

Results from the Survey of Antibiotic Resistance (SOAR) 2002–09 in Turkey

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Objectives: To investigate changes in antibiotic susceptibility of *Streptococcus pneumoniae* and *Haemophilus influenzae* from the Survey of Antibiotic Resistance (SOAR) in community-acquired respiratory tract infections (CA-RTIs) between 2002 and 2009 in Turkey.

Methods: Previously published SOAR data were used for this analysis. MICs were determined using Etest[®] gradient strips or disc diffusion. Susceptibility against a range of antimicrobial agents was assessed using CLSI breakpoints.

Results: A total of 900 *S. pneumoniae* isolates were analysed: 2002–03 ($n=75$), 2004–05 ($n=301$) and 2007–09 ($n=524$). Four antibiotics were tested consistently throughout and three showed a statistically significant decrease in susceptibility ($P<0.0001$): penicillin (74.7% susceptible in 2002–03; 67.8% in 2004–05; and 47.2% in 2007–09); cefaclor (85.3% in 2002–03; 78.7% in 2004–05; and 53.5% in 2007–09) and clarithromycin (85.3% in 2002–03; 82.7% in 2004–05; and 61.9% in 2007–09). Susceptibility to amoxicillin/clavulanic acid did not significantly change (100% in 2002–03; 98.7% in 2004–05; and 97.7% in 2007–09). A total of 930 *H. influenzae* isolates were analysed: 2002–03 ($n=133$), 2004–05 ($n=379$) and 2007–09 ($n=418$). Four antibiotics were also consistently tested: ampicillin, amoxicillin/clavulanic acid, clarithromycin and cefaclor. All showed >90% susceptibility, but only cefaclor susceptibility significantly reduced ($P<0.0001$) over time (99.2% in 2002–03; 96.3% in 2004–05; and 90.4% in 2007–09).

Conclusions: In *S. pneumoniae* from Turkey, there has been a clear statistically significant reduction in susceptibility to key antibiotics since 2002, but not to amoxicillin/clavulanic acid (or amoxicillin). However, susceptibility in *H. influenzae* remained stable. Continued surveillance is required to monitor future changes in antibiotic susceptibility for CA-RTI bacteria.

Introduction

Community-acquired respiratory tract infections (CA-RTIs) such as otitis media (a complication of upper respiratory tract infection), rhinosinusitis and pneumonia are one of the most common human diseases. They constitute a major health problem and are associated with tremendous personal, social and economic burden worldwide. These infections not only cause serious illness, pain and discomfort, but can also progress to chronic forms that are often associated with serious complications causing severe morbidity and mortality.^{1–3} The complications and sequelae of otitis media are also important causes of preventable, irreversible hearing impairment in children.³ Morbidity and mortality rates of

all CA-RTIs are especially high in young children, the elderly and immunocompromised patients.

Otitis media is a leading cause of healthcare visits and antibiotic prescriptions.⁴ Some 70%–80% of healthy children have been reported to have at least one episode of otitis media during the first 3 years of life and 40% will have six or more recurrences.⁵ Globally, the acute otitis media incidence rate is estimated to be ~11% (equivalent to 709 million cases each year) with the majority of these occurring in children <5 years of age.³ Similarly, the incidence of chronic suppurative otitis media is estimated to be 4.8% (equivalent to 31 million cases) with 22.6% of cases occurring annually in those <5 years old.³ Otitis media-related hearing impairment has a prevalence of 30.8 per 10000.³ The WHO

estimates that 28 000 deaths every year are attributable to complications of otitis media.⁶

Acute rhinosinusitis is defined as an inflammation of the mucosal lining of the nasal passage and paranasal sinuses lasting up to 4 weeks.⁷ In one study, nearly one in seven (13.4%) of all non-institutionalized adults were diagnosed with rhinosinusitis within the previous 12 months.⁸

Streptococcus pneumoniae and *Haemophilus influenzae* are the two most important bacterial pathogens associated with CA-RTIs.^{9,10} CA-RTIs are a common cause of mortality and one of the main reasons for physician visits.¹¹ As with many bacterial infections, treatment of CA-RTIs is empirical; therefore, it is vitally important to have a clear understanding of local antimicrobial susceptibility data.

In order to combat antimicrobial resistance, prevention of excessive and inappropriate use of antibiotics is essential. An accurate clinical diagnosis and establishing a bacterial aetiology are essential to administering the right antibiotic at the right dose at the appropriate intervals. Many guidelines are available to aid the correct diagnosis of CA-RTIs and to identify which antibiotic is indicated.¹² Practically and ethically, it is not possible to culture and identify the microorganism in each case by performing sinus puncture; therefore, the choice of antimicrobial therapy in CA-RTIs is usually empirical. Hence, current local antibiotic susceptibility data are required or, if they are not available, regional or global data regarding the causative agents of CA-RTIs and their resistance profile are necessary in order to choose the right antimicrobial regimen. The prevalence of antibiotic resistance can vary from country to country even within the same geographical area. For example, data from the ECDC for 2012 show 73.0% penicillin susceptibility [using the CLSI (formerly NCCLS) oral susceptible breakpoint of 0.06 mg/L] in pneumococci from Spain, 76.6% penicillin susceptibility in France, 87.9% in Italy and 91.6% in Portugal.¹³ In addition, antibiotic resistance can change over time. As seen among CA-RTI pathogens, the general perception of antibiotic susceptibility is its inevitable decrease, as seen with penicillin susceptibility in *S. pneumoniae* from the USA (breakpoint 0.06 mg/L), which decreased from 71.6% in 1998 to 56.3% in 2011.¹⁴ However, this is not always the case, as demonstrated in Portugal where penicillin susceptibility decreased between 1989 and 1999 (to the lowest point of 75% susceptibility) and then increased to 82% in 2007.¹⁵ This increased susceptibility trend was statistically significant.¹⁵ A similar phenomenon has also been observed in Spain where only 40% of pneumococci were penicillin susceptible (using the CLSI parenteral susceptible breakpoint of 2 mg/L) in 1996–97, but susceptibility was 71.1% in 2006–07.¹⁶ Susceptibility to ampicillin in *H. influenzae* from Portugal was relatively stable (~90%) over this time period,¹⁵ whereas susceptibility increased in Spain (from 63.4% in 1996–97 to 83.9% in 2006–07).¹⁶ Therefore, there are both temporal and geographical differences in antibiotic susceptibility for CA-RTI pathogens. In this review, we have compared antibiotic resistance rates in *S. pneumoniae* and *H. influenzae* from Turkey between 2002–03, 2004–05 and 2007–09. This analysis was compiled from data presented for the Survey of Antibiotic Resistance (SOAR) in CA-RTIs in Turkey.^{17–19}

Materials and methods

Collaborating centres

The following six centres took part in the study during the following time periods.

SOAR 2002–03: Istanbul University, Istanbul; and Ege University, Izmir.

SOAR 2004–05: Hacettepe University, Ankara; Ege University, Izmir; Marmara University, Istanbul; Istanbul University, Istanbul; Karadeniz Technical University, Trabzon; and Akdeniz University, Antalya.

SOAR 2007–09: Hacettepe University, Ankara; Ege University, Izmir; Marmara University, Istanbul; Karadeniz Technical University, Trabzon; and Istanbul University, Istanbul.

Clinical isolates (from outpatients who attended the university hospitals)

A total of 900 *S. pneumoniae* isolates were analysed: 2002–03 ($n=75$), 2004–05 ($n=301$) and 2007–09 ($n=524$) and a total of 930 *H. influenzae* isolates were analysed: 2002–03 ($n=133$), 2004–05 ($n=379$) and 2007–09 ($n=418$). Isolates of *S. pneumoniae* and *H. influenzae* were obtained from sputum, bronchoalveolar lavage, endotracheal aspirate, middle ear effusion and blood from adult and paediatric patients with clinical indications of CA-RTI using routine clinical collection methods. Organisms were identified using conventional methods (optochin susceptibility/bile solubility for *S. pneumoniae* and X and V factor requirement for *H. influenzae*). Also, automated systems were used where applicable. Duplicate isolates from the same patient were not accepted. The presence of β -lactamase was determined by a chromogenic cephalosporin (nitrocefin) disc method.²⁰

Susceptibility testing

Antibiotic susceptibility testing for all microorganisms was evaluated by Etest[®] except erythromycin, clindamycin, trimethoprim/sulfamethoxazole, tetracycline and chloramphenicol, which were evaluated by disc diffusion. MICs were determined using a gradient strip Etest[®] susceptibility method according to the manufacturer's instructions (bioMérieux, Marcy l'Etoile, France). Disc diffusion susceptibility testing was carried out according to CLSI methodology.^{21,22} All incubations were conducted in a 5% CO₂ atmosphere, except for macrolide Etests where ambient atmosphere was used when evaluated against *S. pneumoniae* during SOAR 2004–05 and against *S. pneumoniae* and *H. influenzae* during SOAR 2007–09. Quality control strains *S. pneumoniae* ATCC 49619, *H. influenzae* ATCC 49247, *H. influenzae* ATCC 49766, *Escherichia coli* ATCC 25922 and *E. coli* ATCC 32518 were included on each day of testing.

Results of susceptibility testing were accepted if the results of the control strains were within published limits. Any Etest[®] MIC results that were between doubling dilutions were rounded up to the next doubling dilution MIC for data analysis. Susceptibility to the study antimicrobials was calculated based on CLSI breakpoints at the time of testing^{23–25} except for macrolides when incubation was made in CO₂. The breakpoints used are shown in Table 1.

The antimicrobials tested were as listed below.

SOAR 2002–03

S. pneumoniae: penicillin, amoxicillin/clavulanic acid, cefaclor, cefprozil, cefuroxime, clarithromycin and azithromycin.

H. influenzae: ampicillin, amoxicillin/clavulanic acid, cefaclor, cefprozil, cefuroxime, clarithromycin and azithromycin.

SOAR 2004–05

S. pneumoniae: penicillin, amoxicillin/clavulanic acid, cefaclor, cefprozil, azithromycin, clarithromycin, erythromycin, clindamycin, trimethoprim/sulfamethoxazole, tetracycline, chloramphenicol and ofloxacin.

H. influenzae: ampicillin, amoxicillin/clavulanic acid, cefaclor, cefprozil, azithromycin, clarithromycin, trimethoprim/sulfamethoxazole, tetracycline, chloramphenicol and ofloxacin.

Table 1. Breakpoints used to determine susceptible (S), intermediate (I) and resistant (R) categories based on CLSI breakpoints at the time of testing^{22–24}

Antimicrobial	CLSI MIC breakpoints (mg/L)					
	<i>S. pneumoniae</i>			<i>H. influenzae</i>		
	S	I	R	S	I	R
Penicillin (oral)	≤0.06	0.12–1	≥2	NT	NT	NT
Ampicillin	NT	NT	NT	≤1	2	≥4
Amoxicillin/clavulanic acid ^a	≤2	4	≥8	≤4	—	≥8
Cefaclor	≤1	2	≥4	≤8	16	≥32
Cefprozil	≤2	4	≥8	≤8	16	≥32
Cefuroxime ^b	≤1	2	≥4	≤4	8	≥16
Ceftriaxone	≤1	2	≥4	NT	NT	NT
Azithromycin (ambient)	≤0.5	1	≥2	≤4	—	—
Azithromycin (CO ₂) ^c	≤4	8	≥16	≤8	—	—
Clarithromycin (ambient)	≤0.25	0.5	≥1	≤8	16	≥32
Clarithromycin (CO ₂) ^c	≤0.5	1	≥2	≤16	32	≥64
Ofloxacin	≤2	4	≥8	NT	NT	NT
Antimicrobial	CLSI zone breakpoints (mm)					
	S	I	R	S	I	R
	≥21	16–20	≤15	NT	NT	NT
Erythromycin	≥19	16–18	≤15	NT	NT	NT
Clindamycin	≥19	16–18	≤15	≥16	11–15	≤10
Trimethoprim/sulfamethoxazole	≥23	19–22	≤18	≥29	26–28	≤25
Tetracycline ^d	≥21	—	≤20	≥29	26–28	≤25
Chloramphenicol						

NT, not tested.

^aAmoxicillin/clavulanic acid was tested at a 2:1 amoxicillin/clavulanic acid ratio; breakpoints are expressed as the amoxicillin component. Although amoxicillin was not tested against *S. pneumoniae*, the percentage susceptibility to amoxicillin and amoxicillin/clavulanic acid is expected to be the same.

^bBreakpoints used are for cefuroxime axetil.

^cbioMérieux Etest[®] breakpoints used for macrolides when incubated in CO₂.

^dTetracycline disc breakpoints for *S. pneumoniae* are those current for the study periods^{22–24} but are lower than CLSI breakpoints issued more recently.

SOAR 2007–09

S. pneumoniae: penicillin, amoxicillin/clavulanic acid, cefuroxime, cefaclor, ceftriaxone, clarithromycin, erythromycin, clindamycin, trimethoprim/sulfamethoxazole, tetracycline, chloramphenicol and ofloxacin.

H. influenzae: ampicillin, amoxicillin/clavulanic acid, cefuroxime, cefaclor, ceftriaxone, clarithromycin, trimethoprim/sulfamethoxazole, tetracycline, chloramphenicol and ofloxacin.

Statistical analysis

Where data were available for all three SOAR study periods (SOAR 2002–03; SOAR 2004–05; and SOAR 2007–09), changes in antibiotic susceptibility were analysed by the Cochran–Armitage test (XLSTAT, Addinsoft, Paris, France). Data are also presented where susceptibility is only available for two time periods, but were not analysed statistically due to an inadequate number of timepoints.

Results

S. pneumoniae

Percentage susceptibilities for the antimicrobials tested against *S. pneumoniae* over the three time periods of analysis are

shown in Figure 1. In 2002–03, 74.7% of pneumococci were susceptible to penicillin, but this decreased to 67.8% in 2004–05 and decreased further to 47.2% by 2007–09. This trend was statistically significant (Table 2).

A similar decrease in activity was also observed for cefaclor and clarithromycin, which was also statistically significant ($P < 0.0001$). In contrast, amoxicillin/clavulanic acid susceptibility (and presumably amoxicillin susceptibility) did not change significantly over the 7 year time period ($P = 0.116$): 100% of isolates were susceptible in 2002–03, 98.7% in 2004–05 and 97.7% in 2007–09 (Table 2). The other antibiotics were not tested over all time periods and thus temporal trends were not evaluated statistically; however, most showed reduced susceptibility over time (Figure 1). The exception was susceptibility to ofloxacin, which increased from 72.1% in 2004–05 to 88.9% in 2007–09 (Figure 1).

H. influenzae

In 2002–03, the prevalence of β -lactamase production was 4.5% ($n = 133$); it was 5.5% ($n = 379$) in 2004–05 and 2.6% ($n = 418$) in 2007–09. This prevalence did not significantly change over the study period ($P = 0.119$).

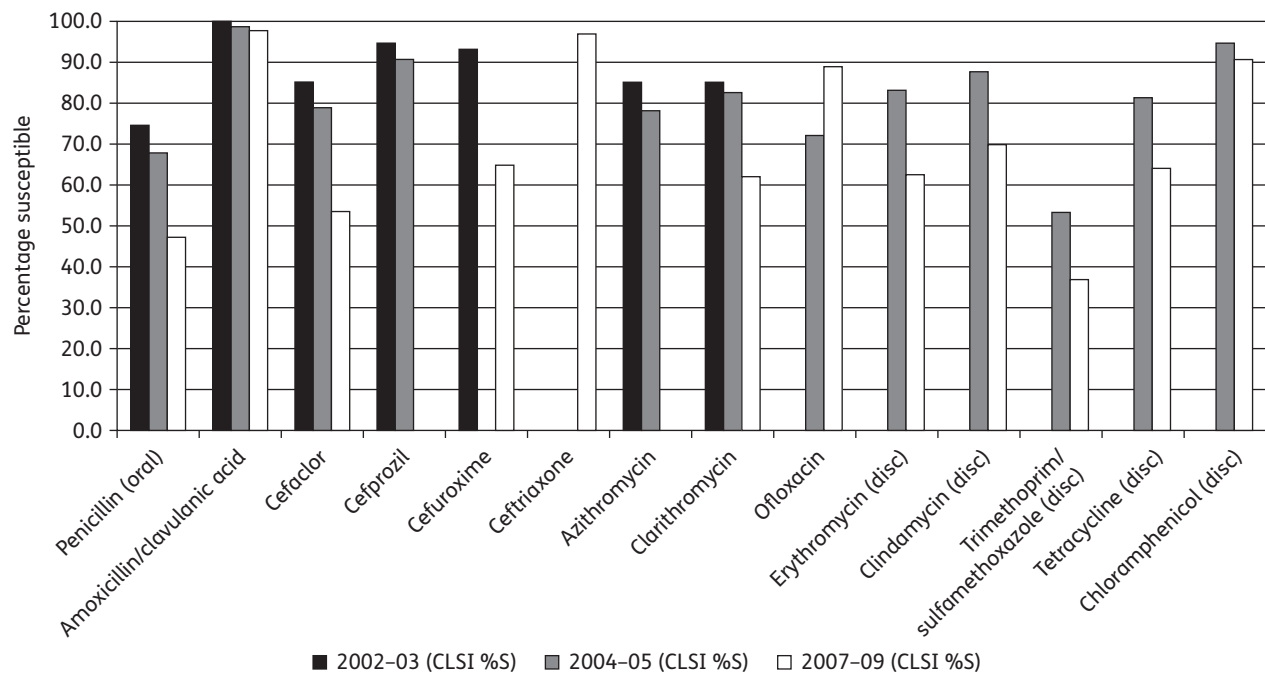


Figure 1. Percentage susceptibility for antimicrobials against *S. pneumoniae* during 2002-03, 2004-05 and 2007-09.

Table 2. Statistical analysis of antimicrobial percentage susceptibility (%S) in *S. pneumoniae*

Antimicrobial	CLSI %S			P value	Conclusion
	2002-03	2004-05	2007-09		
Penicillin (oral)	74.7	67.8	47.2	<0.0001	significant decrease in susceptibility
Amoxicillin/clavulanic acid	100.0	98.7	97.7	0.116	non-significant change in susceptibility
Cefaclor	85.3	78.7	53.5	<0.0001	significant decrease in susceptibility
Clarithromycin ^a	85.3	82.7	61.9	<0.0001	significant decrease in susceptibility

^aClarithromycin data in 2002-03 from Etests incubated in 5% CO₂ and ambient atmosphere in 2004-05 and 2007-09, with differing associated breakpoints used as shown in Table 1.

Between the 2004-05 and 2007-09 study periods in Turkey, the prevalence of β -lactamase-negative ampicillin-resistant (BLNAR) strains was 0.5% and 2.2%, respectively. Based on CLSI guidelines, rare BLNAR strains of *H. influenzae* should be considered resistant to ampicillin/sulbactam, amoxicillin/clavulanic acid, cefaclor, cefamandole, cefetamet, cefonicid, cefprozil, cefuroxime, loracarbef and piperacillin/tazobactam, despite apparent *in vitro* susceptibility of some BLNAR strains to these agents. Therefore, although susceptibility to amoxicillin/clavulanic acid was 100% in 2007-09 according to our susceptibility data, in clinical practice it would be prudent to assume that these BLNAR are non-susceptible to amoxicillin/clavulanic acid (effective susceptibility of 97.8% in 2007-09).

The percentages of isolates of *H. influenzae* susceptible to the antimicrobials tested over the three time periods are shown in Figure 2. The susceptibility to the majority of the test antimicrobials was relatively stable over the 7 year study period. Around 90% or more of the *H. influenzae* isolates were susceptible to all

test antimicrobials over each time period, except for trimethoprim/sulfamethoxazole (76.5% susceptible in 2004-05 and 71.3% in 2007-09) and tetracycline (78.0% susceptible in 2004-05 and 68.9% in 2007-09; Figure 2). Amoxicillin/clavulanic acid was the most active with 100% susceptibility in 2002-03 and 2007-09 and 99.5% susceptibility in 2004-05 (Figure 2 and Table 3). Despite 90.4% susceptibility in 2007-09, cefaclor susceptibility significantly decreased between 2002-03 and 2007-09 with a P value of <0.0001 (Table 3). Ampicillin and clarithromycin did not show significant changes in susceptibility (Table 3).

Discussion

This review analysed susceptibility data for *S. pneumoniae* and *H. influenzae* from the SOAR study for Turkey over three separate study periods: 2002-03, 2004-05 and 2007-09. There are several limitations to this study. In the period 2002-03,

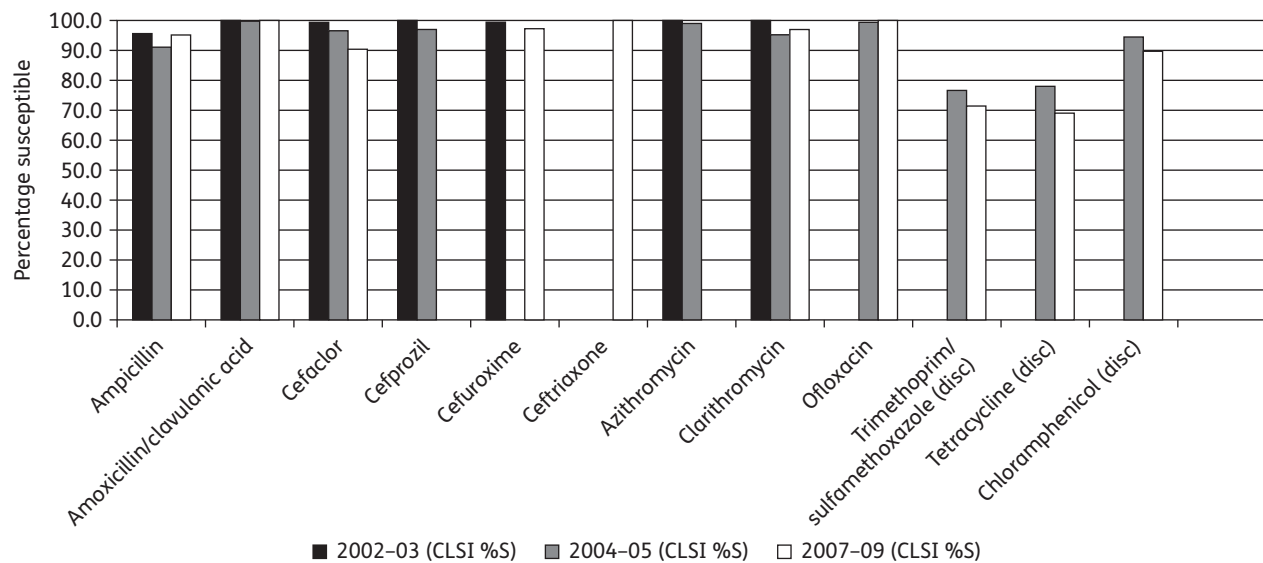


Figure 2. Percentage susceptibility for test drugs against *H. influenzae* during 2002–03, 2004–05 and 2007–09.

Table 3. Statistical analysis of percentage susceptibility (%S) to antimicrobials in *H. influenzae*

Antimicrobial	CLSI %S			P value	Conclusion
	2002–03	2004–05	2007–09		
Ampicillin	95.5	90.8	95.2	0.379	non-significant change in susceptibility
Amoxicillin/clavulanic acid	100.0	99.5 ^a	100.0 ^a	0.539	non-significant change in susceptibility
Cefaclor	99.2	96.3	90.4	<0.0001	significant decrease in susceptibility
Clarithromycin ^b	100.0	95.2	96.7	0.287	non-significant change in susceptibility

^aThe percentage susceptibility of BLNAR was 0.5% (2004–05) and 2.2% (2007–09). Rare BLNAR strains of *H. influenzae* should be considered resistant to amoxicillin/clavulanic acid, despite apparent *in vitro* susceptibility.

^bClarithromycin data in 2002–03 and 2004–05 from Etests incubated in 5% CO₂ and ambient atmosphere in 2007–09, with differing associated break-points used as shown in Table 1.

S. pneumoniae and *H. influenzae* isolates were collected from only two centres and the numbers of isolates were lower than those seen in 2004–05 and 2007–09, respectively. Nevertheless, there are comparisons that can be made between the study periods.

For *S. pneumoniae*, there was a clear and statistically significant temporal trend for reduced susceptibility to penicillin, cefaclor and clarithromycin. Only ~50%–60% of pneumococci were susceptible to these antibiotics in 2007–09 despite susceptibility being around 75% or above in 2002–03. Similar statistically significant decreases in penicillin susceptibility have also been shown for invasive pneumococci from Turkey collected between 2003 and 2005 (87% and 76%, respectively).²⁶ However, in this 2003–05 study, susceptibility to erythromycin was stable at ~90% susceptible.²⁶ In another Turkish study performed in 2005–06, penicillin susceptibility was ~60%,²⁷ which is in keeping with the results presented here for the same time period.

Within the rest of Europe, Antimicrobial Resistance Interactive Database (EARS-Net) data (invasive isolates) indicate either increasing penicillin susceptibility between 2002 and 2012 in Portugal (from 80.4% to 91.6%), Spain (from 66.6% to 73.0%)

and France (from 63.8% to 76.6%) or fairly stable penicillin susceptibility in Italy (88.9% in 2002 to 87.9% in 2012).¹³ Other studies on non-invasive *S. pneumoniae* isolates from Spain and Portugal also confirm an increasing trend in penicillin susceptibility over an earlier time period between the late 1990s to 2007.^{15,16} The same studies also showed an increasing trend for macrolide susceptibility in Spain and Portugal.^{15,16} However, data from EARS-Net showed stable macrolide susceptibility in Spain and Portugal between 2002 and 2012 (~80% and ~75%, respectively).¹³ These countries, therefore, differ quite considerably in their resistance trends, but nevertheless have higher penicillin and macrolide susceptibility levels than Turkey.

Similarly, low susceptibility levels to penicillin and macrolides have been reported in Greece for 2011–12 (63.2% and 71.2%, respectively)¹⁴ and it is tempting to speculate that pneumococcal resistance is widespread in the Mediterranean region. However, a detailed investigation of invasive *S. pneumoniae* between 2003 and 2005 revealed heterogeneity regarding countries in the southern and eastern Mediterranean. For example, Cyprus and Morocco showed relatively high susceptibility to penicillin and

erythromycin overall at 84%–88%,²⁶ whereas isolates from Malta were highly susceptible to penicillin (95%) but less susceptible to macrolides (65%).²⁶ Tunisia, despite being a close neighbour of Morocco, had low susceptibility to penicillin (71%) and erythromycin (66%).²⁶ Antibiotic susceptibility of *S. pneumoniae* was also evaluated from other countries in Africa and the Middle East during 2002–03 in parallel with the data presented here for Turkey. Penicillin susceptibility ranged from 6% in Egypt to 90% in Pakistan¹⁷ and macrolide susceptibility ranged from 54.8% in the United Arab Emirates to 98% in Egypt.¹⁷

Elsewhere, susceptibility data for non-invasive strains from the USA between 1998 and 2011 have also shown a trend of decreasing susceptibility to penicillin and macrolides with susceptibility of 58.5% and 60.6%, respectively, in 2009.¹⁴ This is similar to that observed in the 2009 data from Turkey reported here.

Susceptibility to amoxicillin/clavulanic acid in *S. pneumoniae* from Turkey did not significantly change over time and remained high at 97.7% in 2007–09. Similar levels of amoxicillin/clavulanic acid susceptibility were found in Spain and Portugal between the late 1990s and 2007.^{15,16} However, susceptibility was lower in the USA (81.1% in 2011).¹⁴ Interestingly, CLSI guidelines^{21–25} state that penicillin susceptibility can predict amoxicillin/clavulanic acid susceptibility, but clearly penicillin non-susceptibility does not predict amoxicillin/clavulanic acid (or amoxicillin) non-susceptibility. This warrants further investigation.

Although not evaluated statistically, this decreased susceptibility trend in *S. pneumoniae* from Turkey was also observed for other classes of antimicrobial agent with the exception of fluoroquinolones (ofloxacin), for which susceptibility was seen to increase to 88.9% in 2007–09. High fluoroquinolone (levofloxacin) susceptibility was also observed in Spain (up to 2007), Portugal (up to 2007) and the USA (up to 2011).^{14–16}

Antibiotic resistance in *H. influenzae* remained very stable between 2003 and 2009 in Turkey with a low prevalence of β -lactamases (4.5%) compared with other countries in Africa and the Middle East (evaluated in SOAR 2002–03). Only Pakistan had a lower prevalence (3.2%) while the highest rate was 34.2% in Jordan.¹⁷ Other studies have found higher β -lactamase prevalence than observed in Turkey: Greece 13.8%,²⁸ Portugal 10%–12%¹⁵ and Spain 15.7% in 2006–07. However, the prevalence in Spain during 1996–97 was significantly higher at 25.7%.¹⁶

Only cefaclor showed any significant change in susceptibility between 2002–03 and 2007–09 in *H. influenzae* with a reduction in susceptibility from 99.2% to 90.4%. The least active agents against *H. influenzae* were trimethoprim/sulfamethoxazole (71.3% in 2007–09) and tetracycline (68.9% in 2007–09). A study of *H. influenzae* from Portugal also found susceptibility to trimethoprim/sulfamethoxazole to be the lowest for those antimicrobial agents tested in 2007, at ~86%.¹⁵

Susceptibility to amoxicillin/clavulanic acid in *H. influenzae* remained high at 99.5%–100% from 2002 to 2009 and this high level of susceptibility has also been observed in Portugal,¹⁵ Spain,¹⁶ Greece²⁸ and the USA²⁹ over similar time periods. Inferring amoxicillin/clavulanic acid susceptibility using BLNAR status suggests that in 2007–09, susceptibility may be lower at 97.8% but this can still be considered high.

The data show that there is a worrying trend of reducing antibiotic susceptibility in pneumococci in Turkey with only fluoroquinolones and amoxicillin/clavulanic acid (or amoxicillin)

unaffected. This may relate to very high levels of antibiotic use in Turkey.²⁸ However, high quinolone use is also reported in this country without associated resistance and therefore there may be other factors, such as local clonal spread, associated with these resistance trends.

Conversely, antibiotic susceptibility in *H. influenzae* from Turkey remained very stable between 2002 and 2009 and levels of β -lactamase were low compared with many other parts of Europe. These data are also not consistent with the high antibiotic use in Turkey³⁰ and therefore other factors may be involved. For example, a study in 2002–03 showed that even healthy asymptomatic children in Turkey have high carriage rates of *S. pneumoniae* (23.4%) and *H. influenzae* (15.8%). Of these isolates, 75% of *S. pneumoniae* were penicillin resistant and 86% erythromycin resistant.³¹ High β -lactamase prevalence in *H. influenzae* (20%) was observed.³¹

These data show that continued country-specific surveillance is required in order to fully understand the dynamics of antimicrobial resistance. The SOAR study will continue in Turkey in the future and new data will further assist in the understanding of antimicrobial resistance in this country.

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