

# A Machine Augmented Systematic Literature Review: Prevalence of Coinfections in COVID-19 Patients during Early and Late Pandemic Periods

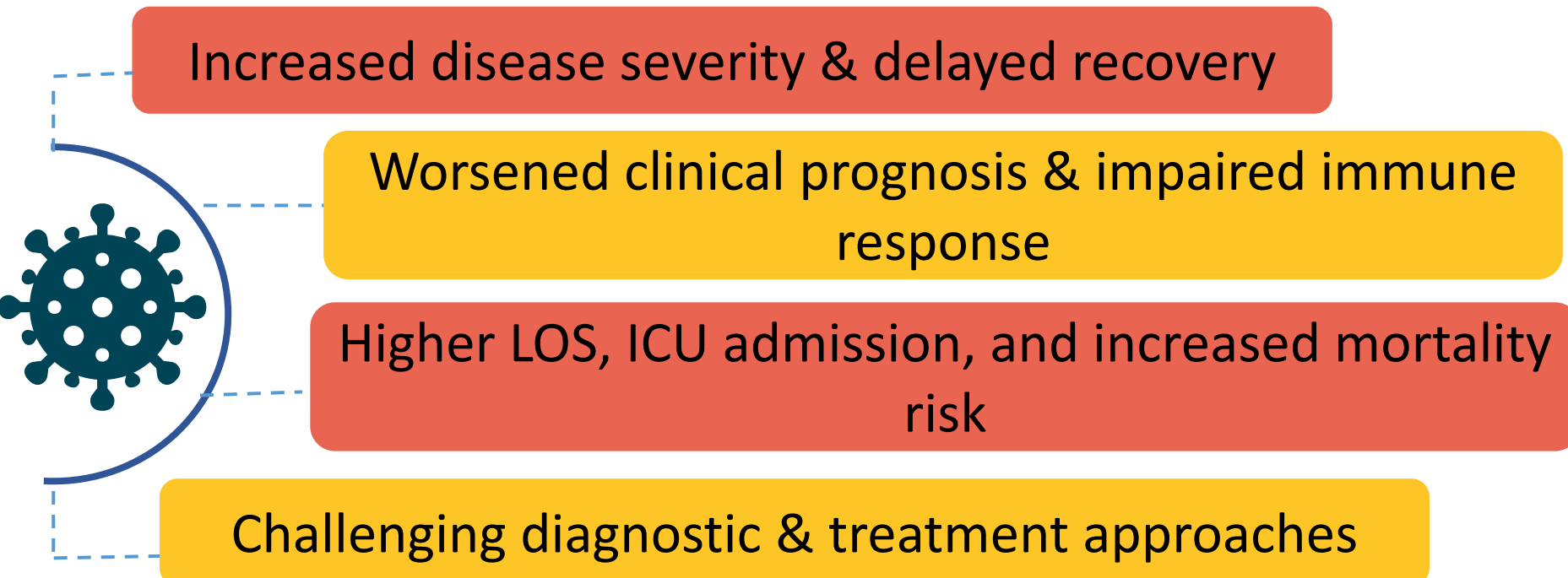
Patel D<sup>a</sup>, Chhaya V<sup>a</sup>, Patel R<sup>a</sup>, Khambholja K<sup>a,b</sup>

<sup>a</sup>Genpro Research Pvt Ltd, Gujarat, India, <sup>b</sup>Genpro Research Inc., Boston, USA

## INTRODUCTION

- As of 2023, COVID-19 remains to be **leading cause of hospitalization and deaths** due to infections, globally.<sup>1</sup>
- The disease burden and mortality risk are further elevated due to **coinfections** with other respiratory pathogens. Recognized as major concern among healthcare professionals.<sup>2</sup>
- Contributing or responsible factors for coinfection involve **prolonged hospital stays** (especially in ICU), **advanced age**, **male gender**, **organ failure** and other **immunocompromising factors**.

### Impact of Coinfections:



- The prevalence of coinfections in COVID-19 patients have been uncertain or less explored, especially during the early stages of pandemic.

### Research Gaps:

- No consistent definition of coinfections** existing leading to overlapping of assessment with secondary infection led to over or underestimate of prevalence during early phases of pandemic.<sup>3</sup>
- Varying prevalence data** on COVID-19 coinfection epidemiology in early pandemic period.
- Advent of **sub variants of SARS-CoV-2** and new waves of COVID-19 pandemic may impact the existing understanding of coinfections.

Need for **robust epidemiological evidence** evaluating the varying coinfection prevalence among early and late pandemic periods.

- Objectives:** To compare the coinfection prevalence in COVID-19 patients from early and late pandemic periods and its impact on hospitalization and mortality.

## METHOD

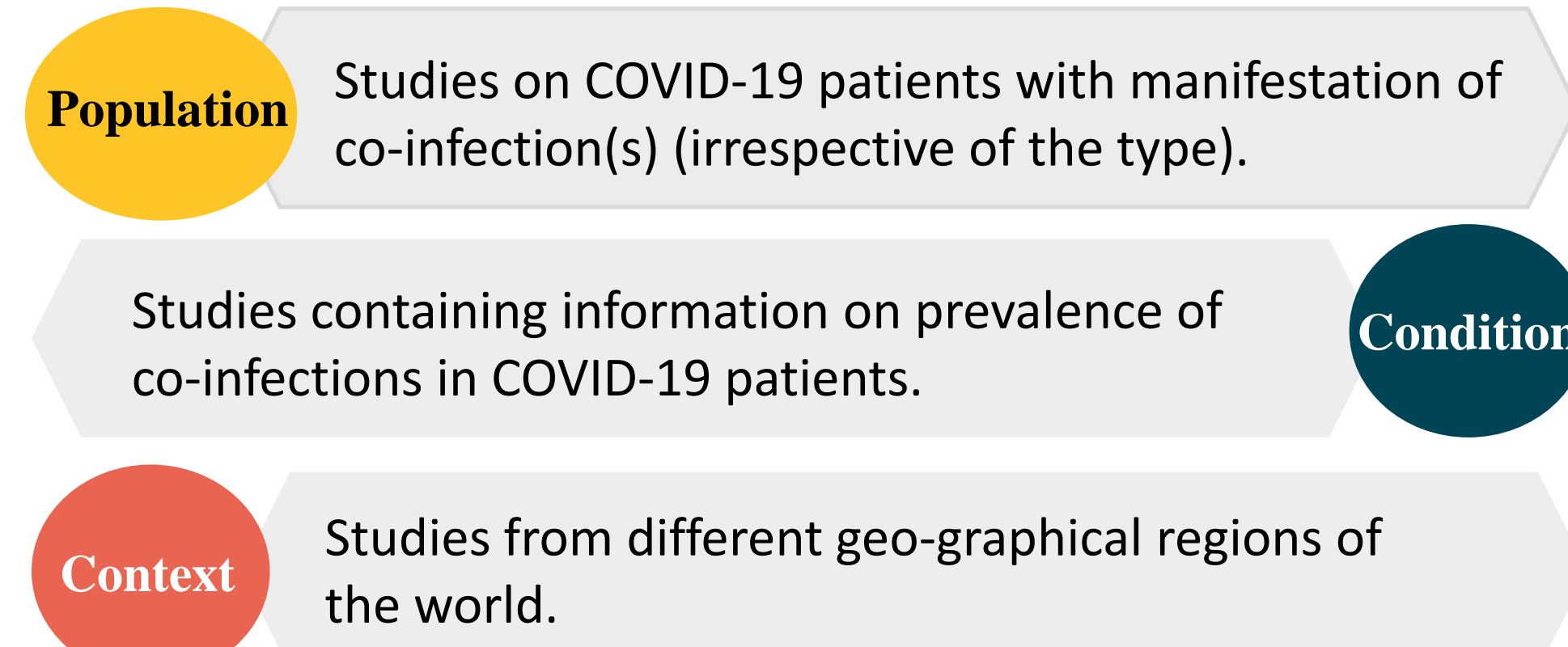
- This epidemiological systematic review was conducted with support of Genpro's proprietary platform for evidence synthesis named **MaiA**.



### Eligibility Criteria:

Inclusion	Exclusion
<ul style="list-style-type: none"> <li>Study type: Prospective and retrospective observational study, case series, systematic reviews, cross-sectional study</li> <li>Studies on coinfections, detected within 48-72 hours of hospital admission</li> </ul>	<ul style="list-style-type: none"> <li>Study type: Case report, review, pre-print, letter or commentary article</li> <li>Studies not in English language</li> </ul>

- Study retrieval and selection based on **CoCoPop** (Condition, Context, Population) framework.



- A subgroup analysis was performed based on the coinfecting pathogen (bacterial, viral, or fungal).

- Data from studies were distributed among two groups –

**Early Pandemic period:** Studies from **Dec2019 to May2021**

**Late Pandemic Period:** Studies from **Jun2021 to Dec2022**

- Risk of bias (RoB) among the included studies was assessed using JBI critical appraisal tools.

## RESULT

- Of 2486 retrieved articles, the review included a total of 72 articles.

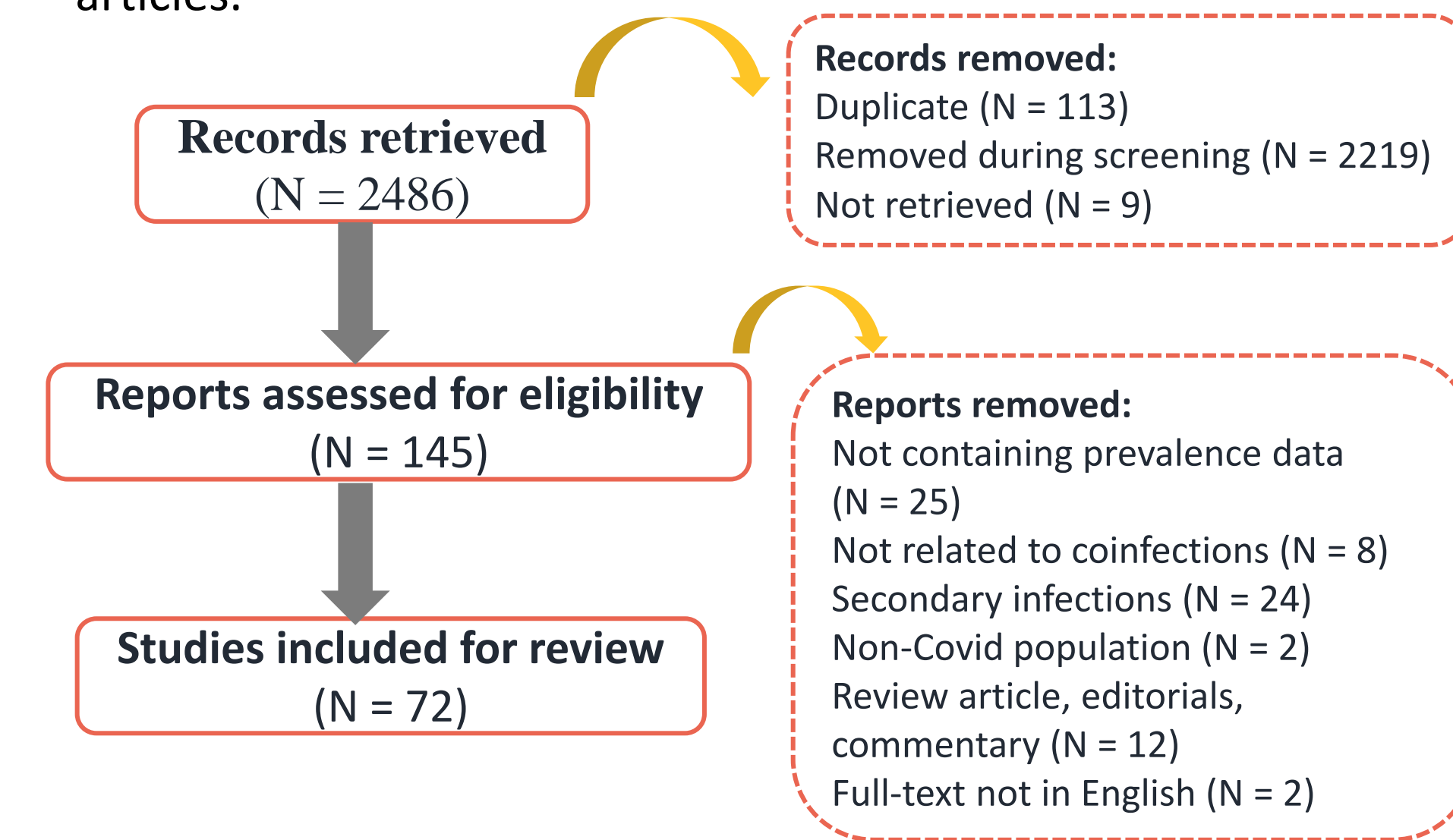


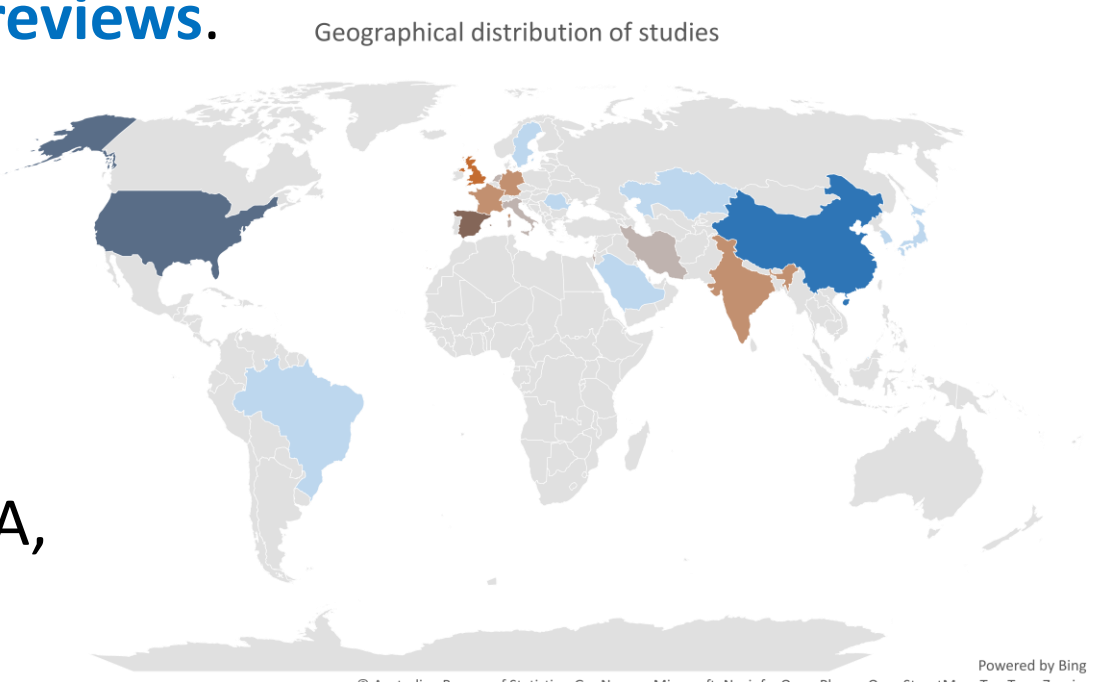
Figure 1: PRISMA flow diagram for SLR

### Report characteristics

- Of 72 included studies - there were **53 observational studies** and **19 systematic literature reviews**.

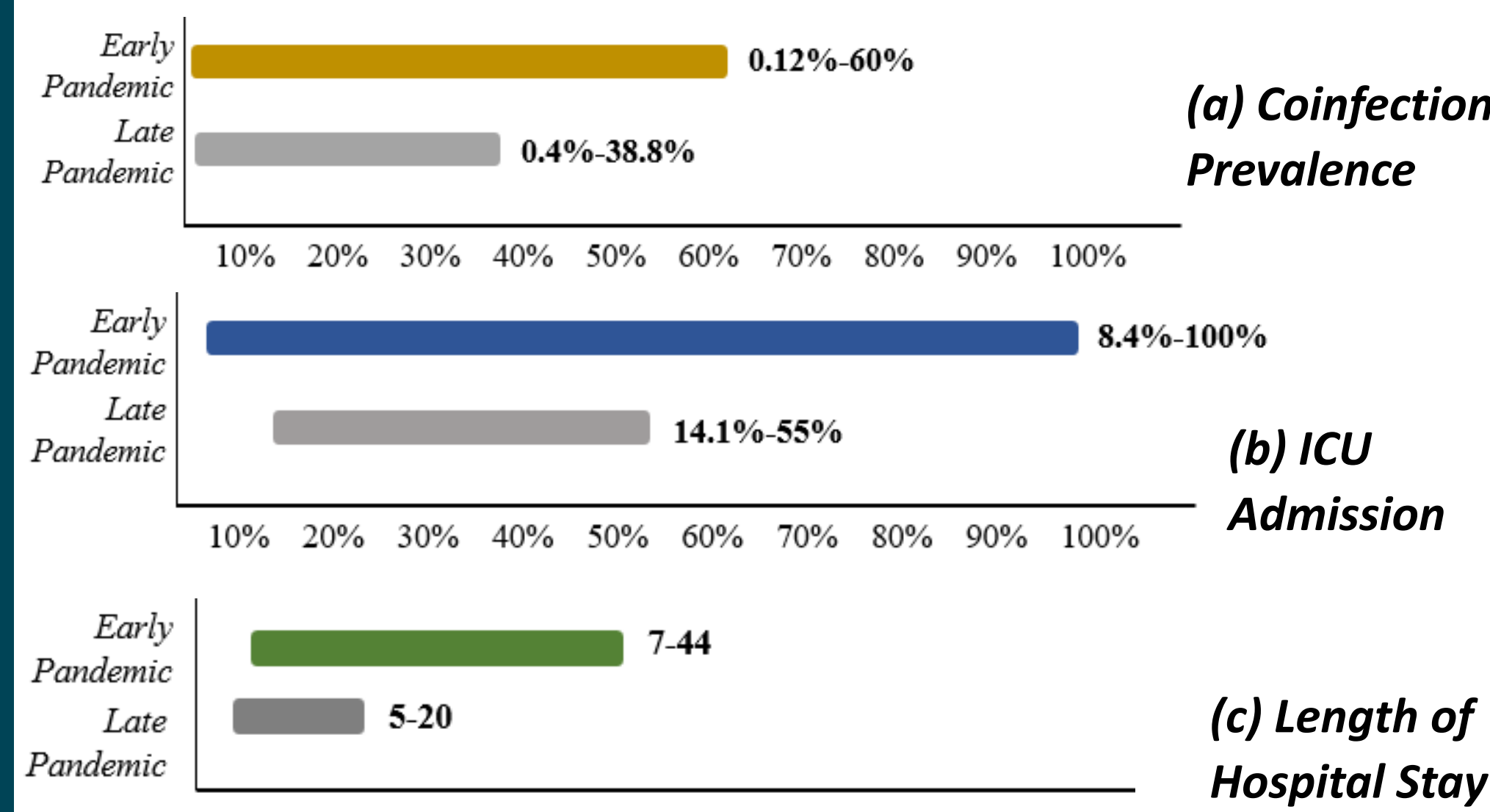
### Geographic distribution:

- 20 global studies,
- 18 from Europe,
- 15 from Asia, 7 from USA,
- 11 from other regions

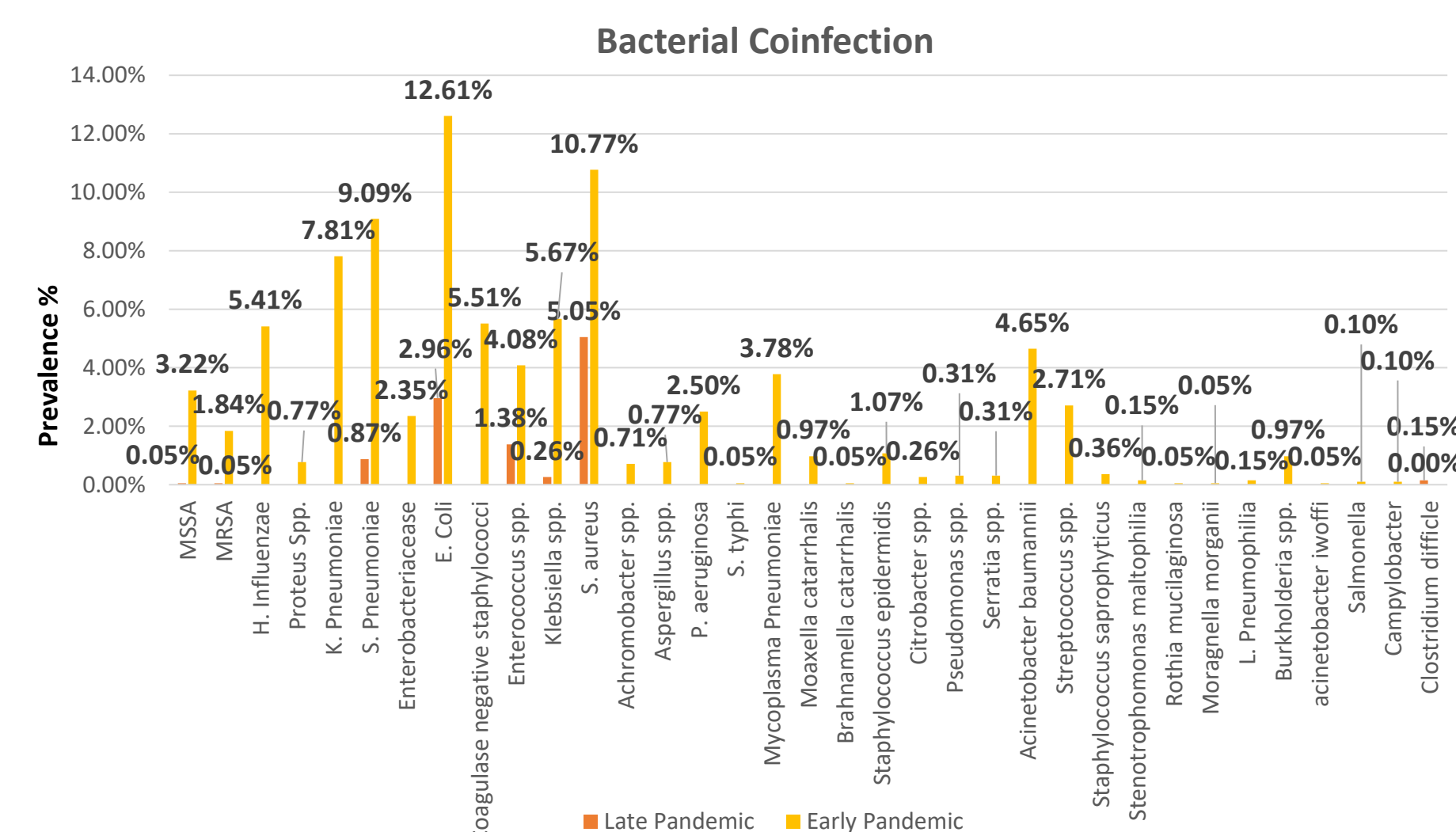


### Epidemiological characteristics in Early and Late Pandemic Periods

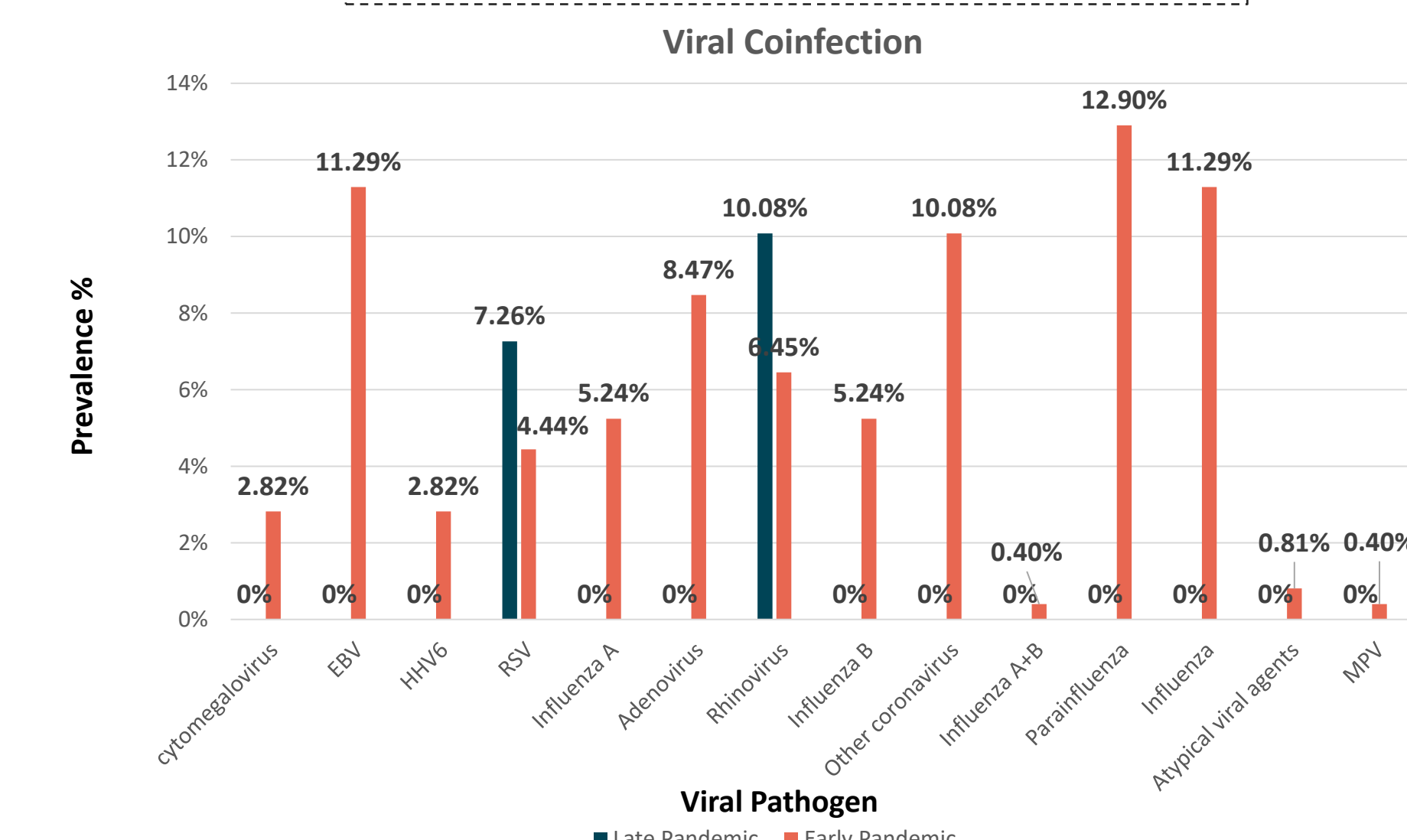
- A decreasing trend observed for coinfections prevalence, ICU admission rate, and length of hospital stay from Early to late pandemic period.



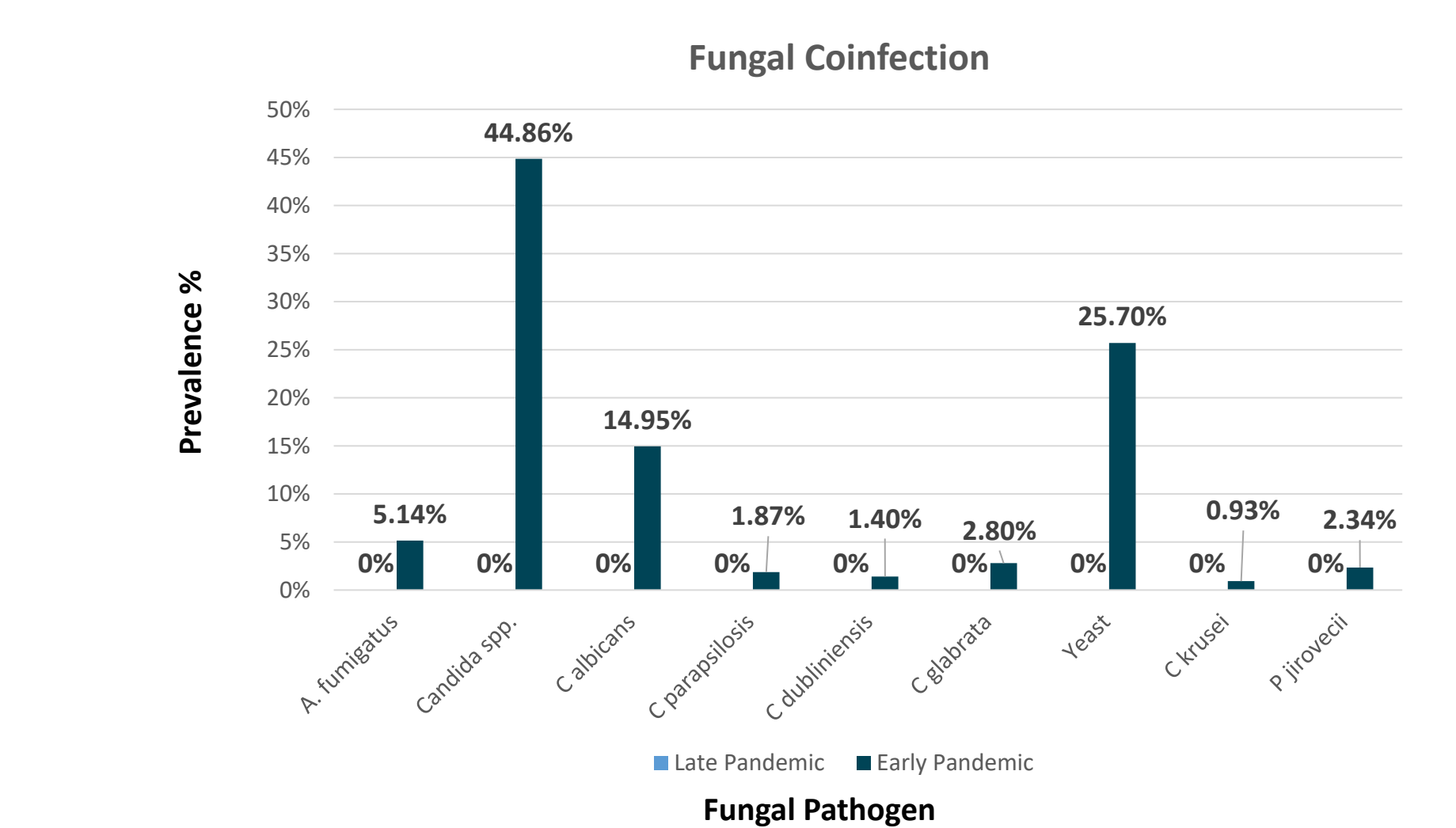
### Pathogen-wise distribution



### (a) Prevalence of Bacterial Coinfection

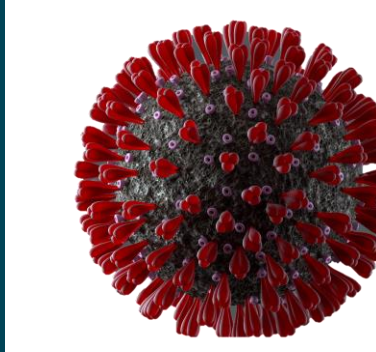


### (b) Prevalence of Viral Coinfection



### (c) Prevalence of Fungal Coinfection

- The highest mortality rate in coinfecting COVID-19 patients was **87% in early pandemic** whereas it was **67.8% during late pandemic period**.
- Risk factors:** Among the included articles, **older age** and **male gender** were found to have higher prevalence compared to population of younger age and females.
- The most common comorbidities among coinfecting patients (overall) were diabetes mellitus, hypertension, cardiovascular diseases, chronic respiratory disorders, and malignancy(ies).



- Impact of variants:** One observational study determined impact of variants (**Alpha, Delta, Omicron**) the in-hospital mortality was found to be independent of SARS-CoV-2 sub variants.
- None of the included SLRs investigated COVID-19 sub-variants and coinfection burden.

### Quality assessment

- Study design and statistical analysis-based requirements were majorly fulfilled by the included studies. 31 of 49 observational studies did not identify confounding factors. Among SLRs, 6 of 17 studies did not assess publication bias and 2 studies did not present recommendations for policy and practice.

## DISCUSSION & CONCLUSION

- A downward/decreasing trend observed in coinfections prevalence from early to late pandemic period.
- The lower coinfection rate in late pandemic period can be attributed to effective vaccination strategies and improved diagnostic and management approaches.
- Efficiently conducted review in shorter timeframe and high-quality, using AI-integrated tool **MaiA** for end-to-end process (literature search to manuscript finalization).
- Recommendations:
  - Coinfection definition used inconsistently in previous reviews - need for implementation of **strict coinfection definition** to avoid overlap with secondary infections.
  - Lack of paediatric studies - **collaborative efforts** required from paediatricians, infection specialists, epidemiologists, and researchers.
  - Continual **surveillance**, early and accurate **diagnostic approach**, and appropriate **monitoring strategies** to rule out coinfections earlier during infection.
  - Effective **microbiological investigations** to curate proper antibiotic regimen
  - Robust **reporting practices** at patient and hospital levels to reinforce infection control practices.
  - Efforts required to carry out **large-scale epidemiological studies** to determine the disease burden of COVID-19, with focus on LMICs.
  - Researchers, clinicians, and industry could collaboratively work and to improve vigilance towards co-infections and lay strategies for its management of COVID-19 patients with coinfections.
  - Rigorous **antibiotic stewardship programs** assessing coinfections prevalence is recommended.

## REFERENCES

- Pifarré AH, et al. Years of life lost to COVID-19 in 81 countries. Sci Rep. 2021 Feb 18;11(1):3504.
- Alshaikh FS, et al. Prevalence of bacterial coinfection and patterns of antibiotics prescribing in patients with COVID-19: A systematic review and meta-analysis. PLoS One. 2022;17(8):e0272375.
- Van LJ, et al. Beyond Guidelines and Reports on Bacterial Co-/Superinfections in the Context of COVID-19: Why Uniformity Matters. Antibiotics (Basel). 2022 Oct 20;11(10):1446.

## CONTACT

Email : [Mw.info@genproresearch.com](mailto:Mw.info@genproresearch.com)  
Website : [www.genproresearch.com](http://www.genproresearch.com)