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Empirical treatment of influenza-associated pneumonia in primary care: a descriptive study of the antimicrobial susceptibility of lower respiratory tract bacteria (England, Wales and Northern Ireland, January 2007—March 2010)

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ABSTRACT

Objectives To determine the susceptibility of lower respiratory tract (LRT) isolates of *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae* to antimicrobial agents recommended by UK guidelines for treatment of pneumonia associated with influenza-like illness.

Methods Analysis of antimicrobial susceptibility data from sentinel microbiology laboratories in England, Wales and Northern Ireland was carried out. Subjects comprised patients who had an LRT specimen taken in a general practitioner surgery or hospital outpatient setting between January 2007 and March 2010. The main outcome measurements were antimicrobial susceptibility trends of LRT isolates over time, between patient age groups and in different geographical regions.

Results Susceptibility to tetracyclines or co-amoxiclav was high. Of the 70 288 and 45 288 isolates with susceptibility results for tetracyclines or co-amoxiclav, 96% and 92%, respectively, were susceptible. Overall susceptibility to ciprofloxacin, ampicillin/amoxicillin and macrolides was lower than for tetracyclines or co-amoxiclav and varied markedly by organism. There were few clinically relevant variations in susceptibility to doxycycline or co-amoxiclav over time, geographically or between age groups.

Conclusions The data support the use of doxycycline or co-amoxiclav as appropriate empiric treatment for LRT infection caused by the pathogens investigated, for patients in primary care.

BACKGROUND

Influenza may be complicated by pneumonia, which has two recognised types: primary viral and secondary bacterial infection.[1 2] Examination of pathological specimens from the 1918—1919 influenza pandemic suggested that secondary bacterial infection was the major cause of deaths associated with influenza-like illness (ILI) during that pandemic.[3] The prognosis of patients presenting with bacterial pneumonia rapidly worsens with delay in treatment, and effective empirical treatment (before or in the absence of a specific microbiological diagnosis) is therefore a critical aspect of successful pandemic influenza planning.[4 5]

Guidelines for the clinical management of patients with ILI during an influenza pandemic were compiled and published in 2007 by the British Infection Society, British Thoracic Society and Health Protection Agency (HPA) in collaboration with the Department of Health.[1] These guidelines regarded the pathogens likely to be associated with secondary bacterial pneumonia as *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae*. The guidelines suggest oral empirical treatment with either a tetracycline (usually doxycycline) or co-amoxiclav for patients in primary care. More recently, Department of Health guidelines introduced specifically for the 2009 H1N1 pandemic have reiterated the use of doxycycline or co-amoxiclav treatment for adult patients with influenza complicated by lower respiratory tract (LRT) infection that are not admitted to hospital.[6] Co-amoxiclav is recommended for children (except patients with penicillin allergy, who should be given clarithromycin).

This paper seeks to assess microbiological evidence as to whether co-amoxiclav or tetracyclines are appropriate empirical treatment for bacterial pneumonia in patients treated in the primary care setting. The analysis draws on susceptibility data for LRT isolates of *S pneumoniae*, *S aureus* and *H influenzae* as reported to LabBase2, the HPA's national communicable disease database. The database collects isolate data from laboratories across England, Wales and Northern Ireland and was extended to cover LRT isolates in 2006 as part of the pandemic influenza preparedness arrangements. The surveillance aims to support the timely modification of empirical treatment in the event that antimicrobial susceptibility patterns change.

METHODS

Antimicrobial susceptibility data for LRT isolates of *H influenzae*, *S pneumoniae* and *S aureus* reported between January 2007 and March 2010 were extracted from LabBase2 for laboratories in England, Wales and Northern Ireland. LRT isolates were primarily obtained from sputum, but other sources included alveolar lavage, bronchial/endotracheal aspirate, LRT, lung, pleura or pleural fluid.

The data included all susceptibility test results for tetracycline, co-amoxiclav, ciprofloxacin, ampicillin/amoxicillin and macrolides for all three organisms as reported by hospital laboratories. Data on ciprofloxacin susceptibility in *S pneumoniae*

were excluded as ciprofloxacin is known to be ineffective against this organism[7 8] and pneumococcal isolates are rarely tested for ciprofloxacin susceptibility. Susceptibility data for macrolides were estimated by pooling results for azithromycin, erythromycin and clarithromycin; where conflicting results were reported for the same isolate for different macrolides, the resistant result was retained in the data set. To classify *S aureus* as either methicillin resistant (MRSA) or susceptible (MSSA), results for antistaphylococcal β-lactamase-stable penicillins were pooled. Penicillin was used as a proxy for co-amoxiclav susceptibility in pneumococci due to the small number of test results available for co-amoxiclav. Demographic information was collected, including geographical region, date of birth and isolate source description (ie, general practitioner (GP) surgery, outpatient). The analysis was confined to specimens taken in GP surgeries or from hospital outpatients.

Where multiple successive isolates were reported from the same patient, results for the first isolate only were included in the analysis. Data were analysed using Stata v11 (Stata Corp.). Data for each organism were stratified by the quarter in which the specimen was collected, region, patient age, sex and source. Wilson's method[9] was used to calculate 95% CIs (shown graphically as error bars) for the percentage of susceptible isolates.

Two Poisson models with robust standard errors were used in the analysis, with incident rate ratios (IRRs) expressed as the outcome measure. The first of these models explored the major focus of the paper which was evaluating changes in antimicrobial susceptibility over time by organism. The second model examined changes in susceptibility by organism and patient age group. As likelihood ratio testing (for the purposes of model building) is problematic for a model with robust standard errors, the final Poisson models were constructed by identifying key variables and interactions in logistic regression models.

The logistic regression models were constructed using a backwards elimination approach that incorporated categorical variables for organism, age group, quarter (1, January–March; 2, April–June; 3, July–September; 4, October–December), sex, laboratory region and isolate source (GP or outpatient) to measure susceptibility over time in years (coded as a continuous variable). Patients were categorised by age at specimen date as <45, 45–65, 65–74 and 75+ years, with the group with the largest number of susceptibility results (45–65 years) chosen as the baseline group. The North West was used as the baseline laboratory region because the greatest amount of susceptibility data was reported by this region. Likelihood ratio testing was used to identify variables that could be satisfactorily dropped from each model. Variables were only excluded from the model if the ORs for the remaining variables did not change markedly.

After the variables for inclusion in the models had been determined, possible interactions between either organism and year or organism and patient age group were investigated and, if significant, retained for use in the Poisson model. Organism-specific IRRs for changes over time or by patient age group were obtained by using linear combinations of the appropriate coefficients (using the 'lincom' command).

Data from the National External Quality Assurance Scheme for susceptibility testing (in which all clinical microbiology laboratories in England, Wales and Northern Ireland take part) were reviewed for the three organisms and antibiotics (tetracycline or co-amoxiclav/penicillin).

RESULTS

Overview

A total of 86 845 LRT isolates of *H influenzae*, *S pneumoniae* and *S aureus* were identified from specimens reported from GP surgeries or outpatients. Over 96% of isolates were obtained from sputum, with the remaining isolates obtained from bronchial aspirate (2.4%), alveolar lavage (0.9%) or endotracheal aspirate, LRT, lung, pleura and pleural fluid specimens (<1%). *Haemophilus influenzae* accounted for the majority (62%, 53 895) of isolates, with an equal split between *S aureus* (19%, 16 860) and *S pneumoniae* (19%, 16 090). It should be noted that methicillin susceptibility was not reported for a subset of 962 *S aureus* isolates and therefore the total number of *S aureus* exceeds the sum of known MRSA (3458, 22%) and MSSA (12 440, 78%). A total of 57 827 (67%) specimens were sourced from GP surgeries, with the remaining third of specimens from outpatients. The median age for all patients included in the study was 63.6 years, while the mean age for GP and outpatient specimens was 61.5 and 54.2 years, respectively. A two-sample Wilcoxon rank-sum test confirmed that there was strong evidence of a difference ($p<0.001$) between the ages of GP patients and hospital outpatients.

The total number of hospital laboratories that reported isolates to the surveillance scheme each year increased during the course of the study from 85 to 99. The mean annual number of laboratories reporting per country was 87, 4 and 1.3 for England, Wales and Northern Ireland, respectively. The proportion of isolates for which susceptibility results were available varied by antibiotic (range 41–81%) and was highest for tetracycline (81%) and co-amoxiclav (64%). Susceptibility to tetracyclines or co-amoxiclav was high (96% and 92%, respectively; table 1). The proportion of *S aureus* isolates tested for co-amoxiclav was 10% and the estimated 78% of isolates susceptible to co-amoxiclav should therefore be considered with some caution. As expected all reported MSSA isolates were susceptible. However, there were a small number of MRSA isolates

Table 1 Antimicrobial susceptibility of lower respiratory tract isolates, England, Wales and Northern Ireland (January 2007–March 2010)

		No. of isolates tested (% susceptible)				
	Total isolates	**Tetracyclines**	**Co-amoxiclav**	**Ciprofloxacin**	**Ampicillin/ amoxicillin**	**Macrolides†**
H influenzae	53 895	46 342 (99)	43 685 (93)	27 175 (99)	49 834 (77)	24 583 (15)
S pneumoniae	16 090	12 876 (91)	–*	–	4919 (97)	14 800 (87)
S aureus	16 860	11 070 (94)	1603 (78)	8146 (61)	1047 (23)	15 410 (68)
MSSA	12 440	8131 (95)	1230 (100)	5825 (83)	836 (28)	12 230 (79)
MRSA	3458	2665 (94)	359 (5)	2279 (4)	204 (2)	2970 (24)
Total	**86 845**	**70 288 (96)**	**45 288 (92)**	**35 321 (90)**	**55 800 (77)**	**54 793 (49)**

*If benzyl-penicillin is used as a proxy for co-amoxiclav, susceptibility is 95% (based on 13 243 isolates tested).
†Combined susceptibility results for azithromycin, erythromycin and clarithromycin.
MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

that were reported as susceptible to co-amoxiclav, which is likely to be a reporting or testing artefact. In contrast, reports for tetracycline susceptibility in *S aureus* were robust (66% of isolates were tested) and there was little variation in susceptibility between MSSA (95%) and MRSA (94%). The overall susceptibility of isolates to ciprofloxacin (90%—excluding *S pneumoniae* isolates), ampicillin/amoxicillin (77%) and macrolides (49%) was markedly lower than for tetracyclines or co-amoxiclav.

Co-amoxiclav susceptibility of *S pneumoniae* was estimated using benzyl-penicillin as a surrogate as pneumococcal isolates are not routinely tested for co-amoxiclav susceptibility and numbers were therefore low. Of the 16 090 isolates tested for either penicillin or co-amoxiclav, a total of 1131 (7%) isolates were tested for both antibiotics and, of these, 17 were reported as penicillin resistant but co-amoxiclav susceptible, 1100 had dual susceptibility and the remaining 14 were resistant to both antibiotics. There were no reports of isolates susceptible to penicillin but resistant to co-amoxiclav. It should be noted that >50% of the co-amoxiclav susceptibility data available for *S pneumoniae* were reported by just three laboratories and may therefore not be representative of all sites. However, these

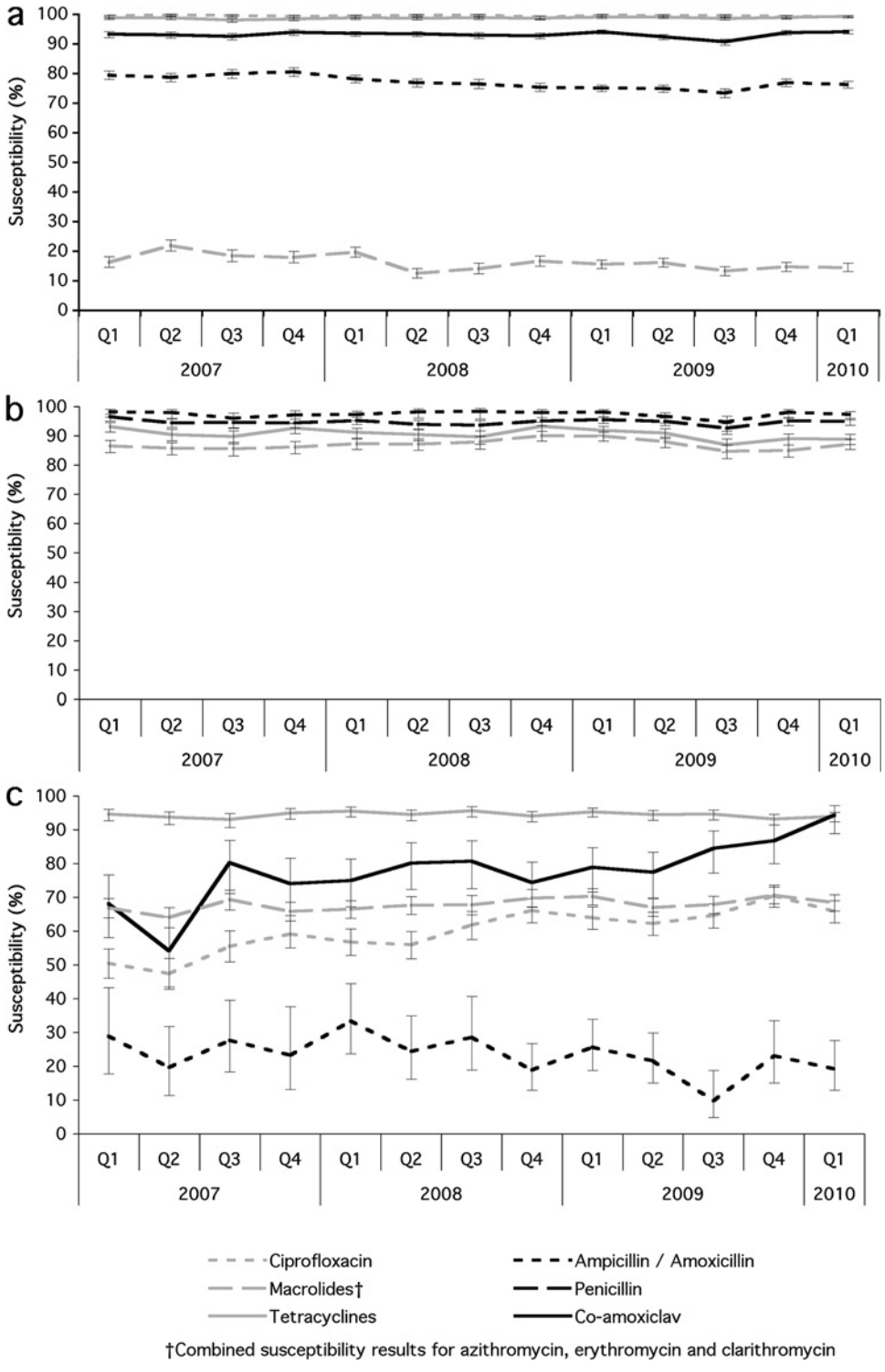

Figure 1 Percentage susceptibility of *H influenzae* (A), *S pneumoniae* (B) and *S aureus* (C) from lower respiratory tract isolates from patients seen by general practitioners and in outpatients between January 2007 and March 2010.

results suggest that pneumococcal susceptibility to co-amoxiclav may be closer to 99% than the 95% estimate based on penicillin susceptibility.

Changes in susceptibility over time

The percentage susceptibility of each of the three organisms to the antibiotics tested is shown in figure 1A–C. In general, changes in susceptibility over time were small. However, *S aureus* susceptibility to co-amoxiclav in the second quarter of 2007 dipped due to a peak in the relative proportion of MRSA to MSSA (ratio of 1:1.1 for 2007 quarter 2 compared with a mean ratio for the whole time period of 1:3.4) and also reflects the small number of isolates tested for this quarter (n=85).

Table 2 outlines IRRs for the annual rate of susceptibility change for each antibiotic investigated accounting for seasonal variation and other important confounders such as patient age group, sex and source. The results suggest that susceptibility to tetracycline, co-amoxiclav and ciprofloxacin has remained relatively constant for all organisms except *S aureus*, for which the estimated 9% annual increase in susceptibility to co-amoxiclav and ciprofloxacin is most likely to be driven by the decreasing proportion of MRSA relative to MSSA; the IRR for methicillin susceptibility in *S aureus* was 1.04 (1.03 to 1.04 p<0.001) after adjusting for patient age, sex, organism, year, quarter, source and laboratory region.

The susceptibility of isolates to ampicillin/amoxicillin (figure 1A–C and table 2) declined at a rate of 2% per year for all organisms during the study period (IRR 0.98, p<0.0001) and there was no evidence to suggest that this trend differed between the three organisms investigated (interaction parameter p value=0.707). There was an estimated annual decrease of 10% in *H influenzae* susceptibility to macrolides during the study period.

Changes in susceptibility by age group

Table 3 outlines susceptibility data by patient age group. Where differences in susceptibility between age groups were identified the trend was generally towards decreased susceptibility with increasing age.

Adjusted IRRs for antimicrobial susceptibility by patient age are outlined in full as a supplementary table online. There was no evidence of a difference in the susceptibility of organisms to either penicillin (p=0.751) or ampicillin/amoxicillin (p=0.500) after adjusting for annual and seasonal variation, patient sex, isolate source and laboratory region. However, there was some evidence that susceptibility to tetracyclines differed between age groups (p=0.018) and that this difference was greatest for *S pneumoniae* after adjusting for other relevant factors.

Co-amoxiclav susceptibility varied between age groups (p<0.0001) and was lower in *S aureus* isolated from older patients. The reported decrease in *S aureus* susceptibility to co-amoxiclav with increasing age (p<0.001) is likely to be due to the high proportion of MRSA in elderly patients as this trend is not mirrored separately for either MSSA or MRSA (p=0.839). Ciprofloxacin susceptibility varied (p<0.0001) and for isolates of *S aureus* decreased from an IRR of 0.68 in patients aged <45 years to 0.46 in those aged 75+ years. There was strong evidence of variation in macrolide susceptibility between age groups (p<0.0001), and adjusted IRRs decreased with increasing age for all organisms, although it should be noted that *S aureus* isolated from the youngest age group did not fit this trend.

Changes in susceptibility by reporting region

There was a small (generally ±5%) but significant (p<0.001) difference in susceptibly between geographical regions for all antibiotics. However, it should be noted that the number of LRT isolates reported by each region varied markedly (range, 201 to 22 810 isolates; median, 6370).

Results from the multivariable analysis suggest that the North East and London generally had lower levels of susceptibility than other regions once factors such as isolate source, patient age and sex, and pathogen had been accounted for. However, in the case of

Table 2 Adjusted incident rate ratios (IRRs) for the annual rate of susceptibility change in lower respiratory tract isolates of *H influenzae*, *S aureus* and *S pneumoniae* in England, Wales and Northern Ireland (January 2007–March 2010)

		Annual rate of susceptibility change		
Antibiotic	**Organism**	**IRR† 95% CIs**	**Likelihood ratio test p value**	**No. of observations**
Ampicillin/amoxacillin *Adjusted for age group and sex	All organisms	0.98 (0.98 to 0.99)	<0.0001§	55 176
Tetracyclines *Adjusted for source and sex	*H influenzae* *S aureus* *S pneumoniae*	1.00 (1.00 to 1.00) 1.00 (0.99 to 1.00) 0.99 (0.98 to 1.00)	<0.0001	69 913
Co-amoxiclav *Adjusted for age group and sex	*H influenzae* *S aureus*† *S pneumoniae*	1.00 (1.00 to 1.00) 1.09 (1.06 to 1.12) 1.00 (0.99 to 1.00)	<0.0001	57 895
Ciprofloxacin *Adjusted for age group, source and sex	*H influenzae* *S aureus* *S pneumoniae*	1.00 (1.00 to 1.00) 1.09 (1.07 to 1.11) –	<0.0001	34 799
Macrolides ‡*Adjusted for age group and source	*H influenzae* *S aureus* *S pneumoniae*	0.90 (0.87 to 0.92) 1.01 (1.00 to 1.02) 1.00 (0.99 to 1.00)	<0.0001	53 934

*IRRs estimated using Poisson regression models with robust standard error. All models were adjusted for seasonal variation (calendar quarter) and laboratory region as well as age group, sex and isolate source where indicated.
†Benzyl-penicillin used as a proxy for co-amoxiclav.
‡Combined susceptibility results for azithromycin, erythromycin and clarithromycin.
§Likelihood ratio test p value refers to the significant trend across all organisms rather than for the interaction. All the other p values outlined in the table refer to the interaction between organism and year.

Table 3 Antimicrobial susceptibility of lower respiratory tract isolates by organism and age group, England, Wales and Northern Ireland (January 2007–March 2010)

			Tested (%S)				
	Age (years)	**Total isolates**	**Tetracyclines**	**Co-amoxiclav**	**Ciprofloxacin**	**Ampicillin/amoxicillin**	**Macrolides**
H influenzae	<45	9658	7573 (99)	7461 (94)	4510 (99)	8432 (80)	4623 (18)
	45–64	18 068	15 864 (99)	14782 (93)	9150 (99)	16 868 (77)	8078 (16)
	65–74	15 160	13 228 (98)	12458 (93)	7852 (99)	14 292 (76)	6825 (15)
	75+	10 663	9363 (99)	8682 (93)	5424 (99)	9921 (74)	4765 (14)
	Unknown	346	314 (98)	302 (92)	239 (98)	321 (79)	292 (20)
	Total	**53 895**	**46 342 (99)**	**43 685 (93)**	**27 175 (99)**	**49834 (77)**	**24 583 (15)**
			Tested (%S)				
	Age (years)	**Total isolates**	**Tetracyclines**	**Penicillin***	**Ciprofloxacin**	**Ampicillin/amoxicillin**	**Macrolides**
S pneumoniae	<45	2931	2218 (92)	2459 (96)	–	857 (99)	2709 (90)
	45–64	5730	4618 (90)	4778 (95)	–	1806 (98)	5288 (87)
	65–74	4298	3506 (90)	3506 (94)	–	1340 (97)	3920 (86)
	75+	3008	2426 (91)	2460 (94)	–	899 (96)	2767 (86)
	Unknown	123	108 (90)	40 (93)	–	17 (100)	116 (85)
	Total	**16 090**	**12 876 (91)**	**13 243 (95)**	–	**4919 (97)**	**13 243 (95)**
			Tested (%S)				
	Age (years)	**Total isolates**	**Tetracyclines**	**Co-amoxiclav**	**Ciprofloxacin**	**Ampicillin/amoxicillin**	**Macrolides**
S aureus	<45	5618	3307 (94)	487 (89)	2916 (67)	229 (33)	5177 (65)
	45–64	4403	3009 (94)	431 (80)	1969 (66)	289 (23)	4027 (73)
	65–74	3369	2381 (95)	351 (72)	1533 (60)	258 (20)	3073 (72)
	75+	3381	2298 (94)	325 (67)	1654 (44)	264 (17)	3051 (63)
	unknown	89	75 (97)	9 (67)	74 (61)	7 (29)	82 (67)
	Total	**16 860**	**11 070 (94)**	**1603 (78)**	**8146 (61)**	**1047 (23)**	**15 410 (68)**
			Tested (%S)				
	Age (years)	**Total isolates**	**Tetracyclines**	**Co-amoxiclav**	**Ciprofloxacin**	**Ampicillin/amoxicillin**	**Macrolides**
MRSA	<45	652	441 (96)	54 (4)	432 (9)	16 (0)	512 (20)
	45–64	851	660 (92)	91 (7)	554 (6)	52 (4)	740 (24)
	65–74	780	618 (94)	101 (6)	494 (3)	60 (0)	686 (28)
	75+	1151	930 (93)	109 (4)	782 (1)	73 (3)	1013 (22)
	unknown	24	16 (94)	4 (25)	17 (0)	3 (0)	19 (26)
	Total	**3458**	**2665 (94)**	**359 (5)**	**2279 (4)**	**204 (2)**	**2970 (24)**
			Tested (%S)				
	Age (years)	**Total isolates**	**Tetracyclines**	**Co-amoxiclav**	**Ciprofloxacin**	**Ampicillin/amoxicillin**	**Macrolides**
MSSA	<45	4668	2793 (94)	429 (100)	2462 (77)	210 (34)	4604 (70)
	45–64	3306	2279 (95)	339 (99)	1410 (91)	237 (27)	3236 (84)
	65–74	2367	1685 (95)	247 (99)	1033 (87)	198 (26)	2330 (85)
	75+	2035	1315 (95)	210 (100)	863 (84)	187 (22)	1997 (84)
	Unknown	64	59 (98)	5 (100)	57 (79)	4 (50)	63 (79)
	Total	**12 440**	**8131 (95)**	**1230 (100)**	**5825 (83)**	**836 (28)**	**12 230 (79)**

*Benzyl-penicillin used as a proxy for co-amoxiclav.
MRSA, methicillin-resistant *Staphylococcus aureus*; MSSA, methicillin-susceptible *Staphylococcus aureus*.

the North East region, lower susceptibility is likely to be a reflection of the low number of reports and potential reporting bias. The East Midlands region generally had higher levels of susceptibility in comparison with all other regions.

DISCUSSION

The 2007 guidelines identify *H influenzae*, *S pneumoniae* and *S aureus* as the major bacterial pathogens for influenza-associated pneumonia. In order to test the evidence base for these guidelines, this study has focused on assessing the antimicrobial susceptibility profiles of these organisms. The data reported here support the *in vitro* efficacy of doxycycline or co-amoxiclav against these three pathogens. Moreover the antimicrobial susceptibility profiles of *H influenzae*, *S pneumoniae* and *S aureus* obtained showed little change over time. In addition, there was little variation either geographically or between age groups for susceptibly to tetracyclines or co-amoxiclav. The validity of these data are supported by the National External Quality Assurance Scheme susceptibility testing results from UK laboratories, which show that the sensitivity of detection of resistance to tetracycline or co-amoxiclav/penicillin in these three organisms was 95–100% in 2007–2008 (personal communication V James, UK NEQAS Organiser).

LabBase is a good source of microbiological data, with comparison of MRSA bloodstream data reported to this voluntary system and to the mandatory reporting scheme indicating that up to 70% of infections in England may be captured.[10] However, clinical data are not captured and, as the data reported represent a sample of all LRT isolates sent to microbiology from primary care and outpatients, it is therefore not possible to determine whether the isolates reported in this study were from

patients with ILI-associated pneumonia. The mean GP patient age of 61 years was similar to the 66 year mean age reported for diagnosis of chronic obstructive pulmonary disease (COPD) by UK GPs between 1990 and 1997.[11] The GP patient specimens included could therefore reflect the organisms associated with LRT infection in chronic lung disease. Nonetheless, these data clearly indicate that LRT isolates of the pathogens studied retain high levels of susceptibility to the antibiotics recommended in the UK guidelines.

Much GP prescribing for LRT infection is empirical, and isolates referred for laboratory testing are likely to be from patients where treatment failure has occurred or who have received prior courses of antibiotics for chronic respiratory conditions, and are therefore enriched for organisms resistant to treatment.[12 13] Thus the 92% and 96% of primary care LRT isolates found to be susceptible to co-amoxiclav or tetracycline (respectively) may well be a conservative estimate, with real susceptibility rates in the ILI-associated pneumonia population being higher. The proportion of MRSA LRT isolates reported via the scheme may also be overestimated in comparison with *H influenzae* or *S pneumoniae* because this organism is more frequently associated with more severe disease presentation,[14] thereby increasing the likelihood that an LRT specimen will be taken.

Susceptibility to ampicillin/amoxicillin and macrolides was well below that recorded for tetracyclines or co-amoxiclav, suggesting that the former drugs are less appropriate for empirical treatment. However, susceptibility to ciprofloxacin for *H influenzae* or ampicillin/amoxicillin for *S pneumoniae* was high (>95%) and these antibiotics may be preferable to tetracyclines or co-amoxiclav where the organism is known. The observed decrease in susceptibility of *H influenzae* to ampicillin/amoxicillin from ~80% at the start of the study period to 76% in the first 3 months of 2010 is supported by work from Jansen *et al*, who noted a similar decrease between 1997/8 and 2004/5 in a range of countries across Europe.[15] The British Society for Antimicrobial Chemotherapy (BSAC) also report a similar decline in *H influenzae* susceptibility to either ampicillin or amoxicillin (84.6% and 77.2% susceptible, respectively, for the whole time period) between October 1999 and April 2007 in community-acquired respiratory infections in the UK and Ireland.[16] During the study period (January 2007–March 2010) there were no changes in susceptibility that should cause clinicians to alter their prescribing behaviour away from the 2007 guidelines and 2009 update. The observed decrease in ampicillin/amoxicillin susceptibility and increased *S aureus* susceptibility to ciprofloxacin are for antibiotics already known to have suboptimal activity against the organisms associated with secondary bacterial infection following ILI.

A weakness of the current study is that other organisms may also cause ILI-associated pneumonia.[3 17–19] *Streptococcus pyogenes* is a particularly important respiratory pathogen which is not covered by the 2007 guidelines.[20] The surveillance programme described here is being expanded to include *S pyogenes*. Current rates of antimicrobial resistance in invasive *S pyogenes* infection are 11% for tetracycline, while penicillin (a proxy for co-amoxiclav) resistance remains very rare[21] and suggests that these antibiotics are likely to be appropriate for LRT infections presenting in primary care, although further work is required to confirm this recommendation. It should also be noted that the number of laboratories in Wales and Northern Ireland that reported isolates during the study period is very low and the data presented in this study may therefore better reflect susceptibility trends in England. The HPA is working to improve the ascertainment of LRT isolates from regions with inadequate reporting coverage. These changes should help better capture the true scale of LRT infections across regions in England, Wales and Northern Ireland.

The high *in vitro* susceptibility of LRT isolates of *H influenzae, S pneumoniae* and *S aureus* to co-amoxiclav or tetracycline strongly supports the use of these antibiotics for empirical treatment of influenza-related pneumonia in a primary care setting. The susceptibility trends for each organism have remained fairly stable over time and spatially, with little variation between patient age group, thereby making any new changes easier to identify. The ongoing and improved reporting of LRT isolates will ensure that robust surveillance continues to inform national empirical treatment in the event that susceptibility patterns change.

What is already known on this topic

Secondary bacterial pneumonia may be a complication of influenza. Published guidelines for the clinical management of influenza-like illness (ILI) in the UK recommend doxycycline or co-amoxiclav for the empirical treatment of ILI-associated pneumonia for patients in primary care.

What this study adds

This study discusses current susceptibility data for lower respiratory tract isolates of *Streptococcus pneumoniae*, *Staphylococcus aureus* and *Haemophilus influenzae* from hospital outpatients and GP patients in England, Wales and Northern Ireland. The results support the use of a tetracycline (doxycycline) or co-amoxiclav for the empirical treatment of secondary pneumonia in a primary care setting. There was little variation of clinical significance in antimicrobial susceptibility to tetracycline or co-amoxiclav over time, between patient age groups or geographically.

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Competing interests None.

Ethical approval The HPA has National Information Governance Board for Health and Social Care approval for the collation of surveillance data in accordance with section 251 of the NHS Act 2006. No additional ethical approval was required to undertake this study.

Contributors All authors made critical contributions either to the conception of the LRT surveillance scheme or for the analysis and interpretation of the data. All authors have helped draft and revise the article and have approved the final version. The guarantor is APJ.

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