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# Impact of reduced numbers of isolates phage-typed on the detection of *Salmonella* outbreaks

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## SUMMARY

The aim of this study was to assess the effects of reductions in the number of isolates tested by phage-typing on the recognition of outbreaks of salmonellosis. Five outbreaks (categorized as 'small', 'medium' or 'large') which occurred in England in 2005 were used as examples. The outbreaks were caused by serotypes which were subdivided by phage-typing. Results indicated that reducing the number of isolates phage-typed would have an impact on the surveillance system, with one outbreak likely to have been missed altogether. However, this does not have a great effect on the 'time-to-detection' for the other outbreaks. Assuming no testing for phage-typing was undertaken it is likely that two out of five outbreaks would not have been detected. Assessing the value of phage-type information is important not only in deciding on the efficiency of the current surveillance system but also in providing a basis upon which to assess more detailed typing methodologies such as an antibiogram of molecular profile.

**Key words**: Detection, outbreaks, *Salmonella*, typing.

## INTRODUCTION

*Salmonella* is a major cause of foodborne infection in England and Wales with 37 298 cases of human infection confirmed by the Health Protection Agency (HPA) Laboratory of Enteric Pathogens from 2004 to 2006 [1]. In general, such infections fall into two categories – sporadic, and outbreak-associated. Early recognition of an outbreak is essential for the development of intervention strategies and the subsequent implementation of disease control measures.

There are three common ways an outbreak of salmonellosis can be detected. It is often recognized in primary care through the patient attending general practitioner clinics. It can also be identified by environmental health officers and other health-care professionals observing an unusual increase in cases. The other way of detecting an outbreak is through surveillance systems [2, 3]. These systems are particularly useful for detecting inter-regional or national outbreaks that may be difficult to recognize by other methods [4].

Inter-regional or national outbreaks occur more commonly nowadays than 40 years ago when outbreaks typically affected a small number of people in a restricted geographical area, with a few notable exceptions [5]. A number of reasons exist for the change in epidemiology of foodborne outbreaks. These include the globalization and centralization of food production [6], the increasing antimicrobial resistance of some common pathogens [7] and change in the consumers' habits by depending less on home-made

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meals using raw ingredients [8]. Moreover, there have been drastic changes in our awareness and attention to food and water as a source of illness transmission. This increased awareness combined with diagnostic (identification of virulent strains of familiar pathogens or novel pathogens) and technological (e.g. reporting and recording systems) advancements has lead to a significant increase in detection and reporting of such outbreaks [8].

An automated exceedance reporting system for outbreak detection was developed in 1996 and used for the number of weekly reports for every recorded pathogen in England and Wales. In brief, an expected count and an upper threshold are estimated using historic data received at the HPA Centre for Infections. This is done using a Poisson regression model allowing for overdispersion, temporal trends and past outbreaks. To overcome seasonality, only the same weeks around the week of interest over the past 5 years are used. If the weekly reported count of a specific *Salmonella* serotype/phage-type exceeds the estimated threshold then it is flagged up as a potential outbreak. An 'exceedance score' is calculated as (observed-expected)/(threshold-expected), the expected count and the threshold being estimated from the regression model. The higher the exceedance score is above 1, the higher the observed count is above the outbreak threshold. The program is run on a weekly basis for both regional and national data [4].

The aim of this study was to investigate whether *Salmonella* outbreaks can still be detected by the exceedance reporting system if only a sample of isolates are phage-typed. A secondary aim was to investigate the impact on outbreak detection if no phage-typing is performed on *Salmonella* serotypes. Finally, the effect of reduced typing with respect to the time it takes for an outbreak to exceed the upper threshold of the system was examined. Five outbreaks categorized as small, medium and large that occurred during 2005 across England were used as examples.

## METHODS

### Study design

All records pertaining to human isolates of *Salmonella enterica* infection, reported in England and Wales, were extracted from the LabBase2 HPA dataset. A total of 90 167 cases of *Salmonella* infection reported between January 2000 and December 2005 were included in the study.

Forty-seven confirmed *Salmonella* outbreaks were flagged up by the surveillance system within 2005. Of these, five were selected without knowledge of the exceedance score of the exceedance reporting system for these outbreaks. The objective was to achieve variety on the size of the outbreaks, the spread of the cases, the area that they occurred, the serotypes and phage-types. Two small outbreaks of a maximum 10 cases, two medium (between 10 and 50 cases) and one large (of at least 50 individuals affected) were included in the study.

The weekly counts of *Salmonella* phage-types from the beginning of the study up to and including each outbreak time-period are shown in Figure 1. The details of the five outbreaks used are given below.

### Outbreak A (small): *Salmonella* Enteritidis phage-type (PT) 8 outbreak in the South East region

An example of a small outbreak of *S*. Enteritidis PT8 occurred in a defined area of South East England in 2005, with a total of four cases all of whom reported within the same week, starting on 20 September 2005, which was flagged by the exceedance reporting system. An additional six illnesses unrelated to the outbreak were reported in the same region that week bringing the total number of *S*. Enteritidis PT8 cases to 10. Figure 1 shows the total number of *S*. Enteritidis PT8 cases from the beginning of the study up to and including the week of the outbreak.

### Outbreak B (medium): *S*. Enteritidis PT4 outbreak in South East/South West regions

A total of 37 cases of *S*. Enteritidis PT4 were reported for an outbreak that occurred during the 9 weeks from 25 October 2005 to 26 December 2005. Of the 9 weeks, only week 3 was flagged using the exceedance reporting program since the majority of the cases occurred within that week (21 outbreak-related cases out of a total of 31 reported for this specific phage-type in the South West/South East) (Fig. 1).

### Outbreak C (medium): *S*. Enteritidis PT4 outbreak in the North East region

Outbreak C is an example of a *S*. Enteritidis PT4 outbreak that occurred in the North East region during 3 weeks in June and July 2005. Twenty-two cases of *S*. Enteritidis PT4 were reported in the North East region the week commencing 26 June 2005, 31 cases

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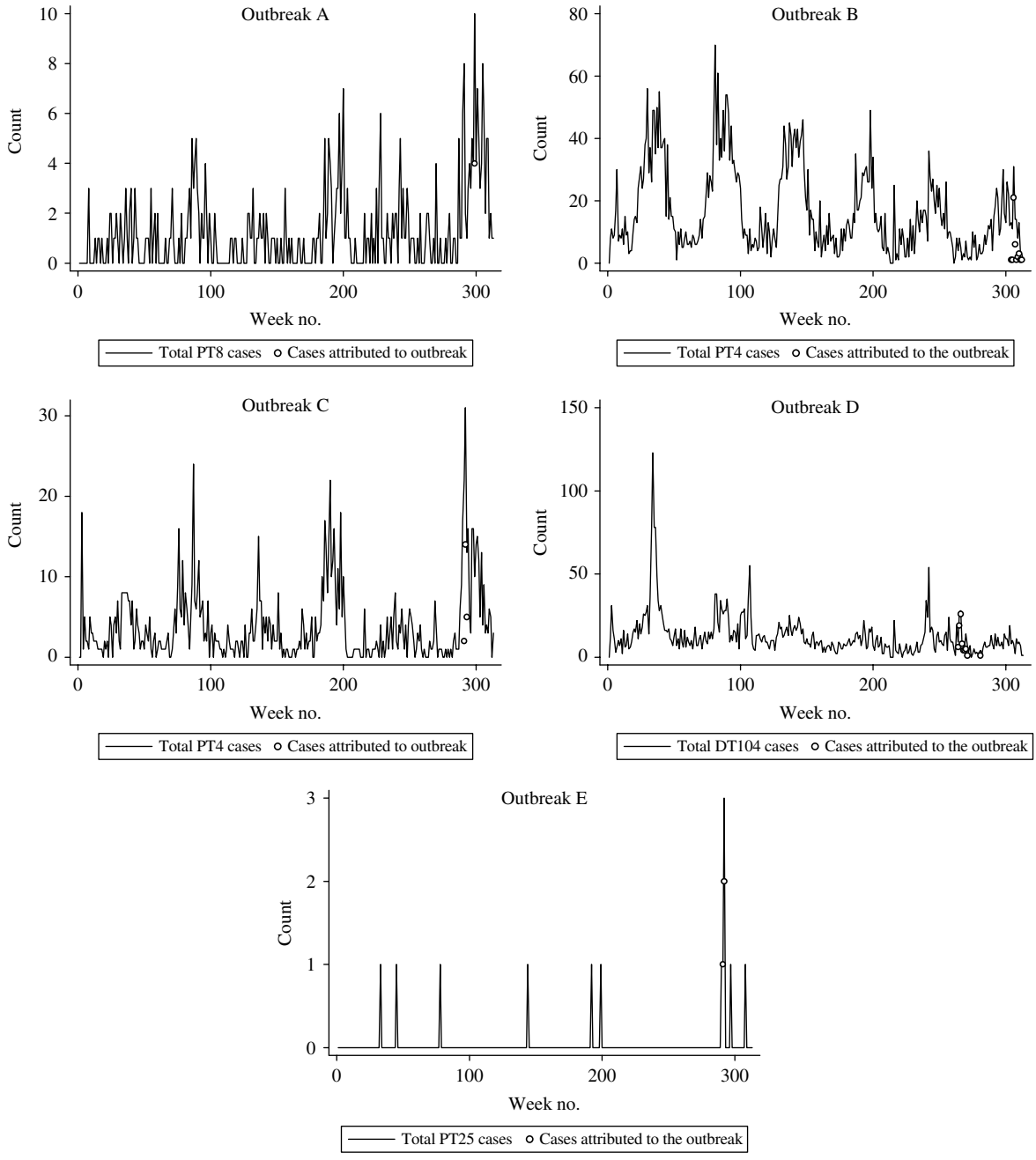


**Fig. 1.** Weekly counts by *Salmonella* phage-types from the beginning of the study up to and including each outbreak time-period.

the following week and 13 cases the week after. Of these, 4, 14 and 5 cases, respectively, were part of the outbreak whereas the rest were considered to be sporadic cases. Using the complete dataset for North East region for *S*. Enteritidis PT4, the count for each of these weeks exceeded the estimated threshold. This means that the exceedance reporting system currently operating detected the outbreak from week 1 and also flagged up each of the subsequent two weeks (Fig. 1).

### Outbreak D (large): *S.* Typhimurium definitive phage-type (DT) 104 national outbreak

An example of a large (national) outbreak of *S*. Typhimurium DT104 occurred between 18 January 2005 and 23 May 2005. A total 74 cases were identified as part of the outbreak and were all reported within 9 weeks. The total number of *S*. Typhimurium DT104 cases reported on a national level during the same time period was 111. The exceedance reporting system

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flagged up week 2 and also weeks 3 and 7 of the outbreak (Fig. 1).

### Outbreak E (small): *S.* Enteritidis PT25 outbreak in the South East region

Three cases were identified as part of an outbreak of *S.* Enteritidis PT25 in the South East region during 2 weeks between 21 June 2005 and 4 July 2005. The one case reported in the first week was not flagged as a potential outbreak by the exceedance reporting program in contrast to the two cases occurring in week 2 (Fig. 1).

### Strain subtyping

The serotypes chosen for investigation were serovars *S.* Enteritidis and *S.* Typhimurium. Isolates of these serotypes had been subdivided by phage-typing, using the schemes of Ward *et al.* for *S.* Enteritidis [9] and Anderson *et al.* for *S.* Typhimurium [10].

### Outbreak detection and simulations

The outbreak detection program was initially run on the full dataset for each serotype and the number of flagged weeks and the exceedance scores were recorded. A percentage of the isolates from all those between 2000 and 2005 were randomly selected and used to re-calculate the exceedance score. This was repeated between 10% and 90% in steps of 10% to mimic a reduction in samples of isolates phage-typed. The process was repeated 100 times at each reduction.

For the duration of each outbreak, the mean and the interquartile range for the exceedance score from the 100 simulations for each reduction were calculated as well as the proportion of simulations where the exceedance scores were $>1$.

The effect of not undertaking any phage-typing was examined by ignoring the phage-type information and attempting to detect the outbreak by simply using the serotype information. For example, for outbreak A the exceedance score was calculated using data for all cases of *S.* Enteritidis that included other types of phage-types apart from PT8.

## RESULTS

The percentage of isolates phage-typed and the exceedance scores including all phage-types and ignoring the phage-type information are given in Table 1. Although percentages of isolates phage-typed are presented ranging from 10% to 90%, a 60% level was chosen for the purpose of describing the results.

### Reduced number of isolates phage-typed

The reduction of phage-typing did not have a great effect on outbreaks A and B. For the week that outbreak A lasted, 81% of the simulations' exceedance scores were $>1$ when 60% of the isolates were phage-typed. For the same reduction of isolates phage-typed, 89% of the simulations of week 3 for outbreak B had an exceedance score of at least 1. The other weeks of outbreak B were never flagged up by the exceedance reporting system.

However, reduction of phage-typing greatly reduced the chance for outbreaks C and D to be detected and probably meant that outbreak E would have been missed altogether. For outbreak C, the first 2 weeks could still be 'detected' in 88% and 100% of the simulations, respectively, when there was a reduction in isolates phage-typed of 60%. However, for week 3, only 36% of the simulations exceeded 1 for 60% of the samples typed. For weeks 2 and 3 of outbreak D, the proportion of simulations flagged up were 95% and 100%, respectively, when phage-typing occurred on 60% of the samples. For week 7 this dropped to just 21%. For outbreak E, two cases were reported and detected by the exceedance reporting system for the week 2 of the outbreak. Only 4% simulations could be detected when 60% of the isolates were phage-typed (Table 1).

The mean exceedance scores and their corresponding interquartile ranges for the weeks the outbreaks were flagged up by the exceedance reporting system are shown in Figure 2.

### No phage-typing

When no phage-typing was performed the chance of missing outbreaks was greatly increased. Outbreaks A, C and D would still have been detected. However, outbreaks B and E would never have been flagged as their exceedance scores for all weeks were $<1$. Of the 9 weeks where the five outbreaks exceeded the threshold to be flagged, 5 weeks (56%) were not triggered when no phage-typing was performed (Table 1).

### Time to detection

The outbreaks were initially detected by the surveillance system (100% of isolates phage-typed) on weeks 1, 3, 1, 2 and 2 for outbreaks A, B, C, D and E,

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Table 1. *Percentage of simulated counts above the threshold for different percentages of isolates phage-typed for each week of the five* Salmonella *outbreaks in 2005 used as examples*

| | Week no. | Outbreak cases* | Total cases† | Percentage of isolates phage-typed | | | | | | | | | Exceedance score | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | | 10% | 20% | 30% | 40% | 50% | 60% | 70% | 80% | 90% | All PT sampled | No PT given |
| **Outbreak A** | 1 | 4 | 10 | 5% | 25% | 48% | 60% | 75% | 81% | 87% | 98% | 100% | 1·92 | 1·04 |
| *S.* Enteritidis PT8 | | | | | | | | | | | | | | |
| South East region | | | | | | | | | | | | | | |
| **Outbreak B** | 1 | 1 | 13 | No detection | | | | | | | | | −0·32 | 0·30 |
| *S.* Enteritidis PT4 | 2 | 1 | 11 | No detection | | | | | | | | | −0·27 | −0·49 |
| South East/South | 3 | 21 | 31 | 10% | 27% | 34% | 54% | 79% | 89% | 98% | 100% | 100% | 2·08 | 0·47 |
| West region | 4 | 6 | 14 | No detection | | | | | | | | | 0·43 | −0·31 |
| | 5 | 1 | 14 | No detection | | | | | | | | | 0·42 | 0·82 |
| | 6 | 2 | 8 | No detection | | | | | | | | | −0·08 | −1·09 |
| | 7 | 3 | 13 | No detection | | | | | | | | | 0·46 | −0·62 |
| | 8 | 1 | 3 | No detection | | | | | | | | | −0·48 | −0·15 |
| | 9 | 1 | 3 | No detection | | | | | | | | | −0·44 | −1·44 |
| **Outbreak C** | 1 | 2 | 22 | 29% | 42% | 68% | 77% | 84% | 88% | 90% | 98% | 100% | 2·68 | 3·77 |
| *S.* Enteritidis PT4 | 2 | 14 | 31 | 50% | 67% | 89% | 95% | 98% | 100% | 100% | 100% | 100% | 4·01 | 3·11 |
| North East region | 3 | 5 | 13 | 6% | 8% | 13% | 21% | 22% | 36% | 46% | 56% | 80% | 1·19 | 0·54 |
| **Outbreak D** | 1 | 6 | 9 | No detection | | | | | | | | | 0·45 | 0·64 |
| *S.* Typhimurium DT104 | 2 | 19 | 27 | 17% | 38% | 59% | 79% | 88% | 95% | 99% | 100% | 100% | 2·76 | 1·54 |
| National | 3 | 26 | 28 | 25% | 66% | 72% | 95% | 97% | 100% | 100% | 100% | 100% | 3·04 | 0·84 |
| | 4 | 8 | 9 | No detection | | | | | | | | | 0·60 | 1·15 |
| | 5 | 4 | 6 | No detection | | | | | | | | | 0·29 | −0·66 |
| | 6 | 4 | 7 | No detection | | | | | | | | | 0·32 | 0·14 |
| | 7 | 5 | 14 | 2% | 1% | 8% | 6% | 18% | 21% | 33% | 46% | 63% | 1·09 | 0·66 |
| | 8 | 1 | 7 | No detection | | | | | | | | | 0·11 | −0·52 |
| | 9 | 1 | 4 | No detection | | | | | | | | | 0·08 | −0·23 |
| **Outbreak E** | 1 | 1 | 1 | No detection | | | | | | | | | 0·00 | −0·02 |
| *S.* Enteritidis PT25 | 2 | 2 | 3 | 0% | 0% | 0% | 1% | 1% | 4% | 16% | 26% | 57% | 4·46 | 0·36 |
| South East region | | | | | | | | | | | | | | |

PT, Phage-type.
* Cases reported as part of the outbreak.
† Total number of cases for the specific phage and region.

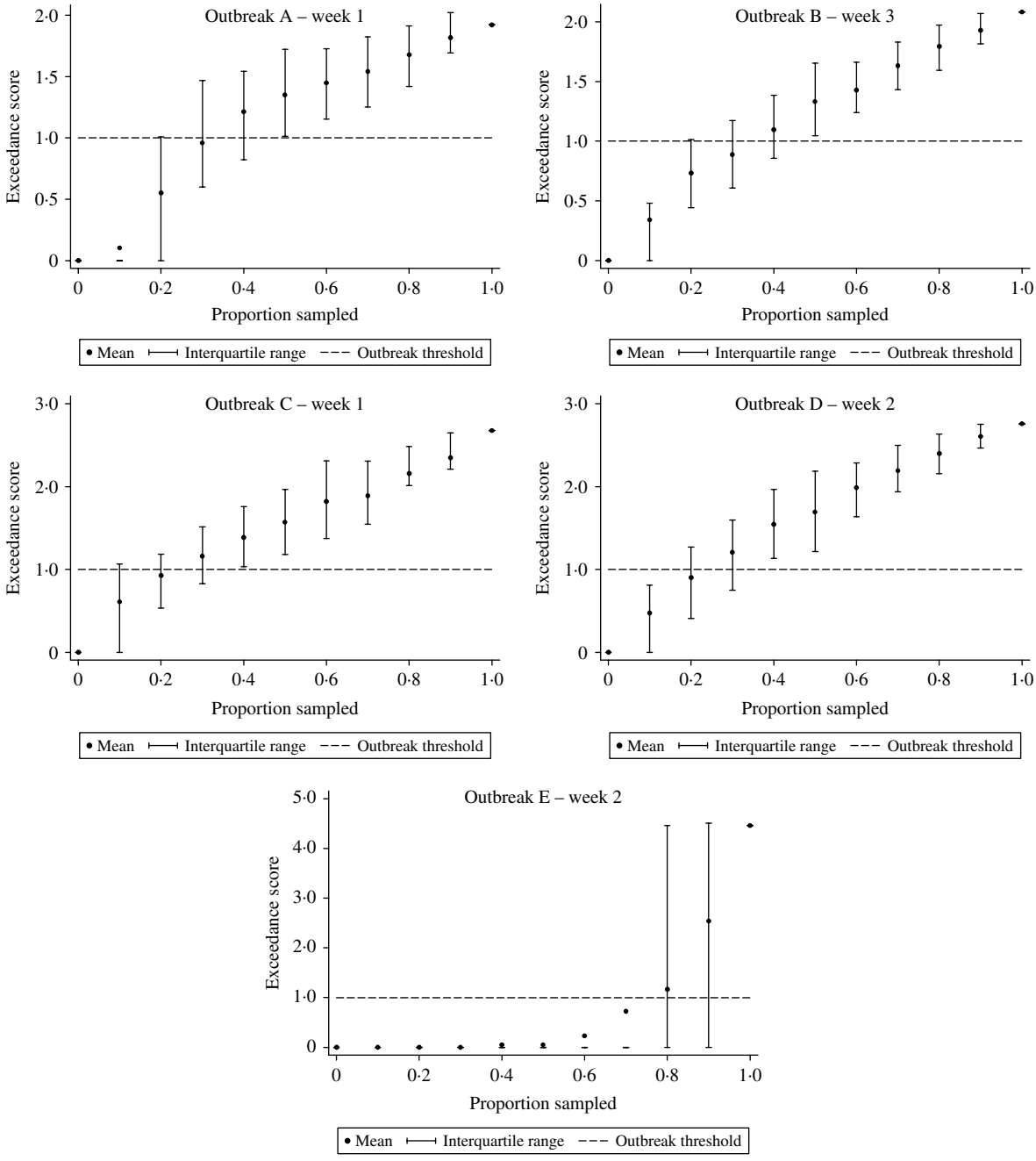


**Fig. 2.** Mean exceedance score and interquartile range for each outbreak at different percentages of isolates phage-typed following 100 simulations.

respectively. When the proportion of isolates phage-typed was 60%, the percentage of simulations with an exceedance score >1 was 81%, 89%, 88% and 95% for outbreaks A, B, C and D, whereas it was only 4% for outbreak E (Table 1).

## DISCUSSION

A small number of outbreaks of *S.* Enteritidis (four outbreaks) and *S.* Typhimurium (one outbreak), which occurred in England in 2005 were used to investigate the effect of reducing the number of referred isolates of *Salmonella* for phage-typing on the recognition of outbreaks. Reducing the number of isolates phage-typed would not have had an important effect on two of the five outbreaks examined, but would have had some effect on another two, and a small outbreak would be likely to be missed altogether.

The reason why reduced phage-typing or no phage-typing at all appears to affect the detection of some

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outbreaks more than others is connected with the characteristics of the outbreaks. The size and the spread of the cases is certainly a factor, i.e. plenty of cases occurring within the same week means that an outbreak is more likely to be flagged up. The exceedance reporting system is set up to detect acute national outbreaks but is also run separately for each of the nine regions. Apart from the characteristics of the outbreak, an important factor for the detection of outbreaks is how frequently cases of the specific serotype and phage-type have occurred in the past. If a serotype is uncommon then phage-typing may be redundant in the detection of the outbreak. For more common serotypes, rarer phage-type information is more important in detection of outbreaks. All of these factors play an important role in the detection of outbreaks as established by the current surveillance system in England and Wales, and it is a combination of these that determines the impact of phage-typing on outbreak detection.

When phage-typing information was ignored, two outbreaks would not have been detected by the system, whereas three outbreaks would have been detected. The outbreaks used as examples were of common serotypes (*S*. Enteritidis and *S*. Typhimurium). For rarer serotypes a lesser impact on outbreak detection would be expected.

The time taken for an outbreak to be detected is crucial to allow for formulation of timely intervention strategies to prevent further infections. The first week of the outbreaks detected by the exceedance reporting system could still be detected in four out of the five outbreaks examined when reducing the number of isolates phage-typed to 60%.

The results presented here can be used in combination with other information by policy makers to decide whether performing phage-typing is a worthwhile practice. Furthermore, it can be used to as a preliminary tool to assess the impact of more detailed typing methodologies such as the effect of an antibiogram of molecular profile. In general, providing more detailed information will improve detection, however, an optimization needs to be achieved balancing the extra cost and time spent for the additional tests against the benefits gained from more accurate outbreak detection.

The exceedance reporting system by its nature will be the slowest method of detection of outbreaks as it requires referral and typing to have been performed. While it is clear that reduced typing will have some impact on detection, it is possible that other decision-based approaches to detection will have already identified the problem.

## DECLARATION OF INTEREST

None.

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