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1 **Decrease of hospital- and community-acquired bloodstream infections due to**
2 ***Streptococcus pneumoniae* and *Streptococcus pyogenes* during the first year of the**
3 **COVID-19 pandemic: a time-series analysis in Paris region**

4

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21 Hôpitaux de Paris' are given at the end of the article

22

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25

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27 infection incidence

28 **Competing interests:** The authors declare that they have no competing interests.

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32 **HIGHLIGHTS**

- 33 • The impact of the COVID-19 pandemic on invasive infections due to *Streptococcus*
34 *pneumoniae* and *Streptococcus pyogenes* was assessed in a group of 25 university hospitals of
35 Paris area.
- 36 • Monthly bloodstream infections incidence rates decreased for the two pathogens during
37 the two COVID-19 lockdown periods of 2020 after 2018 and 2019 steady states.
- 38 • Containment policies, including social distancing, masking and hand hygiene
39 strengthening in the community and the hospital settings are likely to reduce bloodstream
40 infections due to these pathogens.

41

42 **MAIN TEXT**

43 During the COVID-19 pandemic, several containment measures have been implemented to
44 limit the spread of the virus. The diversity of these measures has been previously described and
45 their impact on the COVID-19 pandemic have been largely commented [1]. Nevertheless, data
46 on the collateral effects [2] on such large containment measures on the transmission of
47 pathogens other than the one causing the pandemic should be further analyzed.

48 Measures adopted to mitigate the COVID-19 pandemic, i.e., masking, social distancing, and
49 strengthening of hand hygiene, are also those implemented in hospitals and in the community
50 to control pathogens with droplet transmission. *Streptococcus pneumoniae* and *Streptococcus*
51 *pyogenes* are pathogens with nasopharyngeal carriage and known to be mainly transmitted via
52 droplets. Both have the ability to cause invasive diseases, including bloodstream infections
53 (BSIs) [3,4]. Hence, COVID-19 prevention could favorably impact the epidemiology of these
54 infections.

55 On the opposite, coughing during COVID-19 infection worsened the spread of those bacteria
56 and super-infections are reported in COVID-19 patients, particularly with *S. pneumoniae* [5].

57 In addition, inpatients accumulate risk factors for hospital-acquired infections (invasive support
58 and monitoring, corticosteroid therapy) [6]. Therefore, we sought to analyze the impact of the
59 COVID-19 pandemic on the epidemiology of BSIs due to *S. pneumoniae* and *S. pyogenes* in a
60 large public multihospital institution in the Paris region.

61
62 Assistance Publique - Hôpitaux de Paris (APHP) is a consortium of 37 university-hospitals
63 (20,000 beds) covering the Paris region (12 million inhabitants). This work was conducted in a
64 subgroup of 25 hospitals (70% of the beds) using the same laboratory information system (LIS),
65 allowing standardized data extraction of BSIs. The study covers 2020, the first year of COVID-
66 19 pandemic and, as control, the years 2018 and 2019. A blood culture set (BC set) was defined
67 as the combination of one aerobic and one anaerobic blood culture bottles drawn through the
68 same puncture. Only the first BSI episode with the same microorganism for a given patient was
69 included in the study when several BC sets were positive. Blood cultures drawn in the first two
70 days of admission were considered community-acquired and those >48 hours after admission,
71 hospital-acquired. All laboratories participate in the national accreditation process “COFRAC”
72 with internal and external quality controls and use the EUCAST European quality standards for
73 drug susceptibility testing.

74 Time-series modelling was used to quantify changes in incidence rates of BSIs during 2018 and
75 2019. The model was calculated with a linear trend and seasonal components to account for
76 possible changes in the incidence over time, independent of the pandemic. The predicted values
77 for 2020 were calculated with 95% prediction intervals. The validity of the model was tested
78 with Durbin-Watson and Shapiro-Wilk normality tests. All BSIs data were extracted
79 anonymously following current French rules.

80 We observed a global decrease of BSIs incidence rates in 2020 by 34% for *S. pneumoniae* and
81 28% for *S. pyogenes* as compared to 2018 and 2019. The temporal course showed a substantial

82 reduction in the monthly incidence rates of BSIs between March and May 2020, coinciding
83 with the implementation of COVID-19 first drastic containment measures (Figure 1). At the
84 end of the lockdown, there was a slight increase in BSI incidence rates, but rates remained lower
85 than expected according to the two previous years. During the second lockdown, at the end of
86 the year 2020, containment measures were more relaxed than in the first quarter (back to office
87 work, opened schools). Concomitantly, there was a small increase in BSI rates, remaining lower
88 than predicted values during the winter season, and no classical seasonal peak for *S.*
89 *pneumoniae* (Figure 1). All rates observed during 2020 remained below predicted values of the
90 model and during lockdowns, several rates were even lower than the predicted 95% lower
91 limits. The decrease in the BSIs incidence in 2020 remained significant after stratification on
92 the origin of the BSIs, i.e., community- or hospital- acquired.

93 **DISCUSSION**

94 We witnessed a decrease in both community- and hospital-acquired bloodstream infections due
95 to *S. pneumoniae* and *S. pyogenes* concomitantly to the large implementation of preventive
96 measures to curb the COVID-19 pandemic. These findings are in line with several reports based
97 on either the whole population with data issued from nationwide surveillance systems [7,8], or
98 on inpatients such as the pediatric population [9,10]. On the opposite, one study reported an
99 increase of such infections during intervals when COVID-19 incidence slowed down, that is to
100 date not clearly explained [11].

101 The issue of poor case ascertainment and notification could be raised to explain the decreases
102 while countries were responding to the surge of COVID-19. However, we studied
103 *S. pneumoniae* and *S. pyogenes* invasive infections diagnosed in the hospital setting, where an
104 increase in the number of blood cultures collected, in particular during the first wave has been
105 reported [12]. Hence, the reductions by 34% for *S. pneumoniae* and 28% for *S. pyogenes*
106 observed in 2020 in our facilities are likely to be consistent with actual decreases in incidence

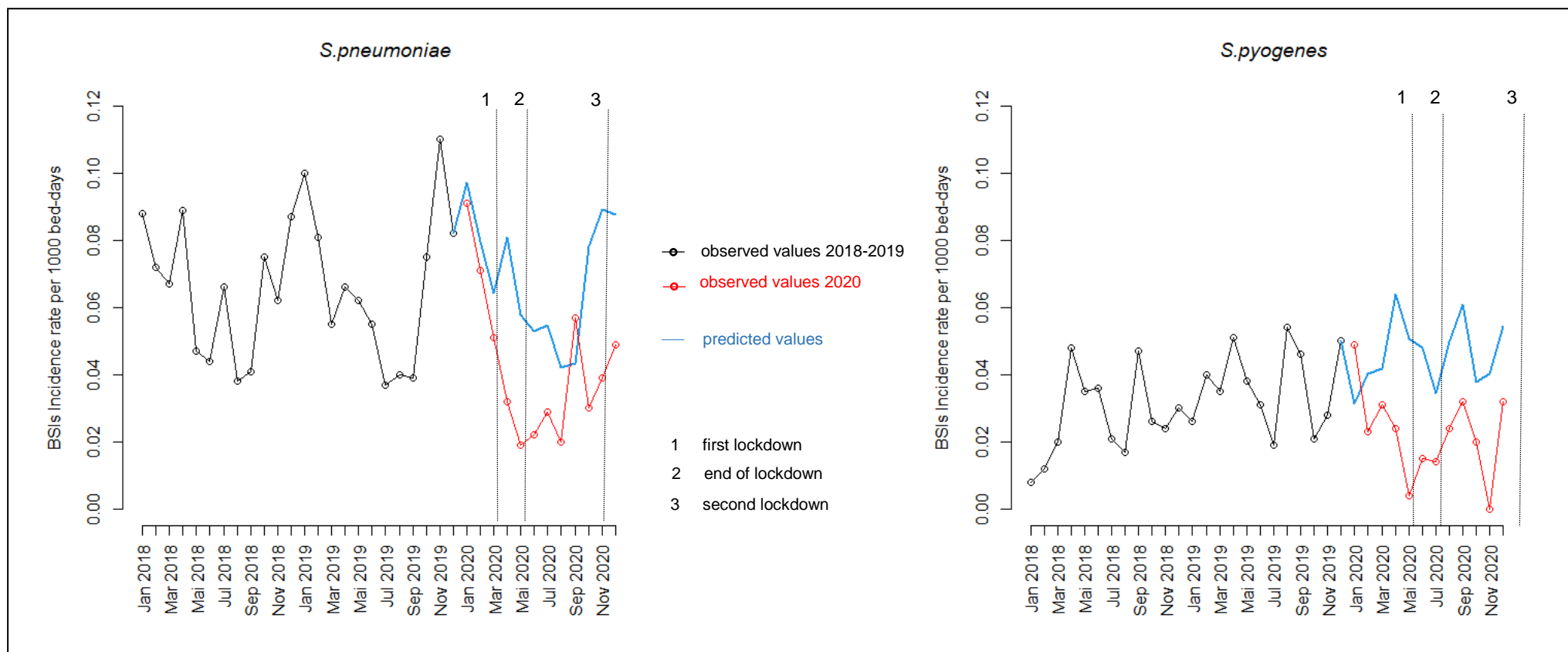
107 rates. These reductions are probably linked to basic COVID-19 bundle prevention procedures.
108 Regarding hospital-acquired cases, the consumption of alcohol-based hand products was
109 multiplied by 2.5 in 2020 in the 25 participating hospitals, which likely has an impact on cross
110 transmission. In addition, universal masking adopted during the pandemic was not
111 recommended in hospitals before that period, and besides performing high-risk invasive
112 procedures, facemasks were only recommended in specific situations such as childbirth to
113 prevent *S. pyogenes* transmission, or for all droplet-generating procedures. In the community,
114 similar precautions were widely adopted and the adherence to those were enforced by lockdown
115 periods, which decreases opportunities for transmission.

116 The major strength of the present study is that it covers a large regional population and allowed
117 to distinguish community- from hospital-acquired cases. Nevertheless, we had no access to
118 comprehensive medical records preventing analysis of data at the individual level (COVID-19
119 status, prior hospitalization, antibiotic use). Similarly, analysis of rates of lower respiratory tract
120 infections were not feasible because it requires clinical and radiological data for interpretation.

121 The containment measures implemented during the COVID-19 pandemic appear to have
122 positively impacted other infections transmitted by the same routes, including influenza.
123 Decreasing such infections should conduct to prevent antibiotic use, which is a worldwide
124 priority. However, the highly restrictive measures may not be accepted outside a health crisis.
125 Therefore, health authorities should promote lighter hygienic measures that are acceptable on
126 the long term to influence public health by decreasing transmission of respiratory pathogens.
127

128 Figure 1. Impact of containment measures on monthly incidence rates per 1000 bed-days of BSIs due to *S. pneumoniae* and *S. pyogenes*.
 129 Red lines represent observed data; blue lines represent model estimates based on observed data. The start and the end of the containment measures
 130 are indicated by a vertical dashed line.

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181 **Appendices**

182 **Members of the Collégiale de Bactériologie – Virologie – Hygiène (CBVH):** Guillaume
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197 Billarant

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199 **Declarations**

- 200 • Ethics approval and consent to participate: Data were extracted anonymously following
201 current French rules
- 202 • Consent for publication: All patients admitted to APHP hospitals are informed about
203 the potential use of data for research purpose.

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207