


# Trends in Antibiotic Consumption and Resistance in Portugal, 2013–2023

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**ABSTRACT:** **Introduction:** Antimicrobial resistance (AMR) remains a major public health challenge globally and in Portugal, where antibiotic consumption has historically exceeded European averages. In response, the Plano Nacional de Prevenção da Resistência aos Antimicrobianos (National Programme for the Prevention of Antimicrobial Resistance) 2019–2023 established national targets to reduce inappropriate prescribing, consumption, and resistance. **Objectives:** To analyse national trends in antibiotic consumption and resistance in Portugal between 2013 and 2023, and to evaluate progress relative to the 2019–2023 national program targets. **Methods:** Surveillance data from 2013–2023 were obtained from the European Centre for Disease Prevention and Control (ECDC), the World Health Organization (WHO), and the Direção-Geral da Saúde (DGS). Four indicators were analysed in line with the 2019–2023 National Programme for the Prevention of Antimicrobial. **Resistance targets:** outpatient antibiotic consumption, hospital carbapenem use, prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA), and prevalence of carbapenem-resistant *Klebsiella pneumoniae* (CR-Kp). Results were compared against national targets and EU/EEA averages. **Results:** Between 2013 and 2023, outpatient antibiotic consumption in Portugal increased and exceeded the 2023 national programme target, remaining above the EU/EEA average. Broad-spectrum antibiotics continued to account for a disproportionate share of prescribing. Hospital carbapenem use remained within national ceilings but above EU means. Resistance trends showed marked progress in reducing MRSA prevalence, which fell below the 2023 national programme target (<35%). CR-Kp approached, but did not exceed, the ceiling (15%). Compared with EU averages, Portugal demonstrated higher resistance rates for both MRSA and CR-Kp, though the gap has narrowed over time. **Conclusion:** Portugal achieved measurable progress in stewardship during 2013–2023, particularly in reducing MRSA prevalence. However, outpatient antibiotic consumption increased during this period and exceeded programme targets, and carbapenem resistance in Gram-negative pathogens continues to pose a critical threat. Sustained, targeted stewardship interventions, especially in primary care, are essential to consolidate and expand national progress.

**KEYWORDS:** Antimicrobial Resistance; Antibiotic Consumption; Antimicrobial Stewardship; Portugal; MRSA; *Klebsiella pneumoniae*



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## INTRODUCTION

In recent decades, AMR has emerged as one of the most pressing global public health threats of the 21st century. The WHO has identified AMR as one of the top ten global health challenges, with resistant infections estimated to cause nearly 1.3 million deaths annually and con-

tributing to almost five million deaths worldwide <sup>[1,2]</sup>. The main drivers of AMR are the overuse and misuse of antibiotics in human and veterinary medicine, as well as other multisectoral industries, combined with insufficient development of novel antimicrobial agents <sup>[3]</sup>.

Recognising the magnitude of the problem, Portugal has progressively implemented stewardship policies and awareness campaigns since the early 2000s. Early initiatives included the “Uso Prudente de Antibióticos” campaign, aimed at improving public and professional awareness [4]. In 2007, the Programa de Prevenção e Controlo de Infecções e Resistência aos Antimicrobianos (PPCIRA) was established under the Directorate-General of Health, providing a central governance structure for infection prevention and resistance control [5].

These efforts evolved into more structured national strategies, culminating in the Plano Nacional de Prevenção da Resistência aos Antimicrobianos (PNPRAM) 2019–2023, which adopted a One Health framework spanning human, veterinary, agricultural, and environmental sectors [6]. While broad goals were outlined for all sectors, specific quantitative targets were set for human health: (i) reduction of outpatient antibiotic consumption; (ii) limitation of hospital carbapenem use within targeted limits; (iii) reduction in prevalence of *Staphylococcus aureus* resistant to methicillin; and (iv) reduction in carbapenem-resistant *Klebsiella pneumoniae* isolates. Importantly, these goals aligned Portugal's strategy with the European Commission's One Health Action Plan Against AMR and the WHO's Global Action Plan on AMR [1,3].

In 2021, PPCIRA published an interim report on PNPRAM implementation, addressing several objectives and providing early insights into Portugal's progress. However, the inclusion of COVID-19 pandemic data complicates interpretation, as reductions in outpatient prescribing during lockdown periods may not reflect sustainable changes in clinical practice [7]. Furthermore, a comprehensive end-of-cycle report for 2023 has yet to be published. A consolidated analysis across the four human health indicators is therefore needed to evaluate true progress, identify persistent gaps, and inform the design of the next national stewardship strategy.

This article aims to assess Portugal's progress towards the PNPRAM 2019–2023 targets within the human health sector. Using national and European surveillance data, we evaluate trends in outpatient antibiotic consumption, hospital carbapenem use, and resistance in *Staphylococcus aureus* and *Klebsiella pneumoniae*. By benchmarking outcomes against programme goals, this analysis provides a timely evaluation to inform the next phase of Portugal's antimicrobial stewardship strategy.

## METHODS

This study is a retrospective, descriptive analysis of antimicrobial consumption and resistance trends in Portugal between 2013 and 2023. The analysis focused specifically on the four quantitative targets defined for the human health sector in the PNPRAM 2019–2023. These indicators were benchmarked against programme objectives and, where applicable, against European Union (EU) averages.

### Data Sources

Antibiotic consumption data were obtained from the European Surveillance of Antimicrobial Consumption Network (ESAC-Net), coordinated by the ECDC. These data are reported annually by INFARMED, the Portuguese National Authority of Medicines and Health Products, and expressed as Defined Daily Doses (DDD) per 1,000 inhabitants per day (DHD), in accordance with WHO methodology [8–10].

Hospital consumption data for carbapenems (ATC code J01DH) were extracted from PPCIRA surveillance reports and ESAC-Net submissions [7,8].

Antimicrobial resistance data were obtained from the EARS-Net, coordinated by the ECDC. These data provided annual percentages of resistant isolates for *S. aureus* (resistant to methicillin) and *K. pneumoniae* (resistant to carbapenems), derived from invasive clinical isolates submitted by Portuguese laboratories. National reports published by PPCIRA in 2021 were also consulted, providing interim assessments of PNPRAM implementation [7,11].

European Union comparator data for both consumption (ESAC-Net) and resistance (EARS-Net) were used to contextualise Portugal's performance relative to EU/EEA averages. Where possible, EU weighted means were applied [8,11].

### Indicators Assessed

The analysis was structured around the four central PNPRAM human health indicators:

- Outpatient antibiotic consumption:  $\leq 17.0$  DHD by 2023.
- Hospital carbapenem consumption:  $< 1.0$  DHD.
- MRSA:  $\leq 35\%$  prevalence.
- CR-Kp:  $< 15\%$  prevalence.

### Analytical Approach

Time-series analysis was conducted for each indicator, using annual national data points between 2013

and 2023. Outpatient and hospital antibiotic consumption were plotted as line graphs, with PNPRAM targets superimposed as reference thresholds. For antimicrobial resistance, proportions of resistant isolates were plotted annually, with EU averages included for comparison.

Progress towards PNPRAM objectives was assessed using two complementary approaches:

- (i) Absolute target comparison, in which 2023 values were evaluated against national target thresholds; and
- (ii) Trend analysis, in which direction and magnitude of changes between 2013 and 2023 were assessed to capture broader dynamics.

Where EU averages were available, benchmarking was performed to evaluate whether Portugal's trajectory was converging with or diverging from EU/EEA norms.

Descriptive statistics (absolute values, percentages, and relative changes) were applied; no inferential statistical testing was undertaken, as the study relied exclusively on aggregated surveillance data.

### Limitations

This study is subject to several limitations inherent to secondary data analysis. Firstly, reliance on national and European surveillance platforms means that data accuracy depends on completeness of reporting by participating institutions. While EARS-Net and ESAC-Net maintain quality assurance protocols, variability in laboratory participation and diagnostic capacity across years may influence results.

Secondly, interim assessments such as the PPCIRA 2021 report included trends influenced by the COVID-19 pandemic, particularly reductions in outpatient consumption during lockdowns. These anomalies may overestimate progress towards stewardship objectives and should be interpreted cautiously [7].

Thirdly, at the time of writing, a full end-of-cycle report for PNPRAM 2019–2023 had not been published. While 2023 surveillance data were available through ECDC, national synthesis and policy evaluation remain pending [8,11].

Finally, this study was limited to the human health sector. Although PNPRAM adopted a One Health approach, data from veterinary and environmental sectors were outside the scope of this analysis. The findings should therefore be interpreted as a partial evaluation of the programme's broader goals.

## RESULTS

### Outpatient Antibiotic Consumption

Between 2013 and 2019, outpatient antibiotic consumption in Portugal steadily increased from 16.1 to 17.9 DHD. Temporary reductions were observed in 2020–2021 during the COVID-19 pandemic (reaching 13.7 DHD in 2020), but these were short lived. Consumption rates rebounded in the following years, reaching 17.99 DHD in 2023. This exceeded the PNPRAM 2019–2023 target of  $\leq 17.0$  DHD [6], although it remained slightly below the EU/EEA average of 18.5 DHD for the same year [11], as illustrated in Figure 1.

### Hospital Carbapenem Consumption

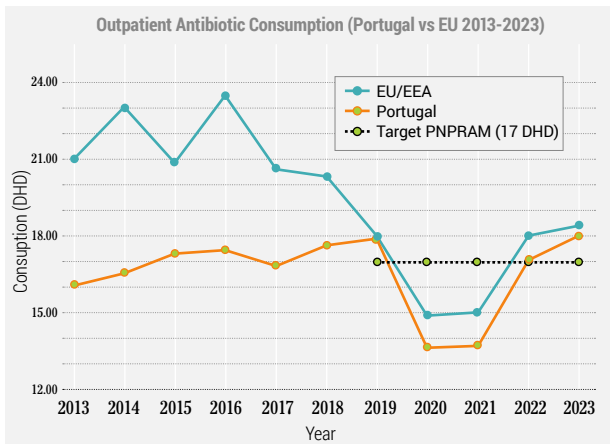
From 2013 to 2023, hospital carbapenem consumption in Portugal consistently remained below the PNPRAM 2019–2023 target of  $\leq 1.0$  DHD [6]. In 2013, usage was 0.113 DHD, gradually declining to 0.082 DHD by 2018. A modest rebound followed during the COVID-19 pandemic years, with consumption rising to 0.089 DHD in 2021 and stabilising thereafter, reaching 0.097 DHD in 2023. Throughout the period, Portuguese values exceeded the EU/EEA mean, which increased from 0.061 DHD in 2013 to 0.070 DHD in 2023 [11]. While national consumption stayed well under the PNPRAM ceiling the persistent gap above EU/EEA averages highlights opportunities for further optimisation, as illustrated in Figure 2.

### Methicillin-resistant *Staphylococcus aureus*

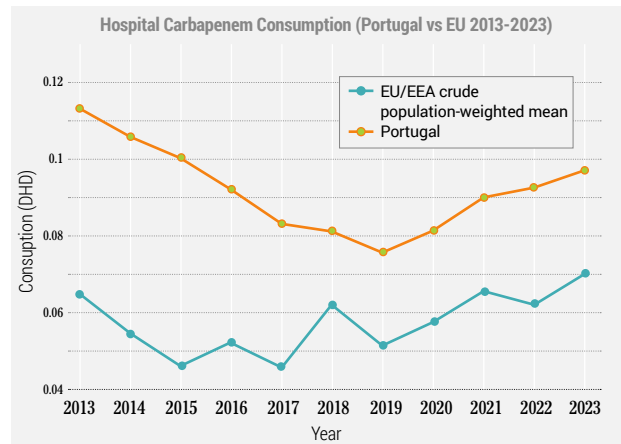
Between 2013 and 2023, the prevalence of MRSA among invasive *S. aureus* isolates in Portugal decreased markedly, from 46.8% in 2013 to 23.1% in 2023 [11]. This represents a sustained downward trend across the decade, with the most notable reductions occurring after 2016. By 2019, MRSA prevalence had fallen below the PNPRAM ceiling of 35% [6] and continued to decline steadily in subsequent years, reaching its lowest recorded level in 2023. These improvements place Portugal closer to, though still above, the EU/EEA average reported over the same period [11], as illustrated in Figure 3.

### Carbapenem-resistant *Klebsiella pneumoniae*

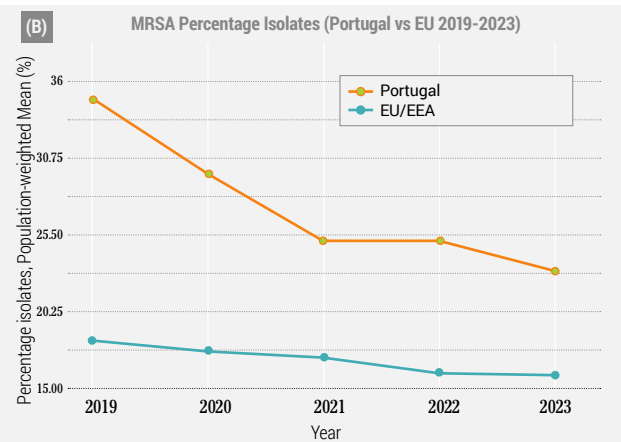
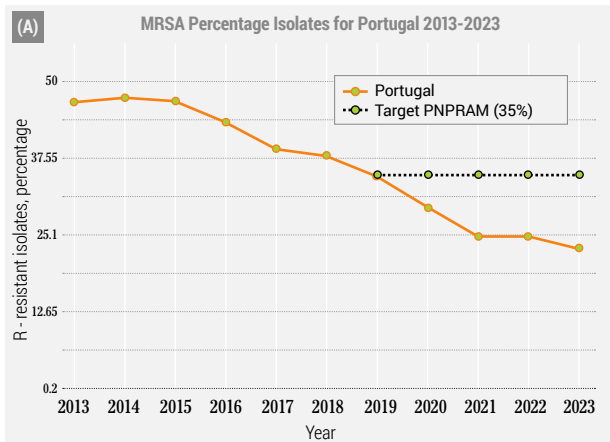
Between 2013 and 2023, the prevalence of carbapenem resistance among invasive *K. pneumoniae* isolates in Portugal rose substantially. Resistance increased from 1.8% in 2013 to 11.7% in 2018, before stabilising around 11% between 2018 and 2022. In 2023, prevalence rose again to 13.1%, remaining just below the PNPRAM ceiling of 15% [6]. While Portuguese rates were above EU/EEA averages



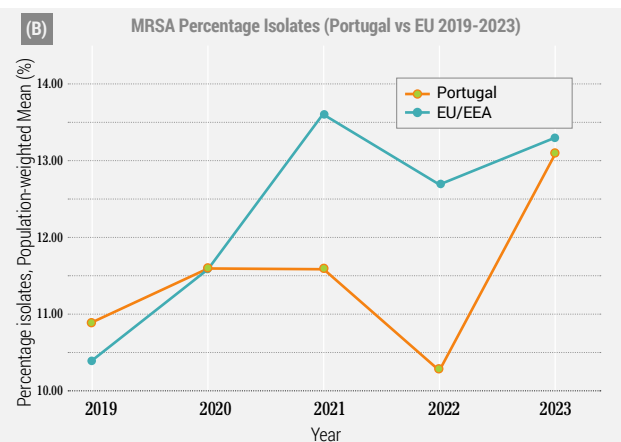
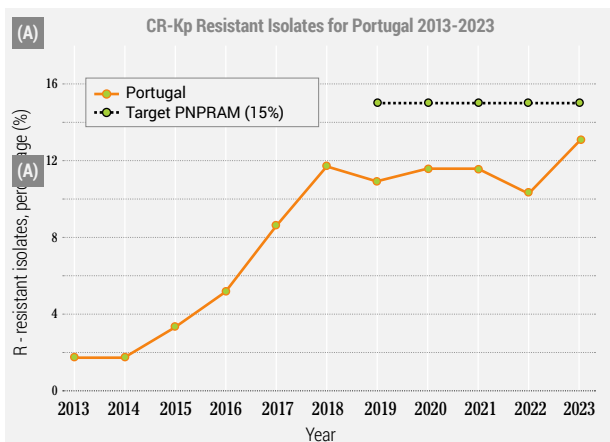
**FIGURE 1.** Outpatient antibiotic consumption in Portugal versus the EU/EEA, 2013–2023, expressed in defined daily doses per 1,000 inhabitants per day (DHD), with PNPRAM target line ( $\leq 17.0$  DHD). Data from ESAC-Net [8].



**FIGURE 2.** Hospital carbapenem consumption in Portugal versus the EU/EEA, 2013–2023, expressed in DHD, with PNPRAM target line ( $< 1.0$  DHD). Data from ESAC-Net [8].



**FIGURE 3.** Prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA). (A) Portugal, 2013–2023, with PNPRAM target line ( $\leq 35\%$ ). Data from EARS-Net [11]. (B) Portugal versus EU/EEA, 2019–2023, population-weighted means. Data from EARS-Net annual epidemiological report [12].



**FIGURE 4.** Prevalence of carbapenem-resistant *Klebsiella pneumoniae* (CR-Kp). (A) Portugal, 2013–2023, with PNPRAM target line ( $< 15\%$ ). Data from EARS-Net [11]. (B) Portugal versus EU/EEA, 2019–2023, population-weighted means. Data from EARS-Net annual epidemiological report [12].

earlier in the decade, they have been overtaken since 2020, with both Portugal and EU/EEA showing a persistent upward trajectory as illustrated in Figure 4 [11].

Taken together, these findings show that Portugal achieved measurable progress against PNPRAM 2019–2023 targets [6], particularly with reductions in MRSA prevalence [11] and the containment of carbapenem use within hospital settings [6]. However, outpatient antibiotic consumption remains above the national ceiling [8], and CR-Kp continues to pose a significant challenge [11]. While Portugal has avoided surpassing programme thresholds [6], the persistence of high consumption and resistance rates [11] highlights the need for sustained and strengthened stewardship interventions moving forward.

## DISCUSSION

This analysis highlights contrasting patterns in Portugal's progress against PNPRAM 2019–2023 goals, with notable successes in resistance outcomes but persistent challenges in antibiotic consumption.

### Outpatient Antibiotic Consumption

The persistently elevated level of outpatient antibiotic consumption remains one of the central challenges for Portugal's stewardship efforts. Despite a temporary decline during the COVID-19 pandemic, community use rebounded to 17.99 DHD in 2023, exceeding the PNPRAM ceiling of 17.0 DHD. This pattern indicates that reductions achieved during periods of restricted social interaction and reduced healthcare utilisation were not sustained once normal prescribing pressures returned. The 2021 PPCIRA interim report highlighted Portugal as one of the five worst-performing countries in Europe regarding the ratio of broad- to narrow-spectrum antibiotics, reflecting diagnostic uncertainty, patient expectations, and regional variability in adherence to prescribing guidelines [7]. Compared with EU/EEA averages, Portugal continues to rank among the higher-consuming countries, underscoring the need for intensified measures in the outpatient sector. Addressing this gap will require stronger integration of rapid diagnostic tools, reinforcement of clinical guideline adherence, and expanded public education to reshape attitudes toward antibiotic use.

### Hospital Carbapenem Consumption

Although Portugal's hospital carbapenem use has remained within national ceilings, it consistently exceeds EU/EEA averages, which raises concern consid-

ering the parallel rise in CR-Kp isolates [6,12]. This association highlights a central stewardship challenge: even modestly elevated carbapenem consumption can drive selective pressure favouring resistant Gram-negative pathogens. Evidence from European and global studies confirms that higher carbapenem exposure correlates with greater prevalence of CR-Kp and other carbapenemase-producing *Enterobacteriaceae* [13]. Given that CR-Kp has continued to increase in Portugal despite adherence to the <1.0 DHD carbapenem ceiling, it may be necessary to reevaluate this threshold and set a more ambitious national target. Establishing stricter consumption limits – aligned with EU best performers – could provide a stronger safeguard against the expansion of carbapenem resistance.

### Methicillin-resistant *Staphylococcus aureus*

The reduction of MRSA in Portugal stands out as one of the clearest successes of national stewardship and infection control policies, with prevalence declining well below the PNPRAM ceiling of 35% [6]. Despite this progress, Portugal still records rates above the EU/EEA mean [12], highlighting the need to consolidate and extend these achievements. The interim PPCIRA 2021 report also documented improvements in other priority pathogens, including a decline in vancomycin-resistant *Enterococcus faecium* (VRE) and reduced prevalence of *Pseudomonas aeruginosa* resistant to carbapenems and piperacillin-tazobactam [7]. These outcomes indicate that targeted stewardship interventions and robust infection prevention measures can yield tangible benefits across multiple species. Looking forward, the strategies that contributed to reducing MRSA should serve as a model for addressing persistent challenges in Gram-negative resistance, particularly CR-Kp.

### Carbapenem-resistant *Klebsiella pneumoniae* and other emerging Gram-negative threats

Notably, since 2020, EU/EEA averages have exceeded Portugal's levels, underscoring that this is not only a national but also a pan-European challenge [12]. The persistence of double-digit resistance rates is clinically significant, given the limited therapeutic alternatives and the association of CR-Kp with increased morbidity, mortality, and healthcare costs [13]. While the 2021 PPCIRA interim report highlighted declining resistance rates for several pathogens up to 2020, more recent data reveal renewed increases since 2021. The prevalence of CR-Kp has risen steadily, accompanied by upward trends

in carbapenem-resistant *A. baumannii* and extended-spectrum  $\beta$ -lactamase (ESBL)-producing *E. coli* [7].

These developments point to a shift in Portugal's AMR landscape, where Gram-negative resistance is re-emerging as the most urgent threat. Addressing this requires pathogen-specific interventions, supported by strengthened diagnostic capacity, rapid detection and isolation of carriers, and more robust infection-control practices in both hospital and long-term care facilities. Without targeted responses, the incremental progress achieved against Gram-positive pathogens risks being offset by rising resistance in Gram-negative bacteria.

Improving stewardship outcomes in Portugal will ultimately depend on addressing systemic drivers such as diagnostic uncertainty and variation in prescribing practices, which continue to encourage broad-spectrum use in community care. Strengthening access to rapid diagnostic tools and reinforcing adherence to clinical guidelines could reduce inappropriate prescribing and ease pressure on resistance trends. Looking ahead, the successor to PNPRAM 2019–2023 offers an opportunity to set more ambitious and transparent targets, ensuring that recent gains are consolidated while tackling emerging Gram-negative threats with renewed urgency.

## CONCLUSION

Portugal has made measurable progress in antimicrobial stewardship, particularly through reducing MRSA prevalence and maintaining hospital carbapenem consumption below PNPRAM ceilings. These achievements reflect the impact of coordinated national strategies and surveillance frameworks. However, outpatient antibiotic consumption continues to exceed national targets, broad-spectrum prescribing remains widespread, and CR-Kp has emerged as a persistent challenge.

The 2021 PPCIRA interim assessment illustrated success in curbing resistance among several pathogens, but more recent data reveal a resurgence in Gram-negative threats, including carbapenem-resistant *A. baumannii* and ESBL-producing *E. coli*. This shift underscores the need for sustained vigilance, pathogen-specific interventions, and strengthened infection-control measures across both hospital and community settings.

Looking forward, Portugal's stewardship policies must build on prior successes while setting more ambitious goals to reduce antibiotic overuse, expand diagnostic capacity, and reinforce governance. Continued alignment with European and global One Health initiatives will be critical to ensure that the progress achieved is not

reversed, and that the next phase of stewardship delivers durable reductions in resistance burden.

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## DISCLOSURES:

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