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Patterns of community antibiotic use with reference to the AWaRe classification of the World Health Organization

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Background: Monitoring consumption through quality indicators and providing feedback is an important activity within programmes for improving antibiotic prescription. This study aims to describe the use of antibiotics for systemic use in community setting in Italy and to compare prescription patterns among regions based on quality prescription indicators to identify any inter-regional variability.

Methods: The 2021 consumption (calculated as DDDs per 1000 inhabitants per day) of antibiotics for systemic use (reimbursed or purchased privately) in community setting were considered. The WHO AWaRe system was used to classify antibiotics into Access, Watch and Reserve groups, using the 60% of prescribed antibiotics belonging to the Access group out of the total DDDs as AWaRe target. The correlation between regional consumption and percentages of DDDs in the Access group was assessed through linear regression. A further indicator 'ratio of broad to narrow-spectrum antibacterials' was also calculated to compare the spectrum of prescribed antibiotics.

Findings: Overall community antibiotic consumption in Italy in 2021 was 15.6 DDDs per 1000 inhabitants per day, with an increasing trend from north (13.0 DDDs) to south (19.5 DDDs) and the percentages of non-reimbursed consumption decreasing from north (33.1%) to south (21.5%). Only three regions out of 21 reached the AWaRe target (regional range 47.4%–62.9%), with a negative correlation between regional consumption and percentages of antibiotics belonging to the Access group (correlation coefficient −0.8; $R^2 = 0.64$; *P* value < 0.001). The 'ratio of broad to narrow-spectrum antibacterials' was 8.5 at national level, with the highest value in the centre (11.0) compared to the south (9.1) and north (7.0).

Conclusion: The percentage of consumption of Access group antibiotics correlates very well with regional consumption in Italy, indicating that regions with higher antibiotics consumption also have worse prescribing patterns with a greater impact on bacterial resistance. Additional data are needed to better describe prescription patterns from an antimicrobial stewardship perspective.

Introduction

Antibiotic consumption monitoring is essential for setting goals and following up activities aimed at optimizing antibiotic use.[1] For this reason, the WHO developed the AWaRe system that classifies antibiotics into three groups: Access (narrower spectrum agents with lower resistance potential), Watch (broader spectrum agents and higher resistance potential) and Reserve (antibiotics of last resort).[1] The WHO's 13th General Program of Work 2019–2023 established a country-level target of at least 60% of antibiotics belonging to the Access group.[1] The AWaRe classification system and related target are widely used in many countries of the world.[2–4]

Italy has a consumption of antibiotics higher than the European average with frequent use of broad-spectrum agents and a strong heterogeneity of consumption between regions.[5–8]

This analysis aims to describe the consumption of antibiotics for systemic use in community setting in Italy in 2021, including the private purchase, by taking in consideration the percentage of antibiotic consumption belonging to the Access group and the ratio of consumption of broad- to narrow-spectrum antibiotics, and to compare prescription patterns among regions.

Methods

The 2021 consumption data for antibiotics reimbursed by the Italian National Health Care Service (NHCS) or purchased privately by patients (i.e. non-reimbursed) were considered. In Italy, all antibiotics for systemic use are reimbursable by NHCS, but sometimes the cost of the antibiotic may be borne by the patients when it is not prescribed using the National Health Care Service form. This happens especially when the antibiotic is prescribed by a private doctor (e.g. dentist) and patient prefers to go directly to the community pharmacy and pay for the medicine rather than go to their general practitioner. The following data sources were used: (i) the OsMed flow for medicines dispensed by community pharmacies and reimbursed by NHCS and (ii) the Drug Traceability flow only for all medicines purchased by community pharmacies regardless the

reimbursement by the NHCS; the private purchase of antibiotics is derived by difference comparing sell-in (i.e. Drug Traceability flow) and sell-out (i.e. the OsMed flow).

Antibiotics for systemic use were categorized according to the Anatomical Therapeutic Chemical (ATC) classification established by WHO and DDDs were used as measurement units.[9] Consumption was calculated as DDDs per 1000 inhabitants per day.[5] The percentage of Access group antibiotics consumption (Table S1, available as Supplementary data at *JAC-AMR* Online) out of the total DDDs was also calculated.[1] A further indicator 'ratio of broad to narrow-spectrum antibacterials' was provided to compare the spectrum of prescribed antibiotics.[7,10]

Italian regions were grouped into three geographical areas (north, centre and south) according to the Italian National Statistics Institute (ISTAT) classification.[11] To optimize the comparability between regions, the population resident in each region was recalculated taking into account the different compositions by age and sex.[5]

A linear regression was performed to evaluate the correlation among overall community consumption at regional level and percentages of antibiotics belonging to the Access group. Stata Statistical Software (Release 17.0. College Station, TX, USA: StataCorp LLC) was used for statistical analysis, with *P* values <0.05 considered significant.

Table 1. Community consumption of antibiotics for systemic use (J01) by region, with the percentage of non-reimbursed antibiotics consumption, percentage of antibiotics belonging to the Access group according to WHO AWaRe classification system and the ratio of consumption of broad- to narrow-spectrum antibiotics (Italy, 2021)

Region	General population			
	Overall consumption[a]	Percentage non-reimbursed (%)	Percentage in the Access group (%)	Ratio *b/n*[b]
Bolzano AP	8.1	30.9	60.5	12.0
Friuli-Venezia Giulia	11.0	24.5	62.9	7.0
Veneto	11.9	32.8	56.9	6.5
Trento AP	12.0	20.0	58.5	7.6
Valle d'Aosta	12.3	32.5	57.1	6.3
Emilia-Romagna	12.7	28.3	60.2	6.0
Piedmont	13.2	32.6	57.3	7.9
Liguria	13.7	41.6	57.7	13.7
Lombardy	14.0	34.3	58.8	6.6
All northern regions	13.0	33.1	58.6	7.0
Tuscany	14.1	29.8	58.2	7.0
Marche	15.3	18.3	50.8	10.8
Umbria	15.8	19.6	55.6	10.5
Lazio	17.2	23.3	50.5	15.8
All central regions	15.9	24.5	53.1	11.0
Sardinia	12.3	17.1	49.7	16.7
Molise	16.5	20.0	51.6	8.2
Basilicata	16.8	14.9	51.1	7.7
Abruzzo	17.1	16.4	49.9	14.1
Sicily	18.2	21.4	50.5	7.2
Puglia	18.4	15.8	49.2	10.9
Calabria	19.4	20.6	50.5	7.1
Campania	24.7	26.7	47.4	9.5
All southern regions	19.5	21.5	49.1	9.1
Italy	**15.6**	**26.3**	**53.6**	**8.5**

[a]DDDs per 1000 inhabitants per day.
[b]Ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones to consumption of narrow-spectrum penicillins, cephalosporins and erythromycin.
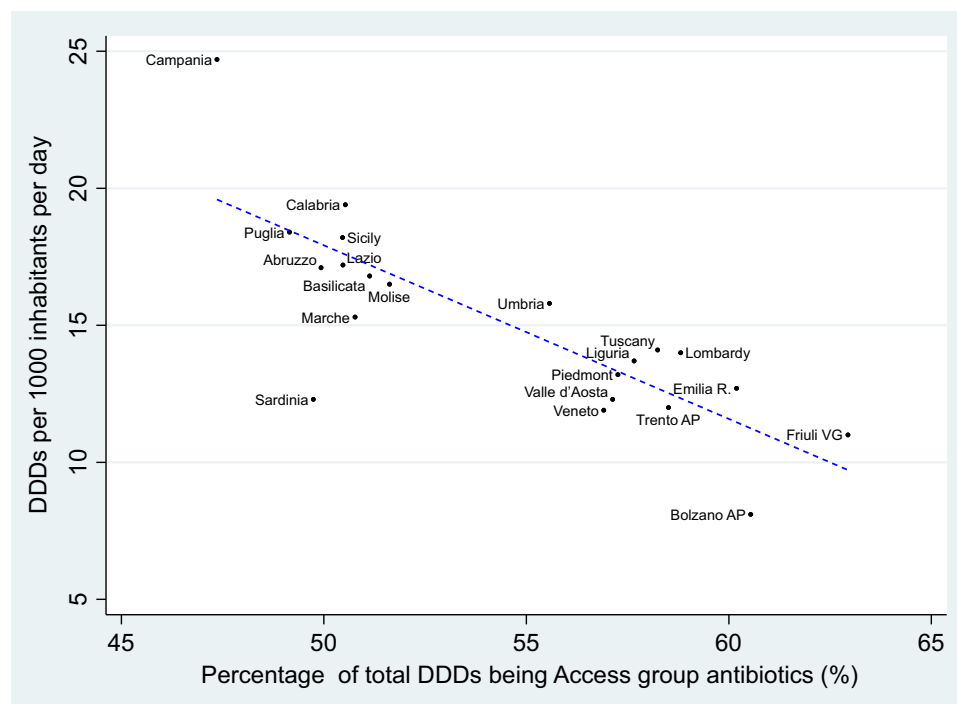
Figure 1. Correlation[a] between overall community consumption of antibiotics for systemic use (J01) by region and percentage of antibiotic consumption belonging to the Access group according to WHO AWaRe classification system (Italy, 2021).[a]Correlation coefficient $=-0.8$; $R^2 = 0.64$; $P < 0.001$.

Results

In Italy in 2021, the community antibiotic use at national level was 15.6 DDDs per 1000 inhabitants per day, varying significantly by geographical area with an increasing trend from north (13.0 DDDs) to south (19.5 DDDs) (Table 1). Conversely, considering the percentages of non-reimbursed consumption on overall consumption, a trend in the opposite direction was observed, with a decrease from north (33.1%) to south (21.5%) (Table 1). The geographical variability was more evident when reimbursed and non-reimbursed consumption were considered separately, rather than overall consumption (coefficients of variation 29%, 31% and 24%, respectively) (Figure S1). In 2021, both overall and reimbursed consumption were higher in the southern regions (overall = 19.5 DDDs per 1000 inhabitants per day; reimbursed = 15.3 DDDs per 1000 inhabitants per day), followed by the central regions (overall = 15.9 DDDs per 1000 inhabitants per day; reimbursed = 12.0 DDDs per 1000 inhabitants per day) and the northern regions (overall = 13.0 DDDs per 1000 inhabitants per day; reimbursed = 8.7 DDDs per 1000 inhabitants per day). In 2021, the national consumption of antibiotics of the Access group out of the total DDDs was 53.6% with a regional range from 47.4% to 62.9% and only three regions out of 21 (Friuli-Venezia Giulia, Autonomous Province of Bolzano and Emilia-Romagna) reached the target of 60% (Table 1). In this analysis, DDDs not included in the 'Access' group belong to the 'Watch' group, since 'Reserve' antibiotics are for hospital use. A strong negative correlation was observed between overall consumption of antibiotics and percentages of consumption of Access group antibiotics (correlation coefficient −0.8; $R^2 = 0.64$;

P value < 0.001); regions with higher consumption also had less frequent use of narrow-spectrum antibiotics (Figure 1).

In 2021 the indicator 'ratio of broad to narrow-spectrum antibacterials' was 8.5 at national level. It was highest in the central regions (11.0), followed by the southern regions (9.1) and the northern ones (7.0) respectively; however, two northern regions (Autonomous Province of Bolzano and Liguria) showed a value above the national average (Table 1).

The antibiotics with the greatest impact on resistance (third generation cephalosporins, macrolides and fluoroquinolones) were prescribed more in the southern and central regions than in the northern ones both in absolute terms (8.8, 6.4 and 4.6 per 1000 inhabitants per day, respectively) and as a percentage of the total antibiotic consumption (45.1%, 40.2% and 35.3%, respectively) (Figure S2; Table S2). Sardinia, which is included in the southern area, had consumption rates similar to the northern regions but a pattern of use in terms of antibiotic type in line with the southern ones (Figure S2; Table S2).

Discussion

The observed community consumption of antibiotics in Italy in 2021 was high at the national level and in most regions. The prescribing pattern was also not satisfactory with a national average for Access group antibiotics of 53.6% in 2021, far below the WHO target of 60% (out of total DDD).[1,12] For reference, in the same year, the EU/EEA average was 60.7%, with other southern European countries such as Spain and Greece reporting percentages of 62.3% and 51.9%, respectively.[7] This indicator showed a strong negative correlation with the consumption rate in the Italian regions. The excessive

use was therefore associated with a preferential use of antibiotics with a high impact on antimicrobial resistance. Heterogeneity between regions was also visible when considering the percentage distribution of classes of antibiotics prescribed.

Although the indicator proposed by WHO (AWaRe) is based on the percentage of Access antibiotics, it should be noted that this group includes antibiotics with different spectrums of action and indications. For example, amoxicillin, cloxacillin and amoxicillin-clavulanate all belong to the Access group but have different characteristics; for the treatment of acute otitis media, simple amoxicillin is indicated as first choice while amoxicillin-clavulanate is a second choice; similarly, from an antibiotic stewardship perspective, cloxacillin would be preferable to amoxicillin-clavulanate in the treatment of mild soft tissue infections and bacterial lymphadenitis.[1,13] Considering these potential limitations, a few countries have adapted the AWaRe classification to their specific objectives and prescribing needs.[14–16]

To have a broader perspective on comparing the spectrum of prescribed antibiotics and to overcome the potential limitations of AWaRe indicator, the present analysis also provided results on the ratio of broad- and narrow-spectrum antibacterials for systemic use.[10] This indicator showed a greater deviation from the EU/EEA country average, compared to the AWaRe one, and a different pattern of inter-regional variability (no clear north–south trend).

Another relevant finding of the present analysis is that the variability between regions was slightly attenuated by analysing the overall community consumption, although relevant differences in overall consumption still persisted across regions. A positive association between the propensity to private health care spending and socio-economic status across regions was also found by other Italian authors.[17] However, in the context of antibiotics use, other factors can be involved in this trend, such as prescriber's attitude or differences in cultural and educational background.[18]

This study, even with the limitations of the information sources (no diagnosis for the prescription and no information on the effective use), allows us to make a detailed description of the prescription patterns of antibiotics at the national and regional level. It also provides interesting insights on qualitative indicators to be used for monitoring antibiotics use. In particular, the percentage of consumption attributable to the Access group (WHO AWaRe indicator) correlates very well with the overall community consumption in the Italian regions. However, the variability in the type of antibiotics used is not fully described by the WHO AWaRe indicator. Therefore, additional indicators could be used to have a more complete picture of consumption patterns from an antimicrobial stewardship perspective.

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The authors report no conflict of interest.

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Data availability
The data that support the findings of this study are available from the author 'AC' upon reasonable request.

Supplementary data
Figures S1 and S2 and Tables S1 and S2 are available as Supplementary data at *JAC-AMR* Online.

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