How AI can help with antibiotic decision-making in hospitals?
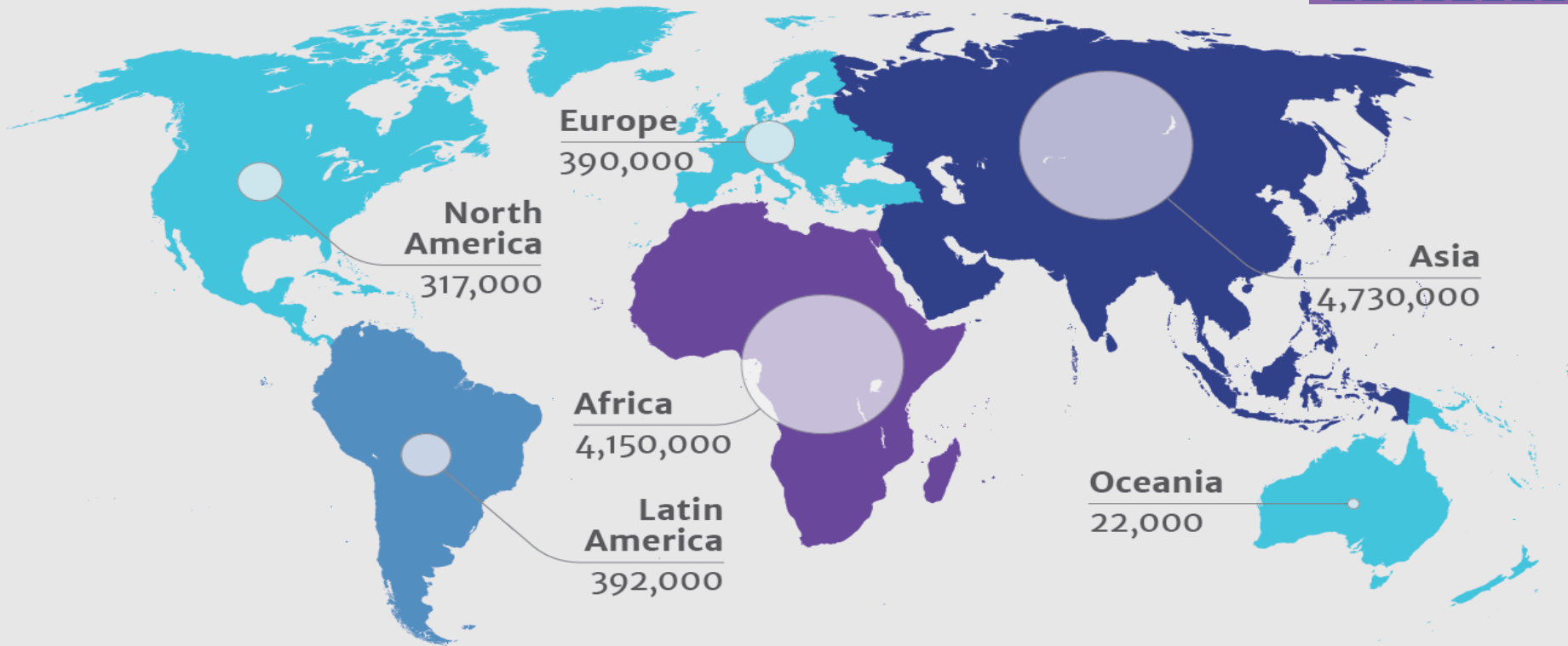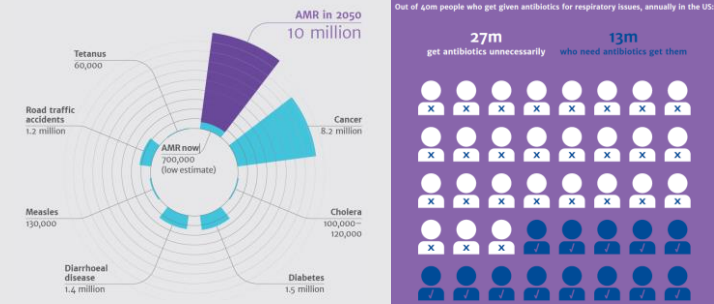
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3rd of November 2020

ANTIMICROBIAL RESISTANCE
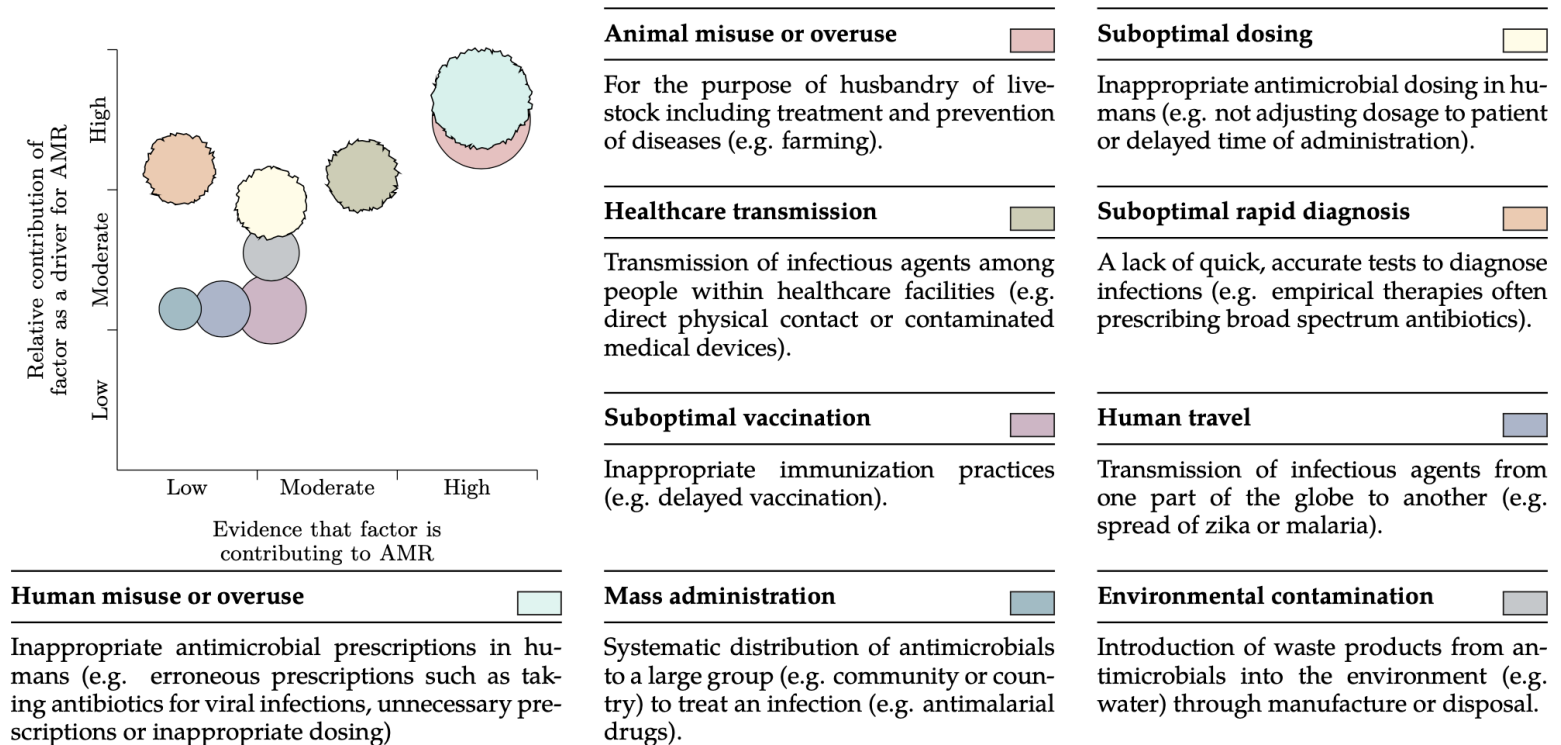

Deaths attributable to AMR every year by 2050

Europe
390,000

North America
317,000

Asia
4,730,000

Africa
4,150,000

Latin America
392,000

Oceania
22,000

number of deaths

Mortality per 10,000 population

5   6   7   8   9   10   >

Table 2.1: Leading drivers of antimicrobial resistance.

Animal misuse or overuse

For the purpose of husbandry of live-stock including treatment and prevention of diseases (e.g. farming).

Suboptimal dosing

Inappropriate antimicrobial dosing in humans (e.g. not adjusting dosage to patient or delayed time of administration).

Healthcare transmission

Transmission of infectious agents among people within healthcare facilities (e.g. direct physical contact or contaminated medical devices).

Suboptimal rapid diagnosis

A lack of quick, accurate tests to diagnose infections (e.g. empirical therapies often prescribing broad spectrum antibiotics).

Suboptimal vaccination

Inappropriate immunization practices (e.g. delayed vaccination).

Human travel

Transmission of infectious agents from one part of the globe to another (e.g. spread of zika or malaria).

Human misuse or overuse

Inappropriate antimicrobial prescriptions in humans (e.g. erroneous prescriptions such as taking antibiotics for viral infections, unnecessary prescriptions or inappropriate dosing)

Mass administration

Systematic distribution of antimicrobials to a large group (e.g. community or country) to treat an infection (e.g. antimalarial drugs).

Environmental contamination

Introduction of waste products from antimicrobials into the environment (e.g. water) through manufacture or disposal.

An info-graphic to show the considered potential contribution of each factor as a driver for antimicrobial resistance including further explanation and examples. The diameter of bubble represents the potential population affected [23, 25]. Irregular circles represent drivers that could be addressed through the implementation of decision support systems in healthcare settings.
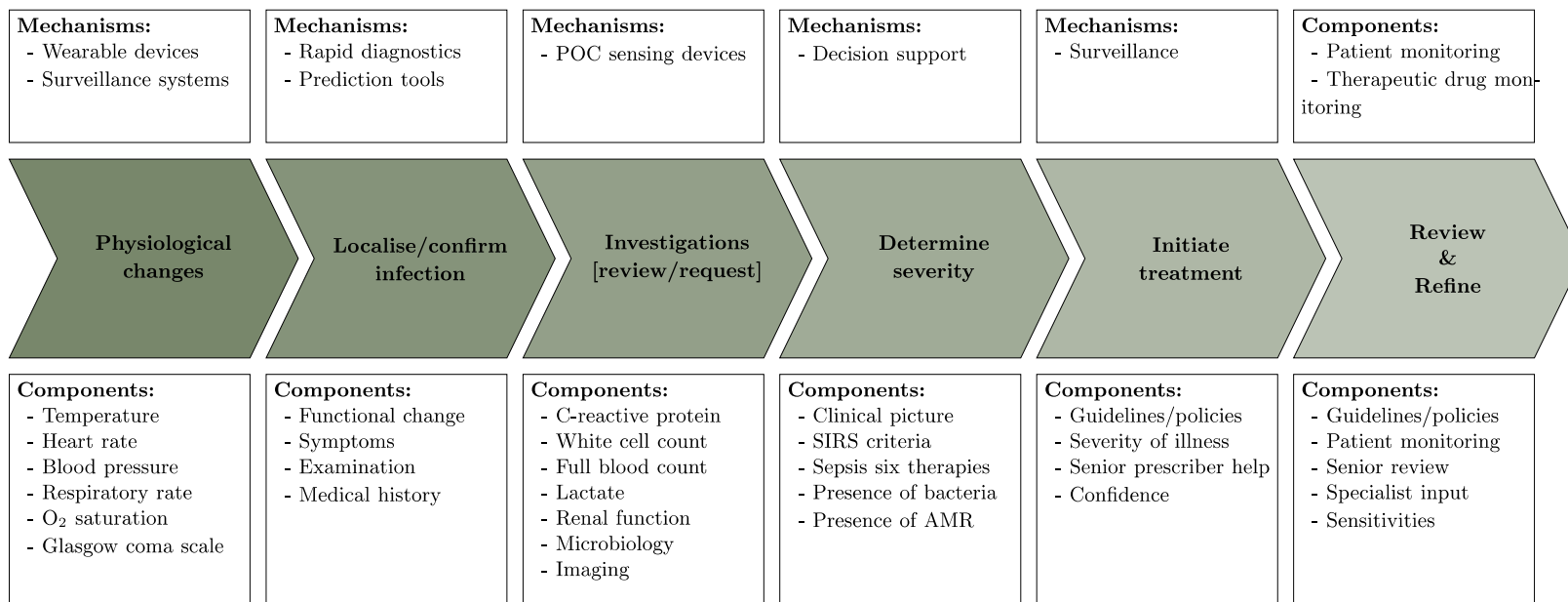
THE INFECTION MANAGEMENT PATHWAY

Mechanisms:	Mechanisms:	Mechanisms:	Mechanisms:	Mechanisms:	Components:
- Wearable devices - Surveillance systems	- Rapid diagnostics - Prediction tools	- POC sensing devices	- Decision support	- Surveillance	- Patient monitoring - Therapeutic drug monitoring

Physiological changes	Localise/confirm infection	Investigations [review/request]	Determine severity	Initiate treatment	Review & Refine

Components:	Components:	Components:	Components:	Components:	Components:
- Temperature - Heart rate - Blood pressure - Respiratory rate - O_2 saturation - Glasgow coma scale	- Functional change - Symptoms - Examination - Medical history	- C-reactive protein - White cell count - Full blood count - Lactate - Renal function - Microbiology - Imaging	- Clinical picture - SIRS criteria - Sepsis six therapies - Presence of bacteria - Presence of AMR	- Guidelines/policies - Severity of illness - Senior prescriber help - Confidence	- Guidelines/policies - Patient monitoring - Senior review - Specialist input - Sensitivities

Figure 7.1: Acute infection management pathway. The stepwise Bayesian like infection management pathway followed by clinicians as described in [5]. Boxes below describe parameters commonly required during such phases of the infection management pathway. Boxes above suggest methods, systems or techniques to improve data collection on such phases. The module(s) providing support on each of the steps are: case-based reasoning (CBR), probabilistic inference (PI) and antimicrobial resistance surveillance (AMR).

EPiC IMPOC - SYSTEM ARCHITECTURE
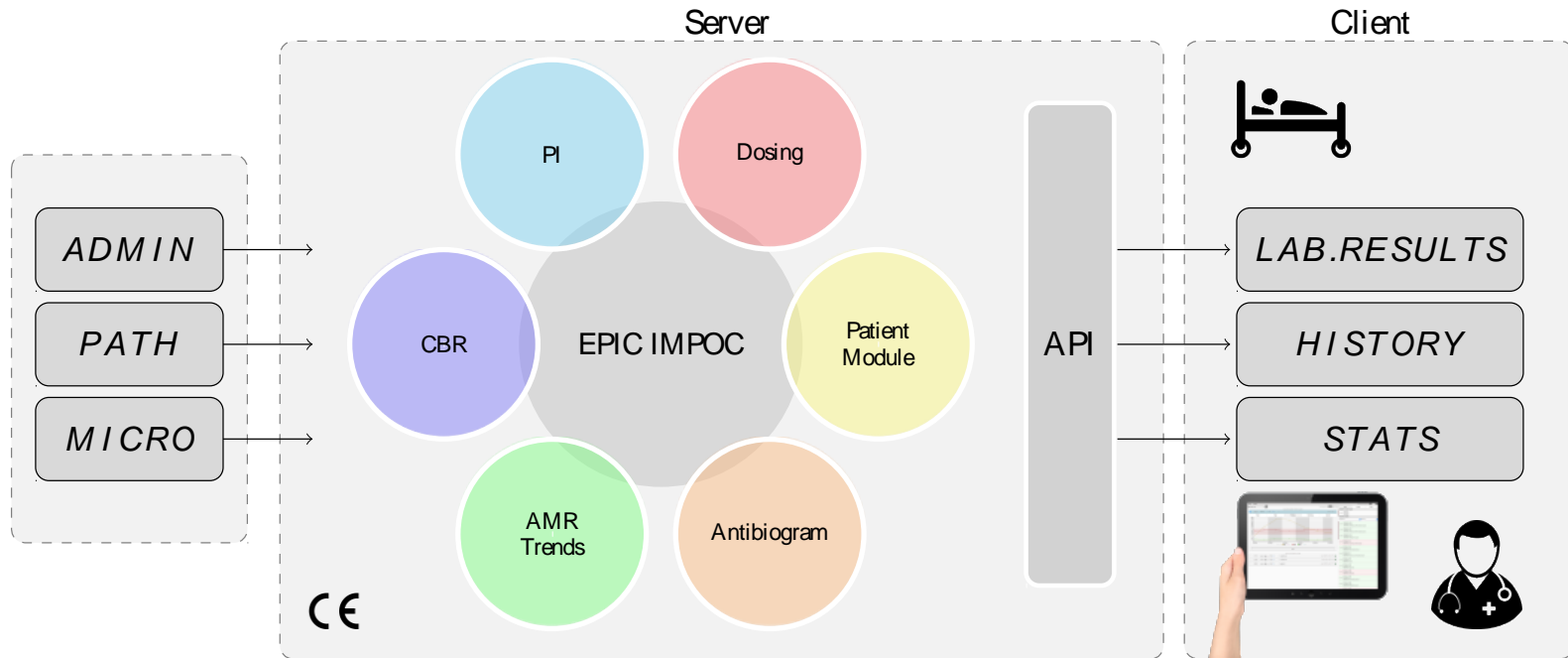
Figure 3.1: EPiC IMPOC high level system architecture diagram. It describes the main components of the CDSS. The external databases are the aptient administration system (ADMIN), pathology laboratory tests (PATH) and microbiology results (MICRO). The server application has the following modules: case-based reasoning (CBR), probabilistic inference (PI), patient engagement module, therapeutic drug monitoring and AMR surveillance. The information is accessed through an API and it is presented on hand-held computer devices or desktop computers to clinicians.

B Hernandez et al *Data-driven web-based intelligent CDSS for infection management... – Health Informatics (2017)*
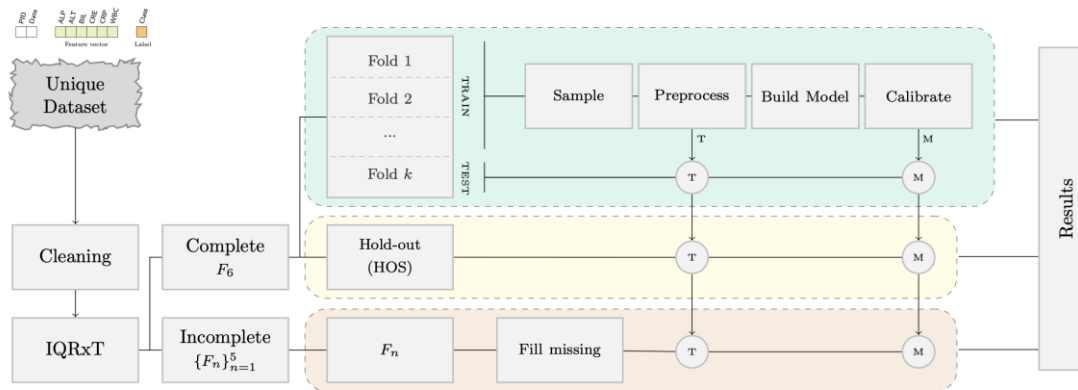
Figure 6.1: High-level methodology diagram for model creation and evaluation. First, data cleaning and outlier removal is performed. The remaining observations are grouped as complete or incomplete profiles. The former is further split into cross-validation Set (CVS) and hold-out set (HOS). Ten-Fold stratified cross-validation is performed on CVS and two outputs are obtained in this step: a preprocessing equation to transform new observations (T) and a calibrated model (M). It is important to highlight that sampling and preprocessing are performed using the train set while calibration is achieved from the test set. Finally, the performance of calibrated models is evaluated in HOS and $\{F_n\}_{n=1}^{5}$.

The prospective evaluation

104 patients
(35% diagnosed with infection in 72h)
(42% had microbiological investigations)

On day of admission
AUCROC 0.84 (95% CI:0.76 – 0.91)

*

B Hernandez et al *Supervised learning for infection risk...* - BMC medical informatics (2017)
TM Rawson et al *Supervised learning prospective study...* - JAC (2019) *
B Hernandez – PhD Thesis (2019) – http://spiral.imperial.ac.uk/handle/10044/1/73000

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Figure 5.1: The CBR cycle. Diagram showing the different phases for a cycle within the case-based reasoning methodology as outlined by Aamodt and Plaza [7].
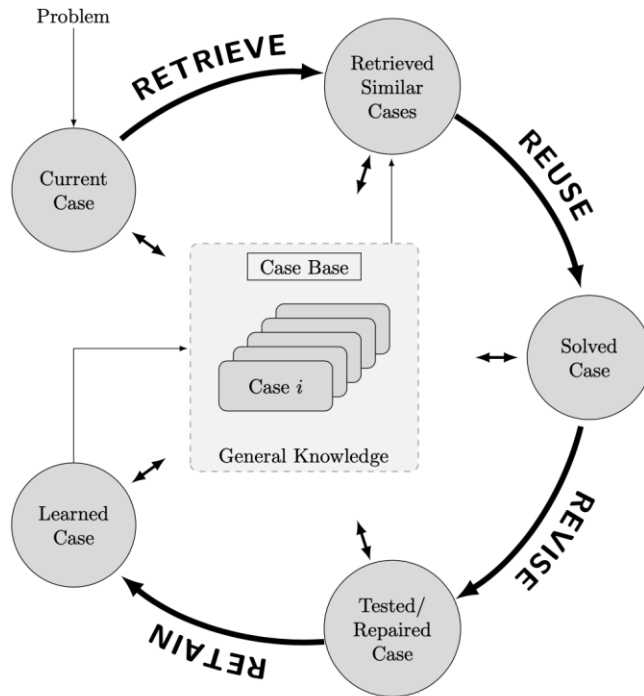
The E. Coli case study

145 patients (all received antibiotics)

Antimicrobial Spectrum index (ASI)

Physicians   - 83% appropriate
CBR   - 90% appropriate

*

B Hernandez et al *Data-driven web-based intelligent CDSS for infection management…* – Health Informatics (2017)
TM Rawson et al *A real-world evaluation of CBR to support antimicrobial prescribing…* - CID (2020) *

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Table 4.8: AMR summary for *Escherichia coli* in urine samples.

Antimicrobial	R(%) (95% CI)	References	T_M(%) (95% CI)	References	T_Y(%)	Pearson	Isolates
Cephalexin (CELX)	**11.1** (10.9, 11.3)		**0.055** (0.045, 0.065)		0.7 ↑	-0.25	79090
Ciprofloxacin (CIP)	**16.3** (16.0, 16.5)	[37, 39]	**0.046** (0.031, 0.062)	[14, 39]	0.6 ↑	-0.46	79239
Ampicillin (AMPC)	**69.6** (68.2, 70.9)	[39]	**0.038** (-0.058, 0.134)		0.5 ↔	-0.18	4729
Trimethoprim (TRI)	**37.8** (37.4, 38.1)	[12][37][38][39]	**0.033** (0.020, 0.046)	[39]	0.4 ↑	-0.14	79133
Amoxicillin-Clavulanate (AUG)	**10.9** (10.7, 11.2)		**0.018** (-0.022, 0.059)		0.2 ↔	-0.42	79093
Meropenem (MER)	**0.2** (0.1, 0.3)		**0.002** (-0.002, 0.006)		0.0 ↔	0.02	9875
Nitrofurantoin (NIT)	**2.7** (2.6, 2.8)	[12][37][38][39]	**-0.006** (-0.013, 0.001)		-0.1 ↔	-0.18	79108
Amikacin (AMI)	**1.1** (0.9, 1.2)		**-0.011** (-0.022, 0.000)		-0.1 ↔	-0.23	9786
Cefotaxime (CTX)	**60.8** (59.9, 61.8)		**-0.012** (-0.083, 0.059)		-0.1 ↔	0.01	9803
Tazocin (TAZ)	**24.2** (23.3, 25.0)	[37]	**-0.023** (-0.078, 0.032)		-0.3 ↔	0.01	9878
Gentamicin (GEN)	**9.3** (9.1, 9.5)	[38]	**-0.033** (-0.061, -0.005)		-0.4 ↓	-0.62	63399
Ertapenem (ERT)	**2.0** (1.7, 2.3)		**-0.033** (-0.050, -0.017)		-0.4 ↓	-0.31	8882
Ceftazidime (CAZ)	**57.3** (53.3, 58.2)		**-0.038** (-0.113, 0.037)		-0.5 ↔	-0.04	9810
Mecillinam (MEC)	**5.4** (4.9, 5.8)		**-0.048** (-0.071, -0.024)		-0.6 ↓	-0.29	9083
Cefoxitin (CXT)	**26.0** (25.1, 26.8)		**-0.069** (-0.123, -0.016)		-0.8 ↓	0.15	9798

Keys: CI=confidence interval; R=resistance; T_M=monthly trend; T_Y=yearly trend; ↑=significant increase; ↓=significant decrease.
Significance: A trend is significant if the CI does not include 0.
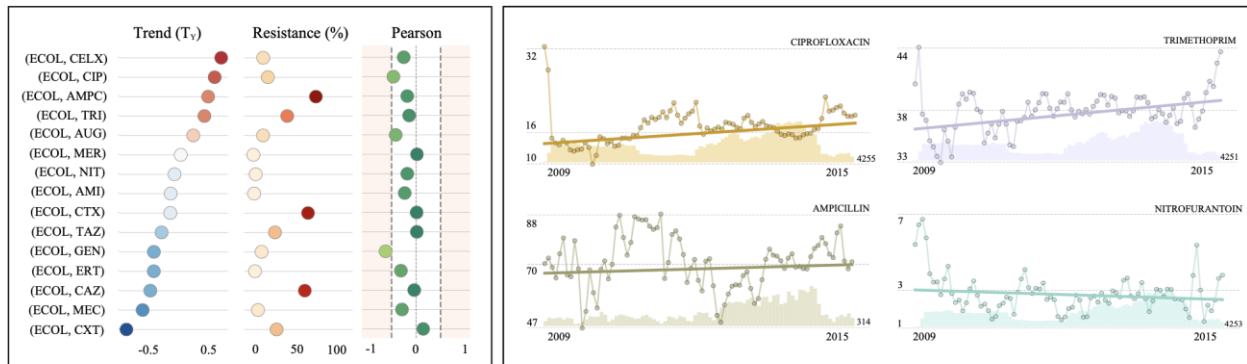
Figure 4.9: AMR summary for *Escherichia coli* in urine samples.

EPiC IMPOC – AMR MODULE (II)

Table 4.7: Antimicrobial spectrum of activity (ASAI) summary in urine cultures.

Antimicrobial	ASAI_N (N_{gn}–N_{sp})	ASAI_P (N_{gn}–N_{sp})	Narrow	Intermediate	Broad	Category	ASAI_N	ASAI_P
Tazocin (TAZ)	71.4 (7–22)	100.0 (3–4)			[32, 33]	Broad		
Meropenem (MER)	83.9 (7–22)	75.0 (4–5)			[32, 33]	Broad		
Amikacin (AMI)	75.0 (8–23)	66.7 (3–4)				Broad		
Ceftazidime (CAZ)	64.0 (7–22)	66.7 (3–4)			[32]	Broad		
Ertapenem (ERT)	56.7 (6–18)	75.0 (4–5)				Broad		
Amoxicillin (AMO)	50.0 (4–5)	73.8 (5–27)	[34]	[32]		Intermediate		
Gentamicin (GEN)	63.7 (9–24)	54.0 (6–27)	[33]			Intermediate		
Tigecycline (TIG)	33.3 (3–5)	100.0 (2–4)				Intermediate		
Amoxicillin-Clavunalate (AUG)	38.1 (7–18)	86.3 (6–31)	[34]	[33]		Intermediate		
Nitrofurantoin (NIT)	36.2 (7–17)	66.7 (6–32)	[33]			Intermediate		
Cefotaxime (CTX)	24.7 (5–18)	75.0 (4–5)				Intermediate		
Cephalexin (CELX)	33.3 (6–14)	54.2 (6–29)				Intermediate		
Ciprofloxacin (CIP)	34.9 (9–25)	27.0 (6–26)			[32, 35]	Intermediate		
Mecillinam (MEC)	17.5 (6–18)	50.0 (2–3)				Intermediate		
Cefoxitin (CXT)	11.7 (5–16)	68.6 (4–8)			[34]	Intermediate		
Trimethoprim (TRI)	20.1 (8–20)	13.8 (5–29)	[34]	[33]		Intermediate		
Vancomycin (VAN)	100.0 (1–1)†	75.0 (5–25)	[33, 34]			Narrow		
Aztreonam (AZT)	41.5 (7–10)	–	[34]		[32]	Narrow		
Clindamycin (CLI)	100.0 (1–1)†	36.0 (5–27)			[33]	Narrow		
Erythromycin (ERY)	100.0 (1–1)†	34.0 (5–26)				Narrow		

† represents insufficient number of species not displayed in graphical summary.
Note: The effective threshold was set at 0.05.
Note: The antimicrobials have been sorted using the geometric mean of the indexes.
Keys: ASAI_N=antimicrobial spectrum of activity index for Gram-negative; ASAI_P=antimicrobial spectrum of activity index for Gram-positive; N_{gn}=number of genera; N_{sp}=number of species;

−1   −0.5   0   0.5   1

EPiC IMPOC – DEMONSTRATION

Imperial College
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epic impoc

enhanced, personalized and integrated care
for infection management at point of care

Health Protection Research Unit in HCAI and AMR | Medicine

Centre for Bio-Inspired Technology Biomedical Engineering | EEE

Imperial College London

?

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3rd of November 2020