Routine telephone review of asthma

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Mortality associated with foodborne bacterial gastrointestinal infections

Statistical method is worth examining

Editor—Helms et al report a significant association between common foodborne infectious, including campylobacteriosis, and increased short term and long term mortality.1 As this conflicts with conventional clinical wisdom,2 it is worth scrutinising the statistical method supporting the claim.

Helms et al compare ill cases with healthier (general population) controls by using a comorbidity index to adjust for the fact that underlying conditions were more common among patients than in the control group, particularly AIDS related illness, metastatic cancers, and lymphomas or leukaemia. But even after adjusting for comorbidity, the relative mortality fell only from 3.10 to 2.56.

Both the small impact of comorbidity adjustment and the association between infections and morbidity can be explained by known limitations of the Charlson comorbidity index. For example, for lung cancer survival, the Charlson index explained only 2.0% of the variation in survival.3 It has not been validated for gastrointestinal infections in AIDS and leukaemia patients. Thus Helms et al rely on an index that accounts for relatively little of the variance in mortality rates. They attribute the remainder to bacterial pathogens. But underlying illness provides a more plausible explanation.4

Severe illness predicts increased mortality, infections, and comorbidity. The comorbidity index does not fully reflect mortality consequences of illness, so residual confounding by illness, even after conditioning on the index, creates a statistical association between infection and mortality, although the former does not cause the latter.

Imperfectly controlled residual confounding can explain counterintuitive statistical associations between exposures and health outcomes.5 Before accepting that infectious diarrhoea triples death rates, as Helms et al say, it is appropriate to consider more carefully the non-causal association between infection and mortality from incompletely controlled confounding.

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Competing interests: LC has conducted research since 1995 on campylobacter causes and risk analyses. This work has been partly supported by funds received from the US Food and Drug Administration and from the Animal Health Institute. This comment reflects the author's opinions only, and has not been supported by any funders.


Case selection and clinical data are important

Editor—The article by Helms et al raises the importance of case selection and clinical data on the estimates of short and long term mortality from clinical illness.6 Clinicians’ understanding of an illness entails identifying symptoms and signs, in relation to age, sex, and geography, the three variables for which the authors selected controls. But clinicians also decide on the necessity for diagnostic laboratory tests. Results deemed likely to influence patients’ management or outcome affect the likelihood of investigations.7 Variations in laboratory testing protocols and methods affect what is detected and reported.

Medical epidemiologists are aware that the infecting dose affects severity. In general, the larger the infecting dose, the more severe the illness and the more likely the patient is to present to a clinician,7 so that severe illnesses are more likely to be represented in those studied.

Medical microbiologists are aware, as acknowledged by the authors, that among the several thousand different salmonellas, some, such as Salmonella typhi, S choleraesuis, S dublin, and S enterica seem predisposed to severe illness and bacteraemia. Similar variation in severity occurs with Shigella and Campylobacter.

One way to deal with the estimate of short and long term mortality is to obtain clinical information concerning mortality. Helms et al think that deaths occurring within one year may relate to the bacterial cause of illness. If a review of the death certificates might give an incomplete picture, examining hospital records could reduce the difficulty.

The method used, as suggested by Evans’s commentary,7 relates to estimates of an exposure that affects mortality, making full use of the extraordinary data available in Denmark and other Scandinavian countries. Incorporating clinical information about cause of death might clarify whether the observations concern clinically severe cases, or represent other factors, not related to the gastrointestinal infection.

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Competing interests: RAF reviewed published and unpublished epidemiological data relating to campylobacter on behalf of Bayer and the US Food and Drug Administration’s centre for veterinary medicine.


Mechanism needs to be explained

Editor—Helms et al show that gastroenteritis due to one of four common bacterial pathogens increases nearly three times the likelihood of death within a year, even after certain comorbidities are controlled for.1 There seems intuitively no reason why a clinically self limiting acute gastroenteritis should cause death except (unusually) as an immediate result of the infection. Could the people at greatest risk of these infections have a lifestyle of dependence on fast food and unsatisfactorily cooked or stored food that is associated with greater mortality? Were Helms et al able to compare the lifestyles of their patients and their controls in a way that might show relative social deprivation?2 Or do the authors think that these
four infections may cause death by some specific mechanism in the subsequent 12 months? If so, can they suggest what it is?

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Competing interests: None declared.


Authors’ reply

Editor—Our study was unique because it included patients with infectious gastroenteritis, by and large people who sought care from their family doctor and had no severe underlying illness. The concerns that O’Brien and Feldman raise about bias introduced by case selection is likely to be less relevant in Denmark as the Danish counties reimburse laboratory costs, and for epidemiological reasons doctors often request stool specimens. Our study was the first to determine mortality while adjusting for background mortality. This was pivotal because gastrointestinal infections often affect elderly people. Furthermore, we adjusted for comorbidity by using data from the national discharge registry. We applied the principles described by Charlson et al., but calculated new empirical weights based on the actual survival rates of the large background population. This approach was used to ensure that the weights were valid and appropriate in the given context. This approach takes care of most of the concerns expressed by Cox. We also found excess mortality in the subanalysis, when all individuals with underlying illness had been excluded.

Many acute infections, including foodborne bacterial infections, are associated with short term and long term complications. These include acute complications such as severe dehydration, misdiagnosis of abdominal cramps, leading to surgery, or spread of the pathogens into the bloodstream. Salmonellas are a well known cause of focal and vascular infections. The Guillain-Barré syndrome is a severe reactive complication to a campylobacter infection, albeit each of these events is uncommon, taken together they may account for our findings.

We agree with O’Brien and Feldman that both the infecting dose and subtype of bacterial species are of importance. In the analyses we looked at the effect of specific zoonotic salmonella serotypes. Beyond Salmonella enteritidis, S typhimurium, and S dublin, we could not see any differences, probably because the number of each of the exotic serotypes was too small to see this. Finally, antimicrobial drug resistance may be associated with adverse public health effects.

The biological plausibility is supported by the fact that our estimates are in line with common knowledge of the different agents. For example, mortality after salmonella infection was higher than after campylobacter infection, and in the group of Salmonella infections, serotype dublin, known to be invasive, was associated with a marked excess mortality. Although long term mortality was observed for Salmonella, Campylobacter and Yersinia enterocolitica, the proportion of deaths attributable to the infection was highest in the acute phase. The table was prepared based on the figures in our table 2. The relative mortality has been converted to the attributable proportion of deaths among exposed, that is, a measure of the probability of a death being related to the gastrointestinal infection. In our opinion, the pattern presented in the table makes sense from a clinical point of view, and supports the notion that our findings are more than artefacts.

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Mortality in Swedish women with cosmetic breast implants

Study found increased risk of suicides and cancer deaths

Editor—The increased suicides and lung cancers among implant patients reported by Koot et al is consistent with a study by Brinton et al at the US National Cancer Institute. However, Brinton et al found an increased risk of suicides and cancer deaths compared with other patients having plastic surgery.

If plastic surgery patients have more psychological problems than the general population, as Koot suggests, that would not explain the difference between suicide rates of breast augmentation patients compared with other plastic surgery patients. There are other, more likely explanations. Notably, unlike most other plastic surgery patients, implant patients suffer from well documented complications such as chronic pain and implant breakage that increase in likelihood every year. Our centre receives letters every week from women whose implants are broken and who cannot afford explant surgery. Many of these women are quite desperate, especially when silicone is migrating to other organs or causing pain or deformities. Even in countries with national health care, these problems can be difficult to remedy and could potentially cause an increase in suicides.

A flaw of the Koot et al study is that it included women who had breast implants for less than one year, which weakens the statistical power. In contrast, the Brinton et al study included women who had breast implants for at least eight years and found increases in deaths from suicide, lung cancer, and brain cancer compared with plastic surgery patients who reported similar smoking and lifestyle habits.

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Body dysmorphic disorder should be considered

Editor—Koot et al reported an increased risk of suicide among patients who had received cosmetic breast implants. The somatoform disorder known as body dysmorphic disorder entails a preoccupation with a defect in appearance, and the defect is either imagined, or, if a slight physical defect is present, the patient’s concern is markedly excessive with subsequent impairment of social or occupational functioning. The patient’s distress may lead to suicidal ideation, suicide attempts, and
completed suicide. It has been estimated that between 6% and 15% of patients having cosmetic surgery and dermatology suffer from this disorder. Consequently, cosmetic surgeons should seek psychiatric consultations preoperatively for the purpose of ruling out body dysmorphic disorder and have it treated if present. Perhaps only then can the elevated suicide rate associated with breast implants be diminished.

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“Evidence of absence” can be important

Editor—Alderson and Chalmers are rightly critical of those who make inappropriate claims, but they are themselves guilty of this.1 Compare these statements: “It is never correct to claim that treatments have no effect or that there is no difference in the effects of treatments”, and “Absence of evidence is not evidence of absence.” The first is the opening sentence of their paper, the second is the title of a paper by Altman and Bland that they cite in its support.2 The two are mutually exclusive, because if the first were true then there could never be “evidence of absence.” In describing their method, Alderson and Chalmers specify that they only classified statements as claiming no effect or no difference if they were without qualification about clinical or statistical significance. Although this could have been described more clearly, it is reassuring, as it shows that they accept that it is possible to have evidence of absence, even if this contradicts their eye catching but inaccurate conclusion that one of the main differences between the two types of consultation was the undertaking of opportunistic health promotion. It would have been interesting to know if anything other than asthma management (for example routine blood pressure measurements) was going on in these 20 minute appointments. We believe that further investigation of these problems is required before recommending this method of managing asthma.

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Further investigation is required

Editor—Pinnock et al conclude that telephone consultation for asthma review is an efficient option for patients in primary care.3 We have several concerns about this study.

Firstly, a large number of patients (654/932) chose not to take part, and a further 307 were excluded for other reasons. It is not inconceivable that patients who dislike telephone consultations could have entirely opted out even before the study started.

Secondly, the assumption that actual observation of patients’ inhaler technique and peak flow measurement is equivalent to asking patients about their technique or measurements causes concerns. Patients commonly deny problems using inhalers but often fail to demonstrate effective usage.

Thirdly, the conclusion that both interventions were equally effective is somewhat spurious since, using their own instrument, neither intervention produced a difference in outcome three months later. It might be better to say both were equally ineffectual.

Lastly we found in our randomised control trial of telephone triage versus face to face consultations for appointments on the same day that one of the main differences between the two types of consultation was the undertaking of opportunistic health promotion. It would have been interesting to know if anything other than asthma management (for example routine blood pressure measurements) was going on in these 20 minute appointments. We believe that further investigation of these problems is required before recommending this method of managing asthma.

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Authors’ reply

Editor—We acknowledged in our discussion that only a third of eligible patients participated in our trial raising concerns about generalisability. Having identified a group
reliant to attend asthma clinics, achieving a high response rate to a postal invitation was always going to be difficult. As detailed in the paper, of the 307 excluded for other reasons, 50% had chronic obstructive pulmonary disease and were therefore not eligible.

We were concerned about the barrier to checking inhaler technique imposed by telephone consultations and discussed this issue at the study training meeting. The trial nurses agreed on a pragmatic approach: if asthma control was good there was little need for concern, but if suboptimal control was identified they considered poor inhaler technique as a possible cause and could arrange a surgery appointment. Our results do not suggest detriment to those in the telephone group but we agree this point warrants further investigation.

We do not agree with Hynih and Lavars that inability to perform a peak flow compromises care. A one off peak flow reading is of limited value in assessing the control of a variable condition such as asthma. We opted to use the three asthma morbidity questions which are recommended for monitoring control1 and which are reflected in the Short-Q morbidity score. Furthermore, we used validated patient based outcomes (for example, the Juniper mini asthma related quality of life questionnaire), which are used increasingly in clinical trials.2 Surgeon based outcome measures would have discouraged recruitment among reluctant attendees who would potentially discourage recruitment among those in the telephone group but we agree this point warrants further investigation.

‘Using the telephone alters the dynamics of consultations,’ and we would echo McKinstry et al’s call for further investigation. We believe, however, that our results are encouraging and are likely to be of considerable interest to clinicians concerned about meeting quality targets for annual reviews.

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Consumption of coffee during pregnancy

Article raises more questions than it answers

Editor—Wisborg et al’s article raises more issues than it settles.1 Firstly, coffee contains not only caffeine but a mixture of different ingredients (milk, sugar, stabilisers, flavour, and other alkaloids from coffee beans). Attributing the result of drinking coffee to just one constituent seems illogical. If Wisborg et al want to prove what they contend, they should contrast the group taking eight cups of ordinary coffee to those taking eight cups of decaffeinated coffee.

Secondly, in many parts of the world, tea, chocolate, and cola are consumed on a large scale and in high doses, like traditional Chinese tea in Hong Kong. Yet Hong Kong has one of the lowest perinatal mortality rates in the world. In Japan and China tea is regarded as part of the healthy diet to be consumed regularly. The same also applies to cola in America and many parts of the world. So what will be the combined effect of coffee, tea, chocolate, and cola should the woman be drinking marginal amounts of coffee (four to seven cups)?

One of the gold standards in establishing causal relations between two factors is to show the dose dependent relation. Wisborg et al’s study showed that, statistically speaking, there is a one off increase in stillbirth after eight or more cups of coffee. To illustrate the dose dependent relation better, the last group should have been subdivided into those taking eight to 11 cups, and those taking 12 cups or more.

Caffeine is used widely to treat migraines. If caffeine leads to stillbirth in the form of coffee, it may carry the same risk for women taking it for their migraine. Should we ban coffee, it may carry the same risk for women taking 12 cups or more. If caffeine is used widely to treat migraines.

If caffeine leads to stillbirth in the form of coffee, it may carry the same risk for women taking it for their migraine. Should we ban coffee, it may carry the same risk for women taking 12 cups or more. If caffeine is used widely to treat migraines.

Competing interests: None declared.

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Data do not support claim

Editor—Wisborg et al found an association between maternal coffee consumption and risk of stillbirth, and claim that after adjustment for potential confounding factors the association remained significant.1 However, I am not convinced that the data they present support that claim.

The claim of a significant association seems to be based on the statistical significance for the odds ratio that compares the highest consumption group with the
zero consumption group. This odds ratio is in any case only marginally significant at the 5% level, as the 95% confidence interval extends as far as 1. More importantly, Wisborg et al do not present the results of an overall test of differing risk of stillbirth among all the coffee consumption groups.

From a statistical point of view, it is not good practice to rely on pairwise comparisons between specific groups if the overall group effect is not significant. We are not told whether it is significant or not, but given that neither the low nor medium consumption group differs from the zero consumption group, and the high consumption group differs only marginally from the zero consumption group; my guess is that it isn’t.

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Competing interests: None declared.


Authors’ reply

Editor—In a prospective study we found that coffee drinking during pregnancy was associated with an increased risk of stillbirth, but not with death in infancy.1 Our results on stillbirth seemed to indicate a threshold effect around four to seven cups per day, but the risk estimate in women with the highest intake of coffee was based on only 11 stillbirths and we therefore had no possibility to explore further the relation between coffee and stillbirth in women drinking eight or more cups of coffee per day. Ludvig claims that a dose dependent association is the gold standard for establishing a causal relation. This is not correct. A monotonic, unidirectional dose-response curve is neither necessary nor sufficient for establishing a causal relation.2

Our result may represent a causal relationship or be due to other factors associated with coffee drinking and stillbirth. Sindos et al are particularly concerned about the possibility of unadjusted confounding, because no information was included about drug abuse. Drug abuse, especially of cocaine, among pregnant women, is fortunately a minor problem in Denmark and identified drug abusers are not included in our cohort.3 Drug abuse including cocaine is thus of little or no relevance as a confounder in our cohort.

Caffeine is regarded as the key component in studies of the potential effects of coffee. The path to death is usually multifactorial, composed of several component causes.4 Caffeine may just be one causal component that in some settings together with other causal components leads to death but in other settings one or more of the other component causes are missing, or the time specific distribution of these component causes is different. As for Jacobs’s criticism of our statistical approach we believe that pairwise comparisons between each level of coffee intake and the reference category is technically appropriate, even if other approaches could have been chosen. Coffee is a commonly consumed stimulant and if our results represent a true causal relationship it has important health implications. However, the question on a causal relation is still open. Thus in an ongoing randomised study including 1000 pregnant women we are further exploring the effect of coffee with and without caffeine.

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Doctors as servants of patients

Long term patients are underused resource

Editor—Your coverage of Ian Kramer’s contribution to the debate raised by the chief medical officer1 is useful if slightly inaccurate (Kramer is a former vice chairman of our organisation). The relationship between provider and servant is too old fashioned for the modern world. We are partners in the shared care of the individual patient, which involves other health professionals too. Other patients can have an important role in explaining, empathising, listening, advocating, and much more.

Long term patients as repeated users of the healthcare system are an incredibly underused resource in how that system works for, or sometimes against, them. If the input of patients as participants is to be valued, perhaps it should be paid for, but we would be half way there if this was, firstly, encouraged; secondly, resourced; and, most importantly, were it ever listened to and acted on at a higher level than the colour of the new and overdue upholstery or curtains.

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1 Macdonald S. Doctors are servants of patients says chief medical officer. BMJ 2003;326:569. (15 March)

Modesty may be deceptive

Editor—Professor Liam Donaldson is right in his sentiments, if impolitic in their expression.2 However, I would rather express my own humility than have it expressed on my behalf. I suspect this would apply to most of my colleagues. Given our respective roles, it may be for me to assert that I am a servant of my patients, and for Donaldson to assert that he is the servant of the government. Even then, protestations of modesty deserve a cynical scrutiny. Who better than Swift to provide one?

“Our betters tell us they are our humble servants, but understand us to be their slaves.”

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surely we can do better than this

Editor—Given the context of the modern healthcare market, and our developed appreciation of dynamics between patients and doctors, the comments of Professor Liam Donaldson seem a little trite and superficial.3 The welfare of the patient may be our concern, but so is the welfare of our patients. Similarly, as professionals, we have a duty to do good to society in general, just as we have a duty to truth and intellectual honesty.

Reducing these complexities to the feudal simplicity of a “master–servant” relationship demeans both participants, just as ignoring the role of patients in setting the political and practical agenda (not least through the ballot box)—when did we as a society last elect a government with a mandate to raise taxes?4 diminishes their responsibility in the medical world that follows. Donaldson may regard us as our patients’ servants. I hope that he does not forget that, as an administrator and political appointee, he is ours.

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