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Stroke care in Italy: An overview of strategies to manage acute stroke in COVID-19 time

Marialuisa Zedde[1], Francesca Romana Pezzella[2], Maurizio Paciaroni[3], Francesco Corea[4], Nicoletta Reale[5], Danilo Toni[6] and Valeria Caso[3]

Abstract

Purpose: To analyse structural and non-structural modifications of acute stroke care pathways undertaken at healthcare institutions across the regions of Italy due to the coronavirus disease 2019 (COVID-19) pandemic.

Methods: Research on National decrees specific for the pandemic was carried out. The stroke pathways of four Italian regions from North to South, such as Lombardy, Veneto, Lazio and Campania, were analysed before and after the pandemic outbreak.

Findings: On 29 February 2020, the Italian Minister of Health issued national guidelines on how to address the COVID-19 emergency. Stroke management was affected and required changes, basically resulting in the need to prioritise the ongoing COVID-19 emergency. In the most affected regions, the closure of departments and hospitals led to a complete reorganisation of previously functioning stroke networks. With the closure of several Stroke Units and Stroke Centres, the transportation time to hospital lengthened significantly, especially for the outlying populations.

Discussion: The COVID-19 pandemic outbreak has been spreading rapidly in Italy and placing an overwhelming burden on healthcare systems. In response to this, political and healthcare decision-makers worked together to develop and implement efforts to sustain the national healthcare system while fighting the pandemic. Stroke care pathways changed during the pandemic and different organisational models were applied in the most affected regions.

Conclusions: Stroke treatment pathways will need to be redesigned so to guarantee that severe and acute disease patients do not lose their rights to the access and delivery of care during the COVID-19 pandemics.

Keywords

Stroke, stroke management, COVID-19, pandemic, Italy

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Background and purposes

Introduction

After the first Italian case was diagnosed on 20 February 2020 at the Codogno Hospital (Lodi, Lombardy, Italy), on 29 February 2020, the Italian Minister of Health issued national guidelines on how to address the COVID-19 emergency.[1] This led to a profound restructuring of the Italian hospital system; a greater number of hospital beds were dedicated to COVID-19 patients. At larger hospitals, those with more than 500 beds, COVID Units and COVID-free areas were set up to admit and quarantine COVID-19

[1]Neurology Unit, Stroke Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy
[2]Stroke Unit, San Camillo Forlanini Hospital, Rome, Italy
[3]Stroke Unit and Division of Internal and Cardiovascular Medicine, Santa Maria della Misericordia Hospital, University of Perugia, Perugia, Italy
[4]Neurology and Stroke Unit, San Giovanni Battista Hospital, Foligno, Italy
[5]President Federazione A.L.I.Ce Italia Odv
[6]Emergency Department Stroke Unit, Hospital Umberto I, Sapienza University Rome, Rome, Italy

Corresponding author:
Marialuisa Zedde, Neurology Unit, Stroke Unit, Azienda Unità Sanitaria Locale-IRCCS di Reggio Emilia, Reggio Emilia, Italy.
Emails: zedde.marialuisa@ausl.re.it; marialuisa.zedde@gmail.com

patients safely. Intensive care unit (ICU) beds were almost entirely dedicated to COVID-19 patients, and additional ICU beds were added up until two to three times more than the baseline numbers. Whereas, in other cases, entire hospitals were assigned to treat and care for only COVID-19 patients. Finally, smaller institutions were often temporarily closed, because both patients and personnel had acquired COVID-19 in hospital.[2]

However, even in times of pandemic, a national healthcare system still needs to guarantee the best possible services to patients affected by non-communicable diseases. Specially, by maintaining its ability to operate effectively, particularly for those patients with ongoing acute conditions such as stroke and myocardial infarction, where treatments are almost always extremely time-sensitive. Given this, the management pathways for acute conditions needed to adapt immediately to the novel realities associated with COVID-19. These changes though also had to simultaneously provide for an effective management of the infectious emergency.

As the Italian healthcare system is directed at regional levels, and among the regions the protocols regarding stroke treatment and care can differ significantly, this study will carry out an analysis of structural and non-structural modifications of acute stroke care pathways undertaken at healthcare institutions across the regions of Italy due to the pandemic.

Organisation of the Italian National Health Service

The system is strongly decentralised, with 19 regions and 2 autonomous provinces that are given significant autonomy in their managing of the services, while the central government is still responsible for the overall system structure and guidelines on services that should be provided (i.e. minimum assistance levels).[3]

These characteristics might explain why the response to the pandemic has been so diversified among the Italian regions, even based on the locally recorded load of infections, as shown in Figure 1.

As a consequence of an economic crisis, which caused a decrease in gross domestic product (GDP) of over 8%, between 2008 and 2015, the public financing of the health systems progressively decreased.[4] Unfortunately, with the spending review carried out in 2012, funding for the national health service was further reduced starting by €0.9 billion in 2012,[5] €1.8 billion in 2013 and €2.0 billion in 2014, representing reductions of the required funding of 0.8% in 2012, 1.6% in 2013 and 1·8% in 2014. According to a study by the independent research centre Gruppo Italiano per la Medicina Basata sulle Evidenze,[6] between 2010 and 2019, there were progressive cuts to the health sector, amounting to around €37 billion.

During the period of the €37 billion cuts, at least 50% of these occurred to staff levels, with the loss of 42,800 healthcare workers, effectively reducing services for citizens and worsening the working conditions of those who remained. Additionally, there was a gradual aging of the health personnel because of the failure to replace those who retired.

Data from the Italian Ministry of Health[7] reported that the mean age of an Italian physician was 50.8 years in 2010, whereas in 2017, this number reached 52.9 years[8] with more than 50% of all physicians being >55 years.[9]

Region	Cases	Deaths
Lombardy	67931	12579
Emilia Romagna	23062	3147
Piedmont	21955	2485
Veneto	16404	1154
Tuscany	8603	686
Liguria	6764	990
Marche	5877	834
Lazio	5895	363
Campania	4135	317
Trento	3614	376
Puglia	3622	351
Friuli V.G.	2792	241
Sicily	2835	206
Abruzzo	2667	271
Bolzano	2410	251
Umbria	1353	60
Sardinia	1236	93
Calabria	1047	76
Valle d'Aosta	1093	126
Basilicata	350	24
Molise	282	18
Total	186957	24648

Figure 1. Map of COVID-19 distribution in Italy by regions (the table reports the absolute number of cases and deaths) updated on 21 April 2020. The size of red circles is proportional to the number of cases in each region. In the map, the regions described in the text are marked by white capital letters (L = Lombardy; ER = Emilia Romagna; V = Veneto; U = Umbria; La = Lazio, C = Campania). Modified from data provided by Italian Civil Protection Agency: http://opendatadpc.maps.arcgis.com/apps/opsdashboard/index.html#/b0c68bce2cce478eaac82fe38d4138b1.

Indeed, the mean age of Italian physicians who died while still in clinical service[10] is 66.6 years. Figure 2 shows the age distribution of physicians in European Union countries (data refer to 2017) and it is well evident that Italy has the higher rate of physicians aged >55 years and >65 years, so the majority of Italian doctors are expected to retire in the coming decade and a non-negligible percentage is working beyond the retirement age.

In Italy on 20 April 2020, 169,325 people have been infected, of which about 10% (17,997) were health professionals.[11] Of the 21,551 deceased, at least 130 physicians[10] and more than 25 nurses have died because of the COVID-19 infections including those who have voluntarily returned to work to overcome shortages.

Methods and results

Stroke management in Italy before COVID-19 time

In Italy, the estimated annual number of strokes is around 120,000 and about 10% of all deaths in 2014 are due to stroke, whereas stroke is the main cause of disability and the second leading cause of dementia with loss of independence in daily activities.[12] Most neurovascular units are online, and the organisational model adopted is that of 'hub and spoke'.[12]

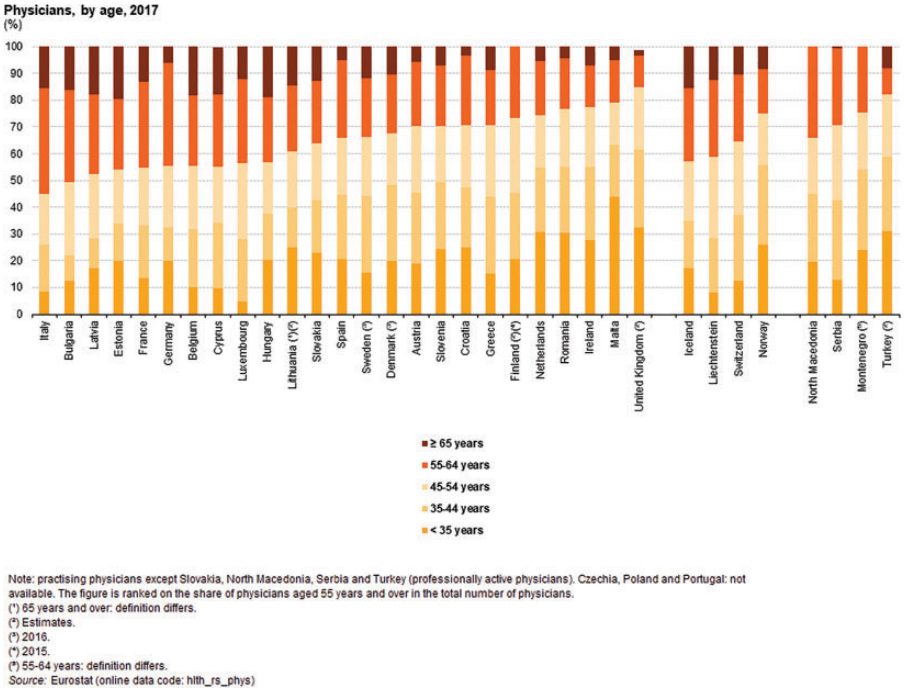
From 2003 to 2017, 190 neurovascular centres, or Stroke Units, were gradually authorised. Figure 3 shows for each region the number of centres according to the ratio of 1 centre per 200,000 inhabitants, defined as an average between the ratio 1: 150,000 and 1: 300,000, as specified for these centres by a government decree in 2015 (D.M.70/2015).[13] The monitoring of intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT) treatments takes place respectively through the SITS-ISTR register and the REI (Italian Endovascular Registry).[14]

Over the years, the management path of acute stroke in Italy has reached a level of organisation, capillary diffusion and efficiency that, in most regions, the number of IVT is greater than 10% of hospitalisations for acute ischemic stroke. In 2018, 12,469 IVT and 4343 EVT were performed, with a relative increase of 18.8% and 65.2%, respectively, compared to the treatments carried out in 2017, against a very modest increase in the number of treating centres.

In 2018, the three Italian regions most affected by the pandemic (Lombardy, Emilia Romagna and Veneto) carried out 4554 IVT and 1788 EVT treatments, or 36.5% and 41.2%, respectively, of all reperfusion treatments carried out throughout the country.

Stroke management during COVID-19 outbreak

COVID-19 has often abruptly disturbed the geography of Stroke Units, especially in Lombardy. The regional organisation of the Italian National Health Service



Note: practising physicians except Slovakia, North Macedonia, Serbia and Turkey (professionally active physicians). Czechia, Poland and Portugal: not available. The figure is ranked on the share of physicians aged 55 years and over in the total number of physicians.
(*) 65 years and over: definition differs.
(*) Estimates.
(*) 2016.
(*) 2015.
(*) 55-64 years: definition differs.
Source: Eurostat (online data code: hlth_rs_phys)

Figure 2. The rate of physicians aged 55 years and over in EU (data from 2017). In Italy, 55.1% of physicians are ≥55 years (and expected to retire in the coming decade) in comparison with 45.1% in France, 44.7% in Germany, 34.1% in Spain, 29.7% in Austria and 15.1% in United Kingdom; the mean rate of EU is 35.7%.

REGIONS	POPULATION	IVT centers	IVT treatments	EVT centers	EVT treatments
Liguria	1,575,000	10	571	2	191
Friuli VG	1,223,000	3	426	2	88
Alto Adige	511,750	1	172	1	76
Trentino	534,405	1	161	1	2
Abruzzo	1,328,000	7	401	4	87
Veneto	4,925,000	22 (22)	1,485	6 (6)	360
Tuscany	3,753,000	22	1,129	3	395
Emilia Romagna	4,451,000	14 (12)	1,264	5 (5)	585
Marche	1,551,000	7	365	1	82
Umbria	894,762	5	221	2	49
Piedmont	4,424,000	24	1,091	5	343
Sardinia	1,663,000	3	381	3	135
Lombardy	10,000,000	38 (8)	1,805	8 (6)	843
Lazio	5,882,000	20 (20)	1,049	7 (7)	476
Valle d'Aosta	128,298	1	20	1	14
Calabria	1,973,000	5	307	3	96
Sicily	5,082,000	17	696	3	163
Puglia	4,087,000	9	526	4	191
Basilicata	574,782	2	43	0	0
Campania	5,869,000	8 (8)	356	2 (2)	167
Molise	314,725	1	0	0	0
Totale	60,744,722	220	12,469	63	4,343

Figure 3. Number of stroke centres and IVT/EVT treatments in Italy, by region, in 2018 with the population of each region (absolute number of inhabitants). The regions described in the paper are marked in red and the number of IVT and EVT centres active during the pandemic are reported in red colour only for these regions (source: mainly unofficial data). IVT = i.v. thrombolysis; EVT = endovascular treatment. Adapted from RAPPORTO 2018 SULL'ICTUS IN ITALIA: https://www.osservatorioictusitalia.it/wp-content/uploads/2018/12/Rapporto-2018-sullictus-in-Italia.pdf.

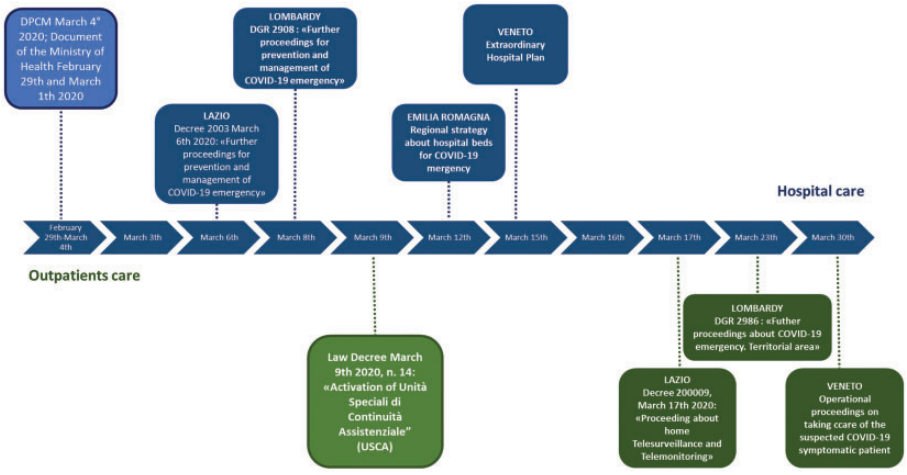


Figure 4. Timeline of institutional decrees and proceedings pertaining to the management of patients affected by COVID-19 infection.

with different institutional proceedings for inpatient and outpatient services (Figure 4) has determined different organisational needs and responses.

In Lombardy, the reorganisation of the stroke network and other time-dependent disease networks (trauma, acute myocardial infarction, neurosurgery and cardiac surgery) has led to an increase in the number of available ICU and sub-intensive ICU beds for COVID-19 patients. However, the number of stroke units (hub and spoke) has been reduced from 28 to 10. All stroke patients are currently transferred by ambulance to these 10 hub Stroke centers.[15] In the case of a self-presenting stroke patient, IVT should be offered in the Emergency Room, and then the patients should be transferred to the nearest stroke hospital. If there is a suspicion of stroke and COVID-19

comorbidity, patients should be preferentially treated in a COVID hospital, possibly in a Stroke Unit or in a COVID-19 ward with neurological consultations.

In Emilia Romagna, in the early days of the epidemic, there was a heterogeneity of involvement in the various provinces of the region, triggering conflicting responses regarding how to best implement the pre-existing stroke pathways which are organised on a provincial basis and by macro-areas. In the most affected provinces, the IVT spoke hospitals had become COVID hospitals, and the organisation was changed from a drip and ship organisation to a mothership organisation. The same scenario happened, at least partially, in the macro areas covering multiple provinces, moving neurologists from the no longer operating spoke to the hospitals where the hub is located. Some interprovincial drip and ship routes in densely populated areas and with an IVT rate for ischemic stroke greater than 15% have remained essentially unchanged with a reorganisation of the personnel in charge of transport. Another aspect of this reorganisation is that in itself, the drip and ship system, due to the measures of social distancing and the consequent lower circulation of vehicles, is carried out with shorter travel times than before the crisis. Where the organisation of pathways had already been settled on a strong mothership, the same model has been guaranteed with few changes. At hub hospitals serving a population of 1M, the need to ensure safe treatment, even for patients already known to be positive or suspect of being COVID positive, has led to a partial separation of intra-hospital routes and hospital areas in the pre-existing Stroke Units. In response to the significant reductions in outpatient rehabilitation treatment services, public awareness programs have been set up by the national patient organisation A.L.I.Ce (Associazione per la Lotta all'Ictus Cerebrale).[16] Ad hoc prepared materials have been made available, including video formats which benefit patients who partake in at-home neuromotor rehabilitation exercises.[17] In this context, home respiratory rehabilitation exercises have also been proposed for patients with COVID-19.

A similar example also comes from Veneto, where the experience of reorganising stroke pathways for one hub centre has been described.[18] The interesting aspect of this organisational model is undoubtedly its flexibility.[19] One of the most significant changes has been the use of a mobile CT unit outside the hospital – a neuroradiological hot-spot for COVID-positive or suspected COVID patients. While awaiting their nasopharyngeal swab results, these patients are treated with IVT and EVT and then admitted to either temporary stroke wards or COVID wards (COVID-ICU wards if thrombectomy needs to be performed under general anaesthesia). Still, in all cases, the stroke team is fully responsible for the decision-making on stroke care. The COVID emergency has led to a significant decrease in the number of stroke admissions and, therefore, in treated patients, compared to numbers from the same period one year ago. Furthermore, many of the admissions are late stage, often with large vessel occlusions and severe stroke, consequently requiring an increase in primary EVT treatments with lesser possibility of bridging therapy.

In Lazio, the COVID-19 network has been quickly implemented from scratch, mirroring a hub and spoke model. Like other regions, some neurology and stroke unit departments have been transformed into COVID-19 dedicated departments. In Lazio, a lower number of diagnosed COVID-19 cases have been observed compared to the northern regions. Being so, the Lazio Region left its hospital network unchanged. However, treatment times are likely to have lengthened, as the added sanitisation procedures, especially for radiology emergency services, must have negatively impacted the management time/burden of vascular emergencies.

Although the southern regions of Italy have reported being less affected by the pandemic, several hospitals have been transformed into COVID-19 dedicated hospitals and measures have been prepared to identify suspected cases before the access to EDs through pre-triage. Being so, the impact of the pandemic has not determined a substantial modification of the pre-existing stroke pathways. That is, the centres identified in the regional resolutions as hubs for IVT and EVT have remained unchanged, with only patient management procedures having been changed to ensure the safety of the procedures. For example, Campania[20] has recently reorganised the stroke network based on the number of stroke hospitalisations per province and the respective population density, establishing three second-level Stroke Units and four first-level Stroke Units for the province of Naples and a second-level Stroke Unit for each of the remaining provinces. An additional first-level Stroke Unit, based on population density has also been established. This organisation has not undergone radical changes, when compared to those changes implemented for the stroke network of the Lombardy Region. However, it is expected that, although most areas have not changed their stroke pathways, the fear of hospital access, the need for pre-triage and to exclude the coexistent presence of COVID-19 can lead to a global increase times in the management of acute stroke already in the pre-hospital phase.

Finally, in Umbria, the patient's door to needle time and door to groin time were doubled even though stroke pathways have not been changed through regional decree. In small hospitals, telemedicine

facilities were completely dedicated to the management of COVID-19 patients in COVID Units, being not available for telestroke.

Interpretation

Stroke patterns in time of COVID-19 pandemic

Since the outbreak of the pandemic, in the Veneto Region, there has been an overall 50–60% reduction in the number of stroke patients arriving at hospitals, compared to the same period a year ago.[18]

This phenomenon, which, although not systematically, has been also observed and reported by neurovascular teams throughout Italy (a National survey is going on). Generally, patients with mild stroke-like symptoms do not go to the hospital and do not seek medical attention. Instead, more than often, they wait for the symptoms to improve or resolve, which could explain both this recorded reduction in admissions for suspect of stroke and/or significant delays in arrival to the hospital. These issues make some stroke patients ineligible for acute treatment. Additionally, more patients have been arriving too late to be eligible for reperfusion treatment.

Baracchini et al.[18] reported that the number of patients who underwent IVT or bridging therapy (combined intravenous and thrombectomy) decreased (26% and 30%, respectively), while the number of primary EVT increased by 41%.

The mandatory change in the organisation of stroke pathways, especially in the regions most affected by the pandemic, could, therefore, have effects on the number of reperfusion treatments in the acute phase, both IVT and EVT, but the extent of these can be assessed with precise data in the next months. This aspect is certainly a limitation of this study. Interestingly, the factors that predict a fatal outcome of COVID-19 infection are one or more of the following: age >65 years, obesity, diabetes, high blood pressure and the number of comorbidities. The same factors relate to a high risk of cerebrovascular events, and patients with these features probably have had a greater fear to go to the hospital for stroke symptoms. The analysis of the Italian technical-scientific agency on public health (Istituto Superiore di Sanità)[21] on the first 3200 deceased patients, confirmed a risk profile mainly overlapping with the population at high risk of stroke: mean age 78.5 (median: 80, range 31–103, interquartile range – IQR 73–85), 30% had a history of ischemic heart disease, 22% atrial fibrillation, 73.8% hypertension and 33% diabetes mellitus.

Another overlooked issue is the underestimation of acute stroke in patients already hospitalised because of COVID-19 and their management. Cerebrovascular diseases in patients with COVID-19 have been studied in a single-centre, cohort study that was published without peer-review on a pre-print server.[22] According to this study, acute stroke may complicate or co-exist with COVID-19 disease; 5%, 0.5% and 0.5% of the patients developed acute ischemic stroke, cerebral venous sinus thrombosis and cerebral haemorrhage accordingly. Moreover, the percentage of acute stroke in intubated patients has been certainly underestimated.

Longstanding and new proposals for stroke management in the pandemic era

The challenges and limitations faced in the management of patients with acute stroke in this historical phase induce vascular neurologists, in collaboration with the entire neurovascular team, to come up with alternative solutions:

- Improve education of health professionals and the public during pandemic giving the following messages:

1. Stroke is an emergency, and treatment is available. The benefit of being treated for life-threatening disease far outweighs the risk of being infected.
2. High-standard treatment is guaranteed during the pandemic.
3. Stroke patients will be managed under a 'protected stroke code' to avoid infection.

- Set up tele-stroke networks by:

1. Implementing the existing telestroke networks and avoiding futile transports.[23]
2. Starting telestroke pathways from the patient's home employing territorial emergency doctors and nurses who carry out evaluations, so to eliminate any contact and the possibility of contagion. This also saves time and sometimes avoids the use of secondary transportation.
3. Using telemedicine at an in-hospital level to evaluate patients who are suspected of having an acute neurological pathology in the COVID Units or even in ED's, when there is no possibility of guaranteeing cold areas.

- Reorganise stroke pathways with a "protected stroke code" by:

1. Evaluating patients with unknown COVID-19 status under "protected stroke code" with appropriate personal protective equipment.[24,25] A suggested model could be that all COVID-19 suspected patients are first managed in a grey

area and then transferred to a Stroke Unit if COVID-19 negative, or to a COVID-19 area if positive.[18]

- Facilitating new stroke treatment options:

1. Promoting the approval of tenecteplase in acute stroke to European Medicines Agency and Agenzia Italiana del Farmaco.

The only drug currently approved for this use is alteplase, even though in other countries, tenecteplase is considered a viable alternative with much faster bolus administration without the need for continuous infusion.[26]

Conclusions

COVID-19 has challenged the Italian healthcare system, and consequently, led to a radical reorganisation of regional stroke pathways. However, the full impact of this on stroke management still needs to be evaluated.

In the event of a second wave of COVID-19, stroke treatment pathways will need to be flexible enough so that they can be readjusted for acute treatment, secondary prevention, and rehabilitation through the use of telemedicine. This is so that severe and acute disease patient rights to access and delivery of care are guaranteed.

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Informed consent

Not applicable.

Guarantor

MZ.

Contributorship

MZ, FRP, FC and VC conceived the study and planned it. MZ wrote the first draft of the manuscript. All authors reviewed and edited the manuscript and approved the final version of the manuscript.

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ORCID iD

Marialuisa Zedde https://orcid.org/0000-0001-7530-818X

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