Risk factors for winter outbreak of acute diarrhoea in France: case-control study

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The earth may move, but let’s keep our feet on the ground
Matthew Hotopf, Simon Wessely

Havelock Ellis, the Edwardian Dr Ruth, was concerned with what he called “the problem of sexual abstinence.” Abstinence was, he claimed, responsible for neurasthenia, spinal irritation, hysteria, hypochondriasis, myalgia, and anorexia. This led him to ask a surprising question: would it be right for a physician to “prescribe” sex, even out of wedlock? He answered this question with a firm “no,” the justification of which reads like modern evidence based medicine: “In giving such a prescription the physician has in fact not the slightest knowledge of what he may be prescribing. He may be giving his patient a venereal disease [or] an illegitimate child, the prescriber is quite in the dark.”

Meanwhile non-epidemiologists will dismiss or endorse Davey Smith and colleagues’ study according to their own prejudice. “Epi-sceptics” will doubt the association with an argument akin to “I don’t care what the evidence shows, my grandfather smoked until he was 98 and it never did him any harm.” In contrast, “epi-enthusiasts” will greet it as a justification for their habits along similar lines to the drinker’s justification: “It has been scientifically proved that drinking half a bottle of wine every day makes you live longer.” As you read this, we confidently predict that “Sex makes you live longer” will occupy more newspaper inches over the holiday period than the Queen’s speech. The public will hear what they want to hear, and they will be deaf to the problems of bias, confounding, reverse causality, or chance, the quartet of spoilsport alternatives epidemiologists use to judge each others’ associations.

This paper is especially susceptible to confounding and reverse causality. Confounding occurs when a risk factor which independently causes the outcome is associated with the exposure under study. In this case age is a good example: the less sexually active subjects were also older. The authors ignore some of the traditional confounders (physical activity and alcohol) and also fail to address psychological confounders—for example, depressed mood and “vital exhaustion.” Both of these may be risk factors for early death, and they are certainly predictors of reduced sexual activity. Reverse causality occurs when the “exposure” is really an early sign of the outcome. Early heart disease is likely to lead to reduced sexual activity and death. Sexual activity is downstream in the direction of causality from disease. Although the authors claim to have accounted for coronary heart disease by using baseline reporting of chest pain, this is a blunt instrument. It would not take many cases of early undetected heart disease to give the results reported here.

Thus we salute an elegantly written analysis that for once deals with activities and outcomes close to all our hearts. We suspect that in the longer run Davey Smith and colleagues have not provided evidence to satisfy Havelock Ellis, but instead they may have provided an excellent worked example for students of evidence based medicine to grapple with the issue of confounding. We would also draw attention to an important failing. The authors begin with a literary guide to adolescent angst. We feel that their omission of Holden Caulfield and, most particularly, Alex Portnoy, would have given both these characters something to complain about.

Risk factors for winter outbreak of acute diarrhoea in France: case-control study
Laurent Letrilliart, Jean-Claude Desenclos, Antoine Flahault

Abstract

Objectives: To assess the potential role of consumption of shellfish (particularly raw oysters) and tap water in the winter epidemic of acute diarrhoea in France.

Design: Population based, case-control study during the 1995-6 winter epidemic of acute diarrhoea in France.

Setting: A national network comprising 1% of general practitioners in France.

Subjects: 568 pairs of cases and controls consulting in general practice and interviewed by 209 doctors from 26 December 1995 to 31 January 1996. Cases and controls were matched for age, doctor, and time of consultation.

Main outcome measures: Adjusted relative risk of diarrhoea estimated from conditional logistic regression.

Results: The risk of acute diarrhoea was not increased in people who had recently eaten raw oysters (odds ratio 1.1; 95% confidence interval 0.9% to 1.4%) or other shellfish such as clams, cockles, and mussels, or in those people who usually consumed tap rather than bottled water (0.8; 0.6% to 1.1%). The risk was, however, increased in people who had had recent contact with a person with diarrhoea, either within the household (adjusted odds ratio 5.0) or in the workplace (3.1), and in people who lived with a child ≤2 years of age (1.6). Recent treatment with either oral penicillin or cephalosporin was also independently associated with acute diarrhoea in winter.

Conclusions: The winter epidemic of acute diarrhoea in France is probably not caused by consumption of either shellfish or tap water. A viral aetiology, however, is suggested by the speed with which the acute diarrhoea is transmitted.
Do shellfish cause the winter outbreaks of diarrhoea in France?

Introduction

In developed countries acute diarrhoea is a major cause of morbidity and medical expense. Each year in the United States about 99 million people experience acute diarrhoea or vomiting, of whom 8.2 million seek medical help (0.036 per person year). According to data from France’s electronic surveillance of communicable disease, about 3.3 million people in France consulted a doctor in 1995 for acute diarrhoea, totalling 0.057 consultations per person year.

In France large outbreaks of acute diarrhoea begin regularly at the end of December or early in January (fig 1). During the epidemic of January 1996 we estimated that about 670 000 people had consulted a doctor for acute diarrhoea throughout continental France.

The consumption of shellfish has been implicated in the winter outbreaks of acute diarrhoea in France because of the increased consumption of shellfish, particularly raw oysters, between Christmas and the New Year; the annual peak of diarrhoea occurs just after 1 January, when shellfish is consumed on a large scale. Another theory is that drinking water becomes contaminated by pathogens and toxic agents that have been washed into the public water supply during flooding. Although one adverse effect of antibiotics is acute diarrhoea, the role of antibiotics in morbidity has yet to be ascertained.

Little is known about the risk factors for acute diarrhoea in Europe, particularly during winter outbreaks. We therefore conducted a case-control study among doctors in France during the winter of 1995-6 to identify the predominant modes of transmission and risk factors for the winter outbreak of acute diarrhoea.

Patients and methods

About 1% of general practitioners participate in the French communicable disease surveillance scheme called Sentinelle; our population based, case-control study was of the patients of these doctors. Our doctors took part in the study on a voluntary and unpaid basis, as they do for the surveillance scheme.

Cases

Cases were patients who had consulted one of the doctors in the Sentinelle scheme for acute diarrhoea—that is, had had loose stools for < 15 days—during the winter outbreak of acute diarrhoea from 26 December 1995 to 31 January 1996. Each doctor was asked to include the first three of their patients who had either presented to the surgery or required a home visit for acute diarrhoea.

Controls

Controls were matched to cases of acute diarrhoea for age (0-4 years, 5-14, 15-59, and ≥ 60), doctor, and time of consultation (within two days). The first patient to meet these criteria was included as a control by the doctor. Patients who reported gastrointestinal symptoms over the past three months were not eligible for inclusion in the study.

Data collection

The doctors were asked to collect data on cases and controls during the consultation; the parent or guardian was consulted if the patient was < 12 years of age. Data included demographic characteristics (age, sex, and whether the patient resided in a rural or urban area); attendance at a nursery, school, retirement home, or other; the presence of a child ≤ 2 years of age at home; consumption of raw shellfish within 10 days before consultation (oysters, clams, cockles, and mussels); if patients had consumed cockles and mussels they were asked whether they had eaten them raw or cooked; consumption of tap water (always or often compared with sometimes or never); and type of oral antibiotic treatment, including trade name of drug, during the month before consultation. Antibiotics were subsequently classed into four groups: penicillins, cephalosporins, macrolids, and combined other families. Transmission from person to person was ascertained by asking the patient whether they had had any contact with a person with diarrhoea within the previous 10 days and, if so, whether this had occurred in the household, workplace, or a confined setting such as a nursery, school, retirement home, or other. Information was also obtained on the date of onset of diarrhoea in the contact; only this date was recorded because repeat contacts may have occurred. From the date of the onset of diarrhoea in the contact we estimated a surrogate variable for the incubation time.
as the time lag between the onset of diarrhoea in the case minus that in the contact—from these data we could approximate the median incubation time for the diarrhoea.

At the time of the study 299 of the 438 doctors who participated in the Sentinelle scheme took part in the case-control study; data included 588 cases and 568 controls, constituting 568 matched pairs.

Statistical analysis
Data were stored in a database (version 7, Oracle, Redwood City, CA). Statistical analysis was performed on sas software (version 6, sas Institute, Cary, NC). Matched odds ratios and their 95% confidence intervals were used to estimate relative risks in univariate analyses. Conditional logistic regression* was then used to assess the independent contribution of risk factors for acute diarrhoea identified in univariate analyses: all variables with P < 0.20 in univariate analyses were introduced in the initial multivariate model and deleted through a backward procedure; variables with a significance level of 0.05 (two tailed formulation) were kept in the final model.

Results

Demography—Cases and controls did not differ by sex and place of residence but controls were on average 2.1 years older than their matched case (SE 0.41 years) and were on average included into the study 1.1 days after the matched case. Controls were more likely than the cases to attend their general practitioner’s surgery: 454 out of 562 (81%) v 331 out of 565 (59%).

Consumption of shellfish and tap water—The risk of acute diarrhoea was not increased among people who had consumed shellfish (raw or cooked) in the 10 days before the onset of acute diarrhoea (table 1); even when there was an increase in consumption of shellfish we did not find a higher risk of acute diarrhoea. Usual consumption of tap water was not associated with acute diarrhoea (table 1).

Confined setting—Acute diarrhoea was not associated with being in a confined setting such as a nursery, school, or retirement home (table 1). The presence of a child ≤2 years of age in the household was, however, associated with an almost twofold increased risk of acute diarrhoea (1.9; 1.3 to 2.7). Patients who had recently been in contact with a person with diarrhoea were 4.3 times more likely to develop acute diarrhoea (3.1 to 6.0). The risk of acute diarrhoea was greatest after exposure to a person with diarrhoea in the household (5.0; 3.4 to 7.3). The distribution of the time interval between the date of onset of diarrhoea in exposed cases and the date of onset of diarrhoea in a contact (reported by 181 of the 241 cases exposed to a person with diarrhoea) ranged from 0 to 18 days, with a median time of 2.0 days (fig 2).

Antibiotics—Treatment with antibiotics was associated with acute diarrhoea in the month before consultation (1.7; 1.1 to 2.4). An increased risk of acute diarrhoea was associated with penicillins (1.6; 1.0 to 2.6) and cephalosporins (1.8; 0.9 to 3.8) (table 1).

Multivariate analysis—The consumption of clams and tap water, attendance at a retirement home, the presence of a child ≤2 years of age at home, contact with a person with diarrhoea (dummy variables for household contact, contact in the workplace, and contact elsewhere), and treatment with penicillins, cephalosporins, and macrolids were introduced in the initial multivariate model. In the final model, contact with a
Discussion

The large size of the samples in our study (568 pairs of cases and controls) implies that the consumption of shellfish was not important in the winter epidemics of acute diarrhoea in France from 26 December 1995 to 31 January 1996. Although an epidemic of acute diarrhoea due to the consumption of raw oysters was described in a coastal area in France during the last week of 1992, the statistical power of our study in detecting any effect of eating raw oysters was estimated after the study as 90% (for a minimal relative risk of 1.5). This rules out the consumption of raw oysters as a cause of the national epidemic in 1996. Even after stratification for coastal areas, our results remained quite similar (data not shown). Neither consumption of shellfish nor consumption of tap water was associated with acute diarrhoea. Exposure to a contact with diarrhoea within the past 10 days, particularly within a household, was identified as the main risk factor for acute diarrhoea. The median incubation time for acute diarrhoea was estimated to be two days. Living with a child ≤2 years of age without knowing that he or she had diarrhoea (adjusted odds ratio 1.6) and exposure to antibiotics within the month before consultation (odds ratio 1.7) were associated with the occurrence of acute diarrhoea; penicillins and cephalosporins were identified as independent risk factors, with adjusted odds ratios of 1.9 and 2.5. In both univariate and multivariate analyses the recent intake of macrolids was not associated with the occurrence of acute diarrhoea.

Although studies have shown a risk of acute diarrhoea within confined environments such as nurseries, schools, and retirement homes, this was not the case in this study. There may be a selection bias with attendance at nursery and school as children with diarrhoea are more likely to stay at home.

Validity of study

The difference observed between cases and controls in the place of consultation may indicate a selection bias for the controls. This should not, however, have had much of an impact on the other results as the place of consultation is related more to the state of the patient than to the cause of his or her disease. In fact, cases are more likely to request a home visit because of their acute condition compared with controls who may have less impairment. The presence of a child of ≤2 years of age in the household made no difference as to whether the controls were seen by their doctor at home or if they went to the surgery.

Of the cases included in the study, 92% met the criteria of the World Health Organisation for acute diarrhoea—that is, three or more stools passed for at least 24 hours.† For controls the observed rate of consumption of tap water (66.4%) was consistent with that estimated from a representative sample of the population in early 1995 (64.4%).†

Most cases of acute diarrhoea are likely to be caused by infection.‡ Given that stool cultures were not requested in this study, we could not identify the causal agent.

A French phenomenon?

Although, both in the United Kingdom and in the United States,§ more people are admitted to hospital for diarrhoea during the winter than at other times of the year, no definite seasonal pattern is reported from these countries for morbidity in the general population.

Antibiotic intake

Diarrhoea is a common side effect of treatment with antibiotics and has been reported in up to 20% of people taking antibiotics.¶ The main antibiotics implicated in diarrhoea are ampicillins, amoxicillins, cephalosporins, and lincosamids.‖‡ Our results confirm the risk of acute diarrhoea related to penicillins (including ampicillins and amoxicillins) and to cephalosporins but not to macrolids. We could not evaluate the role of lincosamids in the occurrence of acute diarrhoea—for example, clindamycin is well recognised in diarrhoea caused by Clostridium difficile.© In addition, lincosamids are rarely prescribed by general practitioners in France, so this antibiotic family was not reported for any case or control.

Conclusions

Our results indicate that the winter outbreaks of acute diarrhoea in France are caused primarily by a person coming into contact with someone with diarrhoea, implying a viral aetiology, and not by the consumption of shellfish or tap water.

Table 2 Association of risk factors with acute diarrhoea in conditional logistic regression model

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Adjusted odds ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contact with person with diarrhoea:</td>
<td></td>
</tr>
<tr>
<td>No contact</td>
<td>1.0</td>
</tr>
<tr>
<td>In household</td>
<td>5.0 (3.4 to 7.3)</td>
</tr>
<tr>
<td>In workplace</td>
<td>3.1 (1.6 to 6.3)</td>
</tr>
<tr>
<td>Other*</td>
<td>2.7 (1.2 to 5.8)</td>
</tr>
<tr>
<td>Child ≤2 years of age at home</td>
<td>1.6 (1.1 to 2.4)</td>
</tr>
<tr>
<td>Oral penicillins</td>
<td>1.9 (1.1 to 3.3)</td>
</tr>
<tr>
<td>Oral cephalosporins</td>
<td>2.5 (1.1 to 5.9)</td>
</tr>
</tbody>
</table>

* Includes contacts in retirement home, school, and other setting.

Key messages

- Acute diarrhoea has a strong seasonal pattern in France with a large outbreak starting regularly at the beginning of January and lasting about four to six weeks.
- The results of this case-control study ruled out the consumption of shellfish and tap water as causes of the winter outbreak of acute diarrhoea in France.
- β-Lactam antibiotics, including penicillins and cephalosporins, were associated with the outbreak.
- The speed with which acute diarrhoea is transmitted is compatible with a viral aetiology.
death rates of characters in soap operas in british television: is a government health warning required?

Tim Crayford, Richard Hooper, Sarah Evans

Abstract

Objective: To measure mortality among characters in British soap operas on television. Design: Cohort analysis of deaths in EastEnders and Coronation Street, supplemented by an analysis of deaths in Brookside and Emmerdale. Main outcome measures: Standardised mortality ratios and the proportional mortality ratio for deaths attributable to external causes (E code of ICD-9) (international classification of diseases, ninth revision). Results: Staying alive in a television soap opera is not easy. Standardised mortality ratios for characters were among the highest for any occupation yet described (771 (95% confidence interval 415 to 1127) for characters in EastEnders), and this was not just because all causes of death were overrepresented. Deaths in soap operas were almost three times more likely to be from violent causes than would be expected from a character's age and sex. A character in EastEnders was twice as likely as a similar character in Coronation Street to die during an episode. Conclusions: The most dangerous job in the United Kingdom is not, as expected, bomb disposal expert, steeplejack, or Formula One racing driver but having a role in one of the United Kingdom's most well known soap operas. This is the first quantitative estimate of the size of the pinch of salt which should be taken when watching soap operas.

Introduction

Death is a fact of life in soap opera. It is only natural that producers should exaggerate the danger of real life to make series interesting, but by how much do they do this? What sorts of occupations would be as dangerous as being a character in a soap opera? Could Brookside Close be the most dangerous street in Britain? We set out to answer these questions in a hard hitting analysis of mortality in British television soap operas. British soap opera has been a mirror to many contemporary social themes over the past 15 years, dealing with topics ranging from HIV and breast cancer to theft, mugging, and murder. This fact and the huge audiences that each programme draws each week has helped make soap opera one of the many ways by which people now normalise their own lives. In this respect, soap operas presumably contribute to people's knowledge of death as they have already done for subjects such as mental illness.

Could it be, however, that these mirrors of our daily lives do not quite reflect reality when dealing with death? Or are deaths in soap operas just convenient ways to raise audience figures while distorting the perception and possibly fear of violence in society?

Methods

We studied mortality in four British soap operas on television—Coronation Street, EastEnders, Brookside, and Emmerdale—from 1983, when the newest of the four, EastEnders, was first broadcast, to the middle of 1997. A literature review using Medline found little other literature specifically on mortality in soap opera. We next sought data from the producers on the dates of deaths or losses to follow up of all named characters, together with their ages and the dates of their first