Epidemiology and Infection

Operational burden of implementing *Salmonella* Enteritidis and Typhimurium cluster detection using whole genome sequencing surveillance data in England: a retrospective assessment

Piers Mook, Daniel Gardiner, Neville Q Verlander, Jacquelyn McCormick, Martine Usdin, Paul Crook, Claire Jenkins, Timothy J Dallman

# Supplementary Material

**Supplementary Technical Description S1. Regression approaches used to investigate associations between population size of geographical area, month of cluster detection and count or presence of clusters for 0, 5 and 10 SNP clusters**

For the HPT analysis, tabulations revealed that there were few instances in which there was more than one outbreak for the organism and SNP types that could be analysed, so a dichotomous outcome variable was created and analysed in each case (where the categories were either ‘no outbreaks’ or ‘one or more outbreaks’). For the national analysis, the *S*. Enteritidis 10 SNP outcome variable was also dichotomised as it was not feasible to estimate an ordinal logistic regression model (where the categories were 0, 1, 2 or more) due to small numbers. Small counts were again the reason for dichotomising the *S*. Typhimurium 5 SNP outcome.

Mixed effects regression models were fitted to the HPT outcomes with the HPT as the random effect, while fixed effects models were used for the other two levels. Mixed effects models were attempted at the centre level but they could not be fitted. If the variance component was not significant as judged by an approximate likelihood ratio test (LRT) and removal of the random effect did not result in a marked change in the odds ratio (OR), then a fixed effects model was used. For HPT and PHEC, the covariates were population and calendar month (April used as the default comparison month; June used in the centre level analysis of 0 SNP *S*. Enteritidis clusters) as continuous and categorical variables, respectively. For the national analysis, two month season (April/May used as the default comparison season; February/March used in national level analyses of 0 and 5 SNP*S*. Typhimurium clusters) as a categorical variable was used as the covariate. When population was one of the covariates, its appropriate functional form was determined by comparison with more complicated polynomials, with the simplest function being used that did not result in a significantly worse fit. Statistical testing of the fixed effects was by means of the LRT, where possible, with 5% taken as the significance level. If LRT was not possible, Wald testing was used. The judgement as to whether a fixed effects regression should be performed in place of the random effects one was done after the determination of the relationship between population and outcome. Linearity of the association between population and outcome on the canonical link scale appeared to be satisfactory in all cases, as was omitting HPT from the HPT model. No evidence of over-dispersion in the Poisson regression models.

**Supplementary Table S1. Identified 0-SNP clusters of *S*. Enteritidis and *S*. Typhimurium and their associated size and duration by HPT (local), PHEC (regional) and national levels, April 2014 to March 2015**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Geographical level** | **Serovar** | **Total n of clusters** | **Total n of cases in clusters** | **Median no. of cases (range)** | **Median duration of cluster (range)** |
| East Midlands PHEC | Enteritidis | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | East Midlands HPT | Enteritidis | 1 | 2 | 2 (2-2) | 6 (6-6) |
| Typhimurium | 2 | 4 | 2 (2-2) | 6.5 (5-8) |
|  East of England PHEC | Enteritidis | 1 | 3 | 3 (3-3) | 6 (6-6) |
| Typhimurium | 1 | 2 | 2 (2-2) | 7 (7-7) |
|  | Anglia HPT | Enteritidis | 1 | 2 | 2 (2-2) | 1 (1-1) |
| Typhimurium | 1 | 2 | 2 (2-2) | 4 (4-4) |
|  | Essex HPT | Enteritidis | 3 | 6 | 2 (2-2) | 1 (1-7) |
| Typhimurium | 1 | 2 | 2 (2-2) | 7 (7-7) |
|  | South Midlands and Hertfordshire HPT | Enteritidis | 4 | 8 | 2 (2-2) | 2.5 (1-8) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
| London PHEC | Enteritidis | 1 | 8 | 8 (8-8) | 14 (14-14) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | North East and North Central London HPT | Enteritidis | 5 | 10 | 2 (2-2) | 2 (1-7) |
| Typhimurium | 2 | 4 | 2 (2-2) | 3.5 (3-4) |
|  | North West London HPT | Enteritidis | 1 | 3 | 3 (3-3) | 3 (3-3) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | South London HPT | Enteritidis | 2 | 5 | 2.5 (2-3) | 4 (3-5) |
| Typhimurium | 2 | 4 | 2 (2-2) | 1 (1-1) |
| North East PHEC | Enteritidis | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | North East HPT | Enteritidis | 7 | 27 | 2 (2-15) | 1 (1-15) |
| Typhimurium | 3 | 6 | 2 (2-2) | 3 (1-8) |
| North West PHEC | Enteritidis | 2 | 4 | 2 (2-2) | 4.5 (1-8) |
| Typhimurium | 1 | 2 | 2 (2-2) | 7 (7-7) |
|  | Cheshire and Merseyside HPT | Enteritidis | 4 | 23 | 4.5 (2-12) | 6 (1-10) |
| Typhimurium | 1 | 2 | 2 (2-2) | 1 (1-1) |
|  | Cumbria and Lancashire HPT | Enteritidis | 2 | 5 | 2.5 (2-3) | 6.5 (1-12) |
| Typhimurium | 1 | 11 | 11 (11-11) | 15 (15-15) |
|  | Greater Manchester HPT | Enteritidis | 1 | 2 | 2 (2-2) | 3 (3-3) |
| Typhimurium | 1 | 2 | 2 (2-2) | 1 (1-1) |
| South East PHEC | Enteritidis | 2 | 4 | 2 (2-2) | 2.5 (2-3) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | Kent HPT | Enteritidis | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Typhimurium | 1 | 2 | 2 (2-2) | 1 (1-1) |
|  | Surrey and Sussex HPT | Enteritidis | 1 | 3 | 3 (3-3) | 7 (7-7) |
| Typhimurium | 1 | 3 | 3 (3-3) | 4 (4-4) |
|  | Thames Valley HPT | Enteritidis | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Typhimurium | 1 | 2 | 2 (2-2) | 8 (8-8) |
|  | Wessex HPT | Enteritidis | 2 | 4 | 2 (2-2) | 1 (1-1) |
| Typhimurium | 3 | 6 | 2 (2-2) | 1 (1-3) |
| South West PHEC | Enteritidis | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | Avon, Gloucestershire and Wiltshire HPT | Enteritidis | 5 | 11 | 2 (2-3) | 8 (1-8) |
| Typhimurium | 2 | 4 | 2 (2-2) | 2.5 (1-4) |
|  | Devon, Cornwall and Somerset HPT | Enteritidis | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Typhimurium | 1 | 2 | 2 (2-2) | 3 (3-3) |
| West Midlands PHEC | Enteritidis | 2 | 7 | 3.5 (2-5) | 10 (4-16) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | West Midlands East HPT | Enteritidis | 3 | 30 | 3 (2-25) | 4 (2-27) |
| Typhimurium | 1 | 2 | 2 (2-2) | 2 (2-2) |
|  | West Midlands North HPT | Enteritidis | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | West Midlands West HPT | Enteritidis | 1 | 2 | 2 (2-2) | 1 (1-1) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Yorkshire and Humber PHEC | Enteritidis | 1 | 2 | 2 (2-2) | 1 (1-1) |
| Typhimurium | 2 | 5 | 2.5 (2-3) | 7 (6-8) |
|  | North Yorkshire and Humber HPT | Enteritidis | 6 | 13 | 2 (2-3) | 2 (1-8) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | South Yorkshire HPT | Enteritidis | 1 | 2 | 2 (2-2) | 1 (1-1) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
|  | West Yorkshire HPT | Enteritidis | 3 | 6 | 2 (2-2) | 6 (1-7) |
| Typhimurium | 3 | 6 | 2 (2-2) | 1 (1-2) |
| National | Enteritidis | 85 | 330 | 2 (2-62) | 6 (1-30) |
| Typhimurium | 33 | 134 | 2 (2-31) | 6 (1-27) |

**Supplementary Table S2. Identified 5-SNP clusters of *S*. Enteritidis and *S*. Typhimurium and their associated size and duration at HPT (local), PHEC (regional) and national levels, April 2014 to March 2015a**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Geographical level** | **Serovar** | **Total n of clusters** | **Total n of cases in clusters** | **Median no. of cases (range)** | **Median duration of cluster (range)** |
| London PHEC | Enteritidis | 1 | 8 | 8 (8-8) | 14 (14-14) |
| Typhimurium | 0 | 0 | 0 (0-0) | 0 (0-0) |
| Yorkshire and Humber PHEC | Enteritidis | 1 | 6 | 6 (6-6) | 9 (9-9) |
| Typhimurium | 1 | 5 | 5 (5-5) | 15 (15-15) |
| National | Enteritidis | 38 | 588 | 7 (5-239) | 18.5 (4-134) |
| Typhimurium | 10 | 112 | 7 (5-36) | 16 (1-29) |

a Only geographical levels with one or more cluster are shown

**Supplementary Table S3. Identified 10-SNP clusters of *S*. Enteritidis and *S*. Typhimurium and their associated size and duration at HPT (local), PHEC (regional) and national levels, April 2014 to March 2015 a**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Geographical level** | **Serovar** | **Total n of clusters** | **Total n of cases in clusters** | **Median no. of cases (range)** | **Median duration of cluster (range)** |
| National | Enteritidis | 16 | 505 | 14.5 (10-239) | 33.5 (16-134) |
| Typhimurium | 4 | 111 | 26.5 (15-43) | 32 (16-61) |

a Only geographical levels with one or more cluster are shown

**Supplementary Table S4. Total number of 0, 5 and 10 SNP clusters of *S*. Enteritidis and *S*. Typhimurium and their associated size that have at least one case in a geographical level, regardless of responsibility for managing the investigation, in England, April 2014 to March 2015**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Geographical level** | **Serovar** | **0 SNP** | **5 SNP** | **10 SNP** |
| **Total n of clusters** | **Total n of cases in clusters** | **Total n of clusters** | **Total n of cases in clusters** | **Total n of clusters** | **Total n of cases in clusters** |
| East Midlands PHEC | Enteritidis | 30 | 34 | 17 | 34 | 11 | 28 |
| Typhimurium | 10 | 46 | 5 | 45 | 2 | 37 |
|  | East Midlands HPT | Enteritidis | 30 | 34 | 17 | 34 | 11 | 28 |
| Typhimurium | 10 | 46 | 5 | 45 | 2 | 37 |
| East of England PHEC | Enteritidis | 31 | 47 | 21 | 48 | 11 | 43 |
| Typhimurium | 12 | 22 | 5 | 10 | 2 | 8 |
|  | Anglia HPT | Enteritidis | 13 | 17 | 12 | 23 | 8 | 19 |
| Typhimurium | 6 | 10 | 3 | 6 | 2 | 5 |
|  | Essex HPT | Enteritidis | 6 | 11 | 9 | 10 | 5 | 6 |
| Typhimurium | 7 | 8 | 4 | 4 | 2 | 2 |
|  | South Midlands and Hertfordshire HPT | Enteritidis | 13 | 19 | 7 | 15 | 7 | 18 |
| Typhimurium | 2 | 4 | 0 | 0 | 1 | 1 |
| London PHEC | Enteritidis | 32 | 64 | 19 | 70 | 8 | 55 |
| Typhimurium | 11 | 17 | 5 | 9 | 2 | 8 |
|  | North East and North Central London HPT | Enteritidis | 16 | 32 | 7 | 29 | 4 | 23 |
| Typhimurium | 6 | 8 | 2 | 3 | 2 | 3 |
|  | North West London HPT | Enteritidis | 3 | 7 | 5 | 10 | 3 | 6 |
| Typhimurium | 3 | 3 | 2 | 2 | 1 | 1 |
|  | South London HPT | Enteritidis | 16 | 25 | 14 | 31 | 7 | 26 |
| Typhimurium | 4 | 6 | 3 | 4 | 2 | 4 |
| North East PHEC | Enteritidis | 22 | 43 | 18 | 50 | 11 | 41 |
| Typhimurium | 9 | 12 | 3 | 3 | 4 | 4 |
|  | North East HPT | Enteritidis | 22 | 43 | 18 | 50 | 11 | 41 |
| Typhimurium | 9 | 12 | 3 | 3 | 4 | 4 |
| North West PHEC | Enteritidis | 40 | 69 | 28 | 93 | 15 | 83 |
| Typhimurium | 15 | 32 | 4 | 22 | 3 | 20 |
|  | Cheshire and Merseyside HPT | Enteritidis | 15 | 35 | 10 | 44 | 10 | 49 |
| Typhimurium | 6 | 8 | 1 | 2 | 2 | 3 |
|  | Cumbria and Lancashire HPT | Enteritidis | 14 | 17 | 14 | 21 | 8 | 16 |
| Typhimurium | 5 | 17 | 2 | 18 | 1 | 14 |
|  | Greater Manchester HPT | Enteritidis | 15 | 17 | 17 | 28 | 8 | 18 |
| Typhimurium | 6 | 7 | 2 | 2 | 2 | 3 |
| South East PHEC | Enteritidis | 38 | 106 | 25 | 110 | 14 | 100 |
| Typhimurium | 22 | 33 | 7 | 8 | 3 | 17 |
|  | Kent HPT | Enteritidis | 8 | 9 | 8 | 8 | 5 | 5 |
| Typhimurium | 2 | 3 | 1 | 1 | 0 | 0 |
|  | Surrey and Sussex HPT | Enteritidis | 11 | 14 | 13 | 15 | 9 | 11 |
| Typhimurium | 7 | 10 | 1 | 1 | 3 | 7 |
|  | Thames Valley HPT | Enteritidis | 7 | 9 | 8 | 12 | 8 | 12 |
| Typhimurium | 7 | 8 | 3 | 3 | 3 | 4 |
|  | Wessex HPT | Enteritidis | 15 | 74 | 12 | 75 | 8 | 72 |
| Typhimurium | 8 | 12 | 3 | 3 | 2 | 6 |
| South West PHEC | Enteritidis | 29 | 43 | 25 | 52 | 13 | 39 |
| Typhimurium | 13 | 16 | 3 | 6 | 2 | 4 |
|  | Avon, Gloucestershire and Wiltshire HPT | Enteritidis | 19 | 25 | 16 | 22 | 11 | 17 |
| Typhimurium | 5 | 7 | 3 | 3 | 1 | 2 |
|  | Devon, Cornwall and Somerset HPT | Enteritidis | 14 | 18 | 15 | 30 | 9 | 22 |
| Typhimurium | 8 | 9 | 2 | 3 | 2 | 2 |
| West Midlands PHEC | Enteritidis | 24 | 71 | 24 | 100 | 10 | 84 |
| Typhimurium | 8 | 10 | 5 | 6 | 3 | 4 |
|  | West Midlands East HPT | Enteritidis | 14 | 51 | 14 | 69 | 6 | 61 |
| Typhimurium | 4 | 5 | 2 | 2 | 2 | 3 |
|  | West Midlands North HPT | Enteritidis | 5 | 9 | 7 | 14 | 5 | 12 |
| Typhimurium | 3 | 3 | 2 | 2 | 0 | 0 |
|  | West Midlands West HPT | Enteritidis | 8 | 11 | 11 | 17 | 7 | 11 |
| Typhimurium | 2 | 2 | 2 | 2 | 1 | 1 |
| Yorkshire and Humber PHEC | Enteritidis | 31 | 45 | 24 | 45 | 14 | 32 |
| Typhimurium | 13 | 19 | 4 | 8 | 2 | 9 |
|  | North Yorkshire and Humber HPT | Enteritidis | 17 | 25 | 10 | 16 | 6 | 9 |
| Typhimurium | 4 | 4 | 0 | 0 | 2 | 3 |
|  | South Yorkshire HPT | Enteritidis | 4 | 5 | 8 | 8 | 7 | 7 |
| Typhimurium | 3 | 3 | 2 | 3 | 1 | 1 |
|  | West Yorkshire HPT | Enteritidis | 12 | 15 | 18 | 21 | 11 | 16 |
| Typhimurium | 8 | 12 | 3 | 5 | 1 | 5 |
| National | Enteritidis | 147 | 522 | 40 | 602 | 16 | 505 |
| Typhimurium | 64 | 207 | 11 | 117 | 4 | 111 |

**Supplementary Table S5. Associations identified between count or identification of any 0-, 5- or 10-SNP cluster and population of geographical level and month**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Geographical Level** | **Outcome** | **Variable** | **Effect estimatea** | **95% Confidence interval** | **p-value** |
| Local | 0 SNP *S*. Enteritidis clusters  | PopulationJanuary February March April May June July August September October November December  | 1.07 per 100,000 person2.350.300.301.000.301.401.852.355.131.001.000.00 | 0.66-1.740.51 – 10.870.03 – 3.150.03 – 3.150.03 – 3.150.28 – 7.120.39 – 8.880.51 – 10.871.18 – 22.30.18 – 5.560.18 – 5.56n.e. | 0.80.001 |
| 0 SNP *S*. Typhimurium clusters  | PopulationJanuary February March April May June July August September October November December  | 1.74 per 100,000 person1.002.121.001.002.123.374.782.122.122.124.781.00 | 1.05-2.890.06 – 17.30.18 – 25.60.06 – 17.30.18 – 25.60.32 – 35.70.48 – 47.40.18 – 25.60.18 – 25.60.18 – 25.60.48 – 47.40.06 – 17.3 | 0.040.8 |
| Regional | 0 SNP *S*. Enteritidis clusters | PopulationJanuary February March April May June July August September October November December  | 1.52 per 100,000 n.e.1.00n.e.1.00n.e.1.00n.e.1.00n.e.n.e.n.e.1.00 | 0.95-2.43n.e.n.e.n.e.n.e.n.e.n.e.n.e.n.e.n.e.n.e.n.e. | 0.060.19 |
| National | 0 SNP *S*. Enteritidis clusters  | April/MayJune/JulyAugust/SeptemberOctober/NovemberDecember/JanuaryFebruary/March | 1.002.503.002.500.631.00 | 1.10 – 5.681.35 – 6.681.10 – 5.680.20 – 1.910.38 – 2.66 | <0.001 |
| 5 SNP *S*. Enteritidis clusters  | April/MayJune/JulyAugust/SeptemberOctober/NovemberDecember/JanuaryFebruary/March | 1.001.003.000.601.400.60 | 0.29 – 3.451.09 – 8.250.14 – 2.510.44 – 4.410.14 – 2.51 | 0.02 |
| 10 SNP *S*. Enteritidis clusters  | April/MayJune/JulyAugust/SeptemberOctober/NovemberDecember/JanuaryFebruary/March | 1.001.001.000.000.000.00 | n.e.n.e.n.e.n.e.n.e.n.e. | 0.4 |
| 0 SNP *S*. Typhimurium clusters  | April/MayJune/JulyAugust/SeptemberOctober/NovemberDecember/JanuaryFebruary/March | 1.004.004.003.502.002.00 | 0.85 – 18.80.85 – 18.80.73 – 16.80.37 – 10.90.37 – 10.9 | 0.3 |
| 5 SNP *S*. Typhimurium clusters  | April/MayJune/JulyAugust/SeptemberOctober/NovemberDecember/JanuaryFebruary/March | 0.000.000.001.000.001.00 | n.e.n.e.n.e.n.e.n.e. | 0.15 |
| 10 SNP *S*. Typhimurium clusters  | April/MayJune/JulyAugust/SeptemberOctober/NovemberDecember/JanuaryFebruary/March | 0.001.000.001.001.001.00 | n.e.0.02 – 50.4n.e.0.02 – 50.40.02 – 50.4 | 0.5 |

n.e. = not estimable

aOdds ratios presented except for investigations for national level 0 and 5 SNP *S*. Enteritidis clusters and 0 SNP, *S*. Typhimurium clusters which presented relative risks.