Results on the mandatory notification of carbapenemresistant Gram-negative bacteria, Hesse, Germany, January 2012 – April 2013

Abstract

Carbapenems are important therapeutic agents for treating infections caused by multidrug-resistant Gram-negative bacteria. Mandatory reporting of carbapenem-resistant Gram-negative bacteria (CR-GN) can allow for a better understanding of the changing CR-GN burden and can help facilitate intervention. In November 2011, identification of CR-GN with acquired carbapenem resistance became notifiable in Hesse, Germany. Hesse is one of the 16 German federal states, with a population of 6.1 million. We report on CR-GN notified between 1 January and 8 April 2013, when reporting requirements were changed. During this period, 549 CR-GN were isolated from 525 patients. Of these, 67.0% (368/549) were Pseudomonas aeruginosa. The remaining 181 CR-GN comprised 59 (32.6%) K. pneumoniae, 53 (29.3%) Acinetobacter baumannii, 28 (15.5%) Enterobacter spp., 20 (11.5%) E. coli, and 21 (11.6%) other CR-GN. Seventy-three (13.3%) CR-GN were reported to harbour a carbapenemase. Fourteen different carbapenemase types were reported, with the most frequent being OXA-23 (n=18), OXA-48 (n= 16), VIM-2 (n=12), VIM-1 (n=11), and NDM (n=5). Our results suggest the widespread presence of CR-GN, a high diversity of identified carbapenemases, autochthonous transmissions, and regional differences in incidence for the different species and carbapenemases, even in the absence of major outbreaks of infection.

Keywords: population-based surveillance, Gram-negative bacteria, multidrug resistance, carbapenemase, carbapenem, epidemiology, mandatory notification

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Table 1: CR-GN notification and surveillance case definition

- 1. CR-GN with molecular confirmation of any carbapenemase
- 2. CR-GN with phenotypic resistance

Acinetobacter baumannii-complex: Resistant to imipenem or meropenem*

Pseudomonas aeruginosa: Resistant to imipenem and meropenem and ceftazidim

Enterobacteriaceae (if not listed under exceptions): Resistant to imipenem or meropenem or ertapenem

Exceptions:

Proteus spp., *Morganella* spp., *Providencia* spp., *Serratia* spp.: Resistant to imipenem, and – in addition – to ertapenem or meropenem[†]

Enterobacter spp., Citrobacter spp: Resistant to imipenem or meropenem*

Species with intrinsic mechanisms of carbapenem-resistance were not notifiable, e.g. *Stenotrophomonas maltophilia*, *Elizabethkingia meningoseptica*, *Chryseobacterium indologenes*, and *Burkholderia cepacia*.

- * Isolated resistance to ertapenem was not notifiable
- [†] Isolated resistance to impenem was thought to be due to resistance mechanisms other than carbapenemase production and therefore not notifiable

Introduction

Carbapenems are important therapeutic agents for treating infections caused by multidrug-resistant Gramnegative bacteria [1]. A common mechanism of carbapenem resistance is acquisition of hydrolytic enzymes (carbapenemases) inactivating beta-lactams [2]. Most carbapenemases are plasmid mediated, and have been mainly reported in Enterobacteriaceae, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* [3]. The spread of carbapenem-resistant Gram-negative bacteria (CR-GN) is a threat to healthcare delivery [3], [4], [5], [6].

In 2011, the European Centre for Disease Prevention and Control (ECDC) published two reports on the spread of carbapenemase-producing Enterobacteriaceae which recommended making all clinical cases of carbapenemase-producing Enterobacteriaceae (CRE) notifiable to public health authorities [7], [8]. Mandatory CRE reporting can allow for a better understanding of the changing CRE burden and can help facilitate intervention [9].

CR-GN are not notifiable under the German Protection against Infection Act [10]. However, nosocomial outbreaks involving at least two infections are notifiable. In addition, the German Protection against Infection Act allows State authorities to extend reporting requirements.

Hesse is one of the 16 German federal states, with a population of 6.1 million, subdivided into 26 counties. In November 2011, identification of Gram-negative bacilli with acquired carbapenem resistance became notifiable in Hesse [11]. The purpose of reporting and surveillance was 1) to prevent transmission of CR-GN within or among healthcare facilities, 2) to identify outbreaks and potential sources or sites of ongoing transmission, and 3) to better characterise the epidemiology of CR-GN. However, as available information on the occurrence of CR-GN in Hesse was scarce, data to be notified to local public health authorities (LPHA) and data to be forwarded to the state public health authority (SPHA) was limited to laboratory notification data until 8 April 2013, when case definitions and reporting requirements were changed. Here we report on CR-GN notified between 1 January 2012 and 8 April 2013.

Methods

Reporting procedure

Laboratories were required to notify CR-GN that meet the notification criteria within one day to LPHAs, and LPHAs were required to forward case-based data within one week to the SPHA. Data to be forwarded to the state level – and presented here – included demographic characteristics of the patient, specimen type, date of specimen receipt at the laboratory, diagnostics carried out, laboratory results (including antibiogram), and unique identifier within the LPHA.

Case definition

In March 2012, notification and surveillance case definitions were issued (Table 1). Only notifications which met these definitions were included in the analysis.

Analysis

We extracted from the Hessian CR-GN database all cases notified between 1 January 2012 and 8 April 2013. We counted as CR-GN isolates notifications of the first isolate - identified at species level - per patient. Data were extracted as of 2 August 2013. We assigned cases to one of four multidrug-resistant organism (MDRO) network regions (North, Centre, Rhine-Main and South) based on their residence. Patients not residing in Hesse were assigned to the MDRO region in which the treating hospital was located. To avoid double counting patients not residing in Hesse and reported by a different LPHA to the state level, we compared all notifications with previously reported patients for month and year of birth and gender. Where necessary, we asked LPHA for clarification. Population data were provided by the Hesse Statistical Office. We compared proportions using the Pearson chi-square test and calculated 95% confidence intervals (CI) for incidence rates and incidence rate ratios (IRRs). In addition, we report data on notified CR-GN outbreaks. Data analysis



MDRO-		osiella moniae		erichia :oli		obacter pp.		tobacter mannii		lomonas ginosa		her -GN	Total
region	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	
North	13	18.6	1	1.4	1	1.4	5	7.1	48	68.6	2	2.9	70
Centre	5	3.9	1	0.8	5	3.9	12	9.4	99	77.3	6	4.7	128
Rhine- Main	35	11.9	13	4.4	14	4.7	28	9.5	194	65.8	11	3.7	295
South	6	10.7	5	8.9	8	14.3	8	14.3	27	48.2	2	3.6	56
Hesse	59	10.8	20	3.6	28	5.1	53	9.7	368	67.0	21	3.8	549

Table 2: Number of CR-GN isolates reported in Hesse, Germany, by species and MDRO-region, 1 January 2012 - 8 April 2013

was carried out with STATA (StataCorp LP, United States, version 12.1).

Results

From 1 January 2012 to 8 April 2013, notifications of 549 CR-GN isolates forwarded to the SPHA met one of the case definitions. Of these, 67.0% (368) were *P. aeruginosa*, 10.8% (59) *K. pneumoniae*, 9.7% (53) *A. baumannii*, 5.1% (28) *Enterobacter* spp. (18 *E. cloacae*, 9 *E. aerogenes* and 1 *E. sakazakii*), 3.6% (20) *E. coli*, and 3.8% (21) other CR-GN (Table 2).

The 549 CR-GN were isolated from 525 patients. Of these, 20 patients (3.8%) harboured two different CR-GN species, and two patients (0.4%) three different CR-GN isolates. Of the 525 patients, 495 (94.3%) had their permanent residence in Germany (German residents). Fifteen (3.0%) of the German residents and seven (23.3%) of the non-German residents harboured two or more CR-GN (p<0.001). The proportion of patients with permanent German residence differed by species (Pearson chi-square test: p<0.001) and was lowest for *A. baumannii* complex (Table 3).

Nine percent of CR-GN isolates (49 of 549) were from specimens taken from ambulant patients. Of these, 39 were *P. aeruginosa* and 10 non-*P. aeruginosa* isolates, respectively, so that the proportion of *P. aeruginosa* isolates from outpatients among all *P. aeruginosa* isolates (10.6%; 39/368) was significantly higher (p=0.05) than that of the non-*P. aeruginosa* isolates (5.5%; 10/181).

Fifteen CR-GN isolates (2.7%) were recovered from blood, two (0.4%) from cerebrospinal fluid. Of the 15 CR-GN isolated from blood, four were *Enterobacter* spp. and nine *P. aeruginosa*. The proportion of isolates recovered from blood was highest for *Enterobacter* spp. (<0.001) (Table 3).

The incidence of all CR-GN species combined differed by MDRO network region. It was highest in the Centre (9.7 per 100,000 population/year, 95% CI 7.9–11.8 per 100,000 population/year) and the Rhine-Main region (8.5 per 100,000 population/year, 95% CI 7.4–9.6 per 100,000 population/year) and lower in the North (4.5 per 100,000 population/year, 95% CI 3.4–5.9 per 100,000 population/year, 95% CI 3.4–5.9 per 100,000 population/year) and South (4.2 per 100,000 population/year).

Annual incidences of all reported cases, by species and MDRO region, are shown in Table 4. Species-specific incidences were highest for *K. pneumoniae* in the Rhine-Main region, for *E. coli* and *Enterobacter* spp. in the South, and for *A. baumannii* complex and *P. aeruginosa* in the Centre. When compared to the remaining three MDRO regions, only incidences for *K. pneumoniae* (IRR=1.8, 95% Cl 1.0–3.0) in the Rhine-Main region and for *P. aeruginosa* (IRR=1.8, 95% Cl 1.4–2.2) in the Centre were statistically significantly different. However, 13 (18.6%) of the 70 reported CR-GN in the North were *K. pneumoniae* compared to 46 (9.6%) of 479 reported in the remaining three MDRO regions (p=0.02).

Seventy-three (13.3%) CR-GN were found to harbour a carbapenemase. Among carbapenemase-producing isolates, the majority were *K. pneumoniae* (n=23), followed by *P. aeruginosa* (n=20), *A. baumannii* (n=8), *E. coli* (n=7), *A. guillouiae* (n=1), *K. oxytoca* (n=1), and Serratia marcescens (n=1). One *K. pneumoniae*, isolated from a patient with residence in Cyprus, harboured two carbapenemases: VIM-1 and KPC-2.

Reported carbapenemases in the different species were as follows: in *K. pneumoniae* (n=24), 11 OXA-48, 4 VIM-1, 4 NDM-1/-6, 2 KPC-2, 2 KPC-3, and 1 VIM-2; in *A. baumannii* (n=19), 18 OXA-23, 1 OXA-72; in *P. aeruginosa* (n=20), 10 VIM-2, 7 VIM-1, 1 GES-14, 1 IMP, and 1 VIM; in *E. coli* (n=7), 4 OXA-48, 1 GES-20, 1 NDM-1/-6 and 1 VIM-2; in *Enterobacter cloacae* (n=1), 1 OXA-48; in *Serratia marcescens* (n=1), 1 VIM-4; in *A. guillouiae* (n=1), 1 OXA-58; in *K. oxytoca* (n=1), 1 KPC-3.

VIM-type carbapenemases predominated in the North (10 of 13 notified carbapenemases). Of the 10 VIM-type carbapenemases reported from the North, nine were VIM-1. Nine of the 11 VIM-type carbapenemases reported from the Rhine-Main region were VIM-2. NDM-type carbapenemases were notified only in the Rhine-Main region (5 of 38 notified carbapenemases).

Results of the antimicrobial susceptibility testing, as reported by the testing laboratory (mixed CLSI and EUCAST standards), for the three most frequently reported CR-GN *K. pneumoniae*, *A. baumannii*, and *P. aeruginosa* isolates are presented in Table 5. During the study period, six nosocomial CR-GN outbreaks were notified, involving 2 to 5 patients (Table 6).



	l otal N=549	al 49	Kleb pneun N=	Klebsiella meumoniae N=59	Esch R C	Escherichia coli N=20	Enter st N=	Enterobacter spp. N=28	Acinet baun N=	A <i>cinetobacter</i> baumannii N=53	Pseudomone aeruginosa N=368	Pseudomonas aeruginosa N=368	ōĸź	Other CR-GN N=21
1	c	(%)	c	(%)	c	(%)	c	(%)	c	(%)	c	(%)	_ _	(%)
Female sex	188	(35)	16	(28)	ω	(40)	9	(21)	7	(14)	140	(38)	11	(52)
Age (in years)														
Median	63		61		63		68		51		63		68	
<18	19	(4)	0	(3)	2	(10)	0	(2)	-	(2)	12	(3)	0	0
18–64	272	(20)	32	(54)	8	(40)	8	(29)	34	(64)	181	(49)	6	(43)
≥65	258	(47)	25	(42)	10	(20)	18	(64)	18	(34)	175	(48)	12	(57)
Residence in Germany	510	(63)	49	(83)	19	(35)	27	(96)	37	(02)	358	(67)	20	(62)
Reported specimen taken in ambulant sector	49	(6)	S	(5)	.	(5)	7	(2)	N	(4)	39	(11)	2	(10)
Specimen type*														
Blood	15	(3)	-	(1)	0	(0)	4	(13)	~	(2)	6	(2)	0	0
Cerebrospinal fluid	0	0	0	0	0	0)	0	0)	7	(4)	0	0)	0	0
Other clinical specimens [†]	126	(22)	16	(23)	9	(30)	7	(23)	20	(35)	75	(20)	2	(10)
Respiratory tract	209	(36)	11	(16)	2	(10)	9	(19)	15	(26)	172	(45)	ო	(14)
Urine	107	(18)	19	(27)	4	(20)	9	(19)	8	(14)	65	(17)	5	(24)
Anal	62	(11)	17	(24)	7	(35)	5	(23)	0	(4)	28	(2)	ო	(14)
Skin	18	(3)	5	(2)	0	0)	~	(3)	ო	(2)	7	(2)	2	(10)
Swab, location not spec.	35	(9)	~	(1)	0	(0)	7	(2)	4	6	23	(9)	5	(24)
Spec. not specified	ი	(2)	0	(0)	-	(2)	0	0)	2	(4)	5	(1)	-	(2)

Table 3: Characteristics of CR-GN isolates reported in Hesse, Germany, by species, 1 January 2012 – 8 April 2013

MDRO-	Pop.	Т	otal			lebsiella eumonia		Esche col	
region	(in mio.)	Inc.	(95% (CI)	Inc.		(95% CI)	Inc.	(95% CI)
North	1,22	4.5	(3.4–5	.9)	0.82		0.4–1.5		0.0–0.5
Centre	1,04	9.7	(7.9–1	1.8)	0.38		0.1–1.0	0.10	0.0–0.5
Rhine-Main	2,75	8.5	(7.4–9	.6)	1.02		0.7–1.5	0.36	0.2–0.7
South	1,05	4.2	(3.1–5	(3.1–5.6) 0.48			0.2–1.1	0.38	0.1–1.0
Hesse	6,06	7.1	(6.5–7	.9)			0.6–1.0	0.26	0.2–0.4
MDRO-	<i>Enterc</i> sp	<i>bacter</i> p.		etobacter umannii			eudomonas eruginosa	-	ther -GN
region	Inc.	(95% CI)	Inc.	(95% CI)	Inc.	(95% CI)	Inc.	(95% CI)
North	0.08	0.0–0.5	0.33	0.1–0.8		3.11	2.2–4.3	0.16	0.0–0.6
Centre	0.38	0.1–1.0	0.86	0.4–1.6		7.48	5.9–9.3	0.48	0.2–1.1
Rhine-Main	0.40	0.2–0.7	0.80	0.5–1.2		5.56	4.7–6.5	0.33	0.2–0.6
South	0.57	0.2–1.3	0.57	0.2–1.3		2.01	1.2–3.1	0.19	0.0–0.7
Hesse	0.36	0.2–0.6	0.69	0.5–0.9		4.78	4.3–5.4	0.28	0.2–0.5

Table 4: Annual incidence (cases per 100,000 population) of all reported CR-GN-isolates, by species and MDRO-region, Hesse, Germany, 1 January 2012 – 8 April 2013

Inc., incidence

Table 5: Antimicrobial susceptibility of reported K. pneumoniae, A. baumannii and P. aeruginosa isolates, Hesse, Germany,1 January 2012 – 8 April 2013

Antihintia	Klebsiella pneumoniae					cinetob	acter bauma	nnii	Pseudomonas aeruginosa			
Antibiotic	*	R†	% [‡] of I+R	Total	*	R†	% [‡] of I+R	Total	*	R†	% [‡] of I+R	
Piperacillin	0	35	(100)	35	0	34	(100)	34	9	223	(96)	242
Piperacillin/ Tazobactam	0	57	(100)	57	2	37	(100)	39	28	258	(94)	305
Cefepime	1	21	(88)	25	3	27	(100)	30	66	153	(93)	236
Cefotaxime	0	49	(96)	51								
Ceftazidime	1	44	(98)	46	1	42	(96)	45	1	337	(100)	336
Ertapenem	0	27	(100)	27								
Imipenem	7	37	(77)	57	0	52	(98)	53	0	338	(100)	338
Meropenem	2	44	(82)	56	1	49	(98)	51	0	337	(100)	337
Ciprofloxacin	1	54	(95)	58	1	45	(98)	47	39	206	(78)	316
Levofloxacin	1	52	(96)	55	1	39	(95)	42	11	186	(83)	236
Moxifloxacin	0	28	(97)	29	0	22	(92)	24	2	152	(92)	168
Norfloxacin	0	13	(100)	13								
Aztreonam	0	18	(90)	20	0	22	(100)	22	44	118	(94)	173
Amikacin	1	10	(31)	36	2	20	(73)	30	8	60	(29)	236
Gentamicin	3	30	(58)	57	1	32	(72)	46	26	147	(55)	314
Tobramycin	2	29	(82)	38	0	15	(48)	31	8	92	(41)	246
Cotrimoxazole	1	37	(81)	47	0	29	(83)	35				160
Fosfomycin	1	28	(71)	41					0	157	(73)	216
Tigecycline	10	16	(62)	42	12	12	(89)	27				
Colistin	0	3	(8)	36	0	4	(12)	33	7	9	(7)	225

* Intermediate

† Resistant

⁺ Totals used to calculate percentages differ due to not tested/not reported antibiotics



No	Species	Carbononomooo	Ν	lumber of pati	ents
NO.	Species	Carbapenemase	Total*	Infected	Deceased
1	Acinetobacter baumannii	-	2	2	1
2	Acinetobacter baumannii	OXA-23	2	2	1
3	Pseudomonas aeruginosa	_	2	2	0
4	Pseudomonas aeruginosa	-	5	1	1
5	Acinetobacter baumannii	_	3	1	2
6	Pseudomonas aeruginosa	VIM-1	4	4	0

Table 6: Number of patients in reported nosocomial outbreaks, by species, Hesse, Germany, 1 January 2012 – 8 April 2013

* Total of colonised, infected and deceased

Discussion

This is the first report describing population-based surveillance of CR-GN and carbapenemases in Germany. Previously, outbreaks of carbapenemase-producing Gramnegatives, first time identifications of specific carbapenemase-types, and interhospital transmissions had been reported for Germany [12], [13], [14], [15], [16]. Data of the present study describe the widespread presence of CR-GN and a high diversity of identified carbapenemases in Hesse. Of the reported CR-GN, 67.0% were P. aeruginosa, while Enterobacteriaceae represented a far smaller fraction of all reported CR-GN. Prevalence of CR-GN and identified carbapenemases appeared to be uneven among regions. These regional differences occurred in the absence of major outbreaks of infection. In this study, the proportion of patients non-resisdent in Germany ranged from 3% for patients with P. aeruginosa to 30% for patients with A. baumannii. These different proportions of patients with non-German residence may suggest that autochthonous transmissions play a different role for the different CR-GN species.

The successive increase of weekly reports during the first half of 2012 should not be interpreted as a corresponding increase in prevalence of CR-GN but rather due to the expected introduction phase of any new notification requirements. Nevertheless, the ongoing first time notification of new patients is well in line with the expected spread of CR-GN. Many of the patients colonised or infected with CR-GN are hospitalised for prolonged periods or readmitted repeatedly. Duration of colonisation is prolonged for CR-GN and clearance of colonisation occurs infrequently [17]. This underlines the need for the implementation of control measures to limit their spread.

In October 2012, the National Commission for Hospital Hygiene and Infection Prevention (KRINKO) issued recommendations on hygiene measures for patients infected or colonised with multidrug-resistant Gram-negative bacilli [18]. These recommendations include, among others, the screening for high-risk patients and suggest rectal swabs (and, where appropriate, wound and urine) as specimens for Enterobacteriaceae and skin, and mouth and throat swabs for *A. baumannii*. In this study, the clinical significance of the notified isolates can only be assumed from the site of specimen collection as no information on reasons for specimen collection (e.g.

screening) or clinical symptoms were available. Data on the proportion of colonised patients who develop clinical symptoms during a hospital stay is still limited, although available data suggest differences by species [18]. Systematic screening is necessary to identify CR-GN introductions into a hospital [19]. With the successive introduction of systematic screening, the proportion of clinical isolates undoubtedly obtained from infected patients (e.g. patients with isolates recovered from blood or cerebrospinal fluid) among all notifications should further decrease.

Antimicrobial susceptibility data reported to LPHAs were generated at individual institutions rather than a central laboratory, and testing methodologies (and susceptibility interpretation) vary between facilities. Also, the proportion of isolates with resistance should be interpreted with caution due to the small number of antimicrobial susceptibility results available for some of the species/antibiotic combinations; e.g. the 12% resistance to colistin of *A. baumannii* is based on 4 resistant isolates. Nevertheless the antimicrobial susceptibility data presented portray an extended multidrug-resistance among the notified CR-GN, even among antibiotic classes not listed in the notification criteria.

Nine percent of CR-GN isolates were from specimens taken from ambulant patients. Eighty percent (39/49) of CR-GN isolates first notified from the ambulant sector were P. aeruginosa. Many of these patients were treated in hospital-associated cystic fibrosis outpatients departments. Laboratories handling mostly specimens from ambulant patients may not test for antibiotics which need to be administered parenterally, such as carbapenems. Data from population-based surveillance in the U.S.A. suggested most carbapenem-resistant Enterobacteriaceae clinical isolates came from cultures collected outside of hospitals from patients with substantial healthcare exposure [9]. This suggests that in Hesse, underdetection and underreporting of CR-GN may be even more pronounced in the ambulant sector. Underdetection and underreporting of CR-GN also need to be considered when evaluating the burden of CR-GN for the health-care system.

Autochthonous transmissions may explain the regional differences in incidence of CR-GN and identified carbapenemase-types. However, several additional factors may be relevant in explaining these differences: Screening procedures differ between hospitals and laboratory pro-



cedures and reporting practices vary between laboratories. Hospitals treat patients from CR-GN endemic countries with different frequencies and some hospitals have country-specific focuses. In addition, differences may have occurred by chance.

There are several limitations to our surveillance. Firstly, this is a passive surveillance system relying solely on laboratories to notify CR-GN positive specimens using the reporting criteria. Underreporting is a typical feature of passive surveillance systems. Secondly, different laboratories used different antimicrobials and methods (e.g. CLSI and EUCAST) for their susceptibility testing. Thirdly, availability of molecular identification and typing of carbapenemases is limited to a few laboratories. Molecular typing for the reported CR-GN was incomplete and regional species-specific differences in performing molecular typing may explain the observed regional differences in carbapenemase detection. In addition, we had no information on how laboratories selected isolates for molecular typing and on how many isolates were tested. However, all laboratories have the possibility of forwarding CR-GN for molecular typing to the national reference centre free of charge. In addition, epidemiological data (e.g. travel outside Germany) on the patients was not systematically collected or forwarded to the state level. Nevertheless, LPHAS used notifications to discuss control measures, e.g. with acute and chronic care hospitals.

In April 2013, the reporting requirements were amended to conform to the multidrug resistance definition for Gramnegative bacteria of the National Commission for Hospital Hygiene and Infection Prevention (KRINKO) [18]. For *P. aeruginosa*, notification requirements were restricted to CR-GN isolated from blood and liquor. In addition, intensified surveillance was initiated.

In conclusion, this population-based surveillance describes the widespread presence of CR-GN and a high diversity of identified carbapenemases in Hesse, Germany. Regional differences in laboratory and reporting procedures likely contribute to the described differences in CR-GN occurrence. Nevertheless, the data suggest autochthonous transmissions and regional differences in incidence for the different species and carbapenemases, even in the absence of major outbreaks of infection. Consequently, efforts for infection control need to be intensified. Laboratory capacities, including in the ambulant sector and for molecular testing, should be strengthened.

Notes

Competing interests

The authors declare that they have no competing interests.

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