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# Long-term effectiveness of infection and antibiotic control programs on the transmission of carbapenem-resistant *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex in central Taiwan

*Efficacité à long terme des programmes de contrôle d'infection et d'antibiotique sur la transmission du complexe Acinetobacter calcoaceticus-Acinetobacter baumannii résistant aux carbapénèmes dans le centre de Taiwan*

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## Abstract

**Objectives.** – A carbapenem-resistant *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex (CRA complex) infection is one of most the difficult infections to control worldwide. We evaluated the long-term effects of infection control interventions on the incidence densities of healthcare-associated infection (HAI) and CRA complex infection, and the rates of *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex bacteremia (AB).

**Patients and methods.** – We performed a cross-sectional analysis at the Changhua Christian Hospital from January 2002 to December 2013. Interventions for infection control were implemented from 2002 to 2009 (period 1). From 2010 to 2013 (period 2), infection control programs were improved by in-service education and a hand hygiene campaign to prepare for international and national hospital accreditation. The effectiveness of infection and antibiotic control programs was assessed according to the incidence densities of HAI and CRA complex, rates of CRA complex and of AB, chlorhexidine consumption density, and defined daily dose of antibiotics.

**Results.** – The incidence density of HAI decreased from 4.56‰ to 1.52‰ from periods 1 to 2 ( $P < 0.001$ ). Likewise, the incidence of AB decreased from 177.79 to 137.76 per person-years per 100,000 admissions ( $P < 0.001$ ). The incidence density of CRA complex ranged from 3.17–7.38‰. The chlorhexidine consumption density increased from 5.5 to 45.5 L per 1000 patient-days ( $P < 0.001$ ). The consumption of piperacillin-tazobactam was lower in period 2 than in period 1 ( $P < 0.001$ ).

**Conclusion.** – Education for infection control programs, hand hygiene campaigns, and antibiotics control programs may decrease the incidence density of AB and HAI, and may help control CRA complex infection.

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**Keywords:** Hand hygiene; Infection control; Antibiotic stewardship; Carbapenem-resistance; *Acinetobacter calcoaceticus*-*Acinetobacter baumannii*

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## Résumé

**Objectifs.** – L'infection aux carbapénèmes *Acinetobacter calcoaceticus-Acinetobacter baumannii complex (CRA complex)* est l'une des infections les plus difficiles à contrôler dans le monde entier. Cette étude a évalué les effets à long terme des interventions de lutte contre les infections sur les densités d'incidence de l'infection nosocomiale (HAI) et de l'infection à *CRA complex* ainsi que les taux de bactériémie à *CRA complex*.

**Patients et méthodes.** – Une analyse transversale a été effectuée à l'hôpital chrétien de Changhua de janvier 2002 à décembre 2013. Les interventions pour le contrôle de l'infection ont été mises en œuvre de 2002 à 2009 (période 1). De 2010 à 2013 (période 2), les programmes de contrôle des infections ont été renforcés par la formation continue et une campagne d'hygiène des mains en vue de l'accréditation internationale et nationale hospitalière. L'efficacité des programmes de lutte contre les infections et les antibiotiques a été évaluée en fonction des densités d'incidence des infections nosocomiales et à *CRA complex*, les taux de *CRA complex* et de bactériémies à CRA, la densité de consommation de chlorhexidine, et la dose quotidienne définie d'antibiotiques.

**Résultats.** – La densité d'incidence des infections nosocomiales a diminué de 4,56‰ à 1,52‰ entre les périodes 1 et 2 ( $p < 0,001$ ). De même, l'incidence de l'AB a diminué de 177,79 à 137,76 par années-personnes pour 100 000 admissions ( $p < 0,001$ ). La densité d'incidence de *CRA complex* variait de 3,17–7,38‰. La densité de consommation de chlorhexidine a augmenté de 5,5 à 45,5 litres par 1000 patients-jour ( $p < 0,001$ ). La consommation de pipéracilline-tazobactam était plus basse en période 2 qu'en période 1 ( $p < 0,001$ ).

**Conclusion.** – La formation aux programmes de contrôle des infections, les campagnes d'hygiène des mains et les programmes de contrôle d'antibiotique pourraient diminuer les densités d'incidence de bactériémies à CRA et HAI, et contrôler éventuellement l'infection à *CRA complex*. © 2015 Elsevier Masson SAS. Tous droits réservés.

**Mots clés :** Hygiène des mains ; Bon usage des antibiotiques ; *Acinetobacter baumannii-Acinetobacter calcoaceticus* ; Résistance aux carbapénèmes

## 1. Introduction

*Acinetobacter calcoaceticus-Acinetobacter baumannii complex (ACB complex)* has emerged as an important healthcare-associated pathogen because it can survive a wide range of environmental conditions and persist [1,2]. The extensive use of medical devices in modern medical institutes has contributed to the emergence of ACB complex as a predominant pathogen, and infection caused by multidrug-resistant ACB complex (MDRACB complex) is currently considered the most difficult infection to control. There are several predisposing factors for colonization or infection with ACB complex species [1,3], and widespread environmental contamination has been frequently reported [4,5]. ACB complex infections have increased worldwide, and MDRACB complex has been isolated in Taiwan since 1999 [6]. In Taiwan, ACB complex is a predominant pathogen causing bloodstream infection and is associated with a high risk of antibiotic resistance [7]. Furthermore, patients with MDRACB complex bacteremia have a higher mortality rate than patients with non-MDRACB complex bacteremia [8]; the overall 30-day mortality of MDRACB complex bloodstream infections ranges from 45.3 to 49% [6,9].

We previously demonstrated that MDRACB complex could occur as a result of cross-infection and natural mutation [10]. Cross-infection can be avoided by increasing precautions against contact in clinical practice, whereas natural mutation can be prevented by the de-escalation of broad-spectrum antibiotics. However, the optimal treatment strategy is unknown. Several authors have reported variable degrees of success in controlling MDRACB complex using interventions such as the promotion of hand hygiene, isolation and contact precautions, environmental cleaning, targeted active surveillance, temporary unit closures, and antibiotic control programs [11,12].

Data from the Taiwan Nosocomial Infection Surveillance System (TNIS) revealed a recent overall decrease of hospital-associated infections (HAIs) in intensive care units (ICUs)

of acute care hospitals (medical centers, from 19.8 per 1000 patient-days in 2003 to 9.4 in 2012 per 1000 patient-days; regional hospitals, from 14.1 per 1000 patient-days in 2003 to 5.9 in 2012 per 1000 patient-days) [13,14]. Although the overall rate of HAIs has decreased, the proportion of HAIs caused by carbapenem-resistant *A. calcoaceticus-A. baumannii complex (CRA complex)* is greater than that caused by all other ACB complexes. In particular, from 2003 to 2012, CRA complex increased from 16.4% to 75.3% in the ICUs of medical centers and from 18.2% to 62.1% in regional hospitals [13,14].

Changhua Christian Hospital (CCH) received on-site surveys for hospital accreditation and healthcare-related infection control audit and quality improvement by the Taiwan Joint Commission on Hospital Accreditation (TJCHA). The annual patient safety goals in 2010–2011 included infection control/hand hygiene, and tube safety. CCH also received on-site surveys for hospital accreditation by the Joint Commission International (JCIA), which includes the prevention and control of infections as core standards. Accordingly, CCH organized a campaign for hand hygiene champions and an antibiotic control program. Although controlling the transmission of CRA complex is a high priority for tertiary care hospitals, there is little information about CRA complex control in Taiwan [15]. Therefore, we evaluated the long-term effects of infection and antibiotic control programs on the incidences of CRA complex and *A. calcoaceticus-A. baumannii complex bacteremia (AB)*.

## 2. Methods

### 2.1. Setting and population

The Changhua Christian Healthcare System is in charge of most of the Changhua population in Taiwan and has maintained comprehensive clinical records since 1867. Changhua County, located in central Taiwan, had a population of 140,277 in 2000. CCH is a member of the CCH system; it is an 1800-bed tertiary

referral medical center located in northern Changhua County. CCH has been a JCI-accredited hospital since 2009.

## 2.2. Study design

The study consisted of an 8-year baseline period (January 1, 2002 to December 31, 2009; period 1, before the campaign), and a 4-year intervention period (January 1, 2010 to December 31 2013; period 2, after the campaign). The intervention team included a hospital administrator, infectious diseases physicians, infection control nurses, a hospital epidemiologist, a clinical microbiologist, and a clinical pharmacist.

## 2.3. Case findings and analysis

Cases of AB were identified from microbiological databases and medical records according to the International Classification of Diseases, ninth edition, clinical modifications (ICD-9-CM) at CCH in central Taiwan. We used computerized indices to find cases with the following ICD-9-CM codes: 790.7, 038, 038.11, 038.19, 785.59, and v09.X. Cases in which ACB complex was isolated from blood were selected for review. Each patient had a medical record, which contained medical diagnoses, surgical interventions, and other key information from medical records. The medical records of all AB cases were reviewed by the primary investigator (C.C.H.) to confirm the diagnosis (using the CCH system resources). Cases that were judged to be problematic were reviewed by the secondary investigator (C.Y.J.). Only the first episode of AB in each patient during the study period was included in the statistical analysis. The disease incidence was calculated by considering the entire admitted patient population of CCH as at risk for infection.

All ACB complex isolates cultured from blood were considered clinically significant. AB was defined as the isolation of ACB complex in a patient between January 1, 2002 and December 31, 2013. The exclusion criteria were:

- incomplete data;
- inconsistency between the data from the ICD-9 code and the microbiological dataset.

AB was classified as healthcare-onset or community-acquired according to a modified version of Horan's definition [16]. Healthcare-onset infection was defined as a positive blood culture obtained from a patient at the time of hospital admission or within 48 hours after admission if the patient fulfilled any of the following criteria:

- having received intravenous therapy at home; having received wound care or specialized nursing care through a healthcare agency, family, or friends; or having self-administered intravenous medical therapy within 30 days before AB infection; patients exclusively using oxygen for home therapy were also excluded;

- having attended a hospital or hemodialysis clinic, or having received intravenous chemotherapy or invasive procedures within 30 days before AB infection;
- having been hospitalized in an acute-care hospital for 2 or more days in the 90-day period before AB infection;
- having resided in a nursing home or long-term care facility.

Community-onset infection was defined as a positive blood culture obtained at the time of hospital admission or within 48 hours after hospital admission for patients who did not meet the criteria for healthcare-onset infection.

Several diagnostic systems for microbiological culture were used in the microbiological databases in CCH during the study period, including the API 20NE (API bio-Mérieux, LaBalme, Les Grottes, France) and Vitek-2 automated systems (bio-Mérieux). The Vitek-2 automated system has been used since 2007. Two sets of blood cultures were routinely performed and analyzed using the Vitek GNI card (bio-Mérieux, Hazelwood, MO, USA) with the Vitek-2 system (bio-Mérieux). The CCH laboratory has been certified by the College of American Pathologists since 2009. CRA complex isolates were defined for an imipenem (or meropenem) MIC > 16 mg/L according to the guidelines of the Clinical Laboratory Standards Institute [17]. The AB isolates that did not meet the definition of CRA complex were considered as susceptible ACB complex.

## 2.4. Validity and reliability of methods

We performed a small-scale validity study on our case-finding procedures. We tested the validity of our system by reviewing the complete medical charts of 99 patients who did not have any relevant ICD-9 codes and obtained their records from the microbiological dataset on or before December 31, 2010 (end of the study period). We examined the reliability of our case-finding procedure by randomly selecting 20 records of potential cases having them reviewed independently by 2 infectious-disease specialists (C.C.H. and C.Y.J.). Finally, we increased the reliability of our diagnoses, by having the infectious-disease specialist assess (C.C.H.) all cases judged to be problematic. The panel accepted 80 diagnoses (95%) out of the 84 cases examined, and rejected 4.

## 2.5. Campaign for infection prevention interventions, hand hygiene champions, and antibiotics control program

Hand hygiene champions and antibiotic control program have been promoted since 2010. The campaign for hand hygiene champions and antibiotic control program included contact isolation, cohort, environmental cleaning and meeting, in addition to 5 strategies for hand hygiene champions and 5 strategies for antibiotic control program. The infection prevention measures before and after the campaigns are listed in [Appendix 1](#). The 12-year chronological data for healthcare-associated infections, catheter-associated urinary tract infections, central line-associated bloodstream infections, and ventilator-associated pneumonia at CCH is listed in [Appendix 2](#).

## 2.6. Monitoring healthcare workers' adherence to infection prevention measures

Infection control nurses directly observed the cleaners' habits throughout the study, including on weekends and night shifts. They noted whether environmental sites were cleaned and recorded results every week, and the percentage of properly cleaned items was calculated. Infection control nurses and hand hygiene officers also monitored adherence to hand hygiene, and gowning and gloving in each unit at various times of the day during the study. Hand hygiene observations began when a healthcare worker entered the intervention unit and was observed performing an activity that involved contact with a patient or the environment and ended when that healthcare worker had completed the activity. Infection control nurses and hand hygiene officers performed daily rounds to enforce the use of once daily chlorhexidine baths. In addition, the pharmacy department provided regular reports of chlorhexidine use. All of the above mentioned observations were made by the same infection control nurses and hand hygiene officers throughout the study. The observations were randomly performed once or twice per week, with the requirement of at least 80 observation opportunities per month during period 2.

## 2.7. Statistical analysis

Descriptive statistics by SPSS version 17.0 for Windows (SPSS Inc., Chicago, IL, USA) were calculated to analyze the case characteristics and laboratory parameters for each group. The demographic data and clinical characteristics were compared by using the  $\chi^2$  test or Student's *t*-test when appropriate. A 2-sided test with a *P*-value < 0.05 was considered as statistically significant.

## 3. Results

### 3.1. Overall demographic characteristics of AB and CRA complex

About 573,701 patients were admitted to CCH during the 12-year study period, including 954 adult patients having presented with at least 1 episode of AB. Sixty-four patients were excluded: 34 (55.9%) because of a conflict between the ICD-9-CM coding data and the microbiological dataset, and 30 (41.1%) because of incomplete data. Finally 890 patients were included. [Appendix 3](#) is a summary of the 12-year chronological data for the 890 patients with AB at CCH. The 12-year chronological data for ACB complex isolates including CRA complex and the density of healthcare-associated infection at CCH and Taiwan Nosocomial Infection Surveillance are listed in [Appendix 4](#). The incidence of AB at CCH was  $164.4 \pm 76.8$  per 100,000 patient-years. The cumulative number of admissions was lower in 2003 because of an outbreak of severe acute respiratory syndrome (SARS) in Taiwan. The median age of patients was 72.1 (8–98) years, and 53.3% were male patients. Three hundred and eighty-eight (43.4%) of the 890 AB episodes were due to CRA complex. Moreover, 680 infections (76.4%) were classified as

healthcare-onset, and 210 (23.6%) as community-onset. The comorbidities for AB included diabetes mellitus (25.6%), gastrointestinal disease (25.3%), cerebrovascular disease (17.5%), cardiovascular disease (15.3%), immunodepression (5.6%), and HIV infection (2.7%). The incidence of chronic obstructive pulmonary disease increased gradually throughout the study period ( $P < 0.001$ ). McCabe's classification of chronic underlying diseases allowed identifying 392 (44.0%) cases with ultimately fatal and rapidly fatal illness. The source or complications of AB included 273 (60.7%) cases with respiratory infection, 136 (15.3%) with skin and soft tissue infection, 135 (15.2%) with catheter-associated infection, 82 (9.2%) with urinary tract infection, 21 (2.4%) with intra-abdominal infection, and 243 (27.3%) were not documented. Eight hundred and twenty-seven (92.9%) patients received antibiotics before the AB episode. The choice of antibiotics during the AB episodes included cephalosporin, penicillin, carbapenem, aminoglycoside, and fluoroquinolone antibiotics in 782 (87.9%), 353 (40.0%), 225 (25.3%), 205 (23.0%), and 95 (10.7%) cases, respectively. The use of cephalosporin ( $P < 0.001$ ), penicillin ( $P < 0.001$ ), and carbapenem antibiotics ( $P < 0.001$ ) during AB episodes gradually increased throughout the study period. Third- and fourth-generation cephalosporin antibiotics (e.g., cefepime, piperacillin-tazobactam, imipenem-cilastatin and meropenem) were used most frequently. Two hundred and twenty-four (224/860) patients died during the study period, for a crude 30-day mortality rate of 25.2% (224/860).

### 3.2. Trends of AB and CRA complex

The incidence of AB in adult patients consulting at CCH increased from 127.4 per 100,000 patient-years in 2002 to 132.2 per 100,000 patient-years in 2013 ([Appendix 3](#)). The incidence density of HAI decreased from 5.23 per 1000 patient-days in 2008 to 0.6 per 1000 patient-days in 2012 ( $P < 0.001$ ). CRA complex bacteremia showed a significant increasing linear trend with each calendar year throughout the study period ( $P < 0.01$ ). Furthermore, the distributions and trends of the types and sources of infections differed significantly by calendar year throughout the study period ( $P < 0.001$ ). The number of patients previously treated by antibiotics before the AB episode decreased slightly from 93.8% in 2002 to 92.6% in 2013. The distribution of antibiotic type including cephalosporins (87.9%), penicillins (40.0%), carbapenems (25.3%), and aminoglycosides (23.0%) showed a significant increasing linear trend with each calendar year throughout the study period ( $P < 0.01$ ). The crude 30-day mortality rate was 25.2% (224/890). The AB mortality rate ranged from 20.2 to 32.4% during the study period, but there was no significant increasing linear trend of mortality with each calendar year throughout the study period ( $P = 0.550$ ).

### 3.3. Rates of CRA complex infection and HAI during periods 1 and 2

Eight hundred and ninety patients were admitted during the 2 study periods, 632 and 258 in periods 1 and 2, respectively. There was no significant difference in patient demographics or

Table 1  
Demographic and clinical characteristics of patients with AB by period.  
Les caractéristiques démographiques et cliniques des patients atteints de AB par période.

Variable	P1 (n = 632)	P2 (n = 258)	P-value <sup>a</sup>
Total strains of ACB complex (blood/all samples)	632/16,118	258/4797	<0.001***
Incidence (AB/total admissions per person-years per 100,000 admissions), mean ± SD	177.79 ± 64.5	137.76 ± 102.34	0.421
Incidence density of HAI (%)	4.56 ± 0.48	1.25 ± 0.87	<0.001***
CRA complex (including MDRACB complex, %), mean ± SD	28.7 ± 28.0	66.2 ± 15.0	0.033*
Age, years, mean ± SD	54 ± 8	52 ± 7.4	0.685
Male sex, n (%)	420 (66.5)	150 (58.1)	0.019*
Duration of ICU stay, days, mean ± SD	6 ± 2.6	7 ± 3.1	0.567
Type of infection, n (%)			<0.001***
Healthcare-onset infection	520 (82.8)	160 (62.0)	
Community-onset infection	112 (17.2)	98 (38.0)	
Underlying disease, n (%)			
Cardiovascular disease	95 (15.0)	41 (15.9)	0.746
Gastrointestinal disease	158 (25.0)	67 (26.0)	0.763
Diabetes	215 (34.1)	13 (5.0)	<0.001***
Cerebrovascular disease	114 (18.0)	42 (16.3)	0.531
Immunocompromised state	51 (8.1)	23 (8.9)	0.679
Source of CRA complex infection or colonization, n (%)			0.038*
Respiratory tract	193 (30.5)	80 (31.0)	
Catheter-associated	98 (15.5)	37 (14.3)	
Skin and soft tissue	106 (16.8)	30 (11.6)	
Urinary tract	64 (10.1)	18 (6.9)	
Intra-abdominal	16 (2.5)	5 (1.9)	
Others <sup>b</sup>	155 (24.5)	88 (34.1)	
McCabe's classification of chronic underlying diseases, ultimately fatal, n (%)	299 (47.3)	93 (36.0)	0.002**
Previous antibiotic treatment before AB, n (%)	588 (93.0)	239 (92.6)	0.832
Mortality, n (%)	161 (25.5)	63 (24.4)	0.742

AB: *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex bacteremia; CRA complex: carbapenem-resistant *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex; HAI: healthcare-associated infection; MDRACB complex: multidrug-resistant *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex.

\* $P < 0.05$ ; \*\* $P < 0.01$ ; \*\*\* $P < 0.001$ . P1: 2002–2009, P2: 2010–2013.

<sup>a</sup>  $\chi^2$  test or Student's *t*-test when appropriate.

<sup>b</sup> Including central nervous system infections.

clinical characteristics between the 2 periods (Table 1). A total of 16,118 ACB complexes were isolated, and 632 episodes of AB were identified during period 1. The number of annual isolates of ACB complex, episodes of AB, and annual isolates of CRA complex was lower in period 2 than in period 1 ( $P < 0.001$ ). There was a 72.6% reduction in the incidence density of HAI and a 22.6% reduction in the incidence of AB in period 2 compared to period 1, but there was no significant difference in the number of ACB complex isolates between periods. The incidences of patients with AB in periods 1 and 2 were  $177.79 \pm 64.5$  and  $137.76 \pm 102.34$  per person-year per 100,000 admissions, respectively ( $P < 0.05$ ) (Table 1). The rate of CRA complex increased from 2.5% to 71% during period 1 but decreased to 43.9% in period 2 ( $P < 0.001$ ), and the incidence density of CRA complex ranged from 3.17 to 7.38‰ during the study period (Figs. 1 and 2). Although there were no differences in the incidence of central line-associated bloodstream infection, ventilator associated pneumonia, or catheter-associated urinary tract infection between periods, the incidence of CRA complex decreased significantly from 2008 to 2013 (Appendix 2).

### 3.4. Adverse reactions and healthcare worker adherence to the campaign

Healthcare worker adherence to infection prevention measures did not differ between periods 1 and 2 (Table 2). Twenty

healthcare workers presented with skin reaction to chlorhexidine in period 2; all reactions were diffuse maculopapular rashes, confirmed by a dermatologist. Fifteen of the 20 healthcare workers presenting with an adverse skin reaction to chlorhexidine were diagnosed with underlying dermatitis, and the other

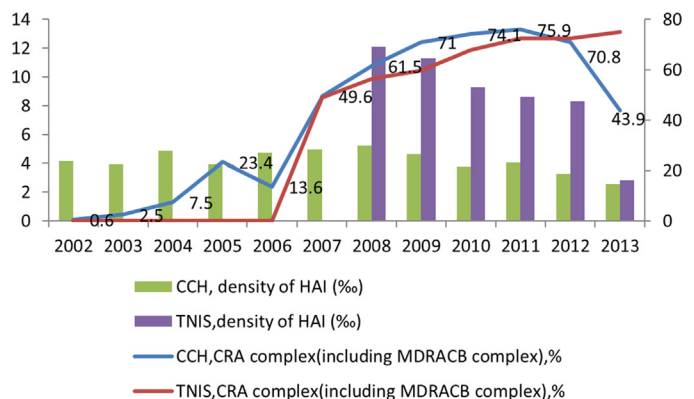


Fig. 1. Twelve-year trends of the rate of CRA complex and density of healthcare-associated infection. CCH: Changhua Christian Hospital; CRA complex: carbapenem-resistant; *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex; HAI: healthcare-associated infection; MDRACB complex: multidrug-resistant *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex; TNIS: Taiwan Nosocomial Infection Surveillance System.  
Tendances sur 12 ans du taux du complexe CRA et densité de l'infection nosocomiale.

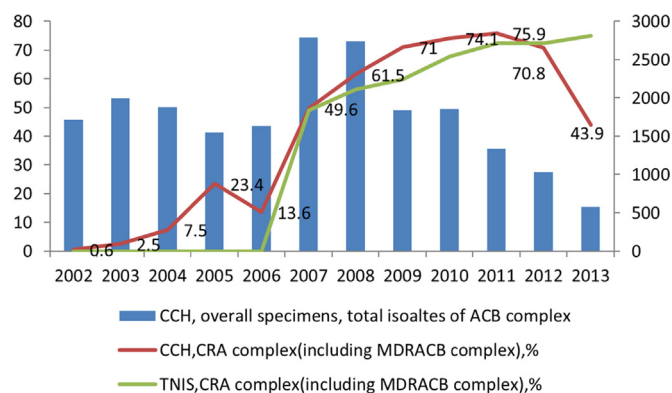


Fig. 2. Twelve-year trends of the rate of CRA complex and total ACB complex isolates. ACB complex: *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex; CCH: Changhua Christian Hospital; CRA complex: carbapenem-resistant *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex; HAI: healthcare-associated infection; MDRACB complex: multidrug-resistant *Acinetobacter calcoaceticus*-*Acinetobacter baumannii* complex; TNIS: Taiwan Nosocomial Infection Surveillance System.  
Tendances sur 12 ans du taux du complexe CRA et total des isolats complexe ACB.

5 had a history of skin allergy to body lotions. No patient presented with severe anaphylaxis.

### 3.5. Antibiotics control program

The pattern of antibiotic prescriptions differed during the study because of the new antibiotic control program. However, antibiotic consumption was not significantly correlated with the decreased incidence density of CRA complex ( $P=0.608$ ). The consumption of some antibiotics differed between periods 1 and 2 (Table 2). The consumption of piperacillin-tazobactam was significantly lower in period 2 than period 1 ( $P<0.001$ ).

## 4. Discussion

We analyzed the long-term effectiveness of a campaign for infection control programs including hand hygiene champions and an antibiotic control program to control CRA complex infection during a 12-year period in accordance with international accreditation programs (i.e., the JCIA) and national accreditation programs (i.e., hospital accreditation and healthcare-related infection control audit and quality improvement by the TJCHA). Accreditation programs improve the management provided by healthcare services [18,19]. Furthermore, our study provided additional evidence of the improvement of infection control and prevention using such measures.

The incidence of AB has been increasing [20]. Wilks et al. described methods to control outbreaks of multidrug-resistant *A. baumannii*-*calcoaceticus* colonization and infection in ICUs without closing the ICU or placing patients in isolation [21]. Rodríguez-Baño et al. reported the use of a comprehensive care program to control endemic multidrug-resistant *A. baumannii* [22]. The TNIS data demonstrated a recent overall decrease in HAIs in the ICUs of acute care hospitals [13,14]. Although the overall rate of HAIs decreased, more HAIs were caused by CRA

complex than by ACB complex. In particular, the rate of CRA complex compared to the rate of ACB complex in the ICUs of medical centers increased from 16.4% to 75.3% and from 18.2% to 62.1% in regional hospitals from 2003–2012 [13,14]. The incidence of AB at CCH in central Taiwan increased according to our study, highlighting the critical need for infection control and prevention measures.

The results concerning the effectiveness of our infection control interventions were mixed and the impact of our hospital's accreditation on infection control remains to be determined. The findings of our study suggest that the educational intervention and hospital accreditation process influenced adherence to infection control measures, especially for hand hygiene [23,24]. Our data corroborated that of a survey of Japanese hospitals, the authors of which identified a significant association between infection control performance scores and hospital accreditation status [25].

Regardless of hand hygiene compliance, we assumed that the cohorting of patients with CRA complex infection in our study still significantly reduced the spread of CRA complex. The use of cohort rooms to isolate CRA complex patients was not monitored, but the incidence density of HAI and rates of methicillin-resistant *Staphylococcus aureus* served as control parameters, while episodes of AB served as an observation parameter to evaluate the impact of isolation precautions on infection control measures, similar to a study by Cheng et al. [26]. The incidence density of HAI decreased because of the increased chlorhexidine consumption density following education and hand hygiene promotion during period 2, whereas that of CRA complex did not. We were unable to determine the proportion of reduced CRA complex incidence density attributable to decreased patient-to-patient transmission, but cohorting likely improved compliance with infection control measures including hand hygiene, as corroborated by previous authors demonstrating the effectiveness of isolation precautions for patients with CRA complex infection or colonization [11,25,27].

Despite the lack of specific antibiotic control measures during the study period, the consumption of antibiotics and carbapenems decreased during period 2. Although we were unable to evaluate the causal relationship between antibiotic consumption and the incidence density of CRA complex, our findings suggest that the reduction in CRA complex incidence density could be related to the level of antibiotic consumption, as consistent with previous reports [28–30]. It is difficult to determine the causal effect underlying the decreased incidence density of HAI and rates of CRA complex, particularly with respect to the rate of antibiotic resistance attributable to antibiotic use and the rate of patient-to-patient transmission.

This study was the first 12-year cross-sectional analysis of AB in central Taiwan. We had previously studied changes in the clinical features of AB in Changhua County, Taiwan between 1998 and 2000 [9] (Appendix 3). The incidence of AB in adults in CCH increased from 127.4 per 100,000 patient-years in 2002 to 132.2 per 100,000 patient-years in 2013. The incidence of AB increased steadily from 1998 to 2009 and then decreased from 2010 to 2012 (Appendix 4). There was a significant increasing linear trend of CRA complex bacteremia during the study

Table 2  
Infection control compliance monitoring and outcomes by period.  
Suivi de la conformité du contrôle de l'infection et résultats par période.

Variable	P1	P2	P-value <sup>c</sup>
Total strains of ACB complex (blood/all samples)	632/16,118	258/4797	<0.001***
Incidence (AB/total admissions per person-years per 100,000 admissions), mean ± SD	177.79 ± 64.5	137.76 ± 102.34	0.421
Incidence density of HAI (‰)	4.56 ± 0.48	1.25 ± 0.87	<0.001***
CRA complex (including MDRACB complex, %), mean ± SD	28.7 ± 28.0	66.2 ± 15.0	0.033*
Adherence to environmental cleaning			
Observations, <i>n</i>	5936	17,224	
Observations per week, <i>n</i> , mean ± SD	–	3 ± 0.9	
Environmental cleaning rate <sup>a</sup> (%), mean ± SD	–	90 ± 12	
Adherence to hand hygiene <sup>b</sup>			
Observations, <i>n</i>	5936	17,224	
Compliance rate (%), mean ± SD	87.2 ± 14.1	98.5 ± 13.2	0.212
Correct rate (%), mean ± SD	91.2 ± 12.1	99.8 ± 3.2	0.202
Adherence to contact isolation <sup>b</sup>			
Observations, <i>n</i>	5936	17,224	
Glove and gown use (%), mean ± SD	79 ± 14	81 ± 15	0.824
Chlorhexidine consumption			
Observations, <i>n</i>	–	17,224	
Chlorhexidine consumption density, L/patient number × 1000, mean ± SD	–	45.5 ± 10.4	
Outcome (per 1000 patient-days), %			
Incidence (ACB complex bacteremia/total admission number per person-years per 100,000 admission), mean ± SD	177.79 ± 64.5	137.76 ± 102.34	0.421
Piperacillin-tazobactam consumption (DDD per 1000 patient-days)	4,591 ± 21.6	4,301 ± 36.6	<0.001***
Carbapenem consumption (DDD per 1000 patient-days)	921 ± 41.5	811 ± 31.6	0.608
CRA complex (%), mean ± SD	28.7 ± 28.0	66.2 ± 15.0	0.033*
MRSA (%), mean ± SD	51.2 ± 6.3	38.3 ± 5.7	0.006**
CR <i>Pseudomonas aeruginosa</i> isolates (%), mean ± SD	5.4 ± 1.4	5.3 ± 1.3	0.908
Density of CLABSI rate (‰), mean ± SD	18.5 ± 9.5	16.4 ± 6.0	0.699
Density of CAUTI rate (‰), mean ± SD	16.9 ± 9.3	10.0 ± 4.4	0.197
Density of VAP rate (‰), mean ± SD	2.9 ± 1.7	0.5 ± 0.9	0.026*

AB: *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex bacteremia; CRA complex: carbapenem-resistant *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex; CAUTI: catheter-associated urinary tract infection; CLABSI: central line-associated bloodstream infection; CR *Pseudomonas aeruginosa*: carbapenem-resistant *Pseudomonas aeruginosa*; DDD: defined daily dose; HAI: healthcare-associated infection; MDRACB complex: multidrug-resistant *Acinetobacter calcoaceticus-Acinetobacter baumannii* complex; MRSA: methicillin-resistant *Staphylococcus aureus*; VAP: ventilator-associated pneumonia. \*  $P < 0.05$ , \*\*  $P < 0.01$ , \*\*\*  $P < 0.001$ . P1: 2002–2009; P2: 2010–2013.

<sup>a</sup> The environmental cleaning rate was defined as the number of sites cleaned/total number of sites observed.

<sup>b</sup> Hand hygiene and contact isolation adherence rates were defined as the number of observations confirming adherence to hand hygiene requirements/number of observations.

<sup>c</sup>  $\chi^2$  test or Student's *t*-test when appropriate.

period explained by an increasing number of healthcare-onset infections. Marchaim et al. reported that the incidence of AB increased in Saudi Arabia from 0.02 per 1,000 admissions in 1997 to 0.738 per 1000 admissions in 2004 [31]. Although the incidence of AB was lower in Taiwan than in Saudi Arabia, it was difficult to compare the incidence we observed in this study to that of other countries because of differences in the methods used. Our study results showed that the incidence of CRA complex bacteremia had increased significantly in CCH since 2008. CRA complex bacteremia increased from 34.5% to 64.8% during the study period mainly because of increasing CRA complex isolates and increasing healthcare-associated AB, but not of community-acquired CRA complex bacteremia. Our results correlated to those of Kuo et al. [6]. Antibiotic use at the onset of infection changed during the study period, because of the increase in CRA complex infections. Antibiotic use changed significantly during the study period; this was explained by the increased incidence of CRA complex as well

as the increased complexity and severity of underlying diseases. The crude 30-day mortality rate was 25.2% (224/890). There was no significant increase in mortality during the study period. The number of patients presenting with CRA complex bacteremia increased but the crude 30-day mortality rate remained between 20.2% and 32.4% during the study period, explained in part by the relatively low virulence of CRA complex and improved supportive care. Jang et al. did not observe any significant difference in the cumulative survival curves of patients presenting with AB and control patients [32]. Likewise, Jamulitrat et al. did not observe any significant difference in mortality rates among 35 patients (52.2%) in imipenem-resistant and imipenem-susceptible ACB complex groups [33]. These results are consistent with ours.

We also analyzed the variables contributing to the decreased incidence density of HAI, rates of CRA complex, and incidence of AB over a 12-year study period (Appendix 4). The in-service education for infection control programs, promotion of hand



hygiene, and enhancement of antibiotic control programs during the preparation for hospital accreditation appear to have been effective in controlling CRA complex infection and AB episodes at CCH. However, the isolation precautions for CRA complex did not allow controlling CRA complex infection during period 1, because of poor compliance, because compliance with infection control interventions is the critical requisite for an effective control of CRA complex infections. We did not perform active screening cultures, which would have allowed an early detection of patients with CRA complex at hospital admission or during hospitalization, consequently prompting contact precautions to reduce person-to-person transmission [34]. There is no optimal surveillance sampling method for MDRACB complex contrary to other multidrug-resistant pathogens [34]. The authors of a previous study reported low MDRACB complex surveillance culture sensitivity for MDRACB complex detection [35]. Sampling is expensive and increases the workload of healthcare workers; consequently we did not implement active microbiological screening, which could be inappropriate for detecting CRA complex carriers. Furthermore, some authors even reported there was no benefit in performing active surveillance cultures for CRA complex [36,37]. Furthermore, compliance with the infection control interventions in our study might have been sub-optimal during period 1. Internal and external audits revealed a significant decrease in the incidence density of HAI during period 2. We assumed that the hand hygiene campaign launched before the hospital accreditation program during period 2 greatly enhanced compliance, which led to an increase in chlorhexidine consumption density.

Our study has several strong points. Most importantly, we accumulated a complete longitudinal dataset over 12 years. We had access to excellent data to evaluate the demographic features of AB. We implemented a campaign for hand hygiene champions, in compliance with the JCIA and TJCHA, and an antibiotic stewardship to control CRA complex infection. We were thus able to provide detailed information for infection control interventions. Our findings provide invaluable epidemiological information about AB and CRA complex in central Taiwan.

Nevertheless, our study had several limitations. The individual effects of interventions were not evaluated, because several actions were introduced simultaneously or sequentially according to requisites from the JCIA and TJCHA. Moreover, the compliance with the various interventions during the study period could not be checked, because part of the study was performed retrospectively. The calculated incidence of AB at CCH was most likely underestimated because 6.9% cases of AB infection were excluded. Furthermore, some cases of AB infection for which blood was not cultured or those treated with broad-spectrum antibiotics before blood cultures might have been overlooked. However, these cases were not likely to account for a large rate of AB cases. Data on antibiotic history was inaccurate for many patients who had received antibiotics in the month before their AB infection episode, including patients with community- and healthcare-onset infections, because part of this study was performed retrospectively. The defined daily doses for the various antibiotics administered during the study period could not be calculated, because some of the

antibiotics had been altered and because of a lack of available manpower. Furthermore, we did not perform pulsed-field gel electrophoresis typing of CRA complex isolates, because there was no evidence of an outbreak during the study period; thus, the role of patient-to-patient transmission in the acquisition of CRA complex could not be documented.

## 5. Conclusion

Our study results suggest that adherence to infection stewardship by means of in-service education, hand hygiene campaigns, and antibiotic control programs is important to decrease the incidence density of AB and HAI and may help control CRA complex infection.

*Author contributions:* Chang-Hua Chen, Chun-Eng Liu, and Maw-Soan Soon designed the research, collected the data, drafted the article, analyzed the data, and interpreted the results. Li-Chen Lin analyzed the microbiological process. Yu-Jun Chang analyzed the statistical data. All authors read and approved the final version of the article.

## Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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## Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.medmal.2015.04.005>.

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