

### Reviewer #1:

Specific Comments to Authors: I thank the authors for their paper and work. It was quite an interesting read. There are a few concerns that need to be corrected:

1. Bacteria names should always be written in Italics.
2. It should be third-line antibiotic or first-line antibiotic in the introduction.
3. In table 1 -> there should be footnote for explanation of "focus of infection"
4. The authors have left out many countries in the table regarding AMR rates -> Latvia (PMID: 34209766); Chile (PMID: 32973892); France, Sweden, Norway etc., and GBD studies have been left out. Data from GBD databases would have enriched the study ([https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)02724-0/fulltext](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)02724-0/fulltext))
5. Authors didn't discuss WHO Global Action Plan on antimicrobial resistance (<https://www.who.int/publications/i/item/9789241509763>).
6. To call it Global Burden in the title -> authors need to more extensively search for local databases or international databases as mentioned above.

### Answering Reviewer #1:

1. All the bacteria names have been rewritten in italics and underlined in yellow. See lines 84,85,110,111,112,115,140,145,186,192,196,197,198,199,203,204,205,208,210,211,213,215,220,228,230, 231,234,236,238,239,275,282,299,392, and column "Pathogen" of the three tables.
2. Thank you for the suggestion. Since this point in the text may be unclear to the reader, we reformulated the sentence to make it more understandable. We specified that "Carbapenems are the third most widely used class of antibiotics worldwide for community-acquired infections in ICU (10.7%) and the first class for hospital-acquired infections (21.5%)" See lines 91-93
3. We replaced in the three tables the term "focus" with "site" of infection to make it more understandable. We also added a footnote to explain the abbreviations used in the "site of infection" column. See lines 240,241,242,244,245,246,247,249,250,251,252.
4. Many thank for your suggestion to enrich the study with data from other studies and GBD databases. We added two new studies: one related to French Guiana (See table 1 and reference [60]) and another to Greece (See table 3 and reference [107]).

We found the two suggested studies - Latvia (PMID: 34209766); and Chile (PMID: 32973892) - very interesting from an epidemiological point of view. Unfortunately, the authors of these mentioned studies aggregated data from different medical wards. Our study focuses only on the Intensive Care Units. We added in the discussion reference and commented on the differences between our study and the previous published on the global burden of antimicrobial resistance: "To our knowledge, this is the first comprehensive review of the global of severe infections due to carbapenem-resistant pathogens focusing on Intensive care units, as well as an evaluation of the limited availability of data. Previous reports focused on the overall antimicrobial resistance

aggregating data from different inpatient wards and not exclusively from Intensive Care Unit" (See lines 434-439).

5. We discussed the WHO Global Action Plan on antimicrobial resistance as suggested. See lines 426-429.

6. We added the section "Methods" in which we submit that we consulted PubMed to search for the epidemiological data of the various countries. See lines 99-107.

#### Reviewer #2:

Specific Comments to Authors: This article reviews the global burden of severe infections caused by carbapenem resistant pathogens in intensive care units. This article has certain clinical significance, but it is not innovative enough. There have been relevant international reports, and the author needs to highlight the characteristics of this article

#### Answering Reviewer #2:

Many thanks for your suggestion, we highlighted the characteristics of our review "To our knowledge, this is the first comprehensive review of the global of severe infections due to carbapenem-resistant pathogens focusing on Intensive care units, as well as an evaluation of the limited availability of data. Previous reports focused on the overall antimicrobial resistance aggregating data from different inpatient wards and not exclusively from Intensive Care Unit" (See lines 433-438).