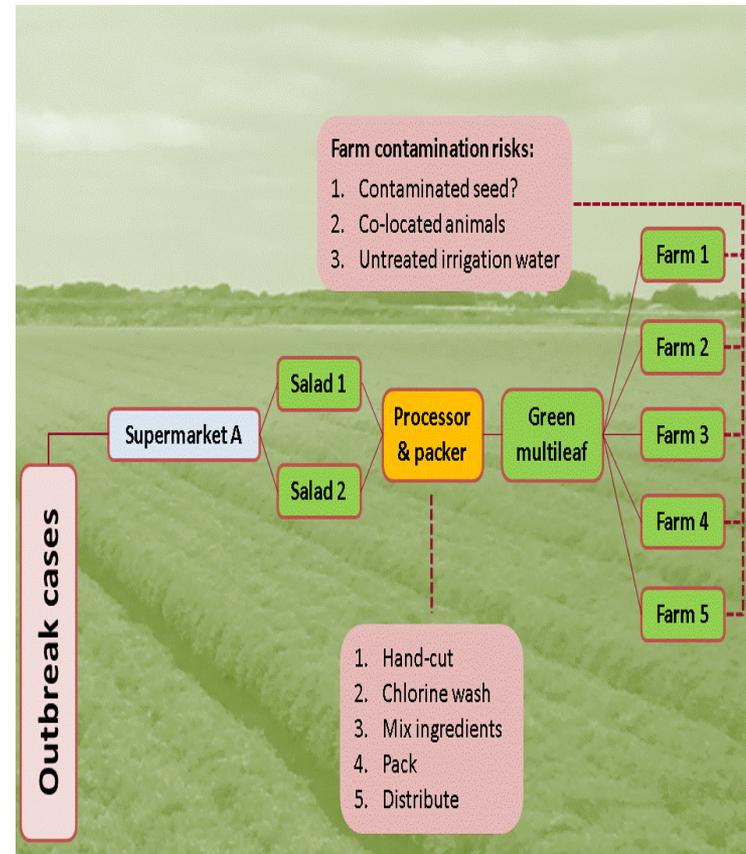
- 11 August 2015 - 4 cases of STEC O157 same SNP type, detected following routine analysis of the WGS data.

- 31 October 2015 – 47 cases, onset 29 July – 30 September, 16 (34%) cases hospitalised

- Nationally distributed
- Adults = 88%; females = 69%

- Exposure frequency analysis ESQs – pre-packed salad 81%

- Case-case study (outbreak cases vs non-outbreak cases as controls) identified pre-packed salad as the primary exposure
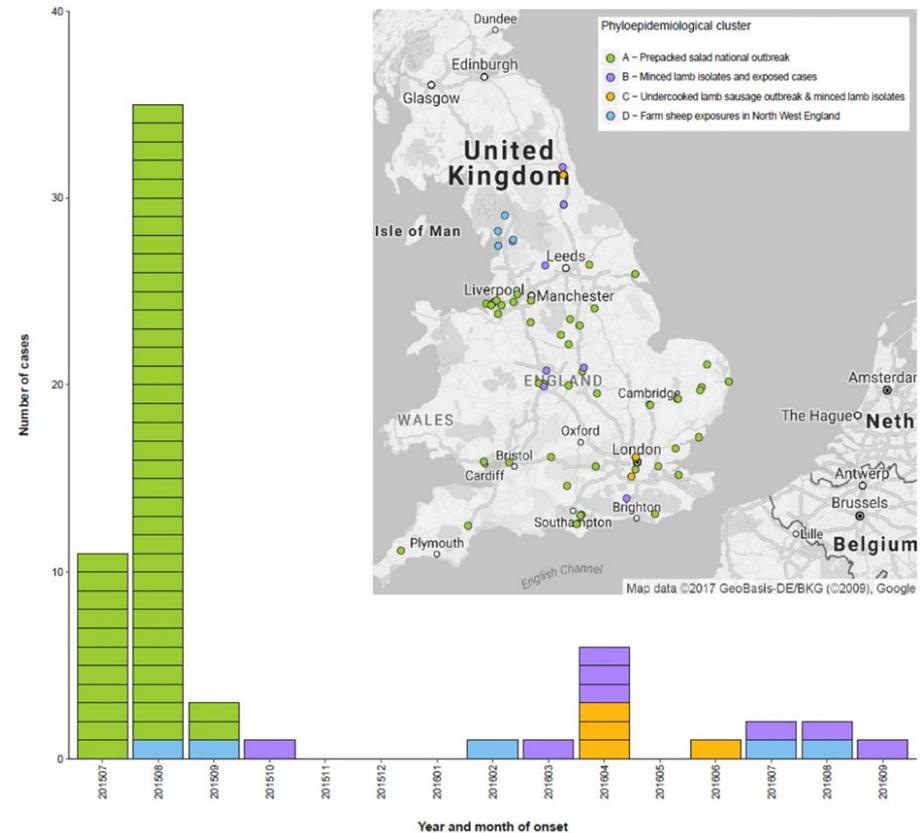
An outbreak of Shiga toxin-producing _Escherichia coli_ O157: H7 associated with contaminated salad leaves: epidemiological, genomic and food trace back investigations[‡]

- Trawl to determine the type of pre-packed salad – 2 product lines bistro salad and mild mixed leaf salad

- Both mixes shared a common ingredient – green multi-leaf lettuce – products were processed and packed by a distributor in the North West

- Distributor was supplied by 5 growers; at 3 farms untreated water was used for irrigation and all farms had poor biosecurity and evidence of animal ingress (wildlife)

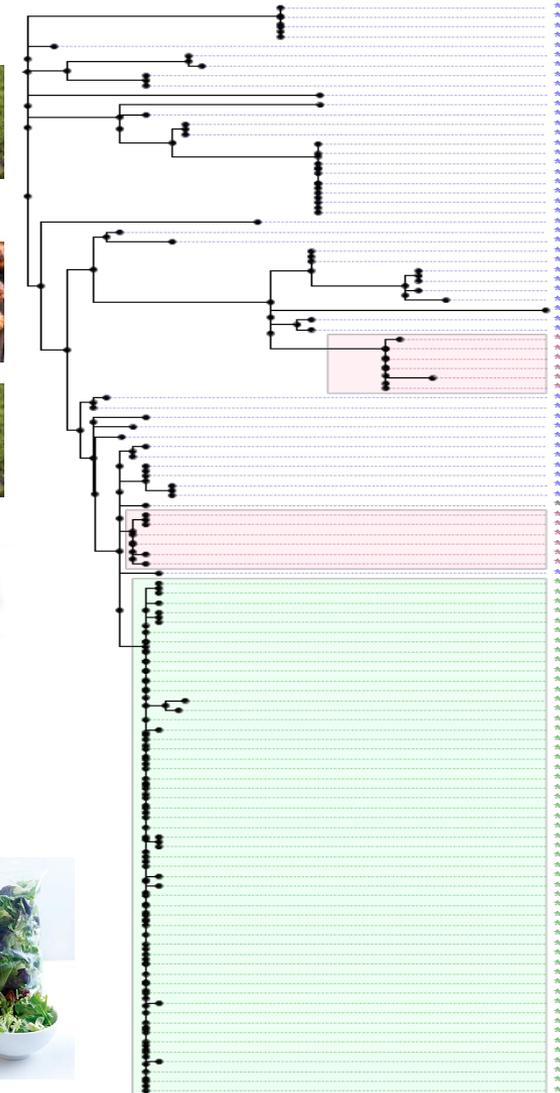- STEC O157 was not detected in any of the food samples tested

WGS provided further evidence of a domestic source - strains closely related to the outbreak strain circulating in the UK – and insight into the route of transmission

10 SNP single linkage cluster

Location of salad growers

Public Health England

Muddy races can lead to STEC cases!

Dr Lisa Byrne, Epidemiologist (Surveillance Lead for STEC and Listeria), Gastrointestinal Infections Unit, PHE National Infections Service.

In August 2018, an outbreak of STEC O157 associated with a mud obstacle race occurred with seven primary cases identified.

Investigations indicated sheep, a primary reservoir for STEC, grazing nearby up to a few days prior to the event were the likely source of infection, through contamination of the race course with faecal matter.
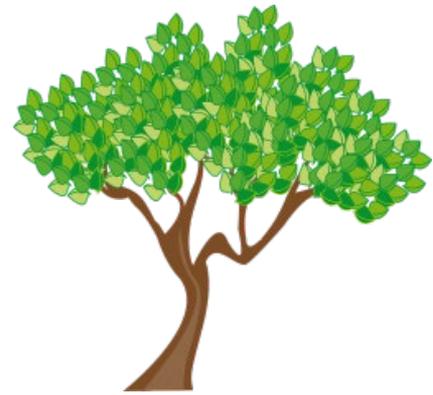

Above: Dr Natalie Adams, GI scientist partaking in a mud obstacle race

Travel data can provide evidence of a non-domestic source

National outbreak of Shiga toxin-producing *Escherichia coli* O157:H7 linked to mixed salad leaves, United Kingdom, 2016

Maya Gobin[1], Jeremy Hawker[1,2], Paul Cleary[1,2], Thomas Inns[1,2], Daniel Gardiner[1,3], Amy Mikhail[4], Jacquelyn McCormick[4], Richard Elson[2,4], Derren Ready[4], Tim Dallman[2,4], Iain Roddick[1], Ian Hall[5], Caroline Willis[6], Paul Crook[1], Gauri Godbole[3], Drazenka Tubin-Delic[7], Isabel Oliver[1,8]

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National outbreak of Shiga toxin-producing *Escherichia coli* O157:H7 linked to mixed salad leaves, United Kingdom, 2016

- 20-26 June 2016 – 24 cases of STEC O157, same SNP type, ultimately165 cases

- 116/165 (70%) adult females, national distributed, 66/165 (40%) cases hospitalised, 9 developed HUS, 2 fatal cases

- Case-control study - illness was associated with mixed salad leaves

- Case-case study - association between outbreak cases and salad consumption

- WGS analysis highlighted the possibility that outbreak strain (and therefore contaminated leaf) originated from a non-UK source
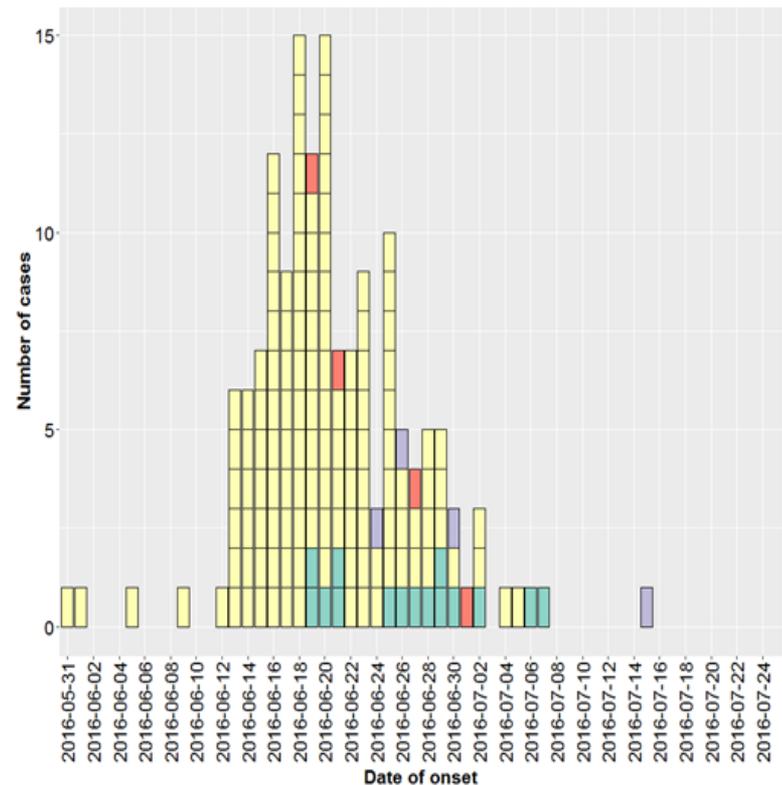
250 SNP single linkage cluster
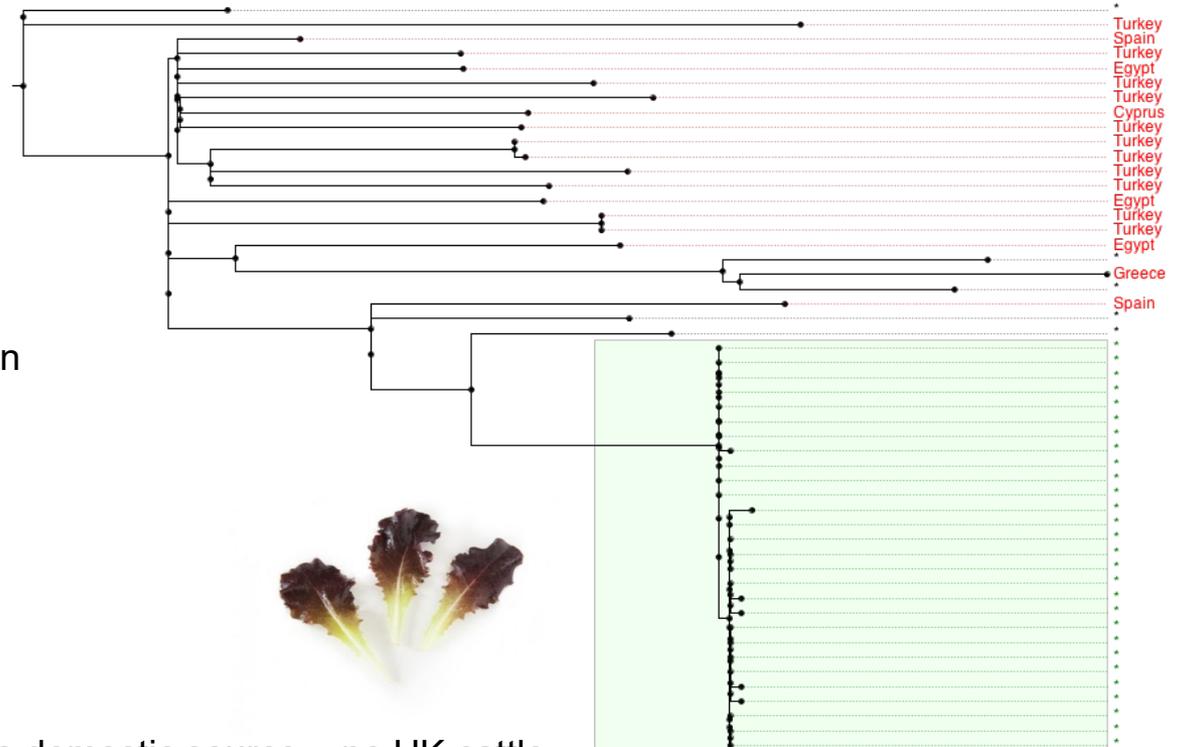
Phylogenetic context

- Sparsely populated 250 SNP single linkage cluster, uncommon in the PHE database

- Long branch length reflect a low level of sampled diversity

Epidemiological context

- No evidence within the cluster of a domestic source - no UK cattle or sheep isolates, or isolates from domestically-produced food or evidence of on-going domestic transmission of closely related strains

- High proportion of cases within the cluster reported recent travel outside the UK

- Outbreak strain multidrug resistant – >80% UK STEC O157 fully susceptible; recent analysis showed MDR in STEC O157 is significantly associated with imported strains

National outbreak of Shiga toxin-producing *Escherichia coli* O157:H7 linked to mixed salad leaves, United Kingdom, 2016

Food chain lab analysis

Investigations focused on one of the three UK producer-suppliers, Supplier A, who supplied salad leaves to catering premises linked to cases outside the south west of England. A forward trace could be established from Supplier A to all catering premises linked to two or more cases.
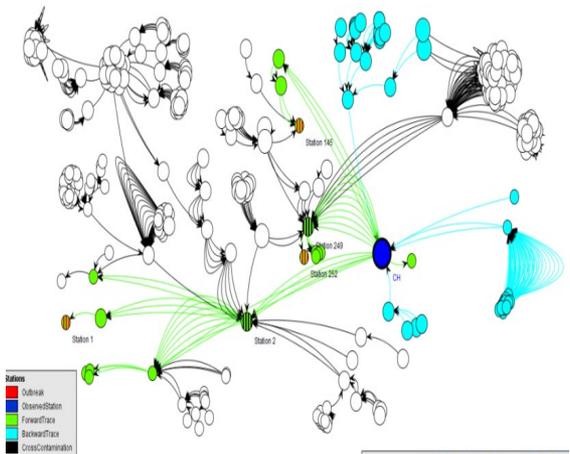
Most plausible source of the outbreak strain based on the exposure window assessment and supply chain timelines was contaminated red batavia leaves imported on 6 June.

Phylogenetic relationships

SNPs

0

250

Dried parsley outbreak - unprecedented level of strain discrimination facilitates understanding relatedness between strains

Raw drinking milk outbreak - robust case definition improves case ascertainment

Domestic salad outbreak - epidemiological data linked to isolates closely related to the outbreak strain provides context and information on likely routes of transmission

Imported salad outbreak - genome wide association of all available data may provide evidence of the geographical origin of the outbreak strain and be able to track transmission on a global scale

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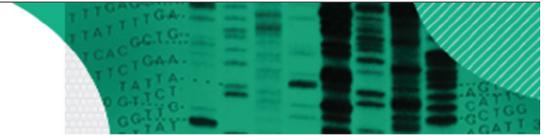
Research Paper

Short-term evolution of Shiga toxin-producing *Escherichia coli* O157:H7 between two food-borne outbreaks

Lauren A. Cowley,[1] Timothy J. Dallman,[1] Stephen Fitzgerald,[2] Neil Irvine,[3] Paul J. Rooney,[4] Sean P. McAteer,[2] Martin Day,[1] Neil T. Perry,[1] James L. Bono,[5] Claire Jenkins[1] and David L. Gally[2]

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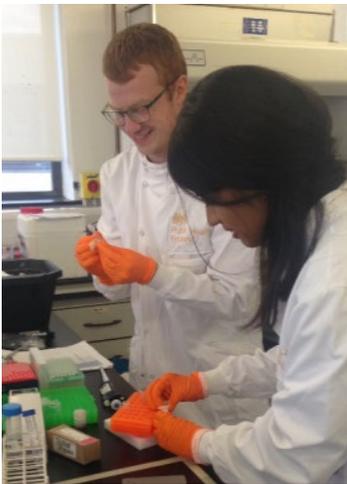
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Comparison of single nucleotide variants identified by Illumina and Oxford Nanopore technologies in the context of a potential outbreak of Shiga Toxin Producing *Escherichia coli*

David R Greig, Claire Jenkins, Saheer Gharbia, Timothy J Dallman
doi: https://doi.org/10.1101/570192

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Food Standards Agency

Animal & Plant Health Agency

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