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Surveillance of microbial resistance in European Intensive Care Units: a first report from the Care-ICU programme for improved infection control

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Abstract

Purpose To report initial results from a European ICU surveillance programme focussing on antibiotic consumption, microbial resistance and infection control.
Methods Thirty-five ICUs participated during 2005. Microbial resistance, antibiotic consumption and infection control stewardship measures were entered locally into a web-application. Results were validated locally, aggregated by project leaders and fed back to support local audit and benchmarking.
Results Median (range) antibiotic consumption was 1,254 (range 348–4,992) DDD per 1,000 occupied bed days. The proportion of MRSA was median 11.6% (range 0–100), for ESBL phenotype of *E. coli* and *K. pneumoniae* 3.9% (0–80) and 14.3% (0–77.8) respectively, and for carbapenem-resistant *P. aeruginosa* 22.5% (0–100). Screening on admission for alert pathogens was commonly omitted, and there was a lack of single rooms for isolation.
Conclusions The surveillance programme demonstrated wide variation in antibiotic consumption, microbial resistance and infection control measures. The programme may, by providing rapid access to aggregated results, promote local and regional audit and benchmarking of antibiotic use and infection control practices.

Keywords Intensive care - Antibiotic consumption - Microbial resistance - Infection control

Introduction

ICU acquired infections, which are often caused by antibiotic resistant bacteria, pose a threat to patients admitted to European ICUs [1-10]. Invasive procedures, high antibiotic usage and transmission of bacteria between patients due to inadequate infection control procedures may explain why ICUs are "hot zones" for the emergence and spread of microbial resistance [1, 4, 6]. There is a clear need for surveillance and early warning systems that can pick up signs of emerging and/or increasing microbial resistance at the local, regional and national level [11]. A further use of a similar system could be to support local audit and benchmarking of microbial resistance and antibiotic use. A prototype programme was developed and used for regular audit of antibiotic use, microbial resistance to antibiotics and infection control procedures in Swedish ICUs. A central component was a web-based application (12http://www4.smittskyddsinstitutet.se/careicu) which included a system for automatic feed-back [7]. The programme was recently revised and adapted to other EU member states. It was launched under the name of controlling antibiotic resistance in ICU [Care ICU, 12] as part of the project improving patient safety in Europe (IPSE), funded by the European Commission Directorate General for Health and Consumer Protection (DG SANCO).

The overall aim of Care-ICU is to hold back the emergence of microbial resistance by judicious use of antibiotics and establish interventions in infection control and antibiotic policy tailored to the needs of each participating ICU. It is our experience that clinicians often lack data on patterns of microbial resistance and antibiotic consumption within their own ICU and hospital. The first important step to amend this is to improve surveillance and provide rapid feedback of microbial resistance, antibiotic consumption and use of hygiene precautions. Therefore, national ICU-networks and individual ICUs were invited to participate in Care-ICU. ICUs from eight countries took part in the first phase of the programme. The purpose of this report is to increase awareness of the usefulness of the programme and provide initial results from diverse settings in Europe, focussing on antibiotic consumption, microbial resistance and infection control.

Materials and methods

This is a descriptive study of the first results of the Care-ICU programme. National ICU-networks and individual ICUs were invited to participate in the web-based data collection. Initially, the participation of a small number of ICUs was sought in each of the countries participating in the IPSE project. The national contact points of IPSE were asked to identify ICUs that would be willing to take part in the large pilot study. Thirty-five ICUs from eight European countries (Croatia 4, Czech republic 3, Estonia 3, Hungary 8, Malta 3, Romania 1, Sweden 10, Turkey 3) participated. One neonatal ICU in Malta contributed with microbial resistance data only, since there is no standard in the WHO DDD system for antibiotic use in neonates. There were 21 ICUs in university hospitals and 14 ICUs in general hospitals (13 teaching, 1 non-teaching).

The data on antibiotic use, microbial resistance and infection control procedures were collected according to the Care-ICU protocol (http://www4.smittskyddsinstitutet.se/careicu accessed 16 June 2008). Following submission of data from the local ICU the national administrator, who was a physician, validated data entries and clarified unexpected entries with the primary site. The project leaders, who performed the aggregation and statistical analyses of the data, identified outliers and notified national administrators for further validation and explanation.

Antibiotic consumption

The data on antibiotic consumption based on the anatomical therapeutic chemical (ATC) classification system were collected and entered into the database using the web application. Antibiotic consumption was expressed as defined daily doses (DDD) per 1,000 occupied bed days (DDD_{1000}). We used the annually updated DDD calculated by the WHO Collaborating Centre for Drug Statistics Methodology as the average maintenance dose per day in adults for the main indication of the drug (http://www.whocc.no/atcddd, accessed 16 June 2008). Calculation of DDD was made easier with an Internet-based "ABC Calc" tool (http://www.escmid.org/esgap, "Scientific issues").

Bacterial isolates, susceptibility testing and breakpoints

Samples were taken on clinical indication and cultured and tested at the local microbiology laboratory. Repeat isolates were excluded and only initial isolates were considered. It was not determined if the isolates represented ICU-acquired infections, community acquired infections or only colonisation of the patients. Data on distribution of species were entered for all isolates including blood isolates. Susceptibility testing was performed at the time of sampling using standardised methods, following national guidelines. Microbial resistance was defined as the proportion of strains showing either intermediate susceptibility or resistance. *E. coli* and *K. pneumoniae* isolates with decreased susceptibility to cefotaxime and/or ceftazidime were defined as extended spectrum beta-lactamase (ESBL) phenotypes. The extent of multidrug resistance among *P. aeruginosa* was characterized by the number of antibiotics among aminoglycoside, ceftazidime, ciprofloxacin and carbapenem to which >90% of isolates of a species were susceptible. These antibiotics were defined as treatment alternatives (TA_{90}) which is a novel index of susceptibility [13].

The density of resistance

We calculated the density, or burden of resistance, defined as number of resistant isolates/1,000 admission days. This index makes it possible to gauge the risk for the individual patient to acquire a resistant pathogen.

Questionnaire on ICU characteristics and infection control

Participating ICUs were asked to provide data on length of stay, number of admissions, severity of illness scores, standard working procedures for hygiene precautions and antibiotic treatment guidelines. Information was also gathered about how often feedback about antibiotic consumption was given by the local pharmacy, and how often feedback about local resistance patterns was given by the hospital microbiology laboratory.

Statistics

Correlations between antibiotic consumption and resistance rates or burden were analysed with the Spearman rank correlation using SPSS version 15. To reduce the effect of mass significance, statistical significance was assumed if $P < 0.01$.

Results

Thirty-five ICUs from eight European countries participated in the collection of data for 2005. The response rate of different items in the protocol varied from 100% (i.e. microbiology) to 26% (consumption of disinfectant in the infection control part of the questionnaire). The median annual number of admissions to ICU was 551 and the median summated length of stay per ICU was 2,595 days.

ICU characteristics and infection control

Bedside facilities for hand disinfection were generally available. Routines for screening for alert microorganisms, presence of isolation precautions and cohort care for patients colonised or infected with alert organisms are shown together with some selected stewardship measures in Table 1 and Fig. 1.

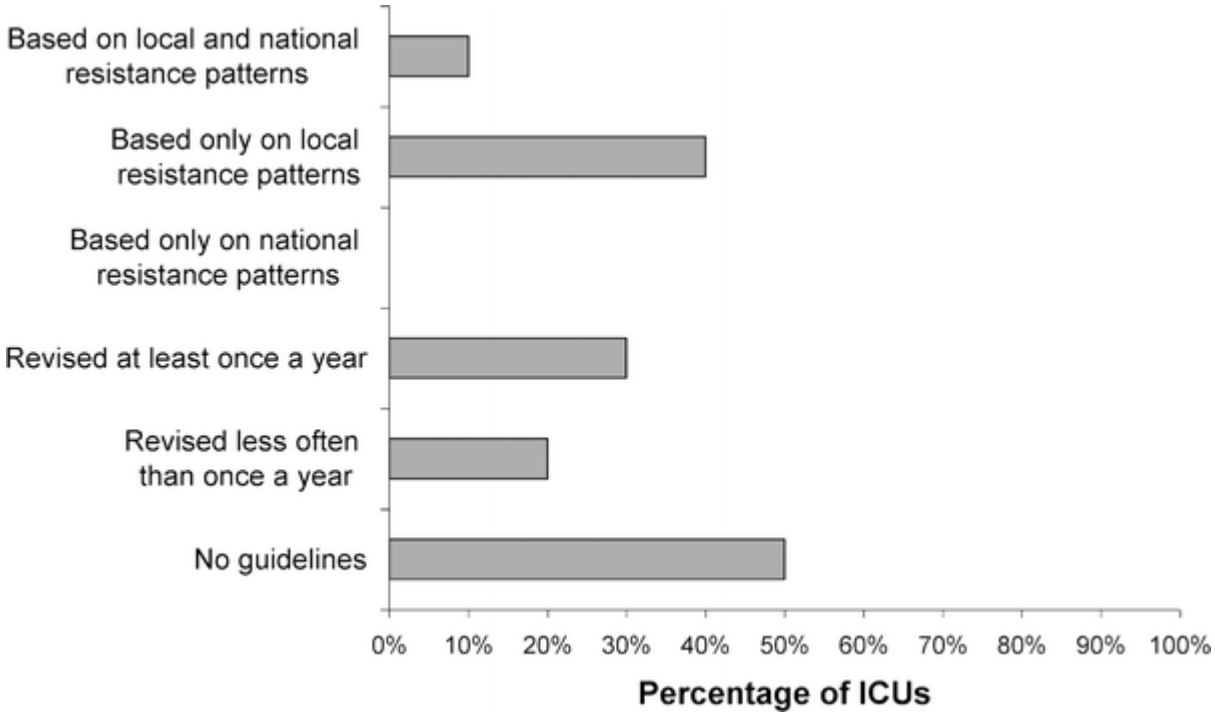

Fig. 1: Presence and basis of antibiotic guidelines for ICU-acquired infections in ICUs replying to this part of the questionnaire (N = 20)

Antibiotic consumption

Antibiotic consumption varied widely, ranging between 348 and 4,992 DDD_{1000} with a median of 1,254 DDD_{1000}. DDD_{1000} split by major antibiotic classes is shown in Fig. 2.

Table 1: Selected stewardship in infection control

ICU short name[a]	Estonia			Croatia				Hungary			Malta	Romania	Sweden	Turkey
	EeMx1	EeMx2	EeNs1	HrMe1	HrMx1	HrNs1	HrSu1	HuMx2	HuMx3	HuOt1	MtMx1	RoMx1	SeMx4	TrMx1
Infection control (IC) committee	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
ICU physician participating in IC committee	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes
Infection control management team	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Instructions for basic sanitary routines in the ICU	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Education about these instructions (times/year)	2–3	1	1	1	2–3	1	4	1	1	NA	2–3	2–3	1	1
Handwashing (soap) facilities in each room	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes
Alcohol based hand disinfection by each bed	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Disinfectant (liters/1000 patient days)	247	75	77	48	108	328	536	NA	149	NA	NA	NA	NA	396
For patients admitted to ICU:														
Which alert organisms are screened for?														
Methicillin-resistant *Staphylococcus aureus* (MRSA)	No	No	No	No	Yes	No	No	Yes	No	No	Yes	No	Yes	No
Vancomycin-resistant enterococci (VRE)	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No
*K. pneumoni*ae with ESBL-phenotype[b]	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No
*A. baumanni*i resistant to carbapenems	No	No	No	No	Yes	No	No	No	No	No	No	No	No	No
Multidrug resistant *Pseudomonas aeruginosa* [c]	No	No	No	No	No	No	No	Yes	No	No	No	No	No	No
C. difficile	No	No	No	No	No	No	No	No	No	No	No	No	No	No
According to the infection control policy that applies to the ICU:														
For which patient groups is “Single room” recommended?														
“High risk” patients awaiting screening results	Yes	No	No	No	Yes	No	No	Yes	Yes	No	No	No	Yes	No
Colonised with MRSA (nasal only)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Colonised with MRSA (other than nasal)	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes	No	Yes	No
Patients with glycopeptide resistant Enterococci	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Yes
Patients with *K. pneumoni*ae with ESBL-phenotype[b]	Yes	Yes	No	No	No	No	No	Yes	Yes	No	No	No	No	No
Patients with *A. baumanni*i resistant to carbapenems	No	No	No	Yes	Yes	No	Yes	No	Yes	No	Yes	No	No	No
Patient with multi-drug resistant *P. aeruginos*a[c]	No	Yes	No	No	No	No	Yes	Yes	Yes	No	Yes	No	Yes	No
Patients with *C. difficile* diarrhoea	Yes	Yes	Yes	No	Yes	No	No	Yes	Yes	Yes	Yes	Yes	No	No
Availability of beds														
Beds in single rooms	4/10	1/10	0/8	0/7	0/6	0/8	1/8	0/8	1/8	0/8	3/13	3/30	1/6	6/61
Isolation beds	1/10	1/10	0/8	0/7	0/6	0/8	0/8	0/8	0/8	0/8	1/13	0/30	1/6	6/61

NA Not Available

[a]The ICU short names consist of the two character Internet top level domain name (*Cz* Czech Republic, *Ee* Estonia, *Hr* Croatia, *Hu* Hungary, *Mt* Malta, *Ro* Romania, *Se* Sweden, *Tr* Turkey) followed by two characters for the type of ICU (*Me* Medical, *Mx* Mixed, *Ne* Neonatal, *Ns* Neurosurgical, *Ot* Other, *Su* Surgical, *Th* Cardiothoracic) and a sequence number

[b]ESBL-phenotype was defined as resistance to third generation cephalosporins (see “Materials and methods” for details)

[c]Multidrug resistance was defined as resistance to ≥ 3 of the 4 tested drugs (aminoglycoside, ceftazidime, ciprofloxacin and carbapenem)

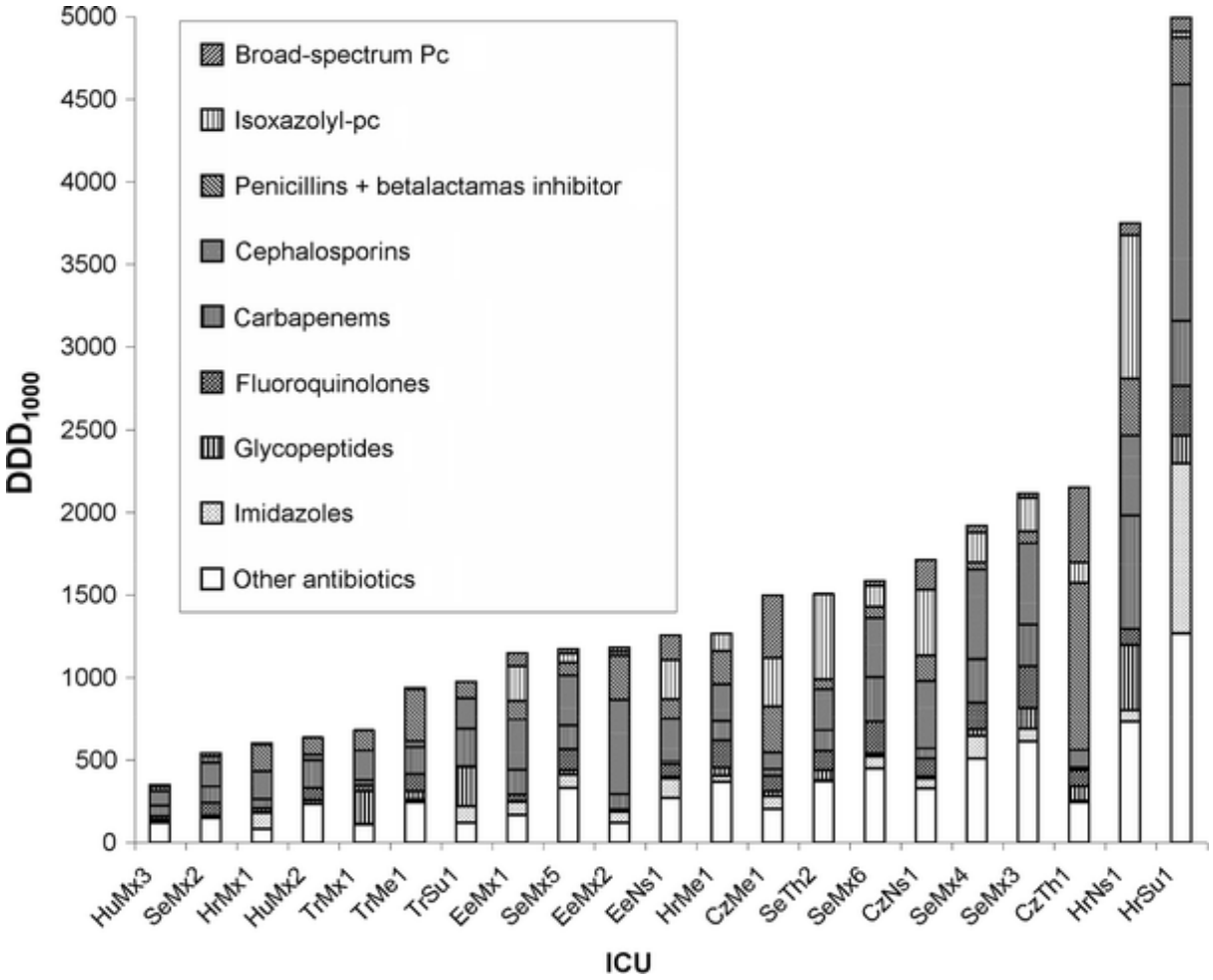

Fig. 2: Antibiotic consumption split by major antibiotic classes. DDD $_{1000}$ Defined daily dose per 1,000 occupied bed days (see "Materials and methods" for details). For ICU short names see footnote Table 1.

Microbial resistance

Thirty-five ICUs contributed data on microbial resistance. The frequencies of microbial resistance among *Staphylococcus aureus*, *E. coli*, *A. baumannii*, *E. cloacae*, *P. aeruginosa* and *K. pneumoniae* for all participating ICUs in each country are shown in Table 2. The pattern of microbial resistance varied greatly between species, ICUs and countries (Tables 2, 3, Fig. 3). A median of 11.6% (range 0–100%) of *S. aureus* were methicillin-resistant (MRSA) and the corresponding figures for ESBL phenotype of *E. coli* and *K. pneumoniae* were 3.9% (0–80%) and 14.3% (0–77.8%), respectively. Many ICUs had a high proportion of antibiotic resistant alert pathogens (Table 3 and Fig. 3). We found no significant correlations between either presence (*I*% + *R*%) or burden (number of resistant patogens/1,000 patient days) of MRSA, cephalosporin resistant *K. pneumoniae*, or carbapenem resistant *P. aeruginosa* on one hand and total antibiotic consumption or consumption of cephalosporins, quinolones or carbapenems on the other hand. Three ICUs had no standard treatment alternative for *P. aeruginosa* ($TA_{90} = 0$) in addition to >35% MRSA and >55% ESBL K. pneumoniae (Fig. 3 and Table 3). These ICUs had no screening routines for alert organisms but recommended single room for certain alert organisms although there were few or no isolation rooms available (Table 1).

Table 2: Microbial resistance (percentage of intermediate susceptible and resistant strains) and number of isolates in parentheses

Species	Croatia	Czech Rep	Estonia	Hungary	Malta	Romania	Sweden	Turkey
Number of ICUs	4	3	3	8	3	1	10	3
Staphylococcus aureus								
Oxacillin	35.2 (91)	3.4 (87)	3.7 (81)	19.6 (291)	60.0 (75)	50.0 (152)	2.2 (136)	92.0 (87)
Aminoglycoside	35.2 (91)	3.4 (87)	4.9 (82)	18.7 (268)	0.0 (65)	44.7 (152)	0.0 (89)	90.2 (82)
Clindamycin	36.3 (91)	9.2 (87)	1.2 (82)	24.7 (263)		0.0 (152)	3.0 (164))	51.7 (87)
Rifampicin	0.0 (91)	0.0 (87)		1.0 (99)	3.3 (61)	38.2 (152)	0.0 (106)	90.1 (71)
Vancomycin	0.0 (91)	0.0 (87)	0.0 (82)	0.0 (266)	0.0 (63)	0.0 (152)	0.0 (128)	0.0 (108)
Escherichia coli								
Third generation cephalosporin[b]	3.6 (83)	1.3 (153)	5.0 (100)	18.0 (172)	3.1 (32)	24.0 (75)	1.6 (123)	42.0 (50)
Ciprofloxacin	11.0 (91)	4.6 (153)	2.0 (100)	18.4 (244)	25.0 (32)	18.7 (75)	5.9 (101)	34.4 (61)
Imipenem	0.0 (65)	0.0 (153)	0.0 (95)[a]	1.1 (189)	0.0 (32)	0.0 (75)	0.0 (64)	0.0 (57)
Aminoglycoside	6.6 (91)	5.2 (153)	4.0 (99)	12.1 (240)	9.4 (32)	26.7 (75)	0.0 (58)	34.5 (55)
Acinetobacter baumannii								
Ceftazidime	53.2 (62)	23.8 (42)		82.3 (113)	90.9 (44)	86.7 (120)	83.3 (6)	89.6 (115)
Ciprofloxacin	90.3 (62)	23.8 (42)	72.7 (11)	92.5 (107)	93.2 (44)	95.0 (120)	20.0 (5)	69.6 (115)
Imipenem	17.7 (62)	4.8 (42)	0.0 (12)	15.2 (112)	90.9 (44)	11.7 (120)	0.0 (5)	38.5 (117)
Aminoglycoside	50.0 (62)	23.8 (42)	66.7 (18)	79.0 (105)	93.2 (44)	98.3 (120)	0.0 (4)	80.2 (111)
Enterobacter cloacae								
Third generation cephalosporin[b]		17.8 (73)	33.3 (6)	18.2 (11)	61.5 (13)	44.4 (18)	20.0 (25)	29.4 (17)
Ciprofloxacin		0.0 (73)	0.0 (6)	16.7 (12)	0.0 (13)	0.0 (18)	2.9 (34)	5.9 (17)
Imipenem		0.0 (73)	0.0 (3)	0.0 (14)	0.0 (13)	0.0 (18)	3.1 (32)	6.3 (16)
Aminoglycoside		0.0 (73)	0.0 (6)	16.7 (12)	30.8 (13)	33.3 (18)	4.5 (22)	17.6 (17)
Pseudomonas aeruginosa								
Ceftazidime	11.0 (127)	34.4 (122)	5.5 (109)	10.7 (373)	9.7 (62)	34.0 (94)	11.0 (73)	48.3 (89)
Ciprofloxacin	36.2 (127)	28.9 (121)	5.0 (100)	20.5 (346)	23.8 (63)	55.3 (94)	12.2 (74)	37.8 (90)
Imipenem	28.3 (127)	30.3 (122)	13.7 (51)	18.8 (377)	25.4 (63)	10.6 (94)	17.3 (52)	48.4 (93)
Aminoglycoside	43.3 (127)	26.2 (122)	4.7 (107)	22.7 (343)	9.3 (54)	57.4 (94)	0.0 (24)	53.5 (86)
Klebsiella pneumoniae								
Third generation cephalosporin[b]	17.8 (45)	9.0 (122)	18.5 (54)	29.0 (62)	16.7 (12)	62.7 (118)	0.0 (18)	52.6 (38)
Ciprofloxacin	21.3 (47)	16.4 (122)	5.6 (72)	13.2 (76)	8,3 (12)	37.3 (118)	0.0 (18)	21.4 (42)
Imipenem	0.0 (49)	0.0 (122)	0.0 (73)[a]	1.1 (94)	0.0 (12)	0.0 (118)	0.0 (14)	13.6 (44)
Aminoglycoside	17.0 (47)	7.4 (122)	5.5 (73)	17.3 (75)	8.3 (12)	69.5 (118)	0.0 (15)	45.0 (40)

[a]Meropenem

[b]Cefotaxime and/or ceftazidime (see “Materials and methods” for details)

Table 3: Burden of microbial resistance (resistant pathogens/1,000 patient days), resistance (percentage of intermediate susceptible and resistant strains) and total number of isolates (N)

ICU	Methicillin resistant *Staphylococcus aureus*			Cephalosporin resistant[a] *Klebsiella pneumoniae*			Carbapenem resistant *Pseudomonas aeruginosa*		
	Burden	***I*% + *R*%**	***N***	**Burden**	***I*% + *R*%**	***N***	**Burden**	***I*% + *R*%**	***N***
CzMe1	0.7	9.5	21	1.5	10.3	39	8.5	53.5	43
CzNs1	0.4	2.3	43	2.5	16.3	43	3.5	28.6	35
CzTh1	0.0	0	23	0.0	0	40	1.6	9.1	44
EeMx1	0.0	0	24	2.7	29.2	24	1.9	9.1	55
EeMx2	0.4	14.3	7	0.0	–	2	0.4	2.5	40
EeNs1	1.0	4	50	1.4	10.7	28	0.0	0.0	14
HrMe1	3.7	57.9	19	0.7	14.3	14	6.1	42.9	42
HrMx1	0.0	0	10	0.0	0	8	2.9	13.9	36
HrNs1	9.5	23.4	47	5.2	26.1	23	5.2	25.0	24
HrSu1	12.6	66.7	15	2.5	–	2	8.8	28.0	25
HuMe1	1.0	23.8	21	0.4	33.3	6	0.8	19.0	21
HuMx1	3.0	13.6	88	0.0	–	2	2.5	14.9	67
HuMx2	0.0	0	56	0.0	0	16	5.7	10.3	156
HuMx3	7.8	29	69	1.2	15.8	19	5.5	36.8	38
HuNs1	1.0	13.6	22	2.4	29.2	24	3.1	30.0	30
HuOt1	0.9	37.5	8	2.1	77.8	9	2.1	38.9	18
HuSu1	2.1	57.1	14	0.3	12.5	8	2.1	36.4	22
HuTh1	1.7	46.2	13	0.3	7.7	13	0.9	12.0	25
MtMx1	5.7	64.1	39	0.2	14.3	7	3.6	30.2	53
RoMx1	4.3	50	152	4.1	62.7	118	0.6	10.6	94
SeMx2	0.6	7.7	13	0.0	–	2	1.3	33.3	6
SeMx3	0.0	0	22	0.0	–	2	0.0	0.0	6
SeMx4	0.0	0	10	0.0	–	2	0.0	0.0	1
SeMx5	0.0	0	33	0.0	–	1	1.6	20.0	15
SeMx6	0.5	4.5	22	0.0	–	3	0.0	–	0
SeTh2	0.0	0	11	0.0	–	3	0.6	25.0	4
TrMe1	3.0	60	5	2.0	–	2	1.0	14.3	7
TrMx1	5.3	94.4	71	1.6	58.8	34	2.9	47.4	78
TrSu1	7.7	100	9	0.0	–	4	6.0	100.0	7

For ICU short names see footnote Table 1

[a] Cefotaxime and/or ceftazidime (see “Materials and methods” for details)

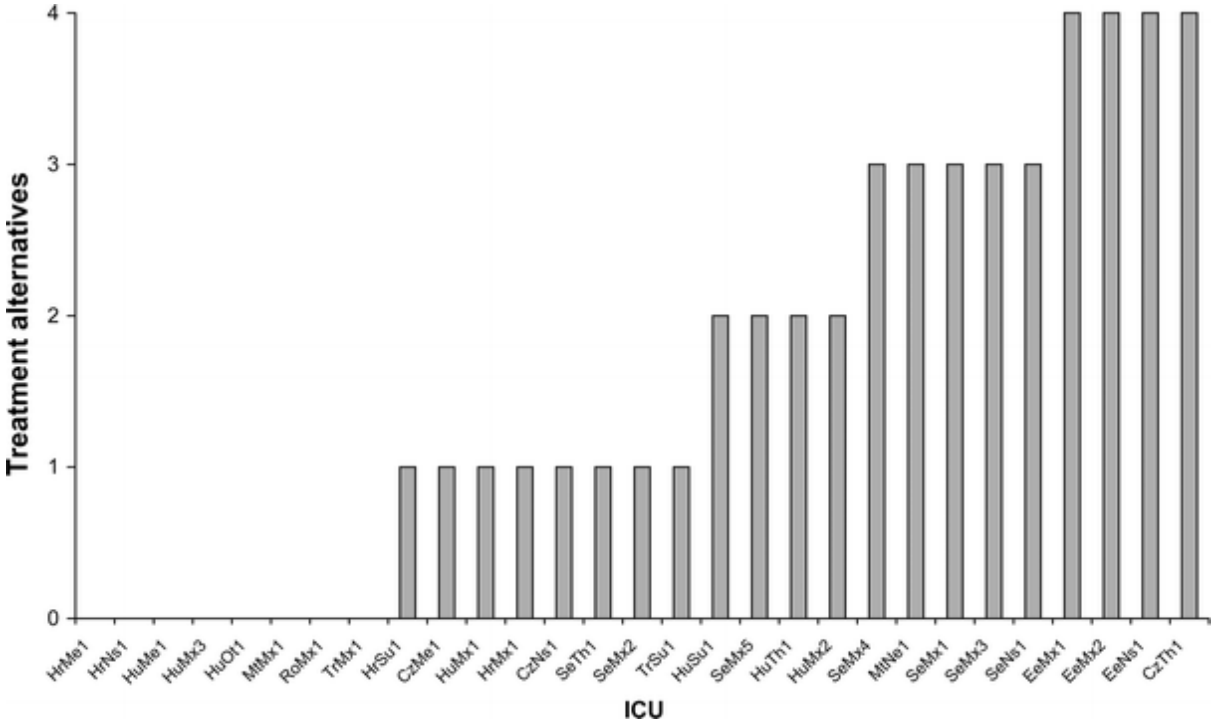

Fig. 3: *TA_{90} for Pseudomonas aeruginosa. TA_{90} is the number of antibiotics to which >90% of isolates of a species were susceptible (see "Materials and methods" for details). For ICU short names see footnote Table 1.*

Discussion

This initial report from CARE-ICU has three main findings. First, antibiotic consumption varied widely from 348 to 4,992 DDD_{1000} with a median consumption of 1,254 DDD_{1000}. Second, levels of microbial resistance were very high in many settings. The finding that more than half of all participating ICUs had no, or only one, conventional antibiotic treatment alternative for *P. aeruginosa* was alarming. Finally, there was a striking lack of isolation rooms for patients colonised or infected with alert organisms.

We calculated antibiotic use as defined daily doses per 1,000 occupied bed days (DDD_{1000}). Although a highly standardised measure that allows the comparison of antibiotic consumption between different settings and countries (http://www.whocc.no/atcddd/ accessed 16 June 2008), a couple of factors complicate such comparisons. First, a common definition for length of stay must be used. Second, antibiotic use was based on the quantities of drugs delivered by each hospital pharmacy, although drugs may be delivered but not administered to patients in the ICU [14-16]. A third source of error is that dosing in the critically ill is influenced by many factors other than the DDD (i.e. increased dosing due to life-threatening disease, reduced dosing due to renal impairment). In spite of these difficulties, hospitals were recently recommended to use the DDD methodology to make national and international comparisons of their antibiotic use possible [17].

We found a median antibiotic consumption of 1,417 DDD_{1000} ranging from 348 to 4,992 DDD_{1000}. This concurs with figures from European and US ICUs in general [14, 18], but like a few ICUs in our programme, relatively low antibiotic consumption has been reported from Switzerland (462–683 DDD_{1000}, 19). The lower antibiotic consumption suggests that it is possible to reduce antibiotic consumption in the critically ill, but it has to be accompanied

with a quality control system to make sure that it does not compromise patient outcomes [19]. We found no clear association between the level of antibiotic consumption and rates of microbial resistance to alert pathogens in CareICU. The absence of correlation between antibiotic consumption and resistance rates may be due to differences in the prevalence of colonisation with resistant alert pathogens at admission and the capacity to avoid cross-transmission of these bacteria in the ICUs. For example, the ICU with the lowest antibiotic consumption showed high rates of resistance with a 29% MRSA rate and a high proportion of carbapenem-resistant *P. aeruginosa*. The most needed intervention in this ICU was probably improvement of hygienic precautions and careful revision of antibiotic guidelines. The greatest consumption of antibiotics reported in our study (4,992 DDD_{1000}) was in a surgical ICU. This unusually large consumption was explained by adding antibiotic treatment on top of a prolonged double-drug peri-operative prophylaxis. Audit of practices lead to a reduction in antibiotic consumption to 1,683 DDD_{1000} for 2006. This change to a more appropriate practice, which was preserved during 2007 (personal communication Smilja Kalenic), is one initial result of local audit and benchmarking. The second highest consumption in a neurosurgery ICU may be partly due to an overestimation of prescribed daily dosages since the DDDs defined by WHO are based on sepsis doses and not doses for meningitis. Lemmen et al. [20] also found high antibiotic consumption in a Neuro-ICU which was reduced following the launching of a routine infectious disease service. Reports from the European Strategy for Antibiotic Prophylaxis also found considerable heterogeneity in the use of antibiotics in 21 European ICUs in six European countries [21].

Resistance proportions were calculated using more than five isolates per species. This is a low number but not too low, since the purpose of this project is to develop an early warning system where the presence of a single positive culture of an alert pathogen should lead to action. We also calculated the density, or burden, of resistance to estimate the risk to acquire a resistant pathogen. However, if colonisation cultures were performed on admission or repeatedly during the ICU stay, this would increase the density of resistance. Therefore to better assess the risk of acquiring a resistant pathogen, density was related to numbers and proportions of resistant isolates.

This study was not designed to evaluate factors and mechanisms that contributed to high rates of MRSA and the ESBL phenotype of *E. coli* and *K. pneumoniae* shown in some settings. High resistance rates in the ICU may reflect high prevalence of the same pathogen in the community (http://www.rivm.nl/earss/, accessed 16 June 2008) and entry to ICUs of these clones. Cross-transmission of alert pathogens between patients in the ICU setting should be suspected if the rates of these strains exceed the rates outside the ICU. By monitoring the ICU-rates of resistance of alert organisms and antibiotic consumption it is possible to identify needs for improvement, which may vary over time. Although this programme was designed for annual follow up it may in the future be used more frequently and serve as an early warning system of increased microbial resistance.

Measures to control the transmission of multidrug resistant bacteria are complicated and costly, and their success depends on many factors [22]. A reduction in antibiotic use can reduce the emergence of resistance during antibiotic therapy but may be of less importance in outbreaks of epidemic clones of MRSA and ESBL phenotype of *K. pneumoniae*. The "search and destroy" strategy including MRSA screening at admission has been advocated and used successfully to control MRSA in many settings [23-26]. However, Harbarth et al. [27] recently found that rapid MRSA screening at admission plus standard infection control measures versus standard infection control alone did not reduce nosocomial MRSA infection

in a surgical department. A study from the UK showed that isolation has no impact on MRSA transmission in the ICU [28], but the results have been questioned due to low hand hygiene compliance and that transmission may have occurred before isolation was started. Current recommendations in most settings include still isolation or cohorting, combined with decolonisation (e.g., mupirocin to the nose and chlorhexidine baths) as major control measures for MRSA [29]. If the MRSA rate exceeds 10%, as it did in half of the ICUs participating in CareICU, it will be impossible to isolate all suspected and proven MRSA-positive patients as the need for isolation rooms will exceed availability. Other measures, including cohort-care of MRSA positive patients, may be used in these settings. An alarming finding was that more than half of all participating ICUs had no or only oneTA_{90} for *P. aeruginosa*. Given the low but increasing resistance to colistin [30, 31] it is unfortunate that we have no data on colistin resistance among *P. aeruginosa*, since colistin is still the drug of choice against multidrug resistant *P. aeruginosa*. We do not know the main reason for the high rates of resistance in *P. aeruginosa*. However, high consumption of carbapenems and quinolones may be responsible, as may the spread of resistant clones [32-35].

This study was done in ICUs that showed a particular interest in issues related to antibiotic consumption and microbial resistance, which probably had a positive influence on the response rate of the extensive dataset. Still, all ICUs were not able to submit complete data, particularly information regarding infection control were missing. The case-mix for each ICU was assessed by classifying units according to the ICU-HELICS-programme (http://helics.univ-lyon1.fr/protocols/icu_protocol.pdf, accessed 16 June 2008). However, differences between ICUs within each category were considerable as indicated by a large variation in ICU mortality from 6 to 48.4% with a median 14.5% (data not shown). A further difficulty was whether to separate different ICUs within the same hospital from each other. One such example was a large academic centre where critically ill were treated within separate ICU-modules in the hospital, each with its own distinctive case-mix. Despite differences in case-mix we chose to present these modules together as a single ICU, since it was served by the same infection control team and was presumably challenged by the same alert pathogens prevalent in the hospital and surrounding environment. However, antibiotic consumption from a multi-module ICU becomes less specific and cautious interpretation of the results is necessary.

Benchmarking and audit of antibiotic use and infection control measures has been facilitated by the Care-ICU programme. The web-based application simplifies data collection and the local multi-professional perspective secures that submitted data is valid. Rapid feedback through the web-based protocol is important for confirmation of data entries locally. Routines were also present for validation both at the national and central level. The programme gives clinicians faster and easier access to results and enables comparisons across hospitals and regions. Continuing efforts are needed to establish best practice as regards antibiotic policy and to improve hygiene measures, which currently vary between and within ICUs, and over time. While there is a lack of evidence as to the most optimal antibiotic strategies for preventing the emergence of bacterial resistance [36], there is consensus that information about usage and cost trends and information about local patterns of bacterial resistance are important steps towards prevention and control of emerging bacterial resistance [22]. A model for action based on results from concomitant surveillance of microbial resistance and antibiotic use has been proposed [11]. According to this model ICUs with high levels of resistance and low antibiotic use should focus on improved control of cross-transmission, identification of colonised patients at admission and optimising of antibiotic dosing. ICUs with high levels of resistance and high antibiotic use should focus on overuse, misuse and co-

usage of antibiotics. Care-ICU provides data for action in agreement with this model and may become an instrument for the promotion of more appropriate use of antibiotics and infection control measures. This may, hopefully, help to reduce emergence and spread of microbial resistance among the critically ill.

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