



# Stroke in Africa: profile, progress, prospects and priorities

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**Abstract** | Stroke is a leading cause of disability, dementia and death worldwide. Approximately 70% of deaths from stroke and 87% of stroke-related disability occur in low-income and middle-income countries. At the turn of the century, the most common diseases in Africa were communicable diseases, whereas non-communicable diseases, including stroke, were considered rare, particularly in sub-Saharan Africa. However, evidence indicates that, today, Africa could have up to 2–3-fold greater rates of stroke incidence and higher stroke prevalence than western Europe and the USA. In Africa, data published within the past decade show that stroke has an annual incidence rate of up to 316 per 100,000, a prevalence of up to 1,460 per 100,000 and a 3-year fatality rate greater than 80%. Moreover, many Africans have a stroke within the fourth to sixth decades of life, with serious implications for the individual, their family and society. This age profile is particularly important as strokes in younger people tend to result in a greater loss of self-worth and socioeconomic productivity than in older individuals. Emerging insights from research into stroke epidemiology, genetics, prevention, care and outcomes offer great prospects for tackling the growing burden of stroke on the continent. In this article, we review the unique profile of stroke in Africa and summarize current knowledge on stroke epidemiology, genetics, prevention, acute care, rehabilitation, outcomes, cost of care and awareness. We also discuss knowledge gaps, emerging priorities and future directions of stroke medicine for the more than 1 billion people who live in Africa.

Stroke is a leading cause of disability, dementia and mortality worldwide and is associated with substantial economic costs. Globally, an average of 1 in 4 adults will have a stroke during their lifetime<sup>1</sup>. Global, age-standardized stroke mortality rates declined substantially between 1990 and 2016, most likely as a result of the increased availability of acute stroke treatments and improved inpatient care in high-income countries; however, the decline in incidence was less steep in Africa<sup>2</sup>. The 2019 update on global stroke statistics identified a consistent increase in stroke incidence in low-income and middle-income countries (LMICs) on the basis of stroke incidence studies performed between 1971 and 2014 (REF.<sup>3</sup>). Between 1970 and 2010, 70% of all stroke deaths and 87% of disability owing to stroke occurred in LMICs<sup>3,4</sup>.

The burden of non-communicable diseases is increasing exponentially in Africa. In addition, infections such as malaria, human immunodeficiency virus (HIV) and tuberculosis persist and are further exacerbated by

poverty and conflict<sup>5,6</sup>. We are also witnessing an increase in the co-morbidity of non-communicable and communicable diseases<sup>7,8</sup>. Less than a century ago, stroke was relatively uncommon in Africa<sup>9,10</sup>. However, in recent systematic analyses by the global burden of neurological diseases investigators, stroke was foremost along with migraine and meningitis in terms of disability-adjusted life years (DALYs) in northern, central, western, eastern and southern Africa<sup>11</sup>. Today, Africa has some of the highest indices of stroke burden in the world<sup>4,12–14</sup>. The increase in stroke burden in Africa is being driven by multiple factors acting across the lifespan. Key drivers include in utero and early-life undernutrition, which are associated with increased cardiometabolic risk factors in mid-life<sup>15–17</sup>, increasing exposure to indoor and outdoor particulate air pollution<sup>18,19</sup>, changes in dietary habits and population ageing<sup>20</sup>. These relationships are only the tip of the iceberg because, for every case of clinical stroke, there are four other cases of covert or ‘silent strokes’, which can cause

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## Key points

- The annual incidence rate of stroke in Africa is up to 316 per 100,000 individuals, which is within the highest incidence rates in the world, and the prevalence rate of 1,460 per 100,000 reported in one region of Nigeria, western Africa, is clearly among the highest in the world.
- Hypertension remains the most important modifiable risk factor for stroke in Africa but others include diabetes mellitus, dyslipidaemia, obesity, stress, smoking, alcohol use, physical inactivity and an unhealthy diet.
- Africa has a slightly greater preponderance of small vessel disease-related stroke and intracerebral haemorrhagic lesions than elsewhere in the world.
- The results of the first African genome-wide association study on stroke are expected soon but genes already known to modify stroke risk in African populations include *IL6*, *APOE*, *APOL1*, *CYB11B2* and *CDKN2A/2B*.
- Pragmatic approaches to improving stroke care in Africa include regular monitoring of risk factors and health services, implementation of prevention strategies, improving acute care and rehabilitation services, and encouraging task sharing; the emergence of standalone stroke care and stroke units in some North African and sub-Saharan countries is encouraging.
- Numerous challenges face stroke medicine in Africa but awareness and the concerted efforts towards securing support for more stroke research and services via organizations such as the African Stroke Organization, World Stroke Organization and WHO hold much promise.

cognitive dysfunction and mental health conditions in later years<sup>19,21,22</sup>.

Stroke medicine in Africa has advanced over the past decade. Our understanding of both traditional and emerging risk factors, including their effect sizes and population attributable risk (PAR), has improved. More information on stroke aetiology and pathophysiological types and subtypes is now available for African populations, including a better understanding of strokes that occur as a consequence of sickle cell disease (SCD), HIV/AIDS or SARS-CoV-2 (COVID-19) infection. Stroke outcomes, rehabilitation, cost of care, quality of life and mortality are receiving more detailed attention, while post-stroke complications, including cognitive impairment and dementia, anxiety and depression,

fatigue, and seizure disorders, are increasingly documented in the growing stroke literature from Africa<sup>4,12</sup>. Candidate-gene studies and ongoing genome-wide association studies (GWAS) have also begun to elucidate the genetic architecture of stroke in Africa<sup>23–25</sup>.

Despite this progress, substantial gaps remain in our understanding of stroke in Africa as well as in stroke care, practice and policy on the continent. The effective organization of preventative, therapeutic and rehabilitative stroke services also remains a challenge in many African countries. However, emerging insights from research and the introduction of novel stroke leadership initiatives offer huge prospects for tackling the growing burden of stroke on the continent with context-sensitive strategies. In this article, we review the unique epidemiological, aetiological and genetic profiles of stroke in Africa and summarize what we know about stroke prevention, acute care, rehabilitation, cost of care, outcomes and awareness. We also identify knowledge gaps, emerging priorities and future directions for stroke medicine and care and the implications for the people of Africa and the global community.

## Stroke epidemiology in Africa

Several epidemiological studies have been undertaken on stroke in Africa with a preponderance of hospital-based over community or population survey studies. Several of the population-based studies have been identified as having methodological shortcomings<sup>26,27</sup> and the only study that fulfilled the gold-standard criteria for a stroke epidemiological study was a prevalence study performed in urban Egypt (Al Quseir) by El-Tallawy et al.<sup>28</sup>.

## Incidence

In 1991, a study involving hospital patients estimated the annual stroke incidence in Harare, Zimbabwe, to be 31 per 100,000 individuals<sup>29</sup>. Other hospital-based incidence studies from Benghazi, Libya (1984 (REF.<sup>30</sup>) and 1993 (REF.<sup>31</sup>)), urban Pretoria, South Africa<sup>32</sup> (1985) and Maputo, Mozambique (2006)<sup>33</sup> reported annual crude incidence rates ranging from 48 to 149 per 100,000 individuals. However, hospital-based studies do not adequately capture the true burden of stroke within a given community because the population at risk is not known, thus interpretation of such studies requires caution. Indeed, a continent-wide meta-analysis<sup>34</sup> and a Nigeria-based meta-analysis<sup>35</sup> of pooled estimates of stroke incidence both found that hospital-based studies estimated lower incidence rates than community-based studies, suggesting that hospital-derived data under-represent the true incidence of stroke.

The earliest known community-based study of stroke incidence in Africa was derived from the Ibadan Stroke Registry and was conducted from 1973 to 1975 in Ibadan, an urban city in southwestern Nigeria. The study reported an annual crude incidence rate of 26 per 100,000 individuals<sup>36</sup>. Similar studies from Lagos and Akure, southwestern Nigeria, were conducted in 2007 and 2010 and reported annual crude incidence rates of 25 per 100,000 (REF.<sup>37</sup>) and 61 per 100,000, respectively<sup>38</sup>. Other community-based studies have been undertaken

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in other parts of the continent<sup>28,39,40</sup> (TABLE 1) and have reported crude annual stroke incidence rates ranging from 95 per 100,000 in rural Tanzania, East Africa<sup>13</sup>, to 260 per 100,000 in urban Egypt, North Africa<sup>40</sup>.

The variation in the reported figures might result from methodological differences, such as completeness of case ascertainment, inclusion of mild or clinically covert strokes, lack of differentiation between first and

Table 1 | Studies of stroke incidence and prevalence in Africa

Country, region	Study period	Type of study	Case definition	Neuroimaging confirmation <sup>a</sup>	Stroke subtyping	Crude annual incidence or crude prevalence rate <sup>b</sup>	Age-adjusted incidence or prevalence rate <sup>b</sup>	Ref.
<b>Incidence: annual range 25–260 per 100,000 from 1973 to 2013</b>								
Nigeria, Ibadan	1973–1975	Community	Not stated	No	Yes	26	Not stated	36
Libya, Benghazi	1983–1984	Hospital	US national survey of stroke	Yes	Yes	63	Not stated	30
South Africa, Pretoria	1984–1985	Hospital	Harvard Cooperative Stroke Registry	Yes	Yes	101	Not stated	32
Zimbabwe, Harare	1991	Hospital	WHO criteria	No	No	31	68	29
Libya, Benghazi	1991–1993	Hospital	Not stated	Yes	Yes	48	Not stated	31
Egypt, Sohag	1992–1993	Community	WHO criteria	Yes	Yes	180	Not stated	39
Tanzania, Hai	2003–2006	Mixed	WHO criteria	Yes	Yes	95	109	13
Tanzania, Dar es Salaam	2003–2006	Mixed	WHO criteria	Yes	Yes	108	316	13
Mozambique, Maputo	2005–2006	Hospital	WHO criteria	Yes	Yes	149	260	33
Egypt, Al-Kharga	2005–2008	Community	WHO criteria	Yes	No	260	560	40
Nigeria, Lagos	2007	Community	WHO criteria	Yes	No	25	54	37
Egypt, Al-Quseir	2010–2011	Community	WHO criteria	Yes	No	181	Not stated	28
Nigeria, Akure	2010–2011	Mixed	Not stated	Yes	Yes	61	61	38
<b>Prevalence: crude range 15–1,331 per 100,000 from 1983 to 2016</b>								
Nigeria, Igbo-Ora, rural	1983–1984	Community	WHO criteria	No	No	56	Not stated	42
Tunisia, Kelibia	1985	Community	WHO criteria	Yes	Yes	42	Not stated	46
Ethiopia, central and rural	1988	Community	WHO criteria	No	No	15	Not stated	44
Egypt, Sohag	1992–1993	Community	WHO criteria	Yes	Yes	508	Not stated	39
Tanzania, Hai	1994–1995	Community	WHO criteria	No	Yes	127	Not stated	43
South Africa <sup>c</sup> , Limpopo province, rural	2001	Community	WHO criteria	No	Yes	243	300	47
Nigeria, Lagos, urban	2007	Community	WHO criteria	No	No	114	204	48
Egypt, Al-Kharga	2005–2009	Community	WHO criteria	Yes	Yes	580	Not stated	40
Nigeria, Niger Delta	2008	Community	WHO criteria	No	No	851	1,230	49
Benin, Cotonou, urban	2008–2009	Community	WHO criteria	Yes	Yes	460	771	50
Morocco, Rabat	2008–2009	Community	WHO criteria	Yes	Yes	284	292	51
Nigeria, Kwara, semi-urban	2009–2010	Community	WHO criteria	No	No	1,310	Not stated	52
Tanzania, Hai	2009–2010	Community	WHO criteria	No	No	2,420 (>70 years of age)	2,300 (>70 years)	53
Egypt, Assiut	2010	Community	WHO criteria	Yes	Yes	963	980	45
Egypt, Al Quseir <sup>d</sup>	2010–2011	Community	WHO criteria	Yes	Yes	655	Not stated	28
Nigeria, SE	2011	Community	WHO criteria	No	No	163	163	54
Egypt, Qena	2011–2013	Community	WHO criteria	Yes	Yes	922	567	55
Nigeria, Niger Delta	2014	Community	WHO criteria	No	No	1,331	1,460	14
Nigeria, Odeda	2015	Community	WHO criteria	No	No	711	Not stated	56
Benin, Parakou	2016	Community	WHO criteria	No	Yes	1,156	3,223	57

<sup>a</sup>‘Yes’ >80%. <sup>b</sup>Per 100,000 population. <sup>c</sup>South Africa, Agincourt Health and Population Unit. <sup>d</sup>The prevalence study performed in urban Egypt (Al Quseir) by El-Tallawy et al. fulfilled the gold-standard criteria for a stroke epidemiological study.

recurrent strokes, and use of neuroimaging for diagnostic confirmation and subtyping. Other sources of variation include inherent geographical differences in the distribution of risk factors, differences in genetic susceptibility to stroke across the populations studied, and cohort or period effects<sup>23,26,41</sup>.

Age-adjusted incidence rates are more representative of the distribution of stroke among the population, especially in Africa, where the population is predominantly <60 years of age<sup>26</sup>. The most recent and rigorous study of stroke incidence in Africa was performed in Tanzania and published in 2010 (REF.<sup>13</sup>). The age-standardized stroke incidence rates from the two surveillance sites in Hai (rural Tanzania) and Dar es Salaam (urban Tanzania) were 109 and 316 per 100,000 person-years, respectively<sup>13</sup>. WHO world population data were used for age-standardization and the researchers used a robust case-ascertainment strategy. If the incidence rates from this study are extrapolated to the rest of Africa, it implies that every minute, six Africans have a stroke. The Dar es Salaam rates were similar to the highest rates in South East Asia and Europe, according to the Global Burden of Disease (GBD) study on global, regional and national burden of stroke, which reported the age-standardized stroke incidence rate as 354 per 100,000 person-years in China and 335 per 100,000 person-years in Latvia<sup>2</sup>.

### Prevalence

The 1982 Igbo-Ora community prevalence study in rural southwestern Nigeria was one of the earliest of such studies to be performed in Africa and found a crude stroke prevalence of 58 per 100,000 (REF.<sup>42</sup>). The largest community prevalence study on stroke in Africa was performed in 1994 in the rural Hai district of Tanzania and reported an age-standardized prevalence of 154 per 100,000 in men >15 years of age and 114 per 100,000 in women >15 years of age<sup>43</sup>. Other crude prevalence estimates of stroke from community studies in Africa range from 15 per 100,000 in rural Ethiopia<sup>44</sup> to 963 per 100,000 in urban Egypt<sup>45</sup>, with more recent studies reporting higher stroke prevalence than older studies<sup>14,28,39,40,45–57</sup> (TABLE 1). Age-adjusted stroke prevalence seems to be higher in some parts of Africa than the global average. For example, two studies from rural communities in the Niger Delta region of southern Nigeria reported age-adjusted prevalence rates of 1,230 per 100,000 (REF.<sup>49</sup>) and 1,460 per 100,000 (REF.<sup>14</sup>). According to data from the GBD study, global age-adjusted stroke prevalence increased from 1,261 (95% uncertainty interval (UI) 1,208.2–1,318.7) per 100,000 person-years in 1990 to 1,300.6 (UI 1,229–1,374.7) per 100,000 person-years in 2017 (REF.<sup>58</sup>). Therefore, although stroke prevalence is declining in western Europe and North America, Africa might have some of the highest stroke prevalence rates in the world.

### Frequencies in hospitals

In Africa, hospital-based studies on stroke seem to be more common than community-based or population survey-based studies<sup>59–68</sup>. The results of these hospital-based studies indicate that stroke is the leading cause of adult neurological admissions and medical coma.

In one hospital-based case series, stroke accounted for up to 78% of adult neurological admissions<sup>69</sup>. In another tertiary centre, stroke accounted for up to 57% of individuals admitted with medical coma<sup>61</sup>. The results of a hospital-based cross-sectional cohort study indicated that stroke constituted ~25% of medical admissions among patients aged ≥60 years in Nigeria, Sudan and Tanzania<sup>67</sup>. A male preponderance in stroke presentation in African hospitals was generally observed in these studies<sup>56–65</sup>. A comparative study found ischaemic stroke to be the predominant stroke phenotype in Africa, accounting for up to 73% of stroke admissions; however, the burden of haemorrhagic stroke was higher in Indigenous Africans than in African Americans or Americans of European descent<sup>70</sup>. Indeed, a separate study, performed in southwestern Nigeria, reported that haemorrhagic strokes constituted ~45% of all stroke admissions<sup>65</sup>.

### Mortality and fatality rates

The results of population-based studies suggest that mortality after stroke is high in Africa — estimates of stroke-related deaths as a proportion of overall mortality range from 5.5%<sup>62</sup> to 11%<sup>63,71,72</sup>. The crude stroke mortality rate in a 1992–1995 study in Agincourt, South Africa, was estimated at 127 per 100,000 in individuals >35 years of age, although a 2016 study from the same site found a mortality rate of 114 per 100,000 (REFS<sup>47,73</sup>). A Tanzanian study on stroke mortality at three sites (one urban, two rural) found yearly age-adjusted stroke mortality of up to 88 per 100,000 for men and 44 per 100,000 for women<sup>71</sup>. However, the results of stroke mortality studies in Africa require cautionary interpretation, owing to low levels of standardized death registration and the use of verbal autopsies.

Evidence suggests that the case fatality rate for stroke could be higher in parts of Africa than in the rest of the world. In hospital-based studies from Africa, incident case fatality at 30 days ranges from 16.2% to 46%<sup>73,74</sup>. A systematic review and meta-analysis of stroke case fatality in sub-Saharan Africa was published in 2021 and reported a pooled estimated 1-month case fatality rate of 24.1%, with high heterogeneity and rates up to 83.3%<sup>75</sup>. These data contrast with the 1-month case fatality rates in high-income countries reported in a 2009 review by Feigin et al., ranging from 8% in France to 49.2% in Estonia<sup>76</sup>. In Africa, case fatality rates are generally higher for haemorrhagic strokes than ischaemic strokes<sup>74,77–82</sup>. Studies with a longer follow-up period, such as those performed by Walker et al. in Tanzania, have reported case fatality rates of up to 84.3% at 3 years post-stroke (rural Tanzania) and 82.3% at 7 years post-stroke (rural and urban Tanzania)<sup>72,83</sup>. Advanced age, stroke severity at presentation, in-hospital complications (especially aspiration pneumonia and sepsis) and poor functional status have been identified as predictors of post-stroke mortality<sup>72,83–86</sup>. Evidence indicates that early stroke fatality is further accentuated by poor control of metabolic risk factors (blood pressure, blood sugar), delayed stroke recognition and hospital presentation, and difficulties accessing early post-stroke care<sup>75,85–87</sup>. In addition, the nature and organization of stroke services in Africa

present inherent challenges, including limited access to diagnostic and time-dependent interventional services such as reperfusion therapies and stroke surgery, lack of stroke units and difficulty with patient retention during post-stroke rehabilitation<sup>88</sup>.

#### **Disability-adjusted life years**

Data regarding stroke DALYs in Africa are sparse. One systematic review found that the burden of disease owing to stroke in South Africa was 564,000 DALYs in 2008 (REF.<sup>89</sup>). In the few available studies, estimated DALYs lost due to stroke ranged from 1,070 DALYs per 100,000 person-years in South Africa to 7,738 DALYs per 100,000 person-years in Kenya. Women seem to have more stroke-associated DALYs than men and DALYs were higher for ischaemic stroke than haemorrhagic stroke<sup>89,90</sup>. Data from the GBD study indicate that, although stroke-associated DALYs decreased in all regions of the world between 1990 and 2016, the region with the smallest reduction was sub-Saharan Africa<sup>2</sup>. According to the same data, 80% of all incident strokes, 77% of all survivors of stroke, 87% of all deaths from stroke and 89% of all stroke-related DALYs occur in LMICs, including those in Africa<sup>91</sup>.

#### **Quality of life and cost of care**

Several studies have examined quality of life after stroke in Africa. The results of these studies consistently indicated that survivors of stroke have poorer quality of life in multiple domains than stroke-free controls<sup>92,93</sup>. The most commonly reported predictors of quality of life were post-stroke disability, depression and stroke severity. The estimated cost of care per patient with stroke ranges from US\$ 145 to US\$ 4,860, depending on the care setting<sup>94</sup>. Cost of stroke care is higher in urban areas than in rural areas and higher in private health facilities than in government health facilities<sup>94–98</sup>. Data from Africa have also identified a high burden of stroke on the psychological and emotional domains of quality of life of caregivers. Multiple studies have reported that female spouses are the predominant caregivers<sup>99–101</sup>; in a 2019 study from Lagos, Nigeria, up to 86.7% of caregivers were women<sup>101</sup>.

#### **Risk factors**

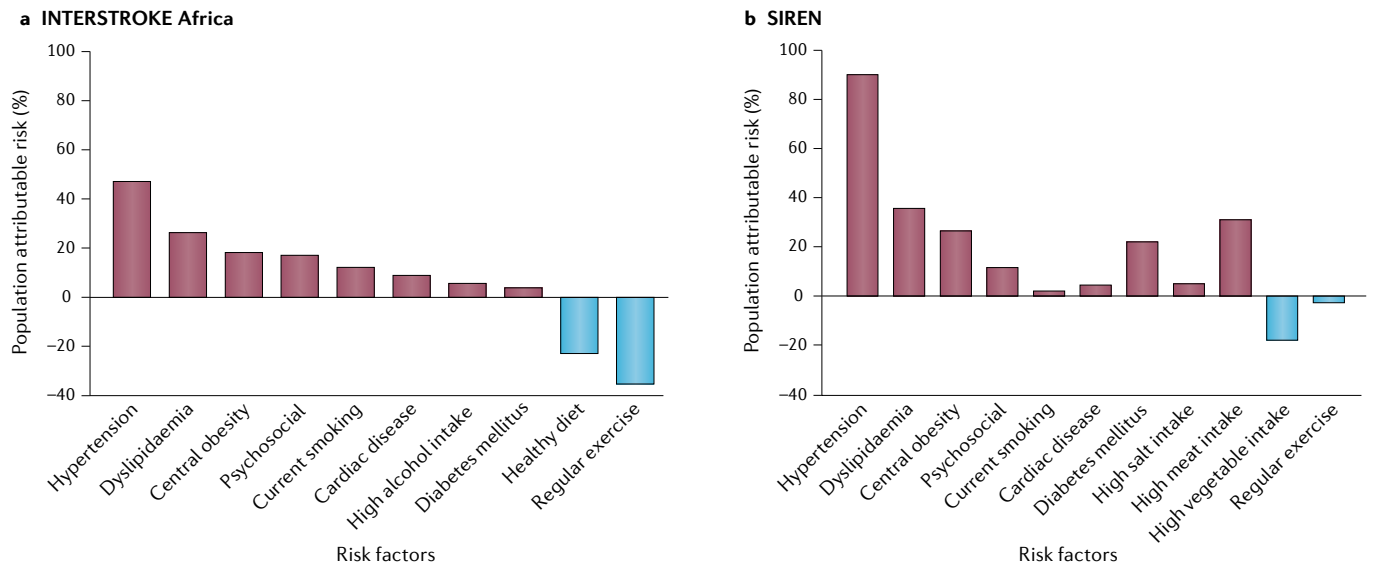
Age is the major non-modifiable risk factor for stroke. A comparative, hospital-based study found mean age at stroke presentation to be at least 10 years lower in Indigenous Africans than in African Americans or Americans of European descent<sup>70</sup>, suggesting Africans are more likely to be affected by stroke during the theoretical peak of their vocational productivity. Similarly, another study found patients with stroke in Ibadan, Nigeria, to be younger than patients with stroke in Berlin, Germany<sup>70,102</sup>. Temporal trends from the GBD (1990–2016) study indicate that age-standardized stroke incidence is increasing in southern sub-Saharan Africa, suggesting a persistent burden of underlying stroke risk factors in this region<sup>2</sup>. Observations from the global INTERSTROKE study, which involved five African countries (Mozambique, Nigeria, South Africa, Sudan and Uganda) suggest that the profile of stroke

risk factors is similar between Africa and the rest of the world, although regional differences in effect size exist<sup>103</sup>. This study identified ten top risk factors (hypertension, dyslipidaemia, diabetes mellitus, central obesity, cardiac causes, current smoking, high alcohol intake, unhealthy diet, physical inactivity and psychosocial factors) that accounted for 82% of the PAR for stroke among Africans and 92% of the PAR for stroke in the rest of the world<sup>103</sup>. The disparity could have resulted from an underestimation of risk in Africa owing to a small dataset or to unexplained residual factors, such as infectious diseases, contributing to stroke risk. The Stroke Investigative Research and Educational Network Study (SIREN) is the largest multi-site case–control stroke risk factor study to be performed in Africa to date. The study included 2,118 case–control pairs of Indigenous Africans from 15 sites in Nigeria and Ghana<sup>104</sup>. Using rigorous case ascertainment methodology and a similar case mix as the INTERSTROKE study<sup>105,106</sup>, the SIREN study found that 98.2% (95% CI 97.2–99.0) of the adjusted PAR of stroke was associated with 11 potentially modifiable risk factors: hypertension, dyslipidaemia, regular meat intake, central obesity, diabetes mellitus, low consumption of green leafy vegetables, stress, added salt at table, cardiac diseases, physical inactivity and current cigarette smoking<sup>104</sup> (FIG. 1).

Hypertension was the major modifiable risk factor identified by the INTERSTROKE study, with an odds ratio (OR) of 4.01 (99% CI 2.59–6.21) and PAR of 34.6 (99% CI 30.4–39.1) for the African countries included in the study<sup>103</sup>. In the SIREN study, the OR and PAR for hypertension were even higher, at 19.36 (95% CI 12.11–30.93) and 90.8% (95% CI 87.9–93.7), respectively. The INTERSTROKE study had a smaller sample size of Africans and lower statistical power than the SIREN study, which could account for this disparity. Nevertheless, these data suggest that hypertension is the prime modifiable driver of the stroke burden in Africa, although many Africans also have other vascular co-morbidities that act in concert with hypertension to drive stroke burden. Indeed, >45% of people in Africa over 25 years of age are estimated to be hypertensive, which constitutes the highest burden of hypertension in the world, according to the WHO<sup>107</sup>. Evidence indicates that <50% of individuals with hypertension in Africa are aware that they have the condition or have received a diagnosis and, among those who are diagnosed, at least half are not receiving treatment<sup>108</sup>. Thus, strategies to reduce the impact of hypertension will greatly reduce the risk of strokes among Africans<sup>104,108,109</sup>. In contrast to non-African cohorts, atrial fibrillation has not been consistently reported as a substantial risk factor for strokes in Africa (it accounted for 7% of all strokes in the INTERSTROKE study), although this observation could be the result of under-reporting<sup>110</sup>.

A comparison between data from the SIREN study and data from the population-based Reasons for Geographic and Racial Differences in Stroke (REGARDS) cohort study of African Americans and Americans of European descent living in the USA found higher frequencies of several cardiometabolic factors (hypertension, diabetes mellitus and dyslipidaemia)





**Fig. 1 | Risk factors for stroke in Africa. a** | The population attributable risk associated with 10 potentially modifiable risk factors in the INTERSTROKE study (Africa sub-cohort). The study included 973 case–control pairs of Indigenous Africans from sites in Mozambique, Nigeria, Sudan, South Africa and Uganda. Data from REF.<sup>103</sup> and REF.<sup>105</sup>. **b** | The population attributable risk associated with 11 potentially modifiable risk factors in the Stroke Investigative Research and Educational Network (SIREN) study. The study included 2,118 case–control pairs of Indigenous Africans from multiple sites across Nigeria and Ghana. Data from REF.<sup>104</sup>.

among Indigenous Africans and African Americans than in Americans of European descent<sup>70</sup> (FIG. 2). However, the comparison also identified a higher frequency of several cardiac and lifestyle factors (smoking, high alcohol intake and physical inactivity) among African Americans and Americans of European descent than among Indigenous Africans. These observations underscore the interaction between ethnic (including genetic) and geographical (lifestyle) factors in the vascular pathophysiological cascade<sup>70,102</sup>.

**Stroke with co-morbid conditions.** In Africa, as elsewhere, strokes occur alongside other conditions. In particular, HIV infection increases the risk of stroke<sup>111,112</sup>. Africa bears the largest global burden of HIV infection — 70% of the 36.8 million people who were living with the virus in 2017 were located in sub-Saharan Africa<sup>113</sup>. Africans with HIV and stroke generally have a young age at stroke onset (<45 years), severe stroke presentation, preponderance of ischaemic strokes and advanced immunosuppression<sup>114–117</sup>. The results of a Tanzanian stroke incidence project, which involved community-ascertained controls, found HIV infection to be an independent risk factor for stroke, with an OR of 5.61 (CI 2.41–31.09)<sup>53</sup>. Several mechanistic links between HIV infection and strokes have been suggested<sup>111</sup>, including clustering of cardiometabolic factors, inflammation of the brain vascular endothelium, coagulation abnormalities, vasculitis, HIV-associated vasculopathy and dyslipidaemia owing to anti-retroviral therapies and insulin resistance. However, more studies are needed to unravel the epidemiological contribution of HIV infection to the burden of stroke in Africa<sup>118</sup>.

Africa bears the greatest burden of SCD in the world, as 75% of the >300,000 individuals born with SCD

globally every year are born in sub-Saharan Africa<sup>119</sup>. SCD has been reported to increase stroke risk among children and adults in Africa<sup>120,121</sup>. There is a bimodal age distribution in the incidence of ischaemic stroke in individuals with SCD: most strokes occur before 20 years and after 30 years of age, with peak incidence at 10–15 years<sup>122,123</sup>. In a systematic review and meta-analysis involving 18,977 participants with SCD pooled from 23 African studies, the overall prevalence of stroke was 4.2%<sup>124</sup>. Stroke in individuals with SCD typically presents with transient ischaemic attacks, seizures and focal neurological deficits such as hemiparesis<sup>124</sup>. Cerebral ischaemia in SCD is thought to result from the occlusion of distal internal carotid arteries, middle cerebral arteries and anterior cerebral arteries<sup>120,121,123,124</sup>. Haemorrhagic strokes in SCD usually occur in the third decade of life<sup>121</sup> and are associated with low steady-state haemoglobin levels and high steady-state leukocyte counts<sup>125</sup>. Emerging data from Kumasi, Ghana, indicate higher numbers of stroke admissions and stroke mortality in January–June 2020 than in January–June 2019, suggesting a link between stroke risk and SARS-CoV-2 infection<sup>126</sup>. SARS-CoV-2 infection has been associated with increased fibrin, D-dimers and hypercoagulability, indicating that infection will increase the likelihood of strokes in vulnerable Africans with pre-existing vascular risk factors<sup>127</sup>.

**Drivers of the rising burden of stroke in Africa.** Data accrued over the past two decades and modelling estimates from the GBD study suggest a progressive increase in the burden of stroke in Africa<sup>4,128</sup>. Indeed, stroke and its risk factors (cardiovascular diseases) are now the leading cause of death of the adult population in the continent<sup>129</sup>. The drivers of this increasing stroke burden

in Africa can be categorized into early-life, mid-life and late-life factors (FIG. 3). Early-life factors, including fetal and/or infant undernutrition and low birth weight, have been associated with cardiometabolic disorders such as high blood pressure, dysglycaemia and dyslipidaemia later in life<sup>15,17,130</sup>. This link is thought to be the result of fetal reprogramming and epigenetic changes. A good illustration of the delayed effects of early-life undernutrition is the high burden of hypertension, diabetes and overweight status reported among survivors of the Nigerian civil war (the Biafran War), which occurred in the late 1960s<sup>16</sup>. Many of these individuals were exposed to severe famine in early life as a result of the conflict.

Early-life undernutrition might also partly explain the increased risk of cardiometabolic disorders among individuals who grow up in low-income rural areas but migrate to urban areas<sup>131</sup>. As these individuals approach mid-life with increasing wealth, they adopt lifestyles associated with urban living. Such lifestyles are often characterized by low levels of physical activity, high caloric intake, smoking, high levels of alcohol consumption, high intake of meat and low consumption of green leafy vegetables. Evidence indicates that exposure to stress and air pollution further exacerbates the course of neurovascular disease through the promotion of neuroinflammation and endothelial dysfunction<sup>18,132</sup>. Indeed, neither urban nor rural Africa is spared from the emerging risks of stress and air pollution (indoor air pollution from solid fuels and outdoor ambient particulate matter pollution) and both are likely to contribute

to the increases in stroke incidence that we are observing in Africa<sup>19</sup>. The GBD 2013 study identified a substantial contribution of household air pollution to the risk of stroke in LMICs, with the largest household air pollution-associated risk observed in the West African sub-region<sup>128</sup>.

Late-life factors driving the increasing burden of stroke in Africa include a progressive increase in life expectancy, which is resulting in population ageing<sup>133</sup>. Multiple cohort and population-based studies in Africa have identified ageing as a key non-modifiable risk factor for stroke, indicating that an increase in the number of older people in the population will result in an increase in stroke burden<sup>4,12</sup>. Genetic predisposition to stroke and stroke-related epigenetic modifications operate across the life course. For example, an association has been found between *IL6* rs1800796 and ischaemic stroke among West Africans<sup>134</sup>. The observation that fine particulate matter air pollution is associated with elevated plasma levels of IL-6 (REF.<sup>135</sup>) strengthens the possible link between air pollution and the increasing stroke burden.

Another contributor to the increasing burden of stroke in Africa is the limited availability of medication to control the more common risk factors. Drugs for the treatment of hypertension and diabetes are costly and might not be readily available in most health systems in Africa<sup>136</sup>. Furthermore, the vast majority of African countries do not have health insurance systems that can pay for the medications in full or even in part<sup>137,138</sup>. As a consequence, adherence to chronic

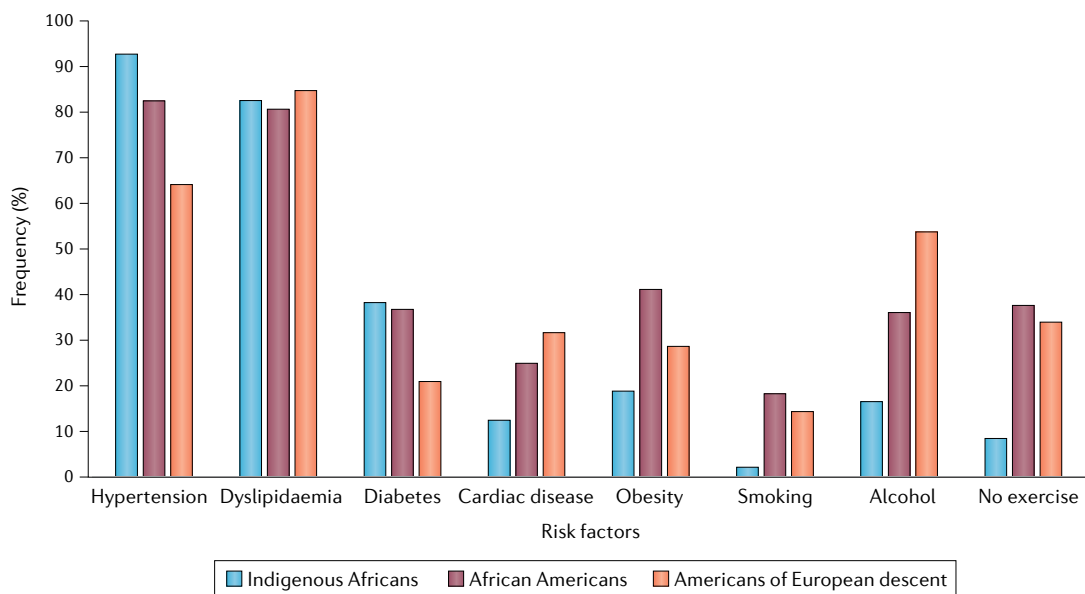
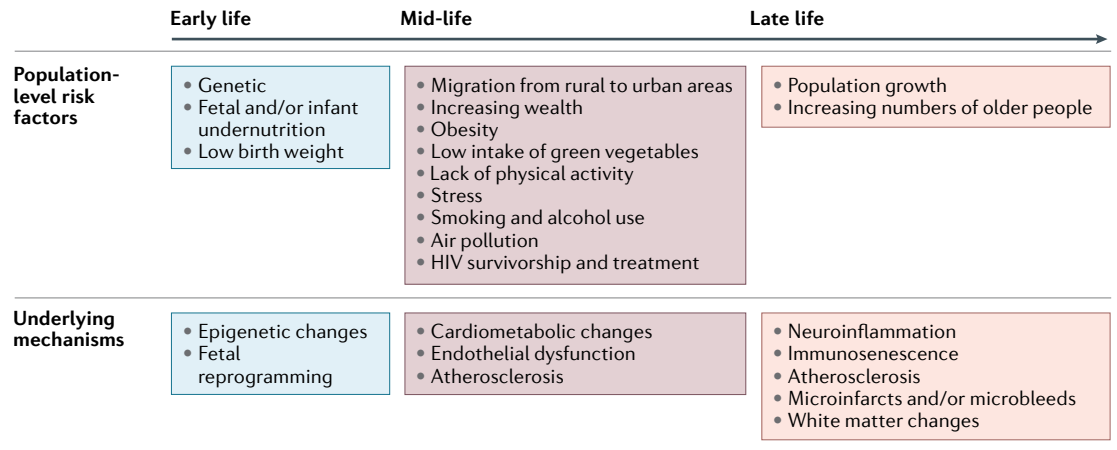


Fig. 2 | **Effect of race and geography on risk factors for stroke.** Graph shows the frequency of eight risk factors in Indigenous Africans, African Americans and Americans of European descent. Study participants were >55 years of age. The data for this analysis came from 1,928 individuals with stroke who met the selection criteria and consisted of 811 Indigenous Africans recruited into the Stroke Investigative Research and Educational Network (SIREN) study, 452 African Americans and 665 Americans of European descent who were participants in the Reasons for Geographic and Racial Differences in Stroke (REGARDS) study. The group of participants of African ancestry had a significantly higher prevalence of hypertension and diabetes, similar frequency of dyslipidaemia and lower prevalence of cardiac disorders than Americans of European descent. However, obesity and lifestyle factors, including smoking, alcohol consumption and physical inactivity, were more prevalent among African Americans and Americans of European descent than Indigenous Africans. These data illustrate the complex interaction between racial (genetic) and geographical (environmental, for example, lifestyle) factors in the neurobiology of stroke. Data from REF.<sup>70</sup>.



**Fig. 3 | A life course approach to factors driving stroke burden in Africa.** The population-level risk factors for stroke change across the lifespan. Here, we summarize the risk factors at each stage of the life course that are driving the increasing burden of stroke in Africa. We also highlight the molecular mechanisms and processes involved in stroke risk at each stage of life. HIV, human immunodeficiency virus.

treatment is a substantial economic load on the patient and their family. Poor health literacy can also contribute to a lack of control of vascular risk factors<sup>139,140</sup>. In the PURE study, which involved >150,000 participants from urban and rural settings around the world, <10% of participants from low-income countries with a previous cardiac or stroke event were on any of the four drugs indicated for secondary prevention, that is, angiotensin-converting enzyme inhibitors, beta blockers, statins or aspirin<sup>141</sup>. In a study performed in the Southwest region of Cameroon, essential cardiovascular disease medicines were only available in 25.3% of public pharmacies and 49.2% of community pharmacies<sup>136</sup>. Medicines for heart failure and dyslipidaemia, including beta blockers, angiotensin-converting enzyme inhibitors and statins, cost the equivalent of 2–13 days' wages for a 1-month supply.

### Stroke phenotypes in Africa

Information on the phenotypic characteristics of stroke types and subtypes in Africa was limited until evidence from the SIREN study became available in early 2018. In the initial data from this study, which recruited index stroke cases from 15 sites in Nigeria and Ghana, of 2,118 individuals with neuroradiologically confirmed stroke, 68% had ischaemic stroke, 32% had intracerebral haemorrhage (ICH) and <1% had ischaemic stroke with haemorrhagic transformation<sup>104</sup>. The SIREN investigators did not recruit participants with sub-arachnoid haemorrhage but it is estimated to contribute to ~5% of all strokes in Africa<sup>142</sup>.

### Ischaemic stroke

In Africa, the most common aetiological subtype of ischaemic stroke is small vessel disease (SVD) (42%), followed by large vessel atherosclerotic disease (17%), cardioembolism (11%) and undetermined (30%)<sup>70,104</sup>. In a meta-analysis of five different stroke studies involving a total of 2,843 participants with ischaemic stroke from both hospital and community-based cohorts in Ghana, Kenya, Nigeria, Mozambique, South Africa,

Sudan and Uganda, we found that SVD accounted for 30% of ischaemic strokes<sup>12</sup>. By contrast, SVD accounted for only 19% of ischaemic strokes from 13 different studies involving 12,931 patients from hospital and non-hospital or community-based cohorts in western Europe and the USA<sup>12</sup>. The preponderance of SVD and the relative paucity of cardioembolic strokes among Africans is similar to observations from other LMICs such as China<sup>143</sup> and Pakistan<sup>144</sup> but in contrast to data from high-income countries. Indeed, studies conducted in mixed ethnic populations in the USA<sup>145</sup> and the UK<sup>146</sup> strongly suggest that SVD is twice as common among participants of African descent than among participants of European descent. Participants of European descent were more likely than participants of African descent to have a cardioembolic or large-artery atherosclerotic stroke.

The above observations indicate that the relative frequencies of ischaemic stroke subtypes across the globe vary by race, geography and, perhaps, gross national income. Therefore, association studies on the genetics of ischaemic stroke among Indigenous Africans are eagerly awaited. However, it seems likely that the high burden of undiagnosed and uncontrolled asymptomatic risk factors (notably hypertension, dyslipidaemia and dysglycaemia) in sub-Saharan Africa is leading to arteriosclerosis and microatheroma formation in deep perforating cerebral vessels and thus causing SVD-related ischaemic strokes<sup>12</sup>. This hypothesis is consistent with the observation that, among Africans, hypertensive disease is more prevalent than atrial fibrillation or atherosclerotic disease (discussed above). Indeed, few studies have researched cervicocephalic atherosclerosis, a marker of epidemiological and stroke transition, among Africans<sup>147</sup>. Neurovascular ultrasonography detected no substantial carotid artery disease in the Tanzania Stroke Incidence Study<sup>148</sup>. However, a study in participants with hypertension and stroke in Nigeria found that carotid intima media thickness was a sensitive indicator of cardiovascular phenotype and had a stronger association with stroke than popular cardiovascular risk calculators



that are used to estimate the time-related risk of cardiovascular disease<sup>149,150</sup>. A more recent study of individuals diagnosed with acute stroke-like syndrome in Malawi reported that 39.4% had extracranial atherosclerosis and 19.2% had intracranial atherosclerosis<sup>151</sup>. Post-mortem studies undertaken ~40 years apart also identified a temporal increase in the frequency and severity of cerebral atherosclerosis among Nigerian Africans in tandem with the overall rise in the burden of cardiovascular disease and stroke occurrence<sup>152–154</sup>.

### **Intracerebral haemorrhage**

Further evidence of poor blood pressure control in sub-Saharan Africa has been gleaned from the aetiological profile of ICH. In the SIREN study, the aetiology of ICH was classified using the structural lesion, medication, amyloid angiopathy, systemic and/or other disease, hypertension, undetermined (SMASH-U) algorithm<sup>155</sup>. Using this method, the most common aetiology was hypertension (80.9%); less common were structural vascular anomalies (4.0%), cerebral amyloid angiopathy (0.7%), systemic illnesses (0.5%) and medication-related aetiologies (0.4%)<sup>156</sup>. Aetiology remained undetermined in 13.7% of participants. Of considerable interest is the observation that, among West Africans, ICH constitutes 53% of all strokes occurring among the young (<50 years of age)<sup>156</sup>. The six factors most associated with stroke in the young (who constituted 25% of the SIREN cohort) were hypertension, dyslipidaemia, diabetes mellitus, low consumption of green leafy vegetables, psychosocial stress and cardiac disease<sup>157</sup>. These further underscore the observation that hypertension is more strongly associated with ICH than ischaemic stroke<sup>103,104</sup> and thus emphasize that large numbers of strokes, particularly among young Africans, could be avoided by better blood pressure control. The PAR of stroke resulting from hypertension in the SIREN study was 88.7% among young West Africans<sup>157</sup>, again highlighting the importance of this vascular risk factor. Furthermore, in a recent cross-sectional study in Ghana, the frequency of refractory hypertension (a rare and severe phenotype of treatment-resistant hypertension) among ~1,200 survivors of stroke was 5.8% compared with 0.7% among ~2,800 stroke-free individuals with hypertension<sup>158</sup>. The prevalence of refractory hypertension was much higher in individuals <60 years of age than in individuals >60 years of age. The odds ratios of refractory hypertension were 13.6 for lacunar stroke, 11.4 for ICH and 3.7 for non-lacunar ischaemic strokes relative to stroke-free hypertension. This further suggests that the phenotypic characteristics of hypertension also exert differential effects on the manifestation of stroke types. Further studies are now required to elucidate the mechanisms underlying these differences and to guide the design of targeted population-level interventions and risk-reduction strategies.

### **Stroke complications and sequelae**

Stroke complications include a range of neurological, psychiatric or other systemic manifestations that occur in the acute, subacute or chronic phases of a stroke. Most data on stroke complications in Africa

come from hospital-based studies and suggest that some form of complication occurs in >80% of inpatients with stroke (TABLE 2). Stroke complications in Africa include delirium<sup>159–161</sup>, post-stroke aspiration pneumonia<sup>85,86,162–166</sup>, bacteriuria and urinary tract infection<sup>167–169</sup>, aphasia and deglutition disorders<sup>170</sup>, anxiety<sup>99,171–173</sup>, fatigue<sup>174–176</sup>, sexual dysfunction<sup>177–179</sup>, pain (central post-stroke pain syndrome)<sup>180–183</sup>, depressive illness<sup>184–193</sup> and cognitive impairment that often leads to dementia<sup>194–197</sup>.

On average, 40–50% of survivors of stroke in Africa develop some form of cognitive dysfunction<sup>194,196</sup>, suggesting that vascular cognitive impairment could become the most common precursor to dementia in Africa. Several hospital-based studies have investigated the prevalence of post-stroke seizures in Africa. The prevalence of early ( $\leq 7$  days of stroke onset) post-stroke seizures were 9.3%<sup>198</sup>, 9.6%<sup>199</sup> and 13%<sup>200</sup> in the three studies that recorded this data. The prevalence of epilepsy among survivors of stroke in Africa was 1.98–16.9%<sup>201–204</sup> (TABLE 3). Factors associated with an increased risk of post-stroke epilepsy included male sex, cortical infarcts and poor access to neurological services. However, the results of these studies need to be interpreted in the context of variation in study methods and case definition and the potential inaccuracy of patient reports owing to the cultural stigma around epilepsy in Africa.

In several studies, the functional outcomes in patients with stroke in Africa were carefully monitored using established scales<sup>43,50,205–214</sup> (TABLE 4). The results of these studies suggest that there is a substantial post-stroke disease burden that needs attention. Evidence from the few available studies in Africa suggests that survivors of stroke are likely to return to work after the first year<sup>215,216</sup>. Shorter post-stroke duration, lower functional independence and worse post-stroke cognitive dysfunction were associated with a lower likelihood of a return to work.

### **Genetics of stroke in Africa**

Evidence indicates that, compared with populations of European descent, stroke in the Indigenous African population has an earlier age of onset and is more likely to be haemorrhagic or SVD-related ischaemic<sup>4,23,70,102</sup>. Differences in stroke severity and outcomes have also been observed between Indigenous Africans and populations of European descent. Broad differences in the demographic structures of the African population and populations in Europe and the USA as well as differences in the availability of health services offer plausible explanations for these disparities<sup>217</sup>. Nevertheless, a possible role of genetic and/or epigenetic factors warrants further exploration<sup>23,24</sup>. For example, differences between chronological age and biological age (which is determined on the basis of epigenetic changes) have been documented among individuals of European ancestry with stroke<sup>218</sup> and whether a similar phenomenon occurs among African individuals needs to be explored<sup>219</sup>. Higher stroke heritability among individuals of African ancestry than among individuals of European ancestry has been reported in the South London Stroke Registry<sup>220</sup> but the exact effect of this heritability requires in-depth studies in Indigenous African populations.

Table 2 | **Stroke complications and sequelae in Africa**

Post-stroke complication	Features	Reported prevalence (%) <sup>a</sup>	Predictors	Countries	Refs
Delirium	Onset 1 week after stroke; confusional states	32–33	Age, NIHSS score	Nigeria	159–161
Aspiration pneumonia	Cause of death after stroke	64–79	Age, stroke severity, consciousness	Benin, Burkina Faso, Ethiopia, Mozambique, Tanzania	85,86, 162–166
Bacteriuria and urinary tract infection	Defined as >10 <sup>5</sup> CFU/ml	9.3–12.3	Infections	Ghana, Nigeria	167–169
Aphasia and deglutition disorders	Aphasia can last for up to 60 months after stroke	~50	Age, left-hemispheric stroke, cognitive impairment	Tanzania	170
Anxiety	Accumulative over 12 months	10–34	Female sex, low socioeconomic status, haemorrhagic lesions, depression	Nigeria, Tanzania	99,171–173
Fatigue	Peak at 6 months after stroke	60	Poor quality of life	Ghana, Nigeria	174–176
Sexual dysfunction	Most common: erectile dysfunction and low libido	>80	Age, male sex	Nigeria	177–179
Pain	Usually musculoskeletal pain or central post-stroke pain syndrome	5–80	Background history of pain, differential thresholds, age at stroke onset	Nigeria, Zimbabwe	180–183
Depression	Most common: mood disorders, suicidality and tedium vitae	16–80; median 30	Age	Democratic Republic of Congo, Gabon, Ghana, Nigeria	184–193
Cognitive impairment	Vascular cognitive impairment, dementia	30–50	Age, low literacy, vascular risk factors, Black race, recent infection, MTLA, WMH	Ghana, Nigeria, South Africa	194–197

On the basis of data from hospital-based studies. For details on post-stroke epilepsy and functional disability, see TABLES 3 and 4. CFU, colony-forming unit; MTLA, medial temporal lobe atrophy; NIHSS, National Institutes of Health Stroke Scale; WMH, white matter hyperintensities. <sup>a</sup>Percentage of individuals with stroke who go on to develop these complications.

### Genomic diversity in Africa

Africa is regarded as the cradle of modern humans, *Homo sapiens*, and African genomes are more diverse than those from any other continent<sup>221–223</sup>; however, only a fraction of the genetic diversity among African individuals has been surveyed — to date, <2% of GWAS were performed on African data<sup>224</sup>. In a high-depth study of African genomes, whole-genome sequencing was performed on samples from 426 individuals from 50 ethnolinguistic groups; the genetic makeup of many of these groups had not been previously studied<sup>225</sup>. The results of this study, published in 2020, identified more than 3 million previously undescribed genetic variants. The implications of the identification of these variants for our understanding of the genetics of the stroke phenotype are immense and are relevant to both Africans and the global population<sup>25,226</sup>. In particular, the Human Heredity and Health in Africa Initiative<sup>222</sup> is facilitating the genetic exploration of African populations, including the SIREN study cohort, by use of approaches including candidate gene studies and GWAS<sup>23,24</sup>. The overall aim is that inclusion of Indigenous Africans in multi-ethnic genomic studies, combined with the use of trans-omics approaches, will facilitate genetic fine mapping, trans-ancestry meta-analysis and development of

ancestry-sensitive polygenic risk scores as well as the discovery of new risk loci, pathophysiological pathways, biomarkers and drug targets for the enhancement of precision stroke medicine<sup>24,25,226,227</sup>.

### Candidate gene studies and GWAS

To date, the majority of genetic studies of stroke in Africa have adopted a candidate gene approach (TABLE 5). Candidate gene studies and GWAS are two methods that are used to detect genetic susceptibility to diseases. The main difference between the two approaches is that candidate gene studies investigate genetic variation within a small number of pre-identified genes of interest, whereas in GWAS, the entire genome is investigated for common genetic variations that are associated with the disease of interest. In northern Africa, candidate gene studies have reported associations between stroke, particularly ischaemic stroke, and polymorphisms in multiple genes, including those encoding apolipoprotein E (*APOE*), IL-1, IL-1 $\beta$ , peroxisome proliferator-activated receptor- $\delta$  (*PPARD*), apolipoprotein A5 (*APOA5*) and aldosterone synthase (*CYP11B2*)<sup>228–242</sup>. In addition, a polymorphism in the gene encoding angiotensinogen (*AGT*) was associated with stroke in an Egyptian cohort consisting of adolescents with SCD<sup>243</sup>. A candidate gene study performed

in Zambia identified an association between *APOEε2/ε4* genotype and an increased risk of both haemorrhagic and ischaemic stroke<sup>244</sup>. Findings from the West African SIREN study included a significant association of variants on *IL6* and *CDKN2A/2B* with risk of ischaemic stroke among men<sup>134</sup> as well as a significant association of variants on *APOLI*, *CDKN2A/2B* and *HDAC9* with risk of SVD ischaemic stroke<sup>245</sup>. This study was the first to identify a stroke-related variant on *APOLI*, although the gene had previously been associated with chronic kidney disease in individuals of African descent<sup>246,247</sup>. A particularly intriguing observation is that, whereas *APOE* alleles influenced the risk of stroke in northern and southern Africa, an *APOLI* risk variant was associated with stroke in western sub-Saharan Africa. Further studies are needed to explore the potential geographical disparity in the effect of these two prominent apolipoprotein genes; the results of such studies could also be relevant to other brain disorders such as Alzheimer disease. The first stroke GWAS in Africa is currently under way and is anticipated to provide further insight into the genetic architecture of stroke in Indigenous Africans by identifying novel stroke-associated variants.

### Stroke services in Africa

Stroke services are organized systems and structures for delivering preventive, therapeutic and rehabilitative stroke care at an institutional, regional or national level. The World Bank's *Disease Control Priorities 3rd edition*<sup>248</sup> identified five major platforms for the provision of essential universal health coverage in LMICs: population-level platforms, community-level platforms, health centres, first-level hospitals and referral hospitals. These platforms provide a model for building chains of stroke care that can be divided into three categories: pre-hospital, hospital and post-hospital services. Pre-hospital stroke services consist of elemental and primary prevention policies, surveillance, pre-hospital emergency care, and outreach and awareness services. Hospital-based stroke services include emergency medical services, acute stroke treatments, secondary prevention and acute rehabilitation. Post-hospital stroke services consist of community rehabilitation, social and family support, and follow-up.

### Population-based services

Stroke shares a common risk-factor profile with many cardiovascular diseases; thus, population-based approaches to stroke prevention in Africa have conventionally focused on non-communicable diseases as a whole. In 2015, non-communicable diseases were

incorporated into the United Nations Sustainable Development Goals: target 3.4 is "By 2030, to reduce by one third premature mortality from non-communicable diseases through prevention and treatment and to promote mental health and well-being"<sup>249</sup>. However, progress reports from Africa published in 2017–2020 suggest low levels of progress towards this target as a result of a lack of political will, poor intersectoral collaboration, absence of universal health coverage, widespread poverty, the challenges involved in making changes to existing health systems and low levels of public spending on health<sup>250–252</sup>. The joint World Stroke Organization (WSO)–WHO–*Lancet Neurology* Commission for Stroke is advocating pragmatic, context-sensitive approaches that involve multiple stakeholders, including healthcare providers, physicians, patients, the general population, policy-makers and payers, with the aim of identifying solutions that will enhance stroke prevention and surveillance services across a range of income levels<sup>253</sup>.

### Pre-hospital acute stroke care

Pre-hospital acute stroke services conventionally function within existing emergency medical services, although they can also be standalone services. Emergency medical services are poorly developed in Africa, except in some areas in South Africa and northern Africa that have a relatively higher income. In a recent survey, established emergency medical services were identified in only 16 African countries; most of the identified services were government operated, had fee-for-service payment structures and poor uptake<sup>254</sup>. Organizations such as the African Federation of Emergency Medicine have developed processes and guidelines for emergency medicine training in Africa, raising hopes of improving access to quality and effective emergency care; however, organizational, fiscal and regulatory challenges remain<sup>255,256</sup>. Few studies have examined the specific factors responsible for pre-hospital delays in stroke presentation in Africa; however, the available evidence suggests that poor stroke knowledge is a major cause of pre-hospital delays in presentation and poor outcomes<sup>257</sup>. Other contributing factors include stroke onset during normal sleeping hours, transportation-related delays, poor availability or a lack of ambulance services, absence of trained first responders and a paucity of neuroimaging services<sup>88,258–260</sup>. Evidence from a 2015 geospatial analytic study indicated that, for 71% of Africans, travel time to the nearest hospital is >2 hours<sup>261</sup>, highlighting a dire need for broad intersectoral strategies to improve access to healthcare.

Table 3 | Estimated prevalence of post-stroke epilepsy in Africa

Country	Year	Study type	Sample size	Diagnostic criteria	Prevalence (%) <sup>a</sup>	Ref.
Burkina Faso	2006–2014	Hospital based; retrospective	1,616	Clinical, EEG, brain CT	1.98	201
Sudan	2006–2008	Hospital based	165	Clinical, eye-witness reports, EEG, brain CT	16.90	202
Benin	2015–2016	Hospital based; retrospective	1,703	Clinical, EEG, brain CT	2.00	203
Ghana	2018–2020	Hospital based; cross-sectional	1,101	Clinical, brain CT, EEG	11.40	204

<sup>a</sup>Percentage of individuals with stroke who go on to develop post-stroke epilepsy.

Table 4 | Estimated frequency of functional disability after stroke in Africa

Country (City)	Year	Type of study	Study population	Sample size	Tools used	Percentage with disability	Ref.
Gambia (Banjul)	1990–1991	Hospital	Not stated	106	Barthel Index	91.5 at 1 month after stroke	205
Tanzania (Hai)	1994	Community and census	85,152 (aged >15 years)	108	Barthel Index	60	43
South Africa (Cape Town)	2004–2006	Hospital	4,524,335	196	MRS, Barthel Index	48 (moderate to severe disability)	206
Benin (Cotonou)	2009	Community	69,869	14,969	MRS, FIM, MADRS	60	50
South Africa (Johannesburg)	Not known	Hospital and community	Not stated	68	Barthel Index	47 at discharge; 93 at 6 weeks after discharge	207
South Africa (Cape Town)	2010	Hospital	Not stated	67	Barthel Index	81.82 at discharge	208
Nigeria (Ibadan)	2013	Hospital	Not stated	128	MRS	60.9	209
Benin (Parakou)	2013	Hospital	Not stated	85	MRS	53 at 1 month after stroke	210
Nigeria (Benin)	Not known	Hospital and outpatient	Not stated	102	MRS	71.6	211
Uganda (Kampala)	2014	Hospital	Not stated	127	Barthel Index	46.1 at 1 month after stroke	212
Egypt (Cairo)	2015–2016	Hospital	Not stated	397	MRS	18	213
Egypt (Cairo)	2018–2019	Hospital	Not stated	61 (posterior circulation stroke)	MRS	72.13 at 3 months after stroke	214

FIM, functional independence measure; MADRS, Montgomery–Asberg depression rating scale; MRS, modified Rankin score.

Onset-to-door or onset-to-needle time is often used as an indicator of timeliness of stroke triage and efficiency of acute reperfusion therapy. Evidence from the European Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS MOST) and Safe Implementation of Treatments in Stroke–Eastern Europe (SITS EAST)<sup>262</sup> study indicates a median onset-to-door time of 140 minutes. Similarly, data from the American Get With The Guidelines – Stroke registry (GWTG-Stroke)<sup>263</sup> indicate a median onset-to-door time of 144 minutes. Indeed, the paradigm of acute stroke care in high-income countries currently emphasizes ultra-early pre-hospital stroke diagnosis, treatment using mobile stroke units and telemedicine for stroke assessments<sup>264,265</sup>. By contrast, a systematic review of studies from Africa found a median time from stroke onset to hospital admission of 31 hours<sup>266</sup>. In a single hospital study from Burkina Faso, median stroke onset to hospital admission time was ~7 hours but only 19% of patients presented within 4.5 hours of stroke onset and were thus eligible for thrombolysis<sup>267</sup>.

#### Hospital-based acute stroke care

The profile, pattern and quality of hospital-based acute stroke care in Africa is heterogeneous. Services for stroke often exist as part of general medical services, although stroke units have now been reported in at least ten countries, including Morocco, Tunisia, Algeria, Egypt, Mauritania, Ghana, Nigeria, Guinea, Central African Republic and South Africa<sup>3,268,269</sup>. In addition, acute stroke services do exist in private hospitals in some parts of Africa.

The WSO has produced the global stroke services guidelines and action plan<sup>270</sup> as a framework to guide the development of stroke services around the world. The framework proposes three tiers of stroke services (minimal, essential and advanced), depending on the availability of multidisciplinary expertise, diagnostic infrastructure and capacity for acute reperfusion therapy. The applicability and effectiveness of this framework in low-resource African settings were recently demonstrated in Conakry, Guinea, where a minimal stroke unit was set up. This unit consisted of a dedicated space equipped with three acute beds, heart rate, blood pressure and blood oxygen saturation monitoring equipment, and a portable oxygen concentrator. Patient outcomes 1 year after establishment of the unit were better than patient outcomes 1 year before the unit was established; introduction of the stroke unit was associated with lower mortality (7.2 versus 22.3%;  $P < 0.0001$ ), fewer medical complications (4.1 versus 27.7%;  $P < 0.001$ ) and a lower rate of pneumonia (3.3 versus 14.5%;  $P < 0.001$ )<sup>268</sup>.

Similarly, the introduction of multidisciplinary stroke care in a South African secondary-level hospital was associated with a substantial reduction in in-hospital mortality and improved uptake of neuroimaging<sup>271</sup>. Neuroimaging services (CT or MRI) are essential for the accurate diagnosis of stroke but the availability, accessibility and affordability of these services are limited in many African settings<sup>88,259,260</sup>. The SIREN Study Team developed a novel computer software application — the AIM on ClearCanvas Enriched Stroke phenotyping Software (ACCESS) — that enables the creation of

simple, standardized annotations for the reporting of brain images of all stroke types. The software enabled concordant and reproducible classification of stroke subtypes by multiple investigators, making it suitable for routine clinical use and multicentre research<sup>272</sup>.

The availability of and access to acute reperfusion therapies in Africa are currently limited but growing. These therapies are now available in Morocco, Tunisia, Algeria, Egypt, Central African Republic and South Africa<sup>88,269,273–276</sup>. Barriers to access include all causes of late hospital presentation, diagnostic delays, the high cost of thrombolytic agents and insufficient numbers of clinicians with the appropriate skills<sup>88,275,277,278</sup>.

Early reports from the countries listed above have consistently shown that intravenous thrombolysis is associated with improved patient outcomes<sup>269,273,274,276</sup>. Door-to-needle times were between 54 and 160 minutes and ≤5% of patients developed spontaneous ICH complications<sup>269,273,276</sup>. Two prospective observational studies conducted at the Ain Shams University hospitals in Egypt reported remarkable success in overcoming barriers to thrombolysis. Implementation of a comprehensive action plan — including government funding of alteplase (tPA) treatment and the introduction of needs-based training programmes for stroke care nurses, doctors and emergency physicians — was associated

Table 5 | Stroke candidate gene studies in Africa

Study	Gene name	Study population	Salient findings
Saidi et al. (2007) <sup>234</sup>	Plasminogen activator inhibitor 1 ( <i>PAI1</i> ); tissue plasminogen activator ( <i>tPA</i> )	Tunisian	<i>PAI1</i> 4G/5G polymorphism associated with increased <i>PAI1</i> expression, decreased <i>tPA</i> expression and increased risk of stroke
Saidi et al. (2007) <sup>233</sup>	Apolipoprotein E ( <i>APOE</i> )	Tunisian	<i>APOE</i> $\epsilon 4$ associated with increased risk of ischaemic stroke, small vessel disease and statin use
Saidi et al. (2008) <sup>230</sup>	Human platelet alloantigen 1–5 ( <i>HPA1–5</i> )	Tunisian	Lower <i>HPA1a</i> frequency and higher <i>HPA1b</i> frequency in the stroke group than in controls
Saidi et al. (2008) <sup>229</sup>	<i>HPA1–5</i>	Tunisian	<i>HPA1a/b</i> and <i>HPA5a/b</i> alleles associated with increased risk of stroke; <i>HPA1b/b</i> and <i>HPA5b/b</i> associated with extent of symptoms and risk of recurrence
Saidi et al. (2009) <sup>235</sup>	<i>APOE</i> ; angiotensin-converting enzyme ( <i>ACE</i> )	Tunisian	Higher <i>APOE</i> $\epsilon 4$ frequency and lower <i>APOE</i> $\epsilon 3$ frequency in the stroke group than in controls; <i>APOE</i> $\epsilon 4$ <i>ACE</i> <i>Del/Del</i> genotype was associated with large vessel stroke and was detected in higher proportions in older (>50 years) patients
Saidi et al. (2009) <sup>231</sup>	Angiotensinogen ( <i>AGT</i> )	Tunisian	Multiple <i>AGT</i> polymorphisms were significantly associated with an increased risk of stroke
Saidi et al. (2010) <sup>228</sup>	Aldosterone synthase ( <i>CYP11B2</i> )	Tunisian	<i>CYP11B2</i> C-344T polymorphisms (T allele bearing) were associated with risk of ischaemic stroke
Chehaibi et al. (2013) <sup>236</sup>	Peroxisome proliferator-activated receptor- $\delta$ ( <i>PPARD</i> )	Tunisian	<i>PPARD</i> +294T/C polymorphism was associated with increased risk of ischaemic stroke
Fekih-Mrissa et al. (2013) <sup>238</sup>	Methylenetetrahydrofolate reductase ( <i>MTHFR</i> )	Tunisian	<i>MTHFR</i> C677T and A1298 polymorphisms were associated with an increased risk of ischaemic stroke
Atadzhanov et al. (2013) <sup>244</sup>	<i>APOE</i>	Zambian	<i>APOE</i> $\epsilon 2/\epsilon 4$ genotype associated with increased risk for both haemorrhagic stroke and ischaemic stroke
Chehaibi et al. (2014) <sup>237</sup>	Matrix metalloproteinase 1 ( <i>MMP1</i> ) and <i>MMP12</i>	Tunisian	<i>MMP12</i> polymorphisms were associated with an increased risk of ischaemic stroke in individuals with diabetes
Diakite et al. (2015) <sup>239</sup>	C2491T	Moroccan	C2491T <i>FV</i> mutation was associated with risk of ischaemic stroke
Diakite et al. (2014) <sup>241</sup>	<i>eNOS</i>	Moroccan	<i>eNOS</i> G894T polymorphism was associated with risk of ischaemic stroke
Rezk et al. (2015) <sup>242</sup>	<i>IL-1</i> cluster genes: <i>IL1B</i> , <i>IL1A</i> and <i>IL1RN</i>	Egyptian	<i>IL1B</i> –511 and <i>IL1A</i> –889 polymorphisms were associated with increased risk of acute stroke
Diakite et al. (2016) <sup>240</sup>	<i>APOA5</i> ; arachidonate 5-lipoxygenase-activating protein ( <i>ALOX5AP</i> )	Moroccan	<i>APOA5</i> T1131C and <i>ALOX5AP</i> SG13S114 polymorphisms were associated with risk of ischaemic stroke
Akinyemi et al. (2017) <sup>134</sup>	<i>IL6</i> ; cyclin-dependent kinase inhibitor 2A/2B ( <i>CDKN2A/2B</i> )	West African (Nigeria and Ghana)	<i>IL6</i> rs1800796 and <i>CDKN2A/2B</i> rs2383207 are associated with risk of ischaemic stroke in men
Akinyemi et al. (2018) <sup>245</sup>	Apolipoprotein 1 ( <i>APOL1</i> ); <i>CDKN2A/2B</i> ; histone deacetylase 9 ( <i>HDAC9</i> )	West African (Nigeria and Ghana)	<i>APOL1</i> rs73885319, <i>CDKN2A/2B</i> rs2383207 and <i>HDAC9</i> rs2107595 are associated with risk of small vessel disease ischaemic stroke



with an increase in the proportion of patients eligible for intravenous thrombolysis from 13.2% to 94.3%<sup>276</sup>.

Strong leadership, improved governmental funding, enhanced stroke awareness, training and partnerships have been reported as factors that have remarkably transformed acute stroke care in the northern African and Middle East region<sup>269,279</sup>. Over a 5-year period, the region recorded a dramatic increase in the number of stroke units, multidisciplinary stroke specialists and centres with capacity for acute reperfusion therapy<sup>279</sup>. Widespread uptake of the Safe Implementation of Treatments in Stroke (SITS) registry and partnership with the Angels Initiative of the European Stroke Organization has resulted in a remarkable transformation of the acute stroke care landscape in North Africa<sup>269</sup>. The lessons from this impressive success story can be deployed and adapted across other African regions.

### **Stroke rehabilitation services**

Stroke rehabilitation is an important component of stroke care. However, the layout, referral pathways, extent of integration into stroke units or stroke multidisciplinary teams, and the time spent on rehabilitation varies widely across Africa. Ideally, stroke rehabilitation should start as soon as possible after a stroke, preferably within a stroke unit, with the aim of achieving early mobilization in order to reduce complications. However, studies of rehabilitation in African stroke units are scarce. Furthermore, the numbers of stroke rehabilitation professionals, including physiotherapists, occupational therapists, and speech and language therapists, seem to be insufficient<sup>280</sup>. In 2017, the WHO launched 'Rehabilitation 2030: a call for action'<sup>281</sup>, which highlights the need for all countries to scale up rehabilitation services and support the use of health information systems to improve patient follow-up for rehabilitation both within hospitals and in the community.

Daily experience from our stroke care practice in Africa suggests that rehabilitation commonly begins soon after admission and is usually supervised by physiotherapists, who are supported by occupational therapists, speech therapists and social workers. Stroke rehabilitation in Africa often occurs in the general medical setting and is provided by professionals who also see patients with other conditions. A review published in 2020 identified poor physician knowledge of the role of rehabilitation, lack of rehabilitation components in the standard of care, long interval from stroke onset to rehabilitation, short duration of rehabilitation and poor financial support of rehabilitation services as inherent problems in the rehabilitation landscape in Africa<sup>280</sup>. Given these challenges, the responsibility of post-discharge rehabilitative care of patients with stroke falls on family members and caregivers. Task shifting and tele-health approaches have been suggested as strategies to mitigate the current scarcity of rehabilitation personnel and improve access to stroke rehabilitation in Africa<sup>281–283</sup>. A study of family-led rehabilitation after stroke (the ATTEND trial) was performed in India and this option could also be explored in Africa<sup>277,284</sup>. In a prospective, single-arm, pre–post study, 20 survivors of stroke recruited from a tertiary medical centre

in Ghana received a smartphone with the 9zest Stroke Rehabilitation Therapy app (9zest) to deliver an individualized, goal-targeted exercise programme 5 days a week. Rehabilitation was remotely supervised by a tele-therapist for 12 weeks. The study demonstrated the feasibility of administering a mobile health-delivered physical therapy intervention in sub-Saharan Africa, with high user satisfaction<sup>285</sup>. Ongoing studies include the MAMBO (Measuring Ambulation, Motor, and Behavioural Outcomes with post-stroke fluoxetine in Tanzania), which aims to determine the safety and efficacy of fluoxetine among Africans with acute stroke and to establish whether the treatment is associated with any improvement in motor outcomes<sup>286</sup>.

### **Stroke support and community outreach**

Stroke support and community outreach can be achieved through direct and indirect services. In Africa, direct stroke support and community outreach are primarily offered by non-governmental organizations (NGOs) or agencies. National departments of health are yet to invest sufficiently in the detection, treatment and care of non-communicable diseases (including strokes). NGOs face funding challenges that affect their capacity to support patients with stroke and their families. Although stroke support services and community outreach seem to have attained some visibility across Africa as a whole within the past decade, in large parts of the continent, these services do not meet the criteria for universal health coverage. The type of stroke support available varies across Africa. Direct services can include home-based care, patient-focused groups and some form of rehabilitation. Indirect services can include telephone support, including emotional support, for the patient with stroke and concerned family members. In addition, many NGOs conduct community-based health-risk assessments to identify individuals with a level of cumulative risk that qualifies them for referral to medical facilities. Hypertension, in particular, is the focus of many stroke-prevention community outreach programmes<sup>108</sup>.

### **Stroke knowledge and perception**

A number of quantitative surveys and qualitative studies have explored stroke knowledge and perception among diverse groups of people in Africa and have revealed largely suboptimal awareness and perceptions that are influenced by religious and cultural beliefs<sup>287–289</sup>. Therefore, community leaders and leaders of faith-based organizations have a vital role in disseminating stroke knowledge across Africa. The percentage of participants who did not recognize the brain as the organ in which stroke occurs varied between 16.9% in a sample of hospital workers and 85.9% in another sample of urban dwellers<sup>287,289,290</sup>. Hypertension and stress were most commonly identified as stroke risk factors and educational attainment was the most common determinant of stroke knowledge<sup>287,291</sup>. Among non-neurologist health workers<sup>292</sup> and adolescent students<sup>293</sup>, stroke-based educational interventions were associated with substantial improvement in stroke literacy. We have also previously shown the feasibility of an educational mobile phone

short messaging service (SMS) including information on stroke for the control of blood pressure among West African survivors of stroke<sup>294,295</sup>. Across multiple sites in Nigeria and Ghana, treatment choices were found to be influenced by beliefs about stroke causation, and the development of culturally sensitive and acceptable community-based educational interventions was necessary for the reduction of stroke burden<sup>291</sup>.

**Expert-consensus practice guidelines**

High-quality, pragmatic guidelines for the management of stroke risk factors and treatment of stroke in LMICs, including Africa, are lacking. The implementation of contextually appropriate, evidence-based, expert-recommended stroke prevention guidelines is particularly important in LMICs. A systematic review of 22 published stroke prevention guidelines found 8 from LMICs (36%) and 14 from high-income countries (64%) but only 1 from Africa (South Africa)<sup>296</sup>. LMIC-issued guidelines were less likely to provide clear recommendations (62% versus 100%;  $P=0.03$ ), utilize high-quality systematic reviews (21% versus 79%;  $P=0.006$ ), engage in good dissemination avenues (12% versus 71%;  $P=0.02$ ) or invite input from an external reviewer (12% versus 57%;  $P=0.07$ )<sup>296</sup>. Thus, the quality and quantity of expert consensus stroke management guidelines in Africa clearly need to improve.

**Clinical trials**

Increasing numbers of stroke-related clinical trials are being performed in Africa<sup>295,297–301</sup> (FIG. 4). The dominant effect of hypertension among African survivors of stroke

means that evidence-based interventions to control this risk factor are an important area of research. The first randomized controlled trials of hypertension control among survivors of stroke in Africa involved multi-modal interventions that aimed to address barriers to hypertension control at the level of the patient, provider and practice. For example, the Phone-based Interventions under Nurse Guidance after Stroke (PINGS) study in Ghana assessed the feasibility and preliminary efficacy of a domiciliary blood pressure-monitoring intervention that was mobile health technology-based and nurse led<sup>295,302</sup>. A cohort of 60 recent survivors of stroke took part in the trial, which had a cluster randomized controlled design; 30 participants received the intervention and 30 participants received usual care using a cluster randomized controlled trial design. The intervention lasted for 3 months and participants were followed-up for a further 3 months. The results indicated that the intervention is feasible and identified a possible efficacy signal in terms of blood pressure control. Specifically, an intention-to-treat analysis found that, at month 3, 67% of participants in the intervention group had systolic blood pressure of <140 mmHg compared with just 47% of participants in the control group ( $P=0.12$ ). At month 9, 73% of participants in the intervention group had systolic blood pressure of <140 mmHg compared with 43% of the participants in the control group ( $P=0.035$ ). Furthermore, medication possession ratio scores (measure of medication adherence) at month 3 and month 9 were higher in the intervention group than in the control group.

The Tailored Hospital-based Risk reduction to Impede Vascular Events after Stroke (THRIVES) study

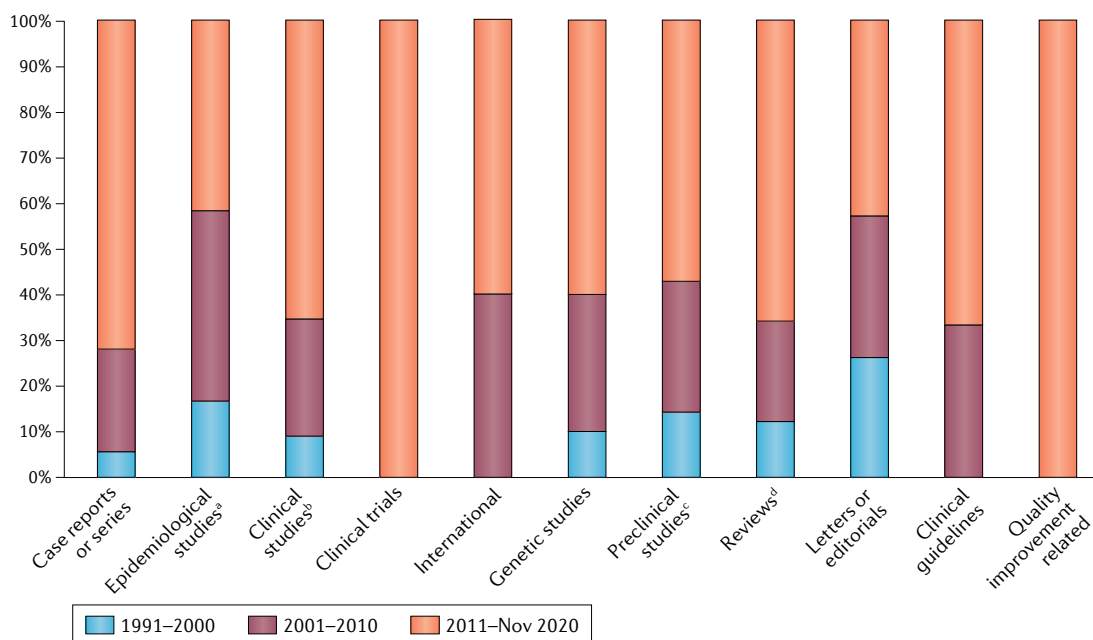


Fig. 4 | **Studies on stroke in Africa.** Here, we summarize the published literature on stroke in Africa, from 1999 to November 2020, and including 107 case reports or series, 29 epidemiological studies, 562 clinical studies, 5 clinical trials, 4 international studies, 30 genetic studies, 21 preclinical studies, 136 reviews, 52 letters or editorials, 6 clinical guidelines and 4 quality improvement-related publications. <sup>a</sup>Includes community-based prevalence and incidence studies on stroke in Africa. <sup>b</sup>Includes hospital-based studies, whether of observational or interventional, retrospective or prospective, longitudinal or case-control designs. <sup>c</sup>Refers to studies that report the testing of a drug, procedure or other medical treatment in animals, where the disease of interest in the study was a stroke. <sup>d</sup>Includes narrative reviews, scoping reviews, systematic reviews and meta-analyses.

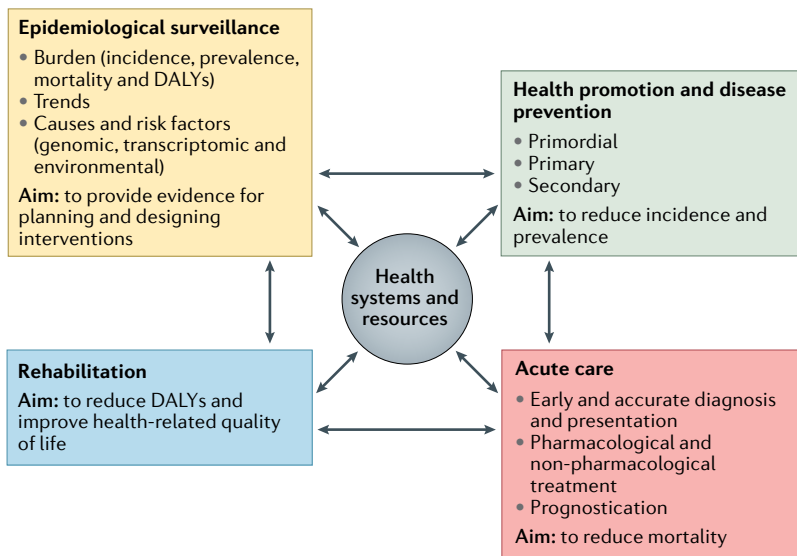


Fig. 5 | **The stroke quadrangle.** The four pillars of the stroke quadrangle are surveillance, prevention, acute care and rehabilitation. Together, these pillars can lead to the reduction of stroke incidence, prevalence, disability and mortality. DALYs, disability-adjusted life years.

in Nigeria was much larger than the PINGS study and randomized 400 survivors of stroke to two treatment groups. One group received usual care and the other received a bundled intervention that included patient report cards, phone text messaging, an educational video and co-ordination of post-hospitalization care<sup>303</sup>.

Table 6 | **Stroke care in Africa: challenges and solutions**

Aspect of stroke care	Challenges	Pragmatic solutions
Surveillance	Valid, reliable data on stroke incidence, prevalence, mortality and disability in Africa are extremely limited; no surveillance system is in place to track trends in the burden of stroke at continental, regional and country levels	Establish stroke surveillance systems to measure and monitor the burden of stroke
Prevention	No robust systems for detection and control of major stroke risk factors such as hypertension, diabetes mellitus and dyslipidaemia; high rates (93%) of uncontrolled hypertension	Increase awareness, screening and control of hypertension, dyslipidaemia, diabetes mellitus and other major stroke risk factors at the primary health-care level in synergy with programmes for NCDs; implement sensitization programme to involve the entire population across the lifespan
Acute care	Scarcity of high-quality hyperacute and acute care services; very low rates of thrombolysis and thrombectomy; few multidisciplinary stroke units	Synergistic action by all stakeholders, including pharmaceutical companies and stroke experts, to improve the availability of services and increase the number of stroke units
Rehabilitation	Few multidisciplinary stroke rehabilitation centres	Increase the number of centres and settings that offer multidisciplinary care; promote recovery and re-integration

NCDs, non-communicable diseases.

After 12 months of administration, systolic blood pressure in the group of participants receiving the THRIVES was not significantly lower than in the group of participants receiving usual care. However, in a sub-group of participants with uncontrolled blood pressure, both usual care and the THRIVES intervention were associated with a reduction in blood pressure, in both arms, compared with the pre-treatment baseline<sup>294</sup>. An ongoing secondary prevention trial — the Stroke Minimization through Additive Anti-atherosclerotic Agents in Routine Treatment (SMAART) trial — is a phase II, open-label, evaluator-blinded trial involving 120 participants from Ghana who have recently survived a stroke. Participants were randomly allocated in a 1:1 ratio to either receive the intervention or usual care. Participants in the intervention arm receive a polypill (Polycap DS, Cadila Pharmaceuticals) that contains 100 mg aspirin, 50 mg atenolol, 5 mg ramipril, 12.5 mg thiazide and 20 mg simvastatin per capsule and taken as two capsules once daily. Participants in the usual care group will receive separate, individual secondary preventive medications prescribed at the physician's discretion. Both groups will be followed for 12 months to assess changes in carotid intima media thickness regression<sup>300,301</sup> and results are expected in late 2021. PINGS-2 is a randomized controlled trial of a theoretical model-based, mobile health technology-centred, nurse-led, multi-level integrated approach to improve longer-term blood pressure control. The trial includes 500 patients who have recently had a stroke recruited from 10 hospitals in Ghana and is currently ongoing<sup>304</sup>.

Evidence for an association between prevalence of tobacco smoking and prevalence and incidence of stroke in Africa is lacking. However, overall epidemiological trends of cardiovascular disease can be used as a proxy for the burden of stroke. For example, in South Africa, despite the use of tobacco taxation measures to discourage smoking, cardiovascular disease is still one of the highest sources of non-communicable disease burden. Although selected countries in Africa are using such fiscal measures to reduce tobacco use, large-scale multi-pronged efforts that include behavioural interventions to reduce the burden of tobacco smoking are lacking. The reality in Africa is that there are well-known inequalities and inefficiencies, both among and within countries, that make it difficult to follow through on the WHO's framework for tobacco control<sup>305</sup>.

**Biobanking and precision stroke medicine**

The stroke research landscape in Africa has witnessed progress and diversification in the past decade. The increasing burden and poor outcomes of stroke on the African continent require an aggressive research agenda to identify, characterize and confront risk factors and to implement evidence-based strategies. Indeed, basic, clinical, translational and health systems research are required to reduce the burden of stroke. In particular, precision medicine-focused trans-omics stroke research approaches are gaining increasing attention while not abandoning the traditional public health-driven approaches<sup>25,306,307</sup>.

The past decade heralded an explosion of genomic research and biobanking in Africa, largely driven by

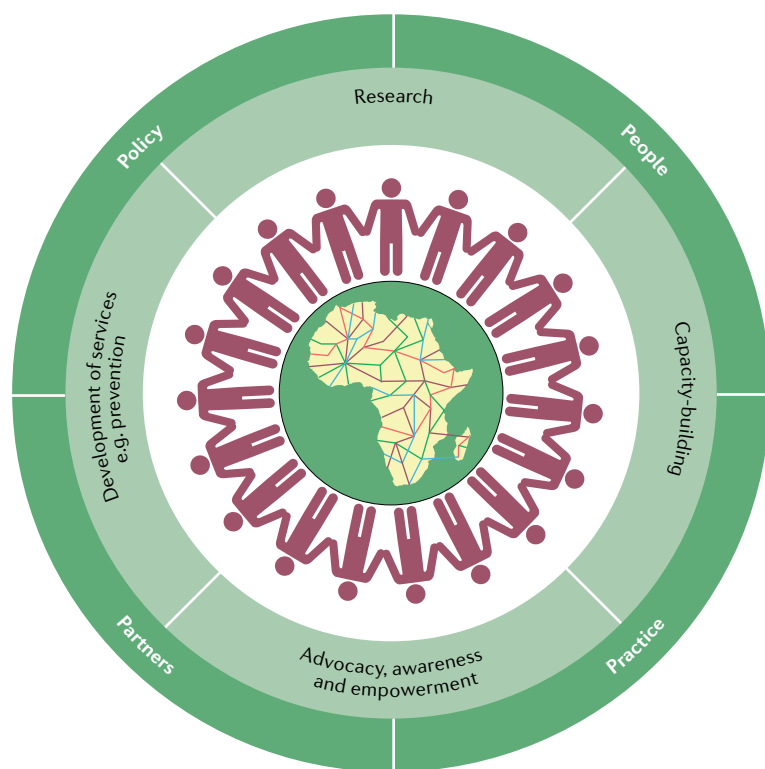
funds provided by the Wellcome Trust and the NIH. The NIH-funded SIREN study is exploring the genetic architecture of stroke among Indigenous Africans. More than 4,000 case-control pairs have already been recruited to the study and several publications on stroke phenomics and preliminary candidate gene analyses have been generated. The SIREN study has also undertaken the first-ever GWAS to unravel the genetic architecture of stroke in Indigenous Africans and the results are eagerly awaited. Stroke neurobanking resources consisting of blood fractions, extracted DNA, neuroimages and databases of clinical information are also being built in Africa and could facilitate data science-driven trans-omics research (including epigenomics, transcriptomics, proteomics and metabolomics) as well as the development of precision medicine products such as Afrocentric risk calculators, polygenic risk scores, biomarkers and drug targets<sup>23–25,227,307,308</sup>. The SIREN neurobiobank comprises a group of constantly monitored ultra-low-temperature (–86 °C) freezers located in Ibadan, Nigeria, constantly powered –20 °C chest freezers located in Ibadan and other recruitment sites, barcode scanners and printers, a laboratory information management system, a secure multi-terabyte server,

user-friendly software for archiving neuroimages, and solar-powered inverter systems to provide uninterrupted electric power back-up<sup>272,309</sup>. The neurobiobank contains >3,800 brain images and 160,000 blood samples including serum, plasma, red cell concentrates and extracted DNA. The ethical, legal and societal implications of stroke neurobiobanking and genomics in the complex African sociocultural landscape are also being explored<sup>310</sup>.

### Future directions

Stroke care in Africa faces numerous challenges related to epidemiological surveillance, health promotion and disease prevention, acute care and rehabilitation: the four domains of the stroke quadrangle<sup>311</sup> (FIG. 5). However, various pragmatic solutions to these challenges exist (TABLE 6). First, epidemiological surveillance can be improved by the establishment of a framework for regular monitoring and evaluation of stroke (including burden and risk factors) and health services at the national level. This framework could involve a combination of community-based surveys and surveillance systems. Second, the implementation of integrated population-wide and individual prevention strategies could reduce exposure to and improve control of modifiable risk factors. Third, the effective planning of acute stroke care services, including workforce training and capacity-building, can improve acute stroke care. Last, the promotion of access to interdisciplinary care, including task sharing approaches, can improve post-stroke rehabilitation services. To coordinate these activities, the newly launched African Stroke Control Observatory Risk reduction Ecosystem (A-SCORE), which will be a major part of the global SCORE (G-SCORE) under the auspices of the WSO–WHO–*Lancet Neurology* Commission on Stroke, should be enhanced<sup>253</sup>. A-SCORE involves policy-makers, patients, payers, providers, the populace and implementation partners. Through surveillance and research, stroke in Africa will become quantifiable and understandable; through prevention, stroke will become avoidable; through provision of acute care, stroke will become treatable; and through rehabilitation, stroke will be surmountable.

Novel stroke leadership initiatives are springing up in Africa and hold great promise for tackling the growing burden of stroke on the continent. For example, the African Stroke Organization is a new pan-African, multidisciplinary coalition of stroke professionals, stroke support organizations and national stroke societies with the vision “to reduce the burden of stroke in Africa”<sup>312</sup> (FIG. 6). The organization aims to achieve this vision through multidisciplinary research and capacity-building, promoting the development of effective stroke prevention and intervention services, enhancing stroke awareness, advocating for survivors of stroke, their families and caregivers, and driving the formulation of stroke-friendly policies<sup>312</sup>. Multiple non-governmental initiatives working as stroke support organizations are springing up across the continent. These organizations are working with survivors of stroke and their caregivers to enhance rehabilitation and life after stroke as well as engaging policy-makers and synergizing with



**Fig. 6 | Conceptual framework of the African Stroke Organization.** The aim of the African Stroke Organization (ASO) is to reduce the burden of stroke in Africa. This figure illustrates the framework through which the ASO plans to meet this goal. The colourful network represents the rich genetic, cultural and geographical diversity in Africa, and the neuronal network of the brain. The interconnected individuals represent the African Ubuntu Philosophy of inclusiveness, cooperation and collaboration. The pale green layer depicts the four core pillars of ASO activities: research; capacity-building programmes; development of stroke services; promotion of stroke awareness, and advocacy and empowerment of survivors of stroke, their families and their caregivers. The dark green layer represents the broader core values of the ASO: working with partners to involve people and positively influence practice and policy. Adapted with permission from REF.<sup>312</sup>, SAGE.



extant stroke prevention initiatives<sup>313</sup>. Furthermore, the African Stroke Organization is launching an annual pan-African scientific conference on stroke to regularly examine gaps in evidence and practice, accelerate translational research, guide priorities for stroke care practice and policy, build future stroke leaders, and strengthen regional collaboration and research output. The first African Stroke Organization Conference is expected to be held in autumn 2021 (REFS<sup>314,315</sup>).

Implementation science is a distinct research priority for stroke in Africa<sup>312</sup>. Existing evidence for the primordial, primary and secondary prevention of stroke needs to be contextualized to target Africa. Barriers to and facilitators of vascular risk factor control, both traditional and novel, need to be unmasked. Accurate, rigorous and detailed epidemiological studies to track the trends of incidence, prevalence, case fatality and mortality, and DALYs will be required to inform detailed and pragmatic planning of population-based strategies to control the escalating stroke burden in Africa. The ongoing African Rigorous Innovative Stroke Epidemiological Surveillance (ARISES) study was designed to address the methodological limitations of previous epidemiological studies<sup>26</sup>. This new study is also using technological innovations, including geographical information systems and mobile health-driven stroke information systems, to gather accurate data on incident strokes in the demographic sites where the study is being conducted. The mobile health-driven stroke information system will be deployed to improve local stroke literacy and enhance near-total case detection. Results are expected in 2025.

Translational interdisciplinary science, including trans-omics technology and data science, will be needed to gain deeper insight into novel stroke-associated genetic loci and pathophysiological pathways. These approaches will also enable the discovery of new, population-specific risk calculators, biomarkers and drug targets with the aim of achieving personalized, or precision, stroke treatment<sup>24,227</sup>. New treatments and novel preventive approaches are needed to inform clinical trials and the development of multicentre and multinational networks to tackle the increasing stroke burden.

The WSO–WHO–*Lancet Neurology* Commission on Stroke<sup>253</sup> conducted a survey of stroke services in five African nations to assess needs and offer pragmatic solutions; however, this effort needs to be scaled up to cover other African countries<sup>316</sup>. Public education is needed to fill the unique gaps in stroke knowledge

present in different African populations and to address the influence of cultural and religious beliefs and practices relating to stroke<sup>289,291</sup>. To fill the critical gaps in the availability of stroke professionals in Africa, focused training in stroke medicine needs to be incorporated into the curricula of postgraduate medical, nursing and allied professional education. Short courses and conference teachings should also be provided. Online resources that are sensitive to the unique epidemiological, cultural and socioeconomic environment in the continent will be very useful for filling knowledge gaps. Large multinational initiatives, such as the Angels Initiative and SITS Registry, have scaled up acute stroke services in Europe, the Middle East and North Africa<sup>269</sup>. We suggest that organizations within Africa develop partnerships with such initiatives to improve stroke services in Africa. African governments and regional organizations need to formulate policies that advance stroke science and care in Africa in tandem with their expressed commitments to actualize Sustainable Development Goal 3.4, which aims to ensure healthy lives and promote well-being and reduce premature death from non-communicable diseases, including stroke, by one-third by the year 2030.

### Conclusions

Alarming, as the current epidemiological evidence shows, the scourge of stroke is on the increase in Africa. Modifiable risk factors such as hypertension are clearly key primary targets for treatment and prevention. As is evident from the experience of higher-income countries, reducing the burden of stroke incidence in Africa will undoubtedly reduce mortality, morbidity, disability and the neurological as well as cognitive sequelae associated with stroke. Fortunately, welcome progress has been made in stroke medicine, awareness, prioritization, care, education, research and policy-making. If such progress continues, the anticipated future toll of stroke on the continent and its over 1 billion people could be substantially mitigated. However, successfully building on current efforts is by no means guaranteed. Patients, providers, payers, policy-makers and the public, in concert with scientists and funders, will need to maintain prospective vigilance of the continental stroke burden, apply vigour to unravelling the unique determinants of stroke in the region, and prioritize the development of contextual preventive and therapeutic solutions to avert and minimize the burden of stroke<sup>316</sup>.

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#### Author contributions

R.O.A., B.O., O.A.A., F.S.S., R.N.K. and M.O.O. researched data for the article, made a substantial contribution to discussion of content, wrote the article, and reviewed and edited the manuscript before submission. F.A.-A., T.A., O.S.O., A.D., R.W.W. and A.O. made a substantial contribution to discussion of content and reviewed and edited the manuscript before submission. P.N. made a substantial contribution to discussion of content, wrote the article, and reviewed and edited the manuscript before submission.

#### Competing interests

The authors declare no competing interests.

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