Title: Estimating the Value of Aztreonam-Avibactam in Treating Metallo-beta-Lactamase-Producing Enterobacterales Infections in Spain using the STEDI AMR Value Framework

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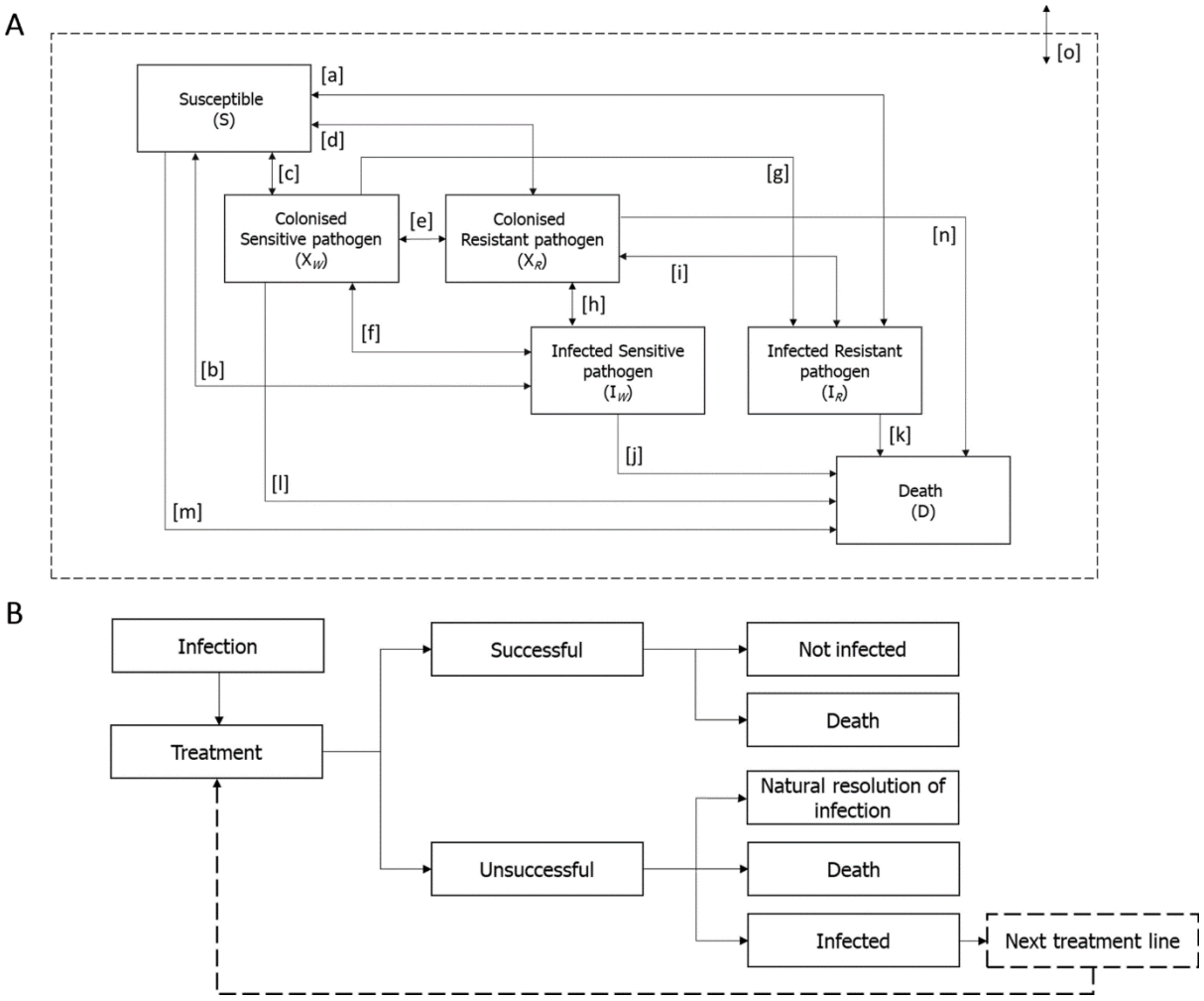
1. Dynamic disease transmission transitions schematic

Figure S1. Dynamic disease transmission schematic and transitions



Overview of the model structure. A) Disease transmission flow diagram and B) treatment decision pathway, sourced from Gordon et al.[15]. Upon becoming infected (A), patients enter the treatment pathway (shown in B). In part A, patients may move between discrete health states representing: Colonised [X]: Patients colonised with the pathogen of interest (XW colonisation with a sensitive pathogen [i.e. no resistance to modelled treatments]; XR colonisation with a resistant pathogen [i.e. resistance to either one, two, or all three modelled treatments]). Infected [I]: Patients infected with pathogen of interest (IW colonisation with a sensitive pathogen [i.e. no resistance to modelled treatments]; IR colonisation with a resistant pathogen [i.e. resistance to either one, two, or all three modelled treatments]). Susceptible [S]: Patients not colonised or infected with a pathogen of interest. Death [D] (absorbing state). Note. the model schematic shows a representation of the transmission dynamics for a single pathogen and treatment, the model considers these dynamics for all pathogen and treatment combinations simultaneously. Details of transitions between health states are outlined below (Table S1).

Table S1. Formulae for the transition between each health state

Label	Transition	Formulae
a	S -> I_R	$\beta_S S X_R/N + \beta_I S I_R/N$
	I_R -> S	P(infection cleared) * I_R * φ
b	S -> I_w	$\beta_S S X_w/N + \beta_I S I_w/N$
	I_w -> S	P(infection cleared) * I_W * φ
c	S -> X_w	$S X_w \beta_X/N$
	X_w -> S	$\gamma_C X_w$
d	S -> X_R	$S X_R \beta_X/N$
	X_R -> S	$\gamma_C X_R$
e	X_R -> X_W	μX_R
	X_W -> X_R	$X_W X_R \beta_C/N$
f	X_w -> I_w	$\lambda_w X_w + \beta_I X_w I_w/N$
	I_w -> X_w	P(infection cleared) * P(no change in resistance|I_w) * I_w * (1-φ)
g	X_W -> I_R	$(\beta_I * X_w * I_R)/N$
h	X_R -> I_w	$(\beta_I * X_R * I_w)/N$
	I_w -> X_R	P(infection cleared) * P(gain resistance to Treatment X|I) * I_w * (1-φ)
i	X_R -> I_R	$\lambda_R X_R + \beta_I X_R I_R/N$
	I_R -> X_R	P(infection cleared) * P(no change in resistance|I_R) * I_R * (1-φ)
j	I_w -> D	P(Death|I_w) * I_w
k	I_R -> D	P(Death|I_R) * I_R
l	S -> D	Not explicitly modelled; captured through hospital discharges
m	X_w -> D	Not explicitly modelled; captured through hospital discharges
n	X_R -> D	Not explicitly modelled; captured through hospital discharges
o	Admissions/ Discharges	Admissions: number of new patients arriving in the infectious environment Discharges: number of current patients leaving the infectious environment

Parameter descriptions:

- Where β_S is the transmission rate from the susceptible to the infected population (I_w or I_R)
- Where β_I is the transmission rate from the colonised to the infected population (I_w or I_R)
- Where β_X is the transmission rate from the susceptible to the colonised population (X_w or X_R)
- Where β_C is the transmission rate informing resistance gain within the colonised community (X_w or X_R)
- Where N is the total number of patients alive in hospital in a given cycle ($S + X_w + X_R + I_w + I_R$)
- Where φ is the proportion successfully treated individuals who do not gain resistance, and are no longer colonised with pathogens of interest
- Where γ is the proportion of individuals that naturally clear the infection
- Where μ is the fitness cost defined as the proportion of individuals colonised with resistant bacteria that lose resistance and return to the sensitive state
- Where λ is the proportion of the applicable colonised community (X_w or X_R) who become infected with a pathogen of interest other than by person to person transmission (β_I and β_S)
- Where P(no change in resistance|I) is the probability that individuals return to each respective colonised state (X_w or X_R) from each respective infected state (I_w or I_R) with no change in resistance
- Where P(gain resistance to Treatment X|I) is the probability that individuals return to each respective colonised state (X_w or X_R) from each respective infected state (I_w or I_R) with a gain in resistance to a given treatment/s
- Where P(Death|I) is the probability of death as a consequence of infection

2. Calibrated transmission parameters

Table S2. Resistance time series used to derive transition parameters

Year	*Cefiderocol* resistance	Source
2014	0.00%	Karlowsky et al. [1]
2015	0.00%	Karlowsky et al. [1]
2016	0.00%	Karlowsky et al .[1]
2017	0.00%	Karlowsky et al. [1]
2018	0.20%	Karlowsky et al. [1]
2019	0.30%	Karlowsky et al. [1]
2020	0.80%	Expert clinical opinion
2021	1.30%	Expert clinical opinion
2022	1.80%	Expert clinical opinion
2023	2.00%	Expert clinical opinion

Transmission parameters were derived empirically, based on calibration of the model to historical resistance data (Table S2), where a trendline was fitted to 2014–2023 resistance levels for cefiderocol

Transmission parameters were calibrated to best fit the trend of observed resistance levels for colistin + meropenem and an infection incidence with goodness of fit assessed though minimising the mean absolute percentage errors (Equation 1) for both resistance and fixed infection prevalence simultaneously using a Generalised Reduced Gradient nonlinear optimisation method.

Equation 1. Mean absolute percentage errors

$$Mean\ absolute\ percentage\ errors = Mean\left(\frac{Predicted\ value_i - Observed\ value_i}{Observed\ value_i}\right)$$

The calibrated was seeded by using the minimum value of each transmission parameter:

- 0.000001 for λ and μ

- 0.0000000001 for β_I, β_S, β_X, β_C, α and ϕ where appropriate

In the cases of cIAI and HAP/VAP, to ensure appropriate model behaviour, an additional model was run in parallel to include a first-line antimicrobial with 0% resistance at baseline based on the associated trendline for the calibration. In these cases, the calibration considered goodness-of-fit assessed though minimising the mean absolute percentage errors of the trend of observed resistance levels for cefiderocol resistance and infection prevalence from the initial model and a first-line antimicrobial with 0% resistance at baseline case from the additional model simultaneously.

The derived transmission parameters for each indication are presented in Table S3. where these parameterisations result in the predicted resistance levels to observed resistance levels for colistin + meropenem shown in Figure S2.

Table S3. Transmission parameters for all modelled indications and pathogens

Parameter	Parameter description	Value
cIAI		
β_I	Effective transmission rate per cycle: colonised → infected	0.03000000
β_S	Effective transmission rate per cycle: susceptible → infected	-
β_X	Effective transmission rate per cycle: susceptible → colonised	-
β_C	Effective transmission rate per cycle: colonised (sensitive) → colonised (resistant)	0.000010000
α	Probability of pathogen developing new resistance per day exposed to treatment	0.250000000
γ_c	Natural clearance rate of pathogen colonisation per cycle	-
γ_I	Probability of natural clearance rate of infection per cycle during unsuccessful treatment	0.030000000
φ	Proportion of infections cleared (i.e. no colonisation remaining) following successful treatment	-
μ_1	Rate of resistance loss due to fitness cost per cycle; resistant to one treatment	0.000100000
μ_2	Rate of resistance loss due to fitness cost per cycle; resistant to two treatments	0.000000010
μ_3	Rate of resistance loss due to fitness cost per cycle; resistant to three treatments	~0.000000000
λ	Proportion of colonised patients who become infected by their colonising pathogen per cycle	0.000520000
HAP/VAP		
β_I	Effective transmission rate per cycle: colonised → infected	0.300000000
β_S	Effective transmission rate per cycle: susceptible → infected	-
β_X	Effective transmission rate per cycle: susceptible → colonised	-
β_C	Effective transmission rate per cycle: colonised (sensitive) → colonised (resistant)	0.000010000
α	Probability of pathogen developing new resistance per day exposed to treatment	0.037620000
γ_c	Natural clearance rate of pathogen colonisation per cycle	-
γ_I	Probability of natural clearance of infection during unsuccessful treatment	0.030000000
φ	Proportion of infections cleared (i.e. no colonisation remaining) following successful treatment	-
μ_1	Rate of resistance loss due to fitness cost per cycle; resistant to one treatment	0.001150000
μ_2	Rate of resistance loss due to fitness cost per cycle; resistant to two treatments	0.000001320
μ_3	Rate of resistance loss due to fitness cost per cycle; resistant to three treatments	0.000000002
λ	Proportion of colonised patients who become infected by their colonising pathogen per cycle	0.000260000

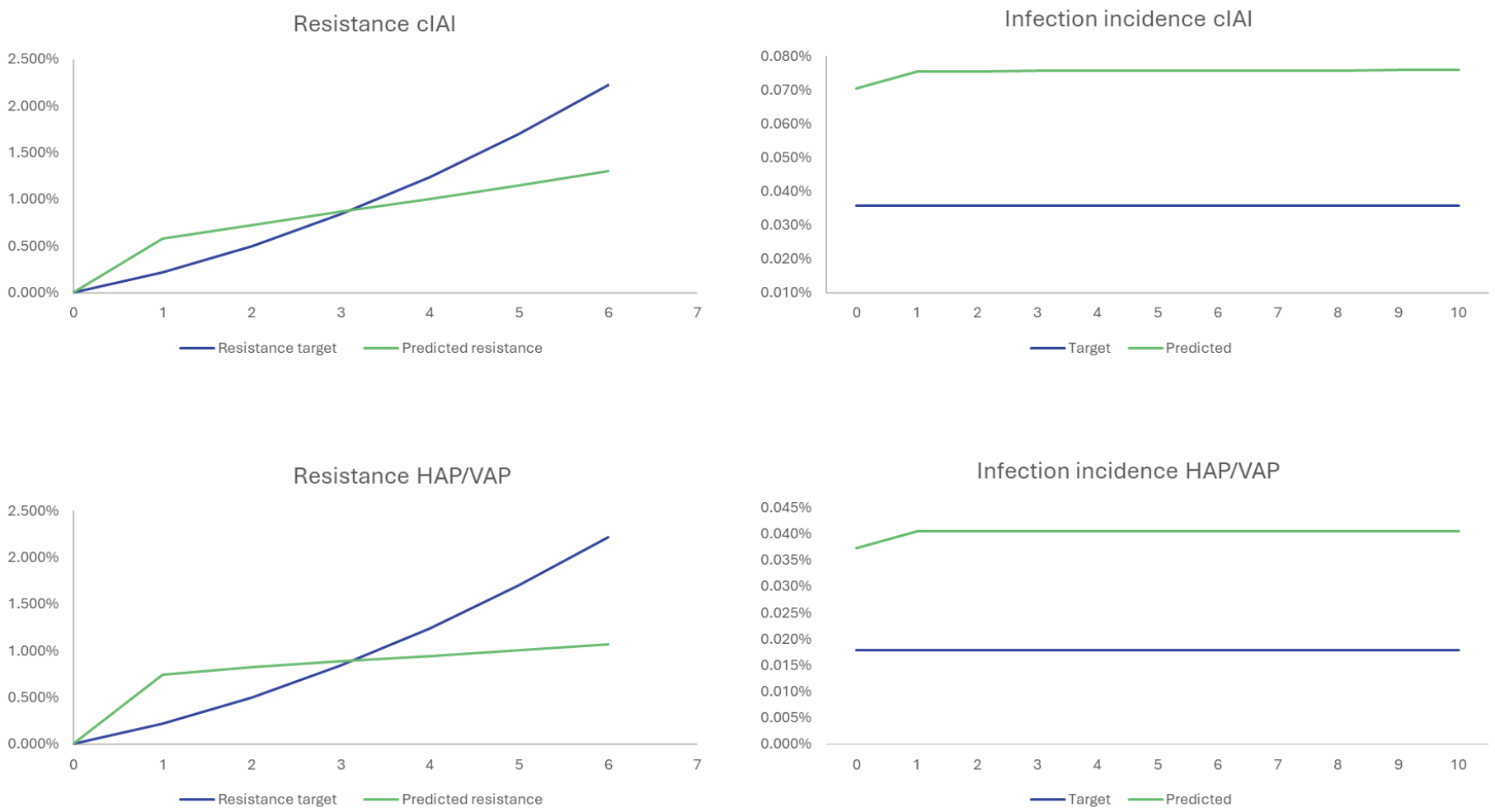


Figure S2. Observed and predicted resistance levels for cefiderocol
green line indicates predicted resistance, blue line indicates resistance in a specific year according to Spain

3. Model assumptions

Table S4. Model assumptions

Assumption	Justification
General	
Homogeneous health states meaning that the patient is in one specific health state at any given time	Model simplification
Colonisation/Infection	
Deaths from the susceptible and colonised health states are not explicitly captured by the model and it is assumed that these are incorporated through patient discharges	Incidence and prevalence of infections and their impact on costs, benefits and mortality are the primary outcome assessed by the model
Patients who are discharged from the infectious environment are not re-admitted	Model simplification required due to assumption of homogeneous health states
Patients who die as a result of infection are able to cause infection in other patients for one additional cycle	Pathogens may still be present in the environment after death; assumption made to prevent underestimation of resistance development in patients who died as a result of infection
The number of admissions and discharges are equal resulting in constant occupancy	Model simplification
All patients are colonised or infected with a pathogen associated with cIAI and HAP/VAP. Following successful treatment of cIAI and HAP/VAP patients remain colonised with a pathogen with the same resistance status at the end of treatment.	Informed by Tlaskalová-Hogenová et al. [2]
Only infections and colonisations associated with pathogen and indication of interest are considered	Model simplification
All infections are considered to be resolved within one model cycle, i.e. all patients are either cured of their infection or have died within one month of initial infection	Model simplification – validated with clinical experts
Infected patients resistant to their current antimicrobial treatment regimen or having exhausted all treatment options have a probability of naturally clearing their infection while on treatment; sensitive pathogens are subject only to the efficacy of the treatment.	Treatment efficacy is derived from trial data and likely to include natural clearances, adding probabilities of cure due to treatment and natural clearance would potentially result in double counting in pathogens sensitive to the current treatment regimen – validated with clinical experts
Patients may not move directly between different infected health states (e.g. Iw -> IR1)	Model simplification
Patients colonised with a resistant pathogen (e.g. R1) may become infected through contact with a patient infected with a pathogen with a different resistance status (e.g. R2); in this case, the newly infected patient becomes infected with the pathogen acquired through contact with the infected patient (R2) and the colonised pathogen is outcompeted.	Model simplification – validated with clinical experts

Resistance	
Patients colonised and not infected with resistant pathogen may lose resistance	Exposure to treatment puts selection pressure benefitting resistance-giving mutations; removing this selection pressure promotes non-resistant pathogens outcompeting resistant pathogen strains
Rate of resistance loss is less in patients with MDR	The potential presence of multiple resistance-giving mutations makes it less likely that all resistance giving mutations are lost in a given model cycle
Treatment	
Duration for successful treatment involves a full course of antimicrobial treatment	Validated with clinical experts
Duration for unsuccessful treatment is less than a full course of antimicrobial treatment; assumed to be three days before treatment is switched	Unsuccessful treatment will become apparent before the full course of antimicrobial treatment is complete - validated with clinical experts
Patients are hospitalised for the entire duration of treatment	Majority of treatments of interest are given by IV infusion and was validated by experts
Patients who have exhausted all their antimicrobial treatment options and fail to clear the infection naturally are assumed to die seven days after their last treatment dose	The prognosis of patients who have no available treatment options is very poor. This assumption as validated by experts.
Different dosing regimens of the same antimicrobial are not considered with respect to cost, treatment duration of efficacy	Model simplification
100% of patients receive empirical therapy, in 0% of patients is antimicrobial susceptibility known at antibiotic treatment initiation and the treatment is targeted	As the population is considered suspected MBL-producing *Enterobacterales* the empirical treatment reflects the treatment practice and resistance is not expected to be known. – validated with clinical experts
Costs and utilities	
Costs and health benefits are only recorded for patients who have acquired an infection	Incidence and prevalence of infections and their impact on costs, benefits and mortality are the primary outcome assessed by the model
No general cost for IV infusion	Model simplification
cIAI: complicated intra-abdominal infection; HAP/VAP: hospital-acquired pneumonia or ventilator-associated pneumonia; ICU: intensive care unit; IV: intravenous; MDR: multi-drug resistance	

4. Model inputs

Table S5. Derivation of prevalence inputs

Description	Value	Source
Prevalence of *K. pneumoniae*	2.5%	CABRA-ES-19 [3]
% Of MBL-producing *K. pneumoniae*	17.3%	CABRA-ES-19 [3]
Prevalence of *E. Coli*	0.04%	CABRA-ES-19 [3]
% Of MBL-producing *E. coli*	40.2%	CABRA-ES-19 [3]
Prevalence of suspected MBL-producing Enterobacterales	0.447%	Calculated
Indication distribution		
cIAI	8.0%	Pfizer. Data on file. Asset DRG [4]
HAP/VAP	4.0%	Pfizer. Data on file. Asset DRG [4]
cIAI baseline distribution		
Susceptible	0.00%	
Colonised	99.96%	100% - % Infected
Infected	0.04%	[Prevalence of HAI]
HAP/VAP baseline distribution		
Susceptible	0.00%	
Colonised	99.98%	100% - % Infected
Infected	0.02%	[Prevalence of HAI]

cIAI: complicated intra-abdominal infections; *E. coli, Escherichia coli*; HAI: hospital-acquired infection; HAP/VAP: hospital acquired pneumonia or ventilator-associated pneumonia; *K. pneumoniae, Klebsiella pneumoniae;* LTO: limited treatment option; MBL, metallo-β-lactamase

Table S6. Utility value calculation

Description	cIAI	HAP/VAP	Source
Utility for general ward	0.73		Lee et al. [5]
Utility for ICU	0.68		Whittington et al. [6]
% of patients in ICU	8.5%	55.7%	REVISIT trial (data on file)
Utility value for infected patients	0.73	0.70	Calculated

cIAI: complicated intra-abdominal infections; HAP/VAP: hospital acquired pneumonia or ventilator-associated pneumonia; ICU: intensive-care unit

5. Enablement inputs

Table S7. Enablement components model inputs – ARR for infection incidence by procedure

Procedure	Infection incidence ARR	Source
Caesarean section	5.5%	Smaill et al. [7]
Transrectal prostate biopsy	5.7%	Zani et al. [8]
Surgical abortion	3.6%	Low et al. [9]
Hysterectomy	12.1%	Mittendorf et al. [10]
Pacemaker implantation	3.1%	Costa et al. [11]
Total hip replacement	5.4%	Al Buhairan et al. [12]
Appendectomy	8.9%	Andersen et al. [13]
Colorectal surgery	26.0%	Nelson et al. [14]
Hip fracture	3.4%	Gillespie et al. [15]
Cancer chemotherapy	10.2%	Gafter-Gvili et al. [16]

ARR: absolute risk reduction

Table S8. Enablement components model inputs – ARR for serious infection incidence by procedure

Procedure	**Serious infections ARR**	**Comments/Rationale**	**Source**
Caesarean section	5.50%	Assume equivalent to ARR for infection incidence	Smaill et al. [17]
Transrectal prostate biopsy	2.98%	Based on the risk difference for hospitalisation related to infections between the antibiotic and placebo groups	Zani et al. [8]
Surgical abortion	3.6%	Assume equivalent to ARR for infection incidence	Low et al. [9]
Hysterectomy	12.1%	Assume equivalent to ARR for infection incidence	Mittendorf et al. [10]
Pacemaker implantation	3.10%	Assume equivalent to ARR for infection incidence	Costa et al. [11]
Total hip replacement	5.40%	Assume equivalent to ARR for infection incidence	AlBuhairan et al. [12]
Appendectomy	1.00%	Based on the number of additional patients with deep SSIs without antibiotic prophylaxis	Andersen et al. [13]
Colorectal surgery	26.00%	Assume equivalent to ARR for infection incidence	Nelson et al. [18]
Hip fracture	1.80%	Based on the number of additional patients with deep SSIs without antibiotic prophylaxis	Gillespie et al. [15]
Cancer chemotherapy	10.20%	Assume equivalent to ARR for infection incidence	Gafter-Gvili et al. [19]

ARR: absolute risk reduction, SSI: surgical site infection

Table S9. Enablement component model inputs - Mortality rate by procedure

Procedure	Mortality rate	Comments/Rationale	Source
Caesarean section	3.0%	Zuares-Easton et al.[20] reports that "SSI is associated with a maternal mortality rate of up to 3%"	Zuares-Easton et al. [20]
Transrectal prostate biopsy	3.4%	Teillant et al.[21] estimated the mortality rate based on SEER Medicare data	Loeb et al. [22] Teillant et al. [21]
Surgical abortion	<0.01%	Calculated using the number of abortion related deaths and number of abortions reported in continuously reporting areas in the US from 2004–2012 from Jatlaoui et al[23].	Jatlaoui et al. [24]
Hysterectomy	0.0%	Mahdi et al reports "SSI was not associated with increased 30-day mortality"	Mahdi et al. [25]
Pacemaker implantation	7.5%	Sandoe et al.[26] reports "infection related mortality being considerably lower than all cause mortality in the same studies; between 0–15% in 12 studies including 100 patients or more reporting this outcome". A midpoint of 7.5% was used for the mortality	Sandoe et al. [26]
Total hip replacement	7.0%	90-day mortality rate used for the two-stage treatment was used as death occurring within this time is more likely to be due to the procedure	Berend et al. [27]
Appendectomy	2.3%	The difference in 30-day mortality rates for patients with deep infections and for patients without deep infections was used	Margenthaler et al. [28]
Colorectal surgery	3.65%	The absolute risk difference in death rates between placebo and treatment groups was estimated at 5.3%. Mortality rate calculated by the following formula: Mortality rate = ARR for mortality / ARR for serious infections	Vincentini et al. [29]
Hip fracture	12.5%	The difference in 30-day mortality rates for patients with deep SSIs and for patients without deep SSIs was used	Duckworth et al. [30]
Cancer chemotherapy	22.5%	The absolute risk difference in death rates between placebo and treatment groups was estimated at 2.3%. Mortality rate calculated by the following formula: Mortality rate = ARR for mortality / ARR for serious infections	Gafter-Gvili et al. [19]

ARR: absolute risk reduction, SSI: surgical site infection

Table S10. Enablement component model inputs - Utility decrement by procedure

Procedure	**Utility decrement**	**Comments/Rationale**	**Source**
Caesarean section	0.320	Results from literature review. The decrement in SSI for a caesarean delivery	Gheorghe et al. [31]
Transrectal prostate biopsy	0.050	The difference in localised cancer state utility and urinary incontinence complication utility. The urinary incontinence utility was used as this is a symptom of urinary tract infections (UTI)	Mowatt et al. [32]
Surgical abortion	0.180	The difference in abortion complications and routine obstetric care EQ-5D utility scores	Lubinga et al. [33]
Hysterectomy	0.140	Difference in well post hysterectomy and convalescence post hysterectomy utility scores	Bhattacharya et al. [34]
Pacemaker implantation	0.198	Results from literature review. Assumed equivalent to the decrement in SSI for cardiac surgery	Gheorghe et al. [31]
Total hip replacement	0.040	Results from literature review. The decrement in SSI for total hip arthroplasty	Gheorghe et al. [31]
Appendectomy	0.300	Results from literature review. The decrement in SSI for outpatient treatment of an open wound, an infected wound or both	Gheorghe et al. [31]
Colorectal surgery	0.044	Results from literature review. The decrement in SSI for colon and rectal resection	Gheorghe et al. [31]
Hip fracture	0.084	Results from literature review. The decrement in SSI for hip and knee surgery	Gheorghe et al. [31]
Cancer chemotherapy	0.140	Difference in the heath state utilities for stable disease and infection without hospitalisation	Brown et al. [35]

SSI: surgical site infection; UTI, urinary tract infection

Table S11. Enablement component model inputs - Life expectancy post procedure

Procedure	Life expectancy (years)	Comments/Rationale	Source
Caesarean section	52.2	Life expectancy based on female general population, assuming average age of 33.46	Ministerio de Sanidad; Spanish life tables [36]
Transrectal prostate biopsy	13.9	Life expectancy based on male general population, assuming average age of 71.68	Darbà et al. [37]; Spanish life tables [36]
Spinal surgery	23.18	Life expectancy based on general population, assuming average age of 62.5	Pereira Duarte et al. [38]; Spanish life tables [36]
Surgical abortion	53.1	Life expectancy based on female general population, assuming average age of 31.1	Eurostat [39]; Spanish life tables [36]
Hysterectomy	39.5	Life expectancy based on female general population, assuming average age of 47	Vazquez-Vicente [40]; Spanish life tables [36]
Pacemaker implantation	8.5	Life expectancy is based on median survival after pacemaker (8.5 years)	Brunner et al, [41]
Total hip replacement	16.3	Life expectancy based on general population, assuming average age of 71.3	Jimenez-Garcia, et al. [42]; Spanish Life Tables [36]
Appendectomy	58.6	Life expectancy based on general population, assuming average age of 25	Carratala-Munuera et al. [43]; Spanish LifeTables [44]
Colorectal surgery	8.3	Life expectancy based on general population, assuming average age of 71, assuming 8 years reduction in life expectancy	de la Portilla et al. [45]; Baade et al. [46]; Spanish life tables [36]
Hip fracture	12.1	Life expectancy based on general population, assuming average age of 86.7	Castillón et al. [47]; Spanish Life Tables [36]
Cancer chemotherapy	11.4	Life expectancy based on general population, assuming average age of 67, assuming 8 years reduction in life expectancy	Pla et al. [48]; Baade et al.[46]; Spanish Life Tables [36]

Table S12. Enablement component model inputs - Utility (post procedure)

Procedure	Utility (post procedure)	Comments/Rationale	Source
Caesarean section	0.885	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Transrectal prostate biopsy	0.800	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Surgical abortion	0.77	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Hysterectomy	0.888	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Pacemaker implantation	0.877	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Total hip replacement	0.781	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Appendectomy	0.892	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Colorectal surgery	0.898	Results from literature review. The utility value for "No SSI"	Gheorghe et al. [31]
Hip fracture	0.744	Utility averaged over age specific utility norms and life expectancy (Table S6)	Szende et al, Population norms [49]
Cancer chemotherapy	0.781	Crude average across cancer types has been calculated from Pourrahmat et al.	Pourrahmat et al. [50]

SSI: surgical site infection

6. Supplementary results

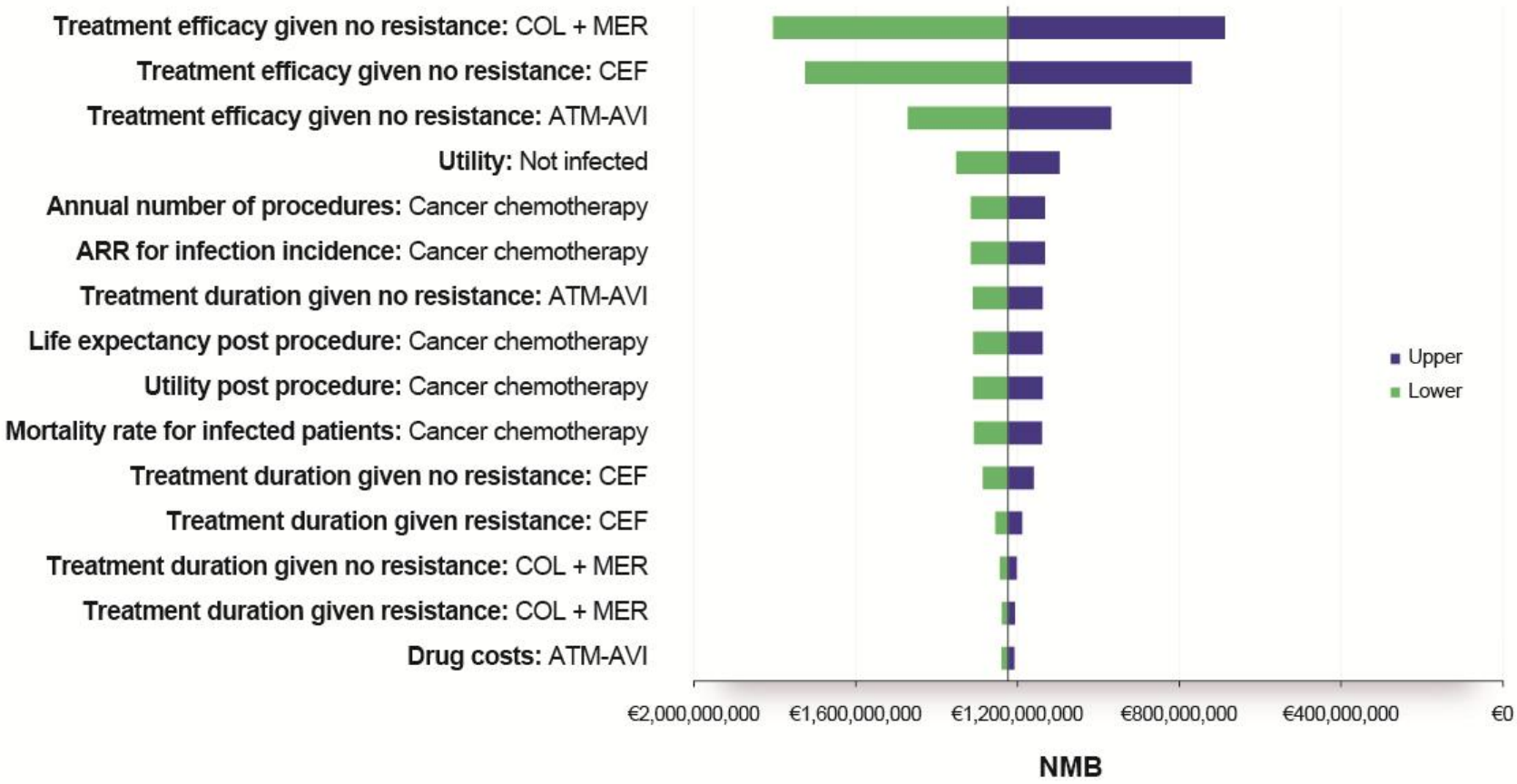
Table S13. Summary of results by transmission & diversity and enablement component

Outcome	Transmission and diversity	Enablement	Combined
Infections	726 avoided	18,744 avoided	19,470 avoided
Deaths	1,720 avoided	2,927 avoided	4,647 avoided
LYs lost	34,716 gained	28,761 gained	63,477 gained
QALYs lost	25,600 gained	21,567 gained	47,168
Net monetary benefit†	€684,371,448	€539,185,390	€1,223,556,839

LY: life years; QALY: quality-adjusted life years

†The WTP threshold was €25,000 per QALY gained

Figure S3. Deterministic sensitivity analysis tornado plot - inputs adjusted ±20% presenting net monetary benefit



ATM-AVI, aztreonam-avibactam; CEF, cefiderocol; COL + MER, colistin + meropenem; NMB, net monetary benefit

Table S14. Deterministic sensitivity analysis outcomes on net monetary benefit

Input	NMB - lower bound	NMB -upper bound
Basecase	€ 1,223,443,941	
Treatment efficacy given no resistance: COL + MER	€ 1,804,482,167	€ 686,946,163
Treatment efficacy given no resistance: CEF	€ 1,724,829,923	€ 769,866,092
Treatment efficacy given no resistance: ATM-AVI	€ 968,668,872	€ 1,470,420,315
Utility: Not infected	€ 1,095,623,965	€ 1,351,489,712
Annual number of procedures: Cancer chemotherapy	€ 1,132,177,973	€ 1,314,935,704
ARR for infection incidence: Cancer chemotherapy	€ 1,132,177,973	€ 1,314,935,704
Treatment duration given no resistance: ATM-AVI	€ 1,310,296,334	€ 1,137,978,560
Life expectancy post procedure: Cancer chemotherapy	€ 1,137,946,617	€ 1,309,167,061
Utility post procedure: Cancer chemotherapy	€ 1,137,946,617	€ 1,309,167,061
Mortality rate for infected patients: Cancer chemotherapy	€ 1,309,167,061	€ 1,307,487,582
Treatment duration given no resistance: CEF	€ 1,309,167,061	€ 1,285,443,942
Treatment duration given no resistance: COL + MER	€ 1,309,167,061	€ 1,243,676,219
Treatment duration given resistance: COL + MER	€ 1,309,167,061	€ 1,238,444,906
Drug costs: ATM-AVI	€ 1,309,167,061	€ 1,207,949,031
Costs: Death	€ 1,309,167,061	€ 1,238,002,914

ATM-AVI, aztreonam combined with avibactam; CEF, cefiderocol; COL + MER, colistin + meropenem; NMB, net monetary benefit

Table S15. Summary of results over 10 years across treatment and prophylactic settings for the full-licenced indication (cIAI, HAP/VAP, cUTI, LTO)

Outcome	Current treatment arm	Introduction of ATM-AVI	Incremental difference
Number of patients treated	29,514	28,252	1,263 fewer patients infected (MBL- producing Enterobacterales)
Hospital length of stay (days)	315,249	315,518	269 additional days
Total costs	€758,678,495	€551,229,659	€207,448,836 cost savings
Infections	180,415	159,332	21,089 infections avoided
Deaths	30,322	24,239	6,084 deaths avoided
LYs lost	383,257	299,272	64,918 LYs gained
QALYs lost	266,700	201,782	64,918 QALYs gained
Net monetary cost†	€7,426,172,503	€5,595,785,736	€1,830,386,768 NMB
ICER	-	-	Dominant (- €3,195/QALY gained)

ATM-AVI: aztreonam-avibactam; ICER: incremental cost-effectiveness ratio; LY: life years; NMB: net monetary benefit; QALY: quality-adjusted life years; WTP: willingness-to-pay

†The WTP threshold was €25,000 per QALY gained

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