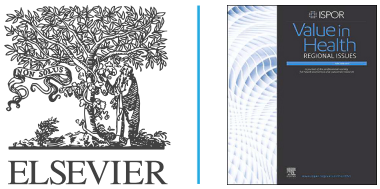

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Economic Evaluation

Development and Real-World Application of a Consumption-Based Model for Projecting the Budget Impact of High-Cost Reserve Antibiotics in a University Hospital

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ABSTRACT

Objectives: Traditional budget impact analysis models, usually based on predefined populations, often fail to capture the complexity of hospital antibiotic use, which is dynamic and often empirical. To address this gap, we developed and applied an adaptable budget impact analysis model based on real-world consumption data of high-cost reserve antibiotics (HCR-ABX), with the objective of projecting their short-term budget impact in a large university hospital over a 3-year horizon.

Methods: HCR-ABX with a purchase cost >€100/defined daily doses (DDD) were selected. The model used retrospective hospital pharmacy data (2021-2024) and incorporated national guidelines on multidrug-resistant infections, regulatory/reimbursement updates, and local resistance trends. These inputs were used to define drug-specific annual variation rates applied in the projection scenarios. Future costs were estimated by combining projected consumption (DDD/100 hospitalization days) with the hospital purchase cost per DDD. Three forecast scenarios (base case, lower impact, higher impact) plus a *Klebsiella pneumoniae* stress-test scenario were modeled.

Results: Despite approximately stable overall HCR-ABX consumption, a shift toward higher-cost agents was observed. The base-case scenario projected a cumulative expenditure of approximately €10 586 248 over 3 years, with increases driven by meropenem/Vaborbactam and cefiderocol. The lower-impact and higher-impact scenarios estimated €10 062 688 and €11 050 385 €, respectively. The *Klebsiella pneumoniae* stress-test scenario indicated a total cost of € 11 321 117 (+6.95% vs base-case scenario), emphasizing the potential financial impact of epidemiological shifts.

Conclusions: The proposed model provides a pragmatic, adaptable framework to assess the hospital budget impact of HCR-ABX and supports antimicrobial stewardship. The approach is replicable and can be refined through future validation against observed data.

Keywords: antibiotic resistance, antimicrobial stewardship, AWaRE, budget impact analysis, high-cost antibiotics.

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Introduction

Antibiotic resistance (AR) can be considered one of the most important public health challenges of our time. A report presented in The Lancet in 2024[1] estimated that AR caused 4.71 million deaths in 2021 of which 1.14 million could be attributed directly to resistant bacteria infections. To counteract AR, the World Health Organization promoted different initiatives focused on the responsible use of antibiotics. One of these programs is the AWaRE classification of antibiotics,[2] a standardized system that classifies commonly used antibiotics into 3 categories (Access, Watch, Reserve) based on stewardship principles and recommendations for appropriate use. During the last decade, these initiatives were supported by the simultaneous approval of new antibiotics, which were progressively more effective and targeted against resistant microorganisms.[3] However, these drugs are significantly more expensive than those used for infections caused by nonresistant microorganisms, as well as older agents for the same conditions,[4] representing a subgroup of Reserve antibiotics commonly designed as high-cost reserve antibiotics (HCR-ABX). This suggests that, without supporting policies, the increasing prevalence of infections caused by resistant microorganisms could also lead to a significant growth in healthcare costs. Several European countries have strengthened

their efforts to fight antimicrobial resistance through coordinated actions, such as the European Commission's One Health Action Plan against antimicrobial resistance,[5] the EU-JAMRAI Joint Action,[6] and the surveillance initiatives of European Centre for Disease Prevention and Control.[7] In Italy, one of the European countries where antibiotic resistance is most critical[8] and antibiotic consumption is among the highest,[7,8] efforts to fight antibiotic resistance have focused on the Piano Nazionale di Contrasto dell'Antibiotico-Resistenza (PNCAR),[9] a 3-year plan developed by the Italian Ministry of Health (Ministero della Salute). Nevertheless, the financial implications of using high-cost reserve antibiotics in hospitals remain poorly characterized, and traditional approaches often fail to capture the empirical and dynamic nature of antibiotic use. In hospital settings, reports on drug consumption are often coupled with budget impact analysis (BIA), developed by hospital pharmacists for budget planning. BIA estimates the financial consequences of adopting a new healthcare intervention within a specific budget context, typically over a short time horizon.[10] However, in major university hospitals where care pathways are highly diversified, it can be challenging to apply traditional BIA models based on a predefined sample size because it is not always available.[11] This is especially true for antibiotics, which are often introduced empirically and then adjusted according to changes in the patient's clinical condition. In hospital settings where patient-level electronic prescribing or clinical information systems do not comprehensively capture all antibiotic prescriptions,[10,12,13] aggregated drug consumption data recorded in hospital pharmacy databases may provide a more realistic and manageable basis for BIA models. By combining historical antibiotic consumption data with other useful information as label extensions, recent local guidelines for the diagnosis and management of infections caused by multidrug-resistant bacteria[14] and current bacterial resistance patterns, the accuracy of these estimates can be significantly improved. As part of antimicrobial stewardship activities implemented in our university hospital in compliance with the Italian National Action Plan on Antimicrobial Resistance (PNCAR), a retrospective analysis of antibiotic consumption and costs over the period 2021 to 2024 was performed. This analysis was followed by the development of an adaptable, consumption-based BIA model for HCR-ABX, applied to project hospital pharmaceutical expenditure over a 3-year time horizon. The study aims to describe both the development and the application of the model, with the objective of supporting hospital decision makers in assessing the financial sustainability of antibiotic use, guiding antimicrobial stewardship strategies, and providing a replicable framework for budget planning in other hospital or regional settings.

Methods

Detailed drug utilization data were retrieved from the pharmacy administrative database of "Policlinico Umberto I" hospital, a large tertiary-care Italian university hospital with approximately 1200 accredited beds and a high case-mix complexity. The database includes records of antibiotics dispensed by the hospital pharmacy, including information on formulation, quantities supplied and acquisition cost, collected for procurement and administrative purposes. Consumption data were stratified by year and analyzed using defined daily doses (DDD) dispensed per 100 hospitalization days as the primary indicator of antibiotic consumption. Based on predefined inclusion criteria, 9 HCR-ABX were selected for the analysis. Eligible antibiotics were those classified as "Reserve" according to the World Health Organization AWaRe framework and associated with a purchase cost exceeding €100 per DDD in the hospital procurement system. This threshold was selected pragmatically to identify reserve antibiotics with the greatest potential impact on hospital pharmaceutical expenditure. In the local hospital context, this value is commonly used for internal budget monitoring to distinguish high-cost antimicrobial agents requiring closer economic evaluation. Reserve antibiotics with a lower cost per DDD were therefore excluded from the model because their individual contribution to overall pharmaceutical expenditure is generally limited. The following antibiotics were included: ceftazidime/avibactam, imipenem/cilastatin/relebactam, meropenem/vaborbactam, ceftolozane/tazobactam, ceftobiprole, cefiderocol, ceftaroline, dalbavancin, and oritavancin. A consumption-based BIA model was then developed to estimate the financial impact of these antibiotics over a 3-year time horizon (2025-2027) from the hospital perspective. The model projects future antibiotic consumption and costs starting from historical data (2021-2024), which are then adjusted by integrating 3 predefined sources of contextual information: (1) Italian national guidelines for the management of infections caused by multidrug-resistant bacteria,[14] (2) regulatory and reimbursement updates issued by the Italian Medicines Agency (AIFA), and (3) local microbiological resistance trends. The role of each information source within the model, as well as the hospital professionals involved, is summarized in Table 1. Four alternative forecast scenarios were defined a priori. These included a base-case scenario, 2

Table 1. Information sources and professional roles contributing to the consumption-based BIA model for HCR-ABX.

Information source	Role in the BIA model	Healthcare professional involved
Antibiotic consumption and expenditure patterns	Performing a prediction for high-cost reserve antibiotics spending based on past consumption (2021-2024)	Hospital pharmacist
Regulatory-approved label extensions and local reimbursement criteria of antibiotics investigated	Predicting the consumption trends of the investigated antibiotics based on newly approved/upcoming indication extensions during the study period or changes in reimbursement criteria (2020-2027)	Hospital pharmacist
Italian "diagnosis and management of infections caused by multidrug-resistant bacteria"[14] guidelines	Assessing potential changes in consumption habits based on the indications provided in the Italian guidelines	Infectious disease specialist
Analysis of bacterial resistance patterns	Investigating trends in resistance to a pathogen for which investigated antibiotics are used	Clinical microbiologist

BIA indicates budget impact analysis; HCR-ABX, high-cost reserve antibiotics.

deterministic sensitivity scenarios (higher impact and lower impact), and an additional "carbapenemase-producing *Klebsiella pneumoniae* (KPC-Kp) stress-test" scenario. The base-case scenario represented the reference projection derived from historical consumption patterns and the integration of clinical guidelines, regulatory and reimbursement updates, and local microbiological resistance trends. In the base-case scenario, drug-specific annual growth or decline rates were applied to each HCR-ABX, with projected consumption/costs for each year derived from the previous year's values. Sensitivity scenarios were defined to explore the potential impact of uncertainty in the projected consumption trends of HCR-ABX. These scenarios were constructed by applying proportional adjustments to the annual variation rates assumed in the base-case scenario. The magnitude of these adjustments was informed by the maximum variability observed in historical HCR-ABX consumption during the study period and applied symmetrically to represent higher-impact and lower-impact trajectories relative to the base-case projection. An additional "KPC-Kp stress-test" scenario was defined to explore the potential financial impact of a substantial increase in infections caused by carbapenemase-producing *Klebsiella pneumoniae*. In this scenario, higher growth assumptions were applied to antibiotics commonly used as first-line treatments for KPC-Kp infections, whereas baseline or sensitivity variation rates were maintained for other HCR-ABX according to their therapeutic role. More specifically, this scenario was designed assuming (1) the standard variation rates of the base-case scenario for HCR-ABX not currently used for the treatment of KPC-Kp infection, (2) the variation rates of the higher-impact scenario for non-first-line treatments, and (3) a shift in the variation rate of +20% each year for first-line treatments as meropenem/Vaborbactam. The inclusion of the KPC-Kp scenario reflects the epidemiological and economic relevance of this pathogen in the Italian hospital setting.[7] For each scenario, annual variation rates in antibiotic consumption were assigned to individual HCR-ABX according to the underlying assumptions of the model. Projected annual and cumulative expenditures were then calculated by combining estimated antibiotic consumption, expressed as DDD per 100 hospitalization days, with the corresponding purchase cost (€) per DDD for each HCR-ABX, as recorded in the hospital pharmacy procurement database and assumed constant over the projection horizon. To avoid implausible extrapolations, predefined constraints were applied to year-over-year consumption variation rates, based on historical utilization. As a robustness check, acquisition costs per DDD were compared across the observation years. All model calculations were performed using Microsoft Excel (Microsoft Corp., Redmond, WA, USA). The key structural assumptions and input parameters used to construct the projection scenarios are summarized in Table 2.

Table 2. Key assumptions and input parameters of the consumption-based BIA model for HCR-ABX.

Model component	Assumption/input	Source
Perspective	Hospital perspective	Study design
Time horizon	Three-year projection (2025-2027)	Study design
Consumption metric	Antibiotic consumption expressed as Defined Daily Dose (DDD) per 100 hospitalization days	WHO DDD methodology
Cost type and unit cost	Direct hospital drug acquisition cost per DDD	Hospital pharmacy procurement database
Scenario	Assumption/input	Basis
Base-case scenario	Drug-specific annual variation rates informed by historical trends, clinical guidelines, regulatory updates and local resistance data	Model assumption informed by historical data and contextual inputs
Sensitivity scenarios (lower-impact and higher-impact scenarios)	Symmetrical adjustments applied to base-case variation rates based on observed variability in HCR-ABX consumption	Observed historical antibiotic consumption variability
KPC-Kp stress-test scenario	Higher growth assumptions applied to first-line agents for KPC-Kp infections while maintaining baseline or sensitivity trends for other antibiotics	Hypothetical epidemiological scenario based on clinical evidence and expert judgment

DDD indicates defined daily dose; HCR-ABX, high-cost reserve antibiotics; KPC-Kp, Klebsiella pneumoniae carbapenemase-producing Klebsiella pneumoniae; WHO, World Health Organization.

Results

Historical Consumption Trends and Expenditure Patterns

The analysis of historical data showed an overall decrease in antibiotic consumption, except for a spike in the immediate postpandemic period. Between 2022 and 2024, total antibiotic consumption varied by only 0.18%, whereas HCR-ABX consumption varied by approximately 10.61%. Over the same period, total expenditure increased markedly from 2022 onward. This divergence reflects a progressive shift toward the use of higher-cost agents within the HCR-ABX group. In absolute terms, expenditure for HCR-ABX increased from €2 556 589 in 2021 to €3 378 185 in 2024, accounting for approximately 60.72% of total expenditure for antibiotics and 1.25% of total hospital pharmaceutical expenditure in 2024. The ±10.61% value derived from consumption data was therefore used as a reference to construct the deterministic sensitivity scenarios, representing proportional upward (+10.61%, higher-impact scenario) and downward (−10.61%, lower-impact scenario) adjustments relative to the base-case projection.

Data-Driven Constraints Applied to Projections

The analysis of overall HCR-ABX utilization patterns allowed the empirical identification of model-level implications, which were subsequently translated into constraints applied to drug-specific projections. In particular, except for periods corresponding to hospital introduction or regulatory label extensions, associated with exceptionally large relative increases (eg, >500%), year-over-year changes in HCR-ABX consumption did not exceed 65%. Accordingly, in the model, year-over-year variation rates were constrained not to exceed this threshold. This

aligns with local resistance surveillance data, which indicated approximately stable resistance trends for carbapenem-resistant *Acinetobacter baumannii* (CRAB), KPC-Kp, *Pseudomonas aeruginosa*, and methicillin-resistant Staphylococcus aureus (MRSA) during the 2021 to 2024 period. In addition, the expected contribution of newly approved antibiotics (such as sulbactam/durlobactam, cefepime/enmetazobactam, and aztreonam/avibactam) is anticipated to remain limited within the projection horizon, given uncertainties regarding their availability and uptake by 2027. Similarly, acquisition costs per DDD remained broadly stable over the observation period (2021-2024), supporting the use of constant unit costs in the model.

Drug-Specific Projections (Observed Drivers and Applied Trajectories)

This section reports the empirical and contextual rationale underlying the drug-specific consumption/costs trajectories used in the BIA model in the base-case scenario. Ceftazidime/avibactam, a beta-lactamase inhibitor combination (BLIC) originally approved in 2016 for the treatment of patients with serious Gram-negative bacterial infections, has shown a gradual decline in consumption over the years, with an average reduction of approximately 20% each year. This trend may, at least in part, be explained by the introduction of competitive drugs (meropenem/vaborbactam and imipenem/cilastatin/relebactam) into clinical practice.[15-17] However, Italian guidelines still recommend ceftazidime/avibactam (along with meropenem/vaborbactam), as a first-line agent for patients with infections caused by KPC-Kp. For this reason, and given the consistent trend of KPC infections, a slow decline trajectory was projected for this HCR-ABX, with a possible plateau beyond 2027. Meropenem/vaborbactam is a new BLIC approved in 2018 with similar indications to those of ceftazidime/avibactam and has rapidly gained popularity,[18,19] including in our setting.[16,20-25] Meropenem/vaborbactam exhibited a sharp increase in consumption between 2021 and 2022 (+1105.13%), followed by a rebound decrease and in a new increase in the growth rate. This pattern is commonly observed during the early adoption phase of new agents or after regulatory label extensions, including the designation as an "innovative drug."[26] In fact, in April 2021, the Italian Medicines Agency (Agenzia Italiana del Farmaco, AIFA) granted the status of "conditional innovative drug" to meropenem/vaborbactam, enhancing its accessibility. This designation grants several benefits, including fast-track access at the local level. Given also its frontline role against KPC-Kp[14] and its competition with ceftazidime/avibactam,[24] its projected variation rate was therefore aligned with a specular trend relative to ceftazidime/avibactam, with an initial increase in the variation rate followed by stabilization by 2027, considering also the expiration of its "innovative" status at the end of 2022. Imipenem/cilastatin/relebactam is a new BLIC approved in 2020; its broad antimicrobial spectrum makes it useful in mixed infections.[27] Imipenem/cilastatin/relebactam exhibited a sharp increase in consumption between 2023 and 2024 (+133.33%). Given its potential as an alternative for treating infections caused by KPC-Kp in selected cases (ie, ceftazidime/avibactam resistant strains)[28] and difficult-to-treat resistant Pseudomonas aeruginosa,[14] its projected variation rate reflects a rebound effect in 2025, followed by a subsequent increase with a gradual trend toward stabilization. Cefiderocol, a new siderophore cephalosporin approved in 2020, is a promising treatment for patients with serious Gram-negative infections, including CRAB infections.[29,30] The utilization of cefiderocol has increased significantly in Italy during the last years,[31] also owing to its designation as "conditional innovative drug," in 2021 and "full innovative drug" in 2023. Cefiderocol showed a trend similar to those of meropenem/vaborbactam, with a sharp increase in consumption between 2021 and 2022 (+467.07%), followed by a rebound decrease and in a new increase in growth rate in 2024, probably due to its "full innovative drug," status. Its use is expected to grow in the coming years in Italy; however, because it is a highly specific and expensive treatment and the incidence of CRAB cases seemed to be stable in our hospital, its growth is projected to gradually slow down and eventually stabilize, in line with patterns observed for other HCR-ABX. Moreover, the recent loss of its "full innovative drug" status (June 2024) could soon have some implications. Ceftolozane/tazobactam, originally approved in 2015, along with ceftazidime/avibactam represents a first-line treatment for *Pseudomonas aeruginosa* difficult-to-treat infections. Ceftolozane/tazobactam experienced a sharp increase in consumption between 2021 and 2022, greater than any other increase recorded for other HCR-ABX (+5709.52%). This steep growth could be attributable to (1) the label extension for complicated intraabdominal infections (cIAI) and hospital-acquired/ventilator-associated pneumonia in late 2019 and (2) the global shortage occurred between late 2021 and 2022. Ceftolozane/tazobactam observed a consumption pattern similar to those observed for cefiderocol and meropenem/vaborbactam. Given the low annual growth rate observed between 2023 and 2024 (+8.57%), this pattern was translated into progressively smaller annual increases in the projected consumption trajectory. Ceftaroline, originally approved in 2012, represents one of the potential alternatives for the treatment of community-acquired pneumonia (CAP) and complicated skin and soft tissue infections (cSSTI), although its activity against Gram-negative pathogens appears limited. In 2015, EMA extended its use to pediatric patients aged ≥2 months, with a further update in 2020 to include neonates, broadening its applicability in clinical practice. Also in 2020, a high-dose regimen was introduced for cSSTI caused by Staphylococcus aureus to optimize therapeutic efficacy in more severe cases. In Italy, ceftaroline is recommended[14] as one of the possible alternatives to glycopeptides for the treatment of cSSTI caused by MRSA. Ceftaroline showed a sharp increase in consumption during the postpandemic period in our setting, after a trend opposite to that observed for teicoplanin and ceftobiprole. Although the number of Staphylococcus aureus isolates is slightly decreasing, the growth appears consistent with the new pediatric label extension, adopted in Italy only in 2023, with the availability of a new high-dose regimen and the growing clinical confidence in its use for MRSA-related infections.[32,33] Based on past drug consumption trends, a significant increase is expected in the coming years, with a tendency to stabilize only because of potential clinical saturation. The projected growth pattern was aligned with that observed for meropenem/vaborbactam. Ceftobiprole, originally approved in 2013, represents one of the potential alternatives for the treatment of HAP, excluding VAP, and CAP. Its broad spectrum makes it a valuable option not just for MRSA but also for some Gram-negative pathogens such as nonresistant Pseudomonas aeruginosa, making it particularly useful in mixed infections.[34] Ceftobiprole, despite the new pediatric indication approved in 2021 and its recognition in Italy as a recommended therapy for nonventilated patients with CAP caused by MRSA,[16] exhibited a progressive decrease in consumption since 2021. This trend may be attributed to a combination of factors, including its uncertain placement in the current therapeutic framework, the introduction of new competing therapies, and the previously described decline in MRSA prevalence. For this reason, a forecasting pattern similar to that of ceftazidime/avibactam was applied. Dalbavancin and oritavancin are 2 lipoglycopeptides originally approved in 2014 and 2015 for

Table 3. Assumed variations for HCR-ABX investigated in the base scenario.

HCR-ABX	2025	2026	2027
Ceftazidime/Avibactam	−20.00%	−10.00%	−5.00%
Meropenem/Vaborbactam	**+20.00%**	**+10.00%**	**+5.00%**
Imipenem/Cilastatin/Relebactam	**−30.00%**	**+10.00%**	**+5.00%**
Cefiderocol	+12.50%	+6.25%	+3.12%
Ceftolozane/Tazobactam	+4.50%	+2.25%	+1.13%
Ceftaroline	**+35.00%**	**+17.50%**	**+8.75%**
Ceftobiprole	−20.00%	−10.00%	−5.00%
Dalbavancin	+0.00%	+0.00%	+0.00%
Oritavancin	+0.00%	+0.00%	+0.00%

Antibiotics associated with the largest projected annual variation rates in the base-case scenario are highlighted in bold. HCR-ABX indicates high-cost reserve antibiotics.

the treatment of bacterial skin infections, including those caused by MRSA.[35] According to Italian guidelines,[14] dalbavancin and oritavancin, together with ceftaroline, represent a possible alternative to glycopeptides for the treatment of cSSTI caused by MRSA. Compared with other antibiotics, dalbavancin and oritavancin have shown modest in-hospital consumption during the last years, with annual variations that were not particularly relevant for reporting purposes. Given their high cost per DDD and their substantial impact on pharmaceutical spending, their consumption was projected to remain stable over the years, consistent with recent utilization patterns. The resulting annual variation rates applied in the base-case scenario are summarized in Table 3.

Budget Impact Projections and Scenario Outputs

The BIA revealed a moderate spending escalation for HCR-ABX over the triennium, in line with trends observed over the previous 4-year period and consistent with the underlying epidemiological data. HCR-ABX are projected to account for approximately €10 586 248 in hospital pharmaceutical expenditure over the next 3 years under the base-case scenario. Projected annual costs are estimated at about €3 421 043 in 2025, €3 531 285 in 2026 and €3 633 920 in 2027. The total amount could potentially be lowered to approximately €10 062 688 in the lower-impact scenario and raised to approximately €11 050 385 in a higher-impact scenario. The most pronounced year-on-year increase in spending (+3.22% in the base-case scenario) is observed in the second year of the projection, whereas the first year registers the lowest impact from consumption changes (+1.27% in the base-case scenario). According to these projections, only the final year of the higher-impact scenario exceeds 2022 expenditure levels, consistent with 2022 representing a pandemic-related outlier in hospital antibiotic spending. Cost projections over the 3-year horizon are shown in Figure 1, with detailed data provided in Appendix Material 1. Regarding the KPC-Kp stress-test scenario, projections indicate

Figure 1. Projected hospital pharmaceutical expenditure for high-cost reserve antibiotics over the 2025 to 2027 period under the base-case, lower-impact, and higher-impact scenarios. Differences between scenarios reflect alternative assumptions on annual consumption variation rates. Vertical dashed lines indicate the timeframe corresponding to the implementation of the Italian National Action Plan on Antimicrobial Resistance (PNCAR 2022-2025).

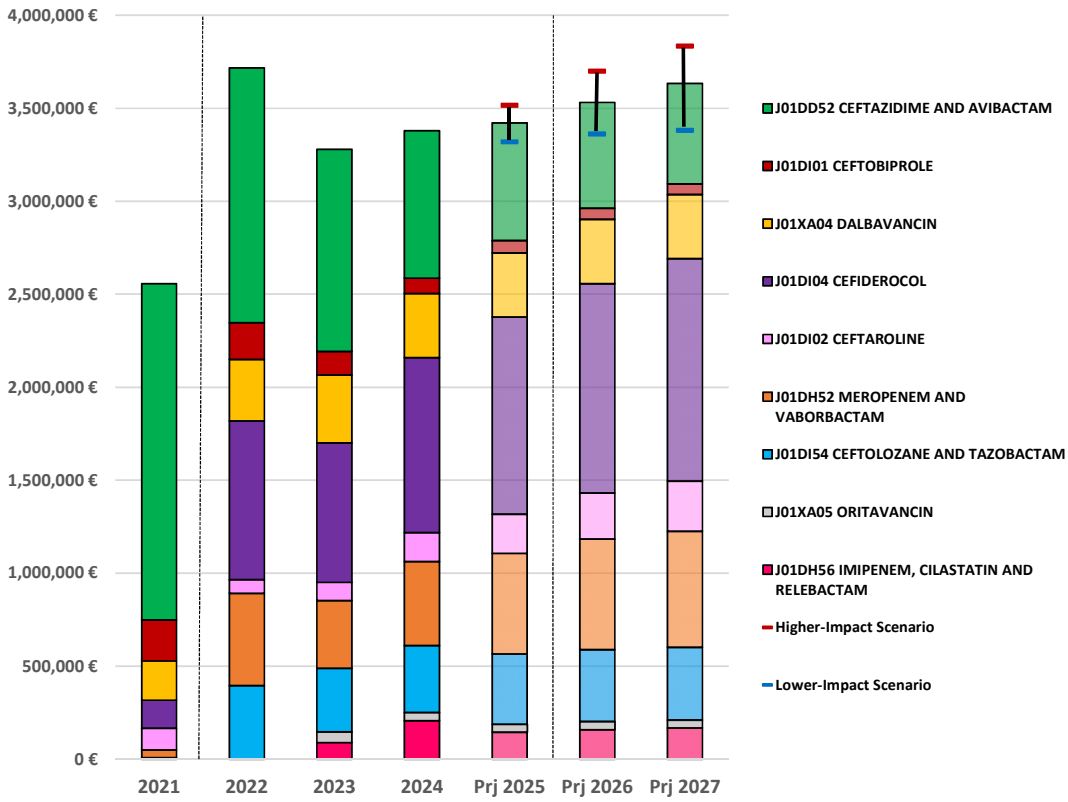


Table 4. Assumed variations for HCR-ABX investigated in the "KPC-Kp stress-test" scenario.

HCR-ABX	2025	2026	2027
Ceftazidime/Avibactam	**−14.30%**	**−7.15%**	**−3.58%**
Meropenem/Vaborbactam	**+22.12%**	**+26.54%**	**+31.85%**
Imipenem/Cilastatin/Relebactam	**−26.82%**	**+11.06%**	**+5.54%**
Cefiderocol	**+13.83%**	**+6.91%**	**+3.46%**
Ceftolozane/Tazobactam	+4.50%	+2.25%	+1.13%
Ceftaroline	+35.00%	+17.50%	+8.75%
Ceftobiprole	−20.00%	−10.00%	−5.00%
Dalbavancin	+0.00%	+0.00%	+0.00%
Oritavancin	+0.00%	+0.00%	+0.00%

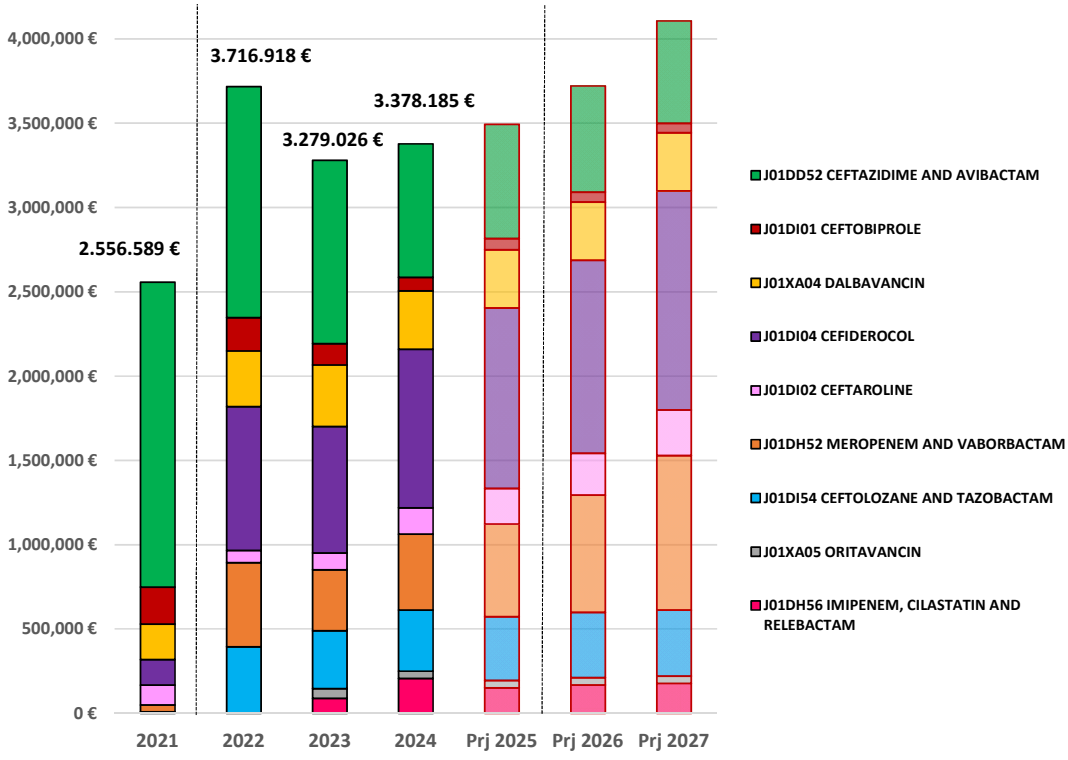
Antibiotics highlighted in bold indicate agents for which annual variation rates differ from the base-case scenario. HCR-ABX indicates high-cost reserve antibiotics; KPC-Kp, *Klebsiella pneumoniae*.

a substantial increase in spending compared with both the base-case scenario and the higher-impact scenario, with annual expenditure exceeding €4 million in 2027 and a cumulative total of about €11 321 117 over the 3-year period (+6.95% compared with the base-case scenario). More in detail, projected annual costs are estimated at about €3 493 786 in 2025, €3 720 847 in 2026 and €4 106 483 in 2027. The assumed growth/decline rates in consumption for each year were summarized in Table 4, whereas the cost projection over the next 3 years was illustrated in Figure 2.

Discussion

AR represents a major threat to global public health; yet, its direct economic impact on healthcare systems, particularly in hospital settings, is often underestimated. This study addresses a dual challenge: the rising use of HCR-ABX and the limitations of traditional BIA in accurately capturing their financial burden in complex settings such as university hospitals. To overcome these challenges, we propose an alternative approach based on real-world antibiotic consumption data. Historical data analysis revealed that overall HCR-ABX consumption remained relatively stable. However, a noticeable shift toward higher-cost agents, such as meropenem/vaborbactam and cefiderocol, was observed. These agents are expected to be the main drivers of expenditure in the coming years. In the absence of major epidemiological changes, these trends appear to be largely driven by regulatory designations and updates in clinical guidelines, which have progressively influenced prescribing patterns. However, a sudden growth in infections caused by resistant pathogens (eg, KPC-Kp) could drastically alter this outlook, leading to a sharp increase in expenditure. The inclusion of the KPC-Kp stress-test scenario illustrates how epidemiological shifts may rapidly translate into increased hospital expenditure, highlighting the model's capacity to support "what-if" analyses and preparedness planning. The methodological contribution of this study lies in its adaptable framework. Although developed in a single Italian university hospital, the model can be replicated by substituting local inputs such as resistance data, guideline updates and drug prices. This flexibility enhances its value for antimicrobial stewardship and short-term budget planning in other hospitals or regional health

Figure 2. Projected hospital pharmaceutical expenditure for high-cost reserve antibiotics under the KPC-Kp stress-test scenario. The scenario simulates an increase in infections caused by carbapenemase-producing *Klebsiella pneumoniae*, with higher growth assumptions applied to first-line agents. Vertical dashed lines indicate the time frame corresponding to the implementation of the Italian National Action Plan on Antimicrobial Resistance (PNCAR 2022-2025).



systems. At a broader level, consumption-based BIA projections may also support regional or national procurement planning and inform price negotiations for HCR-ABX. As with any projection-based approach, this model has inherent limitations. It relies on local data and current resistance patterns, which may vary due to unforeseen epidemiological events, the availability of new antibiotics, or changes in clinical practice. In addition, the analysis is restricted to direct pharmaceutical expenditure and does not capture indirect or downstream costs, such as length of hospital stay, intensive care unit admissions, or other healthcare resource utilization. Moreover, the model does not incorporate patient-level clinical outcomes (eg, mortality or treatment success), as it is based on aggregated antibiotic consumption data. Nevertheless, the model is designed to be periodically updated, allowing refinement of assumptions over time. A future objective will be to validate the model by comparing its projections with actual consumption and epidemiological data observed over the 2025 to 2027 period. This step will be crucial to assess the model's predictive accuracy and to refine its assumptions, ensuring its applicability in future budget planning and antimicrobial stewardship strategies. Such validation will clarify whether a pragmatic consumption-based BIA is sufficient to inform stewardship and budget planning, or whether more advanced decision-analytic approaches (eg, Markov or dynamic models) should be pursued to capture additional complexity.

Conclusion

This study proposes an adaptable consumption-based BIA framework for HCR-ABX. Applied to a large Italian university hospital, the model projected a moderate increase in expenditure driven mainly by newer, costly agents. Its structure enables replication in other hospital or regional contexts, supporting antimicrobial stewardship activities, budget planning, and scenario testing. By integrating real-world consumption data with clinical guidelines, regulatory information, and resistance patterns, the framework provides a pragmatic tool to align clinical priorities with financial sustainability.

Author Disclosures

Author disclosure forms can be accessed below in the Supplemental Material section.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.vhri.2026.101661.

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Ethical Approval: This study relied exclusively on aggregated hospital pharmacy data and did not involve human subjects, individual patient data, or clinical interventions. Therefore, ethics approval was not required.

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