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# Impact of lockdown on cardiovascular disease hospitalizations in a Zero-COVID-19 country

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## **Abstract**

### **Objectives**

There are concerns about the potential effect of social distancing used to control coronavirus disease 2019 (COVID-19) on the incidence of cardiovascular diseases (CVD).

### **Study design**

Retrospective cohort study

### **Methods**

We examined the association between lockdown and CVD incidence in a Zero-COVID country, New-Caledonia. Inclusion criteria was defined by a positive troponin sample during hospitalization. Study period lasted for two months starting the 20<sup>th</sup> of March 2020 (strict lockdown: first month; loose lockdown: second month) compared to the same period of the three previous years to calculate incidence ratio (IR). Demographic characteristics and main CVD diagnoses were collected. Primary endpoint was the change in incidence of hospital admission with CVD during lockdown compared to the historical counterpart. Secondary endpoint included influence of strict lockdown, change in incidence of the primary endpoint by disease and outcome incidences (intubation or death) analysed with inverse-probability-weighting method.

### **Results**

1215 patients were included in the study. 264 were hospitalized in 2020 versus 951 (IR 0.83 [0.72-0.95]). CVD hospitalizations were reduced during strict lockdown (IR 0.71 [0.58-0.88]), but not during loose lockdown (IR 0.94 [0.78-1.12]). The incidence of acute coronary syndromes was similar in both periods. The incidence of acute decompensated heart failure

(AHF) was reduced during strict lockdown (IR 0.42 [0.24 -0.73]) followed by a rebound (IR 1.42 [1–1.98]). There was no association between lockdown and short-term outcomes.

## **Conclusions**

Our study showed that lockdown was associated with a striking reduction in CVD hospitalizations, independently from viral spread, and a rebound of AHF hospitalizations during looser lockdown.

Word count: 250

**Keywords:** SARS-CoV-2, COVID 19, lockdown, heart failure, acute coronary syndrome, epidemiology, hospitalization, myocardial infarction

## Introduction

Since the beginning of the SARS-CoV-2 pandemic, strict social distancing and healthcare reorganization measures have been adopted worldwide to contain transmission and address the surge of critically ill patients in acute care settings.<sup>1</sup> These measures along with border closing and contact tracing contributed to an efficient control of the spread of SARS-CoV-2 in certain isolated territories such as New Caledonia.<sup>2-4</sup> Restrictions related to Covid-19 remain debatable because of their social and economic consequences. Consequently, elimination strategies, which aim to fully prevent any viral circulation, represent a high level of social restrictions. Their impact on healthcare systems and diseases unrelated to Covid-19 remains to be elucidated.<sup>5,6</sup>

New Caledonia, a territory of the French Republic in the Pacific region, has a multicultural and inclusive population with Melanesian, Oceanian, Asian and European cultures characterized by a high incidence of obesity.<sup>7</sup> New Caledonia benefits from a health system and medical infrastructure that meet the highest international standards, guaranteeing safe and efficient care. Early in the COVID-19 pandemic, New Caledonia issued a Zero-Covid strategy starting with complete border closure.<sup>4</sup> Indeed, after the detection of a first local case of COVID-19 in March 2020, a strict one-month lockdown was applied. During this period, no local COVID-19 cases were detected. The strict lockdown was followed by a second month of looser restrictions and social-distancing strategies.<sup>4</sup> Eventually, New Caledonia was declared a Zero-Covid country by the end of May 2020 and maintained this status until March 2021.<sup>8</sup>

After the introduction of the first lockdown measures, local healthcare workers in New Caledonia soon reported changes in hospitalization patterns with a specific signal on acute decompensated heart failure (AHF), acute coronary syndrome (ACS) and acute heart rhythm and conduction disorders as observed elsewhere in the world.<sup>9</sup> Few data on lockdown-related healthcare consequences and patient outcomes have been published despite the fact that it represents the untold toll of the pandemic. The unique setting of New Caledonia during the first lockdown in the absence of viral spread of SARS-CoV-2 represents an exceptional opportunity to analyse the consequences of this healthcare policy. Therefore, we studied the impact of lockdown on the incidence of cardiovascular hospitalizations.<sup>10</sup>

## Methods

### Settings

We conducted this study at the regional hospital of New Caledonia Centre-Hospitalier-Territorial Gaston-Bourret (CHT), the only tertiary hospital in New Caledonia. Unscheduled hospitalisations represented the nearly unique reason of hospital admissions in 2020 in the CHT which is the referral hospital for major surgeries and life threatening emergencies in non-pandemic time. In the present analysis, all adult patients with a positive troponin plasma sample at hospital admission were included. The threshold was  $> 15.6$  pg/ml for women and  $>32.4$  pg/ml for men (Alinity I STAT<sup>®</sup> high sensitive troponin I kit, Abbott, Chicago, USA).<sup>10</sup> Patients who underwent cardiac surgery during the index hospitalisation, imported COVID-19 related myocarditis, patients presenting with post-traumatic myocardial injury, as well as patients admitted for a scheduled dialysis or ambulatory care facilities were excluded. To limit bias due to migration and tourism in the historical group, residents from outside of New Caledonia were excluded because of the border closure during lockdown. The study period lasted from the 20<sup>th</sup> of March, which was the day of the international border closure, to the 20<sup>th</sup> of May 2020. The lockdown period was compared to the same time period of the three previous years (i.e. historical period) to minimize a potential seasonal epidemic effect.

Sensitivity analyses were also conducted. Firstly, time effect was assessed by comparing the two lockdown periods versus the historical period. Period A comprised the four weeks when **strict lockdown** policies were enforced in New Caledonia and period B, the following month, when **loose lockdown** and social distancing policies were implemented. Secondly, the

incidence of different cardiovascular diseases during lockdown was compared to their incidence during the historical period, such as the hospitalizations for AHF, ACS, acute rhythm and conduction disorders, sepsis and surgical emergencies. Thirdly, an analysis was conducted in the subgroup of intensive care (ICU) admissions. Lastly, we analysed the association of lockdown to a composite outcome (intubation and all-cause in-hospital death).

This study was approved by the local ethics committee (identification number 2020-001) and performed in accordance with the declaration of Helsinki.

### **Data collection**

Data on hospitalizations in ICU, specialty wards, as well as emergency department visits were collected. Chronic and acute diagnoses associated to the index hospitalization were collected according to the French coding system CIM 10. Demographic data were recorded on age, gender, billing address, medical history of cancer, neurovascular disease, arterial hypertension, coronary artery disease, chronic heart failure and chronic kidney failure. Clinical characteristics and biological data were extracted from the CHT clinical database (DX Care). Zip codes were used to define two types of urbanicity (see supplementary materials).

Outcome variables included all-cause in-hospital death, the need for mechanical ventilation, a coronary angiography, ICU admission, and Simplified Acute Physiology Score 2 (SAPS2) score. The main diagnosis of cardiovascular disease included type 1 myocardial infarction (ACS with and without ST-elevation (STEMI and NSTEMI)), AHF, as well as acute rhythm and conduction disorders. Data on myocardial injury was also collected, as defined by type 2 myocardial infarction due to sepsis, acute neurovascular disease or surgery.



The maximal troponin measured on plasma sample and the time from admittance to the troponin peak were noted.

## **Endpoints**

The primary endpoint was the incidence of hospital admissions with a positive troponin sample during the 2020 lockdown compared to previous years and the incidence of the main CVD diagnoses, including ACS, AHF and acute rhythm and conduction disorders.

Secondary endpoints included the effects of strict and loose lockdown on primary endpoint, change in incidence of hospitalization for each cardiovascular diagnosis and effects of lockdown on the occurrence of the composite outcome of all-cause in-hospital death and the need of invasive ventilation.

## **Statistical analysis**

We calculated bivariate frequencies of hospitalisation rates, main diagnoses, outcome and preadmission characteristics. Categorical variables are presented as number and percentage. Continuous variables are presented as means and 95% confidence interval (CI95%). The zip codes were used to provide a mapping of patients included in the analysis and to adjust the statistics according to the geographical localization.

The incidence ratios (IR) were calculated as the proportion of related events from the study period in 2020 to the historical period. The incidence of events in the population of New-Caledonia was calculated as the proportion of disease for 100 000 inhabitants. The interaction between period A and B was also tested.

In this retrospective study, data for patients' outcome were censored on September 1<sup>st</sup>, 2020. We then conducted a multivariable logistic regression analysis to estimate the association between the lockdown and the composite endpoint (all-cause in-hospital death or invasive ventilation). To consider the nonrandomized setting, we conducted a propensity-score matched analysis to reduce the bias of confounding factors in the analysis. The individual propensities to be hospitalized with a positive troponin sample in 2020 were calculated with a multiple regression model using the same covariates as previously described. The association between the lockdown period and outcomes was first assessed by a logistic regression analysis (i.e. crude analysis), then by three different analyses using a propensity score. Firstly, we used the propensity score as an additional covariate in the multiple logistic regression analysis with all potential cofounders as covariates. Secondly, we applied the nearest neighbor propensity score matching. Lastly, we used inverse probability weighting. Death and mechanical ventilation were also studied as separate outcomes according to the same methodology. Odds ratios (ORs) and their 95% confidence intervals (CI) were calculated.

The nearest neighbour matching is a method where a patient admitted during the period of interest is matched with a patient admitted during the historical period based on the distance between their propensity score (i.e. a caliper). Caliper value was 0.25 of the standard deviation of the logit of the propensity score.

The subgroup analysis included ICU admissions and SAPS2 score at ICU admission. Patients with missing data on SAPS2 were considered random and excluded from the analysis.

## Results

### 1. Characteristics of the cohort

A total of 1399 patients were admitted with a positive troponin sample during the 2-month period from the 20<sup>th</sup> of March to the 20<sup>th</sup> of May in 2017, 2018, 2019 and 2020. 32 patients were excluded because they underwent cardiac surgery, 104 for non-admittance to hospitalisation, 19 for traumatic injuries, 17 because they were not New Caledonia residents, 8 patients for chronic dialysis and 3 due to missing zip codes. The final study cohort included 1215 patients (an average of 152 patients per month). The evolution of emergency department visits, as well as hospitalizations in ICU and non-ICU ward are described in Figure 1. The median troponin concentration on inclusion was 142 pg/ml [52-1078] and observed at the median day 1 after admission [0-2].

Baseline characteristics of the study population are presented in Table 1. The median age of patients included in the study during the 2020 lockdown was 67 years. Compared to the historic cohort, patients included in 2020 had more comorbidities including neurovascular disease (10.2% vs 5.4%,  $p=0.01$ ) and chronic kidney disease (32.2% vs 23.6%,  $p=0.01$ ).

### 2. Primary endpoints

#### 2.1 Incidence of hospitalizations for cardiovascular disease during lockdown

Concerning the primary endpoint, there were 264 hospitalizations with a positive troponin sample in 2020 vs. 951 during the historical period (mean value of 317 patients over two months). This amounted to an 18% absolute reduction in hospitalizations in 2020 (see Figure 1), with an IR of 0.83 [0.72-0.95]. This reduction in the incidence was exclusively seen during

the first month with strict lockdown (IR 0.72 [0.58-0.88]) and not during the second month of loose lockdown (IR 0.93 [0.78-1.12]),  $p=0.005$ .

The incidence of hospitalization according to urbanicity is illustrated in the supplementary Figure 1.

## **2.2 Incidence of hospitalizations by disease**

The incidence of main cardiovascular diagnoses during the study period is described in the supplementary Figure 2. The number of hospitalizations for Type 1 myocardial infarction did not vary significantly during periods A and B whether it was for a STEMI or a NSTEMI ( $P$  interaction 0.5) (Figure 2). However, the incidence of hospitalizations for AHF dropped significantly during the period A with a decrease of - 42% compared to previous years and increased during period B at + 41% above the usual rate (supplementary figure 3) ( $P$  interaction  $< 0.001$ ). Similarly, the hospitalizations for acute rhythm and conduction disorders decreased during period A and nearly doubled during period B ( $P$  interaction 0.002).

Concerning the diagnosis associated with type 2 myocardial infarction, the number of hospitalizations for acute neurovascular events, sepsis or surgical emergencies with a positive troponin sample did not vary over time.

## **3. Secondary endpoints**

### **3.1 The influence of strict vs. loose lockdown measures on the incidence of cardiovascular hospitalizations**

During the period A, defined as the month of March 2020 when the strict lockdown measures were implemented, a 28.3% decrease in hospital admissions was observed, with 109 hospitalizations compared to a mean of 152 hospitalizations per month during the

historical period of the 3 previous years, with an IR of 0.72 [0.58-0.88],  $p=0.002$ . In During the period B, defined as the second month of lockdown (April 2020) when restrictions were loosened and social distancing policies were applied, a 6.5% decrease in admissions was observed, with 155 patients hospitalized versus an average of 165 patients during the same month of previous years, with unchanged IR of 0.93 [0.78-1.12],  $p=0.452$ .

### **3.2 The influence of strict vs. loose lockdown measures on the composite outcome**

During the inclusion period in 2020, the composite outcome of all-cause in-hospital death and mechanical ventilation was observed in 19.3% of patients vs. 18.4% of patients of the historical cohort ( $p=0.74$ ).

The OR and 95% CI for the outcome endpoint and its two determinants (i.e. death and mechanical ventilation) were calculated for each characteristic studied (Supplementary Table 1). In the crude unadjusted analysis, there was no difference of the composite outcome of all-cause in-hospital death or mechanical ventilation during the lockdown period compared to the historical cohort (OR 1.01 [0.96 - 1.06]). No influence was found for the strict vs. loose lockdown ( $p$  interaction 0.888). No significant differences of the composite outcome were observed after adjustment for propensity score (OR 1.01 [0.97 - 1.05]), neither after propensity score matching (OR 1.02 [0.97 - 1.08]) or after inverse probability weighting (OR 1.01 [0.97 - 1.05]), with no significant interaction of strict vs. loose lockdown. No significant differences were observed when analysing each outcome separately (see Table 2).

## **4. Sensitivity analyses**

### **4.1 Analysis of the impact of strict vs. loose lockdown on the composite outcome**

Additional sensitivity analysis comparing the influence of the strict lockdown month vs. looser lockdown month demonstrated that neither strict nor loose lockdown was associated with an increased rate of in-hospital death or mechanical ventilation (see Supplementary Table 2)

#### **4.2 Subgroup analysis of composite outcome in the subgroup of ICU admissions**

The subgroup analysis of ICU admissions during lockdown showed that there was no significant impact on the composite outcome (see Supplementary Table 3). Interestingly, patients who were admitted to the ICU during the lockdown period had a higher SAPS2 score when compared to the previous years (median 55 [24 - 96] versus 44 [19 - 95],  $P=0.01$ ).

#### **4.3 Subgroup analysis according to admission diagnosis on the composite outcome**

Sensitivity analyses according to the admission diagnosis (ACS, AHF, acute rhythm and conduction disorders, acute neurovascular diseases, sepsis and surgical emergencies) and urbanicity were also conducted according to the outcome (supplementary Table 4). No associations were detected between the diagnosis on admission and the composite outcome.

## Discussion

This study describes the incidence of cardiovascular hospitalizations and their outcomes during a lockdown period in a territory where implemented restrictions successfully prevented the spread of SARS-CoV-2. The overall incidence of hospitalizations for cardiovascular disease with increased myocardial injury biomarkers was lower during lockdown, especially during the first month of strict lockdown when compared to the following month of looser restrictions. However, even though the admissions for ACS remained similar during lockdown when compared to a historical cohort, the admissions for AHF decreased during the period of strict lockdown and rebounded with a dramatic increase during the period of looser lockdown. Interestingly, there was no association of the composite endpoint (all-cause in-hospital mortality and intubation) in patients hospitalized during lockdown.

Our study is unique given the specific setting of New Caledonia, where early border closure and an implementation of strict lockdown resulted in a total control of the outbreak, and no COVID-19 cases were detected in the population during the first wave of the SARS-CoV-2 pandemic. Our results provide a valuable insight into the impact of lockdown *per se*, without the confounding of direct effects of SARS-CoV-2 on cardiovascular disease. Until March 2021, all COVID-19 cases were imported and diagnosed during quarantine with no local transmission of SARS-CoV-2.<sup>8</sup> Analysis of the hidden toll of lockdown is critical in order to identify patients at risk and to prevent any malfunction of the healthcare system, as well as influence future healthcare policies during the pandemic.

In other regions of the world, the effect of lockdown on diseases unrelated to Covid-19 is difficult to interpret because of the confounding factors caused by the viral spread in the population.<sup>11</sup> In the present article, our findings confirm a decrease in admissions for cardiovascular disease during lockdown, which was comparable to those observed in countries with an active spread of SARS-CoV-2, including Italy, United Kingdom and France.<sup>9,12,13</sup>

Our study population is representative of patients at risk of severe COVID-19. Most of the included patients were older than 60 years, had a history of heart failure, and presented a number of cardiovascular risk factors such as metabolic syndrome and hypertension <sup>22,23</sup>. Our results also suggest that patients hospitalized during lockdown had more comorbidities when compared to a historical cohort. Having in mind the reduced incidence of hospitalizations, higher rates of comorbidities demonstrate that only the most severely ill patients presented to the hospital during lockdown. This finding also emphasizes the importance of prevention policies for community medicine and continuity of essential healthcare for patients suffering from chronic illnesses.<sup>14</sup>

Further key insights can be highlighted when looking closely at the admission diagnosis.<sup>15</sup> We studied the consequences of lockdown on the incidence of hospitalizations with increased biomarkers of myocardial injury, as defined by the thresholds of the universal definition of myocardial infarction. <sup>10</sup> We hypothesized that specific factors might have had an influence on CVD presentation such as a decrease in ACS admissions during lockdown, possibly due to a change in lifestyle or reluctance to seek medical help. A previous study reported significant lifestyle changes during lockdown in relation to NSTEMI incidence, with a reduction of passive smoking, working hours, alcohol, junk food and salt consumption, and



an increase in sleeping hours<sup>17</sup>. On the contrary, the hospitalizations for ACS during the lockdown period in New-Caledonia did not change significantly when compared to other countries where the spread of SARS-CoV-2 was high.<sup>12,16</sup> ACS patients may have been compelled to consult hospitals because of the severity of their symptoms. **Our data supports the hypothesis that ACS rates were not influenced by the lower degree of physical exertion and other lifestyle changes during lockdown.<sup>13</sup> Furthermore, there was no increase in hospital workload related to COVID-19, so ACS patients were not underdiagnosed or undertreated, in contrast to countries with active viral spread of SARS-CoV-2.<sup>18</sup> Our study shows that there were no negative effects of early lockdown on the incidence of hospitalizations for ACS.**

The incidence of hospitalizations of patients presenting with type 2 myocardial infarction was not influenced by lockdown, in accordance to previous studies.<sup>19</sup> The elevated troponin concentration in type 2 MI reflects the extent of myocardial injury and thus the severity of the initial illness. No significant difference was found in outcomes associated with type 2 MI in patients hospitalized during lockdown versus the historical period.

Acute heart failure patients with a positive troponin sample are considered as high risk due to increased risk of in-hospital mortality. Our study demonstrated a dramatic decrease in AHF hospitalizations during lockdown, with a rebound phenomenon after the restrictions were lifted. Our results are consistent with previously published findings in countries with active SARS-CoV-2 circulation during the first wave of the pandemic.<sup>20–22</sup> Our study was underpowered to analyse the specific reasons why heart failure patients did not present to the hospital or if they avoided preventive care. Notably, the New Caledonia residents strongly believed in the active circulation of SARS-CoV-2 in March and April 2020. We may

thus hypothesize that the psychological aspect of lockdown was a prominent factor that prevented heart failure patients from seeking medical care during the initial phase of the pandemic. The rebound phenomenon that was observed during the looser lockdown illustrates the importance of ambulatory management of chronic heart failure, including the titration of optimal medical treatment as well as with clinical and biological follow-up.

It is challenging to identify the direct effect of health care policies such as early strict lockdown in the setting of a pandemic. However, in our study we were able to control for bias from the confounding factors. More importantly, our results are free from the influence of the direct effects of SARS-CoV-2 as New Caledonia was a “Covid-free” country during the implementation of the first lockdown. Other strengths of this study include an extensive overview of different causes of myocardial injury during lockdown, that were comprehensively explored in our sensitivity analyses. We used a composite outcome of all-cause in-hospital death and intubation, which is especially clinically relevant during the pandemic.<sup>23,24</sup> We acknowledged that these outcomes can be unevenly affected by both the severity of underlying conditions as well as quality of care. Our results confirmed a preserved quality of care in the acute setting, as even though the incidence of hospital admissions decreased, short-term outcomes remained unaffected. Therefore, the study provides information on the resilience of healthcare system rather than disease-specific factors.<sup>25</sup> It was important to verify this hypothesis when considering the restrictions initially applied to curb the spread of SARS-CoV-2 down to zero detection. Border closure might negatively affect patient care delivery in New Caledonia, as the healthcare system relies on medical evacuations to France or Australia as well as specialized visiting medical or surgical missions, such as cardiac surgery. Aside from hospital overload, Pacific islands as well as

other remote territories had to face specific challenges in their healthcare systems due to the SARS-CoV-2 pandemic.

Several limitations of the present study must be acknowledged. First of all, the retrospective design of the study accounted to a small amount of missing data due to the potential inaccuracy of electronic medical records. **Secondly**, due to lack of randomization there might be residual bias of the outcome analysis. However, the propensity score matching as well as the IPW method allowed us to minimize selection bias and provided consistent findings throughout the different statistical approaches that were used. What is more, our study is in line with a recent meta-analysis focused on the incidence of STEMI during lockdown<sup>26</sup>. Furthermore, our study included both unscheduled and planned hospitalizations, only outpatients were excluded to minimize the selection bias. **Third, the results are based only on in-hospital outcomes without extended follow-up. On one hand, the zero COVID-19 strategy with complete border closure might have direct implications on the incidence of COVID-19 related myocarditis. On the other hand, general stress, and lack of medical care in patients with chronic diseases could have led to an increase in morbidity and mortality in the long term. Unfortunately, our study was underpowered to assess the long-term effects of zero-Covid strategy. Lastly**, our study relies on data from a single centre that could limit the generalizability of the findings. However, the studied site is a referral centre for all critical illness, as it has the only ICU, cardiology ward and angiography facilities for the whole territory.

We feel that it is important to emphasize that the results of this study should not lead to a conclusion that the lockdown had no negative consequences. The fall in the incidence of hospitalization leads to the hypothesis that a significant number of patients did not consult

and stayed home with a myocardial injury. Further studies should focus on the sociological and psychological aspects of the reluctance to seek medical care during the pandemic. Moreover, even though the long term effects of delayed care in a high-risk population are not described here, the rebound phenomenon of AHF hospitalizations emphasizes a major public health issue. At the time of study completion, New Caledonia succeeded in a Zero-COVID-19 strategy but the pandemic consequences such as anxiety or other psychological aspects were most likely present. Policy makers should consider these aspects to enhance outpatient care during lockdown periods.

Word count: **3703**

### **Non-standard Abbreviations and Acronyms**

ACS : Acute Coronary Syndrome

CHT : Centre-Hospitalier-Territorial of New Caledonia Gaston-Bourret

COVID-19 : Coronavirus disease 2019

AHF : Acute Heart Failure

ICU : Intensive Care Unit

IPW : inverse-probability-weighting method

NSTEMI : Non ST-elevation myocardial infarction

SAPS2 : Simplified Acute Physiology Score 2

STEMI : ST-elevation myocardial infarction

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### **Conflict of interest**

Conflicts of interests: AM received honorarium for lectures from Novartis, Roche, Abbott, Orion, Servier, consultation fees from Corteria and Windtree and research grant from 4TEEN4, Adrenomed, Roche, Abbott.

### **Contributors**

PHM, JBB, MDR conceived the study and its design, had full access to the data, and take responsibility for the integrity of the data and accuracy of the analysis. PHM, VC and SG organised and entered data. PHM, NO, MM contributed to data analyses. PHM, VC, MS, EC, AM contributed to data interpretation. PHM and NO drafted the manuscript. All authors critically revised the drafted manuscript and approve of the submitted manuscript

**Disclosure: none**

**Data sharing:**

We are prepared to share our data according to French and New-Caledonian laws on health data upon specific request to PHM.

**Supplemental Material:**

- **Table 1-4**
- **Figure 1 and 2**

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## Tables

**Table 1:** Patient characteristics and outcomes according to the period of inclusion. The composite outcome is defined as the occurrence of death or mechanical ventilation. Results are expressed as mean and standard deviation or number and percentage.

|   | Unmatched Patients |                   | p-value | Matched Patients |                   | p-value |
|---|--------------------|-------------------|---------|------------------|-------------------|---------|
| Characteristics — no. (%)                     | 2020               | Historical period |         | 2020             | Historical period |         |
|   | (N = 264)          | (N=951)           |         | (N = 261)        | (N= 261)          |         |
| Age   | 66 (15)            | 66 (16)           | 0.89    | 66(15)           | 65(15)            | 0.70    |
| <40 y.o.                                      | 16 (6.1)           | 70 (7.4)          | 0.55    | 16 (6.1)         | 13 (5.0)          | 0.70    |
| 40-59 y.o.                                    | 80 (30.3)          | 229 (24.1)        | 0.05    | 77 (29.5)        | 81 (31)           | 0.78    |
| 60-79 y.o.                                    | 113 (42.8)         | 479 (50.4)        | 0.04    | 113 (43.3)       | 119 (45.6)        | 0.66    |
| ≥80 y.o.                                      | 55 (20.8)          | 173 (18.2)        | 0.38    | 55 (21.1)        | 48 (18.4)         | 0.51    |
| Female sex                                    | 128 (48.5)         | 453 (47.6)        | 0.86    | 126 (48.3)       | 116 (44.4)        | 0.43    |
| Geographical region                           |                    |                   |         |                  |                   |         |
| Grand Noumea                                  | 179 (67.8)         | 637 (67.0)        | 0.86    | 176 (67.4)       | 176 (67.4)        | 1.0     |
| Medical history                               |                    |                   |         |                  |                   |         |
| Oncology                                      | 29 (11.0)          | 103 (10.8)        | 0.97    | 29 (11.1)        | 34 (13)           | 0.59    |
| Neurovascular                                 | 27 (10.2)          | 51 (5.4)          | 0.01    | 26 (10)          | 31 (11.9)         | 0.57    |
| Cardiovascular                                | 186 (70.5)         | 646 (67.9)        | 0.48    | 183 (70.1)       | 173 (66.3)        | 0.40    |
| Hypertension                                  | 134 (50.8)         | 464 (48.8)        | 0.62    | 131 (50.2)       | 132 (50.6)        | 1.00    |
| Coronary artery disease                       | 85 (32.2)          | 253 (26.6)        | 0.09    | 83 (31.8)        | 71 (27.2)         | 0.29    |
| Chronic heart failure                         | 68 (25.8)          | 228 (24.0)        | 0.61    | 68 (26.1)        | 61 (23.4)         | 0.54    |
| Chronic respiratory diseases                  | 9 (3.4)            | 59 (6.2)          | 0.11    | 9 (3.4)          | 12 (4.6)          | 0.66    |
| Chronic kidney disease                        | 85 (32.2)          | 224 (23.6)        | 0.01    | 82 (31.4)        | 90 (34.5)         | 0.52    |
| Active Smoking                                | 50 (18.9)          | 212 (22.3)        | 0.28    | 50 (19.2)        | 60 (23)           | 0.33    |
| Metabolic syndrome                            | 125 (47.3)         | 443 (46.6)        | 0.88    | 122 (46.7)       | 120 (46)          | 0.93    |
| Associated Diagnoses and procedures — no. (%) |                    |                   |         |                  |                   |         |
| STEMI   | 29 (11.0)          | 77 (8.1)          | 0.18    | 27 (10.3)        | 33 (12.6)         | -0.49   |
| NSTEMI  | 26 (9.8)           | 86 (9.0)          | 0.78    | 26 (10)          | 25 (9.6)          | 1.00    |
| Acute heart failure                           | 63 (23.9)          | 204 (21.5)        | 0.45    | 63 (24.1)        | 57 (21.8)         | 0.60    |
| Acute neurovasculare disease                  | 33 (12.5)          | 80 (8.4)          | 0.06    | 32 (12.3)        | 29 (11.1)         | 0.79    |
| Acute arrythmias and conduction disorders     | 91 (34.5)          | 262 (27.5)        | 0.03    | 91 (34.9)        | 92 (35.2)         | -1.00   |
| Sepsis  | 44 (16.7)          | 128 (13.5)        | 0.22    | 44 (16.9)        | 44 (16.9)         | 1.00    |
| Coronary angiography                          | 70(26.5)           | 260(27.3)         | 0.85    | 70 (26.8)        | 71 (27.2)         | 1.00    |
| Surgery                                       | 34 (12.9)          | 99 (10.4)         | 0.31    | 33(12.6)         | 30 (11.5)         | 0.79    |
| ICU admisison                                 | 68 (25.8)          | 256 (26.9)        | 0.77    | 68 (26.1)        | 71 (27.2)         | 0.84    |
| Outcome                                       |                    |                   |         |                  |                   |         |
| Composite outcome                             | 51 (19.3)          | 175 (18.4)        | 0.8     | 51 (19.5)        | 46 (17.6)         | 0.65    |
| All-cause death                               | 36 (13.6)          | 115 (12.1)        | 0.57    | 36 (13.8)        | 27 (10.3)         | 0.28    |
| Mechanical ventilation                        | 32 (12.1)          | 109 (11.5)        | 0.85    | 32 (12.3)        | 32 (12.3)         | 1.0     |

Data are presented as mean (standard deviation) or number (percentage).

Definition of abbreviations: *ICU*: Intensive care unit; *Y.O.*: year old; *NSTEMI*: Non ST-segment elevation myocardial infarction; *STEMI*: ST-segment elevation myocardial infarction.

**Table 2:** Association between lockdown and patient outcomes.

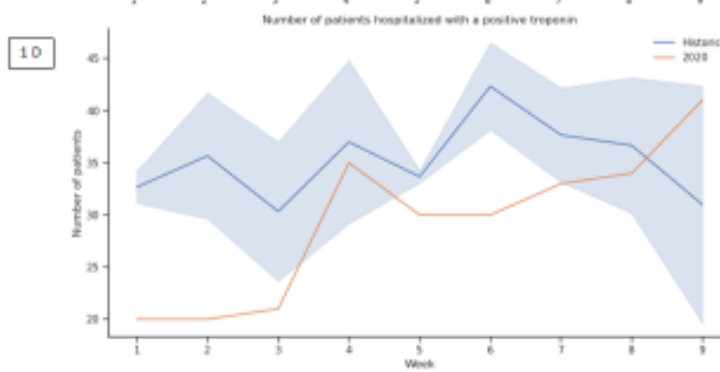
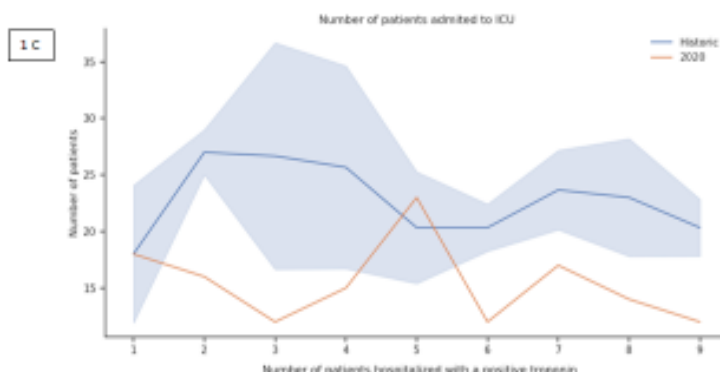
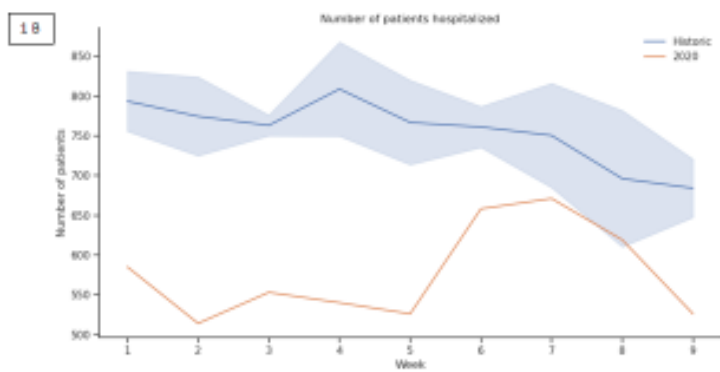
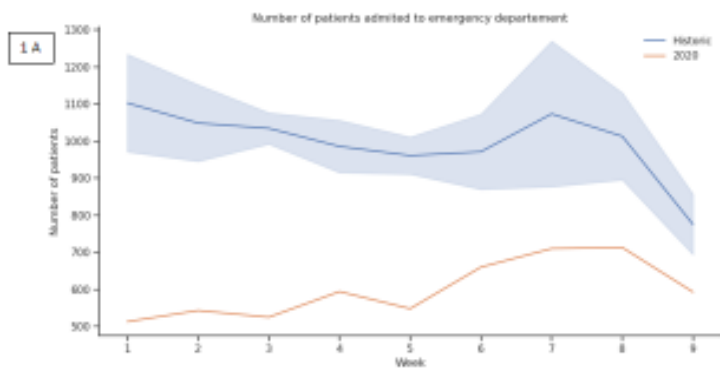
|   | N    | Odds Ratio | 95 % CI       |      |
|---|------|------------|---------------|------|
| <b>Composite primary endpoint of death and mechanical ventilation</b> |      |            |               |      |
| Crude analysis  | 1215 | 1.06       | [0.75 – 1.49] | 0.87 |
| Adjusted for propensity score   | 1215 | 1.07       | [0.66 – 1.72] | 0.83 |
| Matched on propensity score   | 322  | 1.29       | [0.69 – 2.41] | 0.58 |
| IPW stabilized  | 1215 | 1.07       | [0.66 – 1.72] | 0.87 |
| <b>Death</b>  |      |            |               |      |
| Crude analysis  | 1215 | 1.15       | [0.76 – 1.70] | 0.29 |
| Adjusted for propensity score   | 1215 | 1.15       | [0.71 – 1.85] | 0.38 |
| Matched on propensity score   | 322  | 1.70       | [0.88 – 3.26] | 0.99 |
| IPW stabilized  | 1215 | 1.16       | [0.71 – 1.86] | 0.35 |
| <b>Mechanical ventilation</b>   |      |            |               |      |
| Crude analysis  | 1215 | 1.07       | [0.69 – 1.60] | 0.96 |
| Adjusted for propensity score   | 1215 | 1.11       | [0.60 – 2.03] | 0.60 |
| Matched on propensity score   | 322  | 1.18       | [0.52 – 2.70] | 0.99 |
| IPW stabilized  | 1215 | 1.11       | [0.60 – 2.03] | 0.63 |

Data are presented as odds ratio (95% confidence interval).

Definition of abbreviations: IPW: inverse-probability-weighted; 95 % CI: 95 % Confidence interval

## Figure legends

**Figure 1:** Number of hospital admissions in Centre-Hospitalier-Territorial according to the study period and the historical cohort. Emergency department admissions are displayed in figure 1A. Figure 1B shows the number of hospital admissions. Figure 1C shows the Intensive Care Unit (ICU) admissions. Figure 1D shows the number of patients with a positive troponin sample included in the study. Data were collected from the 20<sup>th</sup> of March till the 20<sup>th</sup> of May 2020, and were compared to the same period of the three previous years (i.e. historical period).



**Figure 2:** Incidence of hospitalizations with a positive troponin sample and associate diagnosis during the strict lockdown month of the study period in 2020 (blue line) and during the looser lockdown (yellow line) compared to their historical counterpart of the three previous years. Results are expressed as incidence ratios (IR) and 95% Confidence Interval. A p-value of interaction between the strict lockdown and the loose lockdown period was considered as significant when  $< 0.05$ .

Definition of abbreviations: *ICU*: Intensive care unit; *IR* : Incidence Ratio; *NSTEMI*: Non ST-segment elevation myocardial infarction; *STEMI*: ST-segment elevation myocardial infarction; 95% CI : 95% Confidence Interval.

|                                   | IR [95%CI]<br>Strict Lockdown | IR [95%CI]<br>Loose Lockdown | p-value  |
|-----------------------------------|-------------------------------|------------------------------|----------|
| Hospitalization                   | 0.71 [0.58 - 0.88]            | 0.93 [0.78 - 1.12]           | 0.06     |
| Heart Failure                     | 0.42 [0.24 - 0.73]            | 1.41 [1.00 - 1.98]           | $<0.001$ |
| Acute Coronary Syndrome           | 1.26 [0.82 - 1.93]            | 0.81 [0.52 - 1.26]           | 0.17     |
| STEMI                             | 1.39 [0.72 - 2.68]            | 0.98 [0.55 - 1.71]           | 0.43     |
| NSTEMI                            | 1.18 [0.67 - 2.07]            | 0.63 [0.30 - 1.28]           | 0.17     |
| Acute Neurovascular event         | 0.97 [0.51 - 1.86]            | 1.46 [0.87 - 2.46]           | 0.34     |
| Arrhythmias & Conduction diseases | 0.74 [0.50 - 1.10]            | 1.31 [0.97 - 1.77]           | 0.002    |
| Sepsis                            | 0.83 [0.49 - 1.39]            | 1.23 [0.78 - 1.95]           | 0.26     |
| Surgery                           | 1.18 [0.65 - 2.14]            | 0.92 [0.55 - 1.53]           | 0.56     |
| Coronarography                    | 0.77 [0.52 - 1.14]            | 0.84 [0.59 - 1.20]           | 0.74     |
| ICU admission                     | 0.68 [0.46 - 1.02]            | 0.90 [0.63 - 1.29]           | 0.31     |

