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Disease burden of carbapenem-resistant *Enterobacterales* infections in Korea☆

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SUMMARY

Background: Carbapenem-resistant *Enterobacterales* (CRE) poses a significant public health threat. In Korea, the current surveillance systems do not distinguish between colonisation and infection. This study evaluated the clinical and socioeconomic burden of CRE infections in Korea.

Methods: This retrospective study was conducted at 15 medical institutions. All patients with CRE-positive clinical specimens in 2022 were classified as either 'CRE-infected' or 'colonised'. Clinical data and medical costs were collected for the 'CRE-infected' cohort. A predictive logistic regression model based on sex, age, presence of bacteraemia, and bacterial species was developed to estimate the nationwide incidence of CRE infections. For cases of CRE bacteraemia, the clinical information of the matched control groups (no-infection, 3rd-generation-cephalosporin [3GC]—susceptible infection, and 3GC-resistant infection) was collected.

Findings: Among the 4848 reported CRE cases, 1087 (22.4%) were classified as infections, including 586 bacteraemia cases. The most common infection sites were intra-abdominal (34.0%) and pulmonary (31.3%). Carbapenemase-producing *Enterobacterales* accounted for 74.2% of cases, with *Klebsiella pneumoniae* carbapenemase (84.4%) being the most prevalent. The 30-day and 90-day mortality rates were 29.3% and 40.8%, respectively. The predictive model estimated 7117 CRE infections nationwide, including 1897 cases of bacteraemia. The economic burden of CRE infections in 2022 was estimated to be $517,738,296, with excess costs ranging from $108,382,302 to $401,186,712, compared with carbapenem-susceptible infections and cases without infection.

Conclusions: This study highlights the substantial clinical and socioeconomic burden of CRE infections in Korea. Given the continued increase in reported CRE cases even after 2022, urgent measures are required to address this growing public health challenge.

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Introduction

Carbapenem-resistant *Enterobacterales* (CRE) is an important cause of hospital-acquired infections associated with high morbidity, mortality, and limited treatment options [1]. The Centers for Disease Control and Prevention listed CRE as an urgent threat among antibiotic-resistant pathogens [2] and reported an increase in CRE cases from 2019 to 2022 [3]. Since 2017, CRE isolation from clinical specimens has been a mandatory notifiable event in Korea that requires reporting within 24 h, and the number of reported CRE cases has been steadily increasing [4]. However, the current surveillance systems do not distinguish whether CRE isolation reflects active infection or colonisation. Therefore, determining the number of CRE 'infections' based on this surveillance system is challenging. Previous studies have attempted to estimate the burden of CRE bacteraemia; however, research on the overall burden of CRE infections, including non-bacteraemic cases, is limited.

In Korea in 2020, CRE bacteraemia incurred additional costs of $31,716 and $33,185 per case compared with antibiotic-susceptible bacteraemia and controls without infection, respectively [5]. Another study conducted in Korea reported an even higher additional cost of $72,051 for CRE bacteraemia than for uninfected controls [6]. To establish effective control measures to reduce CRE infections, estimating their socioeconomic impact is essential.

The emergence and spread of antimicrobial resistance pose a global public health concern and a significant socioeconomic burden [7—9]. Therefore, this study aimed to assess the nationwide incidence, clinical impact, and socioeconomic burden of CRE infections in Korea and to estimate the additional medical costs associated with CRE infections compared with antibiotic-susceptible infections and controls without infection.

Methods

To collect representative data, we selected 15 participating hospitals across the Republic of Korea, varying in size and geographical distribution. The nationwide distribution of the study hospitals is shown in Supplementary Figure 1.

Estimation of the clinical burden of CRE infections in 2022

All records of patients who reported CRE isolation from clinical specimens in the participating hospitals in 2022 were identified and classified as having either a CRE infection or colonisation. All patients with CRE isolated from clinical specimens were reviewed through their medical records, including the site of specimen, history of antibiotic use, and laboratory findings, and were classified as having CRE infection or colonisation. This classification of infection versus colonisation, based on patients' medical records, was performed by infectious disease specialists participating from each of the 15 participating hospitals. Demographic data, infection site, bacterial species, presence of carbapenemases, and mortality outcomes were collected for CRE infections. The length of stay (LOS) was defined as the total number of days of hospitalisation from admission to discharge. The LOS after infection was defined as the number of hospitalisation days following the

onset of infection. Mortality outcomes included in-hospital mortality and 7-day, 30-day, and 90-day mortality rates.

The number of bacteraemia cases was confirmed from the total number of reported cases nationwide in the Korea Disease Control and Prevention Agency's reporting data as a constant figure. Therefore, CRE infections investigated in the study hospitals were confirmed by separating the number of bacteraemia cases from those of non-bacteraemic infections.

To estimate the total number of CRE infections, we developed a logistic regression model using data on sex, age, bacterial species, and the presence of bacteraemia from all nationwide CRE cases reported in 2022, all CRE cases reported by 15 study hospitals, and the cases classified as CRE infections. The default prediction of nationwide CRE infection cases was calculated by the highest 10% cut-off of this model's propensity for CRE infection, and results for the 9% and 11% sensitivity cut-offs were also estimated.

Estimation of the total cost of CRE infections in 2022

Direct and indirect medical costs were combined to estimate the total cost of CRE infection. The entire Korean population is covered by the National Health Insurance Service. Direct medical costs include fees for consultation, intervention and surgery, rehabilitation and physical therapy, psychotherapy, anaesthesia, radiation therapy, hospitalisation, meals, medication and prescription dispensing, injection, laboratory tests, imaging examinations, and medical supplies. For each category, costs were divided into reimbursed and non-reimbursed services.

Indirect costs were calculated in two categories: productivity loss due to hospitalisation and the cost of early death before the age of 70 years. Using age- and sex-specific monthly wages and data on the economically active population, we estimated productivity loss for patients aged 15—69 years, as well as the cost of early death based on the number of years lost before the age of 70 years. Monthly wage data by age group and sex were obtained from the 2023 survey on employment conditions by employment type, conducted by the Ministry of Employment and Labour [10]. Data on the economically active population were obtained from the 2023 economically active population survey data from Statistics Korea [11]. All costs were converted into USA dollars (USD) using a 2022 exchange rate of 1294 KRW per USD.

The total costs of CRE bacteraemia and CRE infection without bacteraemia were estimated separately. To calculate the total cost of CRE infection without bacteraemia, all patients who had CRE bacteraemia at any time, including 2022, were excluded to ensure that only non-bacteraemic CRE infections were counted. The number of CRE bacteraemia cases was multiplied by the total cost per case of CRE bacteraemia, and the number of CRE infections without bacteraemia was multiplied by the total cost per case of CRE infection without bacteraemia, which was then summed to estimate the nationwide socioeconomic burden of CRE infections.

Estimation of the additional disease burden of CRE infections compared with controls

To estimate the difference in economic burden between CRE infections and controls, we excluded those with polymicrobial bacteraemia or those whose bacteraemia occurred within 2 days of hospitalisation among the CRE bacteraemia cases. The remaining bacteraemia cases were assigned to the R group, and controls with carbapenem-susceptible *Enterobacterales* (CSE) infections were selected based on the bacteraemia cases.

Control groups with CSE bacteraemia (groups S1 and S2) were selected based on the following criteria: (1) age within ± 10 years, (2) same bacterial genus, and (3) similar primary diagnosis at the time of admission. The S1 group included cases of bacteraemia with 3rd-generation-cephalosporin-resistant (3GC-R) *Enterobacterales*, whereas the S2 group included bacteraemia with 3rd-generation-cephalosporin-susceptible (3GC-S) *Enterobacterales*. The non-infected control N group was selected based on the following criteria, which were modified from those used in a previous study: (1) similar primary diagnosis at the time of admission, (2) similar type of major surgery or procedure, (3) age within ± 10 years, (4) same sex, and (5) exclusion of any cases in which acute bacterial infection occurred during hospitalisation [5].

To evaluate differences in clinical characteristics and outcomes between the CRE infection and control groups, data were collected for the R, S1, and S2 groups. In addition to the variables collected for CRE infection, data on the presence of metastatic infection, clinical severity, antibiotic treatment, and treatment failure were collected. Clinical severity was assessed based on the presence of septic shock, the Sequential Organ Failure Assessment (SOFA) score, and the Pitt bacteraemia score [12]. Variables related to treatment failure included the following: (1) 30-day all-cause mortality; (2) persistent bacteraemia, defined as positive blood cultures for 7 days or longer despite appropriate antimicrobial therapy; and (3) recurrent bacteraemia, defined as bacteraemia with the same species within 30 days after completion of appropriate antibiotic therapy.

To estimate the additional costs of CRE infections compared with controls, propensity score (PS) matching between the R, S1, S2, and N groups was performed using 1:1 nearest neighbourhood matching with replacement, applying a calliper width of 0.01. PS matching was based on variables including age, sex, Charlson Comorbidity Index, and 7-day, 30-day, and 90-day mortality rates. Differences in the total costs between the R group and controls were used to estimate the nationwide excess costs of CRE infections.

Results

Clinical characteristics of CRE infection

In 2022, the total number of reported CRE cases from all participating hospitals was 4,848, accounting for 15.9% of all reported CRE cases in Korea. Of these, 1087 (22.4%) were classified as CRE infections and 3761 (77.6%) as CRE colonisations. Among the 1087 CRE infection cases, 586 were reported to have CRE bacteraemia in 2022, and 501 were infections without reported CRE bacteraemia in 2022 (Figure 1).

The clinical characteristics, microbiological findings, and outcomes are presented in Table I. The mean age of patients with CRE infection was 64.1 years (±16.0), and 60.2% of the patients were male. Intra-abdominal infection was the most common site of infection (369 cases, 34.0%), followed by pneumonia (340 cases, 31.3%) and primary bacteraemia (134 cases, 12.3%). Regarding the bacterial species, *Klebsiella pneumoniae* was the

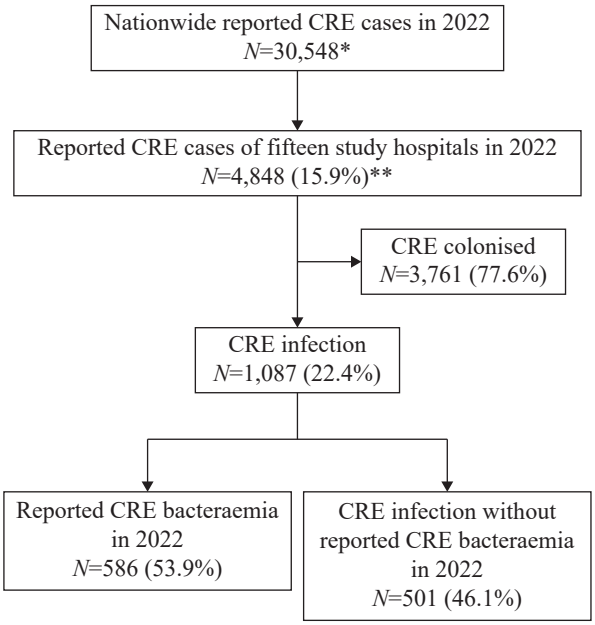


Figure 1. Flowchart of study population. CRE, carbapenem-resistant *Enterobacterales*. *As CRE isolation is a mandatory notifiable event by the Korea Disease Control and Prevention Agency (KDCA), the nationwide number of reported CRE cases can be checked on the KDCA website (https://dportal.kdca.go.kr/pot/is/inftnsdsEDW.do). **Medical records of all patients with CRE isolated from clinical specimens were reviewed to classify them as either infection or colonisation.

most frequently isolated species (77.0%), followed by *Escherichia coli* (7.8%) and *Enterobacter cloacae* (6.8%). Of the 1087 CRE infections, 807 (74.2%) and 249 (22.9%) were carbapenemase-producing and non-carbapenemase-producing cases, respectively. Among the 807 carbapenemase-producing *Enterobacterales* cases, *Klebsiella pneumoniae* carbapenemase (KPC) was the most common enzyme type (84.4%), followed by New Delhi metallo-ß-lactamase (11.4%). The mean LOS was 61.0 days (±111.7), and the mean LOS after infection onset was 33.1 days (±49.3). The 30-day and 90-day mortality rates were 29.3% and 40.8%, respectively.

The clinical outcomes of patients with CRE infection aged ≥70 years are presented in Supplementary Table I. The mean LOS was 50.9 days (±67.0), and the mean LOS after infection was 30.5 days (±49.9). The 30-day and 90-day mortality rates were 30.7% and 41.0%, respectively.

Estimation of the nationwide clinical burden of CRE infection

The nationwide number of CRE infections was estimated by applying a predictive logistic regression model to all 30,548 reported CRE cases in Korea (Table II). The number of CRE infections was estimated to be 7,117, using the top 10% cut-off CRE infection likelihood score. Given that 1897 cases of CRE bacteraemia were reported nationwide in 2022, the estimated number of non-bacteraemic CRE infections was 5220. Using the top 9% and 11% cut-offs of the CRE infection likelihood score, the estimated numbers of CRE infections were 6655 and 7,593, respectively.

Table I
Baseline characteristics and clinical outcomes of patients with CRE infections in 15 hospitals in Korea in 2022

Variables	CRE infection ($N = 1087$)
Age, years	64.1 ± 16.0
Sex	
Male	654 (60.2)
Female	433 (39.8)
Site of infection	
Intra-abdominal infection	369 (34.0)
Pneumonia	340 (31.3)
Primary bacteraemia	134 (12.3)
Urinary tract infection	101 (9.3)
Central line—associated infection	66 (6.1)
Skin and soft-tissue infection	61 (5.6)
CNS infection	3 (0.3)
Phlebitis	1 (0.1)
Vascular infection	1 (0.1)
Osteoarticular infection	1 (0.1)
Others	19 (1.8)
Species	
Klebsiella pneumoniae	837 (77.0)
Escherichia coli	85 (7.8)
Enterobacter cloacae	74 (6.8)
Others	91 (8.4)
Presence of carbapenemase	
CPE	807 (74.2)
Non-CP CRE	249 (22.9)
Unknown	31 (2.9)
Carbapenemase type ($N = 807$)	
KPC	681 (84.4)
NDM	92 (11.4)
OXA	20 (2.5)
VIM	2 (0.3)
IMP	1 (0.1)
GES	0 (0.0)
Others	11 (1.4)
Length of hospitalisation	
Length of stay, days (total)	61.0 ± 111.7
Length of stay, days (after infection)	33.1 ± 49.3
ICU stay, days	14.0 ± 47.3
Mortality	
7-day mortality	142 (13.1)
30-day mortality	318 (29.3)
90-day mortality	443 (40.8)
In-hospital mortality	429 (39.5)

Values are presented as *n* (%) or mean ± standard deviation.
CRE, carbapenem-resistant *Enterobacterales*; CNS, central nervous system; CPE, carbapenemase-producing *Enterobacterales*; non-CP CRE, non-carbapenemase-producing carbapenem-resistant *Enterobacterales*; KPC, *Klebsiella pneumoniae* carbapenemase; NDM, New Delhi metallo-ß-lactamase; OXA, oxacillinase; VIM, Verona integron-encoded metallo-ß-lactamase; IMP, imipenemase; GES, Guiana extended-spectrum ß-lactamase; ICU, intensive care unit.

Based on the 30-day and 90-day mortality rates of 29.3% and 40.8%, respectively, observed in 1087 cases of CRE infection, the number of deaths among 7117 cases of CRE infection was estimated. The nationwide number of deaths within 30 and 90 days was estimated to be 2085 and 2,904, respectively.

Table II
Estimated numbers and total costs of CRE infections according to the sensitivity analyses

Models	CRE bacteraemia (*N*)[a]	CRE infection without bacteraemia (*N*)	Estimated total number of CRE infections (*N*)	Total cost	
				USD, $	1000 KRW, ₩
Model 1: Top 9% cut-off of the model's propensity of CRE infection					
	1897	4758	6655	485,570,285	628,172,566
Model 2: Top 10% cut-off of the model's propensity of CRE infection					
	1897	5220	7117	517,738,296	712,663,854
Model 3: Top 11% cut-off of the model's propensity of CRE infection					
	1897	5696	7593	550,881,094	669,787,678

An exchange rate of 1294 KRW per USD was used in the calculation.
CRE, carbapenem-resistant *Enterobacterales*; USD, USA dollar; KRW, Korean won; KDCA, Korea Disease Control and Prevention Agency.
[a] The number of CRE bacteraemia cases in 2022 is a fixed value, as CRE bacteraemia was reported separately, and the number can be checked on the KDCA website (https://dportal.kdca.go.kr/pot/is/inftnsdsEDW.do).

Estimation of the socioeconomic burden of CRE infection

The mean total cost of CRE infection per case was $78,090, with a direct medical cost of $66,860, productivity loss of $2,930, and a cost of early death of $8301 (Table III). Detailed medical costs associated with CRE infection are shown in Supplementary Table II. Among reimbursed items, the mean costs for hospitalisation, interventions or surgery, and injection treatment were $13,721, $11,728, and $10,929, respectively. For non-reimbursed items, the mean costs of the injection treatment and hospitalisation were $1306 and $1,200, respectively. The total of reimbursed and non-reimbursed medical costs per case of CRE infection was $62,210 and $4,650, respectively.

The costs per case of CRE bacteraemia and non-bacteraemic CRE infections are also presented in Table III. The mean direct medical costs per case of CRE bacteraemia and non-bacteraemic CRE infection were $65,655 and $62,863, respectively. The mean total costs were $81,329 for CRE bacteraemia and $69,628 for non-bacteraemic CRE infections. The costs per case according to major infection types, including intra-abdominal infection, pneumonia, and urinary tract infection, are shown in Supplementary Table III. The total costs per case of intra-abdominal infection and pneumonia were $71,168 and $93,968, respectively.

Using the total cost per case of CRE bacteraemia and non-bacteraemic CRE infection, the national economic burden was estimated at $517,738,296 in model 2, based on the top 10% cut-off (Table II). Depending on the 9%–11% cut-off of the predictive logistic regression model, the economic burden ranged from $485,570,285 to $550,881,094.

Comparison of CRE infections with CSE infections and no infection

In total, 240 patients with CRE bacteraemia were included in the R group. For comparison, 208 cases of 3GC-R CSE bacteraemia (S1 group), 212 cases of 3GC-S CSE bacteraemia (S2 group), and 234 cases without infection (N group) were identified, and their data were collected. The clinical characteristics, outcomes, and costs of the R, S1, S2, and N groups before PS matching are presented in Supplementary Table IV. The mean duration of bacteraemia was the longest in the R group (5.8 days), followed by the S1 group (4.2 days), and the shortest in the S2 group (3.3 days). Clinical severity, as

Table III
The costs per case with CRE infections, CRE bacteraemia, and CRE infection without bacteraemia

Costs	CRE infection (*N* = 1087)		CRE bacteraemia[a] (*N* = 240)		CRE infection without bacteraemia[b] (*N* = 473)	
	USD, $	1000 KRW, ₩	USD, $	1000 KRW, ₩	USD, $	1000 KRW, ₩
Direct medical cost	66,860 ± 95,341	86,496 ± 123,341	65,655 ± 86,232	84,937 ± 111,556	62,863 ± 79,717	81,325 ± 103,128
Productivity loss	2930 ± 13,054	3790 ± 16,888	2790 ± 3848	3610 ± 4978	2158 ± 4678	2792 ± 6052
Cost of early death	8301 ± 16,496	10,739 ± 21,340	12,883 ± 19,298	16,666 ± 24,965	4607 ± 12,228	5960 ± 15,819
Total cost	78,090 ± 108,450	101,024 ± 140,299	81,329 ± 96,115	105,214 ± 124,342	69,628 ± 86,481	90,076 ± 111,879

Values are presented as mean ± standard deviation.
An exchange rate of 1294 KRW per USD was used in the calculation.
CRE, carbapenem-resistant *Enterobacterales*; USD, USA dollar; KRW, Korean won.
[a] For these CRE bacteraemia cases of the R group, we excluded those with polymicrobial bacteraemia or those whose bacteraemia occurred within two days of hospitalisation.
[b] For cases of CRE infection without bacteraemia, those with CRE bacteraemia at any time including in 2022 were excluded to ensure that only non-bacteraemic infections were included.

measured by the proportion of patients with septic shock, SOFA score, and Pitt bacteraemia score, was also the highest in the R group. The R group also had the longest duration of antibiotic administration and the longest time to initiation of appropriate antibiotic therapy.

Supplementary Table V presents the clinical characteristics, outcomes, and costs of patients with CRE bacteraemia and controls after PS matching. Haematologic malignancy was the most common underlying comorbidity in all groups. In the R group, intra-abdominal infection was the most frequent site of infection. LOS in the R group was 11.3 days longer than in the S1 group, 29.5 days longer than in the S2 group, and 41.5 days longer than in the N group. The 30-day mortality rates in the R, S1, S2, and N groups were 31.3%, 30.7%, 21.1%, and 2.5%, respectively. The total cost per patient in the R group was $15,229, $38,891, and $56,370 higher than that in the S1, S2, and N groups, respectively.

Additional socioeconomic burden of CRE infection compared with controls

Using the cost differences between CRE infections and controls of carbapenem-susceptible infections and those without infections, the nationwide excess costs of CRE infections were estimated based on 7117 CRE cases. The estimated excess costs compared with 3GC-R infections, 3GC-S infections, and those without infection were $108,382,302, $276,784,448, and $401,186,712, respectively (Table IV).

Discussion

In this study, we evaluated the nationwide socioeconomic burden of CRE infections in Korea. Using a predictive logistic regression model, the estimated nationwide number of CRE infections in 2022 was 7,117, with an estimated 30-day death of 2085. The total socioeconomic burden of CRE infections was estimated to be $517,738,296, with excess costs of $108,382,302 and $401,186,712 compared with carbapenem-susceptible infections and cases without infection, respectively.

Given the substantial burden of CRE, it is important to establish appropriate infection control interventions to address this issue. Previous studies have reported decreases in the incidence of CRE acquisition, infections, and bacteraemia following the implementation of infection control interventions [13,14]. Considering the high total costs of CRE infections in our study, appropriate infection control measures could help prevent the spread of CRE and reduce the socioeconomic burden of CRE.

Several studies have investigated the CRE burden in Korea. One multi-centre retrospective study reported that the total cost of CRE bacteraemia was $40,464, which is five times higher than that of cases without infection. Based on the nationwide number of CRE bacteraemia cases, the economic burden was estimated to be $39,331,008 in 2020 [5]. Another study estimated the total socioeconomic burden of multi-drug-resistant organism bacteraemia, including medical costs, caregiver expenses, and productivity loss. Hospital costs and LOS for CRE bacteraemia were both higher than those for susceptible bacteraemia and patients without infection. The study reported a socioeconomic burden of $45,850,215 for CRE bacteraemia in 2017 [6]. These studies included only bacteraemia cases and did not account for other types of CRE infections. However, to address the limitations of previous studies, we reviewed all reported CRE cases from participating hospitals, distinguished between CRE infection and colonisation, and estimated the disease burden of CRE infection, including not only bacteraemia but also other types of infections.

In this study, the total cost per case of CRE infection was estimated at $78,090. This figure highlights the substantial economic burden of CRE infection, particularly when compared with a major disease like stroke, the leading cause of death in Korea, which has a disease burden of just $7247 per case [15]. This comparison clearly shows the immense economic burden of CRE infections, even when the impact of other underlying diseases is considered. Additionally, the CRE infection group was associated with higher mortality, longer LOS, and higher total costs than the carbapenem-susceptible infection and non-infection groups. This result is consistent with that of a previous study on *Enterobacterales* bacteraemia in patients with haematological malignancies, which discovered that patients with CRE bacteraemia had higher rates of septic shock and 30-day mortality than those with CSE bacteraemia [16]. A retrospective cohort study conducted in Thailand also showed that CRE infections were associated with higher mortality, longer LOS, and higher medical costs than CSE infections [17]. Similarly, a study conducted in Singapore analysed the costs of

Table IV
Excess cost per case of CRE infection compared with carbapenem-susceptible infections and cases without infection

Excess costs per case of CRE infection	Direct medical cost[a]		Total cost[a]		Nationwide cost[b]	
	USD, $	1000 KRW, ₩	USD, $	1000 KRW, ₩	USD, $	1000 KRW, ₩
3GC-R	13,498	17,462	15,229	19,701	108,382,302	140,212,017
3GC-S	34,716	44,912	38,891	50,312	276,784,448	358,070,504
No infection	47,179	61,034	56,370	72,925	401,186,712	519,007,225

An exchange rate of 1294 KRW per USD was used in the calculation.
CRE, carbapenem-resistant *Enterobacterales*; USD, USA dollar; KRW, Korean won; 3GC-R, third-generation-cephalosporin-resistant; 3GC-S, third-generation-cephalosporin-susceptible.
[a] Costs were compared using cases of CRE bacteraemia and their matched controls, which were selected based on age, bacterial genus, and primary diagnosis for carbapenem-susceptible *Enterobacterales* bacteraemia, and primary diagnosis, major surgery, age, sex, and exclusion of acute bacterial infection history for the no-infection group. Additionally, propensity score matching was performed based on variables including age, sex, Charlson Comorbidity Index, and 7-day, 30-day, and 90-day mortality rates, before conducting further cost analyses for the cases.
[b] The costs were estimated based on the number of CRE infection using the top 10% cut-off of the infection likelihood score.

CRE hospital-associated infections based on direct medical costs and lost bed days and reported that the cost of CRE hospital-associated infections was higher than that of CSE infections [18]. In addition, a study conducted in the intensive care unit in China showed that patients with CRE infections had longer hospital stay and higher hospital costs than those with CSE infections [19].

A retrospective study conducted in a Thai tertiary hospital revealed that the median hospitalisation cost per CRE infection was $10,435, with a median LOS of 31 days [20]. Our study observed a mean direct medical cost of $66,860 per CRE infection with a mean LOS of 61 days. The difference in medical costs might be partly due to the longer LOS; however, other factors may have also contributed. In our study, hospitalisation, intervention, and surgery accounted for the majority of medical costs, whereas the costs of medicine, laboratory, and imaging tests contributed to a major portion of medical expenses in a study conducted in China [21].

A previous study developed a model to estimate the cost of CRE infections and observed variations according to infection type. Intra-abdominal infections were associated with the highest hospital costs, followed by ventilator-associated pneumonia and bacteraemia [22]. In our study, we did not stratify costs by infection type; however, we classified them by the presence of bacteraemia and identified that the costs of CRE bacteraemia and non-bacteraemic CRE infections were similar. The hospital cost per CRE infection was estimated to be between $22,484 and $66,031, which is similar to the estimated medical cost of $66,860 in our study.

This study had several limitations. First, it included only hospitalised patients from secondary and tertiary hospitals. Therefore, the costs associated with post—acute care in nursing homes, outpatient follow-ups, emergency room visits after discharge, readmissions, or quality-of-life effects could not be captured [23]. Second, new beta-lactam/beta-lactamase inhibitors, such as ceftazidime-avibactam, were not available for commercial use in Korea during the study period. Therefore, mortality may be overestimated compared with the period when ceftazidime-avibactam is available [24], whereas antibiotic-related medical costs may be underestimated. Third, to estimate the additional socioeconomic burden of CRE infection, only CRE bacteraemia cases were used. However, since the costs of CRE bacteraemia and non-bacteraemic CRE infections were similar and CSE bacteraemia cases were also used as controls, the observed cost difference might reflect the difference between CRE and CSE infections. Lastly, since there was no data on age- and sex-specific monthly wages for individuals aged 70 years and older, indirect costs were estimated only for patients aged $<$70 years. The 90-day mortality was over 40% in patients with CRE infections aged $\geq$70 years. Of 30,548 reported CRE cases in Korea in 2022, the patients aged $\geq$70 years were 19,399 (63.5%) [25]. Given the high proportion of patients aged $\geq$70 years and their high mortality, the indirect costs reported in this study were likely underestimated. Despite these limitations, this study showed the importance of estimating the nationwide number of CRE infections and assessing the socioeconomic burden, thereby highlighting the substantial socioeconomic impact of CRE infections.

In conclusion, the nationwide burden of CRE infections in Korea could be estimated because CRE isolation is a mandatory notifiable event, even though the reporting system does not distinguish between infection and colonisation. The nationwide number of CRE infections in Korea was estimated to be 7117 in 2022 using the reported CRE cases in the study hospitals. The total socioeconomic burden of CRE infections was estimated at $517,738,296, representing an excess cost of $108,382,102 to $401,186,421 compared with carbapenem-susceptible infections and those without infection. In addition to the substantial medical costs and mortality associated with CRE infections, the annual number of reported CRE cases has greatly increased by approximately 20—30% [26]. Given the significance of CRE, adequate infection control measures and proper investment in managing carbapenem resistance are urgently required.

Korea INfectious Diseases study group

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Ethics statement

This study was approved by the Institutional Review Board of Seoul National University Bundang Hospital (IRB no. B-2312-868-103) and those of all the participating hospitals. Given the retrospective nature of the study, the requirement for informed consent was waived by the IRBs.

Availability of data and material

The data generated during this study is presented in the article and/or supplementary material. Further enquiries can be directed to the corresponding authors.

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Conflict of interest statement

None declared.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jhin.2026.03.012.

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