Control of carbapenemase-producing *Klebsiella pneumoniae*: a region-wide intervention

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Starting in 2010, there was a sharp increase in infections caused by *Klebsiella pneumoniae* resistant to carbapenems in the Emilia-Romagna region in Italy. A region-wide intervention to control the spread of carbapenemase-producing *K. pneumoniae* (CPKP) in Emilia-Romagna was carried out, based on a regional guideline issued in July 2011. The infection control measures recommended to the Health Trusts (HTs) were: phenotypic confirmation of carbapenemase production, active surveillance of asymptomatic carriers and contact isolation precautions for carriers. A specific surveillance system was activated and the implementation of control measures in HTs was followed up. A significant linear increase of incident CPKP cases over time (p<0.001) was observed at regional level in Emilia-Romagna in the pre-intervention period, while the number of cases remained stable after the launch of the intervention (p=0.48). Considering the patients hospitalised in five HTs that provided detailed data on incident cases, a downward trend was observed in incidence after the release of the regional guidelines (from 32 to 15 cases per 100,000 hospital patient days). The spread of CPKP in Emilia-Romagna was contained by a centrally-coordinated intervention. A further reduction in CPKP rates might be achieved by increased compliance with guidelines and specific activities of antibiotic stewardship.

Introduction

The emergence and spread of carbapenemase-producing Enterobacteriaceae (CPE) has been observed throughout the world [1–6]. Infections caused by CPE, a group of organisms characterised by extensive resistance to antimicrobials, are very difficult to treat, with limited therapy options [2,3,6,7]. The first case of carbapenemase-producing *Klebsiella pneumoniae* (CPKP) in Italy was detected in October 2008 [8]. In 2011, the European Antimicrobial Resistance Surveillance Network (EARS-Net) reported that Italy was one of the most affected countries in Europe, with a worrisome increasing trend in CPKP [9].

Several studies have convincingly demonstrated that aggressive control measures are effective in halting the spread of CPE in healthcare institutions [2,3,10-14]. So far, Israel is the only setting with high transmission rate of CPKP where a nationwide intervention has been effectively implemented. The Israeli control activities were based on cohorting CPE carriers and creating dedicated staffing in hospital; the intervention was monitored at national level by a central authority and a task force was created to collect data from hospitals and to participate locally to the outbreak control [14]. This paper describes the impact of a regional intervention to control CPKP and other CPE implemented in Emilia-Romagna, Italy.

The regional setting

Emilia-Romagna is a northern Italian region of 4.4 million inhabitants. The Regional Public Health System includes 17 Health Trusts (HTs) with 60 hospitals and about 550,000 hospital admissions per year. Isolation facilities for infected or colonised patients are unevenly distributed in the HTs of Emilia-Romagna, with some older hospitals having few single rooms.

A regional antimicrobial resistance surveillance system, established in 2003, is based on twice-yearly electronic transfer of microbiological tests performed in public hospital laboratories [15]. The representativeness of the system was estimated to be about 90% of bacterial cultures performed in public hospitals, covering the vast majority of cultures for diagnosis of invasive infections, both in hospital and the community [15]. The proportion of carbapenem-non-susceptible *K.*

pneumoniae isolates from blood increased from 2% in 2009 to 21% in 2011 [15].

Methods

Infection control measures

In July 2011, a regional guideline for the control of CPKP and other CPE was issued (subsequently updated in January 2013) [16]. The guideline was supplemented by a leaflet that informed hospital patients colonised with CPE and their caregivers of the actions to be taken to prevent transmission, as well as specific recommendations for the management of CPE-infected or colonised patients in the community and in long-term care facilities (LTCFs) [17].

The documents were issued after two months of consultations involving all representatives of infection control (IC) teams in the 17 HTs in the region, and other experts in the fields of microbiology, infectious diseases and risk management.

The following infection control measures were recommended:

- CPE diagnosis by phenotypic confirmation of carbapenemase production, by modified Hodge test or by a disk-diffusion synergy test including meropenem and two carbapenemase-inhibiting compounds (dipicolinic acid and boronic acid) [18,19];
- active surveillance of CPE asymptomatic carriers by rectal swabs for close contacts of CPE hospitalised patients (patients staying in the same hospital unit), high-risk patients at hospital admission (i.e. patients transferred from other acute hospitals and LTCFs or coming from endemic countries), and, only for hospitals where CPE were endemic (with sustained intra-facility transmission) or where epidemic clusters were detected the previous year, patients admitted to intensive care units, spinal units, transplant units, oncology and hematology units. CPE screening of carriers was not recommended in LTCFs;
- contact isolation precautions for all CPE infected patients and asymptomatic carriers, during their stay in hospital. It was strongly recommended, where possible, to place these patients in a single room or to cohort them with other CPE-infected patients or asymptomatic carriers; otherwise, they were accommodated in a room with non-carriers and contact precautions were applied. Staff cohorting was recommended and, if this was not feasible, it was recommended that each case be assigned a manager nurse responsible for checking that all health care workers and visitors applied contact precautions. Health Trust general directors were requested to assure the monitoring of compliance with standard and contact precautions and the scheduling of educational activities for health workers aimed at improving infection control skills;
- communication of CPE presence at the time of patient transfer (to receiving institution for patients transferred to other hospitals or to LTCFs, and to the general practitioner for patients returning home).

The guideline, although not explicitly promoting antimicrobial stewardship, recommended using antibiotics sparingly and encouraged laboratories to attach notes to the microbiological results inviting clinicians to carefully evaluate the need for antibiotic treatment.

Specific surveillance

From June 2011, all HTs were asked to send a monthly report to the Regional Agency for Health and Social Care, with the aggregated number of prevalent cases stratified by patients with bacteraemia, patients with other infections and asymptomatic carriers identified by rectal swabs. Data, referring to all patients (hospitalised or not) diagnosed in the area of competence of the HT, were reported separately for public hospitals, private hospitals, LTCFs and other community settings. A report was returned monthly to all HTs. Five HTs, those where CPE were endemic or placed in the same area of an endemic hospital, were asked to provide more detailed monthly reports that differentiated, for hospitalised patients, CPKP incident cases from already known CPKP cases.

Follow-up of implementation of regional recommendations

In the period August-September 2011, after the release of regional guidelines for CPE control, all HTs were requested to confirm through an official written statement that they had produced local operational protocols based on the recommendations of the regional guidelines. A questionnaire-based survey was conducted in May and June 2012 to evaluate the actual implementation of regional guidelines. Individualised feedback, based on the questionnaire results and observed epidemiological trends, was delivered in October 2012 to the directors of the eight HTs which had an average of 2 or more cases of CPE infections per month. The feedback reports pointed out potential failures in the implementation of control measures and provided suggestions for improvement. The HT directors were asked to check for actual implementation of screening activities and of contact precautions in hospitals under their responsibility, by using available data or performing ad hoc audit.

Statistical Analysis

Stata 10.1 (Stata Corporation, College Station, Texas) was used for statistical analysis. The weekly trend line of incident cases of carbapenem-non-susceptible *Klebsiella pneumoniae* (CRKP) in the period 2009–2012 was smoothed by the moving average method (13-period moving average: each point representing the same week and the previous 12). An incident case was defined as the first-ever CRKP isolated in a subject. Analysis of covariance (ANCOVA) was used

to compare the difference between slopes of linear regression of incident cases over time. The time frame up to the 22nd week of 2011 was considered to be the pre-intervention period, while the period starting from the 31st week of 2012 was considered to be the post-intervention period; a window of eight weeks (from the 23rd to the 30th week), during which the HTs produced and implemented local protocols based on the regional guidelines, was removed from this particular analysis.

Multivariate linear regression was performed to evaluate temporal trends and the correlation among independent variables and the monthly CPKP incidence rate in five HTs. The unit of observation was HT-month and a significance level of 0.05 was used. In order to account for the likely correlation among observations coming from the same HT, a multilevel linear regression was also performed, introducing the HT as a random effect variable. However, since the results thus obtained were similar to those yielded by the simpler model, the former is presented here.

Results

Infection trends

The regional system for surveillance of antimicrobial resistance displayed a swift upward incidence trend in the weekly number of patients with carbapenem-resistant *Klebsiella pneumoniae* (CRKP), including isolates from all cultures other than gastrointestinal ones, during 2010 and the first half of 2011. The trend remained stable in the second half of 2011 and the first quarter of 2012, then showed a slight increase in the mid-2012 with a subsequent return to the previous rate (Figure 1). Running two separate linear regressions of incident cases over time, a slope significantly higher than zero ($p<0.001$) was obtained for the pre-intervention period (estimate: 0.10, 95% CI: 0.09–0.12), and a slope not significantly different than zero ($p=0.48$) for the post-intervention period (estimate: 0.02, 95% C.I.: -0.04; 0.08). An analysis of covariance indicated a significant ($p<0.01$) difference in the magnitude of the two slopes. Considering hospitalised patients, the incidence rates

Figure 1

Incident cases of carbapenemase-producing *Klebsiella pneumoniae*, Emilia-Romagna, Italy, 2009–2012

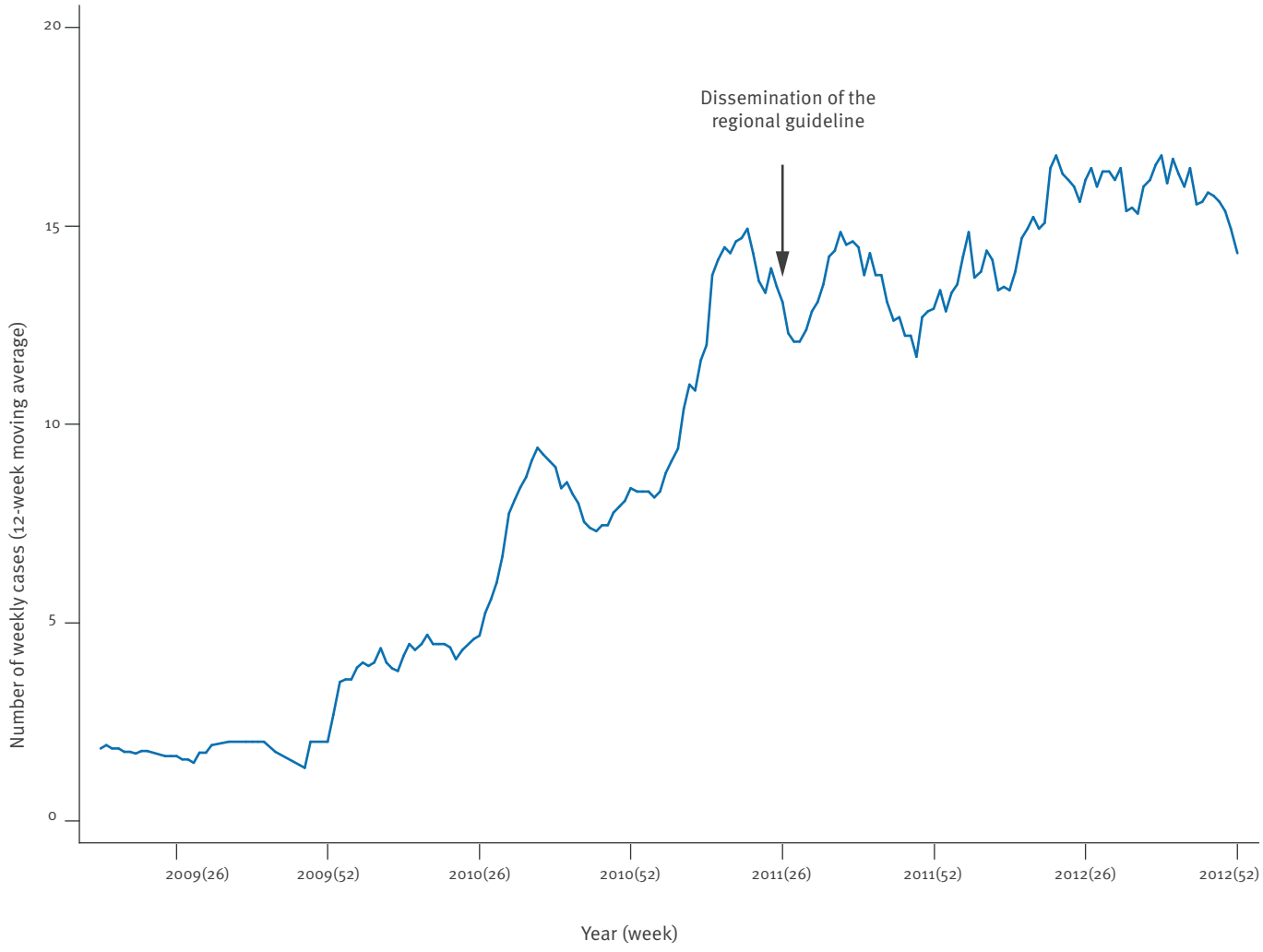


Figure includes all non-gastrointestinal cultures positive for carbapenem-resistant *Klebsiella pneumoniae* reported to the regional antimicrobial resistance surveillance system.

Figure 2

Prevalent cases of carbapenemase-producing *Klebsiella pneumoniae* by sample type, Emilia-Romagna, Italy, July 2011–March 2013

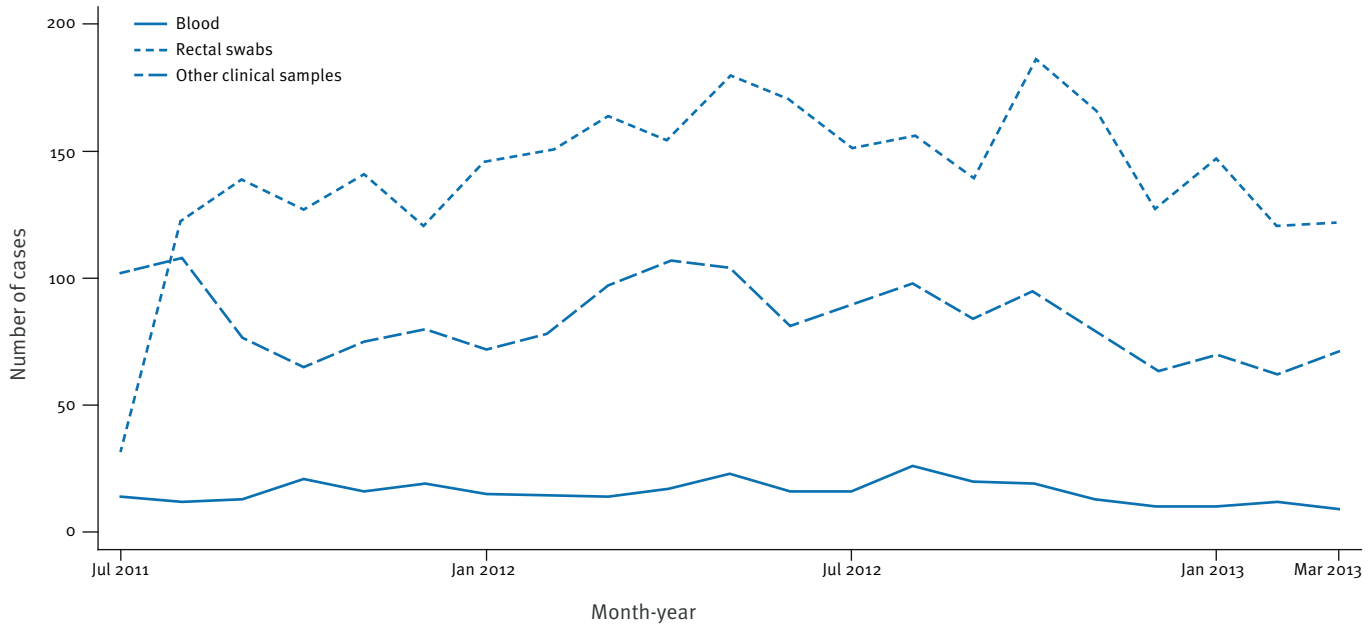


Figure shows all cultures positive for carbapenemase-producing *Klebsiella pneumoniae* reported to the regional carbapenemase-specific surveillance system.

of CRKP isolation from all non-gastrointestinal samples were 16 and 15 cases per 100,000 hospital patient days, after guideline implementation, in the third quarter of 2011 and in the fourth quarter of 2012, respectively, compared to an incidence rate of 7 cases per 100,000 hospital patient days in 2010.

The specific surveillance system for CPE, covering the entire region and providing monthly prevalence data starting from July 2011, showed CPKP as the most prevalent CPE, representing 95% of all cases while *Escherichia coli* and other Enterobacteriaceae accounted for 2% and 3% of total prevalent CPE cases, respectively. Before implementation of regional guidelines, no HT was performing an active search of asymptomatic carriers. Starting from July 2013 the number of CPKP isolated by rectal swab increased (Figure 2) and in September it overtook the number of isolates from clinical samples: the ratio of CPKP isolates from rectal swabs and isolates from clinical samples was 0.3 in July 2011, reached 1.7 in September 2011 and remained quite stable in the subsequent months with a peak of 2 in November and December 2012. Clinical isolates decreased in the period between September 2011 and February 2012, but registered a subsequent growth between March and October 2012 and a further decrease starting from November 2012 (Figure 2). Patients admitted to public hospitals constituted the vast majority of CPKP prevalent cases, accounting for 97% of bacteraemia cases, 93% of asymptomatic

Table

Multivariate linear regression of covariates affecting monthly incidence of carbapenemase-producing *Klebsiella pneumoniae* in five Health Trusts, Emilia-Romagna, Italy, July 2011–March 2013

Variable	Regression coefficient	95% CI	p value
Months since guideline release	-0. 73	-1.21 to -0.25	0.003
Monthly prevalence rate[a]	0.14	0.08 to 0.21	‹0.001
Isolation of identified cases in a single room	-19.30	-26.17 to -12.42	‹0.001
Audit of compliance with contact precautions	-7.58	-13.66 to -1.50	0.015
Intercept	31.06	20.42 to 41.70	‹0.001

CI: confidence intervals.

Incidence defined as new cases per 100,000 patient days: all cultures other than rectal swabs included.

[a] Total cases per 100,000 patient days: all cultures included.

carriers identified by rectal swabs, and 82% of other cases.

Reports from the five HTs providing monthly data on incident in-hospital cases showed a downward incidence rate trend of CPKP cases (isolates from rectal swabs were excluded) after the release of the regional guidelines. The incidence rates observed in these HTs, were 32 and 15 cases per 100,000 hospital patient days in the third quarter of 2011 and in the first quarter of 2013, respectively. In the period between July 2011 and March 2013, the monthly incidence rates showed a significant positive correlation with the monthly prevalence rates and a negative correlation with placement in a single room as main isolation method and with performing observational audit of compliance with contact precautions (Table). Both measures were implemented in one of the five HTs, while one of the two measures was implemented in two HTs. Evaluating the linear trend by HT, we observed a significant reduction in two of the five HTs, an increase in one HT and a non-significant trend in the remaining two (Figure 3). The HT with an increasing trend had incidence rates of seven and 19 cases per 100,000 hospital patient days in the third quarter of 2011 and in the first quarter of 2013, respectively.

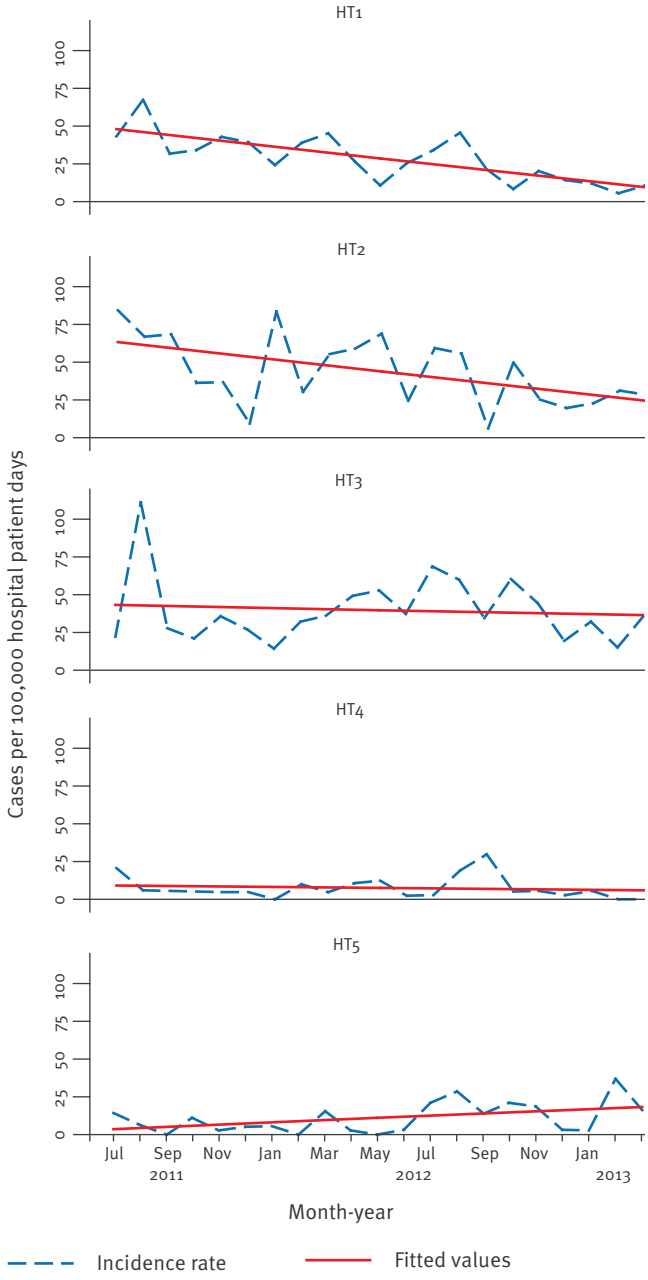
Survey of implementation of regional recommendations to contain CPE (May–June 2012)

All HTs in Emilia-Romagna participated in the questionnaire-based survey. All HTs implemented the appropriate tests for screening and phenotypic confirmation of carbapanemase production. In 16 of the 17 HTs, close contacts of hospitalised patients with CPE were actively screened, while in all HTs at least one of the following groups at risk was screened at hospital admission: (i) patients transferred from other hospitals or from LTCFs; (ii) patients discharged from hospital in the previous 60 days; (iii) patients coming from countries endemic for CPE; and/or (iv) patients admitted to intensive care units, spinal units, transplant units, oncology and haematology units. Isolation in a single room was the main isolation method in eight HTs and cohorting of patients in a dedicated area of the hospital was the main method in one HT, while four HTs mainly applied contact precautions, placing CPE cases in a room shared with non-CPE carriers; the remaining four HTs implemented a mixed approach consisting of two or more methods of physical isolation. In seven HTs, staff cohorting and/or appointment of a unit case-manager nurse was adopted, while in the other 10 HTs neither of the two was adopted. Eight HTs out of 17 reported repeated observational audits of compliance with contact precautions based on a planned schedule, while seven HTs reported random audit activities and two HTs reported no audit activity.

Data on use of hand hygiene products were also requested from the HT hospital pharmacies. The consumption rate of these products significantly increased

Figure 3

Incidence rate of carbapenemase-producing *Klebsiella pneumoniae* in five Health Trusts, Emilia-Romagna, Italy, July 2011-March 2013



HT: Health trust.

Figure shows all cultures positive for carbapenemase-producing *Klebsiella pneumoniae* reported to the carbapenemase-specific surveillance system by five Health Trusts in Emilia-Romagna. The incidence trend over time is plotted by a linear regression line.

during the implementation of regional guidelines for CPE control, and the mean regional rates (litres/1,000 hospital days) were 5.1, 6.8 and 9.4 in 2010, 2011 and 2012, respectively.

Discussion

The intervention implemented in Emilia-Romagna was characterised by a rapid slowdown of the earlier upward CRKP trend, and for nine months, incidence remained stable at to the pre-intervention rate but did not show a dramatic drop, as observed in other contexts (e.g. Israel) [10-14]. After a slight increase observed in the second and third quarters of 2012, a return to the pre-intervention rate occurred, starting in November 2012, with a more noticeable reduction in some hospitals with a high frequency of cases. Considering the five HTs that provided monthly data on incident cases, we observed that the incidence of CPKP infections correlated with prevalence, the availability of single rooms for isolation and the implementation of observational audits for monitoring of adherence to contact precautions (Table). Two out of five HTs considered in this analysis showed significantly decreasing trends, while one had an increasing incidence of CPKP cases (Figure 3). The latter HT was selected to provide monthly incidence data because, even with a low frequency of infection when the regional intervention started, it was located in the same area as a highly affected hospital. This HT had the lowest rate of the five HTs at the beginning of the observation and a rate slightly over the average in the first quarter of 2013. These results highlight how local infection trends can differ significantly from the average observed in a wider setting, such as a region, because of discrepancies in exposure to specific risk factors or in compliance with control measures.

The different response to the activities of control in Emilia-Romagna compared to what was observed in Israel probably depends on the epidemiological context and the type of intervention. In Israel, the incidence observed at the time of the introduction of control activities (55.5 cases per 100,000 hospital patientdays) was significantly higher than that observed in Emilia-Romagna (16 cases per 100,000 hospital patient days). On the contrary, the post-intervention rates observed in the two settings were quite similar: 11.7 and 15 per 100,000 hospital patient days in Israel and Emilia-Romagna, respectively [14]. In Israel, the activities were implemented with very strict systematic cohorting of colonised patients and care staff [12,14]. This approach, while highly effective, was considered unsuitable for Emilia-Romagna, due to the organisation of the regional health system and to high costs. In Emilia-Romagna, contact precautions were implemented without cohorting staff and patients in most HTs. In four HTs, due to scarcity of single rooms, CPE cases were mainly placed in rooms with non-CPE carriers, posing additional difficulties for the correct implementation of contact precautions. Moreover, only eight HTs out of 17 implemented strict monitoring of compliance with contact precautions by observational audit. Still, the control activities implemented in the Region achieved a slowdown of CPKP spread. Incidence remained stable for three consecutive quarters after the launch of the regional intervention and, after a slight increase between April and October 2012, showed a return to the initial rate.

The present study has several limitations. First of all, no control group was available to compare the effect of the intervention, because the study was launched simultaneously across the region. Moreover, the observed results showing a slowdown of CPKP transmission at regional level hide a more heterogeneous result at local level depending on the pre-intervention incidence and on compliance with recommendations achieved during the intervention period [19,20]. The implementation of the regional recommendations at HT level has been monitored through a questionnaire-based survey but specific data on the actual degree of compliance with each of the proposed measures are not available. This an important limitation of the study, but, on the other hand, the increase of asymptomatic carriers identified by the active surveillance and the upward trend of hand hygiene products use are proxies of improvements in compliance with control measures after the start of the regional intervention for CPE containment. There is a consistent and clear temporality between the introduction of the control activities and the change in the slope of the CPKP trend line. Moreover, the reduction of incidence in the hospitals of five HTs correlates negatively with prevalence rate and positively with availability of single rooms for isolation and with monitoring of compliance with contact precautions, showing how control activities can drive the outcome in the expected direction.

Another important issue is the evaluation of the infection trend before the implementation of the regional intervention, which is based on routine data collected through the antimicrobial resistance surveillance system of Emilia-Romagna. This system has the limitation of not including the results of the phenotypic confirmation of carbapenemase production, yet it is a reliable tool for monitoring the trends of antimicrobial resistance, including CRKP before and during the implementation of CPE control measures. Finally, the specific surveillance implemented in Emilia-Romagna did not provide a systematic genotyping of CPKP, though available results indicate that CPKP, which was isolated in this region and more generally in Italy, mainly produces *K. pneumoniae* carbapenemases (KPC) [4,8,21,22].

According to these findings, but in the absence of a controlled study to assess the effectiveness of the intervention, the measures recommended in Emilia-Romagna appear to have contained the spread of CPKP. The intervention in Emilia-Romagna succeeded in curbing CPKP transmission although the activities were hospital-centered and did not include the widespread use of staff and patient cohorting as in Israel. These characteristics of the intervention along with

the incidence, which was lower than in Israel, probably explain why, after stabilising the rate, no evident decrease was observed at regional level, despite an encouraging trend towards reduction in some hospitals (Table and Figure 3). Further reduction might result from increased compliance with standard and contact precautions and from a more effective implementation of antibiotic stewardship. Moreover, the results of this study appear to be of particular interest as they may have direct and indirect effects on the epidemiology of CPE in other Italian regions. In particular, the containment of the spread in Emilia-Romagna reduces the probability of transfer to other regions through colonised patients. In addition, the organisational model can be implemented in other regional contexts. Finally, given the possibility of European citizens to receive free cross-border healthcare, as defined in a recent directive of the European Parliament and of the council [23], there would be also a reduction in the probability of transfer of CPE cases into other European countries.

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Conflict of interest

None declared.

Authors' contributions

C Gagliotti and ML Moro wrote the manuscript. C Gagliotti, V Cappelli, E Carretto, M Marchi, A Pan, P Ragni, M Sarti, R Suzzi, GA Tura, ML Moro and The Emilia-Romagna Group for CPE Control provided feedback, contributed with comments and reviewed the manuscript. C Gagliotti, V Cappelli, E Carretto, M Marchi, A Pan, P Ragni, M Sarti, R Suzzi, GA Tura and ML Moro contributed to implementation of the specific surveillance system for carbapenemase-producing Klebsiella pneumoniae. C Gagliotti and M Marchi performed the data analysis. The Emilia-Romagna Group for CPE Control provided the specific surveillance data.

References

1. Kaiser RM, Castanheira M, Jones RN, Tenover F, Lynfield R. Trends in Klebsiella pneumoniae carbapenemase-positive K. pneumoniae in US hospitals: report from the 2007-2009 SENTRY Antimicrobial Surveillance Program. Diagn Microbiol Infect Dis. 2013;76(3):356-60. http://dx.doi.org/10.1016/j.diagmicrobio.2013.03.032
2. Carmeli Y, Akova M, Cornaglia G, Daikos GL, Garau J, Harbarth S, et al. Controlling the spread of carbapenemase-producing Gram-negatives: therapeutic approach and infection control. Clin Microbiol Infect. 2010;16(2):102-11. http://dx.doi.org/10.1111/j.1469-0691.2009.03115.x
3. Gupta N, Limbago BM, Patel JB, Kallen AJ. Carbapenem-resistant Enterobacteriaceae: epidemiology and prevention. Clin Infect Dis. 2011;53(1):60-7. http://dx.doi.org/10.1093/cid/cir202
4. Canton R, Akova M, Carmeli Y, Giske CG, Glupczynski Y, Gniadkowski M, et al. Rapid evolution and spread of carbapenemases among Enterobacteriaceae in Europe.

Clin Microbiol Infect. 2012;18(5):413-31. http://dx.doi.org/10.1111/j.1469-0691.2012.03821.x

5. Grundmann H, Livermore DM, Giske CG, Canton R, Rossolini GM, Campos J, et al. Carbapenem-non-susceptible Enterobacteriaceae in Europe: conclusions from a meeting of national experts. Euro Surveill. 2010;15(46):pii=19711.
6. Nordmann P, Naas T, Poirel L. Global spread of Carbapenemase-producing Enterobacteriaceae. Emerg Infect Dis. 2011;17(10):1791-8. http://dx.doi.org/10.3201/eid1710.110655
7. Zarkotou O, Pournaras S, Tselioti P, Dragoumanos V, Pitiriga V, Ranellou K, et al. Predictors of mortality in patients with bloodstream infections caused by KPC-producing Klebsiella pneumoniae and impact of appropriate antimicrobial treatment. Clin Microbiol Infect. 2011;17(12):1798-803. http://dx.doi.org/10.1111/j.1469-0691.2011.03514.x
8. Giani T, D'Andrea MM, Pecile P, Borgianni L, Nicoletti P, Tonelli F, et al. Emergence in Italy of Klebsiella pneumoniae sequence type 258 producing KPC-3 Carbapenemase. J Clin Microbiol. 2009;47(11):3793-4. http://dx.doi.org/10.1128/JCM.01773-09
9. European Centre for Disease Prevention and Control (ECDC). Antimicrobial resistance surveillance in Europe 2011. Annual report of the European Antimicrobial Resistance Surveillance Network (EARS-Net). Stockholm: ECDC; 2012. Available from: http://ecdc.europa.eu/en/publications/Publications/antimicrobial-resistance-surveillance-europe-2011.pdf
10. Ben David D, Maor Y, Keller N, Regev-Yochay G, Tal I, Shachar D, et al. Potential role of active surveillance in the control of a hospital-wide outbreak of carbapenem-resistant Klebsiella pneumoniae infection. Infect Control Hosp Epidemiol. 2010;31(6):620-6. http://dx.doi.org/10.1086/652528
11. Borer A, Eskira S, Nativ R, Saidel-Odes L, Riesenberg K, Livshiz-Riven I, et al. A multifaceted intervention strategy for eradication of a hospital-wide outbreak caused by carbapenem-resistant Klebsiella pneumoniae in Southern Israel. Infect Control Hosp Epidemiol. 2011;32(12):1158-65. http://dx.doi.org/10.1086/662620
12. Cohen MJ, Block C, Levin PD, Schwartz C, Gross I, Weiss Y, et al. Institutional control measures to curtail the epidemic spread of carbapenem-resistant Klebsiella pneumoniae: a 4-year perspective. Infect Control Hosp Epidemiol. 2011;32(7):673-8. http://dx.doi.org/10.1086/660358
13. Kochar S, Sheard T, Sharma R, Hui A, Tolentino E, Allen G, et al. Success of an infection control program to reduce the spread of carbapenem-resistant Klebsiella pneumoniae. Infect Control Hosp Epidemiol. 2009;30(5):447-52. http://dx.doi.org/10.1086/596734
14. Schwaber MJ, Lev B, Israeli A, Solter E, Smollan G, Rubinovitch B, et al. Containment of a country-wide outbreak of carbapenem-resistant Klebsiella pneumoniae in Israeli hospitals via a nationally implemented intervention. Clin Infect Dis. 2011;52(7):848-55. http://dx.doi.org/10.1093/cid/ciro25
15. Agenzia Sanitaria e Sociale Regionale (ASSR) Emilia-Romagna. Sorveglianza dell'Antibioticoresistenza e Uso di Antibiotici Sistemici in Emilia-Romagna. Rapporto 2011. Bologna: ASSR; 2013. Available from: http://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/dossier/doss234
16. Agenzia Sanitaria e Sociale Regionale (ASSR) Emilia-Romagna. Indicazioni pratiche e protocolli operativi per la diagnosi, la sorveglianza e il controllo degli enterobatteri produttori di carbapenemasi nelle strutture sanitarie e socio-sanitarie. Bologna: ASSR; 2013. Available from: http://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/rapporti-documenti/indicazioni-pratiche-e-protocolli-operativi-per-la-diagnosi-la-sorveglianza-e-il-controllo-degli-enterobatteri-produttori-di-carbapenemasi-nelle-strutture-sanitarie-e-socio-sanitarie-aggiornamento
17. Agenzia Sanitaria e Sociale Regionale (ASSR) Emilia-Romagna. Indicazioni pratiche per la sorveglianza e il controllo degli enterobatteri produttori di carbapenemasi in Sanità Pubblica e nel territorio: strutture socio-sanitarie, residenze private. Bologna: ASSR; 2011. Available from: http://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/rapporti-documenti/indicazioni-pratiche-per-la-sorveglianza-e-il-controllo-degli-enterobatteri-produttori-di-carbapenemasi-in-sanita-pubblica-e-nel-territorio-strutture-socio-sanitarie-residenze-private
18. Comitato di Studio AMCLI per gli Antimicrobici (CoSA). Indicazioni per lo screening colturale dei pazienti colonizzati da Enterobatteri produttori di carbapenemasi. Milan: Associazione Microbiologi Clinici Italiani (AMCLI); 2012. Available from: http://www.amcli.it/1Mail/2Lavoro/FileInclude/UpDownload.asp?file=Screening_Enterob._prod_di_carbapenemasi.pdf
19. Gagliotti C, Ciccarese V, Sarti M, Giordani S, Barozzi A, Braglia C, et al. Active surveillance for asymptomatic carriers of carbapenemase-producing Klebsiella pneumoniae in a hospital setting. J Hosp Infect. 2013;83(4):330-2. http://dx.doi.org/10.1016/j.jhin.2012.11.024
20. Agenzia Sanitaria e Sociale Regionale (ASSR) Emilia-Romagna. Controllo degli enterobatteri produttori di carbapenemasi in Emilia-Romagna. 2011-2012. Bologna: ASSR; 2012. Available from: http://assr.regione.emilia-romagna.it/it/servizi/pubblicazioni/rapporti-documenti/report-enterobatteri-produttori-carbapenemasi-2011-2012
21. Giani T, Pini B, Arena F, Conte V, Bracco S, Migliavacca R, et al. Epidemic diffusion of KPC carbapenemase-producing Klebsiella pneumoniae in Italy: results of the first countrywide survey, 15 May to 30 June 2011. Euro Surveill. 2013;18(22):pii=20489.
22. Gaibani P, Ambretti S, Berlingeri A, Gelsomino F, Bielli A, Landini MP, et al. Rapid increase of carbapenemase-producing Klebsiella pneumoniae strains in a large Italian hospital: surveillance period 1 March - 30 September 2010. Euro Surveill. 2011;16(8):pii=19800.
23. Directive 2011/24/EU of the European Parliament and of the Council of 9 March 2011 on the application of patients' rights in cross-border healthcare. Official Journal of the European Union. Luxembourg: Publications Office of the European Union; 4.4.2011:L 88/46. Available from: http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32011L0024&from=EN