

The shortage of thrombolytics for stroke: a call for action

Ischaemic stroke is a leading cause of disability and mortality worldwide.¹ Mounting evidence exists in support of thrombolysis for the treatment of patients with ischaemic stroke, and alteplase is also essential for many patients who undergo endovascular thrombectomy.¹ Particularly during the COVID-19 pandemic, novel protocols for stroke treatment flourished, aiming to speed up treatment and avoid unnecessary delays in thrombolysis.² After the pandemic though, a new threat jeopardises the availability of thrombolysis worldwide: the shortage of alteplase and tenecteplase, which is expected to last for at least two more years. However, medical societies have yet to provide guidance on how to cope with this emergency.

From an ethical perspective (according to consequentialist ethics), thrombolysis could be reserved exclusively for the patients who might benefit the most from treatment. Alternatively, if the morality of our actions is guided by the Hippocratic oath (according to deontological ethics), stroke specialists should treat all eligible patients until stocks run out. We could pursue the consequentialist ethical approach by selecting patients for whom the benefit of thrombolysis is expected to be smallest. For instance, patients with lacunar stroke might benefit more from antiplatelet drugs than thrombolysis.³ Besides, recommendations for thrombolysis vary for minor non-disabling strokes, thus allowing for a risk-to-benefit assessment on a case-by-case basis.⁴ Finally, thrombolysis before mechanical thrombectomy is the current benchmark⁵ yet, in the future, evidence might favour direct thrombectomy for certain subtypes of stroke, such as tandem occlusion and large ischaemic core.

From a deontological perspective, thrombolysis can hardly be withdrawn from patients who are borderline because of the expectation to benefit someone else in the future.

The most crucial ethical aspect of the shortage of thrombolytics is arguably that about the regulations of pharmaceutical companies, as those have direct consequences for patients and clinicians. International regulations should perhaps guarantee alternative production systems that bypass patent limitations and penalise supply-chain disruptions undermining the equity of health care access. Worldwide, clinicians are running out of thrombolytic stocks. Therefore, ethical and clinical guidance is urgently needed to ensure the most appropriate treatment in patients with ischaemic stroke.

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The African Dementia Consortium

In low-income and middle-income countries, particularly those in Africa, communicable diseases are still of concern. Accordingly, many clinicians and biomedical researchers have balked at the idea of exploring ageing-related disorders in sub-Saharan Africa. However, longevity is also a characteristic of African populations.¹

Around 70% of all cases of dementia worldwide are due to Alzheimer's disease, but the distribution of dementia subtypes in Africa remains unclear.² Furthermore, little is known about the genetic and epigenetic architecture of dementia phenotypes among indigenous Africans. The *APOE* ε4 allele, which is robustly associated with Alzheimer's disease in most populations, might have more nuanced links to Alzheimer's disease in people with African ancestry.³ The pathology of Alzheimer's disease is also intriguing, as African populations tend not to share risk factors with people living in high-income countries.⁴ Africa harbours the greatest genetic diversity of any continent (low linkage disequilibrium and short haplotype blocks). Thus, increasing the representation of indigenous Africans in genomic research could bring novel insights into the biology of brain health and cognition, facilitate translational genomics, and improve understanding of dementia phenotypes and protective and risk factors.² Furthermore, fine mapping of new loci and variants identified in African populations could help to pinpoint causal genetic variants.



Our African Dementia Consortium brings together dementia researchers in a multidisciplinary framework to generate clinical and socioeconomic datasets. We believe that the Consortium will improve the characterisation of dementia phenotypes in Africans. The Consortium will focus on several research areas, including epidemiological studies on prevalence, incidence, and risk factors;⁴ genetic and epigenetic studies; detection of unique biomarkers; clinical trials; capacity building and networking among dementia researchers living or working in Africa; translational research; implementation science for the translation of research evidence to practice and policy; determinants of brain health; and ethical, legal, sociological, and anthropological issues in brain health. For our future research, the Consortium will build on the biobanking of brain samples, CSF, and blood that is already in place.⁵

Our Consortium includes more than 100 researchers, and more scientists are expected to join. It is coordinated from the Neuroscience and Ageing Research Unit of the Institute for Advanced Medical Research and Training,

College of Medicine, University of Ibadan (Ibadan, Nigeria). Researchers from Nigeria, Ghana, Benin, Cameroon, Kenya, Uganda, Tanzania, Mozambique, and Ethiopia are already part of the Consortium. They are recipients of a grant award from the US National Institute of Aging.

The Recruitment and Retention for Alzheimer's Disease Diversity Cohorts in the Alzheimer's Disease Sequencing Project (READD-ADSP) study, which is led by Margaret Pericak-Vance and her team at the University of Miami (Coral Gables, FL, USA), will explore the genetics of Alzheimer's disease and other dementias in minority ethnic groups and in resource-limited countries, including the aforementioned countries in sub-Saharan Africa. This study aims to recruit 5000 Africans (2500 participants with Alzheimer's disease and 2500 controls). Our African Dementia Consortium will discuss the implementation of READD-ADSP in sub-Saharan Africa at a forthcoming quadrennial symposium on brain ageing and dementia in low-income and middle-income countries, which is to be held in Nairobi, Kenya, on Dec 6-9, 2022.

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For more on READD-ADSP see <https://www.readd-adsp.org/>

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