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Out-of-Hospital Cardiac Arrest During the Covid-19 Pandemic: A Population-Based Study in the Great Paris Area

Prof. Eloi Marijon^{1,2,3*} MD; Nicole Karam^{1,2,3*}, MD; Daniel Jost^{2,4}, MD; David Perrot,^{1,2} MD; Benoit Frattini⁴, MD; Clément Derkenne,⁴ MD; Ardalan Sharifzadehgan,^{1,2,3} MD; Victor Waldmann,^{1,2,3} MD; Frankie Beganton,^{1,2} MS; Kumar Narayanan,² MD; Prof. Antoine Lafont^{1,2,3}, MD; Wulfran Bougouin,^{1,2,5} MD, Prof. Xavier Jouven^{1,2,3}, PhD
On behalf of the Paris-Sudden Death Expertise Center (Paris-SDEC) Investigators

¹*Université de Paris, PARCC, INSERM, F-75015 Paris, France*

²*Paris-Sudden Death Expertise Center, Paris, France*

³*European Georges Pompidou Hospital, Cardiology Department, Paris, France*

⁴*Paris Fire Brigade, Paris, France*

⁵*Jacques Cartier Hospital, Intensive Care Unit, Massy, France*

*Equal contribution

Corresponding author

Prof. Eloi Marijon
Cardiovascular and Sudden Death Epidemiology Unit
Paris Cardiovascular Research Center
56 Rue Leblanc
75987 Paris Cedex 15, France
Tel: +33 6 62 83 38 48
Fax: +33 1 56 09 30 47
E-mail: eloi.marijon@inserm.fr
<http://parcc.inserm.fr>

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SUMMARY (WC=300)

Background

While mortality due to COVID-19 infection is robustly tracked, its indirect impact at the population level through lockdown, lifestyle changes, and reorganization of healthcare systems, has not been evaluated. The aim of the study was to assess the incidence and outcome of out-of-hospital cardiac arrest (OHCA) in an urban region during the ongoing pandemic, compared to non-pandemic periods.

Methods

Since May 15th, 2011, data on every sudden OHCA (N=30,768) has been systematically collected in Great Paris Area, using a real-time multisource surveillance system. We evaluated OHCA incidence and outcome over a six-week period of the pandemic (weeks 12 to 17; March 16th to April 26th, 2020).

Findings

Comparing the 521 OHCA of the pandemic to the 3,052 of the non-pandemic period (weeks 12 to 17, 2012-2019), maximal weekly OHCA incidence increased from 13.42 (95%CI 12.77-14.07) to 26.64 (95%CI 25.72-27.53) per million inhabitants ($P<0.001$), before returning to normal. While patient demographics did not change substantially (mean age 70 ± 17 years, 64% males), there was a higher rate of OHCA at home (460 (90%) vs. 2,336 (77%), $P<0.001$), less bystander cardiopulmonary resuscitation (239 (48%) vs. 1,165 (64%), $P<0.001$) and shockable rhythm (46 (9%) vs. 472 (19%), $P<0.001$), and longer delays to intervention (10 [8.0-13.0] vs. 9 [8.0-12.0] min, $P<0.001$). The proportion of OHCA admitted alive decreased from 22.8% to 12.8% ($P<0.001$). After adjustment for potential confounders, pandemic period remained significantly associated with lower survival rate at hospital admission (OR=0.36,

95%CI 0.24-0.52, $P < 0.001$). COVID-19 infection, confirmed or suspected, accounted for 33% of the increase in OHCA incidence during the pandemic.

Interpretation

A transient two-fold increase in OHCA incidence, coupled with a significant reduction in survival, were observed during the pandemic. While this may be partially related to COVID-19 infections, indirect effects through lockdown and adjustment of healthcare services to the pandemic are likely.

Fundings

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INTRODUCTION

Since the emergence of the infection caused by Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2, causing COVID-19 disease),¹ initially reported in China in December 2019,² then qualified as a global pandemic by World Health Organization on the 11th of March 2020,³ almost 3.9 million cases of COVID-19 have been reported worldwide, with more than 267,00 deaths by May 6th.^{3,4}

Beyond the direct mortality caused by COVID-19 infection, there are growing concerns regarding the consequences of the COVID-19 pandemic on health systems.^{5,6} Lockdown and movement restrictions imposed in several countries, as well as the fear of contamination at the hospital, led patients to refrain from calling emergency medical services (EMS) or presenting to emergency departments, resulting in sub-optimal healthcare and inappropriate delays. Besides, the entire healthcare system had to be reorganized in order to cope with this unprecedented surge of patients with a novel disease and a highly contagious profile. Defferable routine medical activity, including scheduled hospitalisations and consultations, had to be cancelled to recenter the activity on COVID-19 patients, and avoid unnecessary exposure of stable patients to the risk of contamination at the hospital. Altogether, these indirect effects of the COVID-19 pandemic could have detrimental impacts on population health.

Out-of-hospital cardiac arrest (OHCA) could be a valuable surrogate of both population health and efficacy of pre-hospital healthcare system in handling emergencies. While few media reports have suggested an increase in the rate of OHCA in several cities, to the best of our knowledge, only one original report described an increase in OHCA incidence in Lombardy, Italy, a specific setting where the pandemic was particularly violent.^{6,7} In the present article, using a real-time

multisource surveillance system set up in 2011, we assessed the incidence and outcome of OHCA in a urban region (Great Paris Area) during the ongoing COVID-19 pandemic, compared to non-pandemic periods.

METHODS

This study is reported according to Strengthening The Reporting of Observational studies in Epidemiology guidelines.⁸

Paris-SDEC Registry

The Paris-Sudden Death Expertise Center (Paris-SDEC) ongoing registry has been previously described.⁹⁻¹¹ All cases of sudden OHCA occurring, among adults, in the Great Paris Area, including Paris city and its three suburbs (Hauts-de-Seine, Seine-Saint-Denis, and Val-de-Marne), an area covering 762 km², are included in the Paris-SDEC registry, since May 15, 2011. To ensure completeness, an intensive and prospective epidemiological case-ascertainment program is applied. Each case is reviewed separately by two investigators to ensure accuracy of classification. Several quality assessments are performed to ascertain the completeness of collection in the area.⁹ The appropriate review boards approved the study (CNIL approval #912309 and CCTIRS approval #12336).

Population and Study Setting

In the Great Paris Area (6.8 millions inhabitants), patients with OHCA are managed by the Paris Emergency Medical System, a 2-tiered response system, coordinated via a unique dispatcher center (not changed during the pandemic period):^{12,13} (i) a Basic Life Support tier provided by 197 basic life support teams from the Paris Fire Brigade (Brigade des Sapeurs Pompiers de Paris-BSPP), who can apply automatic external defibrillator, and (ii) an Advanced Cardiac Life Support function provided by ambulance teams with a physician, a nurse, and a paramedic (Paris Fire Brigade or Service d'Aide Médicale Urgente—SAMU). The Paris Fire Brigade teams arrive on scene first and provide basic life support according to the

guidelines for OHCA management. The Paris Fire Brigade then calls for advanced life support if considered useful according to case presentation.

Sudden OHCA was defined as any sudden cardiac arrest, after exclusion of cases with obvious accidental causes, irrespective of whether resuscitation was attempted or not. Data were however collected using Utstein templates.¹⁴

Although since the start of this registry, there was no change in system configuration and cases detection during the pandemic, firefighters from the Paris Fire Brigade ; had to constantly adapt their practices, taking contagiousness into account, while complying with international recommendations, for which a dedicated "COVID-19 version" has been published in the meantime. Dispatchers were instructed to investigate, when receiving the call, whether the patient was known to be COVID-19 positive or had symptoms suggestive of COVID-19 infection (fever lasting >48hours before OHCA, with cough, dyspnea, or both). When COVID-19 infection was confirmed or suspected, EMS personnel were instructed to protect themselves by wearing personal protective equipment before initiating attempted resuscitation.¹⁵

Data Collection

General data, including Utstein characteristics of the OHCA, are recorded prospectively.¹⁴ Response time is defined as the delay between EMS call and arrival (Call Answer-to-Arrival time).

For the current analysis, given the French COVID-19 epidemic trajectory, we considered the period extending from March 16th (beginning of the Paris Lockdown) to April 26th, 2020 as the six weeks of the pandemic in the Paris region (corresponding to weeks 12 to 17 of year 2020). We compared patients' characteristics, setting of occurrence, and outcome of this period with weeks 12 to 17

of each year from 2012 to 2019 (non-pandemic reference period #1). We also reported data of patients in the Paris-SDEC registry from 2011 to 2020, excluding weeks 12 to 17 (non-pandemic reference period #2).

In the Great Paris Area, the maximal number of new hospitalizations related to COVID-19 was reached in weeks 13 and 14 (4,402 patients; both intensive and non-intensive care units) (Supplemental Figure), whereas maximal COVID-related in-hospital mortality was observed during weeks 14 and 15 (1,383 in-hospital deaths overall), then it decreased afterwards. A new variable was added to the EMS database, related to COVID-19 status (confirmed or suspected), which allowed us to trace COVID-19 status among OHCA victims (either witnessed and/or admitted alive, N=299). Among those admitted alive, screening for COVID-19 was performed according to clinical suspicion in 20 (32%) of patients whereas 43 (68%) were not tested.

Statistical Analysis

Continuous data were described as mean \pm SD or median [interquartile range], depending on distribution, and categorical data as number (percentage). Continuous variables were compared by applying Student's *t*-test, the Mann-Whitney test, or the Kruskal-Wallis test, as appropriate and categorical variables were compared using the χ^2 test.

The maximal weekly incidence of OHCA during the pandemic period (weeks 13 and 14) was compared with the incidence of OHCA during the non-pandemic period #1 (weeks 13 and 14, from 2012 to 2019). The incidences of OHCA and their 95% confidence intervals (CI) were estimated by considering the population aged ≥ 18 of the four districts. For the weeks 12-17, significant population migration outside Great Paris Area was observed and taken into account in each district, based on the

data of the National Institute of Statistics and Economic Studies (last assessed on May 6st, 2020). Of note, lockdown (started on March 16th) was maintained throughout the pandemic period, and the subset of population who left, did not come back due to movement restrictions.

Additional data on in-hospital mortality as well as hospitalizations related to COVID-19 were collected from the National Institute of Statistics and Economic Studies (last assessed May 1st, 2020).

Multivariable logistic regression analysis was performed to assess the association of pandemic period with survival at hospital admission. Odd ratios (ORs) and their 95% CI were calculated with adjustment for potential confounding factors including sex, age, location, bystander cardiopulmonary resuscitation, use of automatic external defibrillator prior to EMS arrival, shockable cardiac rhythm, at call answer-to-arrival delay. Survival status at hospital discharge was known in 63 (94%) patients.

P values less than 0.05 were considered statistically significant. Statistical analysis was performed using R software, version 3.6.1 (R Project for Statistical Computing).

Role of the Funding Source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all of the data and the final responsibility to submit for publication.

RESULTS

From May 15th, 2011 to April 26th, 2020, there were 30,768 cases of OHCA in the Great Paris Area. The mean age was 68.4±18 years, and 19,002 (62%) were men.

OHCA occurred at home in 23,282 cases (76%) and in public places in 7,334 cases (24%). A witness was present in 18,781 cases (66%), and cardiopulmonary resuscitation was initiated in 11,184 cases (61%). An automatic external defibrillator was used in 368 cases (4%) prior to EMS arrival in the field. Overall, 4,713 OHCA (19%) presented with shockable rhythm (ventricular tachycardia or fibrillation), and finally 6,992 (23%) were admitted alive in one of the 48 hospitals of the area.

Patient characteristics and circumstances of OHCA occurrence are reported in Table 1. During the pandemic period (March 16th to April 26th, 2020), a total of 521 OHCA occurred, giving a maximal weekly incidence of 26.64 (95%CI 25.72-27.53) per million inhabitants (weeks 13 and 14), significantly higher than during the same period between 2012 and 2019: 13.42 (95%CI 12.77-14.07) ($P<0.001$), with a rapid return to usual incidence range afterwards (Figure 1). A geographic heterogeneity was found in terms of OHCA increase, with significantly more OHCA surge in the departments with a low density of medical facilities (North-East of Paris, 13.62, 95%CI 12.79-14.46, OHCA increase per million inhabitants) compared to departments with a high density of medical facilities (intra-muros and West Paris, 28.33, 95%CI 26.94-29.71, OHCA increase per million inhabitants) ($P<0.001$) (Figure 2).

Patient characteristics did not substantially differ in terms of age (69.7 ± 17 vs. 68.5 ± 18 years, $P=0.18$) and male proportion (64 vs. 60%, $P=0.08$). By contrast, major differences were observed in circumstances of occurrence: 460 OHCA occurred at home (90 vs. 77% for the same non-pandemic period, $P<0.001$), less shockable cardiac rhythm at EMS arrival (9 vs. 19%, $P<0.001$), and less use of automatic external defibrillator (<1 vs. 4%, $P=0.001$) (Table 1). Response time, defined as Call Answer-to-EMS arrival was statistically longer.

During the pandemic period, the proportion of OHCA with resuscitation attempt and advanced life support was lower than usual (53 vs. 66%, $P<0.001$), and survival at hospital admission decreased from 22.8% to 12.8% ($P<0.001$), with a return to usual incidence followed by a return to usual survival range towards the end of the period (Figure 3). In multivariable logistic regression analysis, after considering potential confounding factors including sex, age, location, bystander cardiopulmonary resuscitation, use of automatic external defibrillator prior to EMS arrival, shockable cardiac rhythm, at call answer-to-arrival delay, pandemic period remained statistically associated with lower survival at hospital admission (OR 0.36, 95%CI 0.24-0.52, $P<0.001$). Overall, 16 (25%) patients were discharged alive.

A total of 42 patients who had OHCA were suspected to have or had received a diagnosis of COVID-19 (17 and 25 patients, respectively); these numbers account for 33% of the increase in cases of OHCA observed in the Great Paris Area.

DISCUSSION

During the COVID-19 pandemic, the number of OHCA occurring in the Great Paris area almost doubled. OHCA survival rate to hospital admission was dramatically reduced as well, leading to a major rise in OHCA-related deaths during the pandemic that started declining at the end of the study period. While this may be partially related to direct COVID-19 deaths, indirect effects through lockdown, behavior changes and pandemic-related health system issues (overwhelming of emergency medical services and postponement of consultations and scheduled non-urgent procedures) are likely.

Data from the last nine years of the Paris-SDEC registry indicates that the incidence of OHCA has been relatively stable over time in the Great Paris Area,

which is in contrast with the major increase observed during the pandemic period. Both direct and indirect effects of COVID-19 might explain this increased incidence.

The lethality of COVID-19 through acute respiratory distress syndrome or excessive immune response is well established.¹⁶ It is therefore possible that some of the OHCA observed during the pandemic are actually respiratory deaths among COVID-19 patients who were not hospitalized. Besides, COVID-19 can lead to cardiovascular injury and myocarditis; experimental treatments such as hydroxychloroquine or azithromycin might also lead to OHCA.¹⁷ Acute cardiac events can be observed, including acute coronary syndromes, heart failure and arrhythmias, therefore making OHCA a possible presentation. Finally, a major prothrombotic state has been reported during COVID-19 infections, with a consequent increase in thromboembolic events including pulmonary embolisms and acute coronary syndromes.¹⁸ To the best of our knowledge, only one original report described an increase in OHCA incidence in Lombardy, Italy, a specific setting where the pandemic was more violent than what was observed in most regions worldwide.^{6,7} Overwhelming of medical services occurred and rules were set to prioritize hospital admissions and intubation among COVID-19 patients. This could have led to several deaths from COVID-19 occurring at home and being counted as OHCA, as suggested by the high rate of COVID-19 suspicion or diagnosis among OHCA victims, which accounted for 77% of the surge in OHCA cases. Conversely, in our study, we provide a picture of the surge of OHCA in a setting where a severe pandemic was observed, but the healthcare system was still able to handle all COVID-19 cases without specific limitations, leading to a much lower proportion of cases being related to COVID-19 infection.

Among COVID-19 negative patients, an indirect effect, related to changes in public behavior and reorganization of healthcare system, might lead to an increase in OHCA in the pandemic setting.¹⁹ With lockdown and movement restrictions, patients have more difficulty seeking medical advice. They might also be reluctant to present to emergency departments or doctors' offices, due to apprehension of COVID-19 infection, or long waiting times. Besides, stable interventions and consultations had to be postponed in order to favor COVID-19 related activity and avoid exposing patients to an unnecessary risk of contamination at the hospital or medical office. Finally, the effect of increased psychological stress during a pandemic, brought about by fear, restriction and grief due to loss of loved ones, can also potentially trigger adverse cardiac events and arrhythmias, ultimately leading to OHCA.

In addition to the dramatic increase in OHCA incidence, we also noted a drastic reduction in survival to hospital admission. OHCA witnesses and emergency responders may be reluctant to perform cardiopulmonary resuscitation on potentially infected cases, as cardiopulmonary resuscitation is considered an aerosol generating procedure with significant risk of transmission.²⁰ Some hospitals issued directives prohibiting cardiopulmonary resuscitation for potentially COVID-19 cases unless full personal protective equipment is worn,²¹ which may be impractical in the out-of-hospital setting. Besides, more OHCA occurred at home where the witnesses present during time of lockdown are most likely to be family members, and are less likely to perform cardiopulmonary resuscitation.²²⁻²⁴ Finally, OHCA occurring in hypoxemic patients with COVID-19, and OHCA related to advanced cardiac injury such as in late presenters of acute myocardial infarction, might have worse survival compared.

During the last two weeks of the study period, despite the persistence of the COVID-19 pandemic, there was a relative decrease in OHCA incidence although

survival to hospital admission remained low. EMS have been reorganized in some extent allowing a better response to non-COVID related calls. Teleconsultations were developed, and public campaigns were made to encourage seeking of medical attention for non COVID-related symptoms, which probably prompted patients to get early medical care upon onset of cardiac symptoms, before OHCA occurrence. The delay in improvement in survival rate compared to incidence is unsurprising, given the persistent low cardiopulmonary resuscitation rate among family members and bed shortages in intensive care units that obligated EMS to carefully triage OHCA cases likely to benefit from hospital transfer.

Despite being one of the first paper to describe the indirect impact of the ongoing COVID-19 pandemic at the population level,⁶ some limitations need to be acknowledged. First, while we have demonstrated a major increase in absolute OHCA numbers, this change in incidence does not account for the decrease in tourism flow; given the absence of tourists during the pandemic, this might have led to a lower number of OHCA. Second, while COVID-19 status was confirmed in 5% of patients, particularly among those admitted alive, in the others, COVID-19 status was either based on anamnesis or unknown. The exact proportion of COVID-19 related OHCA is therefore unknown. Besides, some OHCA might have occurred in infected patients without being due to the infection. Finally, the study was conducted in the Great Paris Area and specificities related to the location, including healthcare system organization, might not apply to other countries.

CONCLUSION

During the COVID-19 pandemic in the Great Paris Area, we observed a significant increase in the incidence of OHCA, coupled with a major reduction in survival and hospital admission. While this may be partially related to direct COVID-19 deaths,

indirect effects related to lockdown, and reorganization of healthcare systems might account for a substantial part.

Table and Figures

Table 1 – Baseline Characteristics, Initial Management and Outcome of OHCA, According to the Analyzed Period (Pandemic and Non-Pandemic).

Table 2 – Number, Population and Weekly Incidences in the Different Districts of the Great Paris Area (Weeks 5 to 17).

Figure 1 – Weekly Incidences of OHCA During the First 16 Weeks of Years 2012 to 2020. Compared to previous years and to beginning 2020, there was a surge in OHCA incidence starting week 12 of 2020, with a rapid return to normal by week 15.
OHCA: Out-of-Hospital Cardiac Arrest

Figure 2 – Density of Medical Facilities and Surge in Out-of-hospital Cardiac Arrest Incidence Across the Great Paris Area.

Significant differences exist in the density of hospitals and mobile intensive care unit in the Great Paris Area, with a highest density observed in Paris intra-muros. The highest increase in OHCA incidence was observed in areas with low density of medical facilities.

BSPP: Brigade de Sapeurs-Pompiers de Paris; SAMU: Service d'Aide Médicale Urgente

Figure 3 – Proportion of Patients Admitted Alive at Hospital During Weeks 5 to 16 of 2020 Compared to the Same Period in the Previous Years.

Compared to similar periods in the previous years, there was a decrease in OHCA survival at hospital admission during the pandemic period of 2020.

OHCA: Out-of-Hospital Cardiac Arrest

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Declaration of Interest

No conflict of interest to declare.

Contributors Section

EM and XJ had full access to all of the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: EM, NK, DJ, WB, XJ

Literature search: EM, NK, DP, WB

Acquisition of data: EM, NK, DJ, FB, AS, VW, BF, CD

Analysis and interpretation of data: EM, NK, DJ, DP, WB, XJ

Drafting of the manuscript: EM, NK, KN, WB, XJ

Critical revision of the manuscript for important intellectual content: DJ, AS, VW, KN, AL

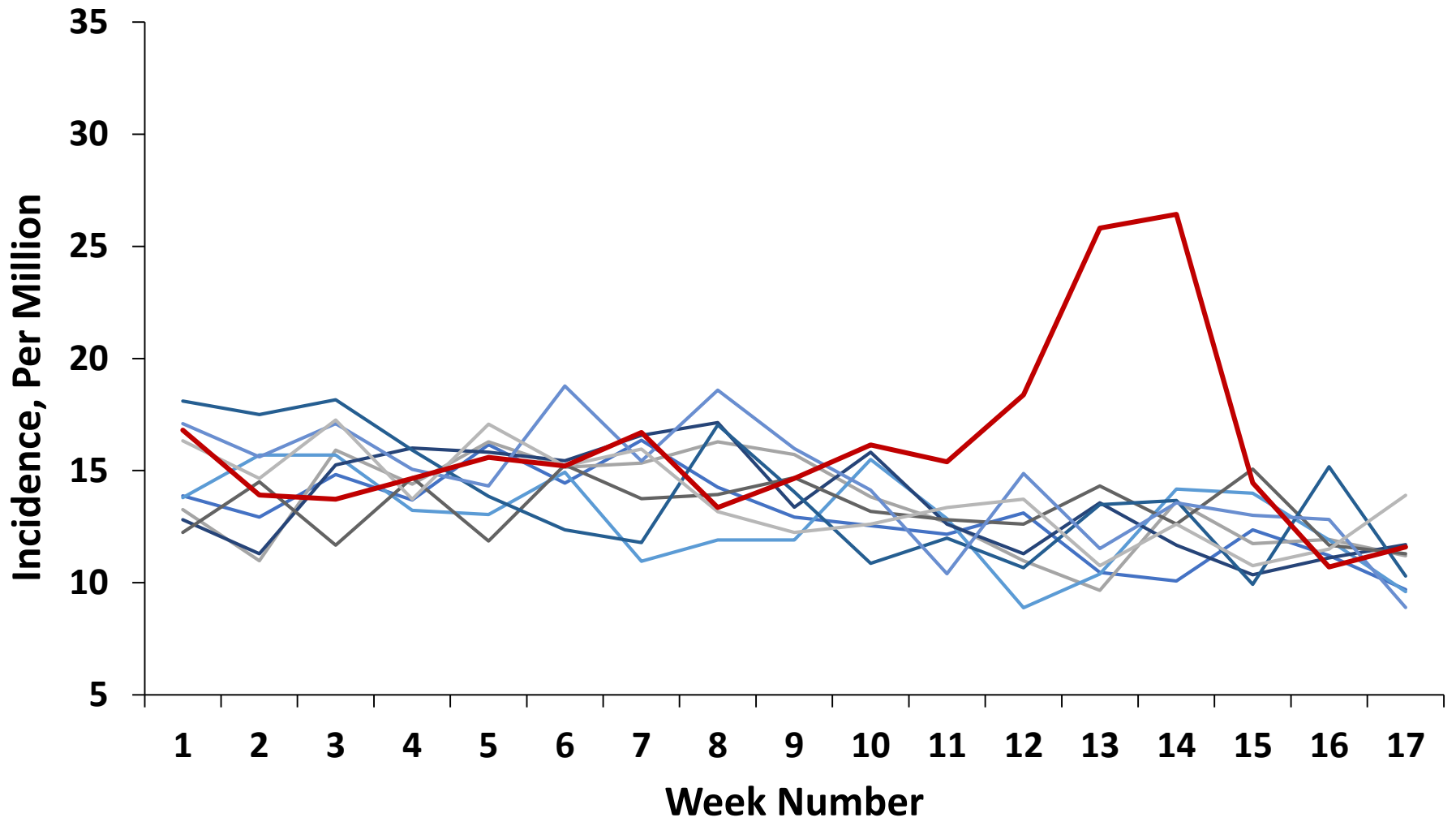
Statistical analysis: EM, NK, BF, DP

Figures: EM, NK, DP

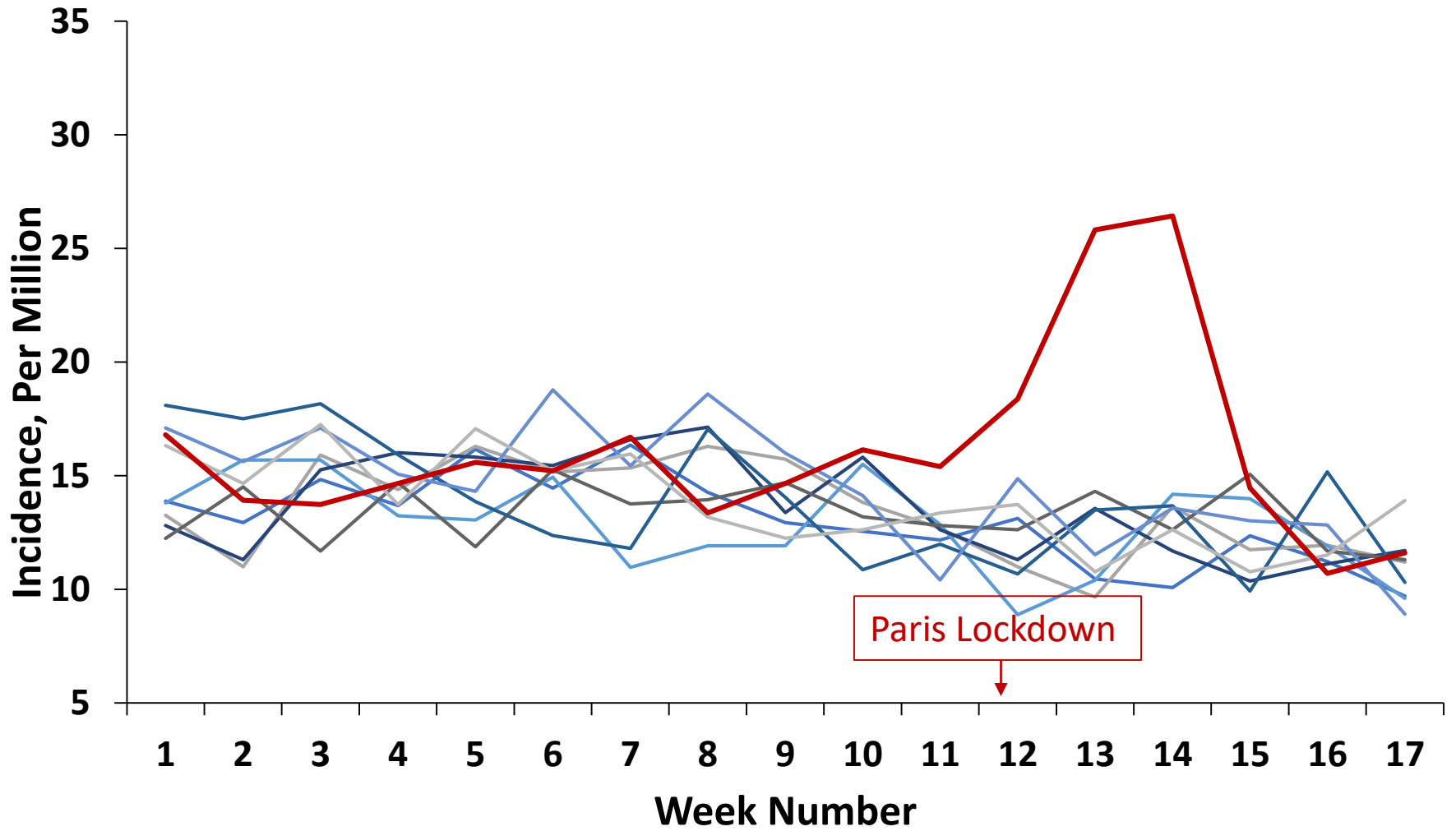
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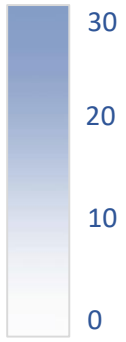


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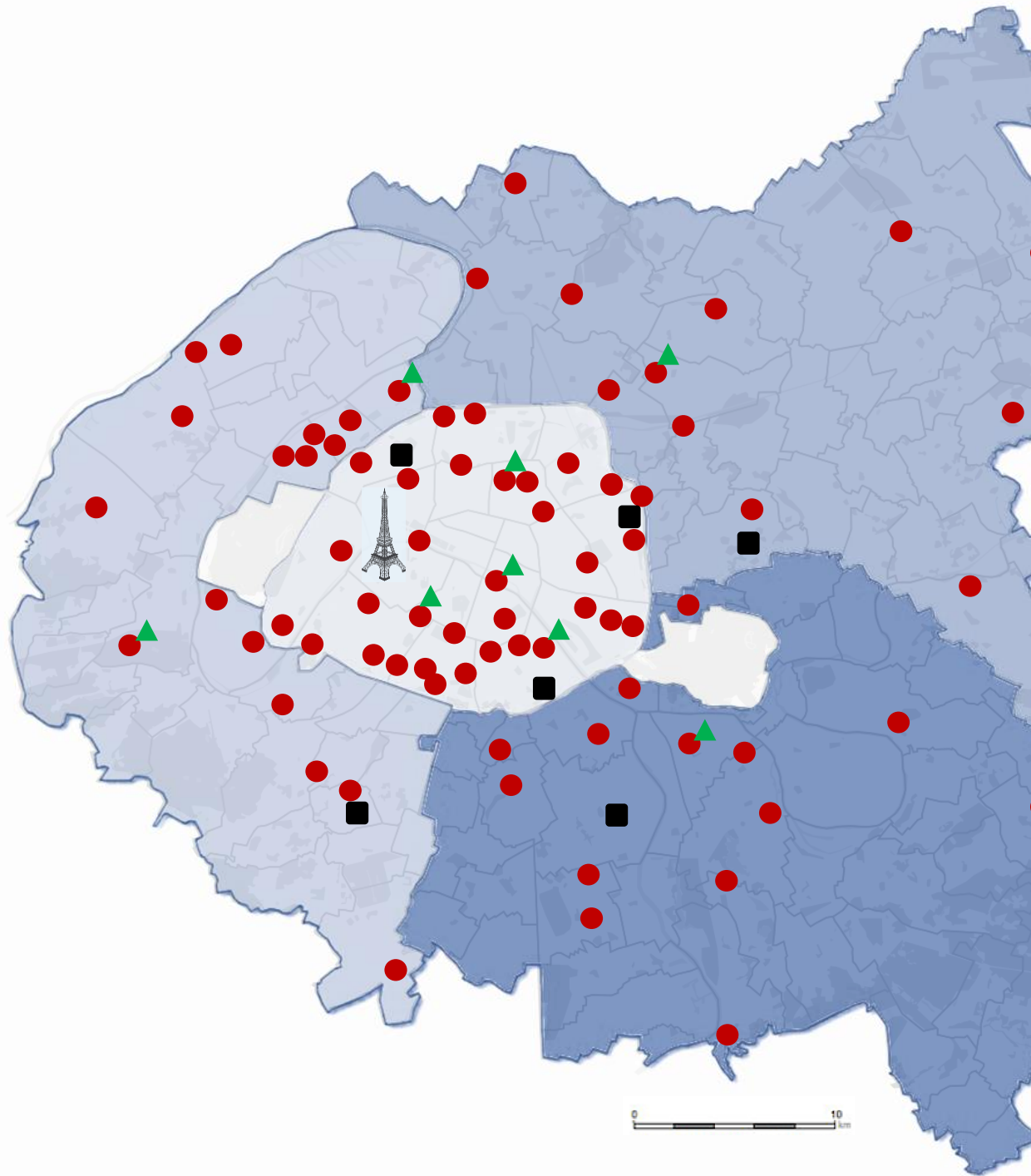


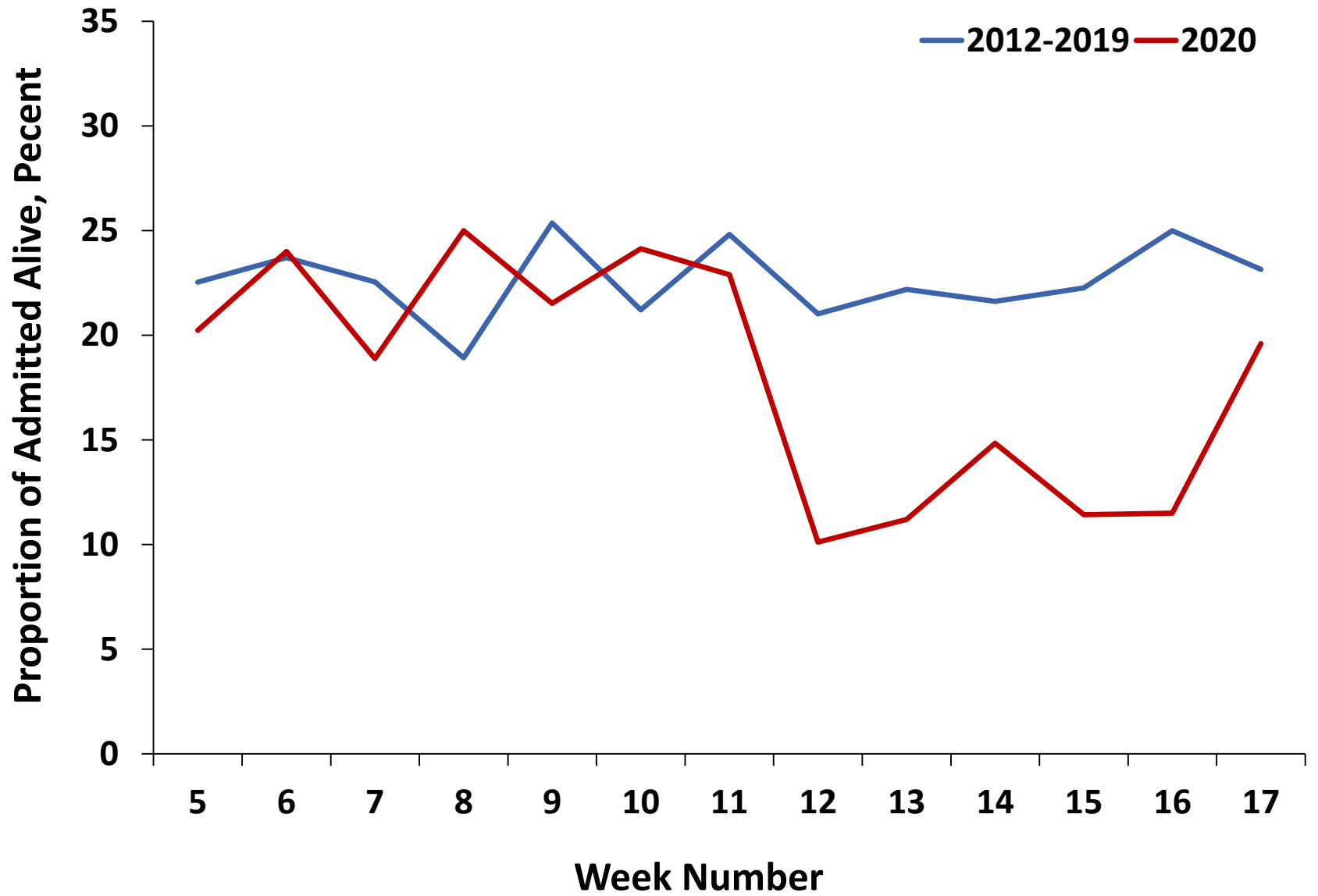
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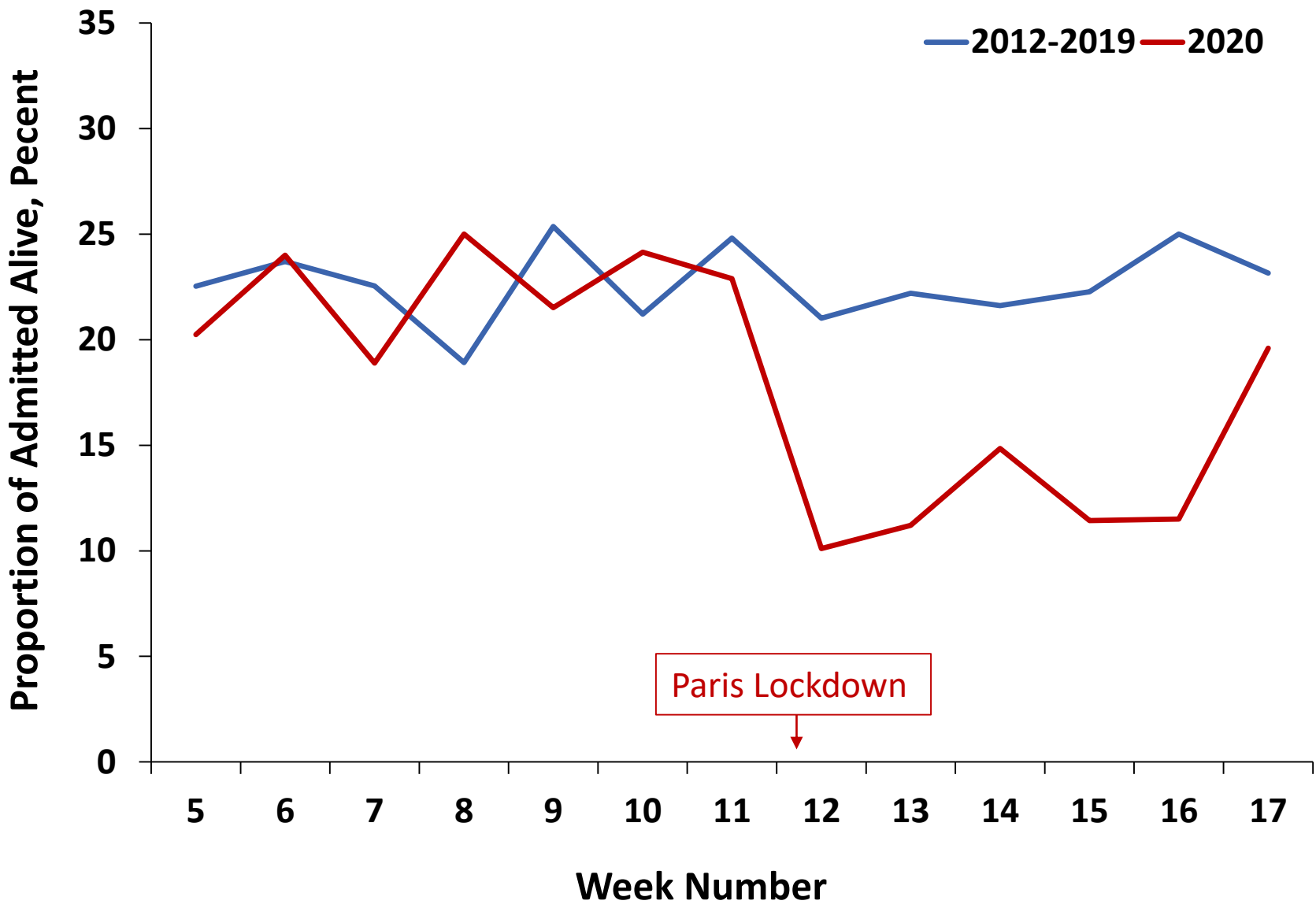
Inflation of OHCA Incidence
Per Million Inhabitants



- Public and Private Hospitals
- ▲ Mobile Intensive Care Units (SAMU)
- Mobile Intensive Care Units (BSPP)







Population Characteristics	Pandemic Period (2020, W12-17) N=521	Non-Pandemic Period #1 (2012-2019, W12-17) N=3,052	Non-Pandemic Period #2 (2011-2020, except W12-17) N=27,195	P Value
Male, n (%)	334 (64)	1,826 (60)	16,842 (62)	0.09
Age, years, mean \pm SD	69.7 \pm 17	68.5 \pm 18	68.7 \pm 18	0.20
Home location, N (%)	460 (90)	2,336 (77)	20,486 (76)	<0.001
Witness, N (%)	294 (59)	1,887 (65)	16,600 (66)	0.003
CPR initiated, N (%)	239 (48)	1,165 (64)	9,780 (61)	<0.001
Public AED use, N (%)	2 (<1)	33 (4)	333 (4)	0.001
Shockable rhythm, N (%)	46 (9)	472 (19)	4,195 (19)	<0.001
Median response time, min				
Call Answer-to-Arrival	10 [8-13]	9 [8-12]	9 [7-12]	<0.001
On road	6 [4-8]	5 [3-8]	5 [3-7]	
Survival at hospital admission, N (%)	67 (13)	695 (23)	6,230 (23)	<0.001
Survival at hospital discharge, N (%)	16 (25)	164 (25)	1450 (25)	0.98

Pandemic period defined as period extending from the 16th of March to the 26th of April, 2020 was considered as the 6 weeks of the pandemic in the Paris region.

Non-pandemic Period #1 defined as weeks 12 to 17 of each year from 2012 to 2019.

Non-pandemic Period #2 defined as data of patients included in the Paris-SDEC registry from 2011 to 2020, excluding weeks 12 to 17.

AED denotes automatic external defibrillator, CPR, cardiopulmonary resuscitation, W, week number.

Percentages were calculated on the basis of the total number of known events.

