

# International Perspectives on the Impact of the COVID-19 Pandemic on Adherence to Prescribed Dual Antiplatelet Therapy: A Window Into Acute Cardiovascular Care

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**Abstract:** An international panel of expert clinicians and researchers in acute cardiac care was convened to review, describe, and contextualize their varied experiences delivering care and maintaining ongoing research during the first year of the COVID-19 pandemic and beyond. A proposed perspective from which care and outcomes could be viewed was the possibility that without routine follow-up and as-accustomed interactions with their care team, patients at risk of acute atherothrombotic events might be less adherent to prescribed antiplatelet medications. This might be manifested by more emergency coronary events or by an increased (and perhaps unidentifiable) incidence of out-of-hospital cardiovascular deaths related to patient anxiety about presenting to hospital during the pandemic. The experiences of the panel members were similar in many regards, which identified opportunities for improvement in cardiac care the next time there is a substantial disruption of usual practice. Regardless of geography or payor system, there was an identified need for better remote care platforms; but stronger infrastructure and consumer facility with remote care technology, improved provider-patient communication to help ensure adherence to primary and secondary prevention medications, and longer-term prescription fills and no-hassle refills on such medications. Profound disruptions in acute cardiovascular research highlighted the need for redundancy or back-up planning for teams engaged in time-sensitive research, to ensure both continuity of protocols and patient safety.

**Key words:** COVID-19, DAPT, patient education

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## INTRODUCTION

The global pandemic of infection that began in Europe and North America late in the first quarter of 2020 with multiple variants of the SARS-CoV-2 coronavirus, subsequently termed COVID-19, has had an unprecedented, unanticipated, and profound impact on the delivery of both acute and chronic care across disease states and across borders. The impact of the pandemic on acute cardiovascular care has been particularly damaging, as it has increased the risk of cardiac events in multiple ways, whereas simultaneously generating a novel apprehension about contagiousness that affected patients' willingness to seek acute care.

Factors perceived to have increased the risks of acute coronary events in at-risk patients include the proinflammatory and prothrombotic effects of the viral infection itself; changes in or absence of routine follow-up to reinforce the need for medication adherence, such as with platelet P2Y<sub>12</sub> receptor antagonists and other preventative therapies; emotional, social, and financial stress; disruption of regular fitness/activity regimens; changing patterns of substance abuse and use (in particular, tobacco); over-stressed human and facility resources at receiving hospitals where patients did seek acute care; and time-dependency of acute cardiac interventions. On the other hand, some patients' risk profiles might have actually improved during "lock-down" periods of the pandemic response, due to factors such as a new-found ability to work from home; decreased stress from commuting and travel; and decreased levels of air pollution.

Patients with coronary artery disease (CAD) prescribed P2Y<sub>12</sub> receptor antagonists are most commonly being treated after either an acute coronary syndrome (ACS) or percutaneous coronary intervention (PCI), or to attenuate high risk due to prior ischemic events or related comorbidity burden (such as diabetes). Similar to blood pressure treatments and lipid-lowering medications, antiplatelet drugs do not relieve patients' symptoms; consistent adherence relies on patient education and collaboration with the healthcare team. Given that the pandemic disrupted this relationship, the likelihood of non-adherence might be assumed to increase, as well as the risk of acute events. Many questions arise: if patients had such events, would they be captured in contemporaneous healthcare data? Would healthcare systems be able to initiate alternative care pathways, such as readily available telehealth visits, to fill the gap created by the pandemic? If telehealth was available, would patients adapt to and benefit from its use? If patients and their caregivers were resistant to visiting a healthcare facility, even with acute symptoms, would the outcomes of any underlying events be worsened? These questions and others, regarding the impact of the pandemic on acute cardiovascular care through the lens of antiplatelet therapy adherence, were discussed by a multinational expert panel representing different perspectives from within varying healthcare delivery systems:

- Dr. Gabriel Steg, presenting the French (single payor) perspective from within acute cardiac care, but also from the national level as a high-level participant in his country's national response.
- Dr. Stefan James, presenting the Swedish (single payor) perspective from with acute cardiac care, but from a country that did not implement large-scale lockdowns and which maintains a rigorous national registry of cardiac events and care.
- Dr. Sanjit Jolly, presenting the Canadian (single payor) perspective on acute cardiac care.
- Dr. Mikhail Kosiborod, presenting the United States (multi payor) perspective on acute cardiac care, particularly in rural and other underserved areas.
- Dr. Marc Bonaca, presenting the United States (multi payor) perspective on acute cardiac care, particularly in urban but also and in rural areas.

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- Dr. Charles Pollack moderated and facilitated the discussion, which also addressed the impact of the pandemic on ongoing cardiovascular research.

## BACKGROUND

The importance of adherence to prescribed P2Y<sub>12</sub> receptor antagonist therapy in at-risk patients prompts little disagreement among cardiologists; debate persists only about the optimal length of dual antiplatelet (DAPT) treatment after PCI or ACS. A meta-analysis of studies comparing the short duration (<6 mo) versus prolonged duration of DAPT (>12 mo or more) suggested that extending DAPT beyond 6 months increased the risk of bleeding without further reducing ischemic events.<sup>1</sup> A subsequent study, however, showed that DAPT continued for >1 year after placement of a drug-eluting stent (DES), compared with aspirin monotherapy, significantly reduced the risks of stent thrombosis and major cardiovascular and cerebrovascular events.<sup>2</sup> Hence, prolonged DAPT beyond 12 months may be considered in selected patients with high thrombotic risk, such as those with prior myocardial infarction (MI),<sup>3</sup> diabetes, and prior PCI.<sup>4</sup> Indeed, early discontinuation of therapy (variably defined as after 1–9 mo<sup>5</sup>) is the most powerful predictor of stent thrombosis for patients treated with DES.<sup>6,7</sup>

Medication adherence among patients requiring DAPT is influenced by multiple considerations but is dependent primarily upon proper prescription, patient education, and reinforcement of that education from interventional cardiologists and follow-up primary care providers.<sup>8</sup> Disruption in continuity of care adversely impacts the consistency of education delivery. The effects of DAPT in at-risk patients go well beyond reduction in the risk of in-stent thrombosis to include secondary prevention of atherothrombotic major adverse cardiac events. Interruption of DAPT—especially in the first weeks to months after an atherothrombotic event—can have disastrous consequences for patients due to stent thrombosis. It is against this background that our expert panel considered the impact of the COVID-19 pandemic on cardiovascular care and research in general, and potentially on DAPT adherence and the concerns for poor outcomes that could result from nonadherence.

## FRANCE: GABRIEL STEG, MD, INTERVENTIONAL CARDIOLOGIST

The COVID pandemic had a dramatic impact in France, particularly during the first and second waves that hit the country from March to May 2020 and from October to December 2020, respectively. These surges led the French government to implement protracted lockdown measures. During that period, France was one of the most brutally affected countries in Western Europe, second only to Italy and Spain. Similar to other countries, however, the incidence of COVID-19 was highly heterogeneous among regions: Eastern France, the North, and Greater Paris were hit particularly hard, whereas the western part of the country had many fewer cases. During peak periods, all hospitals in the affected areas were reorganized to attempt to accommodate a large influx of patients requiring hospitalization for supplemental oxygen and a substantial proportion who needed intensive care. In Greater Paris, for example, hospitals (Assistance Publique-Hôpitaux de Paris, or AP-HP), a network of 39 academic hospitals serving approximately 8 million people, there was a steep increase in the number of patients hospitalized for COVID-19 and of the number requiring admission to an intensive care unit (ICU).<sup>9</sup> The number rapidly exceeded the total number of ICU beds available (Figures 1A and 1B). This resulted in the cancellation of most elective surgical and interventional procedures, as surgical intensive care beds, operating rooms, and even non-ICU beds (and the corresponding staff) were reallocated to COVID-19 intensive care.

In addition, in most cardiology departments, a substantial proportion of coronary care unit beds and standard beds were also allocated to COVID-19 units. In my own institution, during the first wave, half of the entire department, including half of the coronary care unit beds, were reallocated to COVID-19 and were staffed by the cardiology nurses and doctors. After receiving a crash course in COVID-19 care from a multidisciplinary team of intensive care physicians, pulmonologists, and infectious disease specialists, cardiologists handled medical care on these COVID-19 units. COVID-specific consultation systems were set up with internal medicine and intensive care, with a permanent ethical advisory committee on hand to assist with end-of-life decisions. Additionally, approximately 25% of our medical and nursing staff were reallocated, on a volunteer basis, to COVID-19 units outside of cardiology. Practical COVID-19 management guidelines were issued for the entire institutional network, updated on a regular basis, and shared via the institutional website. Older doctors (semi-retired or retired) volunteered to man telephone lines handling patient advice. Thousands of students in medicine, nursing, pharmacy, and dentistry schools were called upon to work as paramedics or research assistants, or to assist with telemedicine consultations. Finally, all research staff were entirely reallocated to COVID-19 specific studies and trials.

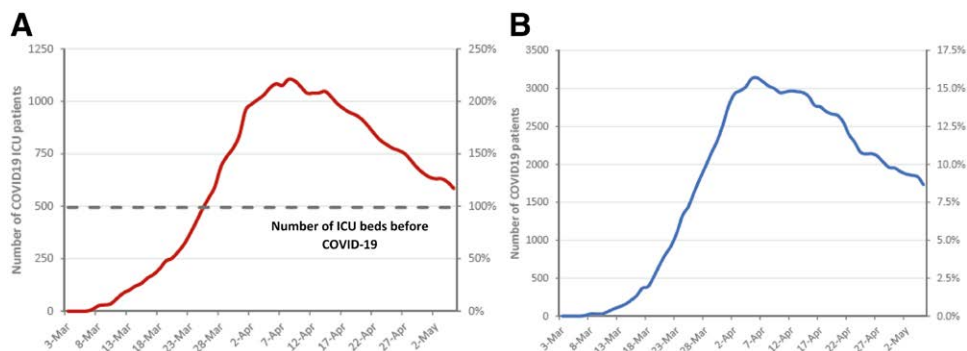
A COVID-19-specific research committee was tasked with developing a global research strategy together with universities and INSERM, the National Institute of Health and Medical Research in France. The committee's main research priorities were establishment of large patient cohorts and registries, biobanking, and randomized clinical trials. During the first 2 months of the first wave, >40 studies were developed and launched. To address the shortage of equipment, particularly small machine parts, a farm of 3D printers was set up by AP-HP to manufacture these items. In parallel, a telemedicine platform (COVIDOM), manned largely by retired or older physicians, was set up to monitor patients who were either sick at home, but did not require hospital admission, as well as patients being discharged from hospitals. That platform facilitated monitoring, via 2-way short messaging systems and phone communications between healthcare professionals and >50,000 patients at home during the first wave. Finally, a contact tracing program—COVISAN—was set up for the greater Paris region, relying on primary care physicians, specialized hospital physicians, private companies, and the regional health authorities.

## Impact on Patients With CAD

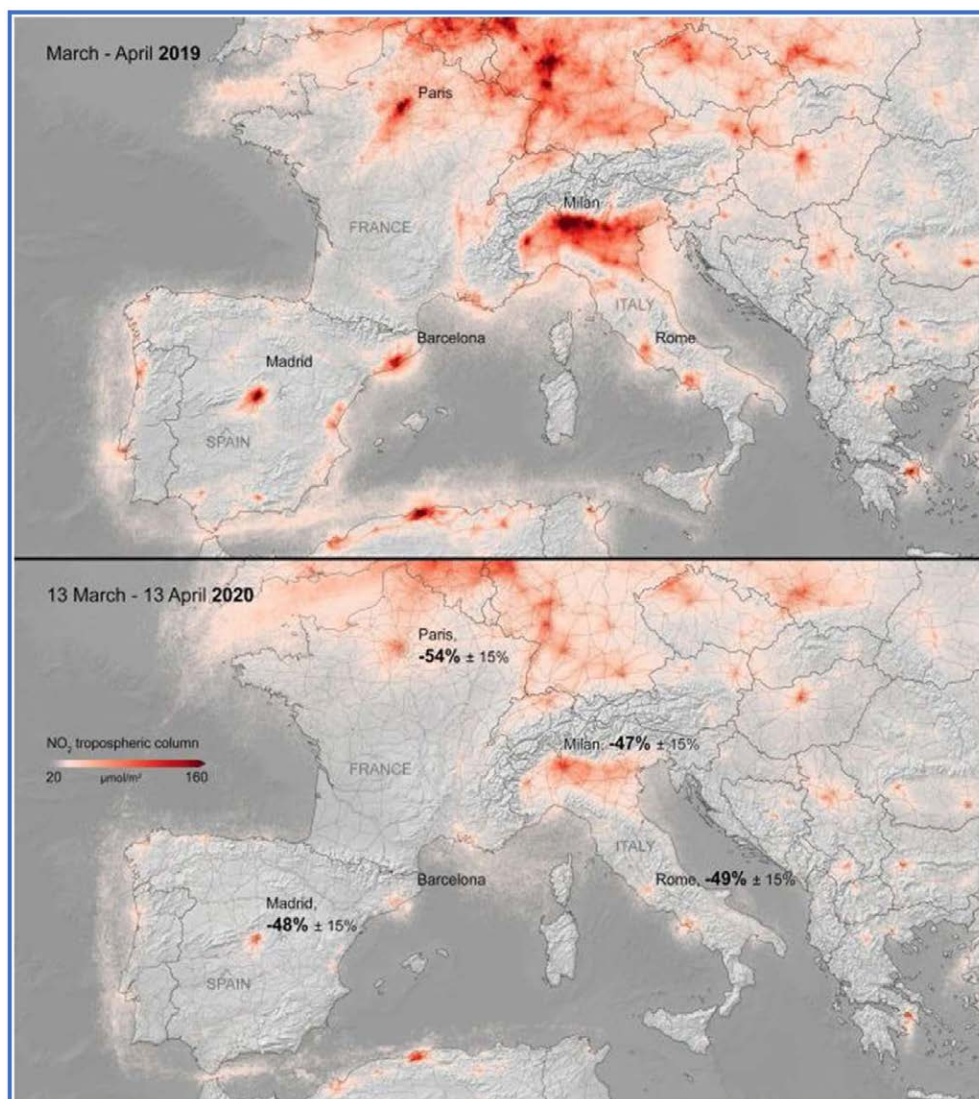
As was seen in other countries, the COVID-19 pandemic peaks resulted in a dramatic reduction in the number of patients admitted with acute MI across France.<sup>10</sup> In a multicenter, nationwide, ongoing, continuous registry of acute MI, the number of MI admissions was reduced by 30% during the lockdown, with a slightly greater decrease for non-ST segment elevation MI (NSTEMI) compared with STEMI (24%). Although the reasons for the decrease in admissions remain conjectural, there are most likely multiple causes.

It is highly plausible that a large fraction of the reduction reflects patient reluctance to go to hospitals at the time of the lockdowns for fear of contamination, but also due to concerns about availability of staff and hospital beds, and a desire not to add to the healthcare system burden. This hypothesis is supported by the decreased incidence of MI being more marked for NSTEMI than for STEMI, a condition in which symptoms may be more severe and presentation more acute than the former. The incidence of acute MI may have truly been reduced during lockdown, due to a substantial reduction in air pollution (Figure 2),<sup>11</sup> a known trigger for acute MI,<sup>12</sup> and to the reduced work and commuting stress.

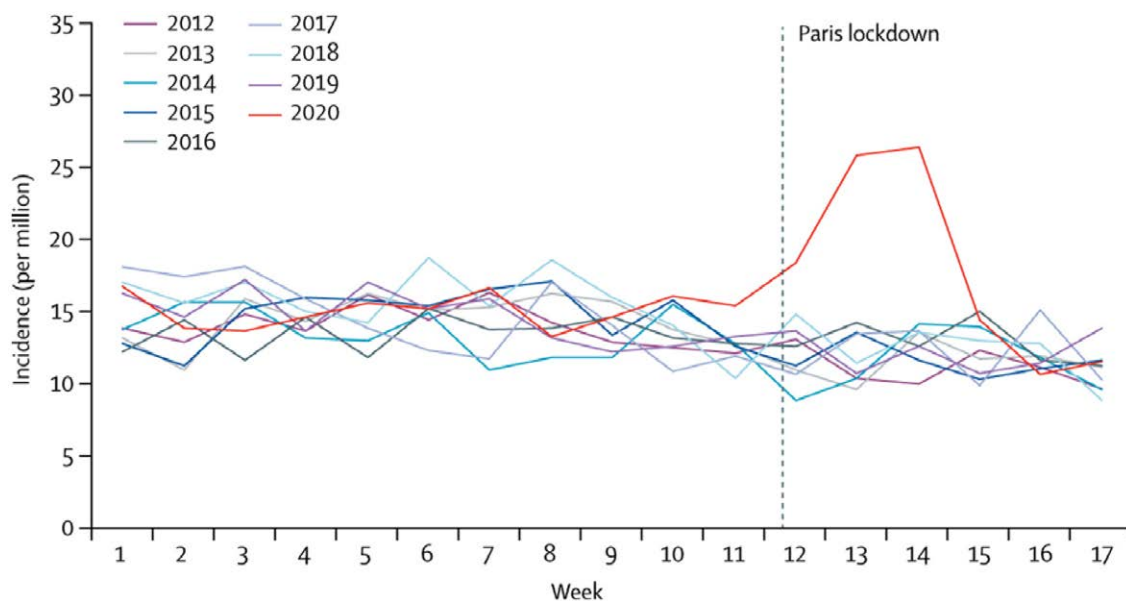
There was also a striking increase in the incidence of out-of-hospital cardiac arrest at the time of lockdowns seen in France<sup>13</sup> (Figure 3) and Italy,<sup>14</sup> which suggests that some patients may have



**FIGURE 1.** A, Number of patients with COVID-19 admitted to ICUs), from the first wave in France starting March 2020. B, Number of patients with COVID-19 admitted to normal hospital beds in the Greater Paris AP-HP hospitals during the first COVID-19 wave.<sup>1</sup> ICU, intensive care unit.



**FIGURE 2.** European air before and after lockdown showing cleaner air after the lockdown. Spring levels of nitrogen dioxide concentration in Europe before, above (year 2019), and after coronavirus containment measures enacted, below (year 2020) (Image: ESA/Copernicus Sentinel data [2019–2020] processed by KNMI/ESA). <https://www.space.com/europe-air-pollution-drop-during-coronavirus-lockdowns.html> (accessed April 25, 2020).<sup>11</sup>



**FIGURE 3.** Weekly incidence of out of hospital cardiac arrest during the first 17 weeks of each year, from 2012 to 2020, showing a marked increase in the incidence in 2020, coinciding the COVID lockdown.<sup>10</sup>

inappropriately delayed seeking medical care and tried to “tough it out” on their own.

An issue that emerged after the lockdown was the problem of patient adherence to prescribed cardiovascular treatments including, but not limited to, antiplatelet therapy in patients with recent ACS or recent PCI and stents. There is yet not much data available in France regarding the issue, but it is likely that canceling direct contact and reduced interactions with healthcare professionals may have reduced patient adherence to preventive therapies and negatively affected their outcome, for example, by increasing the incidence of stent thrombosis in the case of patients prescribed DAPT after stenting. And indeed, there have been case series of stent thrombosis occurring during lockdowns in other countries.<sup>15</sup> In addition, it is plausible that COVID-19 itself, which is accompanied by a major inflammation and prothrombotic state, can increase the risk of stent thrombosis even in patients with relatively mild clinical forms of COVID-19 disease. However, whether the incidence of stent thrombosis actually increased in patients not affected with COVID-19, during the pandemic, remains largely speculative.

### Impact of Telemonitoring and Telemedicine on Patients With Coronary Artery Disease

During the first wave and the attendant protracted lockdown, all clinic visits were suspended, and video consultation systems were set up. Although these allowed secure and effective teleconsultations, they were cumbersome to use and many patients (and physicians) resorted to video communication using simple smartphone applications. The innovative COVIDOM telemedicine platform was mainly designed to monitor patients with suspected or confirmed COVID-19 infection and was not used for telemonitoring of other conditions (which in retrospect should probably have been set up, at least for selected patient subsets with high-risk conditions such as advanced cardiovascular disease). Overall, the frequency and intensity of interactions between patients and cardiovascular care professionals were clearly reduced during the pandemic and this likely affected the ability to diagnose, monitor, and treat these patients.

### Lessons Learned From the Pandemic

First, There are several lessons which were learned “the hard way” for cardiovascular clinicians during the pandemic: (1) The need to communicate with patients. There are many systems that allow 2-way communication with patients. However, they were largely underused during the pandemic, under the assumption that patients needing help would contact physicians first. One of the major lessons learned is that this is not true. Many patients who are facing major issues, including signs of myocardial ischemia or arrhythmias, did not contact the healthcare system and seek help. This implies that physicians need to contact patients proactively on a regular basis and must publicize the pathways for contact. The assumption that “no news is good news” is wrong. Many physicians assumed that patients who did not seek teleconsultation were stable and free of symptoms or major complaints. When the first pandemic waves subsided, it became apparent that many patients in distress or who had major concerns regarding their health or treatment had made decisions on their own, including decisions to discontinue some important chronic treatments. Antiplatelet therapy is a case in point. For many patients, DAPT is only a nuisance, resulting in bleeding (bruising, nose bleeds, gum bleeds or more severe bleeding episodes) whereas the benefits of thrombotic events prevented are not tangible. Therefore, some patients discontinued one or more antiplatelet agents during lockdown. Systems for monitoring adherence must be put in place to allow minimization of treatment disruption, which is well documented to be associated with worse clinical outcomes.<sup>16</sup>

Second, COVID-19 turned out to be a challenge for clinical research, with the need to set up clinical studies and trials to study the pandemic rapidly, in an emergency setting. At the same time, although human and material research resources were quickly diverted to address COVID-19, many non-COVID-19 studies were completely disrupted with problems of drug supply to hospitals and to patients, impaired patient monitoring with fewer patient visits, difficulty in implementing study procedures, visits, event documentation, and monitoring in patients already enrolled in ongoing clinical trials. In the future, it will be critical to allocate sufficient resources to ensure a reasonable amount of study maintenance for non-health emergency-related long-term trials. A critical aspect is the ability to establish

and maintain studies without direct hospital visits by patients. There are now examples of trials in which patient consent, enrollment, and drug supply have been done remotely. Health authorities and regulators should work to allow implementation of such procedures, both for COVID-19 and non-COVID-19 related studies, in particular to avoid derailing the latter.

### SWEDEN: STEFAN JAMES, MD, INTERVENTIONAL CARDIOLOGIST

Sweden's first case of COVID-19 was reported February 4, 2020, and by March 1, only 14 patients had acquired the disease. Ten days later, on March 10, community transmission was declared. The Public Health Agency of Sweden has a national responsibility for public health issues and works to ensure good public health. The agency also works to ensure that the population is protected against communicable diseases and other health threats aiming to contribute to an overall sustainable society. The Public Health Agency is one of several government agencies that must apply the laws and carry out the activities decided by the Parliament (Riksdag) and the government.

From the start, the Swedish strategy against the pandemic, decided by the government by advice from the Public Health Agency, was based mainly on recommendations and voluntary measures and protection of the elderly and vulnerable people in the society. Sweden had one of the most lenient COVID-19 policies during the spring of 2020. This approach received both international praise and criticism. During the first 2 waves of COVID-19, Swedish society remained largely open. Sweden allowed bars, restaurants, and shops to stay open when most western countries opted for a lockdown. During 2020, people were told to keep social distance and to stay at home in case of any symptoms but wearing face masks was not recommended. Sweden was one of the few countries that decided to keep preschools (generally caring for children 1–6 years of age) and schools (with children 7–16 years of age) open. Starting in the fall of 2020, working from home was recommended and more restrictions were imposed on the population.

Sweden is approximately the size of the state of California. However, Sweden is comparatively sparsely populated with 10 million inhabitants or 52 inhabitants per square mile to California's approximately 217 inhabitants per square mile. Generally, the Swedish people have great trust in the government and its national agencies. Like the United States and many western countries, a large proportion (approximately 25%) of the population were born outside of the country. These citizens have on average a lower level of education, lower economic standards and have been shown to be more affected by COVID-19.

In total, there have been 1,303,663 confirmed Swedish cases of the coronavirus according to data reported on December 29, 2021. Since the start of the outbreak, 8214 COVID patients have been in intensive care. Sweden broke with most of the rest of the world and never mandated that people wear masks during the coronavirus pandemic. The numbers also include those who died after receiving intensive care, and patients who have recovered and been discharged. As of December 29, 15,297 people have been confirmed as having died after testing positive for coronavirus in Sweden. This number is higher than most of the neighboring Scandinavian countries but lower than many other countries in the world. During the first days of 2022, the omicron variant caused a massive fifth wave of transmission but the overall effect on the healthcare system remained small. The statistics of hospitalizations and fatalities are very rapidly reported but also very accurate and reliable thanks to the well-developed national registries including mandatory ICD coding, intensive care, and disease-specific clinical registries.

During the first 6 months of the pandemic, the healthcare situation was burdened and numerous operations were postponed. Increasing waiting lists became obvious but the problems were greater for other disease areas than cardiology. Cardiac surgery, percutaneous valve interventions, and ablations were delayed during 2020 and the first half of 2021 but many hospitals were able to transition from open surgery to less invasive alternatives requiring less intensive care resources.

Multiple local reports indicated during 2020 that fewer patients presented to hospitals with MI and some reports from countries that had imposed lockdowns as mean of regressing disease transmission indicated that the incidence of cardiac arrest had increased in hard-hit areas, raising the question if fear of acquiring COVID-19 results in healthcare avoidance with consequent higher cardiac related mortality. The incidence of MI during the ongoing COVID-19 pandemic was examined and published using the nationwide Swedish Coronary Angiography and Angioplasty registry (SCAAR), with access to all patients with MI referred for coronary angiography in Sweden. A total of 17,656 MIs were referred for angiography during the study period, corresponding to an incidence rate of 246 per 100,000 inhabitants per year. A total of 2443 of these occurred during the COVID-19 pandemic and 15,213 during the reference period March 1 to May 7 of the years 2015 to 2019. No differences in age or sex were noted among the patients during the COVID-19 pandemic compared with the reference period patients. The proportion of STEMI versus NSTEMI did not differ during the pandemic compared with the reference period. The daily incidence rate of MI interventions during the COVID-19 pandemic was 36 MIs per day, translating into 204 MIs per 100,000 per year as compared to 45 MIs per day during the reference period, which translates to 254 MIs per 100,000 per year, resulting in an incidence rate ratio of 0.80 (95% confidence interval [CI], 0.74–0.86).

For Stockholm County, which was most severely affected, the incidence rate reductions for total MI interventions was 25% (IRR = 0.75; 95% CI, 0.66–0.84) and was more pronounced for STEMI compared with NSTEMI. No difference was observed in Kaplan-Meier event rates of all cause-mortality within 7 days in the entire country during the COVID-19 pandemic as compared with during the reference period. The reasons behind the declining rates of MI cannot be verified and are probably multifactorial. Fear of acquiring COVID-19 could result in fewer patients with MI seeking acute cardiac care. In addition, patients misinterpreting MI symptoms such as dyspnea as a symptom of COVID-19 might have avoided seeking healthcare in favor of self-quarantine. From the fall of 2020, the admission rates for MI returned to normal despite several new waves of COVID-19 transmission.

The Swedeheart registry showed that reperfusion treatments were not affected by the COVID-19 pandemic. Primary PCI was the primary mode of reperfusion, and the use of fibrinolysis did not increase. The times from symptom onset to electrocardiogram (ECG) or ECG to PCI were not prolonged during the pandemic. The national secondary prevention registry after MI, SEPHEA, showed that the number of patients entered increased steadily from 2005 to 2019. In 2020, the number of eligible patients as well as registered patients decreased, most likely due to the pandemic. During 2020, many centers changed their routines to telephone follow-up instead of physical visits. The proportion of telephone or digital follow-up visits varied from 10% to 50% between sites for the 1-month follow-up and from 20% to 100% for the 12-month follow-up. The proportion of post-MI patients who had started a physical exercise program 2020 was 30% lower as compared to previous years, which is explained by patient's inability and unwillingness to visit healthcare facilities. There is no evidence in the registries or in any other statistics that there were increased rates of stent thrombosis, or of

lower adherence to any specific pharmacological therapy including DAPT or anticoagulation.

Despite a burdened healthcare situation in Sweden during the COVID-19 pandemic, the cardiac care has not been severely affected. Many surgical procedures were postponed during the peak of the pandemic but thanks to hard-working staff most of the waiting lists were cut during the latter phase. Outpatient healthcare visits were transitioned to telephone and digital visits which appeared to be appreciated by patients and staff.

### CANADA: SANJIT JOLLY, MD, INTERVENTIONAL CARDIOLOGIST

In Canada, we have a publicly funded healthcare system. Nearly all patients have healthcare coverage, which helped with overall medication adherence during the pandemic. Early in the pandemic, the telehealth computer systems often failed due to the excessive load. An important step was rolling out telephone billing codes for physicians to allow care to continue via telephone in many provinces, as the approved telehealth computer vendor systems were overwhelmed. This was good for medication renewals and discussions of compliance. In addition, the government instituted legislation allowing pharmacists to renew prescriptions for chronic medical conditions during the pandemic without a physician renewal. These strategies helped reduce the impact of COVID-19 on chronic cardiovascular care, although telehealth was viewed as suboptimal due to a lack of clinical exam, ECG, and blood pressure assessments.

Similar to other geographies, the number of patients presenting with STEMI during the initial phase of the pandemic dropped significantly in Canada.<sup>17,18</sup> The proportion of patients who met recommended first medical contact-to-device times also dropped significantly.<sup>19</sup> Patients were often afraid to come to hospital and would present later or not at all.<sup>17,18</sup> A strategy of providing 3 months of DAPT in prescriptions, which is common in Canada, has previously been shown to improve compliance,<sup>20</sup> this helped mitigate the impact of the pandemic on DAPT adherence in Canada. There were anecdotal cases of stent thrombosis due to a reluctance of patients to contact their physician or go to a pharmacy, but country-level data are not available.

Reduced in-person follow-up has meant that patients were less likely to have atrial fibrillation detected with an in-person ECG. Patients were less likely to have their blood pressure taken and medication doses titrated or bloodwork, including lipids and hemoglobin A1C measurements. These scenarios may have contributed to poorer overall cardiovascular outcomes in these patients. On the other hand, telephone visits made physicians more accessible and may have improved follow-up rates after MI.

In the summer of 2021, the incidence of ACS rebounded to pre-COVID levels. This is likely due to return to normal activities and reduced fear of coming to hospitals. Furthermore, widespread vaccination helped to reduce fear associated with hospital visits.

### Lessons Learned From the Pandemic

In-person follow-up has an important role to play in patients after ACS and in patients with heart failure. Telehealth may supplement care in patients who are stable and have access to home blood pressure monitoring. Elderly patients often have difficulty with video conferencing software used for telehealth and family involvement is critical. The future is likely a mix of telehealth and in-person visits depending on the clinical status of patients.

### Clinical Trials During the Pandemic

Cardiovascular clinical research ground to a halt early in the pandemic with hospitals stopping recruitment and not allowing research nurses or staff on site. Many were redeployed to COVID-19

clinical care or research. Ongoing cardiovascular trials were required to pivot to telehealth visits instead of in-person checks, and often required new set up of systems to courier investigational medications to patients who were being followed. Patients were afraid of coming to hospital for follow-up research visits. Laboratory visits were often delayed and local laboratories were used instead of, for example, an overwhelmed central hospital site that had become a COVID-19 center.

Recruitment into cardiovascular trials gradually restarted but many centers permanently lost research staff who took other positions, or who were let go early in the pandemic. Recruitment in many trials has never returned to prepandemic levels. Rotating waves of COVID-19 would shut down centers in various countries at different times, meaning that international trials often fared better than national trials.

Given their research expertise, a number of cardiology researchers pivoted to COVID-19 trials during the pandemic, to test repurposed medications. These trials were extremely difficult as regulatory agencies often expected the same processes as in prepandemic times, even though contact with patients posed a risk to research staff. The review process at many international regulatory agencies was arduous and slow. A united framework of regulatory agencies to jointly approve pandemic research protocols would have dramatically improved the speed and efficiency of trials during the pandemic. This research could have led to many lives saved.

### RURAL UNITED STATES: MIKHAIL KOSIBOROD, MD, CARDIOLOGIST

Few events in recent history have had as extensive and comprehensive impact on healthcare delivery across all disease conditions and therapeutic areas as has COVID-19. Following the declaration of the pandemic by the World Health Organization, all aspects of care delivery have been markedly affected. Many of these changes will have a lasting impact well beyond the pandemic itself. Some of the key aspects of this transformational change include:

- (1) Fear of exposure to COVID-19 and care avoidance by the patients
- (2) Shift to virtual care
- (3) Temporary discontinuation of routine preventative care, elective screening, as well as imaging studies and interventional procedures for work up of symptomatic patients
- (4) Dramatic and sustained shift in public attention away from chronic disease conditions (including CAD, PAD, heart failure, diabetes, kidney disease, cancer, and others) to COVID-19 care

These trends were especially pronounced in the rural communities in the United States, where the access to care (especially specialty care) was already limited, and numerous barriers to effective preventative care existed even before the pandemic.

Intense fear of exposure drove numerous patients to avoid seeking care in hospitals and clinics in 2020. Because the rural communities were relatively spared, the full impact of COVID-19 early on, and the outbreaks were first confined to the larger population centers. Many in rural communities stayed away from hospital facilities and perceived the threat of COVID-19 as a larger danger than that posed by their chronic disease. This was added on top of already existing barriers to care, including limited or no availability of specialty care near home and the requirement of long-distance travel to tertiary facilities. The impact of these perceived and real barriers to care has been extensive, and well documented—including a marked reduction in patients seen for acute MI and stroke across the emergency departments nationwide. In part this was likely due to patients having MIs and strokes (and sometimes dying) at home.

Although some of these barriers were handled with lightning speed as hospital systems and practices adapted and switched to virtual care, this was only a partial fix, especially in rural communities. Adequate access to virtual care required both availability of broadband internet, and a certain degree of technology savviness from the patients. Suboptimal access to broadband Wi-Fi, and the relatively older rural populations (as compared with urban ones) with more limited technology skills, deprived many of the rural communities from the “full virtual experience” and relegated virtual visits to phone calls in many cases. These interactions, based on their nature, were less engaging and not as meaningful for either patients or clinicians, which in part further contributed to care avoidance and suboptimal management of chronic diseases in these patient groups.

Within a few days to weeks of the pandemic declaration, and with anticipation of healthcare systems and hospitals being potentially overwhelmed by COVID-19 patients requiring intensive care, most institutions canceled elective procedures and surgeries, and paused them from being scheduled in the foreseeable future. Many of these diagnostic and therapeutic procedures included cardiac imaging evaluations, coronary angiography, PCI, coronary artery bypass grafting, and transcatheter aortic valve replacement, and surgical valve replacements, among others. At some institutions, it took many months to accommodate the extensive backlog created by these frequently necessary (but painful) delays in care, and the true impact on patients’ outcomes is difficult to estimate. Due to the already existing barriers to care and fear of COVID-19 (as outlined above), rural residents were again at a disadvantage when the healthcare organizations started “re-animating” their scheduling of elective procedures.

Finally, the nearly exclusive focus in the media on COVID-19, and resultant lack of focus on public messaging in regard to chronic diseases (including CVD and cancer) further contributed to deprioritization of self-management of CAD (among other conditions) by patients. Because of pre-existing barriers to access, rural communities were even more susceptible to this, ultimately resulting in discounting the importance of adherence to lifesaving medications and lifestyle interventions. Many patients discontinued their medications (including, but not limited to DAPT) due to the difficulty of accessing care, renewing their prescriptions, or deprioritizing their own care due to numerous other priorities. Unfortunately, many patients (especially in the rural areas) essentially gave up on self-management techniques during the initial months of the pandemic—in many cases, this went undiscovered by the healthcare professionals until many months later—when the patients finally had an opportunity to be evaluated.

The US Centers for Disease Control surveys of the impact of the COVID-19 lockdown reported that as of June 30, 2020, 40.9% of American adults reported having delayed or avoided any medical care, including urgent or emergency care (12.0%) and routine care (31.5%), because of concerns about COVID-19. Groups among whom urgent or emergency care avoidance exceeded 20% and among whom any care avoidance exceeded 50% included adults aged 18 to 24 years (30.9% for urgent or emergency care; 57.2% for any care); unpaid caregivers for adults (29.8%; 64.3%); Hispanic adults (24.6%; 55.5%); persons with disabilities (22.8%; 60.3%); persons with 2 or more selected underlying medical conditions (22.7%; 54.7%), which of course would include those on antiplatelet therapy; and students (22.7%; 50.3%). One in 4 unpaid caregivers reported caring for adults who were at increased risk for severe COVID-19. Further analysis indicated that adjusted prevalence of urgent or emergency care avoidance was significantly higher among persons with 2 or more selected underlying medical conditions versus those without those conditions (1.9; 1.5–2.4).<sup>21</sup>

Emergency medical services (EMS) care was also doubtless disrupted by the pandemic. Early on, rates of sustained return

of spontaneous circulation for out-of-hospital cardiac arrest were lower throughout the United States, even in communities with low COVID-19 mortality rates. Overall survival was lower, primarily in communities with moderate or high COVID-19 mortality.<sup>22</sup> It may well have been the case that residents of rural communities, who routinely experience delays in EMS response time and longer transport times, were disproportionately affected in this regard.

In addition to the rapid shift to virtual care, other effective interventions in care delivery included (1) prioritizing the order in which elective procedures were reconstituted after “return to normalcy”—whereas those with the higher disease severity would be rescheduled first, followed by those with lower acuity (2) prioritizing the value of frequent y

Much of the research in cardiovascular disease, especially clinical trials—were heavily impacted due to temporary “freezes” across institutions. Although well-intentioned, much of this, in retrospect, was probably avoidable—and the negative impact will likely be felt for many years.

The greater availability of virtual care is here to stay and will change care delivery in the long term. As the pandemic eventually recedes, some of the in-person interactions will return; but the capabilities to effectively deliver care (especially preventative care and chronic disease management) will grow, and allow healthcare organizations to dramatically extend their reach to the rural communities, particularly as the availability of broadband internet improves.

In anticipation of the next public health crisis that disconnects patients on DAPT from your care team, we would advocate for:

1. Greater availability of PPE; shortages of PPE created many unnecessary barriers to optimal care
2. Rapid adoption of practices across the entire organization as new evidence emerges using “command and control center”
3. Continuing expansion and optimization of virtual care infrastructure and protocols
4. Effective communication to patients via nursing and pharmacy staff to ensure adherence—both via virtual visits, phone calls, and patient portals
5. Greater emphasis on producing high-quality evidence—frequently, due to the pressure of the pandemic, the rigorous standards for evidence-based disease management were relaxed due to the pandemic emergency

### URBAN UNITED STATES: MARC BONACA, MD, CARDIOLOGIST AND VASCULAR MEDICINE SPECIALIST

My practice is located in the Mountain Western United States and COVID-19 has had both heterogenous and asymmetric impacts in various areas and populations. In Denver, there is a large and diverse population including Latino and African American communities, which were disproportionately impacted by the pandemic overall, further exaggerating disparities in care in underserved populations. On a practical basis, this means patients were delaying or not showing up for visits and delaying care for cardiovascular procedures that are needed. As a result, people were presenting acutely with more advanced and harder-to-treat disease. In our rural communities, there has also been heterogeneity, and access to care is a major issue. Our institution is a major referral center in the state, and we often would accept patients who were critically ill with cardiovascular disease from other hospitals. We continued to strive to do this, but the resource demands of the COVID-19 pandemic limited the ability to provide this resource. This extends from beyond Colorado as we get calls from neighboring states with the need to transfer patients needing advanced support and with limited resources.

The general impact on patient follow-up among patients on DAPT between March 2020 and March 2021 compared with the year previous was highly variable. Some patients were acutely aware of their risk and wanted to do everything to avoid the hospital, so they were very adherent and wanted to remain on preventive therapies. Others were less likely to follow-up and may have even let prescriptions expire. Our institution is very rigorous about discharging after ACS with DAPT in hand, but persistence in therapy is most concerning, particularly in the first year after the event.

The willingness of those same patients in our community to transition to telehealth or other “novel” means of engagement has again been variable. There are patients who very much value face-to-face interaction and some will drive for several hours to come in for a preventive visit even when offered telehealth. Others find telehealth much more convenient. We are leveraging more asynchronous means of communication like chats through our patient portal, which have been effective. I often use home blood pressure cuffs and other remote tools to try to manage remotely. There have been some strains on resources such as ambulatory blood pressure monitors, but we are filling in the gaps with home cuffs and other tools.

Investigators at another urban referral center in Southern California found that patients who were Asian, Black, or Hispanic had private insurance, and had at least one of several cardiovascular comorbidities used remote cardiovascular care more frequently in the COVID-19 era. Interestingly, clinician ordering of diagnostic testing and medications consistently decreased when comparing pre-COVID-19 versus COVID-19 and in-person versus remote visits, and it was unclear whether these decreases represent a reduction in the overuse of tests and medications versus an underuse of indicated testing and prescribing.<sup>23</sup>

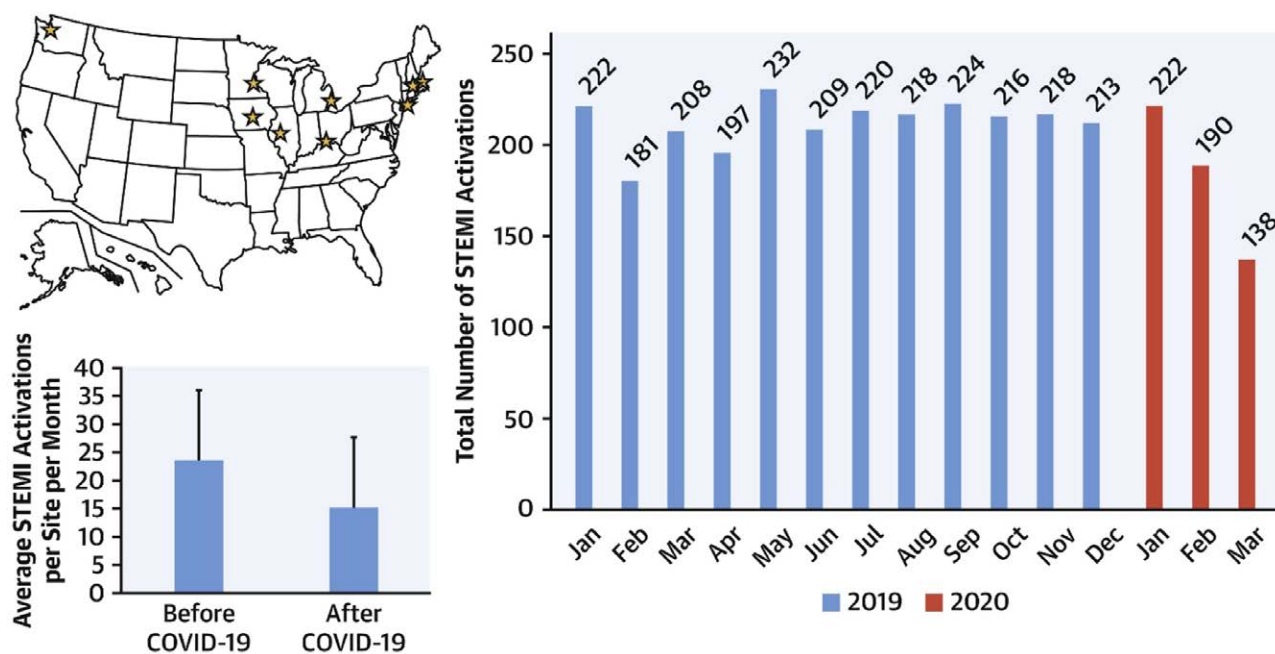
Adherence to DAPT has clearly been variable within our population during the pandemic. Unfortunately this does tend to track with other factors such as socioeconomic status and education. Those

with resources tend to stay connected and are better supported. What we worried about the most were people who are struggling in other ways (eg, loss of a job, caring for a family member, other economic, or social struggles) where adherence with therapy becomes a lower priority. These were not new issues; but in many ways, COVID-19 has worsened the situation as resources are stretched to deal with the pandemic, providers are exhausted, and many are focused on issues outside of cardiovascular care.

Nationally, we have seen some objective indicators of change in the volume of acute cardiac care. Garcia et al analyzed and quantified STEMI activations for 9 high-volume (>100 PPCIs/year) cardiac catheterization laboratories in the United States from January 1, 2019, to March 31, 2020. The model estimate showed a decrease in STEMI activations of 38% (95% CI, 26-49;  $P < 0.001$ ) once the pandemic began. All sites combined reported >180 STEMI activations every month (mean 23.6 activations/mo) in the before-COVID-19 period. In contrast, all sites combined reported only 138 activations (mean 15.3 activations/mo) in the after-COVID-19 period (Figure 4).<sup>24</sup>

The shift to telehealth has been profound and impactful and it is really the new normal. Asynchronous communication through patient portals has enabled a more conversational and iterative engagement with patients. Community Health programs such as CHARLAR and Colorado Heart Healthy Solutions have embraced hybrid approaches and focused very much on behavioral and mental health. This is quite innovative. We can tackle an issue (eg, medication adherence) in isolation without thinking of the whole patient.

Looking back, the biggest difference I would have made in March 2020 would be to change my thinking that this would be over in a year. The notion that we could wait it out and delay things was probably not the best path. If I had known how long this would last (and probably in some form forever) I would have pivoted more quickly to a new normal and reached out to more vulnerable patients and focused on the right care at the right time and not delays. Of



**FIGURE 4.** STEMI Activations During the COVID-19 Pandemic. (Top left) Map of the United States showing the 9 high-volume ST-segment elevation myocardial infarction (STEMI) centers participating in this registry (yellow stars). (Lower left) Bar chart displaying average number of STEMI activations per site per month before and after the COVID-19 pandemic affected the US health care system. (Right panel) Bar chart displaying total number of STEMI activations per month (blue: 2019; red: 2020).<sup>24</sup> STEMI, ST-segment elevation myocardial infarction.



course, this was not really possible in the health system, as much of our more elective care was postponed. I think that although we reached out to patients to engage with telehealth and although this worked for many, we probably need other approaches to reach the most vulnerable. A valuable lesson learned from the urgent need to switch to remote care was that it is not just communication, but engagement that drives better outcomes.

Measures our institution is considering to implement in anticipation of the “next” public health crisis that might disconnect patients on DAPT from their care team are not necessarily novel but are instead more likely to reflect continuation of measures that we are putting in place now. As earlier, this current crisis is not temporary. Whether it is the next variant or the next virus we need to practice in a way that enables us to care for patients through disruptions. There are some systems (eg, direct drug shipments to patients, better tracking programs, reminders, care team approach to adherence) that need to be further developed, including delivery of more personalized care. In a way, this is implementation science “on steroids” because not only do we need to overcome the traditional barriers of education, inertia, cost, and so on, but we also need to overcome a highly dynamic and exhausting environment of news and noise and how these terrible diseases impact individuals, often disproportionately. If a patient cannot feed herself or her family, then adherence to DAPT is likely not her priority.

## SUMMARY

Experiences in acute cardiac care disruption due to the COVID-19 pandemic in diverse geographies and in varying payor systems reflected similar obstacles to care. A pre-existing and likely underappreciated immaturity in remote care platforms was quickly manifest and, in most locations, has now been addressed. Infrastructure problems such as limited broadband access and familiarity with technology by some users are unfortunately likely to persist. Meanwhile, improved provider-patient communication to help ensure adherence to primary and secondary prevention medications that do not themselves treat symptoms, as well as longer-term prescription fills and no-hassle refills on such medications, should be considered. Although potential noncompliance with antiplatelet medications cannot yet be fully assessed from the times when the pandemic would have been most likely to interrupt it, future analyses of hospitalization data, ACS and mortality rates, emergent procedures, and autopsy data may eventually inform us of any pertinent impact on outcomes. Likewise, there is a clear need for redundancy or back-up planning for teams engaged in time-sensitive research, particularly in acute cardiac care, to ensure both continuity of protocols and patient safety.

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## DISCLOSURE

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