Till receipts - a new approach for investigating outbreaks? Evaluation during a large *Salmonella* Enteritidis phage type 14b outbreak in a north west London takeaway restaurant, September 2009

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Selecting suitable controls for outbreak investigations is often difficult and if done inappropriately will lead to biased inferences. Till receipts and other sales records are frequently available on food premises, but their applicability has not been fully explored. Using data from an investigation into a *Salmonella* outbreak affecting 66 individuals exposed in a London takeaway restaurant, this study aimed to evaluate the use of till receipts to assess associations between sales and illness. Cases identified through local case-finding were subjected to a standardised exposure questionnaire. Till receipts over the time period when cases arose were analysed. Estimated food exposures from sales were compared to case reported exposures and till receipts analysis showed strong association between illness and consumption of rotisserie chicken (odds ratio (OR): 2.75; confidence interval (CI): 1.7–4.5). Chicken sales immediately prior to food consumption for cases were compared to two control periods in an ecological case-crossover design. On average there was an estimated increase of 3.7 (CI: 2.2–5.2) extra chickens sold in the hour immediately prior to the consumption in the cases ($p < 0.0001$) and the risk of becoming ill at busy times increased by 5% with each additional chicken quarter sold per hour (OR: 1.05; CI: 1.03–1.08). Microbiological and environmental investigations revealed *Salmonella* Enteritidis phage type (PT)14b in all available cases' stool samples, two environmental samples and leftover chicken from the takeaway. The feasibility of this novel approach to obtain exposure information in the population at risk has been demonstrated, and its limitations are discussed. Further validation is required, comparing results with those in a concurrent classic case-control study.

Introduction

This study is set in the context of a large outbreak in London of *Salmonella* Enteritidis phage type (PT)14b with antimicrobial resistance to nalidixic acid and reduced susceptibility to ciprofloxacin (SE PT14b NxCP). On 16 September 2009, three large London hospitals informed the North West London Health Protection Unit (NWLHPU) of a cluster of patients presenting with diarrhoea and vomiting. All cases had consumed products from a takeaway restaurant, up to 55 hours before becoming ill. The first person with enteric illness presented to the hospital on 9 September. Analysis of stool samples from the initial patients identified *S. Enteritidis* PT14b. Immediate public health measures were taken on the day of reporting and the takeaway shop voluntarily closed on 16 September.

Food poisoning outbreaks related to non-typhoidal *Salmonella* can result in high attack rates [1] and serious complications with associated excess morbidity and mortality amongst those affected [1–3]. The investigation of these outbreaks requires microbiological and epidemiological evidence to ensure appropriate control measures and inform public health action [4].

When a cohort cannot be precisely identified, case-control studies are the method of choice. The feasibility of this study design is determined by available resources and the ability to recruit suitable controls from the population at risk. Greater social mobility and the use of mobile phones make traditional methods of control selection through random digit phone dialling more difficult and less valid, introducing sizable selection bias [5]. Case-nominated controls risk 'overmatching' on the causal exposure, and use of population registers is often not possible, as they do not always identify the population at risk in the outbreak.

Box

Case definitions, outbreak of *Salmonella* Enteritidis phage type 14b related to a north west London takeaway restaurant, United Kingdom, September 2009

A probable case was defined as a person developing diarrhoea or any two or more of the following symptoms: vomiting, fever ($\geq 38^{\circ}\text{C}$) or abdominal pain within 72 hours of consumption of products from the implicated takeaway restaurant purchased between 6 and 16 September 2009.

A confirmed case was defined as a symptomatic person (see above) with a laboratory-confirmed isolate of *S. Enteritidis* phage type (PT)14b with resistance to nalidixic acid and with reduced susceptibility to ciprofloxacin from a blood or stool specimen.

Cases that travelled abroad in the seven days prior to symptom onset and cases with household contact to persons with diarrhoea or vomiting not associated with this outbreak were excluded.

Alternative study designs have been used, such as, case-crossover studies [6], case severity studies [1] and serotype case–case studies [5,7–9]. In addition, analyses-of-sales studies have been reported [10,11]. These were hypotheses-generating consumer record analyses [10], and a comparison of the probability of kebab consumption based on information from the kebab shop owner with exposure information from the cases [11]. However, many of these approaches are contextual and cannot be easily adapted for other outbreak situations.

Based on the initial report of this large cluster of cases with gastrointestinal illness with exposure to food from a north west London takeaway restaurant we sought to establish epidemiological and microbiological evidence for the source and vehicle of the outbreak. In addition, we explored the feasibility and validity of a new analytical approach, using till receipts from the restaurant to both estimate exposures in the population at risk, as well as sales volumes as an exposure in an ecological case-crossover approach.

Methods

Epidemiological investigation

The outbreak was described in time, person and place to generate hypotheses about the possible exposures and exposure mechanisms. Cases were defined as below (box). Following the initial notification, a case-finding exercise was conducted. This involved notification requests from local frontline clinicians (e.g. general practitioners, hospital doctors and microbiologists) for cases with an epidemiological link to the takeaway restaurant. Some reported cases also informed on known fellow diners that became ill. Additionally, national reference laboratory reports for all *S. Enteritidis* PT14b cases during an estimated period when cases may

have been reported (6–30 September) were scrutinised for their plasmid profile and potential exposures. All *Salmonella* reports to the local unit during this period as well as some before and after this period were reviewed for an epidemiological link to the implicated source.

All reported cases who fulfilled the definition of a probable or confirmed case ($n=66$) were interviewed using a standardised questionnaire on food consumption and other risk exposures, which was tailored to this outbreak (based, for example, on the restaurant menu). The questionnaire was administered via telephone, or in person. The prototype had been developed, piloted and tested for validity in other outbreaks prior to this incident. All cases were interviewed within a week of exposure. The data were entered into a secure database, cleaned and cross-checked for inconsistencies. These case exposure data were used for descriptive analysis as well as the two analytical approaches described below.

Microbiology

Stool samples were available for all cases fulfilling the confirmed case definition ($n=31$) and from three of the four food handlers who worked in the takeaway restaurant. The food handlers were asymptomatic but were sampled to ensure that they were not the current or a continued source of the outbreak. Samples were initially cultured for *Salmonella* spp., *Campylobacter* spp., *Escherichia coli* or *Shigella* spp. Positive stool samples for *Salmonella* spp. were sent to the National Salmonella Reference Laboratory, Health Protection Agency (now Public Health England) Centre for Infections, for phage typing [12] and plasmid profiling [13] and tested for resistance to a range of antimicrobials by a standard breakpoint method.

During the investigation by the environmental health team on 16 September, a range of food and environmental samples were obtained and submitted for testing. A total of 30 food samples were taken from the implicated takeaway restaurant, and all raw shell eggs ($n=72$) from the premises were tested for *Salmonella* spp. Twelve environmental samples at the premises as well as leftover food samples from the household of an affected individual were cultured and characterised as above.

Data analysis

All the takeaway restaurant sales during the period at risk of exposure were entered into a cash register machine – regardless of whether payment was by cash or card. This machine automatically registers time and date; the price and product specification were entered manually by staff at the restaurant. Complete till receipt print-outs for the entire period where customers could have been at risk of exposure from contaminated food at the shop (two days prior to the first case until shop closure, 7–16 September 2009, inclusive)

were manually entered in an Excel spreadsheet, cross-checked and cleaned, and used for further analysis.

Till receipts are used for tax purposes and therefore precisely record the sales. Recording was accurate for date, time and price, but in this outlet, 25% of sales were recorded as miscellaneous. Information from the till receipts was used to reconstruct the population at risk, and the exposures in this population at risk for the comparative analysis and to generate sale volumes over time for the ecological case-crossover design.

Method 1 – a comparative approach

A theoretical cohort defining the population at risk, buying food from the restaurant between 7 and 16 September was constructed using sales information from the till receipts and estimated daily customer numbers from the restaurant owner. This was to establish a baseline sales' pattern by estimating the number of persons through the quantity and combination of individual food items bought. Individual food portions consumed by the cohort were calculated from sales, making assumptions about portion sizes and dish combinations. In principle the sale of one main dish (e.g. chicken kebab) or half a rotisserie chicken was equivalent to one portion. Side dishes (e.g. chips), sauces and sundries were counted as individual portions, if they were sold in the absence of a main dish. A person was assumed to consume one main dish (irrespective of an accompanying sundry) or one or more side dishes (in

the absence of a main dish). It was assumed that joint food exposures in the cases were generalisable to the whole cohort. Miscellaneous food items were assumed to occur randomly by staff, person, and food product and have been excluded for the comparative analysis. The derived number of customers was compared with the information from the restaurant owner.

This data set with estimated numbers of individuals in the cohort consuming each food item was merged with the collected exposure information from the questionnaires administered to the cases. The theoretical exposures in the cohort were compared to the exposures in the cases providing estimated odds ratios and chi-squared tests of association. Each exposure was assessed only using single variable analysis. No multivariable analysis was attempted as the underlying assumptions preclude precise knowledge of joint exposure.

Method 2 – an ecological case-crossover analysis

The case-crossover design compares hypothesised risk exposures in the same individual in the interval before onset of illness to one or more intervals when the event does not occur [14]. It is particularly suitable for continuous common source outbreaks [15], where unbiased exposure information (e.g. a menu or purchase records) is available [6,15].

FIGURE 1

Epidemic curve obtained from investigating an outbreak of *Salmonella* Enteritidis phage type 14b related to a north west London takeaway restaurant, United Kingdom, September 2009 (n=66 cases^a)

^a Cases include probable or laboratory-confirmed cases.

TABLE 1

Results of the comparative till receipt analysis, outbreak of *Salmonella* Enteritidis phage type 14b related to a north west London takeaway restaurant, United Kingdom, September 2009

Menu items	Number of cases exposed ^a (percent of 66 total cases) n (%)	Number of portions consumed ^b (percent ^c of the total theoretical cohort of 2,390 exposed)	Odds ratio (95% Confidence interval)	P-value
Rotisserie chicken	41 (62.1)	894 (37.4)	2.75 (1.67–4.52)	<0.0001
Chips	32 (48.5)	508 (21.3)	3.52 (2.16–5.74)	<0.0001
Nan	20 (30.3)	269 (11.3)	3.43 (2.01–5.85)	<0.0001
Doner kebab	16 (24.2)	203 (8.5)	3.45 (1.94–6.13)	<0.0001
Pita	10 (15.2)	299 (12.5)	1.25 (0.64–2.45)	0.522
Chicken doner	8 (12.1)	157 (6.6)	1.96 (0.94–4.12)	0.075
Chicken shish	4 (6.1)	4 (0.2)	51.35 (12.57–209.57)	<0.0001
Mixed kebab	3 (4.6)	9 (0.4)	12.6 (3.61–44.26)	<0.0001
Cheese	3 (4.6)	90 (3.8)	1.22 (0.4–3.73)	0.743
Rice	3 (4.6)	20 (0.8)	5.65 (1.75–18.32)	0.002
Chicken tikka	1 (1.5)	20 (0.8)	1.82 (0–10.88)	0.555
Seekh kebab	1 (1.5)	99 (4.1)	0.36 (0–2.06)	0.287
Shahi special	0 (0.0)	6 (0.3)	0 (0–23.46)	0.684
Paratha	0 (0.0)	14 (0.6)	0 (0–9.98)	0.533

The table is ordered by number of cases explainable by respective exposures (i.e. the numbers of cases who reported the particular exposure, column 1).

^a Based on observed data from the case questionnaires.

^b The sum of portions in this column exceeds the total number in the theoretical cohort (n=2,390) based on the till receipt data, as persons may choose more than one dish. The numbers of portions are calculated for the outbreak period from 7 to 16 September 2009.

^c These are estimated exposures in the theoretical cohort using till receipt data and assuming that joint food exposures in the cases were generalisable to the whole cohort.

This analysis was performed to assess the a priori hypotheses that rotisserie chicken was the causal food source. This hypothesis was developed from customer complaint information, site visits, descriptive analysis and microbiological findings in a left-over piece of rotisserie chicken.

The ecological case-crossover design utilises the complete time series during the study period of sale volumes of rotisserie chicken, whereby the volume of sales in a time interval of one hour before the time of consumption as declared by the case (exposure interval), is compared to the sale volumes in the same hour in the preceding and following day (control intervals). The difference in sales volumes between the exposure interval and the mean of the control intervals was assessed using a paired t-test.

In addition, a conditional logistic regression analysis was used to estimate the risk of illness per additional quarter chicken sold per hour.

All data were entered in EpiData 3.1 and statistical analysis was carried out using STATA SE 11.

Results

Descriptive epidemiology

We identified 72 epidemiologically-linked cases with enteric illness in total, however three of these did not fulfill the clinical case definition and for a further three, not enough information was available to determine

whether they fulfilled the clinical case definition. The remaining 66 cases of enteric illness therefore fulfilled the definition for probable or confirmed cases. Thirty-five of the cases (53%) became ill on a single day (Figure 1). Most cases were male (41, 62%), and under 40 years of age (56, 85%). The mean age was 28 years (median: 26; range: 4–72). The majority of cases (42, 64%) resided near the takeaway restaurant.

The median incubation period was 16 hours (mean: 17; range: 2–55). In addition to diarrhoea, symptoms included abdominal pain (65, 98%), fever (61, 92%), headache (50/64, 78%), vomiting (46, 70%), bloody diarrhoea (10/63, 16%) and myalgia (13/64, 20%). Twenty-two cases (33%) were admitted to hospital with a median stay of four days (range: 1–7 days). None of these required admission to an intensive care unit.

Microbiology

Stool samples were available for 31 of the 66 cases; in all of them *S. Enteritidis* PT14b was isolated. Plasmid profiling was performed for seven of these isolates, and the profile was indistinguishable amongst them, but distinguishable by an additional 4 kb plasmid from profiles identified in other concurrent *S. Enteritidis* PT14b outbreaks in England and Wales.

All stool samples obtained from food handling staff at the venue (n=3) were negative for *Salmonella*. A food sample taken from a cooked leftover rotisserie chicken kept in the refrigerator of one of the cases and purchased at the implicated takeaway restaurant was

TABLE 2

Results of the case-crossover analysis, outbreak of *Salmonella* Enteritidis phage type 14b related to a north west London takeaway restaurant, United Kingdom, September 2009

	Quarters of chicken sold	95% Confidence interval	P-value
Non-exposed times	19.75	17.67–21.83	–
Exposed times	34.59	27.07–42.11	–
Difference	14.84	8.71–20.97	<0.0001 ^a
	Odds Ratio	95% Confidence interval	P-value
Risk of exposure ^b	1.05	1.03–1.08	<0.0001

^a Differences between chicken sales in exposed and non-exposed times were compared with t tests.

^b The lower part shows the result of the conditional logistic regression model estimating the risk of illness per chicken quarter sold per hour.

positive for *S. Enteritidis* PT14b. Environmental swabs taken from the floor of the refrigerator in the food preparation area and from a light switch in the staff toilet were positive for *S. Enteritidis* PT14b. The plasmid profile of the food sample and the environmental samples was indistinguishable from the organism isolated from the stools and the antimicrobial resistance profile was identical in all tested samples. All other samples including 12 environmental, 30 food samples and 72 egg shells from the implicated takeaway were negative for *Salmonella*.

The inspection by the environmental health team raised concerns about food preparation processes, such as the proximity of raw and cooked foods. In addition, an insufficient recording of temperature control, particularly for refrigeration and the rotisserie operation was noted.

Epidemiological analysis

Comparative analysis

Individual portions were estimated from the number of sales. An estimated 2,390 portions were sold during the ten days of the study period (7–16 September), a mean of 239 portions per day (range: 129–287). This broadly agreed with information from the owner, who estimated around 200 customers per day. 25% of all sales were coded miscellaneous.

Table 1 provides an overview of the comparison between exposure information from the cases and estimated exposure in the theoretical cohort from the sales data, ordered by the number of explainable cases through the respective exposure. There was a significant association between consumption of rotisserie chicken and becoming a case in this analysis (odds ratio (OR): 2.75; confidence interval (CI): 1.67–4.52). Although similar or larger effect sizes were observed with other food items, consumption of rotisserie chicken can explain the majority of cases. It is possible that cross-contamination might explain some of these observations of large effect sizes, but which were affecting only few people.

Ecological case-crossover analysis

The times and volumes of rotisserie chicken sales corresponded well with the exposure times of cases (Figure 2), and based on this we formally analysed the correlation between rotisserie chicken sales and illness periods. On average, 34.59 quarters of chicken corresponding to 8.6 chickens (CI: 6.8–10.5) were sold in the hour before the cases had consumed food from the takeaway. This compares with an average of 19.75 quarters, or 4.9 chickens (CI: 4.4–5.5) sales, in the two reference periods. The difference of 14.89 quarters, i.e. 3.7 chickens (CI: 2.2–5.2) is significantly different from zero ($p < 0.0001$) (Table 2). The clustering of cases around the highest sales peaks, particularly on 10 September is shown in Figure 2.

The conditional logistic regression analysis found that the odds of becoming ill increases by 5% with each additional chicken quarter sold per hour (OR: 1.05; CI: 1.03–1.08). A locally weighted scatter plot smoothing (lowess) graph shows that the risk of becoming a case increases linearly, once a threshold of sales of 20 to 24 chicken quarters – i.e. about five to six chicken – per hour (stable 25% background risk) has been exceeded (Figure 3).

Figure 3. Lowess smoother graph denoting the risk of becoming a case per number of chicken quarters sold in the hour before exposure, outbreak of *Salmonella* Enteritidis phage type 14b related to a north west London takeaway restaurant, United Kingdom, September 2009

Discussion

We present the results of the investigation into a large outbreak associated with a north west London takeaway restaurant, using till receipts as a feasible, new analytical approach to validate the hypothesised causal exposure in this outbreak. While acknowledging the limitations of sales data, our analyses of till receipts provided epidemiological evidence of an association between the consumption of rotisserie chicken and developing a gastrointestinal illness. These findings were supported by microbiological and environmental

FIGURE 2

Descriptive plot of the relationship between quantity of chicken quarters sold and number of cases, outbreak of *Salmonella* Enteritidis phage type 14b related to a north west London takeaway restaurant, United Kingdom, 7–16 September 2009

The lines and left y axis denote the number of quarters of rotisserie chicken sold per time (5 minute intervals) and the red dots and right y axis denote the number of cases who were exposed to food from the takeaway restaurant at these times. The figure illustrates that most cases (red dots) occurred shortly after sales peaks.

findings. The ecological case-crossover study demonstrated that a linear relationship between chicken sales and risk of becoming a case occurred as soon as sales exceeded a certain amount. This may indicate that sales pressures led to substandard food handling practices, such as undercooking meat and cross-contamination. It was observed by some cases that raw chickens were being placed above roasted ones in the rotisserie and therefore potential cross-contamination through drippings could have occurred. Prior to serving, the chicken quarters were seared again on a hot

grill before serving, in a rushed period this process may be inadequate, which may have caused the outbreak. This is useful information to change practices so as to prevent future outbreaks, reinforcing the need for scrupulous food hygiene practices at times of high demand.

Few published studies report the use of sales data in outbreak investigations. One of the reasons for this could be that access to sales data is not always granted to investigators, and our study benefits from the voluntary provision of complete till receipts by the restaurant owner. Supermarket bonus cards provide data on grocery shopping habits and have been used to generate hypotheses to inform subsequent analytical studies [10,16]. Purchase records from supermarkets have also been used in a virtual cohort approach [17]. The latter approach has some similarities to our study. Product purchase does not infer consumption, and in this study the unit of analysis was a group of people, which included a primary case (case-purchasing unit) [17].

Bonus card data allow identification of cases within a cohort, yield demographic information and thus allow combination with traditional methodologies. However, the use of bonus card schemes to investigate outbreaks is setting-specific, and limited by their popularity, representativeness and local data-sharing arrangements. The best approximation of this data type for a small caterer was the use of till receipts, which contrary to bonus cards contained all sales during the period at risk.

Synnott et al. calculated the probability that frequencies of observed case kebab consumption were within the expected range of owner-reported sales frequencies in support of their case-control investigation in a small kebab shop outbreak [11]. The analysis was carried out on a single food item, which all cases had been exposed to. In contrast, our study used a comparative approach for all possible exposures in the cohort, providing the exposures in the population at risk.

Our study benefits from extensive case-finding and good quality case exposure information acquired by applying a standardised exposure questionnaire in a standardised way. Till receipts contain readily available data, which are cheap, quick, accessible, and of good quality. Because till receipts are used for taxation purposes, data on price, date and time and food item (where entered) are likely to be accurate and unbiased. However, similar to other outbreak investigations, there remains potential for recall bias arising from the food exposure enquiry of the cases.

The main limitation of using till receipt data stems from the fact that sales data is not direct exposure/consumption data, and that sales data do not allow an accurate calculation of a denominator. This is particularly relevant for the calculation of food exposures in

FIGURE 3

Lowess smoother graph denoting the risk of becoming a case per number of chicken quarters sold in the hour before exposure, outbreak of *Salmonella* Enteritidis phage type 14b related to a north west London takeaway restaurant, United Kingdom, September 2009

The figure demonstrates that the risk of becoming a case was correlated with increasing rotisserie chicken sales in the hour before.

the cohort of takeaway restaurant customers for direct comparison. Assumptions on portion sizes and dish combinations were wide ranging, and sales descriptions were not available for 25% of the sales (miscellaneous category). Future studies using this approach may wish to include 'sensitivity' analyses and vary the underlying assumptions. No information on illness or demography of all the customers was available and cases were included within the cohort. A further limitation is the inability to provide 'adjusted' associations to account for potential confounders due to lack of knowledge of the joint food exposures of the total cohort. It is possible to extrapolate from the joint food exposures in the cases and in the situation here, where the outbreak is likely to have a single causal exposure, the assumption that joint food exposures in the cases are generalisable to the whole cohort is realistic.

The case-crossover study is less vulnerable to these assumptions, and using exposures occurring

immediately prior to when an individual case consumed food, and as this is compared to exposures at the same time of day, they act as their own controls, minimising the potential for selection bias [14,15]. Confounding by subject characteristics is controlled by design [15]. Information bias were largely avoided by use of purchase information [6], but there is a possibility that chicken sales were misclassified as 'miscellaneous' at busy times, although we were able to identify and recode a number of these on the basis of their typical price. While this would not change the direction of observed associations it could have led to an underestimate of the presented effect size.

However; this approach is more complex in terms of exposure data, potentially limiting the number of exposures that can be analysed. An a priori hypothesis is always required before commencing an analytical study, and is crucial in a case-crossover study. Results can be biased if control periods are not representative

of the expected distribution of exposure for follow-up times that do not result in a case [6,14]. The latter is usually unknown, but it is unlikely that the exposure changed systematically during the risk time [6] (same chicken batch) and we minimised this potential by taking the mean of two control periods.

In conclusion we demonstrated that the use of till receipt data for analytical outbreak investigation was feasible and provided additional evidence of an association between the consumption of rotisserie chicken purchased in a specific London takeaway restaurant and subsequent development of gastrointestinal illness. Our approach will need validation and refinement; however, understanding its limitations, the use of till receipt data provides additional information in outbreaks investigated with traditional methods, and is a practical approach to estimate exposures in outbreak investigations, where classical study designs are not feasible due to practical difficulties.

Conflict of interest

None declared.

Authors' contributions

DZ, JZ, WM and YC initially investigated the outbreak, DZ wrote the manuscript, AC and DZ developed the statistical analysis with contributions of JZ, WM, CL and YC. YC is the sponsor and all authors have seen and extensively commented on the manuscript.

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