



An international outbreak of *Salmonella enterica* serotype Enteritidis linked to eggs from Poland: a microbiological and epidemiological study

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Summary

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Salmonella, *Shigella*, and

Background *Salmonella* spp are a major cause of food-borne outbreaks in Europe. We investigated a large multi-country outbreak of *Salmonella enterica* serotype Enteritidis in the EU and European Economic Area (EEA).

Methods A confirmed case was defined as a laboratory-confirmed infection with the outbreak strains of *S* Enteritidis based on whole-genome sequencing (WGS), occurring between May 1, 2015, and Oct 31, 2018. A probable case was defined as laboratory-confirmed infection with *S* Enteritidis with the multiple-locus variable-number tandem repeat analysis outbreak profile. Multi-country epidemiological, trace-back, trace-forward, and environmental investigations were done. We did a case-control study including confirmed and probable cases and controls randomly sampled from the population registry (frequency matched by age, sex, and postal code). Odds ratios (ORs) for exposure rates between cases and controls were calculated with unmatched univariable and multivariable logistic regression.

Findings 18 EU and EEA countries reported 838 confirmed and 371 probable cases. 509 (42%) cases were reported in 2016, after which the number of cases steadily increased. The case-control study results showed that cases more often ate in food establishments than did controls (OR 3.4 [95% CI 1.6–7.3]), but no specific food item was identified. Recipe-based food trace-back investigations among cases who ate in food establishments identified eggs from Poland as the vehicle of infection in October, 2016. Phylogenetic analysis identified two strains of *S* Enteritidis in human cases that were subsequently identified in salmonella-positive eggs and primary production premises in Poland, confirming the source of the outbreak. After control measures were implemented, the number of cases decreased, but increased again in March, 2017, and the increase continued into 2018.

Interpretation This outbreak highlights the public health value of multi-country sharing of epidemiological, trace-back, and microbiological data. The re-emergence of cases suggests that outbreak strains have continued to enter the food chain, although changes in strain population dynamics and fewer cases indicate that control measures had some effect. Routine use of WGS in salmonella surveillance and outbreak response promises to identify and stop outbreaks in the future.

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Introduction

Salmonellosis is the second most commonly reported zoonosis in Europe, after campylobacteriosis, with *Salmonella enterica* serotype Enteritidis being the most commonly reported serotype.^{1,2} Although the number of *S* Enteritidis cases has substantially declined in the past decade, the number of infections increased from 2014 to 2016, and this bacterium remains one of the major causes of food-borne outbreaks.²

On Jan 18, 2016, an urgent inquiry was launched by Scotland on the Epidemic Intelligence Information

System for Food- and Waterborne Diseases and Zoonoses (EPIS-FWD), a platform to exchange information regarding possible public health threats in the EU, hosted by the European Centre for Disease Prevention and Control (ECDC). Scotland reported 21 human cases of *S* Enteritidis, with an uncommon multiple locus variable-number tandem repeat analysis (MLVA) profile 2-9-7-3-2, belonging to two distinct whole-genome sequencing (WGS) clusters. The Netherlands, Denmark, and Finland responded that they had observed *S* Enteritidis cases with the same MLVA profile. The UK

Research in context

Evidence before this study

We searched PubMed without language restrictions using the term “*Salmonella* Enteritidis” combined with “outbreak”. A wealth of evidence exists from previous *S* Enteritidis outbreaks, the most common salmonella serotype in humans in Europe, which have mostly been associated with consumption of eggs, egg products, and poultry meat. The declining trend of salmonellosis cases in the EU has levelled off, and cases of *S* Enteritidis have increased since 2014. Whole-genome sequencing (WGS) is increasingly being used as a confirmatory method in outbreak studies because of its superior discriminatory power and decreasing cost, and it is now more often implemented as routine first-line or second-line typing method for national surveillance of foodborne pathogens. However, the use of different WGS analysis pipelines and hurdles in data sharing make its efficient use difficult in large investigations.

Added value of this study

This study shows how multi-country sharing of real-time WGS data combined with focused epidemiological and food

investigations made it possible to disentangle the largest *S* Enteritidis outbreak in Europe. Coordinated data collection and rapid exchange of information between public health authorities and traceability information by food safety authorities at the EU level was essential in finding the vehicle of infection and in coordinating risk management actions. WGS provided considerable added value in terms of setting a more specific case definition, and resulted in a more conclusive outbreak investigation than would be possible when relying on other, more traditional typing methods.

Implications of all the available evidence

The routine use of WGS in salmonella surveillance and outbreak response could help to detect and resolve international outbreaks and to monitor the effect of control measures, thereby reducing the burden of salmonellosis. The intensified trade of goods and food production practices calls for a WGS network to facilitate global disease surveillance and early recognition of multi-country foodborne outbreaks.

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also reported isolates sharing the associated WGS sequences. Because only a few additional cases were reported subsequently, no further investigation at the EU level was done at that time.

On Aug 25, 2016, the Netherlands reported a re-emergence of *S* Enteritidis cases of the outbreak MLVA profile. Several other European countries observed a parallel increase. In addition, on the basis of WGS analysis, isolates with MLVA type 2-9-6-3-2 appeared to belong to the outbreak. This report describes an international outbreak investigation that revealed the largest known European multi-country salmonellosis outbreak.

Methods

Case definitions

A confirmed case was defined as a laboratory-confirmed *S* Enteritidis infection with the outbreak strain, identified on the basis of WGS analysis, that occurred between May 1, 2015, and Oct 31, 2018 (inclusive). Two distinct single-linkage clusters in which each isolate was within five or fewer single-nucleotide polymorphisms (SNPs) of another isolate were identified, further referred to as WGS cluster 1 (SNP address 1.2.3.175.175.175.%) and WGS cluster 2 (1.2.3.18.359.360.%).³ A probable case was defined as a laboratory-confirmed *S* Enteritidis infection with outbreak MLVA profiles 2-9-7-3-2 or 2-9-6-3-2 that occurred between May 1, 2015, and Oct 31, 2018 (inclusive).⁴

Laboratory methods

ECDC routinely collects and analyses MLVA and associated metadata for human *S* Enteritidis isolates as

part of surveillance across the EU and European Economic Area (EEA).⁵ WGS for case confirmation was done in EU or EEA member states or in an ECDC-contracted laboratory to support countries with a low capacity for WGS. *S* Enteritidis-positive isolates from food products and environmental samples from trace-back investigations were analysed by national competent authorities. Member states without MLVA or WGS capacity were offered typing and sequencing support by the European Union Reference Laboratory for *Salmonella*. The Public Health England pipeline and nomenclature (SNP address) were used for joint multi-country WGS analysis (appendix).⁶⁻⁸

Case finding

The notification of non-typhoidal salmonellosis is mandatory in most countries involved in the outbreak, whereas notification is based on voluntary systems in Belgium, Luxembourg, France, and the Netherlands. In the UK, suspected food poisoning is a notifiable disease, and diagnostic laboratories are required to notify health authorities of isolation of salmonella from all human samples. In some of the countries, local outbreaks (eg, restaurant outbreaks) of cases with the MLVA outbreak profile or WGS outbreak strain were picked up by local health institutes and notified to the national public health institute.

Descriptive epidemiological investigations

Individuals infected with *S* Enteritidis as part of the outbreak were interviewed in Belgium, Croatia, Denmark, France, Hungary, Ireland, Luxembourg, the Netherlands, Norway, Slovenia, Sweden, and the UK. Countries used

See Online for appendix

their routine methods to collect typing data and epidemiological information (clinical symptoms, travel history, and food consumption for 5–7 days [depending on country] before symptom onset). ECDC coordinated the multi-country outbreak investigation by compiling and maintaining a linelist in EPIS-FWD, including microbiological and epidemiological data on cases at the EU level (appendix).

Case-control study

A case-control study was initiated in the Netherlands on Sept 1, 2016, for which confirmed and probable cases recorded between Aug 1, 2016, and Oct 31, 2016, were included. For each case, four controls were randomly sampled from the population registry and frequency matched by age, sex, and postal code. Participants were given a questionnaire to collect information on exposures (including travel history; outlets where groceries were purchased; consumption of various meat, vegetable, dairy, and egg products; eating in food establishments; and contact with animals) in the past 7 days. Exposure rates between cases and controls were compared by calculating odds ratios (ORs) with 95% CIs by use of unmatched univariable and multivariable logistic regression in an iterative process with increasing number of cases and controls (appendix). Statistical analyses were done with STATA (version 15.1). Oral consent was obtained from all participants, but ethical approval was not sought as data were collected under public health legislation.

Environmental and trace-back investigations

Information from case interviews was used to guide trace-back investigations of implicated food items. Because most patients in the Netherlands and the UK initially reported having eaten in restaurants, and no single food item could be identified as a possible vehicle of infection, trace-back investigations were done by the Dutch and Scottish food safety authorities based on food items consumed by patients at restaurants. Data on the ingredients' suppliers were obtained to identify common suppliers between restaurants. Countries shared their trace-back information through the Rapid Alert System for Food and Feed (RASFF), a platform for the exchange of information between national authorities on health risks related to food or feed in the EU. The European Food Safety Authority (EFSA) and the Directorate-General for Health and Food Safety were in contact with national food safety authorities, who were in charge of environmental and trace-back investigations and followed up and coordinated EU-wide trace-forward investigations. Trace-back investigations were done only in Belgium, Croatia, Hungary, the Netherlands, and the UK; investigations were not done in the remaining countries because of the low number of cases in those countries or because there was no commonality in exposure among cases. Rapid outbreak assessments were produced by ECDC and EFSA to share the compiled data on outbreak cases and environmental and trace-back investigations between public health institutes and food safety authorities.

Role of the funding source

The sponsors of the study were involved in data collection, data interpretation, data analysis, writing of the report, and in the study design. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

1209 *S* Enteritidis outbreak cases were identified in 18 EU and EEA countries between May 1, 2015, and Oct 31, 2018, of which 838 were confirmed and 371 were probable (table). Among all cases, the median age was 28 years (range 0–96; IQR 12–53), and 602 (50%) patients were male. Of those with confirmed *S* Enteritidis infection, 112 (13%) reported a history of travel in other EU countries, including Poland (25 [3%] patients), Bulgaria (22 [3%]), Cyprus (14 [2%]), Portugal (11 [1%]), Hungary (ten [1%]), and eight other countries (each with fewer than ten [$\leq 1\%$] cases). Information on clinical symptoms was available for 115 patients, of which 112 (97%) had diarrhoea, 89 (77%) had stomach ache, 73 (63%) had fever, 52 (45%) had vomiting, and 40 (35%) had blood in the stool. 89 (36%) of 246 patients with available information were admitted to hospital. One patient (aged 5 years) in Croatia and three (aged 82 years,

	Cases recorded			Cases interviewed	Ate in a food establishment*	Consumed eggs†
	Confirmed	Probable	Total			
Belgium	14	146	160	36	5	25
Croatia	4	0	4	5	0	5
Czech Republic	0	8	8	0	NA	NA
Denmark	22	0	22	6	4	4
Finland	0	1	1	0	NA	NA
France	29	0	29	4	0	4
Greece	0	2	2	0	NA	NA
Hungary	0	17	17	8	8	6
Ireland	0	16	16	5	Unknown	3
Italy	1	25	26	0	NA	NA
Luxembourg	7	0	7	0	NA	NA
Netherlands	98	109	207	66	49	55
Norway	33	39	72	2	1	2
Slovenia	3	4	7	1	1	Unknown
Sweden	13	14	27	6	Unknown	6
UK	572	6	578	70	59	57
Total	838	371	1209	209	127	162

NA=not applicable (interviews were not done in any of these cases). *Restaurant, catering, or take-away. †Eggs or meals containing eggs.

Table: Number of probable and confirmed cases by country in the EU or European Economic Area from May 1, 2015, to Oct 31, 2018

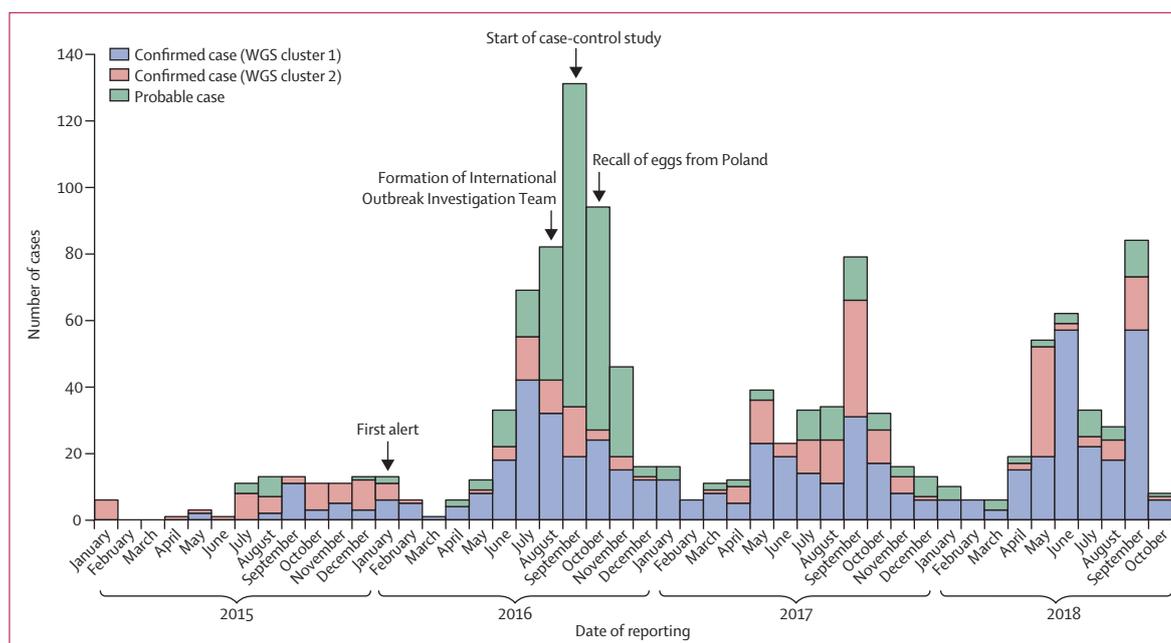


Figure 1: Number of outbreak cases by month and case classification (n=1209) in the EU and European Economic Area between January, 2015, and October, 2017

88 years, and 89 years) in Hungary died because of or with an infection of the outbreak strain.

509 (42%) of 1209 cases were reported in 2016, when the number of cases steadily increased from May and peaked in September (figure 1). Based on interviews with patients, food isolate sequencing, trace-back investigations, and environmental investigations, eggs from an agricultural business consortium in Poland were identified as the outbreak vehicle in October, 2016. Following the withdrawal of the concerned eggs in Europe and the implementation of control measures in Poland, a sharp decrease in the number of cases was observed (figure 1). However, in March, 2017, the number of reported cases increased again, with peaks in May and September. The increase continued in 2018, with a similar temporal pattern.

581 human isolates belonged to WGS cluster 1 and 257 isolates to WGS cluster 2 (figure 2). WGS cluster 1 had a maximum SNP distance of 18 and time to most recent common ancestor (TMRCA) of approximately 4.7 years (95% highest probability density [HPD] 4.0–6.4). Most clinical isolates, all food isolates, and all but one of the primary production isolates in cluster 1 were descended from a clonal expansion 3.0 years previously (95% HPD 3.0–3.2), in late 2014. WGS cluster 2 had a maximum SNP distance of 37 and a TMRCA of around 5.0 years (95% HPD 5.1–5.7). The two WGS clusters had a SNP distance of 78 from each other, with a TMRCA of approximately 34.8 years (95% HPD 23.5–42.5). In contrast to WGS cluster 1, the isolates from WGS cluster 2 were observed across four distinct temporal clades (ie, groups of strains with a common ancestor and its descendants), with three out of four clades persisting past

the implementation of control measures. Bayesian skyline plots, which infer the historical effective population size of the outbreak, showed rapid expansions of WGS clusters 1 and 2 towards the middle of 2015 (figure 2A), which were maintained in both populations until the implementation of control measures. The skyline plots confirm that, despite the interventions, population levels had not returned to pre-outbreak levels by the end of 2017.

209 individuals with confirmed or probable *S* Enteritidis infection were interviewed, of whom 127 (61%) had eaten in a food establishment and 162 (78%) had consumed eggs or products containing eggs (table). No specific food item could be identified from the questionnaires. In Scotland, two restaurant outbreaks were identified, consisting of four and three cases, respectively, in addition to nine cases that were linked to a bakery, and four small restaurant outbreaks that were linked to ten cases in total. In England and Wales, seven restaurants were linked to 29 cases. In four of these restaurants, all identified individuals with *S* Enteritidis infection reported eating eggs or egg-containing dishes. In the remaining three restaurants, investigations identified concerns about cross-contamination during food preparation. In Belgium, 25 people reported having consumed food items from two butchers. In Croatia, five individuals in the same household had all eaten eggs bought from one retail chain. In Hungary, two cases were linked to a meal prepared in a holiday resort, and another six people had eaten meals containing eggs at the same restaurant.

As part of the case-control study, 65 (81%) of 80 questionnaires given to cases and 87 (27%) of 320 questionnaires given to controls were collected in the

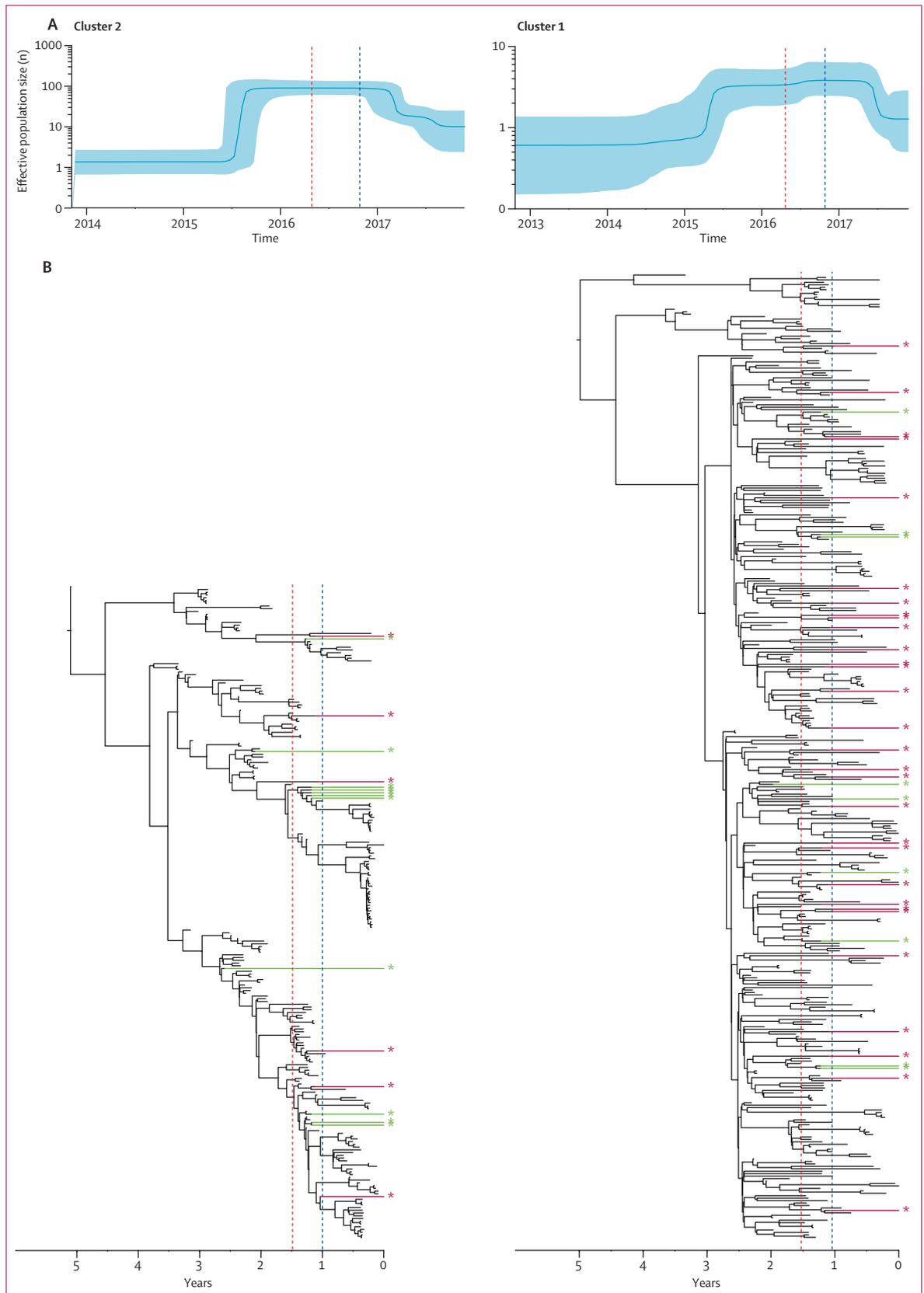


Figure 2: Phylodynamic analysis of whole-genome sequencing clusters 1 and 2
 (A) Bayesian skyline plots showing the temporal changes of the effective population size of the outbreak with 95% highest probability density (blue shading). The red dashed line is when the outbreak was declared (May 1, 2016) and the blue dashed line is when control measures were implemented (Oct 20, 2016). (B) Maximum clade credibility trees. Red stars represent isolates from primary production (30 for cluster 1 and six for cluster 2) and green stars represent food isolates (nine for cluster 1 and 11 for cluster 2). All other nodes represent clinical isolates from humans (355 for cluster 1 and 221 for cluster 2).

Netherlands. In the univariable analysis, illness was significantly associated with eating in a restaurant (49 [75%] of 65; OR 3.4 [95% CI 1.6–7.3]), especially in an Asian-style restaurant (20 [31%]; 7.2 [2.4–25.9]). Consumption of bacon (14 participants), pork chop (12), baked sandwich meat (ten), minced chicken meat (six), gyros (six), kebab (six), minced pork meat (five), and tiramisu (five) were also associated with illness in univariable analysis (appendix). In the multivariable analysis, significant associations with illness remained for eating in a food establishment (OR 3.8 [95% CI 1.6–9.4]) and consumption of pork chop (5.4 [1.4–21.0]) and baked sandwich meat (5.9 [1.4–24.5]; appendix). Because pork chop and baked sandwich meat were eaten by less than 23% of patients, they were deemed an unlikely outbreak source. Consumption of eggs or products containing eggs (reported in 55 [85%] of 65, and 67 [75%] controls) was not significantly associated with illness (OR 1.8 [95% CI 0.8–4.1]; appendix). Because eating in restaurants was also frequently reported by cases in other countries, it was thought to be the most likely source of infection.

In Scotland, investigation of the two restaurant outbreaks identified the potential for cross-contamination within the restaurants, particularly in relation to the practice of batching eggs for use in various dishes. In February, 2016, because individuals with *S* Enteritidis infection frequently reported eating eggs or dishes containing eggs in catering establishments, and because of the potential for cross-contamination, the egg supply chain was investigated in 12 of the restaurants where such individuals had reported eating. A common wholesaler was identified in Scotland for nine of the 12 restaurants, which was supplied with eggs from multiple food business operators, including Polish packing centre A (figure 3). Around 1000 eggs were obtained from the wholesaler, originating from six different suppliers, and all tested negative for salmonella.

In the Netherlands, trace-back investigation in September, 2016, of three cases related to one restaurant, as well as recipe-based trace-back investigations of eight restaurants (later during the investigation, 16 restaurants) where infected individuals had eaten, converged on one supplier, which received eggs from Polish packing centre A via a Dutch egg packing centre. Trace-back of cases linked to two butchers in Belgium, of household members in Croatia, and cases linked to a restaurant and holiday resort in Hungary, also converged on packing centre A. On Sept 23, 2016, Norway reported two *S* Enteritidis isolates with an outbreak MLVA profile from liquid eggs, before pasteurisation, obtained as part of an egg processing company's own monitoring samples. Both samples originated from eggs from Polish packing centre A, with sampling dates of May 5 and Nov 16, 2015. The eggs originated from Polish farms with a salmonella-negative status.

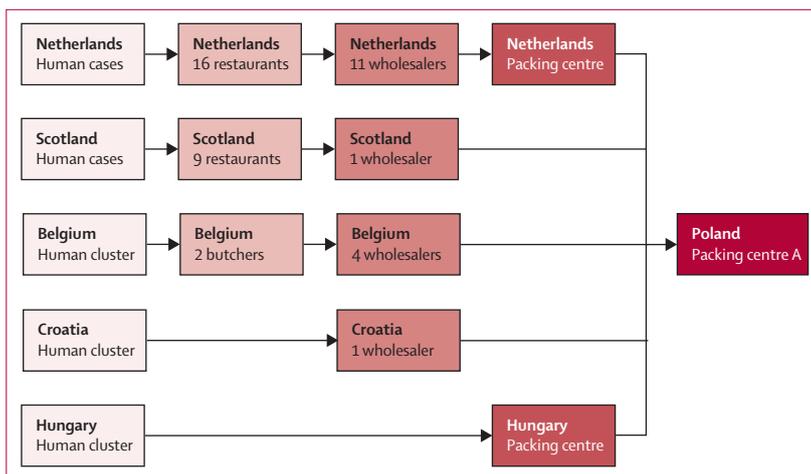


Figure 3: Trace-back investigations and trading connections from countries to packing centre A in Poland

On Oct 12, 2016, 5000 eggs from the Dutch egg packing centre, which originated from the implicated Polish packing centre, were tested for *Salmonella* spp in pools of ten eggs (shells and egg content separately). 66 (13%) of 500 pooled egg shell samples and two (<1%) pooled egg contents samples tested positive for *S* Enteritidis. WGS analyses of ten isolates showed that nine matched the two outbreak WGS clusters, providing microbiological confirmation that eggs from packing centre A were the outbreak vehicle of infection. The isolates from eggs intended for pasteurisation in Norway matched WGS cluster 2 and food isolates from different food types containing eggs from the two butchers in Belgium matched both WGS clusters. In Croatia, 1070 eggs originating from packing centre A were taken from the wholesaler and analysed in pools of ten, of which nine (8%) pooled samples were positive for *S* Enteritidis, and eight (7%) matched the WGS outbreak clusters.

An extensive trace-forward of the concerned eggs, based on information shared by the involved countries in RASFF, was initiated and closely followed up by the European Commission and coordinated by EFSA to organise risk management actions. Since Sept 28, 2016, an estimated 621 consignments with 110 million eggs had been distributed to 18 EU or EEA countries from Polish farms supplying the concerned packing centres. Around 122 consignments with a total of 36 million eggs from farms where *S* Enteritidis had been detected in one or more flocks were also exported to 12 non-EU countries.

In November and December, 2016, WGS analyses were done on ten non-human isolates originating from three *S* Enteritidis-positive farms in Poland providing eggs to three Polish packing centres, including packing centre A. Seven (70%) of these isolates had a MLVA outbreak profile, of which four (40%) belonged to WGS cluster 1 and three (30%) to WGS cluster 2. Most of the *S* Enteritidis-positive farms, as well as the three implicated Polish packing and distribution centres,

belonged to the same consortium and were therefore considered to be linked. In December, 2017, additional WGS analyses were done on 43 *S* Enteritidis-positive isolates sampled between Oct 3 and Dec 13, 2016, from 18 different farms in Poland belonging to the same consortium. Of these, 31 (72%) isolates belonged to WGS cluster 1 and six (14%) to WGS cluster 2, and originated from 15 different farms. In two farms, isolates belonged to both WGS clusters. Breeding flocks and hatcheries upstream in the supply chain of the implicated farms were found to be salmonella-negative.

Eggs from *S* Enteritidis-positive farms were withdrawn from the market and restrictive measures were introduced from Oct 20, 2016, in line with EU legislation.⁹ Eggs originating from *S* Enteritidis-positive farms could only be placed on the market for human consumption if industrially processed (including pasteurisation) to eliminate salmonella. An extensive withdrawal was done in the EU and required several weeks to be completed. New pullets were introduced after the culling of salmonella-positive flocks and poultry houses were cleaned and disinfected. The number of reported cases sharply decreased after the implementation of controls, but the number of cases increased again in May, 2017 (figure 1), albeit with different strain predominance (WGS cluster 2 became dominant). Since 2018, routine sampling of laying hens at the farms have been intensified, but the source of the re-emergence remains unknown.

In England, three isolates from environmental swabs at one restaurant on July 21, 2017, and one isolate from raw pooled egg mix at another restaurant on Sept 4, 2017, belonged to WGS cluster 2. No specific egg producer could be identified as having supplied eggs to the premises at the time of exposure, but a common egg distributor sourcing eggs from multiple countries (including the UK, Germany, Spain, and Poland) and distributing to catering premises was identified. From Feb 1, 2017 to Oct 1, 2017, there were 29 cases linked to these and other catering premises (eight in total) where two or more confirmed patients had consumed food; for the 24 cases for whom consumption information was available, 16 (66%) declared consumption of dishes containing eggs. Interviews of 39 patients not linked to these catering premises over this time period (Feb 1 to Oct 1, 2017) confirmed a higher proportion of people consuming eggs than the expected rate in the general population in England (84% [32/38] vs 54%).¹⁰

Discussion

This prolonged international outbreak highlights the public health impact of multi-country sharing of WGS, epidemiological, trace-back, trace-forward, and microbiological data in real-time. Investigations identified eggs originating from a large agricultural business consortium in Poland as the outbreak vehicle. It is likely that more countries have been affected by the outbreak but were not

detected because molecular typing is not routinely done for cases of *S* Enteritidis in humans in many countries. The ultimate primary source of contamination and incursion of infection onto the egg production farms in Poland remains unknown. Based on the outcomes of the investigations, the source of infection in this outbreak could be at the level of the laying hen farms, but the possibility that *S* Enteritidis might have been introduced at a higher level such as breeding farms cannot be excluded. The decrease in the number of cases and changes in strain predominance indicate that control measures might have had an effect. However, the re-emergence of cases in 2017 suggests that the outbreak strains continue to enter the food chain, but other sources of contamination (eg, other flocks) remain to be identified.

Molecular typing data, particularly WGS analyses, made an important contribution. These analyses were guided by epidemiological and traceability information, which was of equal importance, as confirmation of the food vehicle is unlikely with molecular typing data only. WGS achieves the maximum capability possible for discriminating isolates,^{7,11,12} and is rapidly replacing the current typing methods in Europe.^{13–17} WGS is now often the reference typing method in outbreak studies and is being increasingly implemented as routine first-line or second-line typing method for national surveillance of a number of bacterial and viral infections.^{13–15,18–20} In the USA, the use of WGS in state laboratories participating in a national laboratory network (PulseNet USA) for outbreak detection of foodborne pathogens is quickly expanding, and has been decisive in several salmonella outbreak investigations with regard to the identification of the vehicle of infection.^{20–22} Although MLVA did prove useful as a rapid, inexpensive screening method for detecting probable cases, the application of WGS resulted in a more conclusive outbreak investigation. WGS data provided considerable added value in terms of setting a more accurate case definition and subsequent case confirmation, as well as the typing resolution for microbiological confirmation of the vehicle of infection. Importantly, without WGS, cases with outbreak MLVA profile 2-9-6-3-2 would have been overlooked. Crucial for the success of this outbreak investigation was the strong triggering signal from the WGS data that enabled prioritisation of epidemiological follow-up. A full comparison of WGS and MLVA in this outbreak investigation, as well as country-specific WGS pipelines, will be the subject of future papers.

Several platforms exist to share WGS data globally, such as NCBI and European Nucleotide Archive, in which WGS data can be deposited without costs and restrictions.^{23,24} However, political, ethical, and technical hurdles remain with respect to real-time sharing of WGS data, and the need for a common curated nomenclature for efficient communication and epidemiological anchoring.^{19,25,26} The present outbreak showed that case confirmation using data generated in multiple laboratories and different types

of WGS instruments could be done without prior standardisation, but data interpretation and analyses need to be harmonised if they are done in different institutions. A specific problem faced during multi-country investigations is the use of different typing methods, ranging from various WGS-based methods, MLVA, and pulsed-field gel electrophoresis, to no molecular subtyping at all, hindering efficient communication on the identity of isolates. To facilitate the detection and assessment of typing-based microbiological clusters and related communication between the public health and food and veterinary authorities at the EU and EEA level, ECDC and EFSA have set up a joint molecular typing database, initially based on traditional typing methods, including MLVA for *Salmonella enterica* serotypes Typhimurium and Enteritidis, as well as pulsed-field gel electrophoresis for other serotypes.²⁷

This study has several limitations. First, because countries used their own questionnaire, comparing data for case exposure was difficult. The investigations would have benefited from the use of a readily available standardised outbreak questionnaire.^{28,29} Second, we did a frequency-matched case-control study because it could be set up faster than an individually matched case-control study. Although we adjusted for the matching variables (ie, age, sex, and postal code) in the multivariable analysis, some confounding might have occurred. Third, trace-back efforts were hindered by the complexity of the distribution chain and absence of identification marks on some of the eggs (despite being required by legislation). It is therefore likely that not all eggs originating from the implicated Polish farms were withdrawn from the market. Fourth, two *S* Enteritidis isolates originating from implicated Polish farms did not belong to one of the outbreak WGS clusters, and three isolates had other non-outbreak MLVA profiles (2-10-6-3-2, 2-10-8-3-2, and 2-11-8-3-2), indicating that the outbreak might have been larger than anticipated.

This investigation showed the usefulness and efficiency of coordinated data collection during international outbreaks. The rapid exchange of information between public health authorities facilitated by ECDC, and the traceability information shared by food safety authorities through RASFF, assessed by EFSA, and followed up by the European Commission, were essential in finding the vehicle of infection and in coordinating risk management. This example highlights the importance of systems such as the Epidemic Intelligence Information System to exchange information on outbreaks and the possible source and vehicle of infection; the RASFF system to exchange information on food investigation and contaminated products and their origin, and to coordinate responses; and the Early Warning and Response System for notifications on cross-border threats.

The routine use of WGS in salmonella surveillance and outbreak response holds promise for helping to detect, trace, and halt international outbreaks, and to allow the

effect of control measures to be monitored, thereby reducing the burden of salmonellosis. The changing profile of infectious diseases resulting from increased population mobility and from the intensified trade of goods calls for global sharing of WGS data to facilitate worldwide disease surveillance and early recognition of international food-borne outbreaks.

Contributors

RP, TJD, ASLT, SMK, GA, EA, PMS, DP, ES, and VR prepared the first draft of the manuscript. RP, TJD, ASLT, LL, GH, SD, SK, JP, JMc, HH, LCTB, DB, CJ, LM, BH, SO, PG, IHMF, CvdW, MvdV, EF, GJH, JG, and SLH collected or analysed data at the national level. SMK, DP, and ES coordinated the multi-country outbreak investigation and collected and analysed data on outbreak cases at the EU level. GA, EA, PMS, and VR analysed data on trace-back and environmental investigations and coordinated trace-forward investigations at the EU level. TJD did the phylogenetic analyses. RP, IF, and EF conducted the case-control study. KM coordinated laboratory analyses at the European Union Reference Laboratory for Salmonella. All authors commented on data interpretation and critically reviewed the paper.

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Declaration of interests

We declare no competing interests.

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