Risk factors for the use of prescription antibiotics on UK broiler farms

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Objectives: Despite growing concerns about the emergence of antibiotic-resistant strains of bacteria, little work has been carried out to investigate reasons for prescription antibiotic use in UK farming systems. We carried out a nationwide survey of broiler farms to determine risk factors for the use of prescription antibiotics.

Methods: A cross-sectional questionnaire-based survey of UK broiler farms was undertaken covering flock placement dates from July 2002 until July 2003 and was based on information concerning 54% of the national broiler population reared on 497 farms. Data were collected on all aspects of broiler production and multivariable logistic regression analyses were performed to determine risk factors for two dependent variables; therapeutic and preventive use of antibiotics.

Results: The major indications for the use of antibiotics for therapeutic purposes were enteric and respiratory disease, the strongest association being with the occurrence of necrotic enteritis. No direct association was found between the use of antibiotics for preventive purposes and disease. Multivariable logistic regression analysis indicated that the main drivers for the use of antibiotics for disease prevention may be poultry company disease prevention policies and farm management practices.

Conclusions: With increasing restrictions on the use of antibiotics in food-producing animals, research efforts need to be focused on the epidemiology of enteric and respiratory disease in poultry. The cost of disease to the broiler industry is great, resulting in the use of antibiotics for preventive purposes to safeguard against large financial losses. More research into alternative disease control measures is required.

Keywords: antimicrobial management, poultry, food-producing animals

Introduction

The production of broiler chickens is one of the most intensive types of animal husbandry with over 800 million birds being produced annually in the UK alone.1 It is an industry that has achieved worldwide success in its primary objective of providing a source of affordable animal protein. This success is due to several factors including, importantly, the prevention of disease. This is partly achieved by the use of antibiotics. Increasingly, the use of antibiotics in intensive animal production is linked to the emergence of antibiotic-resistant bacterial strains.2 As a result, by 1999, five antimicrobials (avoparcin, virginiamycin, bacitracin zinc, tylosin phosphate and spiramycin) commonly used as antimicrobial growth promoters (AGPs) in food-producing animals were banned for the purposes of growth promotion by the EC in the first of a two-phase process to ban all AGPs [Regulation (EC) No. 1831/2003] came into full force in the UK banning the two remaining antibiotics that could be used as AGPs: avilamycin and flavomycin. Many studies assume that the removal of AGPs from animal feed will have a positive effect on both animal and human health based on the principal that if fewer antibiotics are used in farming systems, there will be less chance of bacteria developing antimicrobial resistance in food animals and less chance of transmission to people via the food chain.3 In human medicine, where the main reasons for antibiotic use are well known and understood, there is little scientific doubt that limiting antibiotic use in humans has a positive effect on human health. However, this may not be the case for animal health where there have been few studies that have investigated the main reasons for antibiotic use.

The majority of studies that have investigated antibiotic use in food animals are based on data derived from sources that report the type of drugs used, their frequency of use and the quantity used over a certain time period.6–8 To our knowledge,
there have been no studies carried out that look at the specific reasons for antibiotic use beyond being used for therapeutic or prophylactic purposes. It is in the best interests of both human and animal health to use antibiotics in a responsible and efficient manner where they will be most effective for prophylaxis and therapy. In order to ensure antibiotic use in food animals is as efficient as possible, it is necessary to first understand the reasons for their use.

This paper presents the findings of a nationwide questionnaire-based cross-sectional study undertaken in 2003 with the aim of determining the reasons for prescription antibiotic use on UK broiler farms. It is hoped that by gaining a better understanding of the reasons for antibiotic use in UK broiler flocks, future research into these reasons will be better directed.

Materials and methods

Study design

A cross-sectional survey of UK broiler farms was undertaken between March and September 2003. The 11 major poultry companies producing broilers in the UK were invited to participate and 9 agreed. A postal questionnaire, which had been tested in a pilot study, designed to be completed by farm managers was mailed to a stratified random sample of farms selected from lists provided by each company. Epi Info Version 3.3.2 (CDC, Atlanta, GA, USA) was used to calculate sample size estimates, which were based on an expected disease prevalence of 5% with 95% confidence limits and 1% precision. The study covered flock placement dates from the 29 July 2002 to 17 July 2003 and was based on the information concerning 54,945,984 birds reared on 497 farms, which was 54% of the national broiler population at that time (June Agricultural Census 2002–03, Defra).

Data collection

Data on disease occurrence and control, farm management practices, hygiene and biosecurity were collected. Data collected referred to the last crop of broilers to be harvested (reared to slaughter weight) prior to receipt of the questionnaire. Data were collected on two broad categories of prescription antibiotic use: disease prevention (prophylactic) and treatment of sick birds (therapeutic). Within these categories, data were collected about the type of antibiotic used, the number of different products used, the route of administration, clinical indication, duration of antibiotic use and the age of the birds. Data on the administration of prescription antibiotics always referred to medication of the entire flock of birds.

Data on the inclusion rates of avilamycin and flavomycin (AGPs with a spectrum of activity primarily against Gram-positive bacteria) and coccidiostats in feed that were used by farms were collected from the poultry companies. Questionnaires requesting these data for the study farms and corresponding crop placement dates were sent by post or e-mail to company nutritionists, who had better access to this data than the farmers themselves.

Statistical analysis

All analyses were carried out in Epi Info™ Version 3.3.2 (CDC) and STATA 7 (Stata Corporation, College Station, TX, USA). Individual broiler farms were the analytical units. Questionnaire data were entered into two identical Access databases (Microsoft; Redmond, WA, USA). These were compared and corrected to produce a single working database. Univariate and multivariable analyses were carried out using two different binary dependent variables: (i) the use of antibiotics therapeutically; and (ii) the use of antibiotics prophylactically. Univariate analyses of independent binary variables, including variables concerned with disease occurrence and control, farm management practices, hygiene and biosecurity, were carried out using 2 × 2 contingency tables and were tested for significance with χ² tests or Fisher’s exact tests when expected values were <5. Univariate logistic regression models were used to analyse independent categorical variables by creating dummy variables. Continuous variables were analysed using logistic regression models, the best fitting forms of which were assessed using the following fractional polynomials: −2, −1, −0.5, 0, 0.5, 1, 2 and 3.9 Results were considered statistically significant at a P value of 0.05 or below.

Variables showing an association with each dependent variable at a significance level of P < 0.25 after univariable analysis were used to build two multivariable logistic regression models using maximum-likelihood estimation.10 The data had a two-level hierarchical structure; farms were clustered within nine poultry companies, and so ‘poultry company’ was included in each model as a random effect. Correlation analysis was performed on the independent variables to avoid covariance in the final models. Among correlated variables (correlation coefficient > 0.7), those that produced the best fitting model were retained in the model. Forward stepwise models were built manually. Variables were entered individually and those that significantly improved the fit of each model (maximum-likelihood test or Wald test statistic of P < 0.05) were retained in the final models. Once the final models had been developed, all variables not retained in the final models were re-entered individually to check that there were no significant improvements.

Two-way interaction terms were tested between all variables that remained in the final models. The percentage variation attributable to ‘poultry company’, was assessed using the intra-class correlation coefficient (ρ). The fit of random-effects logistic regression models was assessed by comparing the model deviance to the degrees of freedom. For logistic regression models with no significant random effect, the Hosmer–Lemeshow diagnostic test statistic and the area under the receiver operating characteristic curve (ROC) were calculated to assess the fit of the model.

Results

Response rate

Five hundred and five of the 714 poultry farms returned the questionnaire (70.7%). Eight questionnaires were not completed and were excluded from the analysis leaving 497 completed questionnaires and a usable response rate of 69.6%. Although characteristics of non-respondent farms were not examined in this study, in a similar survey carried out during 2002, it was found that average flock size on non-respondent farms was significantly smaller than on respondent farms.11 It should be noted therefore that there may be some degree of non-response bias.

Antibiotic use

Returned questionnaires covered crop placement dates over a period of almost 1 year, from 29 July 2002 to 17 July 2003. During this time, 42.4% (95% CI 37.6–46.8) of the farms surveyed used prescription antibiotics therapeutically, 54.4% (95% CI 49.8–58.9) of farms used them for prophylactic
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purposes and 24.2% (95% CI 20.3–28.5) used antibiotics both for disease treatment and prevention.

Thirty-two per cent of farms used amoxicillin (a penicillin with extended spectrum) to treat disease on at least one occasion, followed by the macrolide antibiotic tylosin (10.4% of farms). Lincomycin, belonging to the lincosamides, was used to treat disease by a much smaller proportion of farms (2.4%) than used it to prevent disease (25.9%). In comparison with penicillin and the macrolide antibiotics, aminoglycoside, fluoroquinolone, lincosamide, potentiated sulphonamide and tetracycline antibiotics were used by only a small percentage of farmers to treat disease (Table 1).

Many of the same antibiotics were used by farmers to treat disease as were used to prevent disease. Antibiotics that were used purely as a preventive measure and never for the treatment of disease were the aminocyclitol antibiotic apramycin and phenoxymethyl penicillin potassium (Table 1).

Lincomycin, potentiated sulphonamides and macrolide antibiotics were used most frequently for the purpose of disease prevention. Seven of the nine poultry companies used lincomycin, tylosin and trimethoprim/sulfadiazine for disease prevention. At farm level, lincomycin was used most commonly (25.9%), followed by a combination of trimethoprim and sulfadiazine (16.8% of farms), and tylosin (11.7% of farms). Aminocyclitol, aminoglycoside, fluoroquinolone, penicillin and tetracycline antibiotics were used by few farms for disease prevention (ranging from 0.6% to 4.5%).

Multivariable analysis

Therapeutic use of antibiotics. Factors associated with the use of antibiotics for therapy, as determined by multivariable logistic regression analysis, are shown in Table 2. Antibiotic treatment was associated with enteric and respiratory disease. The highest odds were with necrotic enteritis (NE), followed by respiratory disease, coccidiosis and wet litter. The use of a live vaccine against infectious bursal disease (IBD) also increased the odds of antibiotic use for therapeutic purposes, as did the addition of whole wheat to feed. The number of hatcheries supplying farms with chicks showed a negative association with the use of antibiotics for the treatment of disease. Poultry company was included in the model as a random effect to account for the clustering effect of the company; however, the random effect was not significant and therefore no variance in the final model could be attributed to poultry company. All two-way interaction terms tested were non-significant. Goodness-of-fit tests performed on the multivariable logistic regression model indicated that the model was a good fit (Hosmer–Lemeshow \( \chi^2 = 10.99, =0.20; \) area under the receiver operating characteristic curve = 0.83).

Preventive use of antibiotics. Factors associated with the use of antibiotics for the prevention of disease, as determined by multivariable logistic regression analysis, are shown in Table 3. A large proportion of the variance in the use of antibiotics for prevention could be attributed to the individual company responsible for the farm (included as a random effect). The intra-class correlation coefficient was calculated to be 54.4%. Comparison of the model deviance to the degrees of freedom indicated a good model fit.

The odds of antibiotic use for preventive purposes increased with the number of hatcheries supplying the farms with chicks and the average slaughter weight of the flock. The use of competitive exclusion (CE) products, which are products containing non-pathogenic microorganisms that are fed to 1-day-old chicks to establish a healthy intestinal microflora, the use of antibiotic growth promoters and controlled feeding regimens were all associated with a reduced risk of the use of antibiotics for preventive purposes (Table 3).

Table 1. Frequency of antibiotics used on 463 broiler farms based on data collected from farmers about their last harvested crop by questionnaire

<table>
<thead>
<tr>
<th>Antibiotic name</th>
<th>Therapeutic use of antibiotics</th>
<th>Preventive use of antibiotics</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Number of companies</td>
<td>Number, % of farms (95% CI)</td>
</tr>
<tr>
<td>Amoxicillin trihydrate</td>
<td>9/9</td>
<td>150, 32.0% (27.8–36.5)</td>
</tr>
<tr>
<td>Lincomycin hydrochloride and spectinomycin sulphate</td>
<td>3/9</td>
<td>11, 2.4% (1.3–4.3)</td>
</tr>
<tr>
<td>Trimethoprim and sulfadiazine</td>
<td>5/9</td>
<td>13, 2.8% (1.4–4.6)</td>
</tr>
<tr>
<td>Tylosin tartrate</td>
<td>6/9</td>
<td>48, 10.4% (7.8–13.6)</td>
</tr>
<tr>
<td>Tilmicosin phosphate</td>
<td>1/9</td>
<td>2, 0.4% (0.1–1.7)</td>
</tr>
<tr>
<td>Phenoxymethyl penicillin potassium</td>
<td>0/9</td>
<td>0, 0.0% (0.0–0.8)</td>
</tr>
<tr>
<td>Trimethoprim, sulfaquinoxaline sodium</td>
<td>1/9</td>
<td>1, 0.2% (0.0–1.4)</td>
</tr>
<tr>
<td>Chlorotetracycline hydrochloride</td>
<td>2/9</td>
<td>3, 0.6% (0.2–2.0)</td>
</tr>
<tr>
<td>Apramycin sulphate</td>
<td>0/9</td>
<td>0, 0.0% (0.0–0.8)</td>
</tr>
<tr>
<td>Neomycin sulphate</td>
<td>2/9</td>
<td>5, 1.1% (0.4–2.7)</td>
</tr>
<tr>
<td>Enrofloxacin</td>
<td>3/9</td>
<td>4, 0.9% (0.3–2.4)</td>
</tr>
<tr>
<td>Difloxacin hydrochloride</td>
<td>2/9</td>
<td>3, 0.6% (0.2–2.0)</td>
</tr>
</tbody>
</table>

The percentage and number of farms and poultry companies that used each antibiotic on at least one occasion is shown; 95% CIs are given in brackets.
This was the pattern of events experienced in a number of European countries when AGPs were banned from use.8,13,14 At present it is unknown what the effects are of the recent AGP ban on the incidence of NE in UK broiler flocks and the consequent use of antibiotics to control such outbreaks. It would be interesting to repeat this study to determine how the use of antibiotics used for therapeutic purposes has changed since the total ban of AGPs in 2006.

Many risk factors have been identified for the occurrence of NE in broiler chickens, one of which is the inclusion of whole wheat in feed.15 The inclusion of wheat in feed was also found in this study to be associated with an increased risk of antibiotic use for therapeutic purposes. Annett et al.16 suggest that the digestion of wheat can result in viscous intestinal contents resulting in an increased intestinal transit time allowing the proliferation of \textit{Clostridium perfringens}, the agent which may predispose birds to outbreaks of NE.

Wet litter and coccidiosis were also strongly associated with the use of antibiotics for therapeutic purposes. ‘Wet litter’ is a term used to describe a deterioration in the litter quality that occurs when the absorbance load of the litter is exceeded.17 Wet litter has been associated most commonly with the occurrence of ‘contact dermatitis’, giving rise to skin lesions that can occur on the foot-pad, hock or breast of birds.17,18 In a previous survey, wet litter was found to be a common occurrence on UK broiler farms, with a reported prevalence of 56.1%.19 Over half of the reported cases were attributed to a disease problem. In the majority of cases (71%), the occurrence of wet litter led to some form of treatment of which 45% was reported to be the administration of antibiotics to therapy, possibly directed at the treatment of secondary infections. It would seem that ‘wet litter’ is an emerging disease problem in UK broiler farms and may be a significant cause of antibiotic use; however, little research has been carried out on the seemingly multifactorial aetiology of this condition. An important risk factor for wet litter outbreaks was found to be the occurrence of coccidiosis, a known cause of diarrhoea in broiler chickens.20 Coccidiosis was also found by this study to be a risk factor for the increased use of antibiotics for therapeutic purposes.

The vaccination of flocks against IBD was associated with an increased use of antibiotics for treatment purposes. The majority of farms (95.1%; 95% CI 88.7–93.8) in this study vaccinated their crops against IBD. It has been demonstrated that IBD vaccination can have a direct impact on the immune function of birds and can suppress it for a period of time,21 thereby rendering them more susceptible to bacterial or viral challenge resulting in treatment with antibiotics.

The only factor that was associated with a decreased use of antibiotics for therapeutic purposes was the number of hatcheries that supplied the farm with chicks (0.63, 95% CI 0.41–0.98, 0.04).
that supplied the farms. Farms that were supplied with chicks from more than one hatchery were associated with a decreased risk of using prescription antibiotics for treatment purposes. However, an increase in the number of hatcheries that supplied farms was associated with an increased use of antibiotics for disease prevention. Studies have shown that 1-day-old chicks are capable of becoming infected in the hatchery. The associations shown by this study may therefore be in response to a perceived increase in disease risk associated with receiving chicks from more than one hatchery. This may explain why on farms that receive chicks from more than one hatchery the frequency of antibiotic use to prevent disease is increased and the frequency of antibiotic use to treat disease is reduced.

No direct association was found between prophylactic antibiotic use and disease, indicating that these antibiotics are doing what they are meant to do, namely prevent disease. If farms with a history of disease were using antibiotics prophylactically to aid in the control of that disease without totally getting rid of the disease, then it is possible that an association between disease occurrence and antibiotic use for preventive purposes would have been found. This study indicates that the main drivers for the use of prescription antibiotics preventively may be influenced by poultry company disease prevention policies, driven largely by veterinarians. Farms in this study ‘belonged’ to nine poultry companies, and ‘poultry company’ was included in the final multivariable model as a random effect where it remained highly statistically significant. The intra-class correlation coefficient indicated that a high percentage of the variation in the final model resided at poultry company level (54.4%). However, it should be noted that independent farms were not represented in this study introducing a possible source of bias. In addition, risk factors for the use of antibiotics for disease prevention identified in the final multivariable model were all factors associated with management practices on farms.

The profit margin on a broiler chicken in 2005 was 1.9 pence per bird. With small profit margins per bird, losses due to disease can be very costly to the poultry industry. It is likely that antibiotics are used preventively by poultry companies, to safeguard against large losses of birds due to bacterial disease. As alternative disease management practices become available, it is likely that the use of antibiotics for disease prevention will fall, underlining the importance of further research into the diseases for which antibiotics are indicated.

The use of CE products was strongly associated with reduced use of antibiotics for preventive purposes. Feeding chicks with non-pathogenic intestinal microorganisms from mature chickens is thought to establish an intestinal microflora that will out-compete pathogenic bacteria that may enter the gastrointestinal tract. Due to the mode of action of CE products, it would be counter-productive to concurrently administer antibiotics for disease prevention. CE products have been demonstrated to be protective against Campylobacter spp., Salmonella spp. and C. perfringens. In our survey, 15.5% (95% CI 12.5–19.0) of farmers used CE products, some as an alternative to use of antibiotics for disease prevention.

Farms that used one of the two AGPs that were still licensed for use during 2003 (avilamycin and flavomycin) were less likely to use prescription antibiotics for preventive purposes, suggesting that AGPs acted through the prevention of infectious disease. When AGPs were licensed for use in food-producing animals (pre-1 January 2006), in addition to growth promoting properties, they afforded antibacterial protection to the animals they were fed, reducing the need to administer additional prescription antibiotics for preventive purposes. The fact that AGPs were commonly used to offer protection against disease highlights the need for more extensive research to be carried out into the epidemiology of infections that AGPs were once used to control.

Farms that used a controlled feeding regimen were significantly less likely to use antibiotics for disease prevention in comparison with farms using an ad libitum feeding method. Several studies have reported that in comparison with an ad libitum feeding regimen, a controlled feeding regimen, where birds are fed specific amounts of food at specific times rather than having access to feed all of the time, reduces the incidence of leg problems and mortality in broilers, reducing the need for farmers to use antibiotics for prophylaxis.

An increase in the final slaughter weight of birds was associated with an increased risk of using antibiotics for preventive purposes. An increased slaughter weight may be indicative of an increased length of time spent by the birds in the house and therefore an increased exposure to pathogens. Farmers rearing birds to heavier final weights might be more inclined to administer antibiotics to reduce the risk of disease that may arise with increased time spent by birds in the house.

In conclusion, this study has shown that the use of antibiotics for treatment purposes remains largely in response to enteric and respiratory disease. With increasing restrictions on the use of antibiotics in the food-animal industry and growing concerns about the emergence of antibiotic-resistant strains of bacteria, this study has indicated that future research efforts need to be focused on the epidemiology of enteric and respiratory diseases in poultry and finding alternative disease prevention methods.

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Transparency declarations

None to declare.

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