



# The Prognostic Impact of Carbapenem-resistant Organism Co-infection in Influenza Inpatients: a Retrospective Cohort Study

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# Where we are?



**Chengdu City,  
Sichuan Province**



## Chengdu Figures

- Area: 14,335 km<sup>2</sup> ≈ 9 London
- Population: 21 million > the Netherlands
- GDP: 2.35 trillion RMB (2024)
- Foreign Consulates: 23
- 4F Class Airports: 2 (81 Int'l Routes)

**1892**

Renji and  
Cunren Clinic



**1914**

Medical School of  
West China  
Union University



**1953**

Sichuan Medical  
College



**1985**

West China  
University of Medical  
Sciences



**2000~Now**

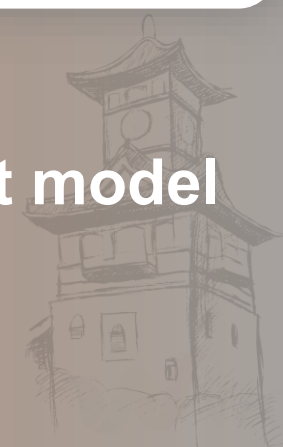
WCSM/WCH,  
Sichuan University



Hospital +Medical School



Highly coordinated management model  
of hospital and medical school



# Campuses: 3+3+3



 676,200 m<sup>2</sup>

 4,900 registered beds

 54 clinical departments

## Main Campus

## Wenjiang

## Jinjiang

## Shangjin

## Tianfu

3 campuses in total: 4,900 beds

1,170 beds

1,200 beds



Our own campus



Fully-entrusted Hospital in Chengdu

## Xiamen

1,000 beds

## Lecheng

200 beds (phase 1)

## Xizang

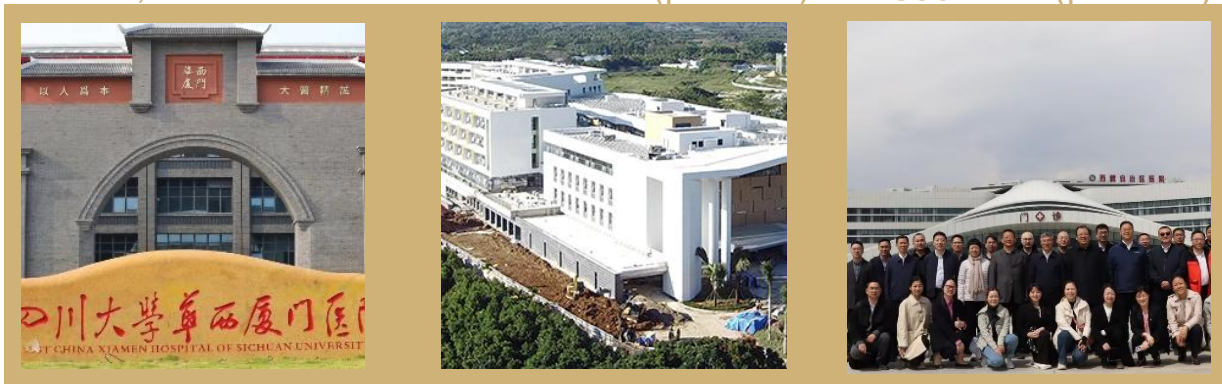
800 beds (phase 1)

## Jincheng

1,000 beds



Fully-entrusted Hospital outside Chengdu

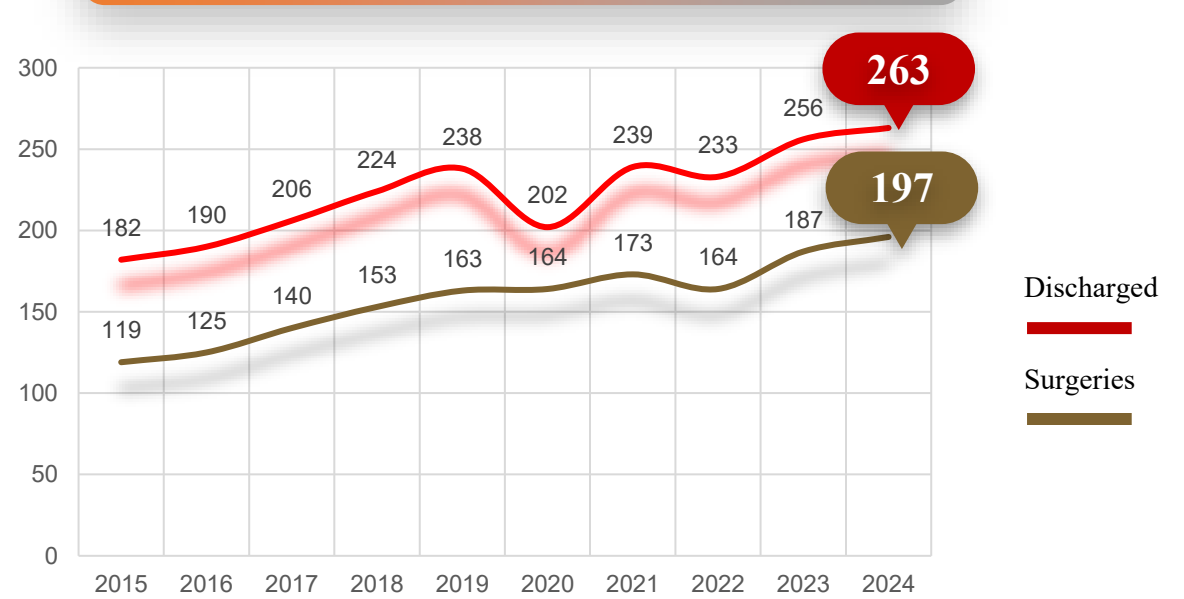


# Healthcare Service Capacity in 2024

Outpatient + Emergency Visits (million)



Discharged Patients & Surgeries (thousand)



**7.35 M**

**5.35 M** Outpatient & ER Visits

**2 M** Internet Hospital Visits

**263 K**

Discharged Patients

**7.05 days**

Average Length Of Stay

**1.71**

Case Mix Index  
**(2<sup>nd</sup> in China)**

**197 K**

Surgeries

**28.31 %**

Day Surgery

**39.34 %**

Level 4 Surgery

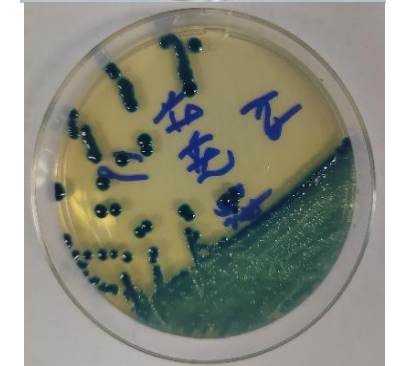
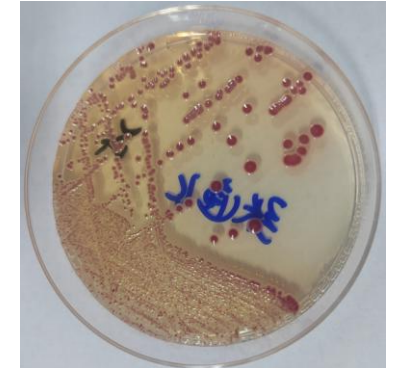
**26.37 %**

Minimally Invasive Surgery

# Background and Objective

- The WHO estimates that global influenza epidemics result in 3 to 5 million severe cases and between 290,000 and 650,000 deaths annually<sup>1</sup>
- Among critically ill influenza patients, the rate of bacterial co-infection ranges from 20% to 51%, with nearly 10% of patients developing hospital-acquired bacterial co-infection<sup>2-4</sup>
- Limited data exist on the impact of co-infection of MDROs, particularly carbapenem-resistant organisms (CRO)
- **To better understand the impact of healthcare associated CRO co-infections on influenza outcomes**

1. *The burden of Influenza*. <https://www.who.int/news-room/feature-stories/detail/the-burden-of-influenza> (accessed 2025-02-06).
2. Bacterial and Viral Co-Infections Complicating Severe Influenza: Incidence and Impact among 507 U.S. Patients, 2013-14. *J Clin Virol* **2016**, *80*, 12–19.
3. Secondary Infections in Critically Ill Patients with Viral Pneumonia Due to COVID-19 and Influenza: A Historical Cohort Study. *Can J Anaesth* **2023**, *70* (3), 374–383.
4. Coinfection and Superinfection in ICU Critically Ill Patients with Severe COVID-19 Pneumonia and Influenza Pneumonia: Are the Pictures Different? *Front Public Health* **2023**, *11*, 1195048.



# Methods: Study design

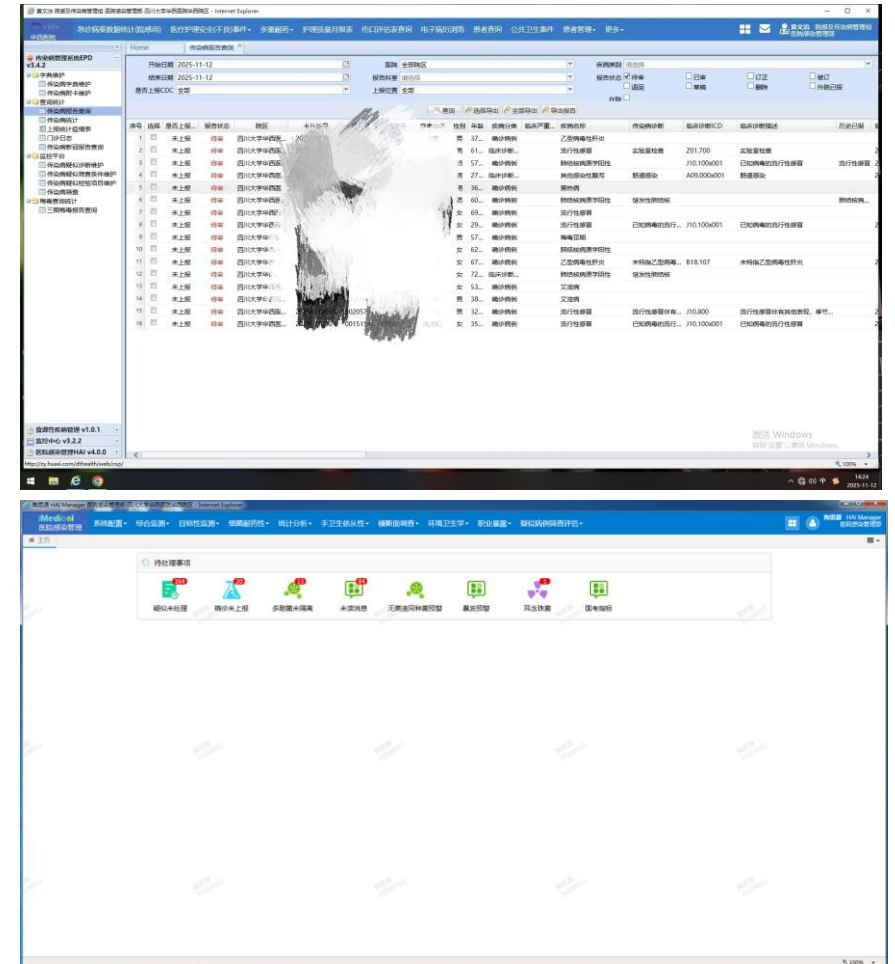
- A retrospective cohort study was conducted
- Adult hospitalized patients diagnosed with influenza between January 1, 2013, and December 31, 2023
  - --The exposed group comprised patients with healthcare-associated CRO co-infections
  - --The non-exposed group included those without CRO co-infections.
- Patients meeting any of the following criteria were excluded:
  - 1) under 18 years old
  - 2) hospitalization duration  $\leq 2$  days or  $> 365$  days
  - 3) infect with CROs within 2 days of admission

# Methods: Case definition

- **CROs:** Carbapenem-resistant *Enterobacterales* (CRE), Carbapenem-resistant *Acinetobacter baumannii* (CRAB), Carbapenem-resistant *Pseudomonas aeruginosa* (CRPA).
  - **CRE:** Carbapenem-resistant *Klebsiella pneumoniae* (CRKP), Carbapenem-resistant *Escherichia coli* (CRECo) and carbapenem-resistant *Enterobacter cloacae* (CRECI)
- **Carbapenem resistance** was defined as WHO guidelines for prevention and control of CRE, CRPA and CRAB
- **Healthcare associated CRO co-infection** was confirmed by a positive culture in the clinical specimens after 48 h of hospitalization, which is followed the criteria publish by MOH in 2001
- **Influenza virus infection** was confirmed follow the guideline published by Influenza Diagnosis and Treatment Expert Panel of the Chinese Ministry of Health in 2011.
- **Poor prognosis** was defined as either in-hospital death or discharge against medical advice (DAMA) due to a perceived hopelessness regarding their treatment

# Methods: Data collection & Statistical analysis

- Basic information was extracted from the infectious disease management system and treatment information was obtained from the HIS
- Data management was conducted using Excel software, while statistical analyses were performed using SPSS version 27.0
- This study was conducted under the supervision of the Ethics Review Committee and was approved by the Biomedical Ethics Review Committee of West China Hospital in 2022 [NO. 2022 Review (229)]



# Results

- **7,050** influenza cases were identified
- **1,546** patients were included in the study
- The average age is 57 years
- Males accounting for 62.23% (926/1546).
- **130 (8.41%)** of these patients were co-infected with CROs
- In hospital mortality rate was 0.71% (11/1,546)
- The poor prognosis rate was 5.11% (79/1,546)

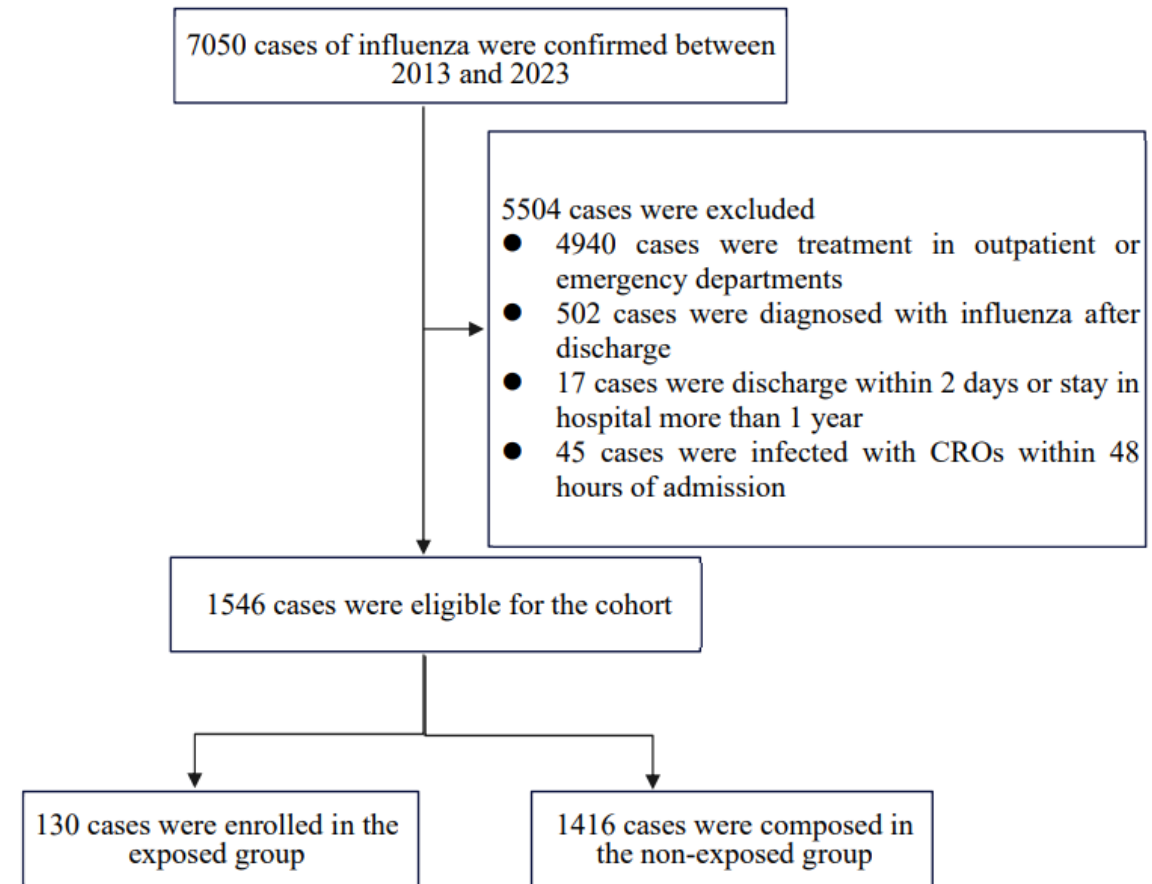
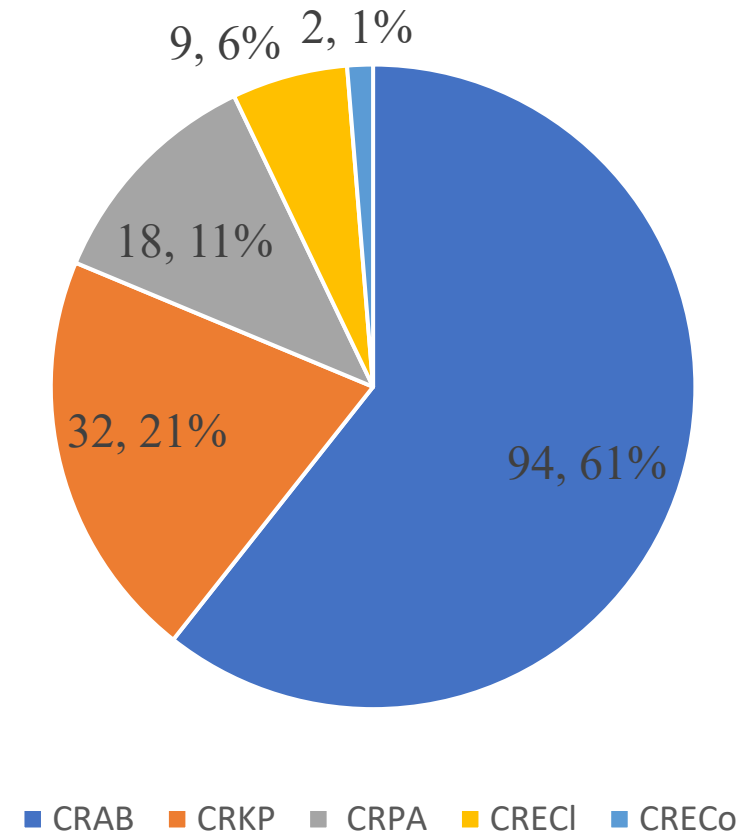


Figure 1. The Flowchart of the study

- Among the 130 patients, a total of 155 carbapenem-resistant pathogens were identified
  - **94 cases of CRAB**, 6.05% (94/1,546, 95%CI [4.89%-7.27%])
  - **32 cases of CRKP**, 2.07% (32/1,546, 95%CI [1.36%-2.78%])
  - **18 cases of CRPA**, 1.16% (18/1,546, 95%CI [0.63%-1.70%])
  - **9 cases of CRECI** 0.6% (9/1,546, 95%CI [0.3%-1.1%])
  - **2 cases of CRECo**, 0.1% (2/1,546, 95%CI [0.0%-0.5%])

Strain distribution profile of the identified CRO



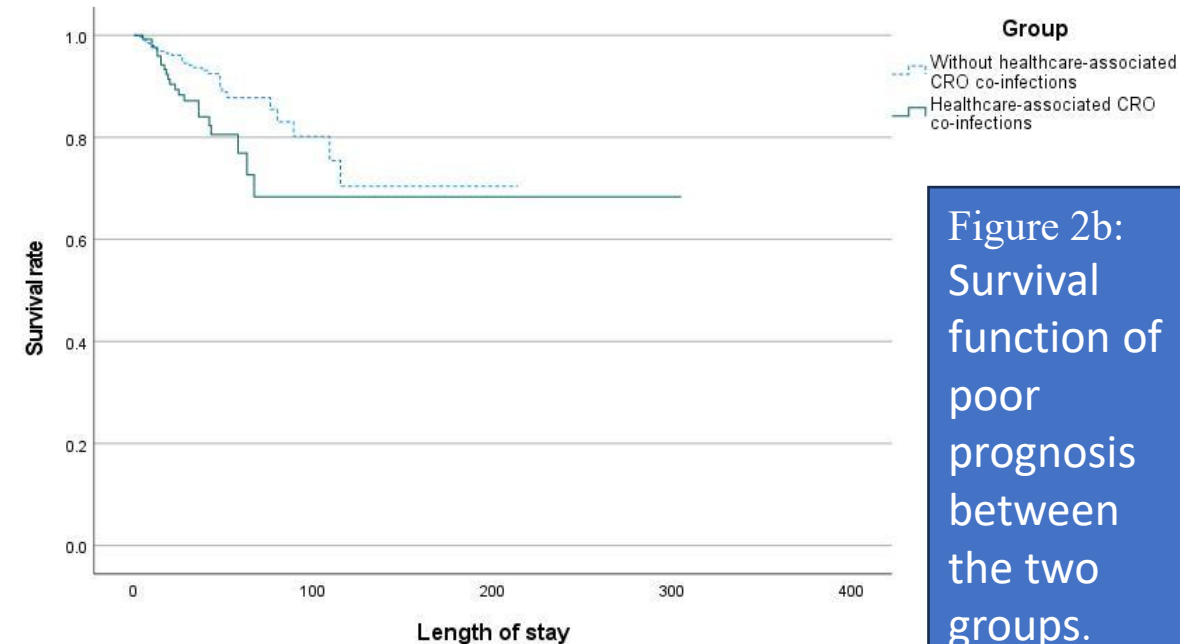
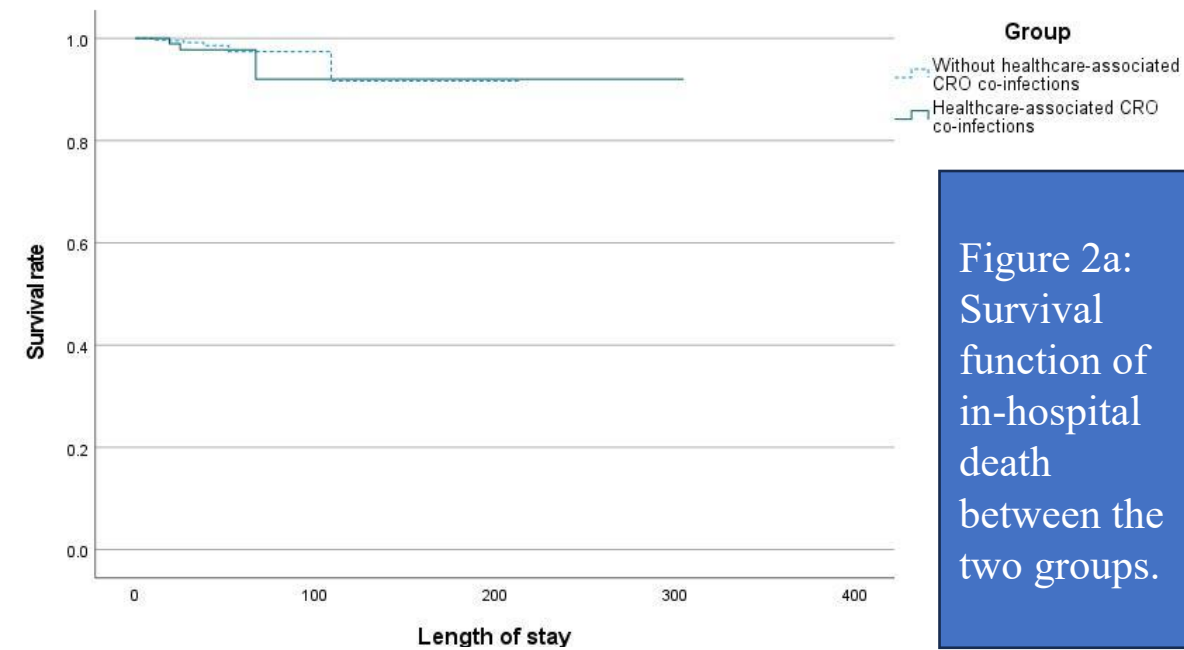
# Comparison between the exposed group and the non-exposed group

- Compared with patients without CRO co-infection, those CRO co-infections had **a significantly higher** proportions of heart failure, COPD, and hypertension
- There was **no** significant difference in **age** and **other underlying diseases**
- Patients with concurrent CRO infections received more corticosteroid treatment and underwent more invasive procedures, including surgeries, mechanical ventilation, central venous catheterization, urinary catheterization, and hemodialysis

Table 1 Comparison of characteristics of exposed and non-exposed groups (N = 1546)

Variant	Non-exposed group	Exposed group	Z/ $\chi^2$	P
	(N=1416)	(N=130)		
	n (%)	n (%)		
Age (years)*	57 (42, 71)	60 (47.75, 73)	-1.644	0.100
<b>Gender</b>			10.457	0.001
Male	864 (61.0)	98 (75.4)		
Female	552 (39.0)	32 (24.6)		
<b>Underlying disease</b>				
Congestive heart failure	120 (8.5)	25 (19.2)	16.208	<0.001
Peripheral vascular disease	38 (2.7)	5 (3.8)	0.595	0.440
Cerebrovascular disease	51 (3.6)	8 (6.2)	2.113	0.146
Dementia	11 (0.8)	0 (0.0)	/	0.614
COPD	264 (18.6)	42 (32.3)	14.002	<0.001
Ulcerative disease	11 (0.8)	0 (0.0)	/	0.614
Diabetes	281 (19.8)	30 (23.1)	0.774	0.379
Hemiplegia	5 (0.4)	0 (0.0)	/	1.000
Malignant tumor	355 (25.1)	25 (19.2)	2.190	0.139
Leukemia	45 (3.2)	3 (2.3)	0.080	0.777
HIV	4 (0.3)	0 (0.0)	/	1.000
Hypertension	443 (31.3)	58 (44.6)	9.659	0.002
Tuberculosis	69 (4.9)	2 (1.5)	3.021	0.082
ACCI*	3 (1, 6)	5 (3, 7)	-3.910	<0.001
<b>Drugs</b>				
Hormonal drugs	650 (45.9)	90 (69.2)	25.963	<0.001
Oseltamivir	256 (18.1)	25 (19.2)	0.106	0.745
Immunosuppressant	139 (9.8)	16 (12.3)	0.819	0.365
<b>Invasive operations</b>				
Surgeries	683 (48.2)	111 (85.4)	65.781	<0.001
Mechanical ventilation	124 (8.8)	92 (70.8)	380.947	<0.001
Urinary catheter	110 (7.8)	68 (52.3)	231.845	<0.001
Central line catheter	106 (7.5)	48 (36.9)	115.040	<0.001
Hemodialysis	41 (2.9)	27 (20.8)	90.462	<0.001
ECMO	26 (1.8)	3 (2.3)	0.002	0.967
<b>Length of stay (days)*</b>	14 (9, 24)	31.5 (18, 50)	-9.918	<0.001

- Compared to the non-exposed group, the exposed group had a **longer length of stay** (days, 14[9, 24] vs. 31.5[18, 50],  $P < 0.001$ )
- **No** significant difference in the in-hospital mortality rate (2.31% vs. 0.56,  $\chi^2 = 0.602$ ,  $P=0.438$ , **HR=1.70**, 95%CI [0.44-6.53]) between two groups
- The poor prognosis rate was **higher** in the exposed group than the non-exposed group (16.15% vs. 4.10%,  $\chi^2 = 7.142$ ,  $P = 0.008$ , **HR=1.98**, 95%CI [1.19-3.30])



# Risk factor for prognosis

- The potential confounding variables for death and poor prognosis were analyzed separately
- Variables with a P-value of less than 0.2 in the univariate analysis were selected for inclusion in the Cox proportional hazards regression model for multivariate analysis.
- CRO co-infection was **not** an independent risk factor associated with in-hospital death (HR=1.152, 95% CI [0.279, 4.754],  $P = 0.844$ )
- Age and hemodialysis were identified as risk factors for in-hospital death
- CROs co-infection (HR = 1.990, 95% CI [1.199, 3.303],  $P = 0.008$ ) and ACCI (HR = 1.146, 95% CI [1.075, 1.221],  $P < 0.001$ ) were independent risk factors for poor prognosis

Model	Beta	Wald	P	HR	HR 95%CI
<b>Death in hospital</b>					
CRO co-infection	0.142	0.039	0.844	1.152	0.279-4.754
Age (years)	0.054	7.476	0.006	1.056	1.015-1.097
Hemodialysis	2.048	8.765	0.003	7.755	1.998-30.095
<b>Poor prognosis</b>					
CRO co-infection	0.688	7.087	0.008	1.990	1.199-3.303
Immunosuppressant	-0.924	3.940	0.047	0.397	0.159-0.988
ACCI	0.136	17.666	< 0.001	1.146	1.075-1.221

# Subgroup analysis of healthcare associated CRO co-infections

Table 3 Univariate analysis of poor prognosis for subgroups

- A univariate analysis of poor prognosis in subgroups of healthcare associated CRO co-infections was conducted.
- The results showed that the effect of CRPA infection on poor prognosis was not significant, whereas co-infections with CRAB ( $\chi^2= 33.642, P < 0.001$ ) and CRE ( $\chi^2= 4.762, P=0.029$ ) were statistically significant

Subgroup	poor prognosis	non-poor prognostic	$\chi^2$	P
<b>CRAB</b>				
exposure group	77 (81.9)	17 (18.1)	33.642	< 0.001
control group	58 (4.1)	1358 (95.9)		
<b>CRE</b>				
exposure group	5 (12.5)	35 (87.5)	4.762	0.029
control group	58 (4.1)	1358 (95.9)		
<b>CRPA</b>				
exposure group	0 (0.0)	18 (100)	/	1
control group	58 (4.1)	1358 (95.9)		

**Table 4 Cox regression of the effect of subgroups on poor prognosis**

- The results of the multivariate analysis indicated that CRAB ( $\chi^2=10.200$ ,  $P=0.001$ ) was an independent risk factor for poor prognosis

Model	Beta	Wald	P	HR	HR 95%CI
<b>CRAB subgroup</b>					
Use of immunosuppressive drugs	-1.388	5.502	0.019	0.250	0.078-0.796
ACCI	0.138	17.626	< 0.001	1.149	1.077-1.225
CRAB co-infections	<b>0.893</b>	<b>10.200</b>	<b>0.001</b>	<b>2.443</b>	<b>1.140-3.307</b>
<b>CRE subgroup</b>					
Use of immunosuppressive drugs	-0.941	3.259	0.071	0.390	0.141-1.084
ACCI	0.146	16.825	< 0.001	1.157	1.079-1.240
CRE co-infections	0.303	0.412	0.521	0.521	0.537-3.415
<b>CRPA subgroup</b>					
Use of immunosuppressive drugs	-1.500	4.313	0.038	0.223	0.054-0.919
ACCI	0.151	17.020	< 0.001	1.163	1.082-1.249
CRPA infections	-12.251	0.001	0.971	0.000	/

# Limits

- The diagnosis of influenza was dependent on both rapid antigen tests and PCR in many of the patients but not all patients with fever received these tests, and the sensitivity and specificity of the tests varied, especially rapid antigen tests which used at the point of care. This may be **over- or under-estimates** of cases.
- We did not conduct **cause-specific mortality** assessments, and all reported mortality rates were crude mortality rate. Additionally, we did not track the outcomes of discharged patients, which may have led to an underestimation of patient mortality.
- This study was a single-center investigation. Future multicenter studies could address the sample size constraints inherent to single-center designs.

# Conclusion

- CRO co-infection independently predicts poor prognosis in influenza patients, underscoring the need for stringent infection control measures and timely clinical interventions targeting these pathogens, especially CRAB.
- Multicenter studies are warranted to validate these findings and refine risk stratification protocols.



华西医院

华西感控



Thank You !

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