**The full title: The Association between Empirical Antibiotic Treatment and Mortality in Severe Infections Caused by Carbapenem-Resistant Gram-Negative Bacteria: A Prospective Study**

[Link is HERE](https://academic.oup.com/cid/advance-article-abstract/doi/10.1093/cid/ciy371/4987600?redirectedFrom=fulltext)\

**Why the paper?**

**Point 1:**

We often wonder whether empiric colistin would have made any difference in term of outcome(s) in patients who have confirmed CRE infection as this was what the paper tried to address.

Additionally, anti-CRE agents that we have so far are either limited in term of their activity against the large family of carbapenamases (i.e. meropenem-varbobactam/ceftazidime-avibactam are active only against certain KPC enzymes) or still in development (aztreonam-avibactam/plazomicin/cefdirocol).

Besides if these agents are to be made available in this country, I believe they should be used prudently by physicians like other broad-spectrum antibiotics.

Thus, this makes colistin (polymixin B) as to-go-to agents for us in CRE infections and answering its use/value in empiric arm would be one of the many conundrums that we have in infectious diseases as well antibiotic stewardship.

**Point 2**

This study was powered to look at the above even when this was only a secondary analysis of AIDA as apposed to a primary analysis (AIDA is a recently published RCT in Lancet ID).

They described the accepted rates for both alpha and beta errors.

(But I am not too clear as to why the reduction was chosen to be at 17%- no citation was made for this)

What we need to be careful with in interpreting this paper?:

Although its title suggests the empirical effect of colistin in CRE GNB infections, majority (77%) of the cases were caused by Acinetobacter baumanii, thus we believe the data extrapolation to other GNB to be somewhat difficult.

**What was the conclusion of this paper?**

Empiric colistin did not reduce the mortality rate in CRE GNB infections (OR rather Acinetobacter baumanii)

The value of external validation/application of this model is interesting.

**The other interesting bit/details**

The authors rightly so avoid the use of RCT term in the article title as the study was not a primary analysis for AIDA. They even performed propensity scoring (PS) to reduce selection bias in an already good study design.

NB. PS made its way to statistics in the year 1983 by both Rosenbaum and Rubin. It is aimed to minimize selection bias associated with a non-RCT study whereby patients assignment to either arm (i.e. this can be more than many arms if the possible assignment is not limited to binary options) may not be equal in term of chance. Failure to address this may lead to biased/wrong parameter (θ) estimates, masking of relationship between variables (e.g. synergy) or worse wrong data interpretation and output.

**Who were recruited in this?**

As this is AIDA cohort, thus the study population was similar.

Seven centers from 3 European countries were involved.

 ○ Italy (1): Monaldi Hospital in Naples;

 ○ Greece (2): Laikon and Attikon Hospitals in Athens;

 ○ Israel (4): Sourasky Medical Center in Tel Aviv, Rabin Medical Center, Beilinson hospital in Petah-Tikva and Rambam Health Care Campus in Haifa.

Included patients needed to be ≥ 18 years of age and

proven to have infections by CRE GNB in any of these 3 sites;

 ○ HAP

 ○ VAP

 ○ UTI

They could only be recruited once in AIDA.

**What were deemed as CRE GNB in this?**

They were;

 ○ *Acinetobacter baumannii,*

 *○ Pseudomonas aeruginosa* or

 ○ any Enterobacteriaceae

**How long was the time window allowed for colistin commencement for it to be considered as part of**

**empiric regimen in this?**

< 48 hours

**An important question into how colistin susceptibility was tested.**

Interestingly, E-test was used to test for this except in one center (Greece), whereby the investigators performed BMD in addition when the colistin MIC via E-test was ≥1 mg/L.

(Colistin E-test is unreliable due to its adherence onto many types of surfaces. Interested readers can find more info on the issue via this LINK)