

# Monitoring of the territorial consumption of antibiotics in local health authority of Vercelli as a measure to contrast AMR

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## **ABSTRACT**

In 2022 the Italian Ministry of Health published the National Antibiotic Resistance Plan (PNCAR) 2022 - 2025 which provides the strategic guidelines and operational indications for dealing with the emergency of antimicrobial resistance (AMR).

ESAC recorded, in the year 2021, an average consumption of 16.4 DDD/1000 inhab. res. die, with a statistically significant decrease in the period 2012 -2021 for class J01, on total territorial and hospital consumption. Italy is one of the countries with the highest consumption of antibiotics, it ranks 9th with a total hospital and territorial consumption of 17.53 DDD/1000 inhab. res. die.

The present study aims to monitor the territorial consumption of antibiotics in ASL VC through the analysis of synthetic indicators and ESAC indicators, comparing them with regional and national values.

Through the IQVIA database, a retrospective descriptive study was conducted on the consumption of antibiotics (ATC J01), for the period 2020 - 2022, measuring the synthetic indicators of consumption (DDD\*1,000 inhab. res. die) and costs (value\*1,000 inhab. res. die). Subsequently, a second analysis was carried out by measuring the ESAC indicators for the year 2022, comparing them with the previous year or period.

With regard to consumption, while a reduction (average -7%) was observed for contracted pharmaceuticals (CONV) in 2021 compared to 2020, followed by an increase in 2022 (average +31%); for private purchase (PRIV), consumption remained constant in 2021 and then increased in 2022 (average +40%). The same trend was observed for the costs of the J01 class.

The ESAC indicators show a mild improvement for ASL VC (variable for regional and national level), except for the use of 3rd and 4th generation cephalosporins which recorded an increase in 2022.

The reduction in the consumption of antibiotics in 2021, followed by an increase in 2022 can be partly explained by the pandemic period that has just ended which led to the return to the community with the resumption of infectious agents in circulation.

It therefore becomes essential to pay particular attention to antibiotic stewardship activities, both in the hospital and on the territory. (community)

## INTRODUCTION

In 2022, the Ministry of Health (Mds) published the National Antibiotic Resistance Plan (PNCAR) 2022 - 2025 to provide strategic directions and operational guidance to tackle the urgent issue of antimicrobial resistance (AMR) in the coming years. The plan follows a One Health approach (1) based on the link between human health, animal health and ecosystem health, and it is endorsed by global organizations, including the World Health Organization (WHO).

In particular, at the national level, the strategy to fight AMR is based on inclusive and integrated governance. This is divided into four horizontal support areas, including information, communication and transparency, and three vertical pillars, including monitoring the appropriate use of antibiotics.

The European System for the Surveillance of Antibiotic Consumption (ESAC) collected data from 29 countries in 2021 and recorded an average consumption of 16.4 defined daily doses (DDD)/1000 inhabitants resident (inhab. res.) per day (range 8.3–25.7), with a statistically significant decrease in the period 2012 -2021 for class J01 on total territorial community and hospital consumption (-2.8%) (2).

Based on the data extracted from the ESAC (3) platform, Italy is one of the countries with the highest consumption of antibiotics; it ranks 9th with a total hospital and community consumption of 17.53 DDD/1000 inhab. res. per day (**Figure 1**).

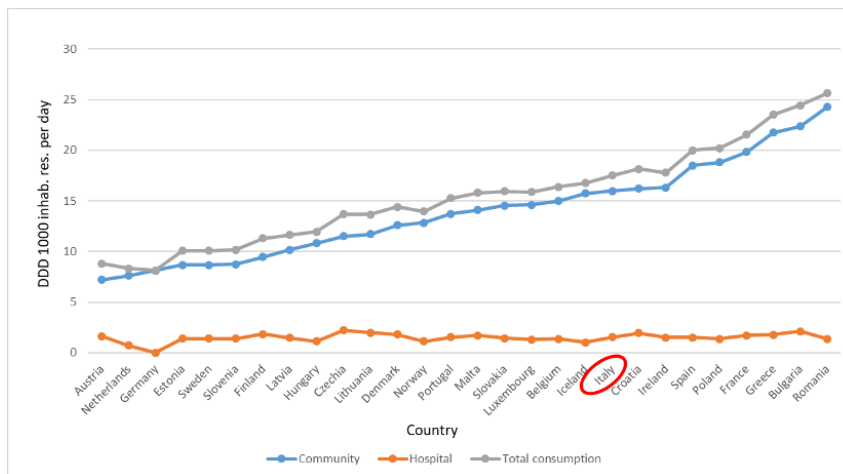


Figure 1. Consumption J01 ESAC.

The Italian Medicines Agency (AIFA), on April 3, 2023, published a report on the use of antibiotics in Italy, referring to 2021 data. The report highlights a decreasing trend for 2021 (-3.3% compared to 2020), although consumption is still higher than in many European countries (4). Also, the OsMed analyzed outpatient prescriptions in General Medicine for specific infectious pathologies and 24%, for almost all the clinical conditions studied (flu, common cold, laryngotracheitis pharyngitis and tonsillitis, uncomplicated cystitis), resulted inappropriate (5).

The report for the antibiotics prescribed under the national health system (Sistema Sanitario Nazionale, SSN) analyses ESAC indicators as measures of appropriateness:

1. Percentage of consumption of penicillin combinations, including beta-lactamase inhibitors (J01CR\_%)
2. Percentage of consumption of III and IV generation cephalosporins (J01DD+J01DE\_%)
3. Percentage of fluoroquinolone consumption (J01MA\_%)
4. Ratio of consumption of broad-spectrum antibiotics to consumption of narrow-spectrum antibiotics within the categories of penicillins, cephalosporins, macrolides and fluoroquinolones (J01 Broad spectrum/narrow spectrum)
5. Seasonal variation in the consumption of antibiotic drugs

At the national level, a reduction in the consumption rate (CR) is observed for penicillin combinations, including beta-lactamase inhibitors, for III and IV generation cephalosporins and fluoroquinolones. At the same time, there is an increase in the consumption of broad-spectrum antibiotics compared to the consumption of narrow spectrum antibiotics. With regard to seasonality, a significant reduction was observed in the period 2020 - 2021, while the value remained constant for the following period (Table 1).

1. J01CR_%			2. J01DD+J01DE_%			3. J01MA_%			4. Broad-spectrum versus narrow-spectrum			5. seasonal variation		
2019	2020	2021	2019	2020	2021	2019	2020	2021	2019	2020	2021	2019-2020	2020-2021	2021-2022
36.9	36	36.2	12.5	11.4	11.2	12.1	12.12	12.1	11	12.3	13.2	67	20	22

Table 1. ESAC indicators 2020 – 2021

The prescriptive context and the geographical differences highlight the importance of continuing to monitor the consumption indicators and costs related to antibiotics.

The objective of the study is to monitor the territorial antibiotic consumption in the local health system (Azienda Sanitaria Locale, ASL) in Vercelli (VC), using synthetic and ESAC indicators updated to 2022 and compared with national and regional values.

## MATERIALS AND METHODS

A retrospective descriptive study was conducted on antibiotic consumption (ATC J01) for the period 2020-2022. The IQVIA database was used as a data source, which collects the databases of drugs dispensed in SSN (CONV) and purchased privately by the population (PRIV).

The data collected from 2020 to 2022 was analysed for consumption synthetic indicators (DDD\*1,000 inhab. res. per day) and costs (value \*1,000 inhab. res. per day).

A second analysis assessed the ESAC indicators for 2022 as following:

1. Consumption (DDD) of combinations of penicillins, including beta-lactamase inhibitors out of total consumption (DDD) of systemic antibiotics (J01). Incidence (%) =  $[(DDD)J01CR / (DDD)J01] * 100$ .
2. Consumption of third and fourth generation cephalosporins out of total consumption of systemic antibiotics (J01). Incidence (%) =  $[(DDD)J01(DD+DE) / (DDD)J01] * 100$ .
3. Consumption of fluoroquinolones out of total consumption of systemic antibiotics (J01). Incidence (%) =  $[(DDD)J01MA / (DDD)J01] * 100$ .
4. Consumption of broad-spectrum molecules over consumption of narrow-spectrum molecules. Ratio:  $[(DDD) J01 (CR+DC+DD+(FA-FA01)+MA) / DDD J01(CA+CE+CF+DB+FA01)]$ .
5. Winter consumption and summer consumption in a one-year interval starting in July and ending in June of the following year.  $[(DDD)J01(winter)/DDD)J01(summer)) -1] * 100$ . The criteria are defined as follows: winter period - October-March; summer period - July-September and April-June (4).

The ESAC indicators were then compared with the data of the previous period to verify the prescriptive behavior of General Medicine of ASL VC.

## RESULTS

For CONV, in 2020, per capita antibiotic consumption was 115.46, 122.58 and 140.49 DDD/1000 inhab per day at company, regional and national respectively. In 2021 there was a slight reduction, while an increase was recorded in 2022 (Figure 2). Figure 2. Pro capita antibiotic consumption CONV ATC J01. ASL VC, Local health system in Vercelli (VC).

For PRIV, in 2020 per capita consumption was 42.73, 49.03 and 49.07 DDD/1000 inhab per day Vercelli, Piemonte and Italy. In 2021 there was a slight growth and in 2022 was registered a strong increase in consumption. (Figura 3)

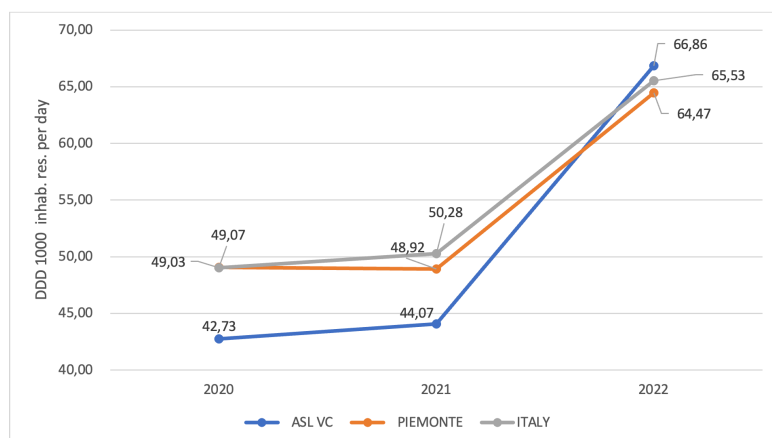


Figura 3. Pro capita antibiotic consumption PRIV ATC J01. ASL VC, Local health system in Vercelli (VC)

Therefore, the total antibiotic consumption trend (2020-2022) follows a similar pattern to the CONV distribution showing an increase at the company (158.19 to 214.82) and

national levels (189.52 to 234.92), and a decrease at the regional level (171.65 to 206.21). (Figure 4).

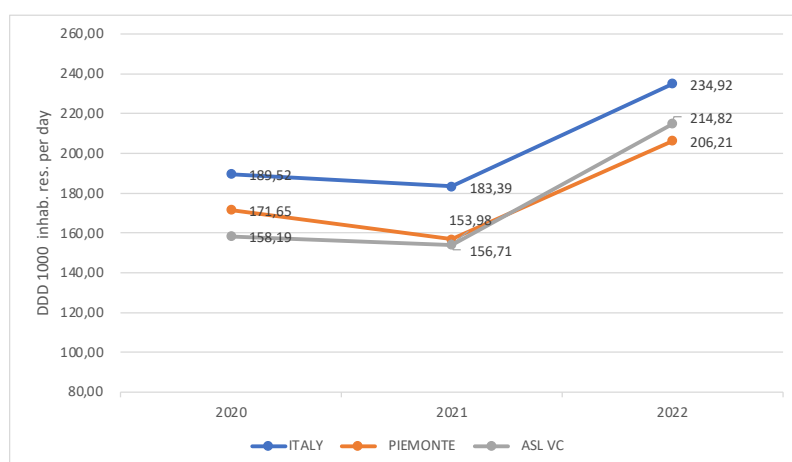


Figure 4. TOT ATC J01 trend ASL VC, Local health system in Vercelli (VC)

The costs were calculated in terms of value/1000 inhab. res. per day, to standardize the levels of analysis and to be able to compare them.

For CONV, in 2020 a per capita costs was observed at company, regional and national level of € 5754.00, € 6167.32 and € 7751.00 respectively per 1000 inhab. res. die. In 2021 there was a slight reduction, while in 2022 there was a significant increase (Figure 5).

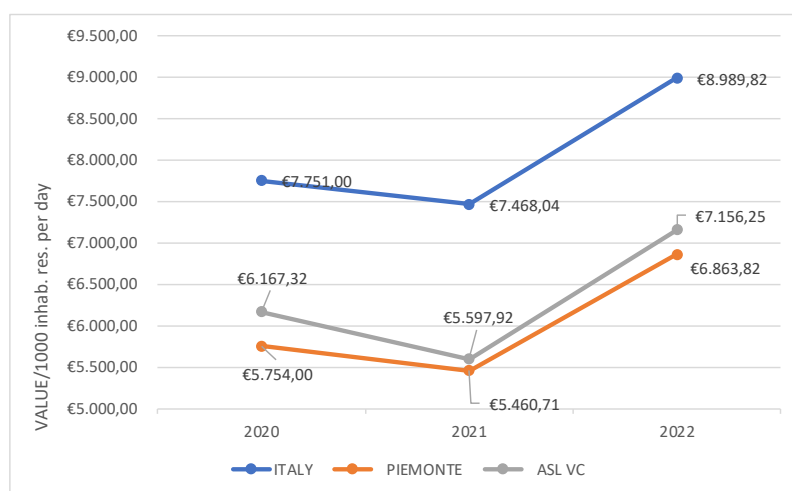


Figure 5. Andamento spesa J01 CONV ASL VC, Local health system in Vercelli (VC)

During the period considered, even PRIV recorded an increase in costs. In 2020, per capita costs at company, regional and national level were respectively € 2056.85, € 2101.95 and € 2968.49 per 1000 inhab. per day. In 2021 the observed values were € 2101.95 at company level, € 2335.02 at regional level and € 2475.04 at national level. In 2022 there was a further rise in expenses. (Figure 6).

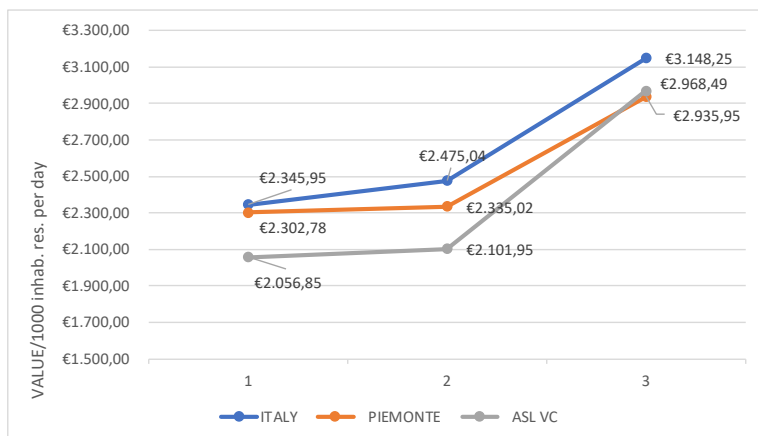


Figura 6. Andamento spesa J01 PRIV ASL VC, Local health system in Vercelli (VC)

The total per capita costs of antibiotics in Vercelli was € 8224.18 in 2020, € 7795.74 in 2021 and € 10124.74 in 2022. Similarly, at regional and national levels, the expenses slightly decreases in 2021 and increased again in 2022. (Figure 7).

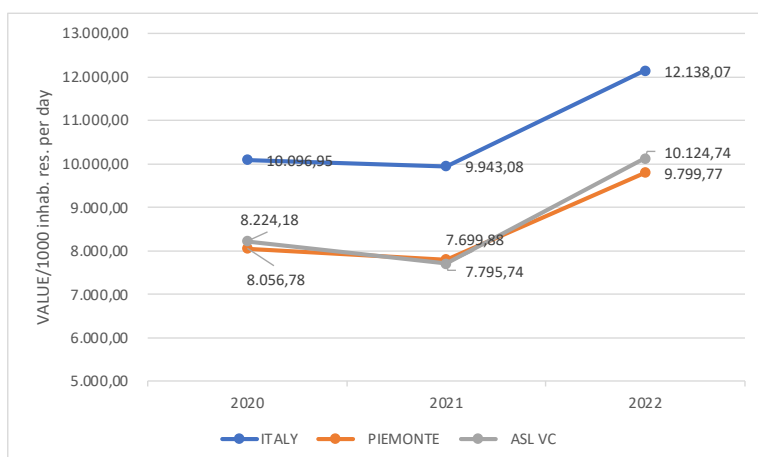


Figure 7. Andamento spesa totale J01 ASL VC, Local health system in Vercelli (VC)

The calculated ESAC indicators are shown in figures 8–12.

The incidence of consumption of penicillin combinations including beta-lactamase inhibitors was similar at regional and local level, and higher compare to the national incidence. This indicator, contrary to what happens at a national level, has had a reduction at a regional and local level. (Figure 8).

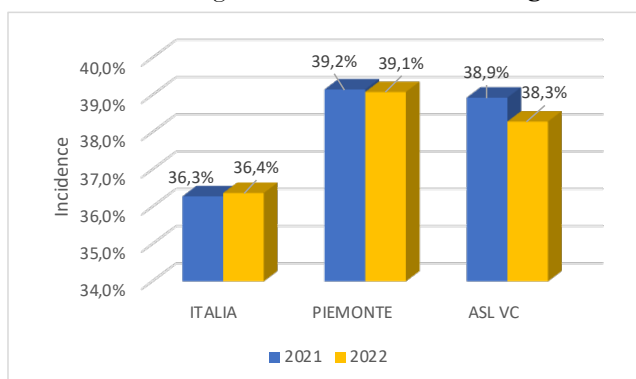


Figure 8. Consumption of penicillin combinations including beta-lactamase inhibitors. ASL VC, Local health system in Vercelli (VC)

The percentage of consumption of third and fourth generation cephalosporins is shown in Figure 9, and the percentage of fluoroquinolone in Figure 10.

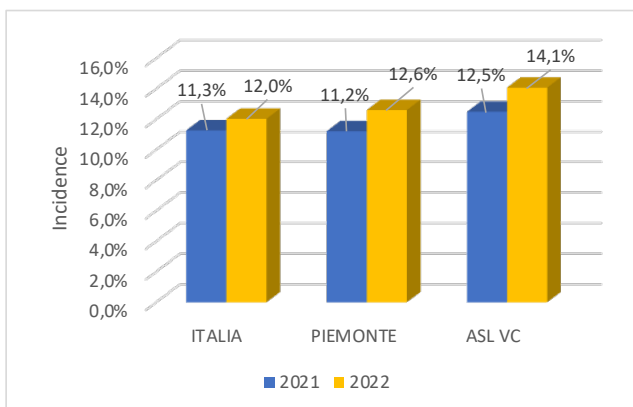


Figure 9. Consumption of third and fourth generation cephalosporins. ASL VC, Local health system in Vercelli (VC)

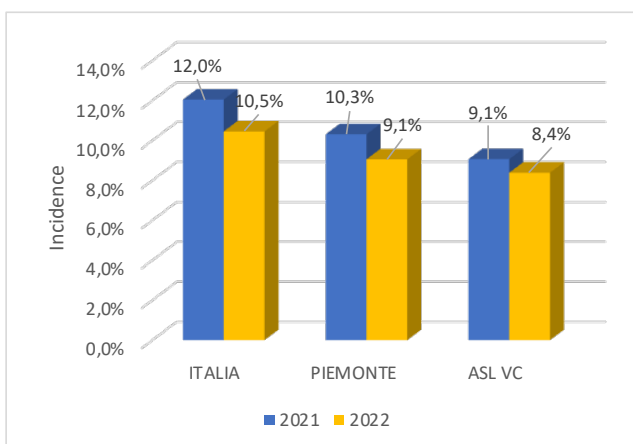


Figure 10. Consumption of fluoroquinolone ASL VC, Local health system in Vercelli (VC)

The indicator values “consumption of broad-spectrum molecules over consumption of narrow-spectrum molecules” are indicated in Figure 11.

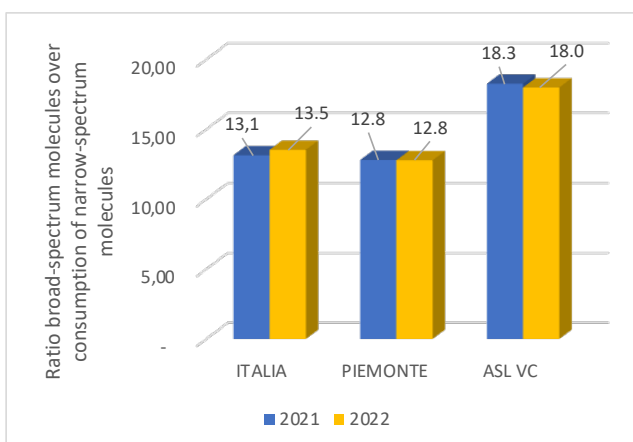


Figure 11. Consumption of broad-spectrum molecules over consumption of narrow-spectrum molecules ASL VC, Local health system in Vercelli (VC)

For the period 2020-2021, the seasonal variation, for ASL VC is lower than Piemonte and Italy.

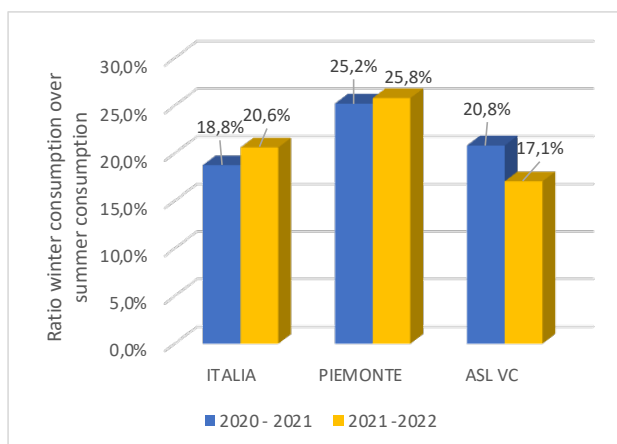


Figure 12. Seasonal variation ASL VC, Local health system in Vercelli (VC)

## DISCUSSION

This study describes the territorial consumption of antibiotics at different levels and the trend on the period 2020-2022.

This work is based on the PNCAR 2022-2025 document, which indicates the monitoring of the consumption of antibiotics as the starting point for adequate actions aimed at appropriate use, essential for contrasting antibiotic resistance.

The study cannot ignore the pandemic period in which it was conducted.

The CONV, in 2021, recorded a slight reduction in consumption, in terms of DDD/1000 inhab. res. per day, 5% at the national and company level and 12% at the regional level. While PRIV consumption in 2021 showed a constant regional value and a slight increase at national and company level (about 3%). The trend observed between 2020 and 2021 could have been influenced by the restrictive measures of the Covid-19 pandemic which reduced access to medical clinics, but also reduced the circulation of infectious agents. In 2022, there was a significant increase in consumption in CONV (+27% in Italy, +32% in Piemonte, +35% in Vercelli), as well as PRIV (+30% in Italy, +32% in Piemonte, +52% in Vercelli).

Certainly, in part, the increase in consumption between 2021 and 2022 can be explained with the end of the emergency period, declared on 31 March 2022, with the return to the community and the resumption of circulation of infectious agents. This increase remains partly unjustified and must make us reflect on the possible actions to be implemented, so long as the increase in AMR observed in hospitals is the result of the use of antibiotics at a local level.

The cost trend reflects the consumption, this because a greater appropriateness leads to economic savings and to better allocation of resources.

For the ESAC indicators, the ASL VC had an improvement in 2022 in the prescription of penicillin associations including beta-lactamase and fluoroquinolone inhibitors, last to be attributed to EMA and AIFA information notes on the use limitations for long-lasting and potentially irreversible side effects (6, 7, 8, 9).



Instead, in 2022 for ASL VC increased the consumption of third and fourth generation cephalosporins, which is higher than the national and regional values.

These antibiotics are classified by WHO as Watch (10) molecules, therefore in need take action to reduce the consumption of these molecules.

The study presented is a descriptive analysis of the consumption of antibiotics, but it is not indicative of appropriate antibiotic use, which needs to be established after a proper diagnosis.

## CONCLUSIONS

The analysis conducted showed that the consumption of antibiotics has increased in the observed three-year period (2020-2022).

As highlighted in the OsMed report, the pandemic has reduced the use of antibiotics, but has not improved the prescribing appropriateness.

In this period, characterized by reduction of the measures for the containment of the SARS-CoV-2 infection and the normalization of clinical activity, needs to be increased the antibiotic stewardship activities, both in the hospital and on the territory, so long as the monitoring data is very important for contrasting the antibiotic resistance.

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