WHAT IS THE STUDY TITLE?  
Consortium on Resistance Against Carbapenems in *Klebsiella pneumoniae* and other Enterobacteriaceae (CRACKLE-2)

**WHAT IS THE PURPOSE OF THE RESEARCH?**

The CRACKLE-2 study investigated types of carbapenem-resistant Enterobacteriaceae (CRE).

The goal of the study was to learn about patients infected with CRE, understand and describe the different types of CRE, and learn how each type affected different patient populations.

The first manuscript focused on carbapenem-resistant Enterobacteriaceae in the United States. The second manuscript analyzed data from around the world, and a specific bacteria that is part of the Enterobacteriaceae family, called *Klebsiella pneumoniae*.

Researchers used a rating scale called DOOR (desirability of outcome ranking), to compare patient outcomes at 30 days after infection.

**WHAT IS THE PRIMARY ENDPOINT?**

The DOOR scale ranks a patient’s outcome from best to worst:

**Best:**
- Alive with no negative events
- Alive with 1 negative event
- Alive with 2 or 3 negative events

**Worst:** Death

Researchers also compared the overall patient death rate and bacterial characteristics between patients from China, South America, and the US.

**MANUSCRIPT OF PRIMARY RESULTS OR CLINICAL STUDY REPORT.**

Molecular and Clinical Epidemiology of Carbapenem-Resistant *Enterobacteriaceae* in the United States: a Prospective Cohort Study

And

Clinical outcomes and bacterial characteristics of carbapenem-resistant *Klebsiella pneumoniae* complex among patients from different global regions (CRACKLE-2): a prospective, multicentre, cohort study

**WHAT HAPPENED DURING THE STUDY?**

In these studies, researchers collected data about patients from electronic health records (EHRs). They also collected a copy of the bacteria, that had been previously collected by the patient’s physician, and analyzed the bacterial DNA.

**WHEN DID THE RESEARCH TAKE PLACE?**

Between April 30, 2016 and November 30, 2018

**IS THE STUDY REGISTERED WITH CLINICALTRIALS.ORG?**

NCT03646227

Changes to your healthcare should not be made based on information in this summary without first consulting a doctor. If you have questions about these results, speak with your doctor.
WHO WAS INVOLVED?
The first analysis of the CRACKLE-2 study included **49 US hospitals in 15 states and the District of Columbia.**

Researchers followed **1,040 patients** with CRE during hospitalization.

The second analysis of the CRACKLE-2 study took place in **71 hospitals** in Argentina, Australia, Chile, China, Colombia, Lebanon, Singapore, and the US.

Researchers followed **991 patients** infected with the most common type of CRE called carbapenem-resistant *Klebsiella pneumoniae* (CRKP).

WHY IS THIS RESEARCH IMPORTANT TO PATIENTS, CLINICIANS, AND OTHER RESEARCHERS?
CRE are of specific concern in the fight against antibiotic resistance. Treatment options are very limited, and there is potential for community spread. Researchers know that CRE infections are a global threat, but they need to learn more about how they are treated, how patients respond to treatment, and what molecular differences exist.

Different types of CRE may need different treatments and have different outcomes. Understanding more about these differences will help researchers know how best to study and treat CRE infections.

WHAT WERE THE RESULTS?
Analysis of the laboratory data categorized the CRE into three groups:

1. **CPE:** drug resistant bacteria with genes for carbapenemase (**59%**)  
2. **Non-CP-CRE:** drug resistant bacteria without genes for carbapenemase (**19%**)  
3. **U-CRE (Unconfirmed CRE):** first tested as drug resistant, but further laboratory tests showed they were not drug resistant (**22%**)  

Patients in each of the groups had poor outcomes. **24% of patients** with CRE infection had died **30 days** after infection. **46% of patients** that were discharged from the hospital after CRE infection were readmitted within **90 days.**

In the US, the most common type of CRE was carbapenem-resistant *Klebsiella pneumoniae* (CRKP).

In the second analysis, researchers learned that both patient and CRKP molecular characteristics differed greatly by region, but little within a region.

Patients in the US with CRKP infection were sicker and had more pre-existing conditions than patients in China or South America.

The overall risk of dying from CRKP infection was **19%**. The risk of dying from CRKP infection was higher in South America than it was in China or the US. The risk of dying from CRKP infection in China and the US were not significantly different.

HOW WILL THE RESULTS HELP PATIENTS AND DOCTORS?
Understanding CREs clinical and genetic characteristics will help focus research and resources on the right methods for combating antibacterial resistance.

The results from these analyses show that CRKP can vary from one region to another, and patients’ outcomes may vary as well.

This important information helps researchers understand that research and treatment strategies for CRKP need to be tailored to a particular region and patient population.

WHAT’S NEXT?
Researchers are using the information from these analyses to inform additional research in carbapenem-resistant pathogens, to design clinical trials using new antibiotics, and to help inform treatment decisions that improve the outcomes of patients.

WHY WAS THIS RESEARCH CONDUCTED? WHAT IS THE RATIONALE?
Carbapenem-resistant Enterobacteriaceae (CRE) is a family of bacteria that resists treatment by a class of antibiotics called carbapenems. The World Health Organization lists CRE as one of the top three drug-resistant pathogens and recognizes CRE as a threat to global public health.

There are many different genes that result in the production of enzymes against carbapenems, called carbapenemases. Enterobacteriaceae that contain at least one of these genes are called carbapenemase-producing Enterobacteriaceae (CPE).

Researchers need to learn more about the characteristics of CRE and how they differ in other regions of the world and in differing patient populations.