International Journal of Infection Control
www.ijic.info ISSN 1996-9783

ORIGINAL ARTICLE

Central line associated bloodstream infections in hospitalised children in Greece before and after implementation of a prevention bundle

***Katerina Mougkou[1], *Despoina Gkentzi[2], Georgia Kourlaba[1], Sofia Kouni[1], Ioannis Kopsidas[1], Charalampia Nteli[3], Theoklis Zaoutis[1,4], Susan Coffin[4]**

1 Collaborative Centre for Clinical Epidemiology and Outcomes Research (CLEO), University of Athens School of Medicine, Greece
2 Department of Paediatrics, University General Hospital of Patras, Greece
3 Paediatric Intensive Care Unit, "P&A" Children's hospital, Athens, Greece
4 Division of Infectious Diseases, Children's Hospital of Philadelphia, UPENN School of Medicine, Philadelphia, PA, USA

* joint first authors

doi: 10.3396/IJIC.v11i3.019.15

Abstract

Data on central line (CL) - associated bloodstream infections (CLABSIs) in neonates and children in Greece are limited. In this study we aimed to assess the epidemiology and microbiology of CLABSIs in children's hospitals in Greece using an active surveillance system and to assess the impact of a central line bundle on the incidence of CLABSIs.

The study was conducted by active surveillance for CLABSIs over an 18-month period (September 2012 – February 2014) in the two largest children's hospitals in Greece. After six months of surveillance, a CLABSI prevention bundle was introduced.

There were 4.07 infections per 1,000 CL days across all participating units in the baseline period. The infection rate during the intervention period decreased by 35% to 2.58 per 1,000 CL days (95% CI: 0.64 (0.55 – 0.75)). Stratified analysis by ward type revealed the highest baseline CLABSI rate for patients in paediatric intensive

Corresponding Author

Katerina Mougkou M.D.,
Research Associate, Collaborative Center for Clinical Epidemiology and Outcomes Research (CLEO), CLEO Room 609, "Aghia Sophia" Children`s Hospital, Thivon & Papadiamantopoulou, Goudi, Athens 115 27, Greece,
Phone: +306974818506,
Fax: +302107777363,
Email: k.mougkou@cleoresearch.org

care units (16.67 per 1,000 CL days), where the greatest reduction (50%) in the CLABSI rate was detected after the intervention. Overall, 48 (60%) of the isolated pathogens were Gram negative, where 4 (8.3%) were found to be resistant to carbapenems and 22 (45.8%) to one or more of third generation cephalosporins.
Implementation of the prevention bundle produced a significant reduction of the CLABSIs in the Greek paediatric hospitals. The high CLABSI rates and the levels of antimicrobial resistance of pathogens identified highlight the importance of establishing antimicrobial stewardship and active surveillance programs in Greece, a country with high rates of healthcare-associated infections during a period of financial crisis.

Keywords: Catheter-related infections; Cross infections and epidemiology and prevention and control; Child, hospitalised; Surveillance.

Introduction

Central line-associated bloodstream infections (CLABSIs) are the most common healthcare-associated infections in high-risk neonates and children and are associated with significant mortality, increased length of hospital stay and increased healthcare cost.[1-3] The Centers for Disease Control and Prevention (CDC) have published evidence-based guidelines that identify many elements of care that, if fully implemented, are able to reduce the risk of CLABSI; these include appropriate hand hygiene, maximal barrier precautions, chlorhexidine skin antisepsis, and daily review of line necessity, with prompt removal of unnecessary central lines.[4] An essential step, prior to the implementation of CLABSI preventative strategies, is the determination of the incidence of CLABSIs within an individual healthcare system. However, few European countries have national reporting requirements or surveillance systems.[5] As a result, little is known about the incidence of CLABSIs and healthcare-associated infections within specific regions of Europe.

In Greece, data on the epidemiology of CLABSIs in hospitalised adults are limited as reporting systems are currently under development;[6-10] most published data are derived from single centre institutions. Even less has been published about CLABSIs in high-risk paediatric populations where central lines are used, such as the neonatal[11] and paediatric intensive care units (NICUs, PICUs) as well as oncology wards[12]. In addition to the limited knowledge of the epidemiology of CLABSI, the emergence and spread of multi-drug resistant organisms (MDROs) in Greece, in both adults[13] and children,[14] increases the need for microbiologic data about the pathogens that cause CLABSIs and other healthcare-associated infections.

In this report, we describe the epidemiology and microbiology of CLABSIs in children's hospitals in Greece using data derived from an active surveillance system and assess the impact of a central line (CL) prevention bundle on the incidence of CLABSIs.

Material and Methods

We conducted an active surveillance for CLABSIs over an 18-month period (Sep 2012 – Feb 2014) in the two largest children's hospitals in Greece, both located in Athens. Surveillance was conducted in two PICUs, three level III NICUs, two oncology units and a bone marrow transplant unit (BMTU). This prospective before-and-after study was performed over two time periods: the baseline period and the intervention period. The baseline period included only active surveillance and lasted for 6 months.

Surveillance was conducted by prospective review of microbiology laboratory results using the CDC definitions.[15] We excluded bloodstream infections that were community onset or secondary to infection at another body site that met CDC criteria. Once a CLABSI event was identified, data were collected in more detail with the use of a separate structured data abstraction form. We collected data about demographics and clinical data such as clinical signs of sepsis, type and insertion date of the catheter, receipt of parenteral nutrition or blood transfusion, prior hospitalisation or surgical intervention, prior use of antibiotics or immunosuppression. Microbiologic data, including the sensitivities of the isolated organisms, were also recorded.

Denominator data, including central line days (CL-days) and patient days (pt-days) were collected by unit-based staff using a standardised form. In NICUs, CL-days and pt-days were stratified by birth weight categories according to CDC definitions.

After six months of baseline surveillance, CLABSI prevention interventions were introduced; these included improving the hand hygiene compliance and implementing a CLABSI prevention bundle. Hand hygiene education focused upon appropriate technique and adherence to the World Health Organization's "5 Moments of Hand Hygiene".[16] The CLABSI prevention bundle included: 1) adherence to maximal sterile barrier precautions for catheter insertion; 2) use of chlorhexidine for skin antisepsis at the time of catheter insertion and for dressing changes for non-NICU patients; 3) proper frequency of dressing changes (48 hours for gauze and 7 days for transparent dressings); and 4) removal of non-essential catheters. Additional interventions included quarterly feedback of the CLABSI rates to each unit's directors, voluntary use of a modified version of the CDC's Central Line Insertion Practices (CLIP) form[17] (PICU and NICU only), and delivery of two seminars on guidelines of CLABSI prevention to physicians and nurses of every unit.

Based on CDC criteria, the CLABSI rate per 1000 CL-days was calculated by dividing the number of CLABSI events by the number of CL-days and multiplying the result by 1000, and the CL Utilization Ratio by dividing the number of CL- days by the number of pt-days.[15]

Categorical variables are presented as absolute (n) and relative (%) frequencies, while the age of patients is presented as a median (25^{th} and 75^{th} percentile), as the Shapiro-Wilk test revealed that it is not normally distributed. To compare baseline patient- and CLABSI-related characteristics between baseline and intervention periods, the Fisher's exact test for binary variables and Mann-Whitney for age were used. P values of <0.05 by two-sided tests were considered significant.

Statistical process control (SPC) charts were used to track changes in monthly CLABSI rates. The mean (centre line) and upper and lower control limit (LCLs) were calculated and displayed as ±2.5 SEs of the mean (Microsoft Excel).

Finally, we conducted two types of analysis to evaluate the impact of the intervention on CLABSI rates. First, we conducted an analysis to compare the pooled mean CLABSI rate of the baseline period with the pooled mean of the remaining months. Second, we divided the intervention period in two 6-month periods to further examine the progressive CLABSI reduction using Poisson regression. We compared the CLABSI rates of each follow-up period with the baseline CLABSI rate. Random effects Poisson regression to account for the clustering of CLABSI rates within units across time periods was used. The results of this analysis are presented as incidence rate ratio (IRR) and 95% confidence interval (95% CI) and p-values. All analyses were conducted using STATA 11.0 statistical software.

Results

During the baseline period, there were 4.07 infections per 1,000 CL-days (34 CLABSIs in 8,356 CL-days) across all participating units. The mean CLABSI rate during the intervention period was 2.58 per 1,000 CL-days (46 CLABSIs per 17,808 CL-days, 95% CI 0.64 (0.55 – 0.75)); this represented a 35% reduction. The monthly CLABSI rates for all units across the whole study period are presented in Figure 1. The CL utilization ratio did not change during the study periods (Table I).

Stratified analysis by ward type (PICU, NICU, BMTU, Oncology unit) revealed that the higher baseline CLABSI rate was observed in the PICUs of participating hospitals (16.67 per 1000 CL-days), with the higher CL utilization ratio on the BMTU (97%) (Table I). Moreover, the greater reduction in the CLABSI rate was detected in PICUs and BMTU. To be more precise, a reduction of almost 50% was revealed in both types of wards (Table I). The monthly CLABSI rates across the whole study period by ward type are presented in Figure 2.

We divided the intervention period into two six-month periods to further examine the progressive CLABSI reduction using Poisson regression. In all units, with the exception of the oncology wards, a progressive CLABSI reduction was detected. However, this reduction did not reach statistical significance in NICUs. On the other hand, the PICUs achieved a 40% reduction in the CLABSI rate during the first six months

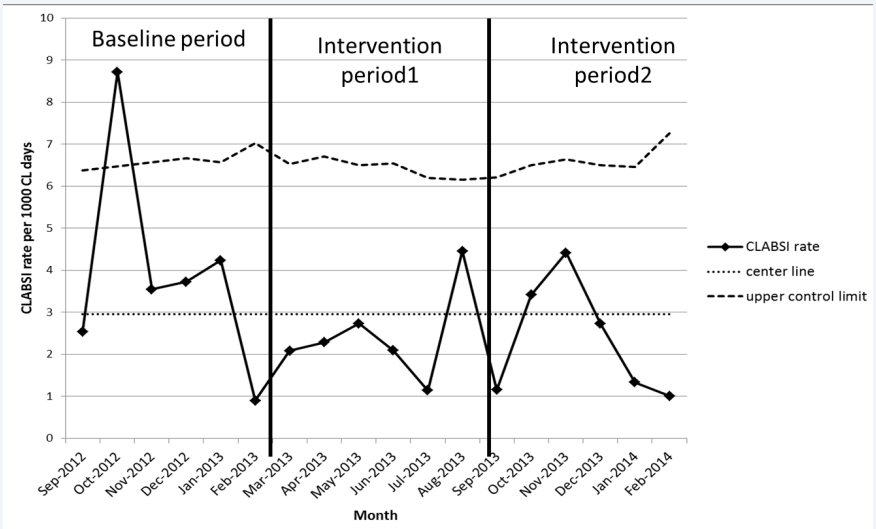

Figure 1. Overall CLABSI rate by month: U-chart

Table I. CL use and CLABSI rates in phase 1 (baseline period) and phase 2 (intervention period)

		ALL UNITS	PICUS	NICUS	ONCOLOGY	BMTU
CLABSI Rate/ 1000 CL days	Phase 1	4	16.6	5.4	1.7	3.4
	(95% CI)	*(2.7 – 5.4)*	*(7.6 – 25.7)*	*(1.6 – 9.2)*	*(0.5 – 2.9)*	*(0.4 – 6.4)*
	Phase 2	2.5	8.25	3.9	1.1	1.6
	(95% CI)	*(1.8 – 3.3)*	*(4 – 12.4)*	*(1.9 – 5.9)*	*(0.4 – 1.9)*	*(0.2 – 3.1)*
IRR (95% CI)		0.64 (0.54– 0.75)	0.5 (0.4– 0.62)	0.83 (0.53 – 1.30)	0.68 (0.39 – 1.20)	0.48 (0.26 – 0.91)
p-value		<0.001	<0.001	0.434	0.193	0.026
CL utilization ratio		0.5	0.5	0.2	0.7	0.9

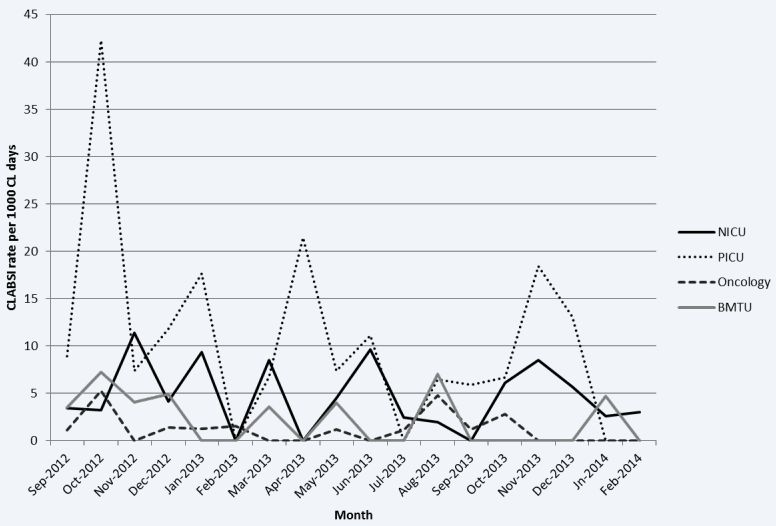

Figure 2. Overall CLABSI rate by month and type of unit

of the intervention period as compared to baseline period, while the reduction was even greater in the second six months of the intervention period (almost 55%). The BMTU also achieved a marked reduction of CLABSI rates (almost 75% in the second six months of the intervention period) while no significant reduction was identified in the first semester (Table II).

Sixty five patients (25 and 40 in baseline and intervention period, respectively) experienced at least one CLABSI event during the whole study period. The baseline characteristics of these patients are presented in Table III. The group of children with CLABSI included 35 males (54.7 %). Median age was 1.1 year (25th, 75th percentile: 0.3, 6.9) and 30 (46.2%) of children had been transferred from another hospital. Twenty-eight of 65 patients (43.1%) were oncology patients, most of whom (50%) had haematological malignancies. No difference was detected in patients' characteristics between the baseline and intervention period.

The majority of CLABSI events were associated with a tunnelled central line catheter (66.3%). The other CLABSI-related characteristics are presented in Table IV.

Table II. The effect of intervention on CLABSI rates: Results from Poisson regression analysis

Overall	No of infections	CL-days	Crude CLABSI Rate (95% CI)	IRR (95% CI)	p-value
0-6 months (baseline period)	34	8356	4.07 (2.70 – 5.44)	1	
7-12 months (intervention period 1)	23	9207	2.50 (1.48 – 3.52)	0.674 (0.560 – 0.809)	<0.001
13-18months (intervention period 2)	23	8601	2.67(1.58 – 3.77)	0.608 (0.503 – 0.736)	<0.001
NICU					
Baseline (6-months)	8	1471	5.44 (1.67 – 9.21)	1	-
7-12 months	6	1629	3.68 (0.74 – 6.63)	0.880 (0.629 – 1.232)	0.459
13-18 months	9	2193	4.10 (1.42 – 6.79)	1.067 (0.774 – 1.470)	0.692
PICU					
Baseline (6-months)	13	780	16.67 (7.61 – 25.73)	1	-
7-12 months	7	781	8.96 (2.32 – 15.60)	0.580 (0.452 – 0.744)	<0.001
13-18 months	8	1037	7.71 (2.37 – 13.06)	0.435 (0.331 – 0.573)	<0.001
Oncology					
Baseline (6-months)	8	4638	1.72 (0.53 – 2.92)	1	
7-12 months	6	5284	1.14 (0.23 – 2.04)	0.638 (0.324 – 1.255)	0.194
13-18 months	5	3926	1.27 (0.16 – 2.39)	0.744 (0.382 – 1.449)	0.385
BMTU					
Baseline (6-months)	5	1467	3.41 (0.42 – 6.39)	1	-
7-12 months	4	1513	2.64 (0.05 – 5.24)	0.739 (0.374 – 1.455)	0.381
13-18 months	1	1445	0.69 (0.00 – 2.048)	0.239 (0.087 – 0.653)	0.005

IRR: Incidence Rate Ratio; CI: Confidence Interval

Table III. Patient-related characteristics of children experiencing CLABSI in baseline and intervention period (n=65)

Characteristics of children	Overall *N =65*	Baseline period *N =25*	Intervention period *N =40*	p-value
Gender (male)	35 (54%)	17 (70%)	18 (45%)	0.044
Age (years)	1.1 (0.3 – 6.9)	2.6 (0.5 – 5.5)	0.6 (0.1 – 7.2)	0.194
Transfer from another hospital	30 (46%)	9 (36%)	21 (52%)	0.194
Oncology patient (yes) *	28 (43%)	13 (52%)	15 (37%)	0.251
ALL/AML	14 (50%)	5 (38%)	9 (60%)	0.066
Solid Tumour	10 (35%)	4 (30%)	6 (40%)	
Stem cell transplantation	4 (14%)	4 (30%)	0	

*Oncology Patient from Oncology unit, BMTU, PICU
ALL: Acute lymphoblastic leukaemia, AML: Acute myeloid leukaemia

Table IV. CLABSI-related characteristics and micro-organisms related to CLABSI in baseline and intervention period (n=80)

Characteristics of CLABSIs	Overall	Baseline period	Intervention period	p-value
Hospitalisation within past 30 days prior to CLABSI	68 (86.1%)	30 (90.9%)	38 (82.6%)	0.293
Type of central catheter				
Tunnelled	53 (66.3%)	23 (67.7%)	30 (65.2%)	<0.001
Umbilical	3 (3.8%)	0	3 (6.5%)	
Non tunnelled	9 (11.3%)	0	9 (19.6%)	
Peripherally Inserted Central Catheter (PICC)	12 (15.0%)	11 (32.4%)	1 (2.2%)	
Other	3 (3.8%)	0	3 (6.5%)	
Blood transfusion within 1 week				
Yes	55 (68.8%)	25 (73.5%)	30 (65.2%)	0.379
N/A	3 (3.8%)	2 (5.9%)	1 (2.2%)	
Surgical procedure within 30 days				
Yes	29 (36.3%)	6 (17.7%)	23 (50.0%)	0.006
N/A	1 (1.3%)	0	1 (2.2%)	
Mechanical ventilation at time of CLABSI	28 (35.0%)	13 (38.2%)	15 (32.6%)	0.602
Urinary catheter at time of CLABSI	27 (34.2%)	9 (26.5%)	18 (40.0%)	0.209
Neutropenia within 1 week	29 (36.7%)	13 (38.2%)	16 (35.6%)	0.672
Immunosuppressive agents within 30 days	33 (41.3%)	16 (47.1%)	17 (37.0%)	0.488
Fever	71 (88.7%)	29 (85.3%)	41 (89.1%)	0.900

Table IV. continued...

Removal of catheter as adjunctive treatment				0.480
No central catheter present at infection onset	1 (1.3%)	1 (2.9%)	0	
Central catheter removed as part of treatment	37 (46.3%)	17 (50.0%)	20 (43.5%)	
Central catheter left in place during treatment	41 (51.3%)	16 (47.1%)	25 (54.4%)	
Unknown	1 (1.3%)	0	1 (2.2%)	
Clinical response at day 3 of treatment				0.237
Uncertain	4 (5.0%)	3 (8.8%)	1 (2.2%)	
Failure	9 (11.3%)	4 (11.8%)	5 (10.9%)	
Probable response	37 (46.3%)	18 (52.9%)	18 (41.3%)	
Definite response	30 (37.5%)	9 (26.5%)	21 (46.7%)	
Pathogen				0.186
Gram positive	20 (25.0%)	5 (14.7%)	15 (32.6%)	
Gram negative	48 (60.0%)	23 (67.7%)	25 (54.3%)	
Fungal	12 (15.0%)	6 (17.7%)	6 (13.0%)	

Thirty-seven (46.3%) catheters from children with CLABSI removed as part of treatment, while in the rest of cases central catheters were left in place. As for the clinical outcome three days after the infection, more than 80% of children with CLABSIs had responded to treatment.

The distribution of the isolated micro-organisms was 60% Gram-negative, 25% Gram-positive and 15% fungi, with no significant difference detected between the baseline and the intervention period. The five most frequently isolated pathogens were *Klebsiella sp*. (15%), *Enterobacter spp*. (13%), *Escherichia coli* (12.5%), *Pseudomonas aeruginosa* (12.5%) and *Candida spp*. (12.5%) (Table IV).

Overall, 4/48(8.3%) of Gram negative pathogens were resistant to carbapenems, while 22/48 (45.8%) were resistant to one or more of third generation cephalosporins. Gram negative pathogens were more likely to be resistant to third generation cephalosporins in baseline period (60.9%) compared to the intervention period (32.0%, p=0.045), while no difference was detected between the two periods in terms of resistance to carbapenems.

Discussion

During the project, we established a CLABSI surveillance program in the largest Greek paediatric hospitals successfully. To our knowledge, this is the first conducted systematic and prospective surveillance study that uses the definitions and procedures standardized by the CDC to explore CLABSI rates in the Greek paediatric population. We also implemented a multifaceted prevention bundle for central line care, including insertion and maintenance practices, resulting in a reduction of the CLABSI rates. This achievement becomes more significant due to the high prevalence of resistant pathogens in Greek hospitals.

We showed that CLABSIs are a significant problem in the Greek paediatric hospitals with infection rates that are considerably higher than the ones in the NHSN report of US hospitals.[17] However, our results are comparable to those reported from the International Nosocomial Infection Control Consortium in countries with limited resources.[18]

This partnership project of two paediatric institutions demonstrates that CLABSI reduction in Greek hospitals is feasible and can have significant public health consequences. Important reductions in morbidity and health care costs could be achieved if the intervention to reduce these infections could be introduced successfully nationwide. Similar results have been published in other European studies when a surveillance network was created among hospitals across the country.[5]

The predominance of Gram negative bacteria causing CLABSIs in our study is in contrast to the epidemiology described in other countries including the United States and Germany where the predominant pathogens are Gram positive. However, this finding was not unexpected given the epidemiology of bacteria previously described in adult populations in Greece where the distribution of pathogens mirrors our findings.[19]

Most concerning was that among the Gram negative bacteria identified, carbapenem-resistant Gram negative bacteria are frequent pathogens in CLABSIs in Greek children's hospitals. Surveillance studies indicate that the percentage of carbapenem-resistant isolates has gradually increased in Europe. In Greece, the proportion of carbapenem resistant *A. baumannii* isolates from adult ICUs patients in tertiary care hospitals increased from 75% to 95% between 2005 and 2010.[20] However, the spread of these resistant bacteria is not yet established in the Greek children's hospitals.[21]

Our study confirms the importance of surveillance in children's hospitals. The significant burden of CLABSIs might be partially attributed to the lack of previous surveillance programs. The high infection rates, central line utilization ratios, and levels of antimicrobial resistance of pathogens identified, compared with international benchmarks, highlight the importance of establishing antimicrobial stewardship and active surveillance programs. Developing a comprehensive education program on evidence-based approaches for all healthcare workers, decreasing device utilization and implementing care bundles will contribute to reducing the burden of CLABSIs and improve the quality of care and patient safety in the hospitalised children in Greece.

This study has limitations but does also have some important public health implications. Participation in the surveillance network was voluntary, limiting the number of participating units to 2 children's hospitals which may limit the generalisability of our findings. An expansion of the network with a mandatory participation would undoubtedly lead to improvement of the representativeness and the generalisability of the results, as well as greatly expand the impact of this work.

In summary, we demonstrated that a multifaceted approach on the prevention of healthcare associated infections, with the establishment of a surveillance program and promoting hand hygiene being essential components of the intervention bundle, can achieve improvement of patient safety by reducing the healthcare associated infections.

Acknowledgements

The authors thank the following individuals for their contributions to this study: Maria Kazantzi, Chrysa Petropoulou, Olga Gerodimou, Ageliki Bilali, Korina Karahristou, Georgia Sideri, Maria Kitra, Stiliani Vore.

References

1. Pittet D, Tarara D, Wenzel RP. Nosocomial bloodstream infection in critically ill patients. Excess length of stay, extra costs, and attributable mortality. *Journal of the American Medical Association* 1994; **271(20):** 1598-1601. http://dx.doi.org/10.1001/jama.1994.03510440058033
2. Elward AM, Hollenbeak CS, Warren DK, Fraser VJ. Attributable cost of nosocomial primary bloodstream infection in pediatric intensive care unit patients. *Pediatrics* 2005; **115(4):** 868-872. http://dx.doi.org/10.1542/peds.2004-0256
3. Carey AJ, Saiman L, Polin RA. Hospital-acquired infections in the NICU: epidemiology for the new millennium. *Clinics in Perinatology* 2008; **35(1):** 223-249. http://dx.doi.org/10.1016/j.clp.2007.11.014
4. O'Grady NP, Alexander M, Burns LA, *et al*. Summary of recommendations: Guidelines for the Prevention of Intravascular Catheter-related Infections. *Clinical Infectious Diseases* 2011; **52(9):** 1087-1099. http://dx.doi.org/10.1093/cid/cir138
5. Schwab F, Gastmeier P, Piening B, Geffers C. The step from a voluntary to a mandatory national nosocomial infection surveillance system: the influence on infection rates and surveillance effect. *Antimicrobial Resistance and Infection Control* 2012; **1(1):** 24. http://dx.doi.org/10.1186/2047-2994-1-24
6. Tarpatzi A, Avlamis A, Papaparaskevas J, *et al*. Incidence and risk factors for central vascular catheter-related bloodstream infections in a tertiary care hospital. *The New Microbiologica* 2012; **35(4):** 429-437.
7. Dima S, Kritsotakis EI, Roumbelaki M, *et al*. Device-associated nosocomial infection rates in intensive care units in Greece. *Infection Control and Hospital Epidemiology* 2007; **28(5):** 602-605. http://dx.doi.org/10.1086/513618
8. Gikas A, Pediaditis J, Papadakis JA, *et al*. Prevalence study of hospital-acquired infections in 14 Greek hospitals: planning from the local to the national surveillance level. *The Journal of Hospital Infection* 2002; **50(4):** 269-275. http://dx.doi.org/10.1053/jhin.2002.1181
9. Apostolopoulou E, Raftopoulos V, Filntisis G, *et al*. Surveillance of device-associated infection rates and mortality in 3 Greek intensive care units. *American Journal of Critical Care* 2013; **22(3):** e12-20. http://dx.doi.org/10.4037/ajcc2013324
10. Alexopoulos EC, Batzi E, Messolora F, Jelastopulu E. Wide range of point prevalences of healthcare-associated infections in Western Greece. *Epidemiology and Infection* 2011; **139(11):** 1734-1739. http://dx.doi.org/10.1017/S0950268810002670

11. Apostolopoulou E, Lambridou M, Lambadaridis I. Nosocomial bloodstream infections in a neonatal intensive care unit. *British Journal of Nursing* 2004; **13(13):** 806-812. http://dx.doi.org/10.12968/bjon.2004.13.13.13503
12. Perdikaris P, Petsios K, Vasilatou-Kosmidis H, Matziou V. Complications of Hickman-Broviac catheters in children with malignancies. *Pediatric Hematology and Oncology* 2008; **25(5):** 375-384. http://dx.doi.org/10.1080/08880010802106622
13. Mouloudi E, Protonotariou E, Zagorianou A, *et al.* Bloodstream infections caused by metallo-beta-lactamase/*Klebsiella pneumoniae* carbapenemase-producing *K. pneumoniae* among intensive care unit patients in Greece: risk factors for infection and impact of type of resistance on outcomes. *Infection Control and Hospital Epidemiology* 2010; **31(12):** 1250-1256. http://dx.doi.org/10.1086/657135
14. Maltezou HC, Kontopidou F, Katerelos P, Daikos G, Roilides E, Theodoridou M. Infections caused by carbapenem-resistant Gram-negative pathogens in hospitalized children. *The Pediatric Infectious Disease Journal* 2013; **32(4):** e151-154. http://dx.doi.org/10.1097/INF.0b013e3182804b49
15. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of health care-associated infection and criteria for specific types of infections in the acute care setting. *American Journal of Infection Control* 2008; **36(5):** 309-332. http://dx.doi.org/10.1016/j.ajic.2008.03.002
16. Pittet D, Allegranzi B, Boyce J, World Health Organization World Alliance for Patient Safety First Global Patient Safety Challenge Core Group of Experts. The World Health Organization Guidelines on Hand Hygiene in Health Care and their consensus recommendations. *Infection Control and Hospital Epidemiology* 2009; **30(7):** 611-622. http://dx.doi.org/10.1086/600379
17. Dudeck MA, Horan TC, Peterson KD, *et al.* National Healthcare Safety Network (NHSN) Report, data summary for 2010, device-associated module. *American Journal of Infection Control* 2011; **39(10):** 798-816. http://dx.doi.org/10.1016/j.ajic.2011.10.001
18. Rosenthal VD, Bijie H, Maki DG, *et al.* International Nosocomial Infection Control Consortium (INICC) report, data summary of 36 countries, for 2004-2009. *American Journal of Infection Control* 2012; **40(5):** 396-407. http://dx.doi.org/10.1016/j.ajic.2011.05.020
19. Koupetori M, Retsas T, Antonakos N, *et al.* Bloodstream infections and sepsis in Greece: over-time change of epidemiology and impact of de-escalation on final outcome. *BMC Infectious Diseases* 2014; **14:** 272. http://dx.doi.org/10.1186/1471-2334-14-272
20. Miyakis S, Pefanis A, Tsakris A. The challenges of antimicrobial drug resistance in Greece. *Clinical Infectious Diseases* 2011; **53(2):** 177-184. http://dx.doi.org/10.1093/cid/cir323
21. Mougkou K, Michos A, Spyridopoulou K, *et al.* Colonization of high-risk children with carbapenemase-producing Enterobacteriaceae in Greece. *Infection Control and Hospital Epidemiology* 2013; **34(7):** 757-759. http://dx.doi.org/10.1086/670997