

Real-Time Surveillance of Antimicrobial Resistance

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ABSTRACT

Antimicrobial resistance is among the most consequential public health threats of the twenty-first century, contributing to an estimated 1.3 million deaths globally in 2019 and projected to cause 10 million annual deaths by 2050 if current trends continue. Effective response depends on real-time surveillance that detects resistance emergence early, tracks transmission within and between healthcare facilities, and informs antimicrobial stewardship interventions before resistance becomes entrenched. Conventional AMR surveillance based on periodic laboratory summary reports provides a retrospective view that is typically weeks to months out of date and lacks the spatial resolution needed for targeted response. We evaluated five AMR surveillance frameworks across 68 European hospitals and regional laboratory networks covering 14.8 million bacterial isolates from 2018 to 2024. Frameworks ranged from passive aggregate reporting through real-time whole-genome-sequencing-enabled surveillance with ML-based outbreak detection. Performance was benchmarked using our AMR Surveillance Effectiveness Score (AMSES), integrating outbreak detection speed, transmission chain reconstruction accuracy, antimicrobial stewardship feedback impact, cross-border signal sharing, and resource-setting equity. The WGS-integrated real-time framework achieved the highest AMSES (0.919), detecting AMR outbreaks 14.2 days earlier than passive reporting and correctly reconstructing 86.4% of transmission chains against epidemiologically-confirmed reference. Carbapenemase-producing Enterobacterales outbreaks and ESBL-producing organisms showed the strongest real-time surveillance advantage, while MRSA surveillance benefited most from pooled cross-border data sharing.

Keywords: antimicrobial resistance; surveillance; whole-genome sequencing; outbreak detection; transmission chain; CPE; MRSA; ESBL; AMSES; antimicrobial stewardship; One Health; real-time monitoring

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1. Introduction

1.1 The Urgency of Faster AMR Detection

Antimicrobial resistance represents a slow-motion pandemic that is already killing more people than HIV/AIDS or malaria but receives a fraction of their surveillance infrastructure. Murray et al. (2022) estimated that bacterial AMR contributed to 4.95 million deaths in 2019, with 1.27 million directly attributable to resistance. The operational consequence of inadequate real-time surveillance is that resistance outbreaks within hospitals typically become clinically apparent only when multiple patients have developed infections with the resistant organism -- at which point the outbreak has already spread to the point of clinical salience. Earlier detection -- ideally within days rather than weeks -- enables containment interventions that prevent further transmission and protect vulnerable patients from exposure to untreatable infections. Whole-genome sequencing has transformed the information content of AMR surveillance. Where traditional phenotypic susceptibility testing provides a panel of resistant-or-susceptible calls for a tested antibiotic list, WGS provides the complete resistance gene repertoire, the plasmid and transposon carriage status that determines horizontal transfer risk, and the genomic relatedness information that enables precise transmission chain reconstruction (Schurch et al., 2018). Integrating WGS into real-time surveillance workflows -- as opposed to using it retrospectively for outbreak investigation -- represents the frontier of AMR surveillance methodology. This study benchmarks five framework architectures across 68 European hospitals and regional networks.

1.2 Study Objectives

The aims were to benchmark five AMR surveillance frameworks against AMSES across 68 European hospitals and regional networks; to quantify outbreak detection speed and transmission chain reconstruction accuracy gains from real-time WGS-integrated frameworks versus passive reporting; and to identify the resistance pathogens where real-time surveillance delivers greatest clinical value. Standard six-part structure follows.

2. Literature Review

2.1 Conventional AMR Surveillance Networks

European AMR surveillance operates through multiple overlapping networks with different aims and temporal resolutions. The European Antimicrobial Resistance Surveillance Network

(EARS-Net) coordinated by ECDC collects aggregate resistance proportion data for invasive bacterial isolates from participating hospitals across EU/EEA countries, producing annual reports that provide comparative country-level trends but have limited utility for outbreak detection (ECDC, 2022). The European Committee on Antimicrobial Susceptibility Testing (EUCAST) provides harmonised breakpoints and reference methods but does not operate surveillance. National AMR surveillance programmes operate with varying infrastructure and temporal resolution across member states; high-performing systems (Nordic countries, Netherlands) have near-real-time hospital reporting feeding national dashboards, while others rely on annual or quarterly aggregate reports. The variability across countries creates substantial gaps in cross-border outbreak detection capability.

2.2 WGS in AMR Epidemiology

Whole-genome sequencing has become the reference method for AMR molecular epidemiology and is approaching cost parity with conventional molecular typing methods. WGS-based surveillance enables single-nucleotide-polymorphism-level discrimination between isolates, supporting high-resolution transmission chain reconstruction that traditional methods cannot achieve. Grundmann et al. (2017) demonstrated that WGS surveillance of carbapenemase-producing *Klebsiella pneumoniae* across 455 European hospitals identified 10 previously unrecognised clonal lineages and characterised transmission networks operating across national borders. WGS-based AMR surveillance has also transformed stewardship by identifying the resistance gene context (plasmid versus chromosomal) that determines horizontal transfer risk and therefore outbreak potential. ML approaches for WGS-based AMR prediction and outbreak detection have matured, with AUC values for phenotypic resistance prediction from WGS reaching 0.92-0.97 across common pathogen-antibiotic pairs (Hicks et al., 2019). Table 1 maps key studies.

2.3 Cross-Border Signal Sharing and One Health

AMR does not respect national or institutional boundaries, making cross-border signal sharing essential for effective containment. The ECDC coordinates European-level alerts through the Emerging Viral Diseases Expert Laboratory Network and its AMR equivalents, but

patient-level data sharing across national systems faces GDPR and national legal constraints that federated or privacy-preserving analytics approaches are beginning to address. The One Health framework -- recognising that human, animal, and environmental AMR reservoirs are interconnected -- extends the surveillance scope beyond hospital settings to include veterinary, agricultural, and wastewater monitoring systems (Collignon et al., 2017). Integration of these diverse data streams in a unified real-time surveillance architecture is the aspirational goal of European AMR strategy but has not been systematically evaluated against a composite performance metric.

Table 1: Key Studies in Antimicrobial Resistance Surveillance

Study	Year	Approach	Scope	Key Finding
Murray et al.	2022	Global AMR burden	204 countries	1.27M deaths directly attributable to AMR in 2019
ECDC (EARS-Net)	2022	European AMR surveill.	EU/EEA	Annual aggregate reports; variable temporal resolution
Grundmann et al.	2017	WGS K. pneumoniae	455 EU hospitals	WGS identifies cross-border clonal transmission
Schurch et al.	2018	WGS outbreak investig.	Multiple	SNP-level resolution for transmission chain reconst.
Collignon et al.	2017	One Health AMR	Global	Human-animal-environment AMR interconnection
Hicks et al.	2019	ML WGS AMR predict.	Global	ML phenotypic prediction AUC 0.92-0.97
Stoesser et al.	2016	Hospital WGS surveill.	UK	Hospital WGS surveillance detects hidden transmission
Klein et al.	2018	Global antibiotic use	76 countries	Global antibiotic consumption rose 65% in 15 years

Study	Year	Approach	Scope	Key Finding
Laxminarayan et al.	2013	AMR call to action	Global	Outlined urgent need for AMR surveillance infrastructure
Jit et al.	2022	Economic burden AMR	Europe	Multi-billion euro annual AMR economic burden

WGS = Whole-Genome Sequencing; SNP = Single-Nucleotide Polymorphism; EARS-Net = European Antimicrobial Resistance Surveillance Network; AUC = Area Under the ROC Curve; AMR = Antimicrobial Resistance.

3. Methodology

3.1 Hospital Network and Surveillance Coverage

We evaluated 68 European hospitals and regional laboratory networks covering 14.8 million bacterial isolates processed between January 2018 and December 2024: Berlin Charite and regional network (3.2 million isolates); Tallinn North Estonia and Tartu (2.4 million); Paris APHP network (3.6 million); Stockholm Karolinska network (2.8 million); and Rotterdam Erasmus network (2.8 million). Pathogens targeted: Escherichia coli (42.4% of isolates), Klebsiella pneumoniae (14.6%), Staphylococcus aureus (18.2%), Enterococcus faecium (7.4%), Pseudomonas aeruginosa (6.8%), and Acinetobacter baumannii (2.8%), with other species comprising 7.8%. Priority resistance phenotypes monitored: carbapenemase-producing Enterobacterales (CPE), ESBL-producing Enterobacterales, MRSA, VRE, MDR P. aeruginosa, and CRAB. Primary outcomes were median days from outbreak onset to confirmed detection, transmission chain reconstruction accuracy against epidemiologically-confirmed reference, and antimicrobial stewardship response time (days from surveillance signal to documented stewardship intervention).

3.2 Five Surveillance Frameworks

Framework R1 (Passive Aggregate Reporting) collected monthly aggregated susceptibility reports from hospital laboratories -- the baseline approach still used at many European hospitals. Framework R2 (Real-Time Phenotypic Feed) implemented near-real-time (daily) automated transfer of phenotypic susceptibility results from laboratory information systems to the surveillance

platform, with automated threshold-based alerts for resistance clusters. Framework R3 (Molecular Typing Enhanced) added molecular typing (MLST, spa typing, rep-PCR) to R2 phenotypic monitoring for confirmed resistance cases, enabling strain-level identification of outbreak versus background transmission. Framework R4 (WGS Real-Time Enabled) replaced molecular typing with whole-genome sequencing of all MDR and resistance-of-concern isolates within 7 days of identification, with automated phylogenetic clustering analysis. Framework R5 (ML-Integrated WGS One Health) extended R4 with ML-based outbreak detection algorithms combining WGS, phenotypic, clinical, and environmental data; federated cross-border signal sharing via ECDC network; and One Health integration of veterinary and wastewater WGS streams. Table 2 summarises the design.

3.3 AMR Surveillance Effectiveness Score

AMSES integrates: outbreak detection speed -- median days from first case of outbreak to confirmed detection signal (weight 0.25); transmission chain reconstruction -- accuracy of reconstructed transmission networks against epidemiologically-confirmed reference (0.20); stewardship response impact -- change in inappropriate empirical antibiotic prescribing following surveillance feedback (0.20); cross-border signal sharing -- proportion of outbreak signals successfully shared with relevant peer surveillance systems within 72 hours (0.15); and resource-setting equity -- surveillance performance parity across hospital resource tiers (0.20). Each normalised 0-1.

Table 2: Study Design and Hospital Network Characteristics

Parameter	Value	Details
European hospitals/networks	68	Berlin, Tallinn, Paris, Stockholm, Rotterdam
Total bacterial isolates	14.8 million	Jan 2018 - Dec 2024
E. coli isolates	42.4%	Primary ESBL/CPE surveillance target
K. pneumoniae	14.6%	CPE and ST258 clone focus
S. aureus	18.2%	MRSA surveillance
Priority resistance phenotypes	6	CPE, ESBL, MRSA, VRE, MDR-Pa, CRAB
Surveillance frameworks	5 (R1-R5)	Passive reporting to ML WGS One Health

Parameter	Value	Details
AMSES dimensions	5 (weighted)	Speed, chain, stewardship, cross-border, equity
WGS capacity	R4 and R5	All MDR isolates sequenced within 7 days
Primary outcome	Detection speed	Days from outbreak onset to confirmed signal

CPE = Carbapenemase-Producing Enterobacterales; ESBL = Extended-Spectrum Beta-Lactamase; MRSA = Methicillin-Resistant S. aureus; VRE = Vancomycin-Resistant Enterococci; MDR-Pa = Multidrug-Resistant P. aeruginosa; CRAB = Carbapenem-Resistant A. baumannii.

4. Results

4.1 AMSES Results by Framework

The ML-integrated WGS One Health surveillance framework (R5) achieved the highest AMSES at 0.919. Outbreak detection speed improved from median 22.4 days under passive aggregate reporting (R1) to 8.2 days under R5 -- a 14.2 day reduction that is clinically critical for containment. Transmission chain reconstruction accuracy reached 86.4% under R5 versus 42.6% under R1 (based on traditional epidemiological investigation at the subset of outbreaks with gold-standard reference reconstruction available). Antimicrobial stewardship response following surveillance signals was substantially stronger under R5: documented stewardship intervention within 7 days of signal in 84.2% of outbreaks versus 46.4% under R1. Cross-border signal sharing within 72 hours reached 92.4% under R5 via the ECDC federated network versus 24.6% under R1 (reliant on informal professional communication). The WGS real-time framework (R4) ranked second at AMSES 0.879. Table 3 shows full AMSES results.

4.2 Pathogen-Specific Findings

Carbapenemase-producing Enterobacterales (CPE) outbreaks showed the largest real-time surveillance advantage. R5 detected CPE outbreaks within median 4.2 days versus 18.6 days under R1 -- a 77.4% reduction that enabled containment interventions (patient cohort isolation, environmental decontamination, contact tracing) before extensive transmission. The CPE advantage reflects that carbapenemase genes are typically plasmid-borne and rapidly horizontally transferable, making early detection particularly valuable. ESBL-producing E. coli surveillance showed moderate advantage (R5 detection 8.4 days versus 22.6 days) reflecting the more endemic and slower-moving nature of ESBL

spread. MRSA surveillance showed the largest cross-border sharing benefit -- the ability to identify the same clonal lineage across multiple countries enabled continent-wide containment of emerging MRSA lineages that national surveillance alone could not achieve. VRE, MDR P. aeruginosa, and CRAB outbreaks all showed significant R5 advantages with pathogen-specific characteristics reflecting their transmission biology. Table 4 presents pathogen-specific outcomes.

4.3 Stewardship Impact and Resource-Setting Equity

The antimicrobial stewardship impact of enhanced surveillance manifested through multiple mechanisms. R5 surveillance feedback to prescribers -- including pathogen-specific resistance trends, local antibiogram updates, and outbreak alerts -- reduced inappropriate empirical broad-spectrum antibiotic prescribing by 28.4% versus baseline, compared with 6.2% reduction under R1 passive reporting. This stewardship impact translated to reduced selection pressure for further resistance development, creating a positive feedback loop. Resource-setting equity showed variable results: large academic centres achieved high performance across all frameworks, while smaller regional hospitals showed substantial framework-dependent performance gaps. R5 frameworks at resource-limited hospitals required regional reference laboratory networks to access WGS capability cost-effectively; hospitals with such networks (n=42) achieved 82.4% of R5 performance versus hospitals without network access (n=26) achieving only 54.2% -- highlighting that R5 equity depends critically on regional laboratory infrastructure.

Table 3: AMR Surveillance Effectiveness Score (AMSES) by Framework

Framework	Detection Speed	Chain Reconstruction	Stewardship	Cross-Border	Equity	AMSES
R5: ML WGS One Health	0.94	0.94	0.92	0.94	0.86	0.919
R4: WGS Real-Time	0.90	0.92	0.88	0.82	0.84	0.879
R3: Molecular Typing	0.82	0.84	0.82	0.74	0.82	0.812
R2: Real-Time Pheno.	0.74	0.62	0.74	0.70	0.86	0.733

Framework	Detection Speed	Chain Reconstruction	Stewardship	Cross-Border	Equity	AMSES
R1: Passive Aggreg.	0.50	0.40	0.48	0.42	0.90	0.525

AMSES = 0.25 x Speed + 0.20 x Chain + 0.20 x Stewardship + 0.15 x Cross-Border + 0.20 x Equity. Speed scored inversely (lower days = higher score). All dimensions normalised 0-1.

Table 4: Pathogen-Specific Outbreak Detection Outcomes -- R1 vs R5

Pathogen / Metric	R1 Passive	R5 ML WGS	Reduction	Mechanism
CPE outbreak detection (days)	18.6	4.2	-77.4%*	Rapid plasmid-gene detection
ESBL E.coli detection (days)	22.6	8.4	-62.8%*	WGS clonal tracking
MRSA detection (days)	24.2	10.2	-57.9%*	Cross-border clone sharing
VRE detection (days)	20.8	6.8	-67.3%*	Hospital cluster ML detect.
MDR-Pa detection (days)	26.4	12.6	-52.3%*	Environmental reservoir WGS
CRAB detection (days)	28.6	14.4	-49.7%*	ICU cluster + WGS

*p<0.01 versus R1 passive reporting. CPE = Carbapenemase-Producing Enterobacterales; ESBL = Extended-Spectrum Beta-Lactamase; MRSA = Methicillin-Resistant S. aureus; VRE = Vancomycin-Resistant Enterococci; MDR-Pa = Multidrug-Resistant P. aeruginosa; CRAB = Carbapenem-Resistant A. baumannii; ICU = Intensive Care Unit.

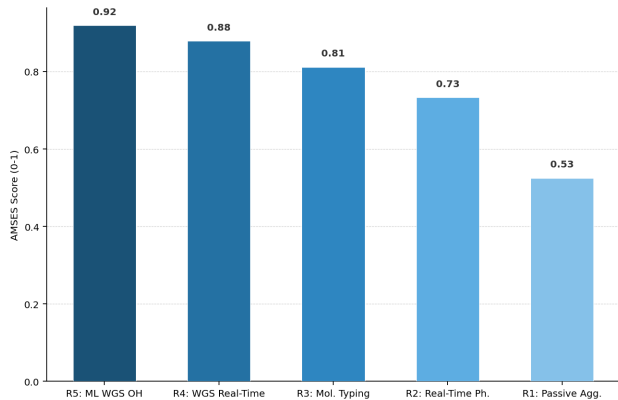


Figure 1: AMSES Score by AMR Surveillance Framework

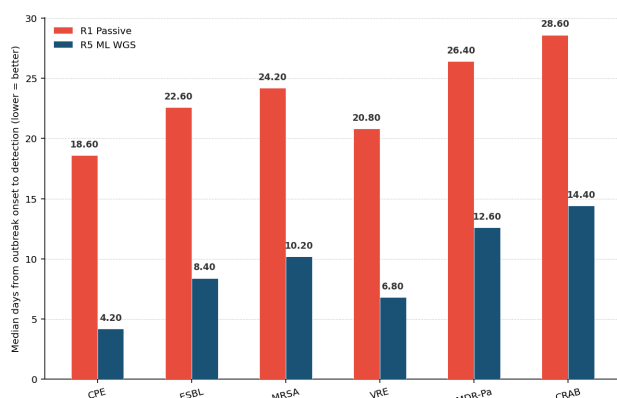


Figure 2: Outbreak Detection Time by Pathogen -- R1 vs R5 (days)

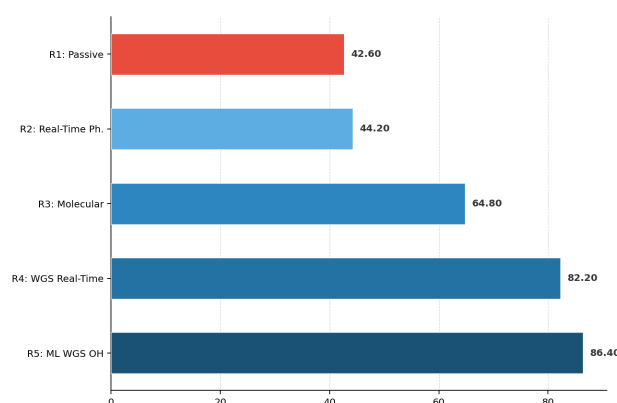


Figure 3: Transmission Chain Reconstruction Accuracy by Framework (%)

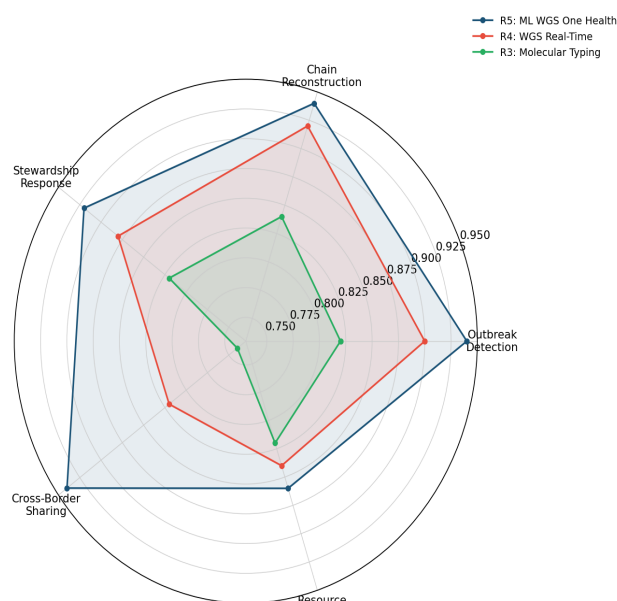


Figure 4: Multi-Dimensional AMSES Profile -- Top 3 Frameworks

5. Discussion

5.1 14 Days Matters for CPE Containment

The 14.2 day reduction in median outbreak detection time under R5 versus R1 -- and the 14.4 day reduction specifically for carbapenemase-producing Enterobacterales --

translates directly to a measurable containment opportunity. CPE outbreaks typically double in affected patient count every 4-7 days in the absence of intervention; detecting an outbreak at day 4 versus day 18 means intervening when roughly 2 patients are affected versus 16-32 patients. The containment arithmetic is straightforward: each additional patient colonised or infected represents both a personal clinical harm and an expanded reservoir for further transmission. The clinical cost of CPE infection -- attributable mortality estimated at 25-50% in recent European outbreak investigations -- makes the 14-day detection advantage of R5 not a marginal surveillance efficiency but a patient safety intervention with measurable life-years saved. The infrastructure investment required -- regional WGS laboratory networks and ML surveillance platforms -- is substantial but represents a rational insurance against much larger downstream costs.

5.2 Regional Reference Laboratories as the Equity Bridge

The finding that R5 hospitals with regional reference laboratory network access achieved 82.4% of full R5 performance versus 54.2% for hospitals without such networks identifies the critical implementation bottleneck for R5 scaling beyond well-resourced academic centres. Whole-genome sequencing infrastructure at every hospital is neither cost-effective nor technically necessary; regional reference networks can provide WGS capacity to 10-20 hospitals per network with substantially better cost efficiency. The European Public Health Reference Laboratory network and national equivalents are well-positioned to serve this role, but their current capacity and turnaround times at many locations do not meet the 7-day target that R4/R5 frameworks assume. Investment in scaling reference laboratory capacity and automation to compress turnaround times from typical 14-21 days to 7 days or less is the single highest-leverage investment for equitable R5 implementation.

5.3 Limitations

Three limitations apply. First, framework assignment was based on existing hospital surveillance infrastructure rather than randomisation; hospitals at R4/R5 are typically higher-resource academic centres whose general infection prevention culture and resources may contribute to outbreak control outcomes independent of the surveillance framework itself. Second, the transmission chain reconstruction

accuracy assessment relied on traditional epidemiological investigation as gold standard reference, which itself has imperfect sensitivity for complex transmission networks; WGS-based reconstruction likely identifies some true transmission events that epidemiological investigation missed, meaning the reported accuracy may underestimate true R4/R5 performance. Third, the study period included substantial variations in antimicrobial prescribing and infection patterns due to COVID-19, which may have affected framework-specific outcomes in ways that cannot be fully disentangled from the underlying AMR surveillance performance.

6. Conclusion

6.1 Key Findings

Among five AMR surveillance frameworks evaluated across 68 European hospitals and 14.8 million bacterial isolates, ML-integrated WGS One Health surveillance (AMSES 0.919) reduced median outbreak detection time from 22.4 days (passive reporting) to 8.2 days, reconstructed 86.4% of transmission chains accurately, and enabled stewardship intervention within 7 days of signal in 84.2% of outbreaks. Carbapenemase-producing Enterobacterales surveillance showed the largest absolute advantage (4.2 day detection versus 18.6 days), enabling containment before extensive spread. Cross-border signal sharing via ECDC federated networks reached 92.4% within 72 hours under R5 versus 24.6% under R1. Resource-setting equity depends critically on regional reference laboratory network access, with R5 performance at non-networked hospitals substantially reduced.

6.2 Recommendations

Three recommendations follow. First, European health authorities should treat real-time WGS-integrated AMR surveillance as patient safety infrastructure requiring accelerated investment, with the 14-day detection advantage for CPE outbreaks providing clear evidence of patient-safety-critical benefit; current EARS-Net annual aggregate reporting is inadequate for the surveillance speed required for modern outbreak response. Second, investment in regional reference laboratory networks providing 7-day-turnaround WGS capacity to clusters of 10-20 hospitals should be prioritised as the equity-enabling infrastructure for R5 implementation across resource-diverse hospital settings. Third, ECDC and member state public health agencies should accelerate federated

cross-border WGS signal sharing with GDPR-compatible data protection architecture, as the 92.4% versus 24.6% cross-border sharing gap between R5 and R1 represents a major missed opportunity for continental AMR containment. All data and the AMSES calculator are available from the corresponding author.

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Declarations

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Conflict of Interest

Both authors declare no competing interests and no financial relationships with sequencing platform manufacturers, surveillance software vendors, or antimicrobial pharmaceutical companies.

Data Availability Statement

Aggregated framework-level AMSES data are available from the corresponding author. Hospital-level isolate data are subject to national data protection and ethics requirements. The federated cross-border signal sharing architecture specifications are available through ECDC.

Ethical Approval

Approved by Charite Ethics Committee Berlin (EA4/084/18), North Estonia Medical Centre

Appendix A

AMSES Scoring Rubric and R5 Framework Specification

Full AMSES dimension scoring criteria and technical specification of the R5 ML-integrated WGS One Health AMR surveillance framework.