# Série dos Seminários de Acompanhamento à Pesquisa

## Prescrição e padrões de uso de antibióticos por pacientes infectados e não infectados com COVID-19

Autora:

Bianca Brandão de Paula Antunes

PUC
RIO

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# Apresentação pessoal

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- **Curso**: Doutorado

- **Período**: 4º

- **Orientador**: Silvio Hamacher

- **Co-orientador**: Fernando Bozza (Fiocruz/IDOR)

- **Área de concentração**: Pesquisa Operacional

- **Linha de pesquisa**: Métodos estatísticos e *analytics*

- **Tema da tese:** Análise do uso de antibióticos e do perfil microbiológico de pacientes internados em UTIs antes e durante a pandemia de COVID-19

# Apresentação pessoal

- **Mestrado** no DEI

- **Título da dissertação:** ICU efficiency assessment using Data Envelopment Analysis

- **Breve resumo**: Avaliação de 93 UTIs brasileiras utilizando Análise Envoltória de Dados (**DEA**) - modelo de programação linear que calcula a eficiência de uma unidade em comparação ao conjunto. Os outputs observados foram **SMR** e **SRU** (mortalidade e uso de recursos ajustados pela gravidade do paciente). Os inputs utilizados eram relacionados à **equipe médica**, **estrutura** e **capacidade** das UTIs.

# Apresentação pessoal

**Artigos publicados:**

- PERES, IGOR TONA ; BASTOS, LEONARDO DOS SANTOS LOURENÇO ; MAYRINCK GELLI, JOÃO GABRIEL ; MARCHESI, JANAINA FIGUEIRA ; DANTAS, LEILA FIGUEIREDO ; ANTUNES, BIANCA BRANDÃO DE PAULA ; MAÇAIRA, PAULA MEDINA ; BAIÃO, FERNANDA ARAÚJO ; HAMACHER, SILVIO ; BOZZA, FERNANDO AUGUSTO . **Sociodemographic factors associated with COVID-19 in-hospital mortality in Brazil**. PUBLIC HEALTH, v. -, p. -, 2021.

- ANTUNES, B. B. P.; PERES, I. T. ; BAIAO, F. A. ; RANZANI, O. T. ; BASTOS, L. S. L. ; SILVA, A. A. B. ; SOUZA, G. F. G. ; MARCHESI, J. F. ; DANTAS, L. F. ; VARGAS, S. A. ; MACAIRA, P. ; HAMACHER, S. ; BOZZA, F. A. . **Progression of confirmed COVID-19 cases after the implementation of control measures. REVISTA BRASILEIRA DE TERAPIA INTENSIVA**, v. XX, p. XX, 2020.

- PRADO, M. F. ; ANTUNES, B. B. P. ; BASTOS, L. S. L. ; PERES, I. T. ; SILVA, A. A. B. ; DANTAS, L. F. ; BAIAO, F. A. ; MACAIRA, P. ; HAMACHER, S. ; BOZZA, F. A. . **Analysis of COVID-19 under-reporting in Brazil. REVISTA BRASILEIRA DE TERAPIA INTENSIVA**, v. 00, p. 00, 2020.

- ANTUNES, B. B. P.; MANRESA, A. ; BASTOS, L. S. L. ; MARCHESI, J. F. ; HAMACHER, S. . **A solution framework based on process mining, optimization and discrete-event simulation to improve queue performance in an emergency department.** In: **International Conference on Business Process Management (BPM),** 2019, Viena, Áustria. Proceedings of the PODS4H 2019 - Process-Oriented Data Science for Healthcare, 2019.

- GELLI, J. G. M. ; ANTUNES, B. B. P. ; MANRESA, A. ; PESSOA, L. . **Minimização do tempo total de fluxo no problema de blocking flowshop com uso de GRASP reativo.** In: LI Simpósio Brasileiro de Pesquisa Operacional, 2019, Limeira, SP. Anais do **SBPO** 2019, 2019.

**Artigos em revisão:**

- ANTUNES, B.B.P; BASTOS, L.S.L; HAMACHER, S.; BOZZA, F. **Using data envelopment analysis to perform benchmarking in intensive care units. Plos One.**

- CUNHA, L.; ANTUNES, B., RODRIGUES, V., CERYNO, P., LEIRAS, A. **Measuring the impact of donations at the Bottom of the Pyramid (BoP) amid the COVID-19 pandemic. Annals of Operations Research.**
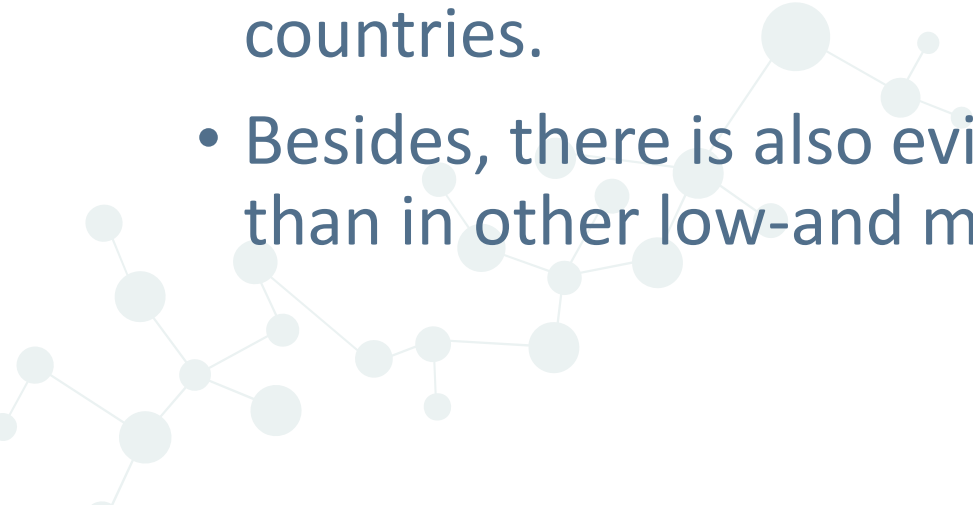
**Artigos em produção:**

- Análise de efetividade da vacinação contra a COVID-19 na Maré.

- Antibiotic prescription and drug use patterns among COVID-19 infected and non-infected patients.

- Comparação do perfil microbiológico de pacientes de UTI antes e durante a pandemia
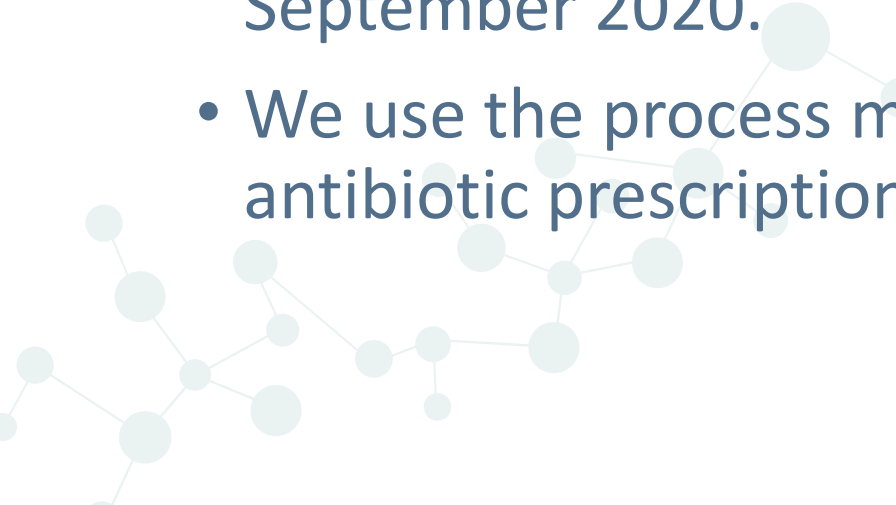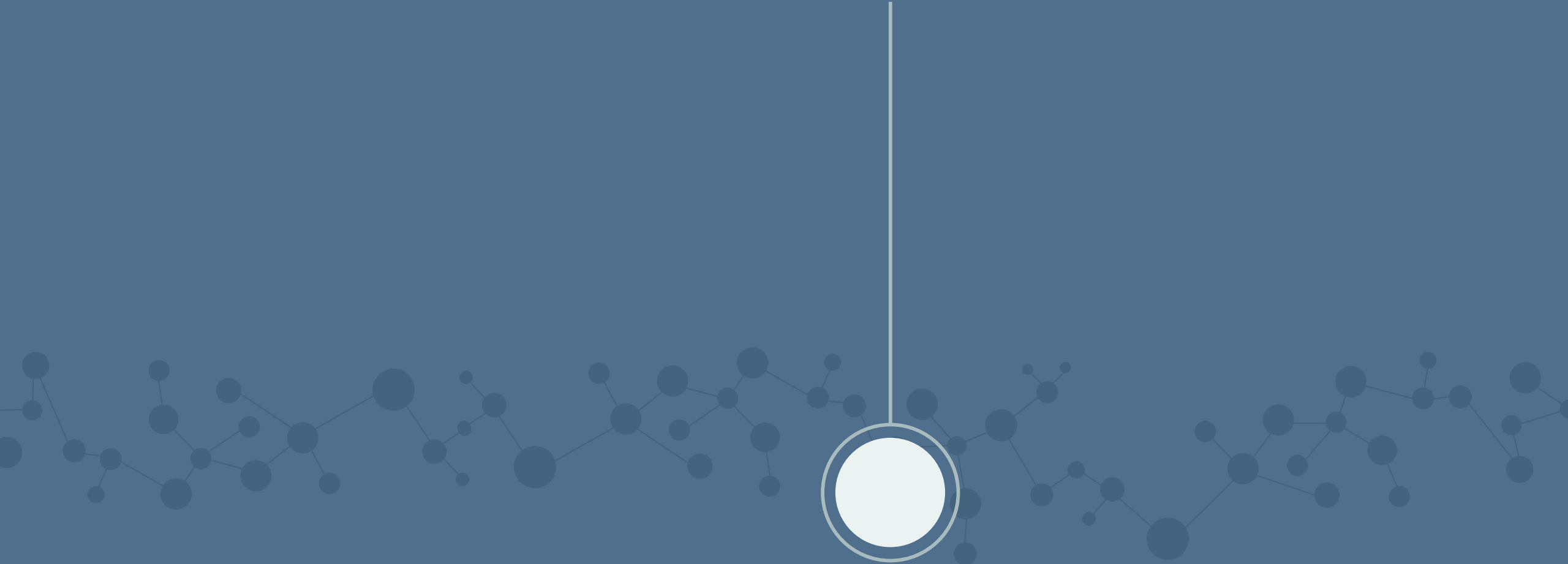
Apresentação do artigo

# Introduction

- The focus on reducing the spread and burden of COVID-19 may cause **unnecessary use of antibiotics**.

- These changes can **increase antimicrobial resistance**, especially in the acute care setting.

- In Brazil, the scenario is even more concerning, as ICU-acquired infections are more common than in the USA and European countries.

- Besides, there is also evidence of **higher use of antibiotics in Brazil** than in other low-and middle-income countries.

# Introduction

- Although it has been reported that there was an increase in the prescription of broad-spectrum antimicrobials, there is still a need to gather evidence to support guidelines concerning the COVID-19 pandemic;

- We aim to describe the clinical characteristics and antibiotic use of 83,964 patients over their stay in Brazilian ICUs from January 2018 to September 2020.

- We use the process mining technique to analyze the patterns of antibiotic prescriptions in COVID-19 infected patients.

# Methods

Primary outcomes

**Defined Daily Dose** (DDD): total grams of an antibiotic administered to a patient at a given time, divided by a reference value

**Days of Treatment** (DOT): number of days in which the antibiotic was administered to a patient

# Results

Table 1 - Clinical characteristics, outcomes, and antibiotic consumption of 83,964 patients divided into COVID-19 infected and non-infected groups

| Characteristic | non-COVID-19, N = 80,724 | COVID-19, N = 3,240 |
|---|---|---|
| Age, Median (IQR) | 66 (49, 80) | 61 (48, 76) |
| <40 | 12,280 (15%) | 390 (12%) |
| 40-49 | 8,653 (11%) | 498 (15%) |
| 50-59 | 10,303 (13%) | 614 (19%) |
| 60-69 | 13,662 (17%) | 602 (19%) |
| 70-79 | 14,791 (18%) | 515 (16%) |
| >=80 | 21,035 (26%) | 621 (19%) |
| Gender | | |
| F | 42,693 (53%) | 1,283 (40%) |
| M | 38,031 (47%) | 1,957 (60%) |
| Admission Source | | |
| Emergency Department | 53,649 (66%) | 2,341 (72%) |
| Surgical Ward | 15,453 (19%) | 23 (0.7%) |
| Medical Ward/Room | 2,925 (3.6%) | 144 (4.4%) |
| Other Locations | 8,697 (11%) | 732 (23%) |
| Modified Frailty Index (MFI) | | |
| Mean (SD) | 1.51 (1.37) | 1.42 (1.34) |
| Median (IQR) | 1 (0, 2) | 1 (0, 2) |
| Non-frail (MFI = 0) | 22,764 (28%) | 1,007 (31%) |
| Pre-frail (MFI = 1-2) | 40,579 (50%) | 1,614 (50%) |
| Frail (MFI >= 3) | 17,381 (22%) | 619 (19%) |
| SAPS-3, Median (IQR) | 42 (34, 51) | 47 (41, 57) |
| Advanced Ventilatory Support | 9,954 (12%) | 1,353 (42%) |
| IMV | 6,292 (7.8%) | 1,039 (32%) |
| NIRS | 3,662 (4.5%) | 314 (9.7%) |
| Vasopressor | 5,654 (7.0%) | 778 (24%) |
| Renal Replacement Therapy | 2,789 (3.5%) | 407 (13%) |
| LOS | | |
| ICU | 3 (1, 5) | 6 (3, 13) |
| Hospital | 5 (3, 11) | 10 (6, 19) |
| LOS > 7 days | | |
| ICU | 14,257 (18%) | 1,400 (43%) |
| Hospital | 29,868 (37%) | 2,037 (63%) |
| Mortality | | |
| ICU | 4,293 (5.3%) | 597 (18%) |
| Hospital | 5,859 (7.3%) | 716 (22%) |
| Use of antibiotics | 33,823 (42%) | 2,265 (70%) |
| DDD/1000 patient-days | 810 | 1364 |
| Discharge | 692 | 1201 |
| Death | 1221 | 1696 |
| DOT/1000 patient-days | 561 | 984 |
| Discharge | 492 | 850 |
| Death | 802 | 1257 |

| ATC5 Code | Name | DDD/1000 patient days | | DOT/1000 patient days | |
|---|---|---|---|---|---|
| | | Non-COVID-19 | COVID-19 | Non-COVID-19 | COVID-19 |
| J01DH02 | Meropenem | 88 | 204 | 67 | 144 |
| J01FA10 | Azithromycin | 76 | 200 | 37 | 98 |
| J01CR05 | Piperacillin with ß-Lactam Inhibitor | 93 | 176 | 101 | 179 |
| J01DD04 | Ceftriaxone | 31 | 144 | 15 | 72 |
| J01XA02 | Teicoplanin | 39 | 125 | 26 | 78 |
| J01CR02 | Amoxicillin with ß-Lactam Inhibitor | 58 | 120 | 41 | 77 |
| J01AA12 | Tigecycline | 52 | 78 | 19 | 25 |
| J01GB06 | Amikacin | 23 | 63 | 15 | 55 |
| J01DD02 | Ceftazidime | 31 | 53 | 16 | 27 |
| J01FA01 | Erythromycin | 40 | 36 | 13 | 11 |
| J02AX05 | Micafungin | 9 | 25 | 5 | 14 |

# Results

Table 2 – Antibiotic consumption in DDD and DOT per 1000 patient-days, ordered by greater COVID-19 patients' DDD. We represented the eleven antibiotics (ATC code 5th level) that accounted for 90% of the antibiotic consumption of COVID-19 patients, in terms of DDD.
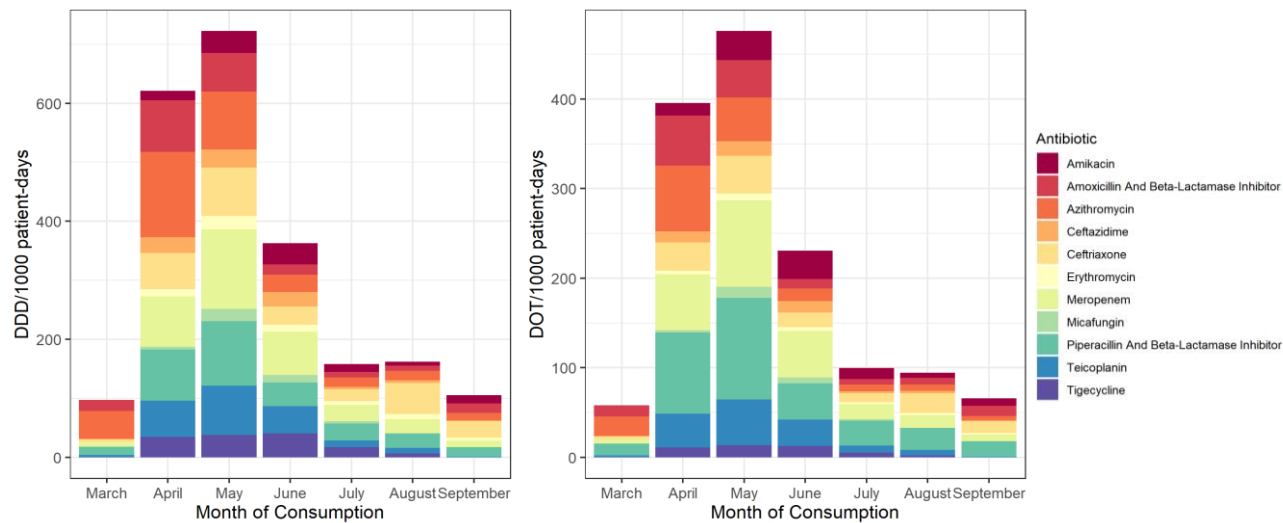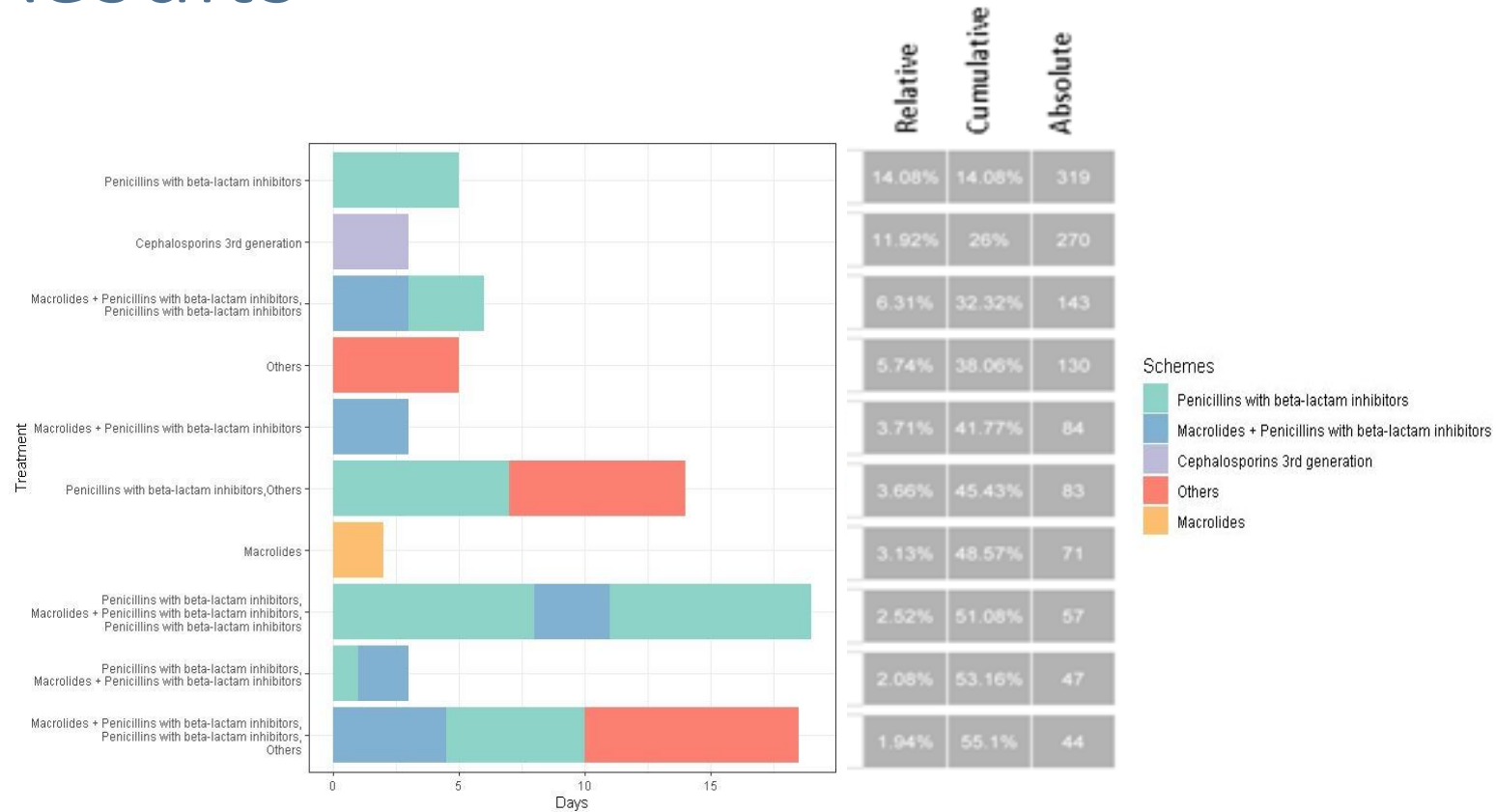
# Results



Figure 1 - Antibiotic consumption by COVID-19 patients in DDD (left) and DOT (right) per 1000 patient-days per month. The eleven antibiotics shown represent 90% of the antibiotic consumption of the COVID-19 patients.

- Higher use of antibiotics in the **first months of the pandemic** in Brazil;
- May was also the month with the **highest occupancy rate** (81%) in the analyzed period.

# Results



Figure 2 – Top 10 most frequent treatments of COVID-19 patients that had an outcome. The size of the bars represents the median duration of each scheme within that treatment. The scheme is the combination of classes (ATC 4th level) taken by the patient on the same day. The columns are the number of patients that followed that treatment (percentage of the total, cumulative percentage, and absolute).

- There was a total of 359 distinct treatments.
- Of the ten most frequent treatments, six lasted less than five days.
- **Penicillins with ß-lactamase** were present in six of the ten most frequent treatments
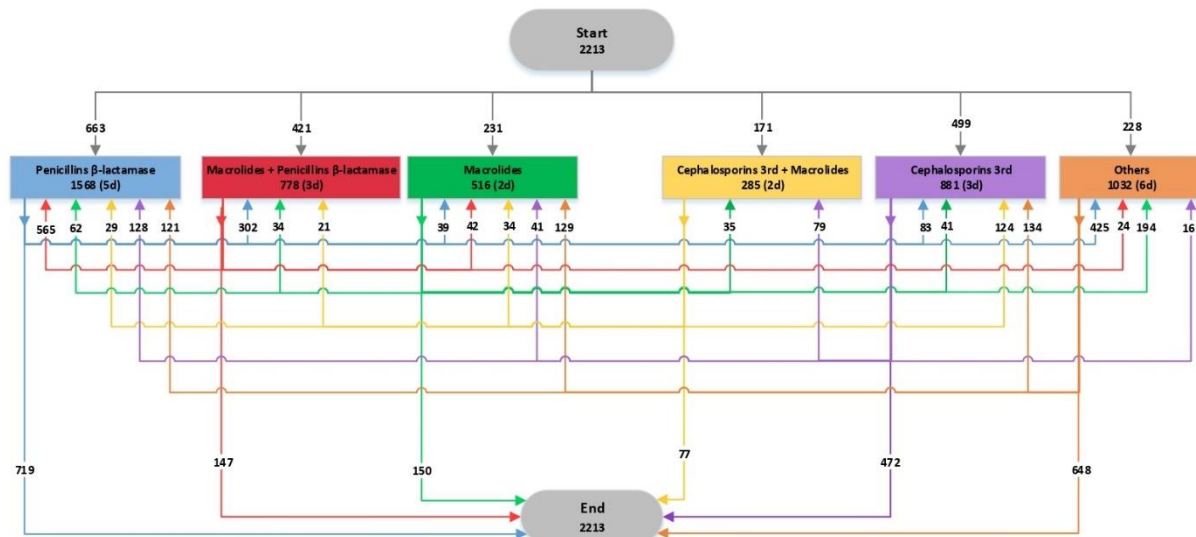
# Results



Figure 3 – Order and frequency of use of the schemes consumed by 97% of the COVID-19 patients that had an outcome and used antibiotics, resulting in 2,213 patients. The scheme is the combination of classes (ATC 4th level) taken by the patient on the same day. The numbers in parentheses are the median duration (in days) of use of that scheme. The numbers in the arrows represent the number of treatments that followed the use of schemes in that order.

- We observed **high variability** in the treatments prescribed to COVID-19 patients.

- Most of the treatments started with **penicillins with ß-lactamase inhibitors** (30%, 663), third-generation cephalosporins (22%, 499), or macrolides in combination with the penicillins (19%, 421).

- Overall, the duration of the antibiotic treatments was on average **9.5 days**.

# Discussion and conclusion

- The proportion of COVID-19 infected patients that used antibiotics in our research (70%) was similar to the number found by Rawson et al. (72%), which reviewed 18 other works.

- One of the hypotheses for the higher use of antibiotics is that the experience with superinfection in influenza has caused the growth, even though there has been no evidence of high levels of co-infection in COVID-19 patients.

- The higher proportion of patients that are mechanically ventilated can also justify the increase in antibiotic consumption.

- The uncertainties regarding the new virus and the lack of antiviral treatments might explain the higher level of antibiotic prescription during the second and third months of the epidemic in Brazil.

# Próximos passos

- Submeter este artigo;

- Fazer análise semelhante para comparar o perfil microbiológico de pacientes sem e com COVID-19;

- Cruzar as duas informações para identificar se o uso de antibióticos durante a pandemia foi condizente com o perfil microbiológico dos pacientes;

- Finalizar os outros artigos em produção/revisão.