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Antibiotic prescribing for respiratory tract complaints in Malta: a 1 year repeated cross-sectional surveillance study

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Objectives: To determine the 1 year antibiotic prescribing patterns by GPs for acute respiratory tract complaints (aRTCs) in Malta.

Methods: In this repeated cross-sectional surveillance study, GPs collected data for patients seen for aRTCs during a designated 1 week period each month, between May 2015 and April 2016. GPs received three text reminders during surveillance weeks and were contacted by phone at most four times during the year. GPs also received 3 monthly individual- and aggregate-level feedback reports on their antibiotic prescribing patterns. Descriptive statistics were used to examine patient, consultation and clinical characteristics, and to describe GPs' prescribing patterns.

Results: Participating GPs (n=33) registered 4641 patients with an aRTC, of whom 2122 (45.7%) received an antibiotic prescription. The majority (99.6%) of antibiotics prescribed were broad-spectrum and the most commonly prescribed antibiotics were macrolides (35.5%), followed by penicillins with a β-lactamase inhibitor (33.2%) and second-generation cephalosporins (14.2%). Specifically, co-amoxiclav (33.2%), clarithromycin (19.6%), azithromycin (15.1%) and cefuroxime axetil (10.9%) represented 78.8% of all antibiotics prescribed. Patients with tonsillar exudate (99.1%), purulent sputum (84%), otorrhoea (78%), tender cervical nodes (74.4%) and fever (73.1%) received most antibiotics. The diagnoses that received the highest proportion of antibiotic treatment were tonsillitis (96.3%), otitis media (92.5%) and bronchitis (87.5%). Wide variation in the choice of antibiotic class by diagnosis was observed.

Conclusions: GP antibiotic prescribing in Malta is high. The abundant use of broad-spectrum antibiotics, particularly macrolides, is of particular concern and indicates that antibiotics are being used inappropriately. Efforts must be made to improve GP awareness of appropriate antibiotic prescribing.

Introduction

Antibacterial medicines, henceforth referred to as antibiotics, revolutionized modern medicine, yet their overuse and misuse have given rise to the global threat of antibiotic resistance (ABR). Antibiotic use is a recognized key driver of ABR, with positive correlations between increased use and the prevalence of ABR.[1,2] Antibiotic overconsumption, in the community specifically, has contributed substantially to the worsening of ABR.[1–3] Antibiotic exposure also has direct repercussions on patients, including alterations to microbiota composition that can lead to further disease, allergies and obesity.[4]

The largest volume of antibiotics is prescribed within primary care,[2] with respiratory tract infections (RTIs) accounting for about 60% of prescriptions.[2,5,6] It has been reported that, within EU countries, 7%–78% of prescriptions are given for RTIs of likely viral aetiology, especially colds, influenza and sore throat.[7] Strategies are therefore needed to promote responsible antibiotic use in this setting. This is particularly essential since RTIs are often self-limiting and do not always necessitate antibiotic treatment, even when caused by bacteria.[8,9]

Decreasing antibiotic prescribing in primary care has been shown to reduce ABR.[3] However, prescribing decisions are often complex and result in wide variations in antibiotic prescribing.[10] Clinical decisions may be further impeded by diagnostic uncertainty, which fuels antibiotic overuse and misuse.[11,12] Since many diagnoses share similar signs and symptoms, and access to diagnostic testing remains limited, GPs risk misdiagnosing RTIs,

misclassifying their aetiology and providing antibiotics inappropriately, erring on the side of caution.[11–13] Perceived patient pressure has also been shown to impact prescribing decisions.[14]

In Malta, antibiotic consumption is high and on the rise.[15] In a 2016 European-wide survey on antimicrobial resistance, Maltese respondents reported the highest antibiotic use within the previous 12 months (48% versus 34% EU average), with 51% of prescriptions given for colds, sore throat and influenza.[7] Since the majority of Maltese antibiotic consumption occurs in the community,[15] it is essential to be able to quantify and describe antibiotic prescribing in primary care to improve antibiotic use. Unfortunately, data on antibiotic prescribing in Maltese primary care is unavailable owing to the lack of electronic prescribing and/or a reimbursement system. Malta is therefore constrained to the use of global data from wholesale distributors to estimate community antibiotic consumption.[15] This does not allow for the depth of analysis necessary to elucidate antibiotic prescribing trends for RTIs. In this study, we sought to determine the 1 year antibiotic prescribing patterns of GPs for acute respiratory tract complaints (aRTCs) in Malta.

Methods

Ethics

Ethics approval was obtained from the University of Malta Research Ethics Committee. The research was conducted in accordance with the Declaration of Helsinki. GPs participated voluntarily and informed consent was obtained. They could drop out at any time, for any reason, without consequence. GP identities were masked using randomly assigned identification codes and no demographic information was disclosed publicly. Furthermore, all patient data collected by GPs was non-identifiable.

Study design and setting

A detailed description of the study design and setting of this repeated cross-sectional surveillance study can be found elsewhere.[16] In brief, Malta is the smallest EU Member State in both size (316 km^2) and population (460 297; 2017 estimate).[17] It is, however, the most densely populated (1450.2 persons/km^2).[17] In Malta, antibiotics are prescription-only medications and more than 90% of antibiotics distributed are procured by private community pharmacies.[15]

This study took place in both public and private healthcare settings. Public services are free at the point of care to Maltese citizens and other residents covered by social insurance.[18] Private services are remunerated on a fee-for-service basis, financed primarily through out-of-pocket payments or voluntary health insurance.[18] Private sector GPs predominantly operate through solo practices within private clinics or pharmacy-based clinics; few work in group practices.[18] Despite associated out-of-pocket costs, private GPs are generally preferred by patients owing to scheduling convenience and better continuity of care.[18] Home visits are still in great demand.

Study participants

All GPs registered on the Malta Medical Council's Specialist Register and GP trainees were invited to participate. Active GPs working either full- or part-time were eligible. Of the 378 registered GPs and 34 GP trainees, 404 (98%) were targeted (Figure S1, available as Supplementary data at *JAC* Online). Eight were excluded at the outset as they were inactive or considered ineligible because they were already involved in project planning.

In November 2014, postal invitations with a 6 week reminder were sent to registered GPs and GP trainees whose contact details were available online. E-mail invitations were also sent via local professional associations and a public invitation was distributed through a local medical professional network called TheSynapse (www.thesynapse.eu). Trainees enrolled in the Specialist Training programme were invited through the Malta College of Family Doctors. Finally, phone calls were made to follow up with as many GPs as possible.

In total, 70 registered GPs and GP trainees responded, of which 35 agreed to participate, 21 declined and 14 were ineligible as they were no longer practising GPs. Prior to surveillance initiation, two registered GPs became ineligible; one transferred to non-clinical work and another stopped working as a GP. Ultimately, 30 GPs and 3 GP trainees participated. GPs exhibited variation across various factors, including locality and sector of practice, years of practice as a GP, age and sex.

Data collection

Surveillance forms, based on tools used in previous research,[19,20] were adapted, piloted and checked for face validity (Figure S2). No major changes were made after pilot testing. GPs collected surveillance data for patients seen for aRTCs during a designated 1 week period, each month, from May 2015 to April 2016, with no substitutions. Forms were completed by GPs during their first consultation with patients of all ages suffering from any aRTC (defined as lower and upper RTIs, allergies and exacerbations of COPD/asthma/bronchitis) and included information on patient and clinical factors, as well as the GP's clinical assessment, diagnosis and prescribed treatment.

Close contact with GPs was maintained throughout data collection. Each surveillance week, GPs received three text messages, including a reminder to prepare for data collection and messages to initiate and conclude it. At the end of each surveillance week, GPs sent all completed surveillance forms to the research team by postal mail in pre-paid envelopes provided to them. Each GP was also contacted by phone at most four times during the year, to address concerns and provide encouragement. Over the year, GPs received 3 monthly individual- and aggregate-level feedback reports on their antibiotic prescribing patterns.

Data analysis

In total, data from 4831 aRTC cases were recorded and inputted in Microsoft® Excel 2010. Following data cleaning, 190 cases were excluded for analysis, resulting in 4641 eligible cases. Descriptive statistics were used to examine patient, consultation and clinical characteristics, and to describe GPs' prescribing patterns. The WHO's 2017 Anatomical Therapeutic Chemical (ATC) classification system was used to classify antibiotics.[21] Antibiotic prescribing indicators were calculated using WHO's manual on investigating drug use[22] and ECDC, European Food Safety Authority and EMA's updated quality indicators for outpatient antibiotic use in Europe.[23] Stata/IC® 13.1 was used for all data management and analyses.

Results

Patient characteristics

Data collection yielded 4831 aRTC cases among 29 510 consultations (16.4%). Of the 4641 aRTC cases considered eligible for analysis, 2462 (53.1%) were female. Median age was 29 years (IQR=12–49), with the highest frequency of cases observed in the 25–44 years age group (n=1312; 28.3%). Smoking was reported in 764 (16.5%) aRTC cases and 963 (20.8%) suffered from comorbidities. The most frequent comorbidities were diseases of the respiratory (n=387; 8.3%) and circulatory (n=323; 7.0%) systems and endocrine, nutritional and metabolic disorders (n=274; 5.9%).

Consultation and clinical characteristics

The majority of aRTC consultations were in January (22.0%). Most patients (*n*=3397; 73.2%) consulted within the first three symptomatic days. The top five reported signs and/or symptoms were sore throat (*n*=2189; 47.2%), rhinorrhoea (*n*=1701; 36.7%), productive cough (*n*=1481; 31.9%), non-productive cough (*n*=1447; 31.2%) and fever (*n*=1363; 29.4%).

Diagnostic tests were seldom performed (*n*=133; 2.9%). A viral aetiology was suspected in 2307 (49.7%) cases, bacterial in 1280 (27.6%) and mixed in 735 (15.8%). The top five reported diagnoses were common cold (*n*=1536; 33.1%), pharyngitis (*n*=743; 16.0%), bronchitis (*n*=570; 12.3%), tonsillitis (*n*=434; 9.4%) and sinusitis (*n*=305; 6.6%). Table 1 depicts the suspected aetiology by diagnosis.

Antibiotic prescription patterns

In total, 2122 (45.7%) aRTC cases received an antibiotic prescription (oral); 1789 (38.5%) were for immediate use and 333 (7.2%) were delayed prescriptions. Few (*n*=51; 1%) solely received instructions to delay antibiotic consumption without being issued a prescription. Antibiotic requests by clients were rarely reported (*n*=76; 2%). However, of those who did request an antibiotic, 51 (67%) received one, 15 (29%) of which were delayed. Of those patients who had taken antibiotics during the previous two weeks (*n*=302), 133 (44.0%) received an antibiotic prescription; 79 (59%) of which were for the same complaint.

Ten (22%) infants under 1 year (*n*=46) and 186 (37.0%) children aged between 1 and 4 years (*n*=503) were prescribed antibiotics. Almost half (*n*=1724; 47.7%) of patients aged over 10 years (*n*=3618) received antibiotics. Notably, 282 (52.7%) patients aged 65 years and older (*n*=535) received antibiotics (Table 2).

The most frequently prescribed antibiotics were macrolides (J01FA) (*n*=757; 35.5%), followed by penicillins with a β-lactamase inhibitor (J01CR) (*n*=709; 33.2%) and second-generation cephalosporins (J01DC) (*n*=302; 14.2%) (Table S1). Specifically, co-amoxiclav (*n*=709; 33.2%), clarithromycin (*n*=419; 19.6%), azithromycin (*n*=322; 15.1%) and cefuroxime axetil (*n*=232; 10.9%) represented 78.8% of all antibiotics prescribed. Eleven cases (1%) received combination prescriptions with antibiotics from two different classes, namely penicillins with a β-lactamase inhibitor combined with macrolides (J01CR & J01FA) (*n*=7) or second-generation cephalosporins combined with macrolides (J01DC & J01FA) (*n*=4). These patients had been diagnosed with pneumonia (*n*=4), bronchitis (*n*=4) or acute exacerbation of COPD/asthma/bronchitis (*n*=3). Table 1 provides an overview of the suspected aetiology and antibiotic prescription patterns by diagnosis.

Patients with tonsillar exudate (*n*=220; 99.1%), purulent sputum (*n*=88; 84%), otorrhoea (*n*=18; 78%), tender cervical nodes (*n*=258; 74.4%) and fever (*n*=997; 73.1%) received most antibiotics (Table 3). Cases with a suspected bacterial aetiology received the greatest proportion of antibiotic treatment (*n*=1213; 94.8%), followed by suspected mixed aetiology (*n*=603; 82.0%). Nonetheless, 268 (11.6%) patients with suspected viral infections received antibiotics, the majority of which were delayed (*n*=231; 86.2%). Delayed prescriptions were less frequently provided to patients with a suspected bacterial (*n*=31; 2.6%) or a suspected mixed infection (*n*=107; 17.7%).

The diagnoses that received the highest proportion of antibiotic treatment were tonsillitis (*n*=418; 96.3%), otitis media (*n*=111; 92.5%) and bronchitis (*n*=499; 87.5%) (Figure 1). Whereas little variation was observed in the monthly class-specific prescription trends, high variation was observed in the choice of class by diagnosis (Figure 2). Notably, co-amoxiclav was the most commonly prescribed antibiotic for most diagnoses, as seen in Table 1. For pneumonia and tracheitis, however, clarithromycin was the first antibiotic of choice (57.0% and 35.3% respectively).

Broad- versus narrow-spectrum antibiotics

The majority (99.6%) of antibiotics prescribed were broad-spectrum (Table S1). The prescribing ratio of broad-spectrum penicillins, cephalosporins, macrolides and fluoroquinolones {J01[CR+DC+DD+(F−FA01)+MA]} to narrow-spectrum penicillins, cephalosporins and macrolides [J01(CA+CE+CF+DB+FA01)] was 33.2.

Discussion

To our knowledge, our study presents the results of the first repeated, cross-sectional surveillance study on the management of aRTCs in Maltese primary care. During the surveillance year, 16.4% of all GP consultations were for aRTC visits, slightly higher than previously reported, although not as high as Irish data which show that 22.6% of patients consulted for respiratory illnesses.[24,25] Similar to previous studies, most GP visits were for sore throat, rhinorrhoea, cough and fever.[14,26]

What is unique about our setting is the haste with which patients consult GPs. Most patients visited within the first three symptomatic days. This type of health-seeking behaviour has similarly been observed in France where antibiotic prescribing is also high.[27] Both French[27] and Maltese patients have quick and direct access to GPs. In low-prescribing contexts, such as the Netherlands and Sweden, patients typically wait at least a week before consulting a doctor.[14,28] At the time of our study, sick leave certificates were required on the first day of illness,[29] further encouraging early consultations. Other high-prescribing countries, such as France and Italy, also require early sick leave certification, whereas low-prescribing countries like Sweden only demand certificates after 1 week of illness.[29] Whilst revision of sick leave policies is being discussed in Malta, it is still up to the employer to decide whether certification is required within the first 3 days. Revision of these policies could help reduce antibiotic overprescribing. Although sick leave certification can be issued by any medical practitioner in Malta, GPs are typically the first point of contact for acute illnesses. Therefore, nationwide campaigns discouraging patients to consult their GPs for simple ailments such as the common cold, as well as informing them about the natural course of infection, are needed.

Quality of antibiotic prescribing

Although Maltese data on antibiotic use in primary care are limited, studies consistently show that Malta is among the highest antibiotic consumers in Europe.[7,15,30] In 2017, ESAC-Net reported that the overall national antibiotic consumption in Malta was 23.4 DDD per 1000 inhabitants per day, which was only marginally above

Table 1. Suspected aetiology and antibiotic prescription patterns for aRTCs by diagnosis

Diagnosis (no. of patients)	Percentage of suspected aetiology and antibiotic prescription (% prescribed antibiotic)			Antibiotic prescription, *n* (%)	Generic name, *n* (%)						
	bacterial	viral	mixed		J01CR02 co-amoxiclav	J01DC02 cefuroxime axetil	J01FA09 clarithromycin	J01FA10 azithromycin	J01MA02 ciprofloxacin	J01MA12 levofloxacin	other J01[a]
Tonsillitis (*n*=429)	79 (98.2)	3 (42.9)	17 (97.3)	418 (96.3)	**213 (51.0)**	58 (13.9)	40 (9.6)	45 (10.8)	3 (0.7)	1 (0.2)	58 (13.9)
Otitis media (*n*=118)	69 (97.6)	8 (55.6)	23 (92.6)	111 (92.5)	**53 (47.7)**	13 (11.7)	12 (10.8)	15 (13.5)	2 (1.8)	0 (0.0)	16 (14.4)
Bronchitis (*n*=562)	60 (94.4)	6 (38.2)	34 (84.7)	499 (87.5)	**134 (26.9)**	29 (5.8)	120 (24.0)	121 (24.2)	7 (1.4)	57 (11.4)	35 (7.0)
Pneumonia (*n*=114)	75 (76.5)	2 (0.0)	24 (77.8)	86 (74.8)	17 (19.8)	4 (4.7)	**49 (57.0)**	2 (2.3)	5 (5.8)	12 (14.0)	1 (1.2)
Sinusitis (*n*=302)	47 (98.6)	29 (12.5)	24 (79.2)	209 (68.5)	**49 (23.4)**	48 (23.0)	31 (14.8)	21 (10.0)	33 (15.8)	5 (2.4)	22 (10.5)
Tracheitis (*n*=50)	32 (93.8)	42 (28.6)	26 (92.3)	34 (66.7)	11 (32.4)	3 (8.8)	**12 (35.3)**	4 (11.8)	1 (2.9)	2 (5.9)	1 (2.9)
Pharyngitis (*n*=737)	25 (97.8)	59 (22.8)	16 (93.2)	392 (52.8)	**109 (27.8)**	46 (11.7)	67 (17.1)	57 (14.5)	22 (5.6)	1 (0.3)	90 (23.0)
Exacerbation[b] (*n*=213)	28 (88.3)	23 (6.0)	48 (60.2)	120 (49.6)	**47 (39.2)**	17 (14.2)	22 (18.3)	15 (12.5)	0 (0.0)	11 (9.2)	11 (9.2)
Influenza (*n*=146)	1 (50.0)	77 (11.6)	22 (90.6)	45 (29.8)	9 (20.0)	1 (2.2)	**21 (46.7)**	7 (15.6)	0 (0.0)	1 (2.2)	6 (13.3)
Allergy (*n*=230)	—	—	—	12 (5.2)	**5 (41.7)**	2 (16.7)	1 (8.3)	4 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)
Common cold (*n*=1527)	1 (77.8)	96 (6.9)	4 (69.0)	149 (9.7)	**54 (36.2)**	9 (6.0)	33 (22.1)	14 (9.4)	0 (0.0)	0 (0.0)	39 (26.2)
Other aRTCs[c] (*n*=100)	22 (66.7)	54 (18.2)	24 (60.0)	28 (28.0)	3 (18.8)	1 (6.3)	7 (43.8)	13 (81.3)	1 (6.3)	2 (12.5)	1 (6.3)
Total, *n* (%)	—	—	—	2103 (45.7)	704 (33.3)	231 (10.9)	415 (19.6)	318 (15.0)	74 (4)	92 (4.4)	280 (13)

Values in bold emphasize the most commonly prescribed antibiotic for that particular diagnosis.
[a]Other J01 includes: J01AA02 doxycycline (<1%), J01CA04 amoxicillin (2.6%), J01DB01 cefalexin (<1%), J01DC04 cefaclor (3.2%), J01DD08 cefixime (2.7%), J01DD13 cefpodoxime (3.0%), J01FA11 miocamycin (<1%), not specified (<1%).
[b]Exacerbation of COPD/asthma/bronchitis.
[c]Including laryngitis, croup, glandular fever etc.

Table 2. Patient age (years) and antibiotic prescription in patients with aRTCs (n=4634)

	Antibiotic/s prescribed, *n* (%)		
Age (years)	yes	no	total
<1	10 (21.7)	36 (78.3)	46 (100.0)
1–4	186 (37.0)	317 (63.0)	503 (100.0)
5–9	201 (43.0)	266 (57.0)	467 (100.0)
10–14	145 (45.4)	174 (54.6)	319 (100.0)
15–18	104 (48.4)	111 (51.6)	215 (100.0)
19–24	198 (46.9)	224 (53.1)	422 (100.0)
25–44	608 (46.3)	704 (53.7)	1312 (100.0)
45–64	387 (47.5)	428 (52.5)	815 (100.0)
≥65	282 (52.7)	253 (47.3)	535 (100.0)
Total	2121 (45.8)	2513 (54.2)	4634 (100.0)

Table 3. Symptom-specific antibiotic prescription in patients with aRTCs

	Antibiotic/s prescribed, *n* (%)		
Symptom	yes	no	total
Tonsillar exudate	220 (99.1)	2 (0.9)	222 (100.0)
Purulent sputum	88 (83.8)	17 (16.2)	105 (100.0)
Otorrhoea	18 (78.3)	5 (21.7)	23 (100.0)
Tender cervical nodes	258 (74.4)	89 (25.6)	347 (100.0)
Fever	997 (73.1)	366 (26.9)	1363 (100.0)
Sibilant rhonchi	183 (65.8)	95 (34.2)	278 (100.0)
Productive cough	956 (64.6)	525 (35.4)	1481 (100.0)
Odynophagia	76 (59.4)	52 (40.6)	128 (100.0)
Otalgia	240 (58.3)	172 (41.7)	412 (100.0)
Hyperpnoea	19 (47.5)	21 (52.5)	40 (100.0)
Dyspnoea	138 (47.3)	154 (52.7)	292 (100.0)
Sore throat	996 (45.5)	1193 (54.5)	2189 (100.0)
Rhinorrhoea	525 (30.9)	1176 (69.1)	1701 (100.0)
Non-productive cough	340 (23.5)	1107 (76.5)	1447 (100.0)
Other[a]	166 (34.2)	319 (65.8)	485 (100.0)

[a]Includes headaches (16.7%), low-grade fever (7.0%), congestion (6.0%), myalgia (5.6%) etc.

the EU average (21.8 DDD per 1000 inhabitants per day).[31] In our study we show that 45.7% of patients received an antibiotic prescription. This closely reflects the findings of the 2016 Eurobarometer survey in which Malta had the highest reported antibiotic consumption in Europe (48% of Maltese people reported taking an antibiotic in the past 12 months, as mentioned earlier).[7] A similar prescription rate of 46.8% has been reported in southern Italy.[32] Southern Mediterranean countries share similar sociocultural characteristics,[12] therefore comparable prescribing rates are expected in such contexts.

General public knowledge on appropriate antibiotic use in Malta has been reported to be lower than in other EU countries.[7] Furthermore, GPs' perceptions of patient expectations for antibiotics have been shown to influence antibiotic prescribing.[14] There is a belief in Malta that patients expect antibiotic prescriptions and quick symptom relief, and that patients tend to believe that a doctor's skills are reflected in his/her prescription rates, although there is little evidence to support this. Indeed, our data and that from other contexts suggest low demand for antibiotics,[11] indicating that GPs may overestimate patient demand. The fact that some patients pay a fee for their visit could influence prescribing decisions.[33] Doctors may feel pressured to prescribe antibiotics to ensure patient satisfaction, avoid losing a regular client and/or reduce the need for reconsultation. However, an antibiotic prescription may not necessarily ensure patient satisfaction; studies have shown that proper communication is considered more important by patients.[34] Delayed prescription has also been shown to successfully reduce antibiotic prescription and consumption; if public awareness of this strategy is good, it has the potential to ensure patient satisfaction,[35] although this should be further investigated in our setting. Our study showed a delayed prescription rate of 7.2%, similar to other European settings.[36] Another possible strategy could be to encourage providing a prescription for symptomatic and analgesic medications so as to meet the expectations of both prescriber and patient. It should address patients' need for a 'quick fix' and fast symptom relief in order to be able to resume work or return to school sooner. Further research to understand how patient expectations in Malta can be met is warranted.

Consistent with similar studies on antibiotic use for RTIs, antibiotic treatment increased with patient age,[14,27,37] with those aged 65 years and older receiving most and children under 5 years receiving least. This difference could be reflective of the Maltese context as children are likely attended by paediatricians who work in separate practices. It could also be attributed to the knowledge that aRTCs in children are often viral and that the elderly suffer from more comorbidities and are therefore more likely to require an antibiotic.

Similar to Belgian prescribers,[38] over 65% of patients with tonsillitis, otitis media, bronchitis and sinusitis were prescribed an antibiotic. Two similar studies carried out in Spain and Sweden also reported high prescription rates for tonsillitis, otitis media and sinusitis, comparable with those in our study, but lower antibiotic prescribing for acute bronchitis.[13,38] There is limited evidence to justify antibiotic use for uncomplicated acute bronchitis, sinusitis and otitis media[39–41] and yet high prescription rates were observed for these conditions. Although consultation incidences and characteristics differ substantially among countries, making comparison difficult, determining the appropriateness of antibiotic prescription by diagnosis requires further investigation, particularly since a high variation in choice of antibiotic class by diagnosis was seen.

This high variability in both suspected aetiology and antibiotic prescribing by diagnosis raises the suspicion that GPs might overestimate the degree to which respiratory infections are bacterial. Rapid diagnostic tests provide guidance for more targeted treatment and have been shown to decrease antibiotic use.[42] Unfortunately they are seldom used in Malta; most GPs do not have access to them and, even if they did, the lack of reimbursement means that this would render an additional cost to the consultation. Diagnostic uncertainty in the management of RTIs results in unverifiable diagnoses and assumptions of aetiology that may lead to unnecessary and inappropriate antibiotic prescribing.[13,43] Malta has a culture of high uncertainty avoidance and, although restricting antibiotic prescription does not pose a

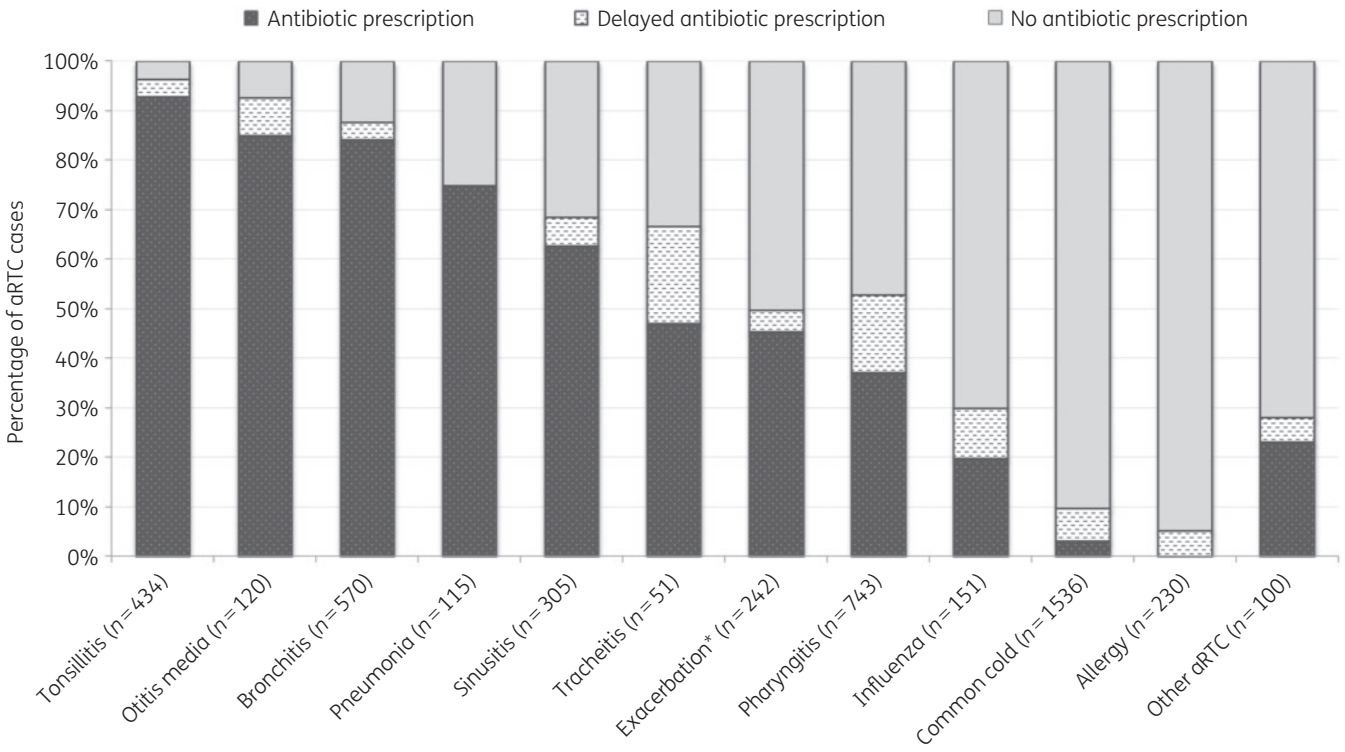

Figure 1. Antibiotic prescription by diagnoses expressed as a percentage of aRTC cases. *Exacerbation of COPD/asthma/bronchitis.

greater risk of complications,[9] prescribing antibiotics just in case can provide a subconscious reassurance of certainty to the GP.[12] It came as no surprise that antibiotics were sometimes prescribed in combinations and that broad-spectrum antibiotics were heavily used.

The continued widespread use of broad-spectrum antibiotics to treat RTIs is consistent with earlier research on antibiotic consumption in Maltese primary care[15] and has been observed in similar southern European contexts, including Spain and Greece.[13,44] Malta has the highest reported ratio of broad- to narrow-spectrum antibiotic use in the EU (22.2 versus 2.3 EU average).[31] Our data shows an even higher ratio of broad- to narrow-spectrum antibiotic use at 33.2. This difference could be explained by the fact that our data are limited to aRTCs only, which contribute largely to the proportion of broad-spectrum antibiotics used in Malta. It could also be a result of sampling bias. Unlike Scandinavian countries such as Sweden, where prescription of the narrow-spectrum antibiotic phenoxymethylpenicillin is common, prescription of phenoxymethylpenicillin in Malta is negligible.[45] In fact, it is currently unavailable in community pharmacies. Although not advised unless there is evidence of resistance, co-amoxiclav is still one of the preferred drugs, prescribed for most diagnoses, similar to Spanish and Irish prescribers.[13,25] Whilst previous reports have consistently indicated that penicillins with a β-lactamase inhibitor are the most frequently prescribed antibiotics in Malta,[15,46] our study shows a preference towards macrolides, as has recently been shown in Greece and the USA.[44,47] Choice of antibiotics varies widely among studies; however, this variability is unlikely explained by differences in the epidemiology of RTIs.

This dependence on broad-spectrum antibiotics in the community is disconcerting, as it has been linked to the development of resistant *Clostridioides* (*Clostridium*) *difficile*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Escherichia coli*, *Haemophilus influenzae* and MRSA.[15] Penicillins with β-lactamase inhibitors, second-generation cephalosporins, broad-spectrum macrolides and fluoroquinolones, in particular, are major drivers of resistance[15] and made up 90% of all antibiotic prescriptions in our study. Given the increasing resistance rates of *E. coli* to fluoroquinolones in Malta, particular efforts should be made to keep prescription of fluoroquinolones for respiratory pathogens low and decrease their use in bronchitis/bronchiolitis, sinusitis and pneumonia. In Europe, there is also increasing concern about the development of macrolide-resistant *S. pyogenes* and high rates have been reported in southern European countries.[48] To this end, stewardship efforts must also specifically target macrolide use. Moreover, although the Maltese national antibiotic guidelines are freely available online, they should be disseminated more proactively. Academic detailing could be one approach whereby focus is placed on discussing specific guideline recommendations, particularly for those diagnoses where the benefits of antibiotic prescription are limited (e.g. uncomplicated bronchitis and sinusitis).

Methodological considerations

Community antibiotic prescribing data from southern European countries are lacking, particularly diagnosis-specific data. This repeated cross-sectional surveillance study is the first of its kind in Malta, to our knowledge. Through easy-to-complete surveillance forms, we were able to acquire robust, diagnosis-specific prescription data, allowing us to determine the proportion of antibiotics prescribed in ambulatory care for RTIs specifically. Furthermore, all data collection tools were adapted from previous studies,

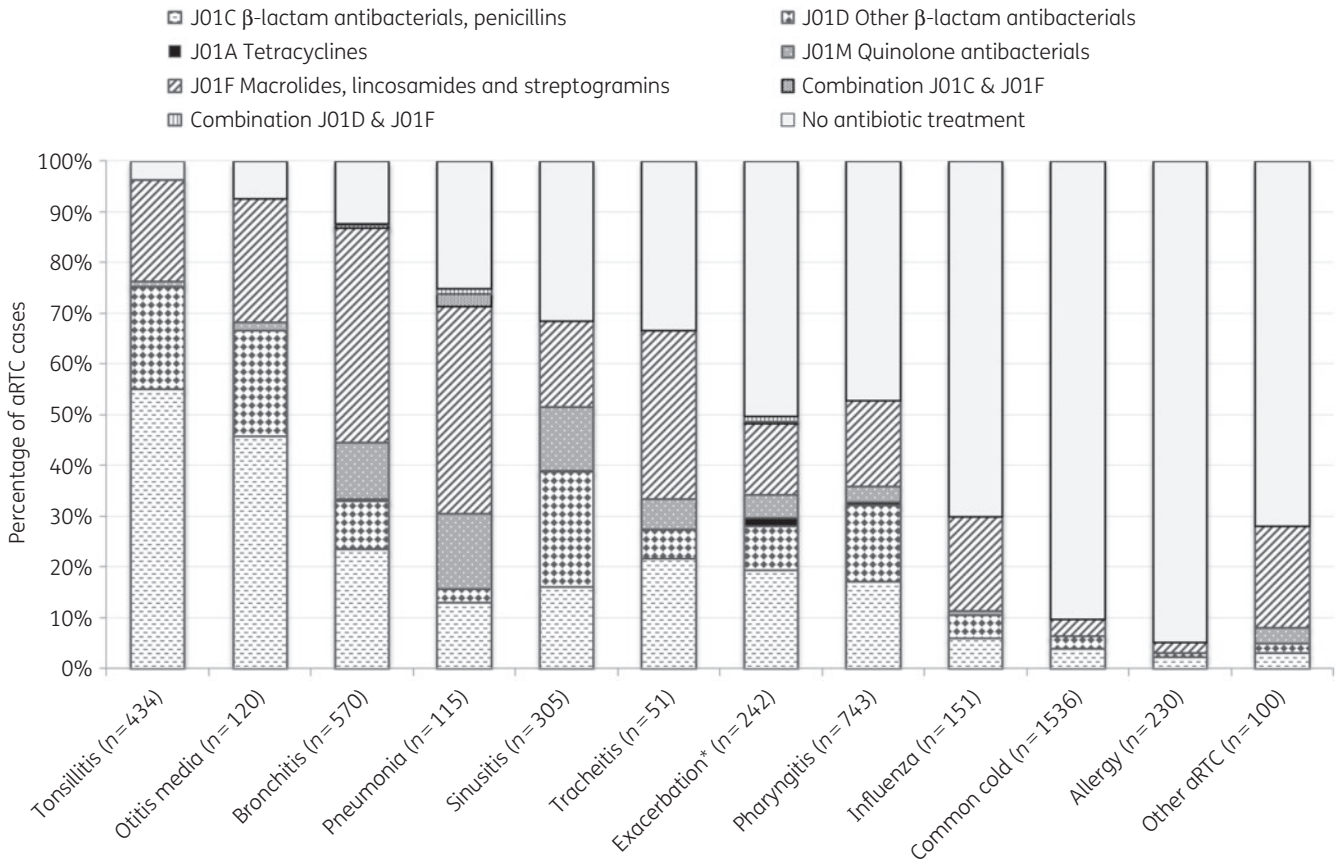

Figure 2. Antibiotic classes prescribed by diagnoses expressed as a percentage of aRTC cases. *Exacerbation of COPD/asthma/bronchitis.

strengthening their validity and allowing for cross-country comparison.

Despite the fact that GPs exhibited variation across factors of interest, the sample may not be representative of all GPs. GPs interested in reducing antibiotic prescribing may have been more likely to partake. The fact that their antibiotic prescribing rates exceed recommendations puts into question what the antibiotic treatment trends are like among non-participants.

Children and the elderly seem underrepresented in our sample, which may be indicative of the fact that children are often seen by paediatricians who are not represented in our study. Elderly persons residing in residential homes, although sometimes captured in our data, are largely lost and underrepresented. It is also possible that they are seen directly at hospital, thereby bypassing primary care.

Although surveillance forms were designed specifically to be quick to complete, in busy clinics, GPs may have underreported data. Similarly, data may have been lost during home visits, where filling in forms may have been considered inconvenient. Since surveillance weeks were static, data were lost for GPs who were unable to report data during the specific week. There is also evidence to suggest that GPs may adjust their diagnosis according to their intention to treat with antibiotics.[11,14,19] Audit and feedback is a behaviour change intervention itself and the fact that GPs were issued 3 monthly feedback reports may have influenced their prescribing practices.[19]

Conclusions

Antibiotics have limited treatment effectiveness for the majority of RTIs and therefore their unrestricted prescription encourages the development of ABR and exposes patients to unnecessary side effects and costs.[1,14] Our study confirms that, in Malta, GP antibiotic prescribing for aRTCs is high and indicates that antibiotics are not being used appropriately. Of particular concern is the abundant use of broad-spectrum antibiotics.

Although altering behaviour is challenging, efforts must be made to improve GPs' awareness of appropriate prescribing by indication and patient group. Stewardship activities should focus on antibiotic use for aRTCs and specifically target overprescribing of broad-spectrum antibiotics, particularly macrolides. Continued prescribing surveillance in the outpatient setting is vital if antibiotic stewardship efforts are to succeed. Sustained audit and feedback with peer comparison could also help improve GPs' prescribing habits.[49]

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Transparency declarations

None to declare.

Supplementary data

Figures S1 and S2, plus Table S1 are available as Supplementary data at *JAC* Online.

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