

# Maintaining stroke care during the COVID-19 pandemic in lower- and middle-income countries: World Stroke Organization Position Statement endorsed by American Stroke Association and American Heart Association

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Jeyaraj D Pandian<sup>1</sup> , Peter D Panagos<sup>2</sup>, Ivy A Sebastian<sup>3</sup>, Gisele Sampaio Silva<sup>4</sup>, Karen L Furie<sup>5</sup>, Liping Liu<sup>6,7</sup>, Mayowa O Owolabi<sup>8</sup>, Valeria Caso<sup>9</sup> and Suhail A Alrukn<sup>10</sup>; World Stroke Organization and American Stroke Association Writing Group

## Abstract

For more than a year, the SARS-CoV-2 pandemic has had a devastating effect on global health. High-, low-, and middle-income countries are struggling to cope with the spread of newer mutant strains of the virus. Delivery of acute stroke care remains a priority despite the pandemic. In order to maintain the time-dependent processes required to optimize delivery of intravenous thrombolysis and endovascular therapy, most countries have reorganized infrastructure to optimize human resources and critical services. Low-and-middle income countries (LMIC) have strained medical resources at baseline and often face challenges in the delivery of stroke systems of care (SSOC). This position statement aims to produce pragmatic recommendations on methods to preserve the existing SSOC during COVID-19 in LMIC and propose best stroke practices that may be low cost but high impact and commonly shared across the world.

## Keywords

Acute stroke therapy, COVID-19, developing countries, pandemic, services, stroke care, stroke systems

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## Introduction

It has been more than a year since the SARS-CoV-2 virus began to impact global health, and now deep into its second wave, it has left no nation unscathed. The world is divided into countries that have heeded the

logic and mathematics of the epidemic and those who regrettably have not. Much of the world is grappling with intermittent surges of mutant variants of the virus. Although the initial wave exhibited a stark dichotomy in

<sup>1</sup>Department of Neurology, Christian Medical College, Ludhiana, Punjab, India

<sup>2</sup>Department of Emergency Medicine, Washington University School of Medicine, St Louis, MO, USA

<sup>3</sup>Department of Neurology, St Stephens Hospital, New Delhi, India

<sup>4</sup>Department of Neurology, Federal University of São Paulo, Clinical Trialist/Neurology, Albert Einstein Hospital, São Paulo, Brazil

<sup>5</sup>Department of Neurology, Rhode Island Hospital Chair of Neurology, The Warren Alpert Medical School of Brown University, Providence, RI, USA

<sup>6</sup>Department of Neurology, Beijing Tiantan Hospital, Capital Medical University, Beijing, China

<sup>7</sup>China National Clinical Research Center for Neurological Diseases, Beijing, China

<sup>8</sup>Department of Neurology, Faculty of Clinical Sciences, Director, Center for Genomic and Precision Medicine, College of Medicine, University of Ibadan, Nigeria

<sup>9</sup>Department of Neurology, Stroke Unit, Santa Maria della Misericordia Hospital, University of Perugia, Perugia, Italy

<sup>10</sup>Department of Neurology, Dubai Medical Collage, Dubai

## Corresponding author:

Jeyaraj Durai Pandian, Christian Medical College, Ludhiana, Punjab 141008, India.

Email: jeyaraj.pandian@cmcludhiana.in

the impact on high-income and low-income countries, there are now few countries unaffected by the pandemic.

Initially, while United States, Canada, and Europe succumbed to second and third waves of the pandemic, large LMICs such as India initially seemed to bend the infection curve with the institution of public health measures. More recently, the surge of cases has overwhelmed the health system.

Severe COVID-19 infection itself is a high risk factor for developing stroke.<sup>1</sup> In a recent systematic review and meta-analysis of 108,571 COVID-19 patients, stroke occurred in 1.4% of the cohort, ischemic stroke (87.4%) being the most frequent stroke subtype.<sup>2</sup> Large vessel occlusion (LVO) was more frequently reported along with multiple territory infarcts, suggesting cerebral thrombosis or thromboembolism as the potential mechanism.<sup>3,4</sup> The widespread roll out of vaccination has led to the identification of unusual mechanisms of cerebral venous sinus thrombosis (CVST).<sup>5</sup>

While high-income countries (HICs) have many diagnostic and therapeutic resources available for the

treatment of acute ischemic stroke (AIS), and recommendations have been published related to maintaining SSOC during the pandemic, LMICs have strained medical resources at baseline, and often face challenges in the delivery of optimal stroke care (Figure 1).

The World Stroke Organization (WSO) and American Stroke Association (ASA) and Heart Association (AHA) joint committee commissioned this project. Two writing group members were nominated from ASA/AHA (PP and KF). The WSO members were selected taking into consideration the geographical representation and the individual expertise in this area (JDP, IAS, GSS, LL, MOO, VC, and SAA).

The purpose of this position statement is to

1. Produce pragmatic recommendations on methods to preserve the existing SSOC during COVID-19 in LMIC.
2. Adapt existing stroke care workflows in a manner that both protects healthcare workers while still

**Figure 1.** Challenges in delivering stroke care during COVID-19 pandemic in low- and middle-income countries.



offering timely acute reperfusion therapy to as many patients as is feasible.

- Propose best stroke practices that may be low cost but high impact and commonly shared across the world.

### Methodology

A writing group was created from World Stroke Organization and American Heart and American Stroke Association (WSO, AHA/ ASA) joint working group. A comprehensive literature search was conducted in Pubmed and Google scholar databases to find articles published between 31 December 2019 to 1 March 2021 on COVID-19 and stroke care. We used the search terms “COVID-19,” “SARSCoV-2” along with Boolean operator “AND” and “OR” with one of the following terms “stroke,” “Stroke care,” “stroke systems of care,” “pre-hospital care,” “neuroimaging,” “thrombolysis,” “mechanical thrombectomy,” “endovascular treatment,” “stroke unit care,” “rehabilitation,” “secondary prevention,” “discharge planning.” We limited the search to original articles and review articles published in English language. The

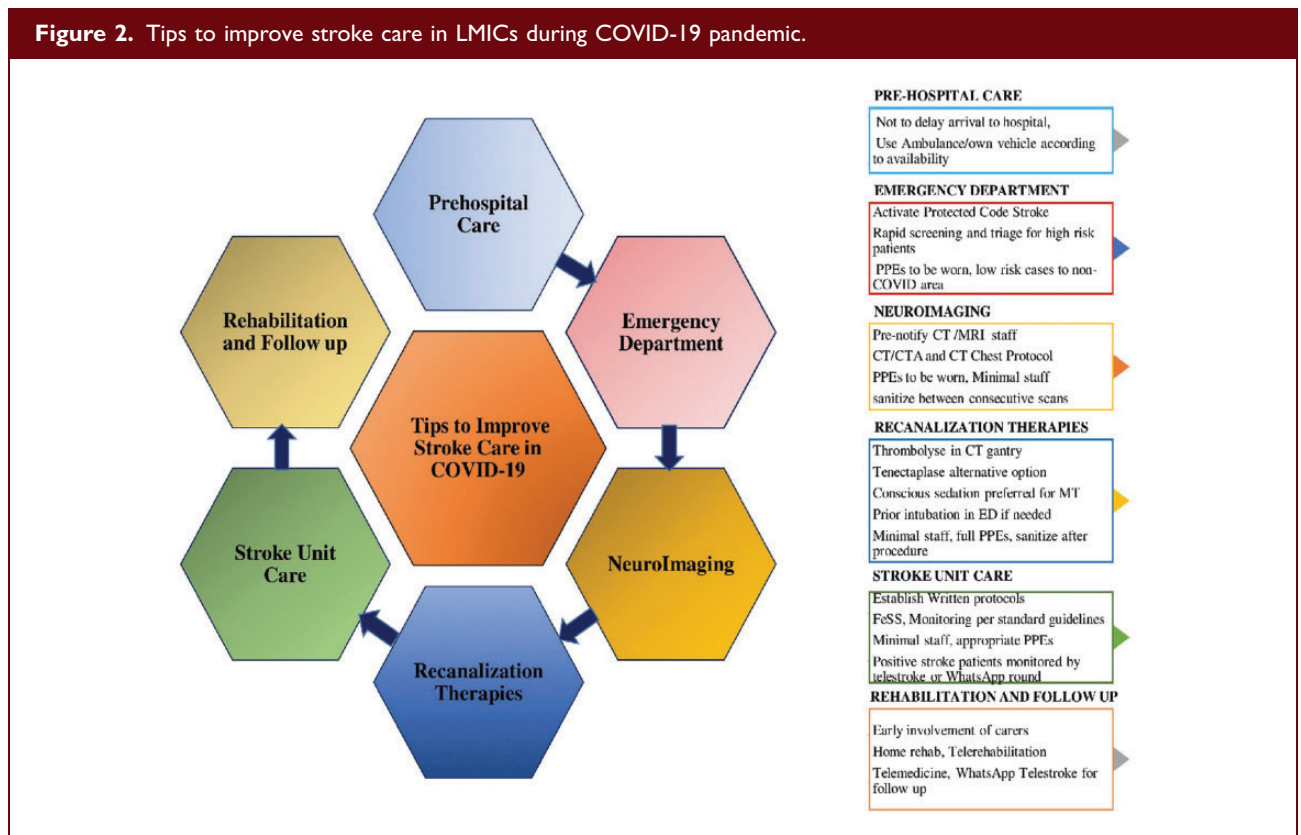
authors drew on their expertise and formulated the recommendations presented below, based on recommendations published by other experts and societies, and best medical experience as no trial-based scientific evidence is yet available. Tips to maintain and improve stroke care in LMICs during COVID-19 are illustrated in Figure 2.

### Prehospital care

The prehospital component of the stroke continuum of care is not well developed in LMICs.<sup>6</sup> Private cars and ambulance were the two modes of conveyance used by patients to reach hospitals in different Asian countries.<sup>7,8</sup> It is recommended that stroke patients use ambulance services to reach the hospital when feasible; however, private conveyance can be used if the need arises. Paramedical and emergency staff should wear appropriate personal protective equipment (PPE) while transporting patients.<sup>7,9</sup>

### Recommendations

- Hospital evaluation should not be delayed for people with suspected stroke. However, patients with minor



symptoms can opt to seek teleconsultation to limit exposure of coming to hospital.

2. An ambulance should be used whenever feasible; however, a personal conveyance can be used if needed rather than delaying acute stroke care.
3. Paramedical staff should wear appropriate PPE during screening and transport.

### Emergency department

As the front-line access point for the healthcare system, emergency department (ED) may be best able to determine the optimal diagnostic and therapeutic disposition of AIS patients with suspected or confirmed COVID-19.<sup>10</sup>

**Staff safety:** Adequate COVID-19 screening may not be possible in stroke patients presenting to ED as they often present with limited available history, unavailable witnesses, aphasic, or confused. “Protected code stroke” (PCS) protocols were introduced early into the pandemic which recommends that ED and stroke team respond with the most appropriate PPE and reduce exposure risk until definitive COVID-19 testing is performed.<sup>11</sup> In most circumstances, ED team must use at least Level 1 PPE (standard infection control precautions such as fluid-resistant mask, disposal apron, and gloves); however, while dealing with COVID-19 suspected or positive patients, Level 2 PPE (contact, droplet, and airborne precautions such as disposable apron and gloves, fluid-resistant mask) must be utilized especially during aerosol-generating procedures. Since PPE is often in limited supply, minimizing the use of scarce PPE is important.<sup>12</sup> Ventilation must be maximized in clinical examination areas, and healthcare professionals must maintain distance where possible.

**Severity classification:** Protocols for rapid triage and evaluation of the stroke patient should be maintained during the pandemic.<sup>13</sup> All patients must undergo nasopharyngeal swab testing at the earliest. In asymptomatic patients, lateral flow tests can suffice for triaging. Symptomatic patients must undergo definitive testing with real-time quantitative reverse transcriptase polymerase chain reaction (RT-qPCR) assays to identify those requiring quarantining procedures. Point-of-care antigen tests can be utilized for rapid triaging; however, results should be confirmed by RT-qPCR.

Delayed presentation for transient ischemic attack (TIA) or minor stroke, due to fear of infection, can lead to worse prognosis.<sup>14</sup>

**Risk stratification:** COVID-19 patients who develop AIS are often older, more likely to be Black, and have a higher frequency of cardiovascular risk factors,<sup>15</sup>

placing such patients at an increased risk of multi-organ involvement.

**Disposition:** Most stroke patients with suspected or confirmed COVID-19 will require admission for time-critical stroke therapies, stabilization, and secondary prevention measures<sup>16</sup> which in a pandemic can lead to prolonged ED boarding times. Temporary stabilizing measures using high flow nasal cannula (HFNC) and non-invasive positive pressure ventilation (NIPPV) can be used in these patients to avoid endotracheal intubation and preserve critical beds.<sup>17</sup> These decisions require coordination in the context of available local resources and transfer to a higher level of care.

### Recommendations

1. Written protocols should be established for rapid triage and risk stratification of stroke patients by epidemiology, symptoms, and investigations.
2. ED staff should don PPE appropriate to the risk stratification during screening and triaging of COVID-19 patients.
3. Temporizing measures like HFNC and NIPPV in stroke patients with COVID-19 can help preserve critical beds.

### Acute imaging

Consensus emerged early in the pandemic that it was essential to preserve the critical elements of guideline defined acute stroke care, including standard acute imaging with CT/CTA or MRI/MRA.<sup>11,18</sup> It was recommended that hospitals design dedicated pathways for high-risk and positive patients for transit or, when possible, assign dedicated CT or MRI rooms.<sup>8,19</sup> Consider concomitant low-dose chest CT, as long as this addition does not incur >5-min delay to treatment. Technicians should don full PPE, and all surfaces in the imaging suite should be disinfected between cases.<sup>18</sup> In order to reduce duplicative scanning (and additional exposure), it was suggested that patients transferred to an advanced stroke center for management of LVO go directly to the angiography suite, bypassing CT, when imaging from the referring hospital was adequate and criteria for mechanical thrombectomy (MT) were met.<sup>20</sup>

### Recommendations

1. All stroke patients must undergo standard acute imaging as per protocol.
2. Dedicated transit pathways or neuroimaging room should be assigned for high-risk COVID-19 patients.

3. Complete sanitization of the gantry between consecutive imaging is mandatory.
4. Patients with LVO should be directly transferred to the angiography suite whenever feasible to limit exposure to additional staff members.

### Thrombolysis

The availability of neuroimaging and thrombolysis is not universal in LMICs.<sup>6,8</sup> During the pandemic, the ability to provide prompt and effective care to the patient must be balanced against the infection risk to the health professionals.<sup>11,21</sup>

Intravenous thrombolysis (IVT) should be administered to all eligible AIS patients within four and a half hours of symptom onset. In hospitals with the capacity to perform advanced neuroimaging (perfusion tomography or magnetic resonance imaging), IVT can be administered up to 9 h after the onset of stroke symptoms.<sup>22</sup> Frequency of neurological examination post-thrombolysis should be decreased, to limit exposure and minimize use of PPE.

Tenecteplase (TNK), as a thrombolytic agent, has already been championed in few centers due to its advantage of requiring only bolus administration.<sup>23</sup> This can be additionally beneficial in times of pandemic by eliminating the need for an hour-long infusion as with alteplase.<sup>24</sup> Hospitals that choose to use tenecteplase for patients with AIS, must implement modifications in the prescription forms and the dose definition used.<sup>24</sup>

### Recommendations

1. IVT within the first 4.5 h of symptom onset or in an extended window in eligible patients after advanced neuroimaging is recommended even during the COVID-19 pandemic in both LMICs and HICs.
2. LMIC are encouraged to publish their individual protocols for a PCS with realistic adaptations such as those published by Indian Stroke Association and Asian Stroke Advisory Panel.<sup>7,9</sup>

The use of tenecteplase for thrombolysis may be considered. However, services that choose to do so should consider substantial modifications to protocols.

### Mechanical thrombectomy

Despite many proposed guidelines to streamline the interventional process for LVO candidates,<sup>25,26</sup> the pandemic was associated with a drop in MT rates.<sup>27</sup>

Decision-making on whether a patient is suitable for thrombectomy and obtaining procedural consent

should be consistent with hospital protocols prior to COVID-19.

A separate angiography suite for high-risk and positive stroke patients is recommended, although may not be always feasible. Conscious sedation is preferred; however, if general anesthesia and ventilation are required, then it should be performed under negative pressure conditions if feasible.<sup>8</sup> Use of high efficiency particulate air-filtered forced units is an alternative to negative pressure units to contain pathogen exposure.<sup>28</sup> Medical staff should be kept to a minimum during procedures to limit exposure. In high incidence areas, Level 3 PPE is recommended irrespective of COVID-19 status of patient, whereas low-incidence areas require at least Level 2 protection in non-suspected patients and Level 3 for suspected and confirmed patients. Thorough disinfection of the angiography suite is warranted after every procedure. Post-recanalization patients should be cared for in designated, isolated areas according to stroke unit (SU) care protocols.

### Recommendations

1. All eligible patients irrespective of COVID-19 status should be offered MT.
2. Conscious sedation is preferred over general anesthesia and mechanical ventilation to reduce aerosolization.
3. Negative pressure units or high efficiency particulate air-filtered forced units should be utilized ideally to contain exposure wherever feasible.
4. Thorough post-procedure sanitization of angiography suite is mandatory.

### SU care

SU care is one of the most cost-effective evidence-based interventions which have shown benefit in improving outcomes in patients with stroke.<sup>6</sup> However, reallocation of SU beds to COVID-19 patients in most countries has entailed utilization of less optimal beds for stroke care. An effort to provide the standard principles of SU care including the nursing care bundle (fever, sugar and swallow (FeSS) protocol), blood pressure (BP) and sugar control, and management of complications should be made for all stroke patients.<sup>7,9</sup> While COVID-19-negative patients should continue to receive care in designated SUs, intermediate-high risk and positive patients need to be managed in designated hospital areas, according to institutional protocols. Although optimal SU care with trained stroke personnel may not be available in these areas, essential components of care like BP monitoring, control of sugar and temperature, and other abnormal physiological parameters should be provided. Decreasing the

frequency of neuro-checks and vitals monitoring is recommended to limit exposure to healthcare workers. Swallow assessment should be carried out in all conscious and non-intubated patients with stroke. A modified approach like repetitive saliva swallowing<sup>29</sup> may be considered to limit contact. Decompressive hemicraniectomies may have to be deferred in positive patients; however, if urgent, decision for surgical intervention may be considered in tertiary or comprehensive stroke centers on a case-by-case basis, keeping in mind the deficit of ICU beds and resources.<sup>9</sup>

#### Recommendations

1. SUs should be maintained wherever possible to care for stroke patients, and not be used for managing COVID-19 patients who do not have stroke.
2. Modified protocols for SU care should be established and followed.
3. High-risk and positive stroke patients should be managed in designated hospital areas, with allocated staff trained to provide essential principles of SU care.

#### Rehabilitation

Post-stroke rehabilitation has been affected because of the restrictions in travel and due to the physical distancing that has to be maintained during therapy. It is difficult to physically rehabilitate a patient without being in close contact with them; especially, patients with aphasia and hemiparesis.<sup>7,9</sup> Physical distancing might be impractical, and in patients requiring rehabilitation, we may need to screen for COVID-19. Even in COVID-19-negative patients, there is a need to reduce the duration of physical contact during each session of neurorehabilitation. Telerehabilitation is a feasible alternative to physical rehabilitation in this COVID era.<sup>30</sup>

#### Recommendations

1. An adequate supply of PPE to the rehabilitation professionals
2. Caregivers could be trained to deliver therapy at home
3. Therapists can make home visits following all safety measures
4. Telerehabilitation using various apps that can be configured to preserve patient and provider privacy.

#### Secondary prevention and discharge plan

All stroke patients should be started on appropriate secondary prevention timely. Stroke patients with COVID-

19 should be evaluated for pro-thrombotic and cardioembolic causes and managed accordingly. All patients should have a discharge plan; however, discharge of COVID-19-positive stroke patients should follow local country guidelines. Follow-up should be arranged either in outpatient clinics or by telemedicine, with appointments provided at the time of discharge.<sup>7,30</sup>

#### Recommendations

1. Secondary prevention medications should be started in a timely manner in all stroke patients.
2. Stroke patients with COVID-19 should specifically be evaluated for prothrombotic and cardioembolic causes.
3. Telemedicine or WhatsApp consultations can be used for follow-up.

#### Telestroke

Telestroke makes it possible to care for stroke patients in locations deprived of specialists physically on-call.<sup>31</sup> Even before the COVID-19 pandemic, several studies attested the safety of acute stroke care via telemedicine.<sup>32</sup> Successful precedents of telestroke have been described in LMICs, with limited access to neurological care.<sup>6</sup>

With the advent of the pandemic, the case for virtual care has become even more compelling.<sup>33</sup> Prehospital triage protocols using mobile telestroke can facilitate in decision-making and transfer of patients requiring MT to comprehensive stroke centers,<sup>34</sup> while maintaining patients with minor strokes in smaller hospitals.<sup>35</sup> An interesting example of telemedicine is the Coronavirus SUS application in Brazil,<sup>36</sup> which utilizes a questionnaire to indicate a possible diagnosis of infection and need for referral.

Telestroke locally expands the concept of PCS, with multiple applications across the stroke care continuum including virtual rounds, follow-up consultations, telerehabilitation,<sup>37</sup> and tele-counseling. Additionally, screening for asymptomatic AF can be done with digital smart devices to complete the diagnostic workup after discharge.<sup>38</sup> The JOIN system is an example of a low-cost telemedicine solution using smartphone technology that allows for rapid data exchange including neuroimaging.<sup>39</sup> Low-cost WhatsApp<sup>®</sup> can also be used as an alternative in resource-poor settings.<sup>30</sup>

#### Recommendations

1. Telestroke can be used as a reliable tool throughout the stroke continuum of care including prehospital notification, mobile telestroke for direct referral for

recanalization, management of positive stroke patients in COVID-19 designated areas, tele-critical care rehabilitation, and follow-up.

### **Vaccine-induced immune-mediated thrombotic thrombocytopenia and CVST**

CVST is a known neurological manifestation of COVID-19 disease. Recent reports of CVST and thrombocytopenia following COVID-19 vaccination (ChAdOx1 nCoV-19 Vaccination, Astra Zenecam and Johnson and Johnson) have been published.<sup>40,41</sup> Patients presented with new onset headache, visual symptoms, and focal deficits with parenchymal hemorrhage. Antibodies to Platelet Factor 4 has been postulated as the mechanism of CVST in these individuals.<sup>5</sup>

Even though this complication is rare following COVID vaccination, the public and the treating doctors should be mindful so that it is recognized early.<sup>42</sup> Patients can also present with venous and arterial thrombosis in other vascular beds. Both American Stroke Association and World Stroke Organization have issued advisories regarding this complication.<sup>43</sup> Surveillance system needs to be created in order to identify post vaccine CVST in LMICs.

### **Recommendations**

1. A high index of suspicion for CVST should be kept in patients with recent COVID-19 vaccination presenting with new onset headache and/or focal deficits.
2. Suspected patients should undergo testing for Antibodies to Platelet Factor 4.
3. Immunoglobulin treatment is recommended in patients with confirmed VITT.

### **Limitations of the study**

During the COVID-19 pandemic, every country's health system adapted differently to cope with the massive strain on its health resources. The regional innovations varied from country to country, depending upon their baseline economic, infrastructural, and human resources. Extracting high-quality evidence for each component of stroke systems of care is difficult in this pandemic situation. The recommendations formulated are empirical and are drawn from the authors' expertise in addition to the existing recommendations in literature published by other experts and societies, as no trial-based evidence is yet available. This position statement aims to focus on how low-resourced countries were able to adapt to the evidence-based interventions for stroke in their respective health systems.

## **Conclusion**

Quo Vadis Corona! It is not hyperbole to say that the pandemic is far from over. Perhaps the largest humanitarian crisis since the Second World War, the virus has transformed life as we know it. The pandemic has laid bare societal inequalities and crushed economies and healthcare ecosystems globally. However, learning from the chronicles of past pandemics, COVID-19 has forced us to rethink our strategies and reinvent our systems. The introduction of "protected pathways," modified stroke protocols and adoption of digitalization into stroke care including telestroke, telerehabilitation, and videoconferencing is crucial to preserve the stroke "chain of survival." While there is still a long way to go, diligently continuing protective measures of handwashing, wearing a mask, and vaccination is paramount to successfully enter the next normal.


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### **ORCID iD**

Jeyaraj D Pandian  <https://orcid.org/0000-0003-0028-1968>

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