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ORIGINAL ARTICLE

Prevalence and antibiotic susceptibility of Acinetobacter baumannii, Pseudomonas aeruginosa and Klebsiella pneumoniae in Estonian intensive care units in comparison with European data

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Abstract

This prospective cohort study was performed from April to December 2003 for the purpose of collecting a maximum of 50 non-duplicate isolates of Acinetobacter baumannii, Pseudomonas aeruginosa, and Klebsiella pneumoniae from each of 4 ICUs to determine minimum inhibitory concentrations. The most prevalent species were Enterobacteriaceae (13%), K. pneumoniae and A. baumannii (both 12%). 60% of A. baumannii strains were susceptible to ampicillin/sulbactam and cefepime, 95% to meropenem and imipenem, and 75% to amikacin. 79% of P. aeruginosa strains were piperacillin/tazobactam, 58% ceftazidime, 81% meropenem, 72% imipenem, 69% ciprofloxacin and 97% amikacin susceptible. The susceptibility of K. pneumoniae to meropenem and imipenem was 99%, to ciprofloxacin was 91% and to amikacin was 98%. Gram-negative bacteria (especially K. pneumoniae and A. baumannii) were prevalent in our ICUs compared to other European studies. Carbapenem susceptibility of Estonian strains was higher, but P. aeruginosa sensitivity to ceftazidime was lower, compared to other EU countries.

Introduction

Monitoring of antimicrobial resistance at the local or national level and comparison of these data with other countries serves several purposes. The first is the question of clinical relevance of empirical antimicrobial therapy guidelines. Since antimicrobial resistance varies highly, it is difficult to compile international therapy guidelines for infectious diseases and it is not always known in which situations and regions these are applicable. A problem of how to treat infections is common, especially in intensive care units (ICUs), where adequate empirical therapy employment may save human lives, as well as financial resources. The most frequent cause of mortality and morbidity in intensive care units is infection caused by Gram-negative resistant pathogens [1,2]. Successful management of these infections relies on adequate antibiotic therapy, which should begin empirically, and be adapted by the spread of local pathogens and their susceptibility pattern.

The second task is to identify the possible threat areas that serve as sources of highly resistant strains. The European Union has been expanded during past y. This expansion has led to a higher risk of pathogen spread between countries and thus has also led to more infections and requires increased antimicrobial resistance surveillance. Unfortunately, the information about prevalent pathogens and their susceptibility, as well the antibiotic usage, is incomplete not only in the Baltic States, but also in the other Central and Eastern European countries. For this reason, the microbiological background of new membership countries of the European Union may contain valuable information concerning the importance and manner of re-estimation of current infection control policy.

The third task includes theoretical questions important for understanding the spread of resistance. The resistance gradient between Northern and Western Europe is well known in the case of Gram-positive bacteria [3]. Putative reasons for the

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gradient include differences in the availability of antibiotics (selection of strains by antibiotic pressure), infection control measures (clonal spread of strains) and probable methodical biases (sampling habits, methods used, quality assurance of laboratory tests). Evaluating and correlating resistance in post-socialist countries (including the Baltic States) with unique socioeconomic backgrounds, treatments and infection control traditions may give a better understanding of this topic, considering that studies for comparison of resistance and putative risk factors of different regions have more than a limited local value.

The aim of the present study is to evaluate the proportion and susceptibility of A. baumannii, P. aeruginosa, and K. pneumoniae based on the spectrum of pathogens in ICUs of Estonian hospitals and to compare these data with other studies from EU countries.

Materials and methods

We included the intensive care units of the 4 largest Estonian hospitals with 342 to 1492 beds, 9 to 28 ICU beds and 2147 to 7704 total patient-d in ICUs. For background data, the percentage of positive cultures and their nomenclature (non-duplicated analyses only) were collected from January to December 2003. Overall sampling frequencies ranged from 11 to 69 microbiological samples per 100 patient-d in these ICUs. A prospective cohort study was performed from April to December 2003 for the purpose of collecting a maximum of 50 consecutive non-duplicate isolates (mostly from the lower respiratory tract, but also from wound material, blood, and urine) of A. baumannii, P. aeruginosa, and K. pneumoniae from each ICU for susceptibility detection. An isolate was defined as the same species of bacteria with the same antimicrobial susceptibility pattern isolated from the same patient.

Organisms were identified by the participating centres using the identification method routinely employed in their clinical microbiology laboratory [4]. Minimum inhibitory concentrations (MIC) were determined in each centre using E-tests based on the manufacturer's instructions (AB Biodisk, Solna, Sweden). To determine ESBL (extended spectrum betalactamase) producers, an E-test with ceftazidime and ceftazidime combined with clavulanic acid was used. The interpretative criteria were those recommended by the NCCLS [5]. Quality control was performed with the following strains recommended by the NCCLS: E. coli ATCC 25922, P. aeruginosa ATCC 27853, and K. pneumoniae ATCC 700603.

The Ethics Review Committee at the Estonian Institute of Experimental and Clinical Medicine approved the study protocol (2003).

Results

The spectrum of pathogens

The aetiology of 1493 pathogens isolated in 2003 is as follows: Gram-positive cocci, 29.2%; Gram-negative rods, 60.0%; anaerobes, 2.0%, and pathogenic fungi, 8.8%. The prevalent species in Estonian ICUs in 2003 were K. pneumoniae, other coliforms, and A. baumannii. Our data indicate a higher proportion of Gram-negative (60% vs median 49.5%) and lower proportion of Gram-positive bacteria (29.2% vs median 44.0%) in Estonia compared with other European studies (Table I) [6–10]. K. pneumoniae was more frequent in our hospitals than in other studies (12.0% vs median 4.1%). The percentage of A. baumannii was higher in our study than in EU studies, but lower than in Turkey. Among Gram-positive bacteria, the principal difference was the incidence of enterococci (2.7% in Estonia vs median 8.5%).

Antibacterial susceptibility

A total of 325 Gram-negative pathogens collected during the study period, including 128 A. baumannii, 99 P. aeruginosa, and 98 K. pneumoniae strains, were tested (Table III). Comparing our results with other studies (Table II or Figures 1–3) [6–8,11,12], our A. baumannii and P. aeruginosa strains were more sensitive to carbapenems than in other European countries (exception was Frank et al. study [12] where Gram-negative bacteria were highly sensitive to most tested antibiotics). In contrast, sensitivity of P. aeruginosa to ceftazidime was lower in Estonia (58% vs median 73%). In other combinations variation was high or no clear differences were observed [6–8,11,12].

Discussion

In our study, the ratio of Gram-positive to Gram-negative pathogens was 1:2 (29% and 60%, respectively). According to data from the literature, Gram-positive microorganisms, especially CONS and S. aureus, were the predominant pathogens in ICUs [6–8,11]. In Estonian ICUs, the domination of Entrobacteriaceae, including K. pneumoniae and non-fermentative microbes such as A. baumannii and P. aeruginosa was estimated. These species are known to be responsible for a wide range of nosocomial infections among ICU patients [13–15].

Table I. Incidence of the most common bacterial species isolated from ICU patients in Estonian and European ICUs.

	Country (reference)/incidence (%)							
Pathogen	Estonia	Sweden: Sörberg et al., 2003	Germany: Jones et al., 2004	France: Jones et al., 2004	Italy: Jones et al., 2004	Europe: Goossens, 2000	Italy: Lizioli et al., 2003	Turkey: Meric et al, 2005
Gram-negative pathogens (included in study)	60	39.5	46.8	55.2	52.5	62.2	33	49.5
Other Entetrobacteriaceae	12.9	12.1	18.3	23.2	19.0	19.3	12.1	1.0
K. pneumoniae	12.0	4.7	5.4	2.7	3.5	8.9	ND	2.1
A. baumannii	12.0	1.9	ND	ND	ND	4.5	ND	26.8
P. aeruginosa	9.0	4.7	10.8	13.8	22.3	15.5	14.5	12.4
E.coli	8.2	7.6	12.3	15.5	7.7	12.2	6.4	7.2
Other Gram-negative non-fermenters	5.9	8.7	ND	ND	ND	1.8	ND	ND
Gram-positive pathogens (included in study)	29.2	45.7	41.7	42.5	44	37.8	56	45.3
S. aureus	11.0	12.5	13.6	17.2	18.1	ND*	20.2	30.9
Streptococci	9.0	6.2	ND	3.3	ND	3.7	5.6	1.0
CoNS	6.1	15.8	16.4	16.7	18.7	25.7[a]	11.3	2.1
Enterococci	2.7	8.5	11.7	5.3	7.2	8.4	8.9	11.3
Gram-positive rods	0.4	2.7	ND	ND	ND	ND	ND	ND
Pathogenic fungi	8.8	ND	ND	ND	ND	ND	10.5	5.2
Anaerobes	2.0	0.7	ND	ND	ND	ND	0.8	ND
Others	0	14.7	11.5	2.3	3.5	0	9.7	0

ND: no data; [a] Both S. aureus and CoNS.

Table II. Antibiotic susceptibility in European ICUs.

Pathogen	Antibiotics	Country (reference)/$MIC_{50/90}$ mg/L and/or% of susceptibility and method							
		Estonia 2003 (current data)[a]	Europe: Garcia-Rodriguez et al., 2002[a]	Europe: Goossens 2000[a,b,c,d]	Italy: Jones et al., 2004[a,b,c,d]	Germany: Jones et al., 2004[a,b,c,d]	France: Jones et al., 2004[a,b,c,d]	Sweden: Sörberg et al., 2003[b]	Germany: Frank et al., 2000[d]
A. baumannii	Ampicillin/sulbactam	6/24; 60%	ND	ND	ND	ND	ND	ND	ND
	Cefepime	8/24; 60%	ND	ND	17.9%	74.2%	28.0%	ND	92%
	Meropenem	0.75/3; 95%	79.6%	ND	74.5%	96.0%	68%	ND	100%
	Imipenem	0.5/1.5; 95%	82.2%	ND	77.9%	96.2%	93.8%	ND	100%
	Amikacin	4/12; 75%	ND	ND	ND	ND	ND	ND	ND
P. aeruginosa	Piperacillin/tazobactam	6/ >256; 79%	83.1%	4–8/64– ≥128	77.7%	85.8%	69.6%	ND	91%
	Ceftazidime	1.5/48; 58%	70.6%	1–2/16–32	56.7%	76.2%	70.2%	97.7%	94%
	Meropenem	1/16; 81%	76.1%	0.5–1/8	57.3%	77.8%	81.1%	ND	91%
	Imipenem	3/ >32; 72%	68.2%	2–4/8–16	59.7%	70.5%	69.5%	74.7%	94%
	Amikacin	4/12; 97%	ND	ND	ND	ND	ND	ND	ND
	Ciprofloxacin	0.25/8, 69%	63.3%	0.12–0.25/8–16	58.4%	68.6%	55.3%	96.1%	81%
K. pneumoniae	Meropenem	0.023/0.16; 99%	98.9%	≤0.06/ ≤0.06–0.12	ND	ND	ND	ND	100%
	Imipenem	0.19/0.5; 99%	98.9%	0.12–0.25 /0.5	100	100	100	ND	100%
	Amikacin	2/3; 98%	ND	ND	ND	ND	ND	ND	ND
	Ciprofloxacin	0.023/1; 91%	83.2%	≤0.06/0.12–0.25	88.2%	85.4%	89.5%	98–100%	94%
	ESBL positive (%)	17%	2.5–39.6% [f]	10.9–19.5%[g]	28.5%	8.2%	5.2%	ND	5.8%

[a]E-test; [b]disk diffusion; [c]agar dilution; [d]microdilution methods; [g]among all Enterobacteriaceae; [f]among Escherichia coli, Klebsiella spp., and Proteus mirabilis.

Table III. The distribution of antibacterial susceptibility[a] among Estonian isolates (number of isolates per MIC)

Pathogen	Antibiotics	MIC value/number of isolates																													
		0.004	0.006	0.008	0.012	0.016	0.023	0.032	0.047	0.064	0.094	0.125	0.19	0.25	0.38	0.5	0.75	1	1.5	2	3	4	6	8	12	16	24	≥32	48	64	96	128
A.baumannii	Ampicillin/ sulbactam	0	0	0	0	0	0	0	0	0	0	0	0	0	1	3	6	16	3	7	15	5	10	10	15	9	10	3	5	3	0	1
	Cefepime	0	0	0	0	1	0	0	0	0	0	0	0	0	0	1	0	1	2	2	4	17	18	30	16	10	9	7	4	4	0	0
	Meropenem	0	0	0	0	0	0	0	0	0	1	1	12	14	13	18	4	14	21	8	10	5	2	0	0	1	0	4	0	0	0	0
	Imipenem	0	0	0	0	0	0	0	0	0	0	1	7	25	19	17	16	12	14	10	2	0	1	0	0	0	0	4	0	0	0	0
P.aeruginosa	Amikacin	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	3	5	12	22	18	14	2	5	12	8	7	2	5	2	4
	Piperacillin/ tazobactam	0	0	0	0	0	0	0	0	0	0	1	1	0	0	1	0	0	8	12	16	7	6	5	6	5	0	1	7	2	1	1
	Ceftazidime	0	0	0	0	0	0	0	0	0	0	0	0	0	2	6	16	17	12	11	7	1	1	3	1	3	7	1	1	1	1	0
	Meropenem	0	0	0	0	0	0	2	0	8	4	2	8	5	6	5	8	11	8	4	5	5	4	2	1	2	0	9	0	0	0	0
	Imipenem	0	0	0	0	0	0	0	0	0	0	1	1	0	0	2	1	7	12	19	16	12	1	2	1	1	1	22	0	0	0	0
K.pneumoniaeppne	Amikacin	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	1	0	7	16	13	22	11	15	5	6	1	1	0	0	0	0
	Ciprofloxacin	0	0	0	0	0	0	0	3	4	11	11	12	13	4	5	2	3	4	2	7	5	2	2	3	0	0	6	0	0	0	0
	Meropenem	1	1	7	17	14	18	17	9	3	1	0	1	1	1	0	1	4	1	0	0	0	0	0	0	0	0	1	0	0	0	0
	Imipenem	0	0	0	0	0	0	1	2	0	3	27	26	19	7	5	2	4	1	0	0	0	0	0	0	0	0	1	0	0	0	0
	Amicacin	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2	13	31	35	8	1	3	0	2	1	0	0	1	0	0	0
	Ciprofloxacin	1	2	9	15	14	12	16	4	3	1	5	0	1	3	2	0	2	1	1	0	0	0	0	1	0	5	0	0	0	0	0

[a] Non-susceptible isolates are highlighted

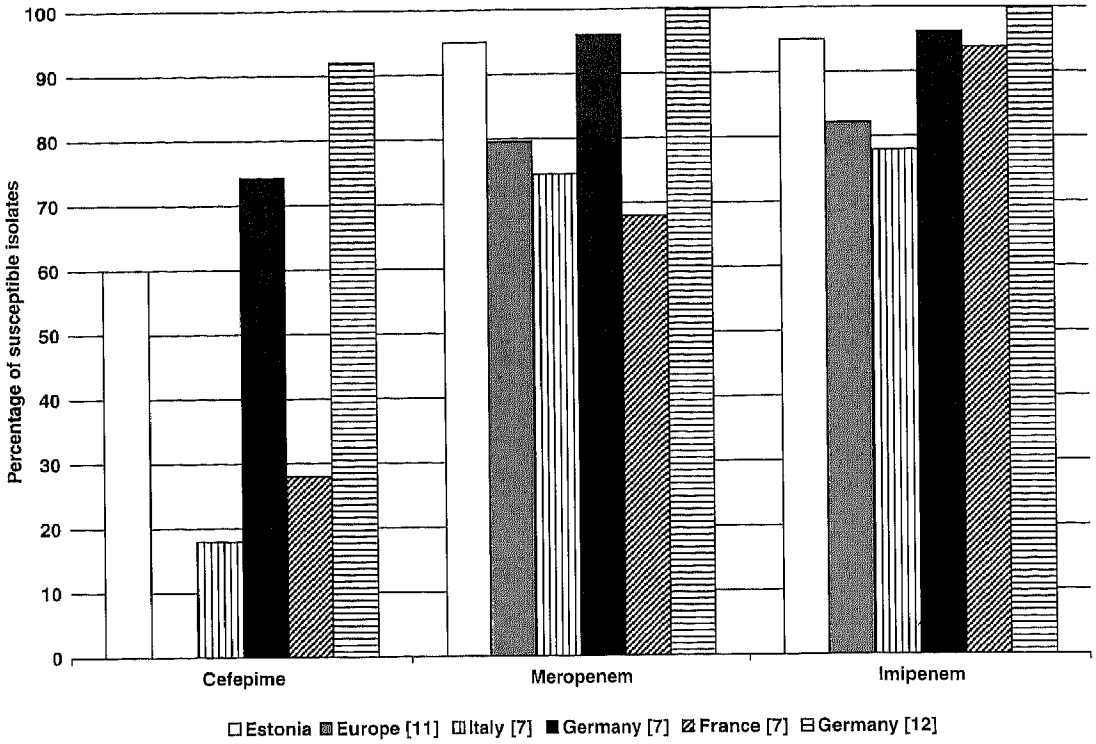

Figure 1. Antibiotic susceptibility of Acinetobacter baumannii in Estonian and European ICUs.

Differences in the proportion of Gram-negative pathogens in Estonia may be related to several factors. Infection control and antibiotic policy was introduced just few y ago and is not well developed in some hospitals, thus clonal spread of nosocomial pathogens (e.g. Klebsiella and Acinetobacter) could be frequent. On the other hand, the domination of Gram-negatives may be related to the structure of samples (e.g. respiratory tract vs blood); the isolates may have either caused infection or reflected colo-

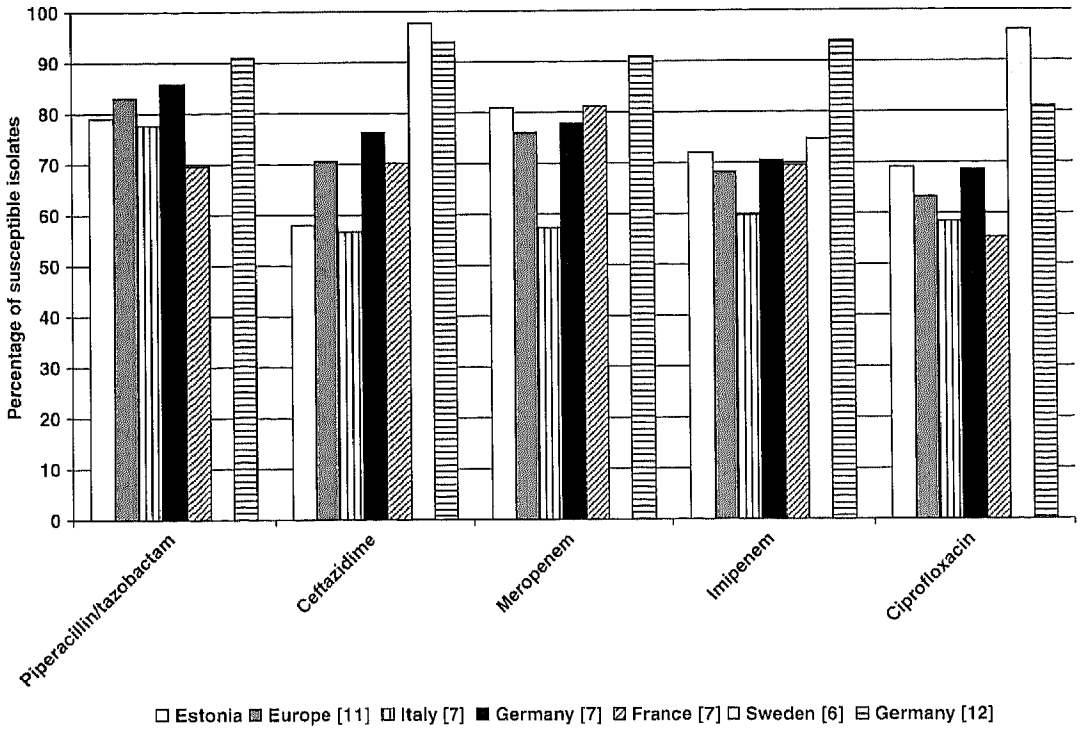

Figure 2. Antibiotic susceptibility of Pseudomonas aeruginosa in Estonian and European ICUs.

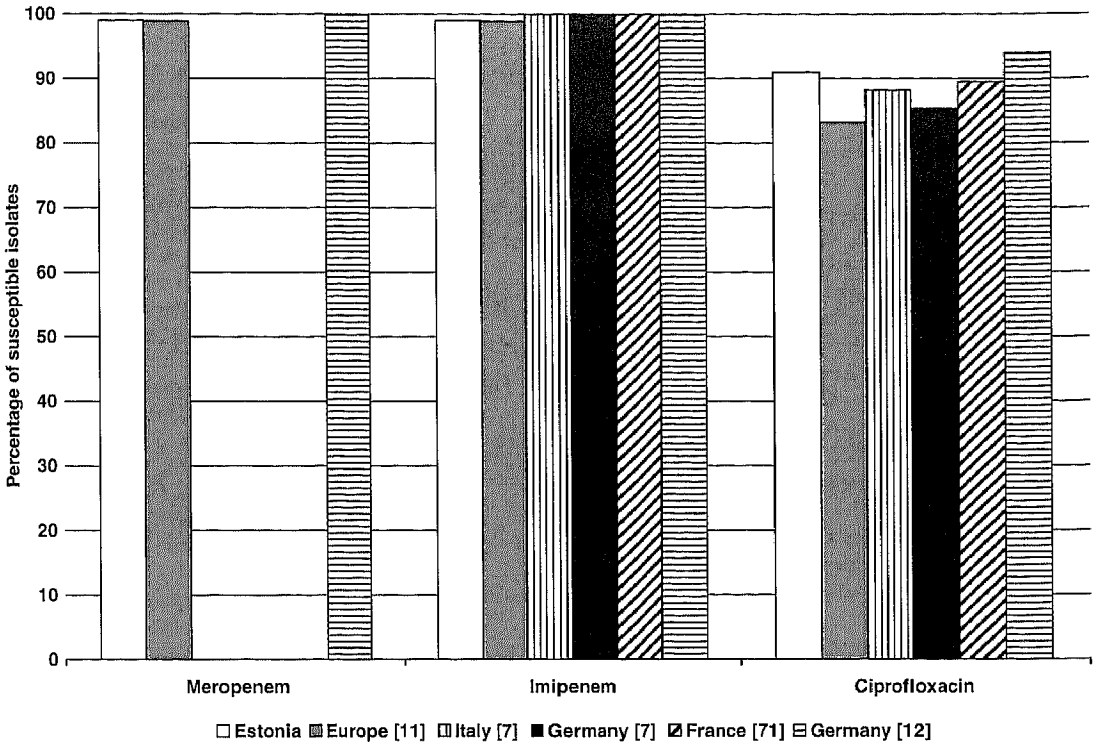

Figure 3. Antibiotic susceptibility of Klebsiella pneumoniae in Estonian and European ICUs.

nization. Overall, the apparent superiority of Gram-negatives is lower in Estonian ICUs since, during recent y, the prevalence of A. baumannii and P. aeruginosa is decreasing, while the tendency towards an increase of Entrobacteriaceae, especially K. pneumoniae, is occurring [16].

For decades, the antibiotic resistance of Gram-negative pathogens has been a troublesome task for Estonian hospitals. In our study, carbapenems and amikacin exerted an influence on 70% or more of A. baumannii strains, and amikacin, carbapenems, and piperacillin/tazobactam on 70% of P. aeruginosa strains. K. pneumoniae strains were successfully suppressed by all tested agents. ESBL-positive K. pneumoniae were found in 17% of cases, belonging to the middle of the range of European data (5% to 62%) [7,17–19]. In general, our results show that the overall antibiotic resistance rates, especially to carbapenems, are still more similar to the data of ICUs in Northern European countries than in Southern European countries [6,8,11]. This finding may be attributed more to the low level of use of those agents than to strict infection control and antibiotic policies in Estonia.

Mapping of resistance prevalence is complicated since internationally published data from the Baltic States and Central and Eastern Europe is lacking. Furthermore, the comparison of results from available studies must be handled carefully. Different sampling habits (sampling frequency and proportion of different materials) and methodology can bias these results. The comparative and quantitative (MIC distributions) data are especially necessary for Gram-negative pathogens not covered by EU surveillance networks and from European regions previously not included in surveillance projects.

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