CHARACTERISTICS OF STROKE IN YOUNG ADULTS IN SOUTHWEST ENGLAND

Dr Oladotun Ayoola ABIDAKUN

Student number: 20076021

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DEDICATION

In loving memory of Jonah Oluyemi Abidakun, my father and mentor. Your spirit of excellence continues to inspire me. This work is dedicated to you.

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ABSTRACT

For many decades, stroke has been regarded as a health condition that affects only older individuals. However, recent studies have proven otherwise by showing that stroke significantly affects younger adults. This study comprehensively characterises stroke in a young adult population presenting at the Bristol Royal Infirmary Stroke Unit in Southwest England. Through a retrospective cohort analysis of 460 patients aged 18 – 55 years using SSNAP data from 2013 to 2021, the research sought to determine the frequency of stroke, identify risk factors, assess clinical presentations, and provide recommendations for improved care. The results of this study indicate that ischaemic stroke is the most common type, with a range of clinical presentations from mild to severe, which differs from older patients who may experience more severe presentations. In addition to traditional risk factors like hypertension, atrial fibrillation and smoking, young adults have unique risk factors like cardiac abnormalities such as patent foramen ovale (PFO), genetic disorders, arterial dissection and migraine. Lifestyle factors like alcohol and illicit drug use were also found to be significant in the results. The findings indicate that young stroke patients often have different risk profiles compared to older individuals. The treatment data revealed that thrombectomy, thrombolysis, and surgery, were used less frequently in young adults in the study. Although 20 patients (11 females, 9 males) did not survive within 30 days of hospitalization, the statistical analysis revealed no significant influence of age or gender on survival rates. The results of this research emphasize the importance of early detection and tailored interventions that are focused on specific risk factors prevalent in young adults. These include targeted screening for genetic disorders and cardiac abnormalities, which are commoner in younger stroke patients, could lead to earlier diagnosis and preventive measures. Additionally, addressing lifestyle factors such as excessive alcohol consumption and illicit drug use through specialised counseling and intervention programs is crucial to reduce the risk of stroke in young adults. In conclusion, the contributions of this research provide valuable insights into the epidemiology, risk factors, and management of stroke in young adults, as well as inform future research and clinical practice

RELATED PRESENTATIONS

Stroke in the Young Adults, Regional Stroke Simulation and Thrombolysis Training Day, Bristol Royal Infirmary, June 2022

Stroke in the Young Adults, Geriatric Medicine Regional Training Day, Gloucester Royal Hospital, March 2024

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Abbreviations

ANOVA	Analysis of Variance
APS	Antiphospholipid Antibody Syndrome
AF	Atrial Fibrillation
AVR	Aortic valve replacement
CADASIL	Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarction and Leukoencephalopathy
CKD	Chronic Kidney Disease
CHF	Congestive Heart Failure
CVST	Cerebral Venous Sinus Thrombosis
CHD	Congenital heart disease
DCM	Dilated cardiomyopathy
DVT/PE	Deep Vein Thrombosis/Pulmonary Embolism
ETOH	Ethanol (alcohol)
GCA	Giant Cell Arteritis
GCNKSS	Greater Cincinnati / Northern Kentucky Stroke Study
HTN	Hypertension
HCM	Hypertrophic Cardiomyopathy
HRT	Hormone Replacement Therapy
IHD	Ischaemic Heart Disease
LVH	Left Ventricular Hypertrophy
LDS	Loeys-Dietz syndrome
MELAS	Mitochondrial Encephalomyopathy with Subcortical Infarction and Leukoencephalopathy
MGUS	Monoclonal Gammopathy of Undetermined Significance
NHANES	National Health and Nutritional Examination Survey
PFO	Patent Foramen Ovale
PVD	Peripheral Vascular Disease
PFO	Patent Foramen Ovale
RHS	Ramsay Hunt syndrome
SITS-ISTR	Safe Implementation of Treatments in Stroke – International Stroke Thrombolysis Registry
SSNAP	Sentinel Stroke National Audit Programme

SCD	Sickle Cell Disease
SLE	Systemic Lupus Erythematosus
SPSS	Statistical Package for the Social Sciences
TTP	Thrombotic Thrombocytopenic Purpura
VSD	Ventricular septal defect

CHAPTER ONE

Introduction

1.1 Chapter Overview

This chapter will serve as the introductory chapter of this thesis, as it will provide an initial understanding of the research focus and the significance of the study. It also outlines the research problem, introduces the research aim and objectives, and highlights the importance of investigating stroke in young adults in Southwest England. The chapter will also delve into the background of stroke, its prevalence, and its shifting landscape, particularly in younger age groups. It will introduce the key classifications of stroke, ischaemic and haemorrhagic, and outline their respective subtypes. Lastly, the risk factors associated with stroke in young adults and the need for age-specific research to address the unique characteristics of this demographic will be discussed in this chapter.

1.2 Background of Stroke in Young Adults

Stroke is a cerebrovascular event characterized by an abrupt disruption in cerebral blood flow, leading to ischaemic or haemorrhagic injury within the brain parenchyma. This pathological phenomenon arises due to either an obstruction within the intracranial or extracranial vasculature, most commonly from thromboembolic occlusion, or the rupture of a cerebral vessel, precipitating intracerebral hemorrhage (Johnson et al., 2016). The consequent deprivation of oxygen and essential nutrients initiates a cascade of ischemic injury, culminating in neuronal apoptosis and infarction within the affected brain regions. The clinical sequelae of stroke are highly heterogeneous, ranging from transient neurological deficits to profound and irreversible neurological impairment, with significant morbidity and mortality. Given its complex pathophysiology and profound socioeconomic burden, stroke remains a critical focus of contemporary neurological research and public health intervention.

Stroke ranks as the second leading cause of death and the third major cause of disability around the world. Although stroke was initially viewed as a medical condition that primarily affects middle-aged and older individuals, several studies have discovered a rise in stroke occurrences among younger adults (George et al., 2017; Krishnamurthi et al., 2015). This implies that the landscape of stroke has shifted, and its impact on younger individuals has gained recognition as a critical health concern.

For decades now, several studies show that the healthcare industry has witnessed a disquieting phenomenon - the marked increase in the incidence of stroke among young adults all around the world. According to Krishnamurthi et al. (2013), although the prevalence of stroke does rise with age, approximately 10% to 20% of such occurrences are observed in individuals between the ages of 18 and 50. In the United States, the incidence of stroke among young adults aged 20–44 has been on the increase, rising from 17 per 100,000 US adults in 1993 to 28 per 100,000 US adults in 2015 (Madsen et al., 2020). Similarly, Ekker et al. (2019) noted that the incidence of stroke in young adults in the Netherlands has exhibited an upward trend, escalating from 14.0/100,000 person-years in 1998 to 17.2/100,000 person-years in 2010. Furthermore, Béjot et al. (2014) pointed out that in France, the incidence of strokes surged from 11.6 per 100,000 young adults in the period of 1985–1993 to 20.2 per 100,000 adults in the period of 2003–2011. In India, the average annual incidence of stroke was only 4 per 100,000 people for patients under 40 years old. However, this incidence sharply rose to a significantly higher rate of 41 per 100,000 for the 40–44 age group (Das et al., 2007). In Africa, the prevalence of stroke in young is also on the rise with about a 12.9% increase in young adults in Nigeria (Mustapha et al., 2012); while Chraa et al. (2014) noted a 28.9% rise in stroke among young adults in Morocco.

In the United Kingdom, the impact of stroke is both significant and unique. According to Bryne et al. (2022), In the UK, more than 100,000 people experience a stroke each year; this equates to one stroke every five minutes, and over 1.2 million people living with the aftermath of a stroke. Stroke ranks as the fourth leading cause of death in the UK and is a leading cause of disability, with nearly two-thirds of stroke survivors leaving the hospital with some form of disability (Stroke Association, 2018). Contrary to the common perception that stroke predominantly affects older individuals, it is increasingly recognized that younger adults are also at risk. Recent data indicates a worrying trend: from 2002 and 2018, there was a 67% increase in stroke incidence among adults under 55 years of age in the UK, while the incidence among older adults decreased by 15% (Li et al., 2022). This rise among younger populations is reflected in broader high-income countries and suggests a significant shift in the demographic affected by this condition. In England, it is estimated that one in six people will experience a stroke in their lifetime. Public Health England (PHE) statistics reveal that

57,000 individuals had their first stroke in 2016, with around 30% of these people expected to experience a recurrent stroke (OpenAccessGovernment, 2018).

Although the majority of strokes (59%) occur in the older population, there is a significant shift with more first-time strokes occurring in middle-aged adults (ages 40 to 69 years). Recent data from Gov.UK (2018) highlights that over a third (38%) of first-time strokes now happen within this age group. Alarmingly, the average age for stroke onset has decreased over the past decade; for men, it fell from 71 to 68 years, and for women, from 75 to 73 years between 2007 and 2016. Moreover, strokes in younger adults, although less common, have a profound economic impact. In 2016, approximately 3% of first-time strokes in England occurred in individuals under 40 years old.

These staggering statistics indicate that young adults, who were once considered relatively immune to the ravages of cerebrovascular accidents, now find themselves confronting the condition in an alarming reality. This emerging trend challenges deeper research into the enigmatic world of stroke in the youthful population. This is because the nature and aetiology of stroke in young adults slightly differ from that of older individuals, and this plays a huge role in the diagnostic evaluation and treatment. This implies that the knowledge obtained from research regarding stroke in older adults is not equally applicable to young adults. When compared with stroke in the older population, stroke in the young has a disproportionately large economic impact, such that it results in the individual becoming disabled throughout their most productive years. This research seeks to evaluate the characteristics of stroke in young adults in Southwest England. The major aim of this research is to shine a spotlight on the phenomenon of stroke in young adults in Southwest England and its implications for healthcare. Through rigorous research and analysis, this study will uncover the multifaceted characteristics of stroke in young adults, from its frequency and risk factors to its clinical presentation and prognosis.

1.3 **Stroke: A Brief Overview**

Stroke, medically referred to as a cerebrovascular accident (CVA), represents a significant and potentially life-threatening neurological event resulting from an acute disruption in cerebral blood flow. This sudden vascular compromise initiates a

complex cascade of pathophysiological processes, culminating in neuronal ischemia, infarction, and varying degrees of neurological dysfunction. The brain, reliant on a continuous supply of oxygen and glucose to maintain cellular metabolism and synaptic activity, is particularly vulnerable to any perturbation in cerebral perfusion. Consequently, when this supply is interrupted, either due to vascular occlusion or hemorrhage, irreversible neuronal injury ensues.

Stroke is broadly classified into two major subtypes: ischaemic stroke, which results from thromboembolic occlusion of a cerebral artery, and haemorrhagic stroke, which arises from the rupture of a weakened intracranial vessel, leading to extravasation of blood into brain parenchyma or subarachnoid spaces. Both subtypes can produce profound neurological deficits, with clinical manifestations contingent upon the anatomical distribution of the affected vasculature. Motor impairments, aphasia, sensory deficits, and visual disturbances are among the myriad presentations, reflecting the heterogeneous impact of stroke on neurological function.

1.3.1 Ischaemic Stroke

Ischaemic strokes occur when a blood clot or other occlusion obstructs a cerebral artery, thus impeding blood flow to a specific region of the brain. When this happens, the part of the brain deprived of blood, also known as the infarct zone, begins to suffer damage within a few minutes and ultimately leads to the hallmark symptoms of stroke. The interruption of blood flow to a specific area of the brain due to a blockage within a cerebral blood vessel can be categorised into three subtypes: thrombotic stroke; embolic stroke, and small vessel disease (lacunar stroke).

Thrombotic stroke is a type of ischaemic stroke that is caused by the formation of a blood clot (thrombus) within an artery that supplies the brain. Thrombotic strokes often occur in areas where atherosclerosis has narrowed the arteries. These clots can gradually grow and block the blood vessels. On the other hand, embolic strokes occur as a result of the migration of a clot (embolus) formed elsewhere in the circulatory system to the brain. These emboli can originate from various sources, such as the heart (in conditions like atrial fibrillation) or a major artery. They tend to cause more sudden and severe symptoms. Lastly, lacunar strokes involve the occlusion of small, deep brain arteries. They are often associated with conditions like hypertension and

diabetes and can lead to specific neurological deficits. The blocked artery results in a cascade of events that deprive the brain tissue downstream of vital oxygen and nutrients, leading to cellular injury and death. The severity of the damage depends on factors such as the size of the blocked vessel and the duration of the ischemia (Kalogeris et al., 2016; Sommer, 2017).

Ischaemic stroke can manifest with a wide range of symptoms, which may vary depending on the specific brain region affected. Common clinical signs and symptoms include a sudden weakness or numbness in the face, arm, or leg, often on one side of the body; a sudden loss of balance, coordination, or severe dizziness; sudden difficulty speaking or understanding speech (aphasia); sudden vision disturbances, such as blurred or double vision; and sudden severe headache (Walter, 2022; Yew and Cheng, 2015).

Ischaemic stroke is a leading cause of mortality and disability which occurs when a blood clot or other occlusion obstructs a cerebral artery and impedes the blood flow to a specific region of the brain. The ensuing deprivation of oxygen and nutrients results in rapid cellular injury and death within the affected area, known as the infarct zone. The primary mechanisms leading to ischaemic stroke can be categorized into three subtypes: thrombotic stroke, embolic stroke, and small vessel disease (lacunar stroke).

The pathophysiology of ischaemic stroke, irrespective of subtype, involves a cascade of events triggered by the obstruction of blood flow. This blockage deprives brain tissue of vital oxygen and nutrients, leading to cellular injury and death. The severity of damage is influenced by several factors, including the size of the blocked vessel and the duration of ischemia.

1.3.2 Ischaemic Stroke in Young Adults

Several studies have shown that ischaemic strokes account for the majority of stroke cases in young adults all around the world (Kissela et al., 2012; Tibæk et al., 2016). According to Krishnamurthi et al. (2013), there are more than 11 million global occurrences of ischaemic strokes every year. Although the incidence of ischaemic stroke generally increases with age, nevertheless, approximately 10% to 20% of

these events affect young adults between the ages of 18 and 50 (Boot et al., 2020). This condition is a major contributor to long-term disability and profoundly impacts the quality of life of young adults.

Ischaemic stroke affects young adults of all races and ethnicities, although the incidence and underlying causes exhibit substantial variation across different countries, genders, and ethnic groups. These differences cannot be solely attributed to variations in healthcare resources affecting diagnostic work-up and treatment. More so, the prognosis for young adults who have suffered an ischaemic stroke varies widely depending on factors such as the size and location of the infarct, the speed of medical intervention, and the presence of comorbidities (Kalaria et al., 2016). While others may experience significant recovery and regain most of their lost functions, others may face long-term disabilities.

1.3.3 Haemorrhagic Stroke

Unlike ischaemic stroke, haemorrhagic strokes are less common and are often more severe. Haemorrhagic strokes result from the rupture of a blood vessel within the brain, leading to bleeding into the surrounding brain tissue. Haemorrhagic strokes can have devastating consequences due to the compression of adjacent brain structures and the toxic effects of blood on neural tissue. This rupture leads to the extravasation of blood into the brain tissue, causing pressure on the brain and potential damage to adjacent structures. Haemorrhagic strokes are primarily categorised into two subtypes: intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH).

Intracerebral hemorrhage (ICH) is the most common form of haemorrhagic stroke which occurs when a blood vessel within the brain itself ruptures. Intracerebral hemorrhage (ICH) is often linked to certain factors such as hypertension, aneurysms, arteriovenous malformations (AVMs), or anticoagulant medication use (Dekker et al., 2018; Murphy and Werring, 2020). Subarachnoid hemorrhage (SAH) occurs as a result of bleeding in the subarachnoid space, which is the area between the brain and the thin membrane covering it, the arachnoid layer. Subarachnoid hemorrhage (SAH) is often caused by the rupture of an aneurysm; nevertheless, it can be caused by other factors such as head trauma or bleeding disorders.

Regardless of the subtype, haemorrhagic stroke disrupts normal brain function by compressing brain tissue and causing bleeding and local inflammation. Depending on the location and extent of the bleeding, patients may experience a range of neurological deficits, such as weakness, numbness, or paralysis on one side of the body (Smith and Eskey, 2011). Haemorrhagic stroke can also lead to altered mental status, including confusion, lethargy, or loss of consciousness. Some individuals may experience seizures as a result of the disruption caused by the hemorrhage.

1.3.4 Haemorrhagic Stroke in Young Adults

Numerous studies have indicated that haemorrhagic stroke constitutes a significant number of all strokes occurring in individuals below the age of 45, with reported incidence rates ranging from 3 to 6 per 100,000 per year for subarachnoid hemorrhage and 2 to 7 per 100,000 per year for intracerebral hemorrhage (Kumar et al., 2020). Generally, the underlying causes of intracerebral hemorrhage in young patients are synonymous with those observed in individuals older than 45, except for a higher prevalence of arteriovenous malformations, drug abuse, and bleeding disorders early in life. Hypertension remains the major contributor to intracerebral hemorrhage in both younger and older individuals, and the majority of hemorrhages occur in the lobar regions of the brain.

1.4 Risk Factors of Stroke in Young Adults

Many risk factors and aetiologies have been associated with the occurrence of stroke in young adults, however, there remains a significant number of young adults with undetermined causes. Past research indicates that the conventional risk factors of stroke common in older adults have been found to be linked with stroke in young adults. These risk factors include hypertension, diabetes mellitus, obesity, dyslipidemia, and tobacco use (George et al., 2017; Kissela et al., 2012; Singhal et al., 2013). Recent studies also suggest that when compared to older adults, the prevalence of the conventional risk factors of stroke is substantively high in young adults, aged 15 - 55 years (Kivioja et al., 2018). In another study conducted by Putaala et al. (2012) in Europe, the top three most common risk factors of stroke in young adults were dyslipidemia (46%), current smoking (49%), and hypertension (36%). More so, these same risk factors - hypertension, dyslipidemia, and cigarette smoking,

were identified as the prevalent risk factors of stroke in young adults in New Zealand and China (Wu et al., 2012; Zhang and He, 2012). These findings suggest that the prevalence of risk factors for stroke in young adults is relatively consistent globally.

Although there is a substantial body of research on the risk factors of stroke in young adults, this dissertation aims to add new insights by focusing on the specific demographic of young adults in Southwest England. This region has unique socioeconomic and environmental factors that may influence the prevalence and impact of these risk factors differently compared to other regions studied. By so doing, the research findings will contribute to a better understanding of stroke in young adults, as well as inform targeted prevention and intervention strategies specific to this region.

1.5 The Bristol Royal Infirmary Stroke Unit

The aim and objectives of this research focus on evaluating the characteristics of stroke in young adults in Southwest England. To achieve these aim and objectives, this research will be carried out at the Bristol Royal Infirmary (BRI), University Hospitals Bristol and Weston NHS Foundation, Bristol. Bristol is the most populous city in the region with an estimated population of 479,000 (mid-2022) (Bristol City Council, 2022). The population diversity of Bristol is quite cosmopolitan with at least 185 countries of birth, 287 different ethnic groups and 90 main languages represented (Bristol City Council, 2021). The BRI is a large teaching hospital in the centre of Bristol, England. It has links with the nearby University of Bristol and the University of the West of England, also in Bristol. The BRI serves a population of 2.3 million people in Bristol and the surrounding areas, including Cheltenham, Gloucester, Bath, Swindon, Taunton, Yeovil, and Weston (Society for Cardiothoracic Surgery, n.d). The Bristol Royal Infirmary Stroke Unit is a tertiary stroke centre in Southwest England with an acute stroke unit attending to an average of 500 stroke patients and 800 TIA patients annually. The BRI Stroke Unit serves as a regional epicenter for stroke care, attracting patients not only from Bristol but also from the surrounding regions of Southwest England. Its catchment area extends its influence to communities and healthcare systems beyond the city limits, making it a focal point for understanding stroke in the context of this geographic region.

The study population for this research will be young adults between the ages of 18 – 55 years, admitted at the Acute Stroke Unit, Bristol Royal Infirmary, University Hospitals Bristol and Weston NHS Foundation, Bristol with a primary diagnosis of stroke coded as I-61, I-63, I-64 between 2013 to 2021.

The Sentinel Stroke National Audit Programme (SSNAP) is a prominent healthcare quality improvement initiative that is based in the School of Population Health and Environmental Studies at King's College London. Its primary mission is to assess and enhance the quality and organisation of stroke care within the National Health Service (NHS). It also serves as the primary repository for stroke-related data in England, Wales, and Northern Ireland. SSNAP has earned recognition as the most effective national clinical audit in the UK for nine consecutive years, as determined by healthcare professionals engaged in audit activities. Stroke cases on SSNAP do not include subarachnoid hemorrhage. For the purpose of this research, the SSNAP data will be leveraged to analyse acute young stroke admissions at BRI from 2013 to 2021. The investigation will focus on aspects such as classification, aetiology, risk factors, management, and outcomes.

1.6 Statement of the Problem

For many years, stroke has been largely viewed as an issue affecting older adults. However, there has been a noticeable increase in the number of strokes occurring in young adults, specifically those aged 18 to 55. This emerging trend presents a significant challenge: there is a lack of comprehensive studies that explore the characteristics, risk factors, and outcomes of stroke in young adults. Existing research has identified several causes and risk factors for ischaemic stroke in young adults. Studies by George et al. (2016) and Ekker et al. (2018) have documented the rising incidence of stroke in this age group by linking it to both traditional risk factors, such as hypertension and diabetes, and lifestyle factors like smoking and obesity. However, these studies often focus on specific populations or have limitations in their scope. For instance, while some research highlights the role of lifestyle factors, it does not fully explore the complex interactions between these factors and other emerging risks, such as genetic predispositions or autoimmune conditions (Putaala et al., 2009; Kivipelto et al., 2022). This lack of detailed research leads to misconceptions among healthcare providers and the general public. The symptoms of stroke in young adults can be

subtle and atypical, often resulting in delayed or incorrect diagnoses (Edlow and Selim, 2011; Wallace and Liberman, 2021). Without proper awareness and knowledge, these delays can worsen the severity of the condition. Moreover, young adults who experience stroke often present with different risk factors compared to older patients. Understanding these unique risk factors is crucial for effective prevention and treatment strategies. The absence of age-specific research also hampers the development of targeted support and rehabilitation programs for young stroke survivors. This gap in research is not just an individual issue but also a broader public health concern, as stroke in young adults can lead to long-term disabilities, loss of productivity, and increased healthcare costs. Given these challenges, it is essential to address the lack of comprehensive studies on stroke in young adults. This study aims to fill this gap by examining the characteristics, risk factors, clinical presentations, and outcomes of stroke in young adults treated at the Bristol Royal Infirmary Stroke Unit. The insights gained from this research will contribute to improving early diagnosis, prevention efforts, and overall healthcare for this often-overlooked group.

1.7 Research Aim

The aim of this study is to comprehensively characterise stroke in young adults presenting at the Bristol Royal Infirmary Stroke Unit, Bristol.

1.8 Objectives of the Research

- To determine the frequency of stroke in young patients presenting at the Bristol Royal Infirmary Stroke Unit, Bristol
- To determine the risk factors and prognosis of stroke in young patients presenting at the Bristol Royal Infirmary Stroke Unit, Bristol
- To provide recommendations to relevant authorities about stroke in young patients presenting at the Bristol Royal Infirmary Stroke Unit, Bristol

The first objective aims to establish the prevalence and incidence rates of stroke in young adults aged 18 to 55, presenting at the BRI Stroke Unit. This data will provide essential epidemiological insights into the scope and scale of stroke in Southwest England, emphasizing its significance as a public health issue. The second objective

focuses on identifying the unique risk factors, such as lifestyle-related factors, comorbidities, and genetic predispositions, that contribute to stroke in young adults. This will enhance understanding of the underlying causes and support the development of effective prevention and intervention strategies. The third objective seeks to detail the clinical manifestations and neurological deficits associated with stroke in young adults. This will aid in the early recognition and diagnosis of stroke, ensuring prompt and appropriate medical care. Finally, the fourth objective is to formulate evidence-based recommendations for healthcare authorities and policymakers. These recommendations will aim to improve stroke prevention, management, and support systems specifically for young adults, ultimately reducing the condition's burden on individuals and society.

Achieving these objectives will provide a comprehensive understanding of stroke in young adults, as well as addressing critical gaps in current knowledge. This research will pave the way for targeted interventions and support systems that will improve early diagnosis and treatment. By identifying unique risk factors, the study will contribute to the development of preventive strategies by addressing the root causes of stroke in this demographic. Besides, understanding the prognosis and outcomes of stroke in young adults will guide healthcare providers in tailoring rehabilitation and support services, optimizing recovery, and enhancing the quality of life. The recommendations generated from this research will have practical implications for healthcare policies, clinical guidelines, and practices, benefiting stroke patients and healthcare systems in the Southwest of England and beyond.

1.9 Rationale of the Study

This study aims to provide a comprehensive characterization of stroke in young adults who present at the Bristol Royal Infirmary Stroke Unit. The rationale behind this research lies in the growing recognition that stroke in young adults, though less common than in older populations, presents unique challenges in diagnosis, treatment, and long-term management. Understanding the specific risk factors, clinical presentations, and outcomes in this demographic is crucial for improving patient care. Young adults with stroke often have different risk profiles and may experience delayed diagnosis due to the unexpected nature of stroke at a younger age. By focusing on

this population, the research seeks to fill gaps in current knowledge and provide insights that can lead to more effective prevention, earlier detection, and better-tailored interventions. Furthermore, by concentrating on patients at the Bristol Royal Infirmary, the study will generate localized data that can inform healthcare planning and resource allocation within the Bristol community. The research aims to contribute to the broader understanding of stroke in young adults and to foster community engagement in stroke prevention and management efforts.

1.10 Thesis Structure: Overview of Organisation and Chapters

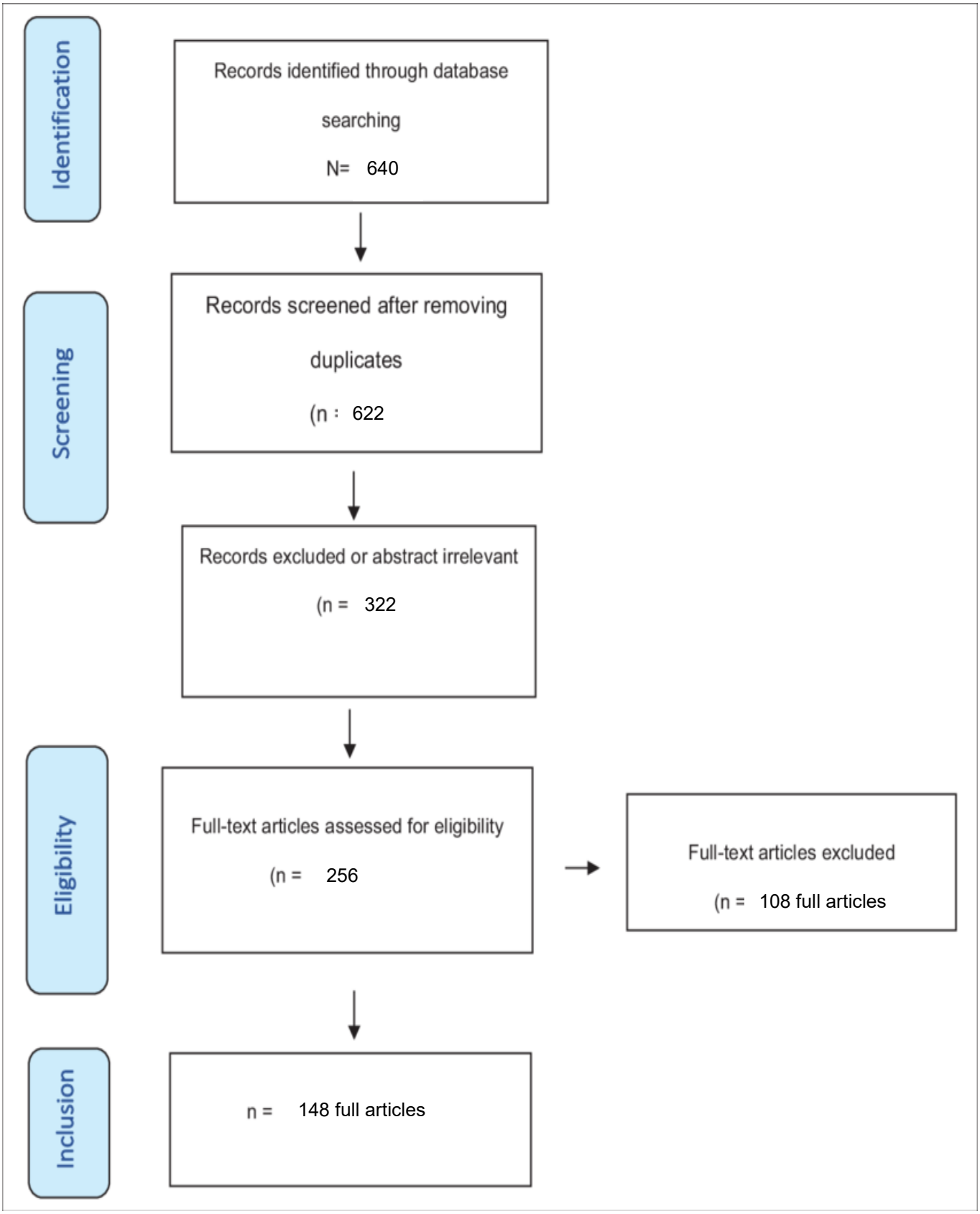
This thesis is structured to provide a comprehensive exploration of the topic, "Characteristics of Stroke in Young Adults in Southwest England". To facilitate navigation and understanding, here is an overview of the organisation and content of each chapter. Chapter One provides an overview of the study's focus, significance, and objectives. In Chapter Two, the existing literature will be explored to examine studies on strokes in young adults, with an emphasis on Southwest England. Chapter Three will outline the research methodology and methods, including the data collection methods, sample selection, and data analysis. Chapter Four will expound on the data analysis and present the findings of the research. Charts and graphs will be used to visualise the findings of the research. Chapter Five will entail a discussion and conclusion section that interprets the research findings, an analysis of the findings in the context of existing literature, and a sum up of the key points of the thesis.

CHAPTER TWO
Literature Review

2.1 Introduction

In this chapter, a systematic review of existing literature will be conducted to evaluate the characteristics of stroke in young adults in Southwest England. To ensure a rigorous and transparent review process, this research adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines. The Study Identification Process began by defining the search strategy and selecting appropriate databases. The primary databases searched included PubMed, ScienceDirect Scopus, Google Scholar, and Web of Science. The search terms were carefully chosen to capture relevant studies while excluding irrelevant ones. A combination of keywords and phrases were used such as “young adults,” “stroke,” “risk factors,” and “outcomes.” Boolean operators (AND, OR) were used to refine the search results and ensure that all relevant articles were retrieved. The inclusion criteria were designed to ensure that only studies pertinent to the review were selected. The included studies that focused on young adults (defined as individuals aged 18-55 years) with stroke; reported on risk factors, clinical outcomes, or epidemiological data related to stroke in this age group; and published in peer-reviewed journals. For the exclusion criteria, specific filters were applied to remove studies that did not meet the age criteria; studies that are not original research, not published in the English language and lacked sufficient data for analysis. Furthermore, each study was screened for relevance based on its title and abstract. Full-text articles were then reviewed to confirm that they met the inclusion criteria. Studies that did not meet the criteria were excluded from the review. The final selection of studies was based on a detailed evaluation of their quality and relevance to the research questions posed. The PRISMA flow diagram is presented below

Figure 2.1: Prisma Flow Diagram



2.2 Young Adults

The definition of "young adults" in stroke research is crucial, as it directly impacts the participant selection and how findings are interpreted. However, the age range for young adults is not consistent across studies, which leads to potential variations in results. For example, Aigner et al. (2017) define young adults as those aged 18 to 45 years, while Ji et al. (2013) extend this range up to 55 years. Other studies, such as those by Barra et al. (2019), Li et al. (2022), and McCarty et al. (2019), also show differences in the age ranges used. These disparities reflect various research goals, study populations, and available data. More so, these inconsistencies in defining the age range for young adults can complicate the comparison of studies and the synthesis of findings. This can lead to differing conclusions about stroke characteristics and outcomes in this group. In this study, the age range of 18 to 55 years is adopted in line with NHS guidelines, to ensure a broad yet relevant scope that encompasses the definitions used in other key studies. This approach allows for a more comprehensive understanding of stroke in young adults within the context of the UK healthcare system.

2.3 Epidemiology of Stroke in Young Adults

2.3.1 Global Geographic Trends

The global incidence of stroke among young adults under 65 has significantly increased in recent decades, with a 25% rise in the incidence rate among those aged 20 to 64 (Krishnamurthi et al., 2015). This surge has sparked debate among researchers, partly due to variations in how stroke data are reported. As Griffiths and Sturm (2011) noted, the epidemiology of stroke in young adults varies across studies, often because incidence rates typically encompass all stroke types, including ischaemic, intracerebral haemorrhage, and even subarachnoid hemorrhage. Despite these complexities, certain trends can be identified. Studies have shown that the incidence of ischaemic and haemorrhagic strokes in young adults generally ranges from 7 to 15 per 100,000 individuals per year (Giroud et al., 2000; Minelli et al., 2007; Vibo et al., 2005).

In the United States, approximately 10-15% of all strokes occur in young adults, with an increasing trend observed in recent years (Maaijwee et al., 2014; Ji et al., 2013).

Madsen et al. (2020) reported that the incidence rate for adults aged 20-44 in the U.S. rose from 17 per 100,000 in 1993 to 28 per 100,000 in 2015. In the Greater Cincinnati/Northern Kentucky region, ischaemic stroke accounted for about 65% of all strokes in young adults aged 20-44, while intracerebral hemorrhage (ICH) and subarachnoid hemorrhage (SAH) constituted 17% and 16%, respectively (Kissela et al., 2012). Moreover, George et al. (2017) highlighted that hospitalization rates for stroke in young U.S. adults aged 18-44 doubled between 2003 and 2012.

In Europe, similar trends are noted. Béjot et al. (2014) observed that stroke incidence among young adults increased from 10.7 per 100,000 between 1994-2002 to 18.1 per 100,000 between 2003-2011. Yesilot et al. (2017) reported a wide spectrum of incidence rates across Europe, ranging from 5.8 per 100,000 in central Italy to 97.7 per 100,000 in China. Additionally, Stevens et al. (2017) projected a 34% increase in the annual number of strokes in Europe from 2015 to 2035. In the UK, stroke incidence and prevalence are rising, with over 113,000 strokes occurring annually. This increase is partly due to an aging population and improved treatment outcomes (Chutoo, 2021; King et al., 2020). Stroke incidence in the UK is expected to rise by 60% between 2015 and 2035. A study in Oxfordshire, England, found a significant increase in stroke incidence among young adults under 55 between 2002-2010 and 2010-2018, with a corresponding decrease in older adults (Li et al., 2022). These findings align with trends observed in UK hospital admissions for young adults (Madsen et al., 2020).

In regions like Russia, China, and India, the rising incidence of stroke among young adults has become a significant public health concern, as it contributes to the increasing stroke burden in these populations (Danaei et al., 2011; De Los Ríos et al., 2012; Hu et al., 2012; Jha et al., 2008; Norrving and Kissela, 2013; Zaridze et al., 2009). Asia, with over 60% of the global population, also reports a high prevalence of young stroke. In India, for example, 12% of all strokes occur in individuals under 40 (Pandian and Sudhan, 2013). Venketasubramanian et al. (2017) observed that young stroke mortality rates in Asia are higher than in Western Europe, the Americas, or Australasia and more closely resemble rates in Eastern Europe. High rates have also been reported among Japanese young adults (70 per 100,000 in the 35-44 age group) (Morikawa et al., 2000) and Hispanics (26 per 100,000 in the 22-44 age group) (Jacobs et al., 2002). These regional differences illustrate the varying impact of stroke globally,

with incidence rates ranging from 5 to 15 per 100,000 person-years in Europe to 20 per 100,000 in North America, Australia, and Asia, and up to 40 per 100,000 in some African nations and Iran (Lavados et al., 2005; Marini et al., 2010; Sarfo et al., 2018; Tsai et al., 2013).

Developing and underdeveloped countries also show significant young stroke trends. For instance, Libya reports an incidence rate of 47 per 100,000 for all strokes under 45 years (Akinyemi et al., 2021). In Africa, higher prevalence rates have been reported, with 12.9% in Nigeria (Mustapha et al., 2012), 31% in South Africa (Hoffmann, 1998), and 28.9% in Morocco (Chraa et al., 2014). A study in Mulago Hospital, Uganda, found that 25% of stroke patients were under 51, with 23% of stroke-related deaths occurring in this age group (Kwarisima et al., 2014). According to Boot et al. (2020), the higher incidence of young stroke in developing countries compared to developed ones can be attributed to disparities in risk factors, such as the prevalence of rheumatic heart disease, HIV infections, and limited resources for managing vascular risk factors.

These regional differences in stroke incidence among young adults can be attributed to several factors. Socioeconomic disparities, access to healthcare, and differences in lifestyle and environmental exposures play significant roles. Studies have shown that higher stroke rates in developing regions are often linked to inadequate healthcare infrastructure, limited access to preventive measures, and higher prevalence of infectious diseases like HIV, which can increase stroke risk (Pandian et al., 2018; Mukherjee and Patil, 2011). In contrast, developed regions may see rising stroke rates due to lifestyle factors such as increased obesity, sedentary behavior, and higher stress levels associated with urban living (Teo and Rafiq, 2021).

2.3.2 Sex Differences in Young Stroke

Sex disparities significantly influence the incidence and outcomes of stroke among young adults. Research indicates that stroke rates are generally higher in men compared to women in the 35 to 44 age group (Syme et al., 2005; Vibo et al., 2005). However, this trend shifts in younger populations. Several population-based studies and case series report a higher incidence of stroke among women under the age of 30 (Broderick et al., 1998; Naess et al., 2002). Boot et al. (2020) reveals that young

men are more prone to ischaemic strokes, particularly those related to large artery disease and small vessel disease. In contrast, women often experience strokes associated with different etiologies. This sex disparity can be attributed to female-specific risk factors, such as the use of oral contraceptives, pregnancy, and the postpartum period. Women also have a higher prevalence of migraine and autoimmune disorders, which further contribute to their stroke risk (Boot et al., 2020).

In France, data reveal that women under the age of 35 experience a higher incidence of stroke compared to men, with a women-to-men incidence ratio of 1.89 (95% confidence interval 1.27–2.80). However, in the 35-44 age group, no significant sex difference is noted, while men exhibit a higher incidence in the 45-84 age range. Similarly, in the Netherlands, a nationwide cohort study found that women aged 18-44 have a higher stroke risk compared to their male counterparts (Giroud et al., 2017). Factors such as pregnancy, postpartum changes, and the use of estrogenic oral contraceptives have been proposed as potential contributors to this increased risk among young women (Ekker et al., 2019).

Sex differences in stroke mortality are also evident. The World Health Organization (WHO) reported that between 1990 and 2006, stroke-related deaths were more frequent among women compared to men (Redon et al., 2011). Madsen et al. (2020) noted that while stroke prevalence is higher among men across all age groups, women often experience more severe outcomes and higher case-fatality rates. This is possibly due to a greater prevalence of embolic strokes in women. A study conducted across eight European countries observed that the annual risk of stroke increased by 9% in men and 10% in women. Asplund et al. (2009) attributed this elevated risk partly to women's longer lifespan and higher prevalence of hypertension and atrial fibrillation, which are significant stroke risk factors. Additionally, Cordonnier et al. (2017) emphasized that other factors such as differences in vascular biology, immunity, coagulation, hormonal profiles, and societal roles contribute to these sex disparities. Specifically, risks associated with pregnancy and the postpartum state further differentiate the stroke risks between genders.

2.3.3 Racial and Ethnic Differences

Racial and ethnic differences play a crucial role in determining stroke incidence and outcomes among young adults. In the United States, research highlights significant disparities between different racial and ethnic groups. Stroke incidence rates are notably higher among Black and Hispanic populations compared to White populations. Specifically, Blacks and Hispanics experience stroke rates of approximately 11 per 100,000 persons per year, while the rate for Whites is lower at 7 per 100,000 persons per year (Kissela et al., 2012; Pathak and Sloan, 2009). This disparity is most pronounced between the ages of 30 and 40 years.

In addition to differences in incidence rates, there are notable variations in hospital outcomes among these groups. Data indicate that Hispanics often have longer hospital stays compared to both Blacks and Whites. Blacks also experience longer hospitalizations than Whites (Feng et al., 2009). This extended duration of hospital stay among minorities can be attributed to a higher prevalence of complications, such as pneumonia, deep vein thrombosis, and urinary tract infections among Black patients compared to their White counterparts (Feng et al., 2009). Furthermore, Black patients are more frequently discharged to rehabilitation facilities, skilled nursing facilities, or long-term care hospitals, in contrast to White patients (Feng et al., 2009).

Mortality rates also exhibit racial disparities. Research shows that Black patients have higher stroke-related mortality rates compared to White patients, while Hispanics generally face a lower early mortality risk (Jacobs et al., 2002; Pathak and Sloan, 2009). These differences in mortality rates can be influenced by various factors, including differences in access to healthcare, quality of care, and underlying health conditions. A deeper examination of these disparities reveals that interdependent risk factors, such as hypertension (HTN), diabetes, and socioeconomic status, significantly contribute to stroke risk and outcomes. For instance, hypertension is more prevalent among Black individuals, leading to an increased risk of stroke within this group. Additionally, chronic conditions such as diabetes, which are also more common in certain ethnic groups, further influence stroke risk and recovery (Jacobs et al., 2002). Socioeconomic status can affect access to timely medical care and rehabilitation services, which can impact stroke outcomes.

An understanding of these racial and ethnic disparities, along with their interdependent risk factors, is essential for developing targeted interventions and improving stroke prevention and treatment strategies. Addressing these disparities can assist healthcare systems in working towards reducing the gap in stroke outcomes among different racial and ethnic groups and enhancing overall care for young adults experiencing stroke.

2.4 Aetiology of Stroke in Young Adults

The causes of stroke in young adults differ notably from those in older individuals. The TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification system is widely used to categorize ischaemic strokes into five primary etiological categories: large-artery atherosclerosis (LAA), cardioembolism (CE), small-vessel occlusion (lacunar), stroke of other determined aetiology, and stroke of undetermined aetiology (Adams et al., 1993). This system helps in understanding the varied origins of stroke and is particularly useful in distinguishing between traditional and less common stroke etiologies. In young adults, traditional stroke etiologies such as cardioembolic, atherosclerotic, and lacunar strokes are increasingly recognized. Studies from both U.S. and international cohorts report a higher prevalence of these traditional classifications compared to other determined and undetermined etiologies (Ji et al., 2012). This trend may be attributed to the high incidence of traditional stroke risk factors such as hypertension, diabetes, smoking, obesity, and dyslipidemia among young adults. For instance, the SITS-ISTR registry found that smoking was twice as common in younger participants (42.7% among those aged 18-50) compared to older participants (22.8% among those aged 51-80) (Toni et al., 2012). Additionally, a cardiovascular health study of U.S. adolescents (NHANES 2005–2010) revealed that about one-third of individuals aged 12–19 years had a body mass index in the 85th percentile or higher and had smoked within the past 30 days. The study also noted that 22% of males and 10% of females had high blood pressure (≥90th percentile), and a significant portion of adolescents did not meet the recommended levels of physical activity (von Sarnowski et al., 2013).

The increasing prevalence of traditional stroke risk factors among young adults is supported by recent trends. The Greater Cincinnati/Northern Kentucky Stroke Study

(GCNKSS) observed a rise in stroke prevalence among young adults, which correlated with an increase in stroke risk factors. From 1993 to 2005, the prevalence of coronary heart disease among young adults increased from 2.5% to 12.0% (Kissela et al., 2012). Additionally, the growing prevalence of obesity and diabetes in the U.S. is projected to result in a significant increase in coronary heart disease cases over the coming decades, with an estimated 100,000 additional cases attributed to obesity (Kissela et al., 2012).

In contrast to older adults, young adults are more likely to experience strokes of other determined aetiology or strokes with undetermined aetiology. For example, the Yonsei Stroke Registry in South Korea reported that patients with strokes of other determined aetiology were, on average, 20 years younger (mean age ± SD, 46.6±16.2) compared to those with cardioembolic, large-artery atherosclerosis, lacunar strokes, or strokes of undetermined aetiology (Nam et al., 2012). Similarly, the Cerrahpasa Stroke Registry in Istanbul found that patients with strokes of undetermined aetiology were younger (mean age 59.6±13.2) than those with other etiologies (mean age 63.0±13.4 years; $P<0.001$) (Ince and Benbir, 2013).

Strokes in young adults from other determined etiologies often involve conditions that are less common but more prevalent in this age group. These conditions include arterial dissection, various arteriopathies, inherited hypercoagulable traits, acquired hypercoagulable states, migraines, and illicit drug use. Arteriopathies such as moyamoya disease, fibromuscular dysplasia (FMD), cerebral angiitis, postpartum angiopathy, radiation arteriopathy, and thrombosed vascular malformation are particularly noteworthy (Sultan and Elkind, 2013).

The aetiology of stroke in young adults is influenced by multiple factors, including age, gender, and geographical location (Jacobs et al., 2002; Marini et al., 2001). Although haemorrhagic strokes are more common in young adults (40–55%) compared to the general stroke population (15–20%), cerebral infarction remains the most prevalent type of stroke among young adults. Brainin et al. (2007) observed that the risk of cerebral infarction is notably higher in regions with increasing rates of smoking and urbanization, especially in developing countries. Atherosclerosis is still a significant

risk factor, accounting for 15–25% of strokes in young adults, with even higher rates observed in certain ethnic groups (Kwon et al., 2000; Lee et al., 2002).

2.4.1 Cardioembolic Strokes

Cardioembolic strokes are a significant cause of ischaemic stroke in young adults; they account for approximately 20% of all stroke cases in this age group (Rasura et al., 2006; Varona et al., 2007). These strokes occur when a blood clot or other debris forms in the heart and travels to the brain, blocking a cerebral artery. The sources of these emboli are diverse, and they can be categorized into major and minor sources of cardioembolism (Choi et al., 2017). Cardioembolic strokes in young adults can arise from various cardiac conditions. According to Ji et al. (2013), significant sources include inherited valvular abnormalities, cardiomyopathies, and patent foramen ovale (PFO). Among young adults with cardioembolic strokes, PFO is particularly notable. This condition is present in about 20% of the general population but is found in up to 50% of young stroke patients (Choi et al., 2017). Recent studies, including those from the Risk of Paradoxical Embolism (RoPE) project, have identified specific neuroimaging characteristics associated with PFO. Larger, superficial strokes are more likely to be associated with PFO, as opposed to smaller or deeper strokes, or those with chronic infarcts (Maaijwee et al., 2014). The RoPE project developed a scoring system that helps predict the likelihood of PFO in patients with unexplained strokes. This system, which considers factors such as age, diabetes, hypertension, smoking, and prior strokes, shows that the prevalence of PFO increases with higher scores. Interestingly, patients with the highest likelihood of PFO had the lowest risk of recurrent stroke (Yusuf et al., 2020).

The prevalence and impact of cardioembolic stroke sources can vary by region. Mitral valve disease, a major cause of cardioembolic strokes, is more common in areas with high rates of rheumatic heart disease. The influence of rheumatic heart disease and mitral valve prolapse on cardioembolic strokes differs across regions and stroke registries, with studies reporting prevalence rates between 40% and 70% (Ghandehari and Moud, 2006; Lee et al., 2002; Varona et al., 2007).

Several factors contribute to the occurrence of cardioembolic strokes in young adults. Atrial fibrillation (AF) is a significant risk factor. This condition causes irregular heart

rhythms, leading to the formation of blood clots in the atria, which can then embolize and cause strokes (O'Carroll and Barrett, 2017). While AF is more commonly associated with older adults, it can also affect younger individuals, particularly those with genetic predispositions or existing heart conditions (Hanon et al., 2013; Sankaranarayanan et al., 2013).

Structural heart abnormalities are another critical factor. Congenital or acquired defects such as atrial septal defects (ASDs) and PFOs can facilitate clot formation and embolism (Wahl and Meier, 2009). Additionally, recreational drug use, particularly cocaine and amphetamines, can induce cardiac arrhythmias and increase the risk of cardioembolic strokes in young adults (Fonseca and Ferro, 2013).

Finally, some young adults have underlying conditions that predispose them to clotting disorders. These include antiphospholipid syndrome and genetic mutations like Factor V Leiden, which increase the risk of developing blood clots (George et al., 2020; van Alebeek et al., 2018). In essence, cardioembolic strokes in young adults are influenced by a combination of cardiac conditions, geographical factors, lifestyle choices, and genetic predispositions.

2.4.2 Patent Foramen Ovale (PFO)

Patent foramen ovale (PFO) is a congenital cardiac anomaly characterised by the persistence of a small opening in the atrial septum, the wall dividing the left and right atria of the heart. This condition is particularly relevant in young adults with cryptogenic stroke, where no other clear cause of the stroke is identified (Hari et al., 2015). PFO is found in approximately 25% of the general population, but its role as a potential risk factor for stroke remains a subject of ongoing research. Studies have demonstrated a notable prevalence of PFO among young adults with cryptogenic stroke. Handke et al. (2007) found that up to 45% of young patients with cryptogenic strokes had a PFO. Similarly, Thaler and Saver (2008) reported that PFO was significantly more common in young patients with cryptogenic strokes compared to those with known stroke etiologies. This suggests that PFO may contribute to the development of stroke in this population, although the exact mechanism remains complex.

The relationship between PFO and stroke, particularly in young adults, is still debated. Large population studies have not consistently shown a direct link between PFO and an increased incidence of first-ever stroke. Thaler and Saver (2008) and Griffiths and Sturm (2011) argue that while PFO is present in about 25% of the population, it is not independently associated with a higher incidence of stroke. However, a non-significant trend has been observed, especially in individuals under 60 with an associated atrial septal aneurysm (ASA) (Thaler and Saver, 2008; Overell et al., 2000). Meta-analyses have provided more insights. For instance, a meta-analysis of nine case-control studies found that young patients with cryptogenic stroke had a six-fold increased likelihood of having a PFO compared to those with known causes of stroke. In contrast, the odds ratio for all young stroke patients was 3.0 (Thaler and Saver, 2008; Overell et al., 2000). The presence of an ASA, found in about 2.2% of the population, appears to further increase this risk, though the impact of large septal defects remains uncertain (Thaler and Saver, 2008). Research indicates that the association between PFO and ischaemic stroke is stronger in younger individuals compared to older ones. Alsheikh-Ali et al. (2009) found that young adults with PFO have approximately a five-fold increased risk of stroke, whereas older individuals exhibit a two-fold increased risk. Despite these findings, the precise conditions and characteristics of PFO necessary to trigger a stroke are not fully understood (Putaala, 2020).

The predominant theory is that PFO may lead to stroke through paradoxical embolism, where a blood clot from the venous system bypasses the lungs and travels to the brain via the PFO. Factors such as the size of the PFO, the extent of the shunt, the tunnel length, and the presence of an ASA may influence the risk of ischaemic stroke associated with PFO (Goel et al., 2009). Additionally, other risk factors that can increase the likelihood of stroke in the context of PFO include immobilization, pregnancy, and both genetic and acquired hypercoagulable states (Putaala, 2020). In essence, although PFO is a common congenital anomaly, its role in stroke, particularly among young adults, is complex and not entirely understood. While PFO is frequently observed in individuals with cryptogenic stroke, the exact mechanisms and additional factors that contribute to this risk are still under investigation.

Current guidelines suggest that screening for PFO in stroke patients is not universally recommended but may be considered in cases where no other cause for the stroke is

identified, particularly in younger patients. PFO is often found incidentally during routine tests, and while it can be associated with stroke, not all cases require closure. The decision to close a PFO is usually made on a case-by-case basis, considering factors such as the patient's risk of recurrent stroke and the presence of other stroke risk factors. Closing the PFO is generally advised for patients with a history of unexplained stroke where no other causes are identified, but it is not recommended for all stroke patients.

2.4.3 Migraine

Migraine, particularly migraine with aura, has been linked to an increased risk of ischaemic stroke in young adults, especially women under the age of 45 (Bousser, 2004; Schwaag et al., 2003). Recent studies affirm that individuals with migraine, especially those with aura, face about a two-fold increased risk of ischaemic stroke compared to those without migraine (Sultan and Elkind, 2013). This association suggests that migraine may be a significant risk factor for stroke in this demographic, although the precise mechanisms remain unclear. The pathophysiological connection between migraine and ischaemic stroke is not fully understood. It is challenging to distinguish whether migraine precedes ischemia to potentially lead to migrainous infarcts, or if ischemia triggers migraine with aura. A meta-analysis by Schürks et al. (2011) did not find an increased risk of cardiovascular mortality among migraine patients, though the study's heterogeneity limited its conclusions. Bousser (2004) noted that migrainous infarcts are rare and typically affect the posterior circulation of the brain.

The role of migraine as a risk factor for ischaemic stroke is particularly pronounced in young women. Bousser (2004) found that women with migraine with aura face a potentially three-fold higher risk of ischaemic stroke, especially when combined with tobacco use and oral contraceptive use. Øie et al. (2020) reviewed several studies, including five meta-analyses, and confirmed that the association between migraine and ischaemic stroke is stronger in women, especially those under 45 years, and further heightened by oral contraceptive use and smoking.

A comprehensive meta-analysis by Spector et al. (2010) assessed the link between migraine and ischaemic stroke across eight cohort studies and thirteen case-control

studies, involving over 600,000 patients aged 30 to 50 years. The analysis accounted for confounding factors such as hypertension, smoking, use of combined oral contraceptives, cholesterol levels, cardiac disease, and family history. The results indicated that patients with migraine with aura had a significantly higher risk of ischaemic stroke, with a pooled adjusted odds ratio of 2.3 (95% CI, 1.5 to 3.3). In contrast, no significant association was found for individuals with migraine without aura. Adelborg et al. (2018) further noted that the increased risk of stroke associated with migraine is most pronounced shortly after the migraine diagnosis, particularly in women, but tends to diminish over the long term by extending up to 19 years.

Furthermore, migraine may also be a symptom of underlying conditions that predispose individuals to both stroke and migraine attacks. Gryglas and Smigiel (2017) discussed how hereditary vasculopathies, such as cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL), and other genetic disorders like mitochondrial encephalopathy with lactic acidosis and stroke (MELAS), are associated with migraine and stroke-like episodes. Several studies have explored the association between migraine and patent foramen ovale (PFO). Dowson et al. (2008), Ailani (2014), Kahya et al. (2015), and Larrosa et al. (2016) found a higher prevalence of PFO in individuals with migraines, particularly those with aura. Lantz et al. (2015) observed that in migraineurs who experienced stroke, the prevalence of PFO was notably higher and the average age of stroke onset was lower compared to controls. Despite these findings, routine detection and closure of PFO for migraine prevention are not supported by overall evidence, as the benefits do not outweigh the risks (Chessa et al., 2009; Butera et al., 2010; Finocchi & Del Sette, 2015). In essence, the relationship between migraine and ischaemic stroke, especially in young adults illustrates the need for further research to clarify underlying mechanisms and to assess the impact of lifestyle factors and comorbid conditions. While migraine with aura is associated with a higher risk of stroke, the complex nature of this relationship and the potential role of PFO in stroke occurrence necessitate a deeper approach to diagnosis and management.

2.4.4 Stroke in the Puerperium

Stroke incidence rates among young adults during the puerperium vary widely, with estimates ranging from 4 to 210 per 100,000 deliveries (James et al., 2005). Miyakis

et al. (2006) observed that stroke complicates approximately 34 in 100,000 deliveries and accounts for at least 12% of maternal deaths. Most strokes associated with pregnancy occur during the peripartum period or in the postpartum phase (Jaigobin and Silver, 2000; Jeng et al., 2004).

The risk of ischaemic stroke significantly increases in the six weeks following childbirth, with a relative risk of 8.7 (Simolke et al., 1991; Sharshar et al., 1995). This period also sees a heightened prevalence of cerebral vein thrombosis (Jeng et al., 2004; Treadwell et al., 2008). During pregnancy, the relative risk of intracerebral hemorrhage is 5.6. When considering both intracerebral and subarachnoid hemorrhages, there is a 2.5-fold increased risk of haemorrhagic stroke during pregnancy and a remarkable 23.8-fold increased risk in the postpartum period (Treadwell et al., 2008). Notably, about half of aneurysmal ruptures in women under 40 occur during pregnancy (Treadwell et al., 2008).

The high risk of stroke during the puerperium is influenced by various factors. While age and underlying conditions like hypertension, pre-eclampsia, and Type 2 diabetes mellitus (T2DM) are significant risk factors, the risk is not entirely dependent on these factors. Stroke during pregnancy and the postpartum period can affect women regardless of age or pre-existing conditions, though older women and those with additional risk factors may have an elevated risk.

The aetiology of stroke during pregnancy includes a range of factors. Haemorrhagic and ischaemic strokes during pregnancy are often related to pre-eclampsia and eclampsia, which account for 25-45% of pregnancy-related stroke cases (Cantu and Barinagarrementeria, 1993; Kittner et al., 1996). Other contributing factors include arterial dissection, peripartum cardiomyopathy, paradoxical embolism, amniotic fluid embolism, postpartum cerebral angiopathy, and cerebral vein thrombosis (Griffiths and Sturm, 2011). These conditions can lead to stroke regardless of the patient's age, though they are often exacerbated by other risk factors.

2.4.5 Antiphospholipid Antibody Syndrome (APS)

Antiphospholipid Antibody Syndrome (APS) is a significant risk factor for ischaemic stroke, particularly in young adults. A cohort study involving individuals with an

average age of 42 years found that ischaemic stroke is the most common manifestation of arterial thrombosis in APS patients (Cervera et al., 2002). This diagnosis aligns with the Sapporo criteria, which are used to assess and diagnose APS (Miyakis et al., 2006; Wilson et al., 1999). There is a general agreement that individuals meeting the criteria for APS are at an increased risk of thrombotic events, including stroke. Case-control studies consistently show a higher prevalence of antiphospholipid antibodies among young adults who have had an ischaemic stroke (Brey et al., 2002; Nagaraja et al., 1997). However, there is a notable lack of research on whether these antibodies persist following an ischaemic stroke in young adults. This gap in the literature highlights the need for further investigation to understand the long-term implications of antiphospholipid antibodies in stroke patients.

2.4.6 Nonatherosclerotic Vasculopathies

Nonatherosclerotic vasculopathies contribute significantly to stroke cases in young adults. These conditions include cervical artery dissection, various forms of vasculitis, infections such as HIV, radiation vasculopathy, and rare disorders like CADASIL, MELAS, RCVS, Moyamoya disease, Sneddon's syndrome, Fabry's disease, and malignancies (Griffiths and Sturm, 2011). Among these, cervical artery dissection is the most prevalent; it accounts for approximately 20-25% of stroke cases in young individuals (Kristensen et al., 1997; Putaala et al., 2009). More so, vasculitis related to infection follows, with prevalence rates varying by geographic region, sometimes reaching up to 7%. Moyamoya disease is notably more common in Asian populations, where it represents 6-15% of nonatherosclerotic vasculopathy cases, in contrast to the 1-5% prevalence of migraine-related cases (Kristensen et al., 1997; Putaala et al., 2009). Overall, nonatherosclerotic vasculopathies collectively account for 7-25% of stroke cases in young adults. These conditions exhibit significant ethnic, geographical, and genetic variations, leading to differing prevalence rates across different populations (Rasura et al., 2006; Varona et al., 2007).

2.4.7 Hypercoagulable Traits

Hypercoagulable states, whether inherited or acquired, are important contributors to stroke in young adults. Research by Kenet et al. (2010) showed the role of various hypercoagulable traits in pediatric stroke. Meta-analyses reveal that certain inherited

conditions, such as protein C deficiency, antithrombin III deficiency, antiphospholipid antibodies, elevated lipoprotein(a), factor V Leiden mutation, protein S deficiency, factor II G20210A mutation, and MTHFR C677T mutation, are more prevalent in children with stroke compared to healthy individuals. In young adults, hypercoagulable traits are also significant. A registry study reported that 15.9% of young adults tested for hypercoagulable panel abnormalities had at least one such condition (Ji et al., 2013). These findings emphasize the importance of screening for hypercoagulable states in young stroke patients, as these factors can significantly influence stroke risk.

2.4.8 Moyamoya Disease

Moyamoya disease is a rare cerebrovascular condition characterised by progressive narrowing of the internal carotid arteries and their major branches, leading to the development of a network of small, abnormal blood vessels to compensate for the reduced blood flow. This disease typically presents in two distinct age groups. According to Sultan and Elkind (2013), in a study of Chinese patients undergoing surgical treatment for Moyamoya disease, there are two primary peaks in incidence: one between the ages of 5 and 9 years, and another between 25 and 44 years. This bimodal pattern is particularly notable in Asian populations, where the disease is more prevalent compared to other regions.

2.4.9 Arterial Dissection

Arterial dissection is a significant cause of ischaemic stroke in young adults, accounting for approximately 10-25% of cases. This condition involves a tear in the artery wall, which can occur either in the cranial arteries or externally in the carotid or vertebral arteries. Dissections in the cervical arteries, particularly the carotid and vertebral arteries, can result in a wide range of complications, including ischaemic stroke. Despite its prominence, the precise cause of cervical artery dissection remains unclear. Studies have identified potential factors such as trauma, infection, fibromuscular dysplasia, and connective tissue disorders, but robust evidence linking these factors to dissection is lacking (Debette and Markus, 2009; Kristensen et al., 1997). Genetic predisposition is suggested by the frequent observation of connective tissue defects in affected individuals and the familial clustering of cases.

Recent research highlights the role of environmental factors and genetic predisposition in arterial dissection. For instance, Morris et al. (2011) found a correlation between the degree of vertebral artery tortuosity and the age of onset of arterial dissection, particularly among individuals with connective tissue disorders. Data from the U.S. National Fibromuscular Dysplasia (FMD) registry further illustrate the impact of arterial dissection and related vascular complications. Among the participants, 19% experienced transient ischaemic attacks or strokes, 20% had a history of arterial dissection, and 17% had aneurysms (Olin et al., 2012). These findings underscore the importance of considering both genetic and environmental factors when diagnosing and managing arterial dissection.

2.4.10 Haemorrhagic Stroke

Haemorrhagic stroke includes both subarachnoid hemorrhage (SAH) and intracerebral hemorrhage (ICH); it represents a significant proportion of all strokes in individuals under 45 years of age. Various studies have consistently reported the incidence rates of SAH ranging from 3 to 6 per 100,000 per year, and for ICH, the rates range from 2 to 7 per 100,000 per year (Jacobs et al., 2002; Marini et al., 2001). These statistics underline the importance of recognizing haemorrhagic stroke as a substantial concern in this demographic. The aetiology of ICH in younger adults shares similarities with those found in older adults, yet some distinctions are noteworthy. In particular, young adults demonstrate a higher prevalence of arteriovenous malformations (AVMs), cavernomas, and bleeding disorders manifesting early in life, as well as drug abuse, which significantly contributes to the risk of ICH (Smajlović, 2015). This increased incidence of specific risk factors in younger populations may reflect both genetic predispositions and environmental influences, such as exposure to illicit drugs. Cocaine and amphetamines, for instance, have been closely associated with an increased risk of haemorrhagic stroke, further complicating the management of stroke in younger patients (Smajlović, 2015).

Subarachnoid hemorrhage (SAH) is similarly prevalent in younger adults, with aneurysms in this group exhibiting similar locations and clinical characteristics as those seen in older adults. The management and diagnosis of SAH also remain consistent across age groups. However, hypertension, which is a well-documented cause of intracranial hemorrhage in older adults, continues to play a crucial role in

younger populations as well (Boehme et al., 2017). The persistence of hypertension as a leading cause across age groups shows the need for effective blood pressure management as a preventive measure against haemorrhagic stroke.

Ethnic and geographical variations also play a role in the incidence and outcomes of haemorrhagic stroke. For example, studies have shown that young Black Americans exhibit higher rates of intracranial hemorrhage, likely due to the prevalence of hypertension within this population (Jacobs et al., 2002). Similarly, Onwuchekwa et al. (2009) reported a relatively high incidence of intracranial hemorrhage among young Nigerians. However, the study's findings were somewhat limited by the lack of access to CT scans, which may have resulted in underreporting. On the other hand, the relatively low proportion of haemorrhagic stroke cases reported in Saudi Arabia, where only 13% of strokes are haemorrhagic, suggests that environmental, cultural, or healthcare-related factors may influence stroke patterns in different regions (Al Rajeh and Awada, 2002).

In contrast to these regions, the Northern Manhattan Stroke Study documented an increased risk of intracerebral hemorrhage among Hispanics; this pointed to the importance of considering ethnic background when assessing stroke risk (Jacobs et al., 2002). This geographical and ethnic variability in haemorrhagic stroke incidence further emphasizes the need for tailored public health strategies and interventions aimed at addressing the unique risk profiles of different populations. These findings show that the complexity of haemorrhagic stroke in young adults necessitates a multifaceted approach that considers not only the traditional risk factors seen in older populations but also the unique challenges posed by younger patients.

2.4.11 Venous Thrombosis

Cerebral venous thrombosis (CVT) is recognized as a relatively rare cause of stroke, but it occurs more frequently among young adults compared to older populations. According to Sultan and Elkind (2013), CVT accounts for a noteworthy proportion of stroke cases in this demographic. The International Study on Cerebral Venous and Dural Sinuses Thrombosis (ISCVT) adult registry highlights that the mean age for CVT onset is 37 years. Several risk factors for CVT have been identified, many of which overlap with those for arterial stroke, such as thrombophilia, oral contraceptive use,

and pregnancy. This overlap complicates the diagnostic process, particularly because CVT can present with non-specific symptoms such as papilledema, seizures, and headaches. These symptoms, although common, can be misleading and lead to potential delays in diagnosis and treatment. The challenge in diagnosing CVT is further compounded by its rarity, which often leads to lower clinical suspicion in young patients presenting with these symptoms.

The importance of prompt and accurate diagnosis cannot be overstated, as delayed treatment can result in severe neurological deficits or even death. Although imaging techniques such as MR venography have improved the detection of CVT, there remains a need for heightened awareness among clinicians, particularly when encountering young patients with unexplained neurological symptoms. The combination of risk factors and varied clinical presentation necessitates a high index of suspicion to ensure timely diagnosis and management of this potentially life-threatening condition.

2.4.12 Genetic Thrombophilia

The role of genetic factors in predisposing individuals to ischaemic stroke has been extensively studied, yet the findings remain inconclusive and somewhat controversial. Factor V Leiden mutation, a common genetic variant associated with increased thrombotic risk, has been the subject of numerous investigations. Alhazzani et al. (2018) conducted a meta-analysis involving 6,860 patients and 18,025 controls, which identified a statistically significant but relatively modest association between the Factor V Leiden mutation and ischaemic stroke. Notably, this association was slightly stronger in individuals who experienced stroke onset before the age of 40, suggesting that genetic predisposition may play a more critical role in younger populations.

In contrast, the prothrombin G20210A mutation, another genetic variant linked to thrombophilia, has shown inconsistent results in relation to ischaemic stroke. Although Jiang et al. (2014) found no significant overall association between the mutation and early-onset ischaemic stroke, they did observe a notable connection in a younger subgroup, with an odds ratio of 5.9 (95% CI, 1.2 to 28.1). This suggests that, although rare, the mutation could significantly increase stroke risk in specific populations, particularly younger individuals.

Moreover, deficiencies in natural anticoagulants such as protein C and antithrombin III, while exceedingly rare (occurring in less than 1% of the population), have been identified as potential contributors to ischaemic stroke. However, these associations have been inconsistent across studies. For instance, although some observational cohort studies suggest a link, these findings have not been consistently replicated in case-control studies or meta-analyses (Folsom et al., 2009; Morris et al., 2010). This inconsistency raises questions about the clinical significance of these deficiencies in the broader population.

It is also crucial to consider the potential synergistic effects of multiple thrombophilic factors, particularly when combined with modifiable risk factors. Some studies, such as those by Pezzini et al. (2005, 2006), have suggested a gene-dose effect, where the presence of multiple prothrombotic variants, coupled with risk factors like tobacco smoking, hypertension, and the use of combined oral contraceptives, may exponentially increase the risk of ischaemic stroke in young adults. This gene-environment interaction shows the complex nature of stroke risk in younger populations and shows the need for a multifaceted approach in both research and clinical practice.

2.4.13 Genome-Wide Risk Variants

Recent advances in genome-wide association studies (GWAS) have provided valuable insights into the genetic underpinnings of early-onset ischaemic stroke to identify specific risk loci that may contribute to the development of this condition in young adults. Cheng et al. (2016b) conducted a comprehensive GWAS involving 4,505 young stroke patients and 21,968 controls across three distinct ethnic groups. This study led to the identification of a novel age-specific locus at 10q25, which was linked to ischaemic stroke across all subtypes. This locus is located near the HABP2 gene, which encodes an extracellular serine protease involved in the regulation of coagulation, fibrinolysis, and inflammatory pathways. The identification of this locus suggests a biologically plausible mechanism through which genetic variation may contribute to the pathogenesis of ischaemic stroke in younger individuals (Cheng et al., 2016a).

The findings from Cheng et al. (2016b) are particularly significant as they highlight a potential genetic basis for early-onset stroke, which has been less extensively studied compared to stroke in older populations. However, it is important to approach these findings with caution, as the identified locus at 10q25, while statistically significant, requires further validation in larger independent cohorts. Moreover, the functional role of HABP2 in stroke pathology remains to be fully elucidated, and additional research is needed to explore how this gene interacts with other genetic and environmental risk factors.

Similarly, Debette et al. (2015) conducted a GWAS as part of the Cervical Artery Dissection and Ischaemic Stroke Patients (CADISP) study, involving 1,393 patients with cervical artery dissection (CAD) and 14,416 controls. This study identified a previously unreported genome-wide risk locus for CAD at the PHACTR1 gene, along with several other loci that showed strong but not definitive associations. The rs9349379(G) allele at PHACTR1 was found to be associated with a reduced risk of CAD, suggesting a protective effect against this particular subtype of stroke. Although these findings are promising, they are also preliminary. The discovery of the PHACTR1 locus adds to the growing body of evidence that genetic factors play a critical role in the susceptibility to specific stroke subtypes, particularly in younger individuals. However, the clinical utility of these findings is still uncertain. The protective effect observed with the rs9349379(G) allele needs to be confirmed in further studies, and the biological mechanisms through which PHACTR1 influences stroke risk must be better understood. Additionally, the potential interactions between these genetic variants and environmental risk factors, such as smoking, hypertension, and lifestyle choices, remain largely unexplored.

2.5 Geographical Variations in the Aetiology of Stroke in Young Adults

The aetiology of stroke in young adults varies significantly across different geographical regions, and this is influenced by both genetic factors and environmental exposures. Moyamoya disease, an uncommon non-atherosclerotic arteriopathy exemplifies this variation. It is particularly prevalent in young adults in East Asian countries. Shang et al. (2020) reported that Moyamoya disease constitutes a significant cause of stroke in young adults within these regions. Baba et al. (2008) observed the highest prevalence in Japan, with rates as high as 10.5 per 100,000

individuals. Similarly, Ahn et al. (2014) found a prevalence of 16.1 per 100,000 individuals in Korea, and Miao et al. (2010) reported a prevalence of 3.92 per 100,000 persons in China. These findings show the regional specificity of Moyamoya disease, which is significantly less common in Western countries, where exact prevalence figures are less clear but substantially lower.

This stark contrast between Asian and Western populations raises important questions about the genetic and environmental factors contributing to the development of Moyamoya disease. Although incidence rates in Asian countries are notably high—0.94 per 100,000 in Japan, 2.3 per 100,000 in South Korea, and 0.43 per 100,000 in China—Western regions such as Washington and California report much lower incidence rates, around 0.086 per 100,000 (Uchino et al., 2005). These disparities suggest that both genetic predispositions and environmental exposures unique to these regions may play critical roles in the pathogenesis of Moyamoya disease.

In contrast to developed countries, where infectious causes of stroke are infrequent, developing countries continue to grapple with a significant burden of infection-related strokes. In regions with limited healthcare resources, such as parts of Southeast Asia, Africa, and the Middle East, preventable infectious diseases remain common causes of stroke in young adults. For instance, Chagas disease caused by the tropical protist Trypanosoma cruzi, has a prevalence of 6.6 million people predominantly in Central and South American countries (Cardoso et al., 2014). The exact incidence of stroke in young adults with Chagas disease is difficult to ascertain, as many infected individuals are asymptomatic, but the disease can lead to cardiomyopathy and significantly increase stroke risk.

Similarly, rheumatic heart disease which results from an abnormal immune response to untreated group A streptococcal infection remains a prevalent cause of cardioembolic stroke in young adults in developing regions. Boot et al. (2020) reported that rheumatic heart disease continues to be a significant health concern, with prevalence rates ranging from 1.8% to 2.0% in Northern America and Europe, to as high as 23.2% in some parts of Asia (Wang et al., 2013a). These infections, alongside other conditions such as HIV, neurocysticercosis, and tuberculosis, contribute to the high incidence of stroke in these regions. Abdallah et al. (2018) highlighted that in Sub-

Saharan Africa, where HIV prevalence is among the highest globally, stroke is often the first manifestation of HIV infection, with young stroke patients with HIV exhibiting more severe strokes and a higher likelihood of coagulopathy compared to their HIV-negative counterparts.

The role of sickle cell disease (SCD) in stroke incidence also illustrates significant geographical variation. SCD is particularly prevalent in Africa, which accounts for 75% of global cases, followed by Southeast Asia, Europe, and the Americas (Piel et al., 2013). The incidence of stroke in individuals with SCD increases with age, reaching 740 per 100,000 person-years in young adults aged 35 to 64 years in the USA. While traditionally considered a monogenic disorder with stroke as a primary manifestation, recent findings from a meta-analysis by Hyacinth et al. (2018) suggest that sickle cell trait may not significantly correlate with the incidence of ischaemic stroke among African Americans, this indicates the need for further research to clarify the relationship between SCD and stroke risk.

Furthermore, neurocysticercosis, a parasitic infection caused by the larval stage of the tapeworm Taenia solium, is another significant but geographically specific cause of stroke. Benjamin et al. (2017) noted that this condition is closely associated with cultural practices and inadequate sanitation, predominantly affecting rural populations in sub-Saharan Africa, Latin America, and Asia. The disease can lead to stroke by causing inflammation and subsequent narrowing or occlusion of cerebral vessels. Moreover, arterial dissection, a less common but important cause of ischaemic stroke in young adults, shows geographical variation in its prevalence. Boot et al. (2020) reported that arterial dissections account for up to 15% of all young stroke cases, with extracranial dissections being more common in Europe, while intracranial dissections are more prevalent in Asia. This regional variation may be influenced by differences in genetic susceptibility, environmental exposures, and access to appropriate imaging technologies.

2.6 Risk Factors of Stroke in Young Adults

2.6.1 Illicit Drugs and Smoking

Illicit drug use is a significant and multifaceted risk factor for ischaemic stroke in young adults. Fonseca and Ferro (2013) emphasized that drugs such as cannabis, opiates, cocaine, amphetamines, and designer drugs can substantially elevate the risk of stroke through various mechanisms. These include acute hypertensive crises, vasoconstriction, platelet activation, accelerated atherosclerosis, toxic vasculitis, cardiac arrhythmias, cardiomyopathy, and the heightened risk of septicemia and endocarditis among intravenous drug users. This broad spectrum of potential mechanisms highlights the complex interplay between illicit drug use and stroke, suggesting that both direct vascular effects and secondary complications contribute to the increased risk.

Cheng et al. (2016a) further elaborated on the impact of the mode and route of drug administration on stroke risk. Notably, the authors found that cocaine use within 24 hours is associated with a six-fold increase in the risk of ischaemic stroke compared to non-use. This significant elevation in risk shows the acute dangers posed by certain drugs, particularly those like cocaine that have potent sympathomimetic effects leading to severe hypertension and vasospasm. Moreover, the study's findings suggest that even short-term or occasional use of such substances can have catastrophic consequences, thereby raising important considerations for both clinical practice and public health interventions aimed at reducing stroke risk among young adults.

Furthermore, cannabis, often perceived as a relatively benign substance, has also been linked to an increased risk of ischaemic stroke. Rumalla et al. (2016) observed that cannabis use is associated with a higher incidence of stroke in young adults, challenging the commonly held belief that cannabis is a safe recreational drug. The mechanisms by which cannabis may increase stroke risk are still under investigation, but proposed pathways include cannabinoid receptor-mediated vasoconstriction and prothrombotic effects, as well as the potential for cannabis to exacerbate other risk factors such as hypertension. These findings call for a reevaluation of the risks associated with cannabis use, particularly as its legalization and use increase in many parts of the world.

Smoking is another critical risk factor that has become increasingly prevalent among young adults that contributes significantly to the incidence of stroke in this population. George et al. (2017) and Hauer et al. (2017) noted that smoking rates among young adults have risen over the past decade, with a substantial proportion of young stroke patients identifying as current or recent smokers. Putaala et al. (2009; 2012) reported that up to 50% of young stroke patients are smokers, a figure that underscores the strong association between smoking and stroke risk in this demographic.

The study by Kivioja et al. (2018) provides compelling evidence of smoking's impact on stroke risk in young adults. They reported a population-attributable risk (PAR) of 19.9% for smoking, with an odds ratio (OR) of 1.78, indicating that smoking significantly contributes to stroke occurrence in this age group. Additionally, a stronger dose-response relationship between smoking and ischaemic stroke risk has been observed in younger adults compared to older populations (Bhat et al., 2008; Markidan et al., 2018). This suggests that young adults may be more vulnerable to the harmful effects of smoking, possibly due to a combination of physiological factors and the longer cumulative exposure to smoking-related toxins over their lifetime.

The geographical variations in smoking prevalence further illustrate the global disparities in stroke risk. O'Donnell et al. (2016) reported that smoking prevalence is highest in Europe (28.7%) and Southeast Asia (24.8%), with the lowest rates observed in Africa (13.9%). The corresponding stroke risk varies widely, with a PAR of 4.5% in Africa and 18.0% in Western Europe, North America, and Australia. These differences highlight the importance of regional public health strategies tailored to the specific smoking patterns and associated stroke risks in different parts of the world.

Reitsma et al. (2017) also noted significant gender and racial disparities in smoking prevalence. The authors found that daily smoking rates are higher in men (25%) compared to women (5.4%), and that smoking prevalence is higher among whites (30.6%) compared to blacks (18.5%) (Pathak and Sloan, 2009). These disparities may reflect underlying socioeconomic, cultural, and environmental factors that influence smoking behavior and, consequently, stroke risk. Moreover, Sultan and Elkind (2013) highlighted the role of sympathomimetic drugs like cocaine, crack, and amphetamines

in contributing to ischaemic stroke in young adults, primarily through mechanisms such as hypertensive effects and platelet aggregation. Bhattacharya et al. (2011) further supported this by showing that patients with cocaine-related ischaemic stroke were, on average, ten years younger than non-cocaine-related ischaemic stroke patients. These findings indicate the profound impact of these substances on younger populations.

2.6.2 Air Pollution

Air pollution has increasingly been recognized as a significant global risk factor for stroke that affectd both young and older adults. The rapid pace of economic development, particularly in low- and middle-income countries, has led to major changes in air quality. These changes are largely driven by increased energy demands, urbanization, expanded transportation networks, and widespread industrialization, which together contribute to the deteriorating air quality (Mateen and Brook, 2011). According to Feigin et al. (2026), air pollution is responsible for 29.2% of the global stroke burden, with a disproportionately high impact in low- and middle-income countries, where it accounts for 33.7% of the burden compared to 10.2% in high-income countries. This significant disparity reveals the uneven distribution of environmental health risks in regions most affected by poor air quality. The disparity in stroke-related mortality due to air pollution can be partly attributed to the fact that a staggering 97% of cities in low- and middle-income countries with populations exceeding 100,000 fail to meet the World Health Organization's (WHO) air quality guidelines. In contrast, only 49% of cities in high-income countries fall short of these guidelines (Mossa-Basha and Wasserman, 2016). These statistics reveal a stark environmental inequity that is likely exacerbating health disparities, including the incidence of stroke, across different global regions.

However, the relationship between air pollution and stroke in young adults remains underexplored, particularly in low-income settings where the impact might be most pronounced. One notable study, a case-crossover analysis from Israel, suggests that air pollution is associated with an elevated risk of stroke in young adults. The study reported an odds ratio (OR) of 1.10 (95% CI 1.02 to 1.20) for young adults, which was higher than the OR of 1.00 (95% CI 0.96 to 1.03) for patients over 65 years of age (Yitshak Sade et al., 2015). This finding is particularly concerning as it indicates that

younger populations, who are typically considered at lower risk for stroke, may be more vulnerable to the adverse effects of air pollution than previously thought. Moreover, the study found that individuals living within 75 meters of a main road faced an even greater risk of stroke (OR=1.26; 95% CI 1.04 to 1.51), further emphasizing the role of proximity to traffic-related air pollution as a critical factor in stroke risk among young adults. Despite these insights, there remains a significant gap in the literature regarding the effects of air pollution on stroke risk among young adults in low-income countries. The absence of data from these regions is particularly troubling given the high levels of air pollution and the potentially greater susceptibility of young populations due to factors such as poorer access to healthcare, higher prevalence of other risk factors, and lower socioeconomic status.

2.6.3 Alcohol

Alcohol consumption, particularly recent and chronic heavy drinking, has been consistently linked to an increased risk of stroke in young adults. Chiu et al. (2015) found that both binge drinking and sustained heavy alcohol use are significant risk factors for stroke in this age group. Hillbom and Numminen (1998) provided further insight into the mechanisms underlying this association, noting that alcohol consumption increases stroke risk primarily through its effects on cardiac arrhythmias, hemostasis, fibrinolysis, and blood clotting. Additionally, heavy drinkers are more prone to head and neck trauma, which can predispose them to cervical artery dissection, a known cause of ischaemic stroke in young adults.

The relationship between alcohol consumption and stroke is also marked by regional disparities, which can be attributed to differences in drinking patterns and the type of alcohol consumed. O'Donnell et al. (2017) noted that the prevalence of alcohol-related stroke is higher in high-income countries compared to low-income countries. This finding may reflect the greater availability and cultural acceptance of alcohol in wealthier nations, where heavy drinking is more common. Furthermore, the study revealed that episodic heavy alcohol consumption is more prevalent among men than women, which could partly explain the higher incidence of stroke in young male adults.

Furthermore, Aigner et al. (2017) conducted a study in European countries and found that engaging in heavy episodic alcohol consumption significantly increases the risk

of stroke in young adults, with a population attributable risk (PAR) of 17.3% (95% CI 14.2 to 20.5) and an odds ratio (OR) of 2.2 (95% CI 1.9 to 2.5). This strong association suggests that alcohol is a critical modifiable risk factor in this population. The study's findings are particularly important in the context of Europe, where heavy episodic drinking is a common cultural practice, especially among young men. These findings show the need for targeted public health interventions aimed at reducing heavy drinking among young adults as a means of preventing stroke. In addition to the direct effects of alcohol on stroke risk, the social and behavioral contexts in which heavy drinking occurs also contribute to the overall risk. Young adults who engage in heavy episodic drinking are more likely to engage in other risky behaviors, such as smoking and drug use, which further compounds their stroke risk.

2.6.4 Oral Contraceptives and Pregnancy

The use of combined oral contraceptives (COCs) has been extensively studied for its association with an increased risk of ischaemic stroke in young women. Roach et al. (2015) conducted a study that demonstrated a 1.7-fold to 6-fold higher risk of ischaemic stroke in women using COCs compared to non-users. This elevated risk is particularly concerning given the widespread use of oral contraceptives globally. The study further showed that the risk of stroke increases with higher doses of estrogen, with a doubling of risk in women taking pills containing ≥ 50 mcg of estrogen (Roach et al., 2015). These findings align with earlier studies that have consistently reported a dose-dependent relationship between estrogen levels and stroke risk. However, the mechanisms underlying this increased risk are multifactorial and include estrogen-induced changes in coagulation factors, increased platelet aggregation, and alterations in lipid metabolism, all of which can contribute to thrombus formation and subsequent ischaemic events.

Despite the clear association between COCs and stroke risk, it is important to consider the role of other factors that may modulate this risk. For instance, smoking, hypertension, and a history of migraines with aura are known to further elevate the risk of stroke in women using COCs. This suggests that the risk associated with oral contraceptive use is not uniform across all women but is influenced by a combination of genetic, environmental, and behavioral factors. The interaction between these factors and oral contraceptive use warrants further investigation to develop more

personalized approaches to contraceptive counseling and stroke prevention in young women.

Furthermore, pregnancy, though generally considered a physiological state, also presents a unique set of risks for stroke in the third trimester, during delivery, and in the postpartum period. Swartz et al. (2017) noted that while pregnancy-related stroke is relatively rare, occurring in fewer than 20 per 100,000 pregnancies, the risks during these critical periods are significant. The mechanisms of pregnancy-related ischaemic stroke are diverse and include a hypercoagulable state due to pregnancy, eclampsia, peripartum cardiomyopathy, amniotic fluid embolism, and reversible cerebral vasoconstriction syndrome (van Alebeek et al., 2018). These conditions can lead to significant maternal morbidity and mortality, particularly if not promptly recognized and managed.

Moreover, pregnancy-related strokes often occur in younger women who may not have traditional risk factors for stroke, thereby making early diagnosis challenging. The hypercoagulable state induced by pregnancy is a well-documented phenomenon, driven by increased levels of procoagulant factors, decreased fibrinolysis, and vascular changes that promote clot formation. This state is further exacerbated in cases of preeclampsia and eclampsia, where endothelial dysfunction and systemic inflammation contribute to an increased risk of stroke. Additionally, the postpartum period is characterised by significant physiological changes, including the reversal of the hypercoagulable state, which can paradoxically increase the risk of thrombotic events as the body readjusts.

2.6.5 Chronic and Recent Infections

Infections have been increasingly recognized as important contributors to stroke risk, particularly through mechanisms that induce a prothrombotic state, endothelial dysfunction, and inflammatory responses. Putaala (2020) emphasized that infections can increase the risk of stroke via various pathways, including endothelial dysfunction, platelet activation, alterations in serum lipids that favor atherogenesis, and the induction of a hypercoagulable state. Infective endocarditis, meningoencephalitis, and HIV are examples of infections that can directly cause stroke, while others, such as respiratory tract infections, primarily serve as significant risk factors (Putaala, 2020).

Furthermore, respiratory tract infections have been proven as the most common acute infections associated with ischaemic stroke. Grau et al. (2010) reported that up to 10.7% of young stroke patients experienced an infection within four weeks prior to the stroke. This finding suggests a temporal relationship between infection and stroke, with the inflammatory and immune responses triggered by the infection potentially playing a role in the pathogenesis of stroke. The exact mechanisms by which respiratory infections increase stroke risk are not fully understood but may involve increased levels of circulating cytokines, acute phase reactants, and procoagulant factors that promote thrombosis. These findings reveal the importance of prompt and effective treatment of infections, especially in individuals who may already be at increased risk for stroke due to other underlying conditions.

Additionally, the COVID-19 pandemic brought renewed attention to the relationship between infections and stroke. Several studies have shown that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is associated with a higher likelihood of thrombotic vascular events, including stroke, than other coronaviruses and seasonal infectious diseases (Fifi and Mocco, 2020). Merkler et al. (2020) reported a 7.6-fold increase in the odds of stroke in patients with COVID-19 compared to those with influenza, highlighting the unique and severe impact of this virus on cerebrovascular health. The predominance of ischaemic stroke in COVID-19 patients, with a significant increase in cryptogenic aetiology as classified by the TOAST criteria, suggests that the virus may induce stroke through mechanisms that are not yet fully understood (Stein et al., 2021).

Studies have also described large vessel involvement in younger patients without traditional stroke risk factors or typical COVID-19 symptoms at the onset of stroke. This has been particularly evident in male and non-white individuals, who appear to be disproportionately affected (Oxley et al., 2020; Escalard et al., 2020). The potential mechanisms for COVID-19-related stroke include endothelial injury, hypercoagulability, and direct viral invasion of the central nervous system, all of which contribute to a prothrombotic state. The recognition of these risks has important implications for the management of COVID-19 patients, particularly those who are

young and otherwise healthy, as they may require more aggressive monitoring and intervention to prevent stroke.

Beyond acute infections, chronic infections such as periodontitis, chronic bronchitis, and infections with Helicobacter pylori, Chlamydia pneumoniae, cytomegalovirus, and HIV have also been linked to a heightened risk of ischaemic stroke (Grau et al., 2010; Carod-Artal and Gascon, 2010). These infections can contribute to chronic inflammation, endothelial dysfunction, and atherogenesis, creating a persistent state of heightened stroke risk. The chronic inflammatory response induced by these infections is believed to promote atherosclerosis, destabilize plaques, and increase the likelihood of thromboembolic events. The management of these chronic infections is therefore crucial not only for preventing their direct complications but also for reducing the long-term risk of stroke.

2.6.6 Cancer

The link between malignancy and stroke in young adults, has garnered increasing attention in recent years. Kivioja et al. (2018) identified active malignancy as a significant risk factor for ischaemic stroke, with an unadjusted odds ratio of 3.67. Although this association lost statistical significance after adjusting for cardiovascular risk factors, it reveals the complex relationship between cancer and vascular health. The findings of Bright et al. (2017), which indicate a twofold incidence of ischaemic stroke among cancer survivors aged 15-39, further highlight the vulnerability of this population. Putaala (2020) elaborates on the mechanisms linking cancer to stroke, including the prothrombotic effects of chemotherapy, the lasting impact of radiotherapy on the vasculature, and the direct effects of malignancy, such as tumor emboli and marantic endocarditis. These findings are relevant in younger cancer patients, who may face unique challenges due to the aggressive nature of their treatments and the longer duration of exposure to risk factors compared to older populations.

The study by Bright et al. (2017) also outlines specific cancer types that pose the greatest risk for future ischaemic stroke, including central nervous system tumors, head and neck tumors, and leukemia. These cancers not only have a direct impact on the cerebrovascular system but also often require intensive treatments that further exacerbate stroke risk.

2.7 Modifiable Cardiovascular Risk Factors

The prevalence and impact of modifiable cardiovascular risk factors in young stroke patients are well-documented, yet they present unique challenges compared to older populations. Smajlović et al. (2013) and Putaala et al. (2009, 2012a) consistently identify hypertension, smoking, and dyslipidemia as the most prevalent risk factors among young adults. However, the study by Putaala et al. (2009) suggests that the burden of these risk factors is substantial, with dyslipidemia affecting 60% of young stroke patients, smoking 44%, and hypertension 39%. These findings are corroborated by the larger European study (Putaala et al., 2012a), which found similar prevalence rates across different regions.

The Stroke in Young Fabry Patients (SIFAP) study further elucidates the clustering of risk factors such as abdominal obesity, tobacco smoking, physical inactivity, and hypertension in young adults (von Sarnowski et al., 2013). This clustering suggests a synergistic effect, where the presence of multiple risk factors significantly increases the likelihood of stroke. Moreover, the study highlights sex differences, with men more likely to exhibit multiple risk factors, indicating a need for targeted interventions based on sex-specific risk profiles. Aigner et al. (2017) also provide valuable insights into the population attributable risk (PAR) of various modifiable risk factors, with low physical activity, hypertension, heavy episodic alcohol consumption, and cigarette smoking together accounting for nearly 80% of the PAR in young stroke patients. This data underscores the importance of lifestyle interventions in this population, where behavioral modifications could have a substantial impact on reducing stroke risk.

The study by Kivioja et al. (2018) adds further insights by identifying strong associations between well-documented cardiovascular risk factors such as atrial fibrillation, cardiovascular disease, and diabetes mellitus, and ischaemic stroke in young adults. The data suggest that these conditions, while traditionally associated with older populations, are increasingly relevant in younger individuals, necessitating a broader approach to stroke prevention that includes aggressive management of these risk factors from an earlier age.

Moreover, studies from diverse geographic regions, including China and New Zealand, indicate that the prevalence of these risk factors among young adults experiencing

strokes is globally consistent (Wu et al., 2012; Zhang and He, 2012). This global perspective shows the universal nature of these risk factors, suggesting that successful prevention strategies in one region may be applicable elsewhere, with appropriate cultural and contextual adaptations.

2.7.1 Obesity and Physical Inactivity

Obesity and physical inactivity are critical risk factors for vascular diseases, including ischaemic stroke among young adults. Research consistently shows that elevated Body Mass Index (BMI) during childhood is associated with a higher risk of early-onset ischaemic stroke, particularly before the age of 55. Gjærde et al. (2017) found that the risk of stroke progressively increases with higher BMI, even starting from the 75th percentile in childhood BMI distributions. This suggests that childhood obesity has long-term implications for cardiovascular health, potentially predisposing individuals to stroke in adulthood.

Putaala et al. (2009) defines obesity as having a BMI of 30 or higher, a condition that affects more than 10% of young adults who experience strokes. The impact of obesity on stroke risk extends beyond just BMI. Winter et al. (2008) highlighted alternative obesity markers such as waist circumference, waist-hip ratio, and waist-height ratio, which may have a stronger association with stroke risk compared to BMI alone. This observation is supported by a European cohort study conducted by Bener et al. (2013), which identified abdominal obesity as a prevalent risk factor among young stroke patients. The study found that abdominal obesity was more common in women (73%) compared to men (64%), and was associated with increased risk of cardiovascular disease and type 2 diabetes.

The association between obesity and stroke risk is quantified by Aigner et al. (2017), who reported a Population Attributable Risk (PAR) of 6.9% for obesity in young adults, with an Odds Ratio (OR) of 1.2. This data reveals the significant impact of obesity on stroke risk, and indicates that even modest levels of excess weight can increase susceptibility to stroke. The parallel increase in obesity prevalence and stroke rates among young adults over the past three decades in both developed and developing countries further illustrates the growing concern (Gjærde et al., 2017; Ng et al., 2014).

Furthermore, geographical and demographic disparities in obesity prevalence among young stroke patients are significant. For example, obesity rates among young stroke patients are higher in the USA (61.1%), Europe (54.8%), and the Eastern Mediterranean (46%) compared to lower rates in Africa (26.9%), the Western Pacific (25.4%), and Southeast Asia (13.7%) (Arai et al., 2016; Yatsuya et al., 2014). Sex differences also emerge; Garawi et al. (2014) noted that obesity is more prevalent among young adult women compared to men. Racial disparities are also significant; Pathak et al. (2009) reported that morbid obesity diagnoses were more common among Black individuals compared to White and Hispanic individuals (10.9% vs. 9.2% vs. 7.8%, respectively; $p<0.0001$).

Additionally, physical inactivity compounds the risk associated with obesity. It is linked to a worsened cardiovascular risk profile and has been shown to significantly elevate stroke risk (Aigner et al., 2017). Among teenagers, physical activity levels vary by gender, with lower levels of activity observed in girls compared to boys (Yatsuya et al., 2014). This sex disparity highlights the need for targeted interventions to promote physical activity, particularly among young women, to mitigate the risk of stroke.

2.7.2 Hypertension

Hypertension or high blood pressure is a major risk factor for ischaemic stroke that affects approximately 35% of young adults (Béjot et al., 2014; Aigner et al., 2017). The Global Burden of Disease Study highlights significant regional disparities in the Population Attributable Risk (PAR) for hypertension. Southeast Asia exhibits the highest PAR for hypertension-related stroke at 54.8%, while Eastern and Central Europe, as well as the Middle East, show a lower PAR of 40.7% (Feigin et al., 2016). These variations show the influence of regional healthcare systems, lifestyle factors, and genetic predispositions on the prevalence and impact of hypertension. The study by Kivioja et al. (2018) showed that hypertension is a critical risk factor for ischaemic stroke, with a PAR of 25.5% (95% CI 22.1 to 28.2). This means that over a quarter of ischaemic stroke cases in young adults can be attributed to hypertension. Additionally, Aigner et al. (2017) found that hypertension is strongly associated with stroke, with an Odds Ratio (OR) of 2.3 (95% CI 2.0 to 2.6). This data indicates that individuals with hypertension are more than twice as likely to experience a stroke compared to those without hypertension.

The global prevalence data reveals significant variations in hypertension rates. The WHO reports that Africa has the highest prevalence of hypertension at 46%, while North America and South America have the lowest at 35% (Canaud et al., 2017). These differences can be attributed to various factors, including dietary habits, levels of physical activity, and access to healthcare. The higher prevalence in Africa may be linked to less access to effective hypertension management and preventive care compared to other regions.

2.7.3 Diabetes Mellitus

Diabetes mellitus is another critical risk factor for ischaemic stroke in young adults, with approximately 10% of young stroke patients diagnosed with the condition (Putaala et al., 2012; van Alebeek et al., 2018). Diabetes significantly increases the risk of stroke, with Aigner et al. (2017) reporting an Odds Ratio (OR) of 1.9 (95% CI 1.5 to 2.3) and a Population Attributable Risk (PAR) of 4.8% (95% CI 2.9 to 6.7). This indicates that diabetes contributes to nearly 5% of ischaemic stroke cases among young adults.

The regional disparities in diabetes prevalence and its impact on stroke risk are notable. Southeast Asia has the highest PAR for diabetes mellitus at 28.6%, suggesting a major burden of stroke attributable to diabetes in this region. In contrast, Western Europe, North America, and Australia have a lower PAR of 3.5% (Feigin et al., 2016). These variations reflect differences in diabetes management, healthcare accessibility, and prevalence of risk factors such as obesity and physical inactivity.

In the United States, there is a pronounced racial disparity in diabetes prevalence. Bhupathiraju and Hu (2016) report higher incidence rates among Black and Hispanic populations compared to White individuals, with non-Hispanic Blacks (16.3% to 20.6%) and Mexican-Americans (17.5% to 20.5%) showing the highest rates. Additionally, Pacific Islanders (18.3%), South Asians (15.9%), and Filipinos (16.1%) have the highest diabetes prevalence among all ethnic groups (Bhupathiraju and Hu, 2016). Geographical differences also exist in the subtypes of diabetes associated with stroke. Type 1 diabetes, which is less common than Type 2, shows varying incidence rates across regions. Kivioja et al. (2018) found that Type 1 diabetes has a notable

incidence rate in Finland (36.5 per 100,000 person-years) and a prevalence of 4.6% among young ischaemic stroke patients, with a stronger association observed in women compared to men. Conversely, Canaud et al. (2017) report a low incidence of Type 1 diabetes in China and Venezuela (0.1 per 100,000 person-years), reflecting regional differences in diabetes types and their associations with stroke.

2.7.4 Dyslipidemia

The prevalence of lipid disorders among young adults has been increasing globally, with significant variations across different regions. According to George et al. (2017), Europe has the highest prevalence of dyslipidemia at 54%, followed by North America at 48%, Southeast Asia at 29%, and Africa at 22.6%. This regional disparity appears to correlate with income levels, as higher income countries tend to report greater incidences of dyslipidemia (Esnault et al., 2016). For young stroke patients, dyslipidemia is very prevalent; it affects approximately 50% to 60% of this demographic. Interestingly, men show a slightly higher prevalence of dyslipidemia compared to women (Putaala et al., 2009; Putaala et al., 2012). This suggests a sex disparity in lipid disorders among young stroke patients, which warrants further investigation. Additionally, dyslipidemia is particularly associated with large artery disease and small vessel disease but is less common in strokes caused by cardiac embolism (Hauer et al., 2017). This association reveals the role of dyslipidemia in specific types of ischaemic stroke, though its overall impact appears less pronounced. Despite these observations, the association between dyslipidemia and the risk of all-cause stroke in young adults is not substantial.

A Population Attributable Risk (PAR) of -2.1% (95% CI -6.7 to 2.6) and an Odds Ratio (OR) of 0.9 (95% CI 0.8 to 1.1) indicate that dyslipidemia is not a significant independent risk factor for stroke in this age group (Aigner et al., 2017). This could be attributed to the multifactorial nature of stroke, where dyslipidemia might not be a predominant risk factor among young individuals. However, in cases of stroke associated with large artery or small vessel disease, dyslipidemia does appear to contribute to the risk, particularly in older adults. This demographic is more likely to experience strokes due to these conditions, which may explain the greater significance of dyslipidemia in their stroke risk profiles. Furthermore, the limited focus of many studies on only high low-density lipoprotein cholesterol (LDL-C) or low high-density

lipoprotein cholesterol (HDL-C) might have overlooked other important lipid variables. For example, the apolipoprotein B (ApoB)/apolipoprotein A-I (ApoA-I) ratio has been identified as a significant predictor of ischaemic stroke (Sabino et al., 2008); this suggests that a broader examination of lipid profiles could yield more comprehensive insights into the relationship between dyslipidemia and stroke risk. Additionally, research by Pathak et al. (2009) outlines racial disparities in the prevalence of dyslipidemia; it notes a higher prevalence among whites compared to Hispanics and blacks in Florida (21.0% vs. 17.1% and 17%, respectively; $p<0.0001$). This finding suggests that ethnic and regional differences influence the prevalence and impact of dyslipidemia on stroke risk.

2.8 Prognosis/Outcome of Stroke In Young Adults

According to Maaijwee et al. (2014), the prognosis for young adults who experience a stroke is not as optimistic as previously believed in the past. This is because of significant implications for both mortality and the physical/psychosocial challenges faced by stroke survivors. Krishnamurthi et al. (2015), noted that although strokerelated mortality has shown an overall decline in recent years, this improvement has been slower in young adults compared to older individuals. One of the primary reasons for this difference lies in the underlying causes of strokes, which have a substantial impact on both mortality and morbidity. In contrast, several studies show that the prognostic outcomes for young stroke patients are generally more favorable than for their older counterparts. A single tertiary stroke centre in Boston reported that 81% of young adult patients (aged 18–45 years) achieved a good outcome, at the time of hospital discharge (Ji et al., 2013).

The prognosis of stroke in young adults hold crucial significance, as young adults often have a longer expected lifespan compared to older stroke patients (Singhal et al., 2013). Besides, most young adults affected by stroke frequently shoulder significant stress, as they are typically primary earners for their families or responsible for childcare. The prognosis encompasses various aspects, including mortality, stroke recurrence, other vascular events, poststroke epilepsy, functional outcomes, poststroke depression, quality of life, return to work, and social consequences (Singhal et al., 2013).

Several studies have shown that the prognosis following a stroke in young adults are closely tied to the stroke's root cause, the extent of central nervous system (CNS) damage, and various other factors. Over the course of 30 days, the case fatality rate tends to be relatively low, especially for ischaemic strokes, ranging from 0% to 6%. In contrast, it can range from 20% to 36% for cases of intracerebral hemorrhage (Jacobs et al.; 2002; Spengos and Vemmos, 2010). When compared to Whites, the NOMASS data revealed that 30-day case fatality rates were higher among young Black and Hispanic individuals (Jacobs et al., 2002).

Among young adults, a higher proportion of strokes are haemorrhagic in nature. The case-fatality rate for ischaemic strokes is estimated to be 3.6%, whereas it significantly rises to 22% for intracerebral hemorrhage (ICH). It is worth mentioning that long-term mortality among young patients who experience ischaemic strokes is also alarmingly high. Studies indicate a cumulative mortality of 12.4% after 10 years and a staggering 26.8% after 20 years, with approximately half of these deaths attributed to vascular causes. This underscores that the underlying factors contributing to strokes at a young age continue to exert an influence on health throughout an individual's life (Maaijwee et al., 2014). Moreover, the journey to recovery for survivors is fraught with challenges that can hinder their ability to fully regain their normal lives. This is particularly pertinent for young stroke survivors who are of working age, as well as those who have dependents such as children or older parents (Maaijwee et al., 2014).

Long-term mortality rates provide a more critical perspective on stroke in young adults. A study by Putalaa et al. (2009) reported cumulative long-term mortality rates of 4.7% at 1 year and 10.7% at 5 years, for both male and female young adults. Similarly, a FUTURE cohort that focused on 30-day stroke survivors, observed a higher 20-year mortality rate compared to expected mortality in the underlying population (Carandang et al., 2006). In some populations, young adults exhibited more pronounced mortality differences. According to Eriksson et al. (2012), the Northern Sweden MONICA Stroke Registry (1985–2005) revealed that young age was associated with reduced survival among diabetic stroke patients. The impact of sex on mortality differences may vary depending on the time frame following the index stroke.

Another study conducted by Leys et al. (2002), which involved 287 young adult stroke patients, the mortality rate was 4.5%, with recurrence rates of 1.4% within the first year, decreasing to 1.6% and 1% in the subsequent two years, respectively. Furthermore, Leys et al. (2002) discovered that seizures affected 6.6% of the patients while myocardial infarction occurred in 0.2% of cases. In a similar study, Musolino et al. (2003), reported a recurrence rate of 7.4%, with over 80% of patients achieving a moderate to excellent outcome. The primary contributor to increased long-term mortality among young stroke patients is cardiovascular causes of death. Consequently, the accumulation of multiple vascular risk factors and the presence of large artery atherosclerosis as an etiological factor are associated with heightened long-term mortality risk (Putaala et al., 2009; Putaala et al., 2012).

In a population-based study conducted by Seminog et al. (2019), it was revealed that in the first decade of the 21st century, stroke-related mortality rates in England were cut in half. More so, stroke event rates experienced a reduction of approximately 20%, and 40% decrease in case fatality. The predominant factor behind the decline in stroke mortality rates (constituting 78% in men and 66% in women), was as a result of a reduction in case fatality (Seminog et al., 2019). The remaining 22% in men and 34% in women was attributed to a decrease in stroke event rates. In addition, there were notable discrepancies between different age groups. In young adults (aged < than 55 years), the reduction in stroke mortality was primarily attributed to improved survival rates, while in older adults (aged 85 years or older), both improved survival and a decrease in event rates played equally significant roles in reducing mortality (Seminog et al., 2019). More so, stroke rates exhibited an increase of 2% per year on average in young adults (aged 35 to 54 years) and contrasted with the declining trend observed in other older adults. In another study conducted in South London, Wang et al. (2013b) observed similar findings regarding age-specific rates reported in a stroke registry. Younger adults displayed an increase in stroke rates per year when compared to older adults in south London.

Furthermore, the risk of stroke recurrence in young adults is alarming. According to Putaala et al. (2010), during the first year following the initial stroke, the absolute risk of recurrence is nearly 3%, diminishing to 1% to 2% in subsequent years. However, this risk remains high for an extended period, with cumulative risks of approximately

10% at 5 years and 15% at 10 years. Additionally, the risk of cardiac events leading to hospitalization 15 years after stroke is comparable to that of recurrent stroke, hovering at approximately 20%. Furthermore, Putaala et al. (2011) using a database of 1,008 consecutive patients aged 15 to 49 with first-ever ischaemic stroke from 1994 to 2007 noted that cumulative recurrent ischaemic stroke rate at 10 years was 40.9% for type I DM (14 events), 29.7% for type 2 DM (15), and 12.0% for nondiabetic patients (94). This was most common in patients with an index cardioembolic infarct, followed by patients with an undetermined cause of infarct and nonatherosclerotic vasculopathy. Brain MRI follow-ups documented silent cerebral infarcts (lacunes) in 9.5% of patients, predominantly among those with embolism from a cardiac source and an undetermined cause of stroke.

Over the long term, poststroke complications extend beyond the physical aspect. According to Roivainen et al. (2013), approximately 5.5% of patients develop poststroke epilepsy within 3 years, increasing to 11.5% within a decade. Similarly, Central poststroke pain, which is often linked to severe stroke symptoms or haemorrhagic transformation of ischaemic lesions, affects 5.9% of survivors. Cognitive challenges are also prevalent, particularly among those with mild motor symptoms. Hunt and Cappuccio (2014) reported declines in cognitive skills in up to 50% of patients, primarily impacting processing speed, working memory, and attention. Other common poststroke issues include fatigue, with 41% of survivors reporting such symptoms compared to 18% in controls, as well as memory impairment (41%), depression (29%), anxiety (19%), and sleeping disorders (36%) (Waje-Andreassen et al., 2013). In terms of sexual functioning and future pregnancies, Van Alebeek et al. (2018), reported impaired sexual activity in almost 30% of stroke survivors 1 year after their strokes. Additionally, higher frequencies of pregnancy loss and pregnancy complications have been observed in women following ischaemic strokes compared to stroke-free mothers and the general population.

Returning to work can be challenging for a substantial proportion of young adults who experienced strokes. In a Finnish study tracking patients who were employed before their strokes, 37.6% were not working at 1 year, 42.0% at 2 years, and 46.9% at 5 years' post-stroke. According to Maaijwee et al. (2014), factors associated with not returning to work included the presence of large ischaemic lesions, neurologic deficits

detected using the National Institutes of Health Stroke Scale at hospital discharge, low income, and cognitive deficits even in cases of good motor recovery. According to Singhal et al. (2013), the estimates of the percentage of young stroke patients returning to work after their strokes vary, ranging from 42% to 53%, with 23% of those who returned requiring occupational adjustments.

According to Putaala (2020), therapy for young stroke patients regarding their prognosis and the repercussion of stroke is crucial and should be comprehensive, involving a multidisciplinary approach. Depending on the individual's needs, this counseling may encompass various specialties such as social work, occupational therapy, psychology/psychiatry, internal medicine, cardiology, urology, and clinical genetics. The study by Goeggel Simonetti et al. (2015) that focuses on stroke outcomes in young adults reveal that approximately 2 out of 5 young patients who experience an ischaemic stroke achieve complete or near-complete recovery, and nearly 9 out of 10 can regain their independence. Putalaa et al. (2009) observed that the fatality rate of young adults who receive counselling remains relatively low, at less than 3%.

In addition, Singhal et al. (2013), noted that functional outcomes revealed that functional independence, defined as no or slight disability and the ability to manage one's affairs without assistance ranged from 78% to 94% in various studies. Predictors of poor functional outcomes included diabetes and severe neurologic deficits upon admission. However, despite the majority of young adults regaining functional independence, there was a high prevalence of poststroke depression, reported in the range of 28% to 46%. Besides, fatigue was another common complaint, reported by 54% of patients. Quality of life was also compromised, particularly in dimensions related to physical functioning, role limitations due to physical health, and social functioning as assessed by the SF-36 questionnaire (Singhal et al. (2013). Toni et al. (2012) observed functional independence to be 72.1% in 18–50-year-olds, compared to 54.5% of 51–80-year-olds. Most of the predictors of functional independence at the 3-month mark included younger age, lower baseline systolic blood pressure, and no prior history of stroke (Toni et al., 2012).

2.9 SSNAP in Stroke Research

The Sentinel Stroke National Audit Programme (SSNAP) is an invaluable resource for stroke research, offering a comprehensive dataset on stroke care and outcomes in the UK. SSNAP is designed to assess the quality of stroke services, providing real-time data on key performance indicators such as treatment times, patient outcomes, and rehabilitation services. However, while it offers a wealth of data, using SSNAP data for research presents both opportunities and challenges that merit critique.

2.9.1 Strengths of SSNAP Data for Research

- **Comprehensive Data Collection:** SSNAP is recognized for its extensive coverage across hospitals in England, Wales, and Northern Ireland, encompassing over 80% of stroke admissions. The dataset captures multiple dimensions of stroke care, including patient demographics, acute care processes, and long-term outcomes. Studies such as those by Bray et al. (2018) and Rudd et al. (2017) have leveraged SSNAP to analyse the impact of organized stroke care on patient outcomes, demonstrating the usefulness of the data in assessing healthcare performance and informing policy decisions.

- **Longitudinal Tracking**: The ability to track patients over time is a significant advantage for research using SSNAP data. For example, Turner et al. (2016) used SSNAP data to assess long-term outcomes such as survival and disability at six months, allowing researchers to explore the trajectory of recovery and the long-term effects of interventions like thrombolysis. This longitudinal aspect is particularly beneficial in evaluating the effectiveness of stroke care pathways and rehabilitation services.

- **Granularity of Data:** SSNAP's granularity enables detailed analyses of specific care processes and patient subgroups. For instance, Hoffman et al. (2020) used SSNAP data to examine inequalities in stroke care and outcomes across different socio-economic and ethnic groups. The dataset's rich demographic variables allowed the researchers to identify disparities in access to care and tailor interventions to address these gaps.

2.9.2 Challenges in Using SSNAP Data for Research

- **Data Quality and Completeness:** One of the major challenges associated with SSNAP data is variability in data quality across different sites. Some hospitals may have more complete data, while others may suffer from missing or incomplete records, which can bias research findings. Bray et al. (2020) identified this issue when using SSNAP to assess the relationship between door-to-needle times and outcomes for thrombolysis, noting that incomplete data submissions from some hospitals limited the generalizability of their results.
- **Confounding Variables:** SSNAP data, while rich in clinical and demographic information, often lacks certain variables that are critical for robust observational research, such as socio-economic status beyond broad regional markers or detailed data on pre-existing conditions. Without controlling for these confounders, studies using SSNAP may overestimate or underestimate the impact of interventions. A study by Morris et al. (2019) used SSNAP data to assess the impact of mechanical thrombectomy on outcomes but acknowledged that the lack of granular comorbidity data limited their ability to adjust for all relevant factors.
- **Limited Scope of Outcomes:** While SSNAP provides data on some long-term outcomes like disability, its focus remains largely on acute care processes and short-term outcomes. This limits the ability of researchers to fully understand the impact of stroke care on long-term quality of life and social reintegration. Studies like that of McMeekin et al. (2019), which sought to evaluate the cost-effectiveness of acute stroke units, found that the lack of long-term quality-of-life data from SSNAP hindered their analysis.
- **Ethical and Data Privacy Considerations**: Using patient-level data from SSNAP also raises ethical issues around consent and data privacy, particularly in light of recent data protection regulations like the General Data Protection Regulation (GDPR). Researchers must navigate these legal requirements carefully, ensuring that patient confidentiality is maintained, which can limit the accessibility of certain data points.

SSNAP data provides a robust foundation for stroke research; it provides detailed insights into stroke care and outcomes across the UK. Studies like those by Bray et

al. (2018), Hoffman et al. (2020), and Turner et al. (2016) highlight the utility of SSNAP in evaluating stroke care pathways, treatment outcomes, and inequalities in healthcare access. However, researchers must be mindful of limitations such as data quality, confounding variables, and the scope of outcomes captured. Addressing these challenges through improved data collection practices and careful study design will enhance the potential of SSNAP data to contribute to meaningful advances in stroke care.

2.10 Gaps in the Literature

The journey through the extensive literature on stroke in young adults has shed light on the complex web of risk factors, etiological contributors, and prognostic outcomes. This comprehensive review has highlighted the evolving epidemiology of stroke, by challenging the conventional belief that it primarily afflicts the older people. However, several notable gaps and areas of potential future research emerge from this review. While many studies have examined individual risk factors for stroke in young adults, there's a limited focus on how these risk factors interact. For instance, how do genetic factors, lifestyle choices (e.g., smoking and physical inactivity), and medical conditions (e.g., diabetes and dyslipidemia) collectively contribute to stroke risk? Understanding these interactions could provide a more comprehensive risk assessment for young adults.

Furthermore, the literature review highlights that the prognosis for young stroke patients is not as favorable as previously believed, with significant challenges in terms of long-term mortality, recurrence, cognitive issues, and quality of life. However, more research is needed to explore these long-term outcomes in greater detail, including factors that influence recovery, rehabilitation strategies, and interventions to improve the quality of life for young stroke survivors. Lastly, the literature is sparse on studies that focus on young stroke, particularly in Southwest England. This research seeks to close this gap by analyzing the characteristics of stroke in young adults in Southwest England.

2.11 Research Hypothesis

This research seeks to characterise stroke in young adults in Southwest England. The key hypothesis is that young adults with stroke have a unique risk factor profile compared to older patients. The expected outcome is that stroke in young adults differs significantly from stroke in older adults in terms of risk factors, clinical presentation, and treatment outcomes. Traditional stroke risk factors, such as hypertension and diabetes, are well known in older populations. However, younger adults may have different contributing factors, including genetic predisposition, cardiac abnormalities such as patent foramen ovale (PFO), arterial dissection, and lifestyle-related risks such as illicit drug use and excessive alcohol consumption.

CHAPTER THREE
Research Methodology

3.1 Chapter Overview

This chapter focuses on the research design and data collection methods adopted in this study. It introduces the retrospective cohort study design used to analyse stroke in this study. It also details the selection of the study population - young adults with stroke. Additionally, this chapter justifies the Bristol Royal Infirmary (BRI) as the research location in the Sentinel Stroke National Audit Programme (SSNAP). Furthermore, this chapter outlines the data collection methods with a focus on the comprehensive SSNAP dataset. More so, this chapter covers the various statistical methods adopted in this research, including R programming, descriptive statistics, proportions, t-tests, and ANOVA.

3.2 PICO(T) Framework

Table 3.1 shows the PICOT table that outlines the entire endeavour of this research.

Component	Details
Population	Young adults aged 18 – 55 years
Intervention	Characterization of stroke in young adults
Comparison	N/A (since this is a retrospective study)
Outcome	- Frequency of stroke in young patients
	- Risk factors and prognosis of stroke in young patients
	- Clinical presentation of stroke in young patients
	- Recommendations to relevant authorities about stroke in young patients
Time	Data collected between 2013 and 2021
Study Design	Retrospective cohort study
Study Site	Bristol Royal Infirmary, University Hospitals Bristol and Weston NHS Foundation, Bristol
Inclusion Criteria	- Age 18 – 55 years
	- Primary diagnosis of stroke (coded as I-61, I-63, I-64)

	- Admitted between 2013 and 2021
Exclusion Criteria	- Diagnosis of subarachnoid haemorrhage
Variables	- Frequency of stroke in the young
	- Patient Characteristics:
	- Demographic Variables:
	- Age
	- Sex
	- Ethnicity
	- County of residence
	- Clinical Variables:
	- Type of stroke
	- Severity of stroke (NIHSS)
	- Exposures:
	- Traditional stroke risk factors
	- Risk factors specific to young people
	- Treatments:
	- Thrombolysis
	- Thrombectomy
	- Surgical
	- Outcomes:
	- Duration of admission
	- Case-fatality rate at 30 days

Table 3.1 PICOT TABLE

3.3 Research Design and Statistical Analysis

This study used a retrospective cohort design to analyse the characteristics of stroke in young adults at the Bristol Royal Infirmary Stroke Unit from 2013 to 2021. This approach was chosen because it allowed for the examination of past clinical records.

The data were sourced from the Sentinel Stroke National Audit Programme (SSNAP), which collects comprehensive stroke-related information, including patient demographics, risk factors, stroke subtypes, treatment approaches, and outcomes. Only patients aged 18 to 55 years with a confirmed diagnosis of stroke (ICD codes I-61, I-63, I-64) were included. Subarachnoid hemorrhage cases were excluded, as SSNAP does not record them.

Risk factors recorded in the SSNAP database were drawn from the patient's medical history at the time of stroke diagnosis, specifically during the initial clinical contact or assessment by the stroke team. The National Institutes of Health Stroke Scale (NIHSS) score, which evaluates the severity of the stroke, is also captured at this initial point of contact. To maintain the integrity of the dataset, only cases with both clinical and radiological confirmation of a stroke are included in the SSNAP database. This ensures that transient ischaemic attacks (TIAs) and conditions mimicking strokes are excluded, allowing the data to focus exclusively on true stroke events and enhancing the accuracy of the audit. In this research the entire dataset of eligible participants in SSNAP was used, as opposed to using a sample. This large sample size provided statistical power and precision for the research analysis. More so, given that stroke in young adults is a relatively rare event, using the entire dataset ensured that enough cases were used to draw meaningful conclusions and make reliable inferences.

The data analysis focused on identifying trends in stroke occurrence, risk factors, treatment, and outcomes. Descriptive statistics were used to summarize baseline characteristics such as age, sex, ethnicity, and stroke type. Chi-square tests were applied to examine categorical variables - the relationship between stroke type and patient demographics. Student’s t-tests and Mann-Whitney U tests compared continuous variables - stroke severity (NIHSS scores) and duration of admission, between the different patient groups. More so, multivariate logistic regression was performed to assess the impact of key risk factors on stroke outcomes. Kaplan-Meier survival analysis was used to evaluate 30-day survival rates and investigate whether factors such as stroke type or sex influenced mortality. Lastly, ANOVA tests were conducted to compare differences in treatment outcomes across stroke subtypes.

A test for normality was not performed in this study because the dataset was large, and statistical tests for normality are not reliable for large sample sizes. Normality tests such as the Shapiro-Wilk and Kolmogorov-Smirnov tests are sensitive to sample size. They often detect small deviations from normality even when the data distribution is suitable for parametric analysis. Given the large number of stroke cases analysed, graphical methods such as histograms and Q-Q plots were instead used to visually assess the distribution of continuous variables. Besides, parametric tests like the t-test and ANOVA are robust to violations of normality when sample sizes are large.

3.4 Ethical Considerations

Although ethical approval was not needed for this study, nevertheless, ethical approval was requested and obtained for the study. This research utilized a fully anonymized study population obtained from the SSNAP. SSNAP is a registry approved by the NHS Health Research Authority to collect clinical data obtained from patients under section 251 of the NHS Act of 2006.

CHAPTER FOUR

Presentation of Results

4.1 Chapter Overview

This chapter presents the results of the analysis conducted in this study. The data for this research was obtained from the Sentinel Stroke National Audit Programme (SSNAP), a major national healthcare quality improvement programme based in the School of Population Health and Environmental Studies at King's College London. A database was developed using the Statistical Package for Social Science (SPSS). The SPSS was used to analyse the data obtained from SSNAP and the results are presented in this chapter. The frequencies and descriptive statistics were computed for each variable in this study. In addition, the analyses of the stroke exposures, treatment measures and outcomes are presented in this chapter. Furthermore, several comparisons between patients who died and patients who survived were computed using the student t-tests for normally distributed continuous data, the Mann–Whitney U test for non-normally distributed data, and the chi-square test for categorical data. A p-value of less than 0.05 was considered to be statistically significant.

4.2 VARIABLES

In research, variables are characteristics, attributes, or properties that can take on different values and can be measured or observed. According to Kaliyadan and Kulkarni (2019), variables are fundamental components of any research that captures the various aspects of a research study and play a key role in hypothesis testing and data analysis. In this research, two types of variables were analysed using SPSS – demographic and clinical variables.

4.2.1 Demographic Variables

The tables of the statistical analyses of each demographic variable are presented in the Appendix Section.

Table 4.1: Demographic Characteristics of Young Adult Stroke Patients (n = 460)

Variable	Category	Frequency (n)	Percentage (%)
Age (years)	Mean (SD)	46.86 (8.12)	-
	Median	50.00	-
Sex	Male	292	63.5
	Female	168	36.5
Ethnicity	British	365	78.6
	African	18	4.0
	Caribbean	13	2.8
	White Other	24	5.3
	Mixed/Other	18	4.7
	Unknown/Not Stated	22	4.7
Country of Residence	United Kingdom	442	96.2
	Belgium	2	0.4
	China	3	0.7
	France	2	0.4
	Singapore	1	0.2
	Unknown	13	2.8

4.2.2 CLINICAL VARIABLES

In this research, the clinical variables are type of stroke and severity of stroke. The tables of the statistical analyses of each clinical variable are presented in the Appendix Section.

Table 4.2: Clinical Characteristics of Young Adult Stroke Patients (n = 460)

Variable	Category	Frequency (n)	Percentage (%)
Type of Stroke	Ischaemic Stroke	407	88.5
	Haemorrhagic Stroke	53	11.5
Stroke Severity (NIHSS Score)	Mean (SD)	4.87 (5.48)	-
	Median	3.00	-
	0 (No Symptoms)	97	21.1
	1-4 (Minor Stroke)	162	35.2
	5-15 (Moderate Stroke)	130	28.3
	16-20 (Moderate-Severe Stroke)	42	9.1
	21+ (Severe Stroke)	29	6.3

4.3 Exposures

In epidemiology, exposures refer to factors or conditions that individuals have been subjected to, and that researchers believe may be associated with the occurrence of a particular outcome or condition (Lee and Pickard, 2013). In this research, the exposures are classified into two main categories: traditional stroke risk factors and risk factors specific to young people. This research explores how these exposures, both traditional and specific to young people, contribute to the occurrence and severity of strokes in the studied population.

In analysing the stroke risk factors, it is important to note that many patients presented with multiple risk factors simultaneously. However, for the purposes of this analysis, the risk factors were entered individually, and this does not capture the clustering effects of the risk factors.

4.3.1 TRADITIONAL STROKE RISK FACTORS

Traditional stroke risk factors are well-established elements that have been widely recognized and studied in the context of stroke occurrences (Donkor, 2018). These factors have demonstrated a consistent association with an increased likelihood of experiencing a stroke and are routinely assessed in all stroke patients. The tables of the statistical analyses of the traditional stroke risk factors are presented in the Appendix Section.

Table 4.3: Traditional Stroke Risk Factors Among Young Adult Stroke Patients (n = 460)

Risk Factor	Category	Frequency (n)	Percentage (%)
Hypertension (HTN)	Present	175	38.0
	Absent	285	62.0
Atrial Fibrillation (AF)	Present	38	8.2
	Absent	422	91.8
Smoking	Current Smoker	69	15.0
	Ex-Smoker	102	22.2
	Non-Smoker	259	62.9
Alcohol (EtOH) Consumption	Current Drinker	52	11.3
	Former Drinker	2	0.4
	Never Consumed Alcohol	406	88.3
Hypercholesterolemia	Present	15	3.3
Diabetes Mellitus	Present	59	12.8
	Absent	401	81.2

4.3.1.1 Hypertension (HTN)

According to Boehme et al. (2017), hypertension is a well-established and significant traditional risk factor for stroke. The relationship between hypertension and stroke is firmly established in the medical literature, with numerous studies consistently demonstrating a strong association (Hisham and Bayraktutan, 2013; Ogunniyi et al., 2021; Wajngarten and Silva, 2019). When blood pressure is consistently high, it can lead to damage in the blood vessels, including those supplying blood to the brain (Pires et al., 2013). This damage increases the risk of both subtypes of stroke i.e ischaemic stroke and haemorrhagic stroke (Wajngarten and Silva, 2019). Additionally, hypertension causes cardiac damage and increases the risk of atrial fibrillation, a condition associated with stroke (Manolis et al., 2012).

Table 4.3 provides insights into the prevalence of hypertension among the 460 patients in the dataset. 38% of the patients (175 out of 460) had hypertension in the dataset. On the other hand, 62% (285 out of 460) did not report hypertension. For these patients that did not report a history of hypertension, they may have other contributing risk factors for stroke, or they may represent a relatively healthier subset of the population.

4.3.1.2 Atrial Fibrillation (AF)

Atrial Fibrillation (AF) is a common heart rhythm disorder characterised by irregular and often rapid heartbeats (Pellman and Sheikh, 2015). AF can disrupt the normal flow of blood through the heart, leading to the formation of blood clots, which can be dislodged and travel to the brain, causing ischaemic strokes. In individuals with AF, the irregular heartbeat can lead to the pooling of blood in the atria, and promote the formation of blood clots (Corradi, 2014). If a clot dislodges and travels to the brain, it can block an artery and result in an ischaemic stroke. Strokes associated with AF are often more severe and have a higher risk of disability and death.

From Table 4.3, Atrial Fibrillation (AF) was reported in 8.2 percent of the patients in this dataset. This suggests that AF may not be a significant risk factor for strokes

among young adults in the study. However, when extrapolated for age, this could be significant. The majority (91.8%) of the patients did not mention a history of AF. This could mean that for most of the study population, AF was not a significant factor contributing to their stroke, or they may not have had a history of this condition.

4.3.1.3 Smoking

Smoking has a strong association with stroke risk, and it contributes to stroke through various mechanisms. Smoking leads to the accumulation of plaque in the blood vessels, atherosclerosis, which narrows the arteries and disrupts blood flow to the brain, increasing the risk of stroke (Pan et al., 2019). Secondly, smoking promotes blood clot formation. Nicotine and other chemicals in cigarettes are prothrombotic, increasing the likelihood of clot formation, which can block blood flow to the brain (Roy et al., 2017).

Table 4.3 shows the distribution of smoking habits among young people in the dataset. The study classified the patients into four categories: those who are current smokers (yes), those who have never smoked (no), those who used to smoke (ex), and those with missing data. From the table, 259 patients (62.9%) in the dataset are non-smokers; this signified that they did not smoke at the time of the assessment and have never smoked. Non-smokers generally have a lower risk of stroke compared to smokers. While this group is not currently exposed to the direct risks of smoking related stroke, it is essential to recognize that other risk factors may still apply. These factors could include secondhand smoke exposure or the presence of other comorbid conditions such as hypertension or diabetes. Another 102 patients (22.2%) in the dataset identified as ex-smokers. This implied that they had a history of smoking but had quit by the time of the assessment. Although quitting smoking reduces the risk of stroke over time, ex-smokers might still carry a higher risk compared to non-smokers. The dataset did not provide details on the duration of smoking cessation, which is crucial in understanding the extent of risk reduction. Furthermore, 69 patients (15.0%) were current smokers; meaning they were actively smoking at the time of the assessment. Current smokers are at a significantly higher risk of stroke due to the

direct and immediate impact of smoking on their cardiovascular system. This group is of particular concern due to the well-established link between smoking and stroke.

4.3.1.4 Alcohol (EtOH) Consumption

Excessive alcohol intake is considered a risk factor for stroke. Alcohol shares a direct and causal relationship to hypertension, atrial fibrillation, and other cardiovascular problems, which can increase the risk of stroke (Hillbom et al., 2011). Additionally, alcohol consumption may contribute to the formation of blood clots and alcoholic cardiomyopathy is a known risk factor for stroke. Moreover, alcohol can increase the level of triglycerides which may contribute to the formation of blood clots.

Table 4.3 provides the frequency distribution of alcohol (EtOH) consumption among the patients in this study. The dataset classified the patients into four categories: those who currently consume alcohol (Yes), those who have never consumed alcohol (No), those who used to consume alcohol (ex). However, the dataset did not explicitly state the amount of alcohol consumed in units. From the table, eleven (11.3 %) percent of the patients reported being current alcohol consumers. The consumption of alcohol is a risk factor for stroke, and this percentage raises concerns, especially among young adults. While moderate alcohol consumption may have cardiovascular benefits, excessive or binge drinking can increase the risk of both ischaemic and haemorrhagic strokes. Additionally, a minimal percentage, 0.4%, of the patients were classified as former alcohol consumers, meaning they have quit drinking. Although quitting alcohol can reduce stroke risk, it is important to note that the effects of past heavy drinking on stroke risk may persist.

An understanding of the reasons for quitting and the duration of abstinence is necessary for a more comprehensive risk assessment. Encouraging former alcohol consumers to maintain sobriety is a crucial aspect of stroke prevention. Lastly, the majority, (88.3%) 406 patients reported never having consumed alcohol. This is an encouraging finding as avoiding alcohol consumption eliminates a significant risk factor for stroke. However, it is essential to recognize that other risk factors may still apply, and these individuals should maintain a comprehensive approach to stroke prevention, including healthy lifestyle choices and managing other risk factors.

4.3.1.5 Hypercholesterolemia

Reported in young stroke patients are a multitude of abnormalities in lipid profile. Although the association between cholesterol levels and stroke occurrence is debated in the literature as elucidated by the Framingham study, it seems that both hypercholesterolemia and hypertriglyceridemia play significant roles as risk factors in the development of atherosclerosis and by extension ischaemic stroke (Castelli et al 1992 & Albucher et al, 2000).

From Table 4.3, 15 patients corresponding to 3.3% were documented to have hypercholesterolemia in this dataset. This lends credence to the fact that hypercholesterolemia as a risk factor for stroke in young adults cannot be ignored.

4.3.1.6 Diabetes Mellitus

Diabetes is a highly prevalent, chronic disease, and a well-established risk factor for stroke. It often coexists with other cardiometabolic risk factors that independently increase the risk of stroke (Visseren et al, 2021). People with diabetes have a 1.5-2 times higher risk of stroke compared with people without diabetes, with risk increasing with diabetes duration. Also, ischaemic stroke patients with T1DM or T2DM exhibit a distinct risk-factor and etiologic profile and a worse vascular prognosis than do nondiabetic patients (Putaala et al, 2011). As echoed by Mosenzon et al (2023), patients with diabetes have worse post-stroke outcomes and a greater risk for stroke recurrence as compared with those without diabetes.

From Table 4.3, diabetes mellitus was present in 13 patients (12.8%) in the study population but absent in the majority of the patients (81.2%) The subtype of the diabetes (T1DM or T2DM) was not stated in the dataset which made further analytical characterization impossible. However, appropriate management of diabetes and other vascular risk factors may improve stroke outcomes and reduce the risk for recurrent stroke.

4.3.2 RISK FACTORS SPECIFIC TO YOUNG PEOPLE

Risk factors specific to young people denote conditions that may predispose individuals to strokes at a young age. This category may include factors such as certain genetic disorders, lifestyle choices, or health conditions that are more prevalent in younger demographic. These risk factors are not routinely assessed unless there is a clinical indication, and the traditional risk factors are absent. The tables of the statistical analyses of the risk factors specific to young people are presented in the Appendix Section.

Table 4.4: Risk Factors Specific to Young People (n = 460)

Risk Factor	Category	Frequency (n)	Percentage (%)
Illicit Drug Use	Yes	35	7.6%
	No	425	92.4%
Hormone Replacement Therapy (HRT)	Yes	9	1.3%
	No	451	97.8%
Genetics (CADASIL, MELAS)	Yes	4	0.4%
	No	456	99.2%
Migraine	Yes	59	12.8%
	No	401	87.2%
Deep Vein Thrombosis (DVT)/Pulmonary Embolism (PE)	Yes	32	7%
	No	428	93%
Non-Haematological Malignancy	Yes	32	7%

	No	428	93%
Haematological Malignancy (Leukemia, Lymphoma, Myeloma)	Yes	5	0.4%
	No	455	99.6%
Endocarditis	Yes	35	7.7%
	No	425	92.3%
Peripheral Vascular Disease (PVD)	Yes	6	1.3%
	No	454	98.7%
Cervical Artery Dissection	Yes	26	5.7%
	No	434	94.3%
Patent Foramen Ovale (PFO)	Yes	48	10.4%
	No	412	89.6%
Sickle Cell Disease/Sickle Cell Trait	Sickle Cell Disease	1	0.2%
	Sickle Cell Trait	1	0.2%
	No	458	99.6%

4.3.2.1 Illicit Drug Use

Illicit drug use is a risk factor for stroke, as many drugs can have adverse effects on the cardiovascular system. Recreational drugs have been implicated in hypertension, vasospasm, thromboembolism and atrial fibrillation, all of which contribute to stroke risk. Chronic drug use can damage blood vessels and the heart, increasing the likelihood of stroke. Additionally, drug use might lead to risky behaviors that further elevate the risk, such as engaging in other unsafe activities such as smoking and excessive alcohol intake. Some recreational drugs reported in the dataset include cocaine, heroin, amphetamine, cannabis, spice and skunk.

Table 4.4 provides the frequency distribution of drug use among the patients in this study. The dataset categorized the patients into two groups: those who reported using recreational drugs (yes) and those who did not use drugs (no). About 7.6% of the respondents admitted to using recreational drugs. This finding highlights the importance of addressing drug use and addiction among this demographic through comprehensive prevention and intervention programs. On the other hand, the majority of the patients, 92.4%, reported not using drugs. This is an encouraging finding, as it indicates that a substantial portion of young adults in the study population are making healthier lifestyle choices by avoiding illicit drugs. Preventive measures that promote a drug-free lifestyle among young adults, coupled with awareness campaigns about the health risks associated with drug use, are essential in maintaining this trend. The data shows that a significant percentage of the young adults in the dataset are nonusers and suggests a lower risk of stroke associated with drug use.

4.3.2.2 Hormone Replacement Therapy (HRT)

Hormone Replacement Therapy, HRT, is a medical treatment that involves replacing hormones, such as estrogen and progesterone, in women who are experiencing menopause or have undergone a hysterectomy (Lobo, 2017). These hormones are typically produced by the ovaries, and their levels decline during menopause, leading to various symptoms, including hot flashes, mood swings, and vaginal dryness (Sullivan et al., 2016; O'Neill and Eden, 2014). While HRT can alleviate menopausal symptoms, it has been subject to debate due to its possible effects on stroke risk. Some studies have suggested that HRT may slightly increase the risk of stroke,

particularly ischaemic stroke (Henderson and Lobo, 2012; Paganini-Hill, 2001). However, the relationship between HRT and stroke risk is complex and may depend on various factors, including the type of hormones used, dosage, and the individual's overall health. Therefore, it's essential to analyse the data to understand how HRT is reported in the dataset and its potential implications for stroke among young people.

From Table 4.4, among the 460 individuals in the dataset, only 1.3% (nine) reported using Hormone Replacement Therapy (HRT) in this dataset. The low percentage of HRT users suggests that many of these young adults may not be using hormonal therapy. Out of the 9 patients, 3 reported using contraceptive pills as a form of hormonal therapy. While the percentages of individuals using contraceptive pills or oral contraceptives are very low, it is essential to note that these contraceptive methods contain hormones. The usage of these contraceptives can impact hormonal profiles and may have implications for their overall health. On the other hand, most of the patients (97.8%) did not report using any form of hormone replacement therapy. This large population can be attributed to the fact they may not have a medical indication for HRT or may have chosen alternative treatments or management strategies.

4.3.2.3 Genetics

The function of genetics in stroke is significantly more intricate. Stroke exhibits heterogeneity, just as its predisposing risk factors, which also possess their unique hereditary influences. Although, the real genetic impact of the origin of strokes is still unknown, monogenic condition is responsible for 1% of strokes, especially in younger patients, but the data is underestimated (Bersano 2016). Genetics may either mediate or moderate stroke via multiple mechanisms (Jha, 2022). Genetic factors are more responsible for small- and large-vessel disease than in the cardio-embolic aetiology of a stroke (Chojdak-Łukasiewicz et al 2021). Genetics can influence a person's risk of stroke by impacting various factors, such as blood vessel health, blood clotting, and the ability to metabolize certain substances (Boehme et al., 2017). According to Lusis (2012), some individuals may inherit genetic variants that make them more susceptible to conditions like atherosclerosis, which can lead to stroke.

From Table 4.4, approximately 0.4% (two) of the patients in the dataset reported had a specific genetic mutation known as CADASIL which involves mutation in the Notch 3 gene on chromosome 19. More so, two patients were diagnosed with MELAS. MELAS, which stands for Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes, is a mitochondrial disorder caused by mutations in mitochondrial DNA (Wang and Le, 2015). It affects the body's energy production and leads to a wide range of symptoms, including muscle weakness, neurological problems, lactic acidosis, and stroke-like episodes. The occurrence of just two patients with a history of MELAS may be attributed to various factors. As earlier stated, MELAS is a rare genetic disorder, and the presence of these cases could be influenced by genetic predisposition, population demographics, potential selection bias, advances in diagnostic practices, or even coincidental occurrences. If there is a genetic predisposition in the population under study, it could contribute to the occurrence of MELAS in the dataset. More so, certain populations or ethnic groups may have a higher prevalence of specific genetic disorders. If the dataset includes individuals from a population with a relatively higher incidence of MELAS, it could explain the presence of these cases. On the other hand, no stroke-related genetic component was found in most of the patients (99.2% or 456 out of the 460).

4.3.2.4 Migraine

Migraine is a neurological disorder characterised by recurrent, severe headaches often accompanied by symptoms such as throbbing head pain, sensitivity to light, sound, and smells, nausea, and vomiting (Migraine, 2020). Migraine is correlated with a heightened susceptibility to ischaemic stroke. The correlations exhibit greater strength in those experiencing migraine with aura compared to those without aura, particularly among females as opposed to males, and among younger individuals. Nevertheless, debates persist over the mechanisms via which migraine may potentially increase the risk of ischaemic stroke (Gryglas and Smigiel, 2017; Gollion et al 2021).

Table 4.4 on migraine provides insights into its prevalence among the study population. Migraine is relatively common among the study population, with approximately 12.8% of the patients reporting a history of migraine. This suggests that migraine may be a significant risk factor in strokes among young adults in the study. Additionally, a significant portion (87.2%) of the patients did not mention a history of migraine. This could imply that for a majority of the study population, migraine may not have been a significant factor contributing to their strokes, or they may not have had a history of migraines. Most of the patients not mentioning migraines may also indicate that other risk factors, such as health conditions or lifestyle factors, played more prominent roles in their stroke. This underscores the multifactorial nature of stroke aetiology in young adults.

4.3.2.5 Deep Vein Thrombosis/Pulmonary Embolism (DVT/PE)

Venous thromboembolism (VTE) consisting of deep venous thrombosis (DVT) and pulmonary embolism (PE) is a multifactorial disease, and advancing age and obesity are recognized as shared atherosclerotic risk factors for VTE and ischaemic stroke (Glynn & Rosner, 2005). While DVT and PE primarily affect the venous system, there is a potential link to stroke. Both conditions involve the formation of blood clots, which can obstruct blood flow. In some cases, a paradoxical embolus in the venous system can be pumped into the arterial system and potentially reach the brain, causing an ischaemic stroke. However, this is relatively rare, and the primary concern with DVT/PE is the risk of pulmonary embolism and other complications. Also, arterial

thrombotic events (ATEs), such as ischaemic stroke, transient ischaemic attack (TIA), or myocardial infarction (MI), share similar risk factors such as concomitant OCP use, smoking, and some acquired thrombophilic disorders — hyperhomocysteinemia and antiphospholipid syndrome (APS), with VTE (Dulicek et al, 2018).

Table 4.4 on Deep Vein Thrombosis (DVT) and Pulmonary Embolism (PE) as risk factors for stroke provides insights into their prevalence among the study population. DVT and PE, which are both related to blood clotting, is not common among the study population, with approximately 7% of the patients reporting a history of DVT or PE. This low percentage of respondents reporting DVT/PE suggests that these conditions may not be potential risk factors for strokes in young adults in this dataset. However, it could be related to an underlying predisposition to thrombotic events. Conversely, the majority (93%) of the patients did not mention a history of DVT or PE. This could indicate that for most of the study population, DVT and PE were not significant factors contributing to their strokes.

4.3.2.6 Non-Haematological Malignancy

Non-haematological malignancies include a diverse group of cancers arising from tissues other than the blood and bone marrow (Kalid et al., 2020). The relationship between non-haematological malignancy and stroke is complex and multifaceted as primary brain tumours, metastatatic tumours and even occult malignancies can increase the risk of stroke (Verhoeven et al., 2023). Occasionally, there is a correlation between the two, since a stroke might serve as an initial indication of an underlying occult cancer. Individuals diagnosed with cancer face a heightened susceptibility to stroke due to a combination of factors, including the direct impact of tumours, the prothrombotic effects they induce, and the consequences of cancer treatments (Dearborn et al., 2014). Furthermore, it is worth noting that numerous types of cancer and strokes share common risk factors, namely smoking and obesity (Tybjerg et al., 2020). Additionally, certain cancers, such as brain tumors, can directly affect blood vessels and increase the risk of stroke. Treatments like chemotherapy and radiation therapy may also impact the vascular system, further increasing the risk of stroke (Dardiotis et al., 2019).

Table 4.4 on non-haematological malignancy as a risk factor for stroke provides insights into its prevalence among the study population. Non-hematological malignancy is significantly rare among the study population, with only 7% of the patients reporting this condition. This low percentage of patients with a history of nonhematological malignancy in this dataset suggests that this may be a potential risk factor for strokes in young adults. Conversely, a majority (93.0%) of the patients did not mention a history of non-hematological malignancy. This could indicate that for most of the study population, non-hematological malignancy was not a significant factor contributing to their strokes, or they may not have had a history of cancer.

4.3.2.7 Haematological Malignancy

According to Méndez-Ferrer et al. (2020), haematological malignancies comprise a range of cancers that originate from the blood and bone marrow, including leukemia, lymphoma, and myeloma. These malignancies arise from abnormal proliferation and differentiation of hematopoietic stem cells and lead to disruption of normal blood cell production and function. In this study, the three haematological malignancies, leukemia, lymphoma, and multiple myeloma were identified in the dataset.

According to Vishwanath (2023), leukemia is a type of cancer that affects the blood and bone marrow, leading to the overproduction of abnormal white blood cells. In some cases, leukemia can be associated with a hypercoagulable state, making individuals more susceptible to the formation of blood clots. The presence of leukemia can contribute to a higher risk of thrombosis, including venous and arterial clots. Leukemia-related hypercoagulability increases the likelihood of clot formation throughout the circulatory system, including within the veins of the brain.

From Table 4.4, only two patients (0.4%) had history of leukemia. This can be attributed to the fact that leukemia is not common among stroke patients. Furthermore, lymphoma is a broad category of blood cancers that primarily affect the lymphocytes, a type of white blood cell (Jamil and Mukkamalla, 2020). Lymphocytes play a crucial role in the body's immune system. Lymphoma is further divided into two main types:

Hodgkin lymphoma and non-Hodgkin lymphoma. In the dataset, two patients (0.4%) had a history of lymphoma. With this prevalence level, lymphoma is relatively rare among stroke patients in the database.

For multiple myeloma, this is a type of blood cancer that affects plasma cells in the bone marrow (Michels and Petersen (2017). Myeloma is characterised by the abnormal growth and accumulation of these plasma cells, which can crowd out healthy blood cells. From Table 4.21, one patient (0.2%) had a history of myeloma, a type of bone marrow cancer. This low representation of myeloma as a risk factor for stroke in this dataset can be attributed to several factors. Myeloma is a relatively rare cancer and accounts for a small percentage of all cancer diagnoses (Kazandjian, 2016). As a result, the likelihood of encountering myeloma as a risk factor for stroke in a general stroke patient population is low. More so, the causes of strokes in myeloma patients can be multifactorial, often involving a combination of factors such as treatment side effects, infection risks, and complications related to the cancer itself. Identifying myeloma as a sole, direct risk factor for stroke can be challenging. Besides, myeloma patients may have other comorbid conditions or risk factors that are more commonly associated with stroke. The presence of traditional stroke risk factors may overshadow the role of myeloma in stroke occurrence.

4.3.2.8 Endocarditis

According to Khalid (2023), endocarditis is a condition characterised by the inflammation of the endocardium and heart valves. Endocarditis serves as a significant contributor to cardiac embolism, given its substantial embolic risk. Furthermore, it is closely linked to elevated rates of morbidity and mortality. Both ischaemic stroke and intracranial haemorrhage are known neurological complications of endocarditis (Holland et al., 2016 and Nitsch et al. 2023).

From Table 4.4, endocarditis is relatively uncommon among the study population, with about 7.7% of the patients reporting a history of endocarditis. This suggests that endocarditis may not be a notable risk factor for strokes among young adults in the study. On the other hand, in a majority (92.3%) of the patients, stroke was not associated with endocarditis.

4.3.2.9 Peripheral Vascular Disease (PVD)

Peripheral Vascular Disease (PVD) is commonly associated with atherosclerosis and by extension an increased risk of complications, including stroke (Alonso et al., 2010). Studies have shown a high prevalence of PVD in patients with stroke, and of stroke in patients with PVD (Banerjee, Fowkes and Rothwell, 2010). Peripheral Vascular Disease (PVD) is relatively uncommon among the study population, with only 6 (1.3%) of the patients reporting a history of PVD. A majority (98.7%) of the patients did not mention a history of PVD.

4.3.2.10 Cervical Artery Dissection

Cervical artery dissection, involving either the vertebral or carotid artery, is a rare cause of stroke in the general population, but one of the more common causes of stroke in patients younger than 45 years of age and some series estimated that vertebral artery dissection may be responsible for at least 20% of ischaemic strokes in young people (Britt, 2023; Goodfriend, 2022). From Table 4.4, cervical artery dissection is uncommon among the study population, as it was implicated in approximately 5.7% of the patients in this study and absent in the majority (94.3%) of the patients.

4.3.2.11 Patent Foramen Ovale (PFO)

Patent foramen ovale (PFO), a consequence of failed closure of the foramen ovale, is the most common congenital heart abnormality of fetal origin and was present in approximately 25% of the worldwide adult population (Homma et al., 2016). PFO has long been associated with cryptogenic stroke. Potential stroke mechanisms include paradoxical embolism from a venous clot which traverses the PFO, *in situ* clot formation within the PFO, and atrial arrhythmias due to electrical signaling disruption (Ioannidis & Mitsias 2020).

Table 4.4 provides insight into the prevalence of Patent Foramen Ovale (PFO) for stroke among the study population. PFO was present in approximately 10.4% of the study population and absent in the remaining 89.6%. This could be related to the proximity of the BRI stroke unit to the Bristol Heart Institute which is the largest

cardiothoracic centre in Southwest England. Hence, some patients from the Bristol Heart Institute end up on the stroke ward on account of peri-procedure stroke.

4.3.2.12 Sickle Cell Disease and Sickle Cell Trait

Sickle cell disease (SCD) is an inherited haemoglobinopthy which results in an abnormality in the oxygen-carrying protein haemoglobin found in red blood cells (Mandal et al., 2020). Of the many severe consequences of SCD, acute stroke and chronic cerebral ischemia are among the most disabling (Platt, 2005). From the dataset, only one patient (0.2%) in the dataset had sickle cell disease. This rarity might be due to the relatively low prevalence of sickle cell disease and the location of the study as sickle cell disease is particularly common in people with an African or Caribbean family background. Furthermore, Sickle cell trait is a genetic condition in which an individual carry one abnormal hemoglobin gene (HbS) and one normal hemoglobin gene (HbA) (Ashorobi et al., 2019). Sickle cell trait is distinct from sickle cell disease, which is inherited when an individual carry two abnormal HbS genes. Individuals with sickle cell trait typically do not experience the same severe health issues as those with sickle cell disease. While sickle cell disease can lead to severe complications, including an increased risk of stroke, sickle cell trait is generally considered a milder condition with fewer associated health problems. In the dataset, one patient (0.2%) was identified as having sickle cell trait. The presence of sickle cell trait in one patient suggests that it is a relatively uncommon risk factor for stroke in this population.

4.4 OTHER INDIVIDUAL STROKE RISK FACTORS IDENTIFIED IN THE DATASET

In addition to the risk factors identified above, several other risk factors were identified in the data set although with lesser frequency. Most of these risk factors are rare in the study population and are not routinely assessed. The table of the statistical analyses of these risk factors are presented in the Appendix Section.

Table 4.5: Other Individual Stroke Factors Identified in the Dataset (n = 460)

Risk Factor	Frequency (n)	Percentage (%)
Thrombophilia	1	0.2%
Antiphospholipid Syndrome	3	0.6%
Chronic Kidney Disease (CKD)	7	1.4%
DiGeorge Syndrome	1	0.2%
Giant Cell Arteritis (GCA)	1	0.2%
Cerebral Venous Sinus Thrombosis	1	0.2%
Gilbert Syndrome	1	0.2%
Hepatitis	2	0.4%
Hypothyroidism	8	1.6%
Graves Disease	2	0.4%
Hyperthyroidism	1	0.2%
Thyroid Cancer	1	0.2%
JAK2 Mutation	1	0.2%
Loeys-Dietz Syndrome	1	0.2%
Prothrombin Gene Mutation	1	0.2%
Ramsay-Hunt Syndrome	1	0.2%
Smith-Magenis Syndrome	1	0.2%
Sneddon's Syndrome	1	0.2%
Thrombotic Thrombocytopenic Purpura (TTP)	1	0.2%
Congestive Heart Failure (CHF)	14	3.1%
Ischaemic Heart Disease (IHD)	41	8.9%
Myocardial Infarction (MI)	20	4.3%

4.4.1 Thrombophilia

Thrombophilia is often associated with genetic factors or acquired conditions with heightened risk of thromboembolic events, potentially leading to an ischaemic stroke (Omran et al., 2021). From the dataset, only one patient in the dataset had a history of thrombophilia. This accounts for about 0.2% of the total dataset, and signifies that this combination of risk factors is extremely rare among stroke patients in this dataset.

This patient's condition may have been a critical contributing factor to their stroke. However, the rarity of this combination within the dataset suggests that it might not be a significant risk factor in this particular population.

4.4.2 Antiphospholipid Syndrome

Antiphospholipid syndrome (APS) is a prothrombotic autoimmune disease with heterogeneous clinicopathological manifestations and is a well-established cause of acute ischaemic stroke (AIS) and transient ischaemic attack (TIA), particularly in younger patients (Mittal et al, 2023). From Table 4.5, only three patients (0.6%) had antiphospholipid syndrome. The presence of just three patients with antiphospholipid syndrome in the dataset indicates that this autoimmune condition is quite rare among stroke patients in this population. The low prevalence of this syndrome within this dataset suggests that it might not be a prominent stroke risk factor for the majority of patients. While it may not be a common factor in this dataset, it can significantly impact those affected by it.

4.4.3 Chronic Kidney Disease (CKD)

It is well established that impaired kidney function is an independent risk factor, above and beyond traditional risk factors, for cardiovascular disease. Kidney function, as determined by the estimated glomerular filtration rate (eGFR), demonstrates an inverse stepwise relationship with incident stroke risk (Kelly et al, 2021). Proteinuria itself is an under-recognized risk factor for stroke, independent of blood pressure and diabetes, and coupled with declines in kidney function, substantively elevates stroke risk (Masson et al, 2015). From Table 4.5, a total of 7 patients (1.4%) had chronic kidney disease (CKD), which although commoner than the other rare risk factors is still a relatively rare stroke risk factor in this age group.

4.4.4 DiGeorge Syndrome

DiGeorge syndrome, also known as 22q11.2 deletion syndrome, is a genetic disorder caused by the deletion of a small piece of chromosome 22 (Sullivan, 2019). This syndrome affects multiple systems in the body and lead to a wide range of developmental and health problems including stroke (Choudhry and Trede, 2013). From Table 4.5, DiGeorge syndrome is a rare condition, with only one patient (0.2%)

in the dataset having a history of this syndrome. This low prevalence of DiGeorge syndrome among the patients suggests that it is not a common traditional risk factor for stroke in this specific population.

4.4.5 Giant Cell Arteritis (GCA)

According to Borchers and Gershwin (2012), Giant Cell Arteritis (GCA) is a form of vasculitis, a relatively rare condition characterised by inflammation of medium to large arteries that mostly affects the temporal arteries and if left untreated, can lead to significant complications, including strokes. From Table 4.5, Giant Cell Arteritis (GCA) was observed in one patient and this constituted only 0.2% of the entire dataset. The rarity of GCA in the dataset could be attributed to its relatively low prevalence in the general population, especially when compared to more common stroke risk factors such as hypertension and diabetes.

4.4.6 Cerebral Venous Sinus Thrombosis

Cerebral venous sinus thrombosis, a thrombus of the cerebral veins and/or cavernous sinuses, is a relatively rare neurological disorder accounting for about 0.5% of all strokes but with a higher incidence in young adults (Alvis-Miranda et al., 2013; Zahoor et al., 2023 and Ferro & Aguiar de Sousa, 2019). From Table 4.5, only one patient (0.2%) with a history of venous sinus thrombosis. This can be attributed to the fact that venous sinus thrombosis is a rare cerebrovascular condition.

4.4.7 Gilbert Syndrome

Gilbert Syndrome is a relatively mild and common liver disorder. It is an autosomal recessive disorder of bilirubin metabolism within the liver in which reduced glucuronidation of bilirubin leads to unconjugated hyperbilirubinemia and recurrent episodes of jaundice (Bosma, 2003). Some studies have suggested a possible association with a slightly higher risk of heart disease and stroke, but this has not been conclusively proven (Zhong et al, 2019). In the dataset, only one patient (0.2%) had Gilbert's Syndrome, which is a very low prevalence.

4.4.8 Hepatitis

Hepatitis are viral infections that primarily affect the liver (Ringehan et al., 2017). The connection between viral hepatitis and stroke risk is multifaceted. According to Fede et al. (2015), chronic hepatitis, especially when it progresses to cirrhosis, can contribute to cardiovascular complications, including hypertension and atherosclerosis. Liver dysfunction may also affect blood clotting factors, potentially increasing the risk of thrombotic events, such as ischaemic stroke. Additionally, the inflammatory response associated with hepatitis can lead to systemic inflammation, which plays a role in the development of atherosclerosis (Zampino et al., 2013). From table 4.5, only two patients, (0.4%) had Hepatitis. While the dataset does not provide specific details regarding the type and severity of hepatitis, it is essential to recognize the potential implications of viral hepatitis as a stroke risk factor.

4.4.9 Hypothyroidism

Hypothyroidism is characterised by an underactive thyroid gland that can result from various causes, including autoimmune conditions, medications, or iodine deficiency (Friedman, 2013). The association between hypothyroidism and stroke risk is complex because several factors contribute to this relationship such as increased atherosclerosis risk, blood pressure changes, cardioembolic strokes, and blood clotting abnormalities (Udovcic et al., 2017). From Table 4.5, 8 patients (1.6%) had hypothyroidism. Hypothyroidism is relatively common compared to some other factors but still not among the most frequent in the dataset.

4.4.10 Graves Disease

According to Davies et al. (2020), Graves Disease is an autoimmune disorder characterised by an overactive thyroid gland. It is one of the leading causes of hyperthyroidism and can have various systemic effects. In the dataset, only two patients (0.4%) had Graves Disease making it a rare risk factor in this dataset.

4.4.11 Hyperthyroidism

Hyperthyroidism is a common endocrine disorder, affecting 0.5% to 2% of the population, and young adults comprise a significant proportion of those with this disorder. Some studies have shown a relationship between hyperthyroidism and stroke risk in young adults (Sheu et al, 2010). From Table 4.5, only 1 patient (0.2%) had hyperthyroidism. This implies that hyperthyroidism is rare among the dataset when compared to other factors.

4.4.12 Thyroid Cancer

Thyroid cancer is a malignancy that develops in the thyroid gland, a vital part of the endocrine system responsible for producing hormones that regulate various bodily functions (Carling and Udelsman, 2014). While thyroid cancer is not traditionally considered a direct risk factor for stroke, there may be indirect connections worth exploring. In the dataset, a single patient (0.2%) had a history of thyroid cancer. The low incidence of thyroid cancer as a risk factor implies that it may not significantly influence the development of stroke in this population.

4.4.13 JAK 2 Mutation

According to Roskoski Jr (2016), JAK2 (Janus kinase 2) is a gene that encodes a protein involved in regulating blood cell production. Mutations in this gene can lead to the overproduction of blood cells, particularly red blood cells, white blood cells, and platelets. Two of the most common blood disorders associated with JAK2 mutations are polycythemia vera (PV) and essential thrombocythemia (ET) (Tefferi and Barbui, 2020). The presence of a JAK2 mutation can potentially contribute to an increased risk of stroke, although the extent of this risk depends on various factors. From Table 4.5, only one patient (0.2%) had a JAK2 mutation. The low prevalence of JAK2 mutations in this dataset might be reflective of the rarity of these mutations in the general population or specific demographics represented in the study.

4.4.14 Loeys-Dietz Syndrome

In the dataset, one patient (0.2%) was identified as having a possible Loeys-Dietz syndrome, which is a genetic connective tissue disorder (Van Laer et al., 2014). The

presence of a possible Loeys-Dietz syndrome in the dataset is a rare occurrence. This genetic disorder is not typically considered a traditional risk factor for stroke, and its low incidence in the dataset reflects its infrequent association with stroke risk.

4.4.15 Prothrombin Gene Mutation

The dataset includes one patient (0.2%) with a prothrombin gene mutation, which is associated with an increased risk of clotting disorders. The presence of a prothrombin gene mutation in the dataset is a relatively rare occurrence. While this mutation can contribute to a heightened risk of clot formation, it is not considered a typical traditional risk factor for stroke.

4.4.16 Ramsay-Hunt Syndrome

Ramsay-Hunt syndrome is primarily associated with conditions like shingles and affects the facial nerve, leading to facial paralysis and various neurological symptoms (Goswami and Gaurkar, 2023). In the dataset, only one patient (0.2%) had RamsayHunt syndrome signifying that it is an uncommon stroke risk factor.

4.4.17 Smith-Magenis Syndrome

Smith-Magenis syndrome is a complex and uncommon condition associated with various neurological and behavioral issues (Rinaldi et al., 2022). It is typically caused by the deletion of a portion of chromosome 17. In the dataset, one patient (0.2%) was identified as having Smith-Magenis syndrome. The presence of Smith-Magenis syndrome in this dataset highlights its rarity as a risk factor for stroke. Given the unique and complex nature of this genetic disorder, it is not typically recognized as a traditional stroke risk factor.

4.4.18 Sneddon's Syndrome

In the dataset, one patient (0.2%) was identified as having Sneddon's syndrome, a rare vascular disorder. Sneddon's syndrome is a condition characterised by livedo reticularis (a mottled, purplish discoloration of the skin) and neurological symptoms such as headaches, strokes, and cognitive impairment (Wu et al., 2014). The low

percentage of patients with Sneddon's syndrome in this dataset suggests that this syndrome is not a common contributing factor to stroke within this specific population.

4.4.19 Thrombotic Thrombocytopenic Purpura (TTP)

Among the patients in the dataset, one individual (0.2%) had Thrombotic Thrombocytopenic Purpura (TTP), a rare and serious blood disorder. Thrombotic Thrombocytopenic Purpura (TTP) is characterised by the formation of small blood clots throughout the body, leading to a low platelet count (thrombocytopenia) (Stanley et al., 2022.). It is an uncommon risk factor for stroke in this dataset.

4.4.20 Congestive Heart Failure (CHF)

Table 4.5 shows the frequency table of Congestive Heart Failure (CHF). From the dataset, congestive heart failure (CHF) is not a prevalent condition among the patients who experienced stroke. Out of the 460 patients in the dataset, only 14 individuals (3.1%) had a history of CHF. On the other hand, the vast majority which comprised of 451 patients (96.9%), did not have CHF. The low prevalence of CHF in this dataset raises several important considerations**.** The limited presence of CHF in the dataset could be due to various factors, including underreporting, under diagnosis, or an inherent low incidence of CHF in the population under study. Additionally, the dataset may not have fully captured the broader population's experience with CHF as a risk factor for stroke.

4.4.21 Ischaemic Heart Disease (IHD)

Ischaemic Heart Disease, also known as coronary artery disease (CAD), relates to a limitation or interruption of coronary blood flow due to the buildup of plaque in the coronary arteries and can manifest as angina or myocardial infarction (Jensen et al., 2020; Saleh and Ambrose, 2018). While the primary manifestation of IHD is heart-related, it is also associated with an increased risk of cardioembolic stroke. Additionally, shared risk factors, such as hypertension and hypercholesterolemia, contribute to both conditions (Boehme et al., 2017).

Table 4.5 on the frequency distribution of Ischaemic Heart Disease (IHD) provides valuable information about the prevalence of these conditions among the study population. IHD was present in 8.9% (41) patients indicating that IHD is not a significant risk factor for strokes in young adults. Out of the 41 patients, 20 were diagnosed with myocardial infarction corresponding to approximately 4.3% of the study population. This rare proportion suggests a that MI is not a notable risk factor for strokes among the young adults in the study population.

4.5 TREATMENT MEASURES FOR STROKE IN THE STUDY POPULATION

The treatment of stroke includes various treatment measures employed in managing stroke patients. In this research, three treatment measures were considered; they include thrombolysis, thrombectomy, and surgical interventions. Each treatment modality played a distinct role in addressing different aspects of stroke and aimed to mitigate the impact of the condition and improve the patient outcomes. The tables of the statistical analyses showing the three treatment measures are presented in the Appendix Section.

4.5.1 Thrombolysis

Thrombolysis is a medical treatment used for acute ischaemic stroke. Thrombolysis is a standard and time-sensitive treatment for acute ischaemic stroke, as it can help restore blood flow to the affected area of the brain. However, its use is subject to several factors, including the time of presentation, patient eligibility, and the availability of medical facilities equipped to administer thrombolysis. It involves the administration of thrombolytics, such as tissue plasminogen activator (tPA), to break down blood clots that are obstructing blood flow to the brain (Wardlaw et al., 2014). In the dataset, 10.7% of patients (49 out of 460) received thrombolysis as a treatment for acute ischaemic stroke, while the majority (89.3%, 411 out of 460) did not receive this intervention. The relatively low percentage of patients who received thrombolysis in this dataset could be due to various reasons, such as low NIHSS score, delayed hospital arrival, contraindications for the treatment, or other factors that might impact the decision to use thrombolysis.

4.5.2 Thrombectomy

Thrombectomy is a medical procedure used in the treatment of acute ischaemic stroke. During a thrombectomy, a catheter is inserted into an artery, usually in the groin, and threaded up to the blocked blood vessel in the brain. A device is then used to physically remove or break up the blood clot causing the stroke, thus restoring blood flow to the affected area of the brain (Albers et al., 2018). In the dataset, only a very small percentage of patients (1.5%, 7 out of 460) underwent thrombectomy as a treatment for acute ischaemic stroke, while the majority (98.3%, 452 out of 460) did not receive this intervention. This suggests that thrombectomy is a relatively less common treatment option for acute ischaemic stroke in this population under study. Thrombectomy is typically recommended for eligible patients with large vessel occlusion strokes, and it can be a highly effective treatment when performed promptly. However, its limited utilization in this dataset could be due to various factors, including patient eligibility especially the type of stroke and low NIHSS score at presentation.

4.5.3 Surgery (Hemicraniectomy)

Surgery in the context of acute stroke treatment typically refers to hemicraniectomy / cranioplasty and haematoma evacuation. Hemicraniectomy plays a crucial role in the management of stroke, particularly in cases of severe ischaemic stroke or intracerebral hemorrhage (ICH) where increased intracranial pressure (ICP) threatens brain tissue viability. According to Ropper (2014), hemicraniectomy involves removing part of the skull to relieve pressure caused by swelling or bleeding in the brain. This procedure allows the brain to expand outward and reduces the risk of herniation and further damage. While hemicraniectomy can improve outcomes by preventing secondary brain injury, it is often reserved for patients with large strokes and significant mass effect. Following hemicraniectomy, cranioplasty is typically performed to replace the removed portion of the skull with a synthetic or autologous bone graft. Cranioplasty restores the protective barrier around the brain and provides cosmetic reconstruction.

From Table 4.29, only 3.0% of patients (14 out of 460) underwent surgery as a part of their stroke treatment, while the majority (97%, 445 out of 460) did not undergo surgical interventions. The low percentage of patients who received surgery for stroke treatment in this dataset suggests that, in the majority of cases, other treatment

modalities or medical management may have been preferred or indicated. It's important to note that the type of surgery and the patient's specific medical condition would influence the decision to proceed with surgical intervention. Additionally, not all strokes require surgery; treatment decisions are typically made on a case-by-case basis. The limited use of surgery as a stroke treatment in this dataset indicates that for many patients, non-surgical approaches, such as medications, thrombolysis, or other medical interventions, may have been deemed more appropriate or effective. Further analysis and clinical evaluation are needed to understand the factors influencing the utilization of surgery in stroke management within this population.

4.6 TREATMENT OUTCOMES

4.6.1 Duration of Admission

From Table 4.30, the mean duration of admission is approximately 14.94 days. This implies that, on average, patients in this dataset spent about 14.94 days in the hospital as part of their stroke care. Additionally, the median duration of admission is 4.00 days. The median is notably lower than the mean and this indicates that there might be some patients with significantly longer durations of admission, which influenced the mean. This also signifies that while most patients had relatively short hospital stays, some had much longer stay.

From the table, the computed mode is 2. This implies that the most common duration of admission is 2 days and indicates that a significant number of patients had relatively short hospital stays. More so, the standard deviation of 26.857 is relatively high. This high spread indicates a wide variation in the duration of admission, which means that some patients had very short stays, while others had exceptionally long ones, contributing to the considerable spread in the data.

The duration of admission represented the length of hospital stays for stroke patients. The data provides a comprehensive overview of the distribution of admission durations. The data on the duration of admission indicates a wide range in the length of hospital stays for stroke patients. While many had relatively short stays, some required much longer hospitalization, likely depending on the severity of the stroke and the necessary treatment. The data is divided into categories representing the number of days' patients

spent in the hospital. The most common duration of admission is 2 days, with 68 patients (14.8%) falling into this category. The range of hospital stays varies widely, from 0 days to 173 days. The majority of patients had relatively short hospital stays, with 34.4% staying 1-2 days, and 51.6% staying 1-4 days. After 20 days, the frequency decreases, and hospital stays of longer durations become less common. While most patients had short stays, there is a noticeable tail in the data, with some patients experiencing much longer hospitalization. It's important to note that the wide distribution of hospital stay durations could be influenced by factors such as stroke severity, treatment requirements, and individual patient health.

The results illustrate a wide range of hospital stays for individuals who have suffered a stroke. The data encompasses short stays of a few days to extended stays of several weeks or even months. The high standard deviation (26.857) indicates considerable variability in the duration of hospitalization. While the mean duration is 14.94 days, it should be noted that this mean is influenced by both shorter and longer stays. Hospital stays of 20 days or fewer are more common, with a cumulative percentage of 51.6% by day 2. This suggests that a substantial portion of patients is discharged relatively early after experiencing a stroke. Although less frequent, there are cases of significantly longer hospital stays (up to 173 days). These prolonged stays may be attributed to the severity of the stroke, complications, or the need for extended rehabilitation.

Figure 4.5 Bar Chart of Duration of Admission

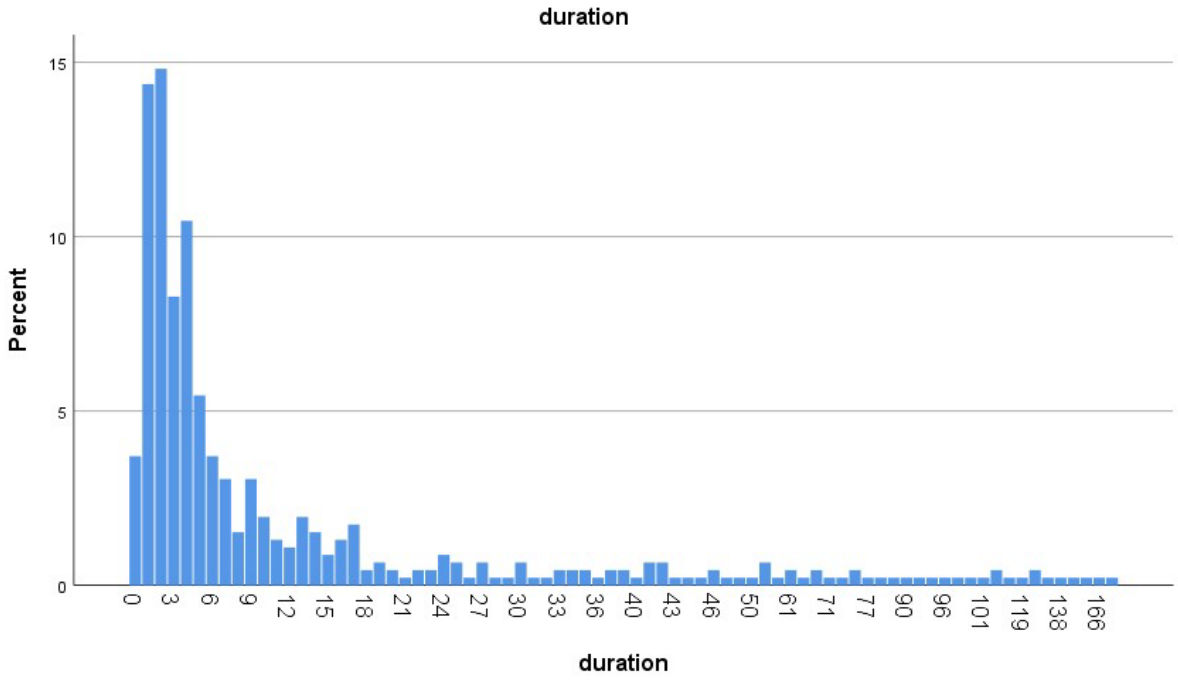


Table 4.31 Frequency Distribution of Patients Alive at 30 days
Alive at 30 days

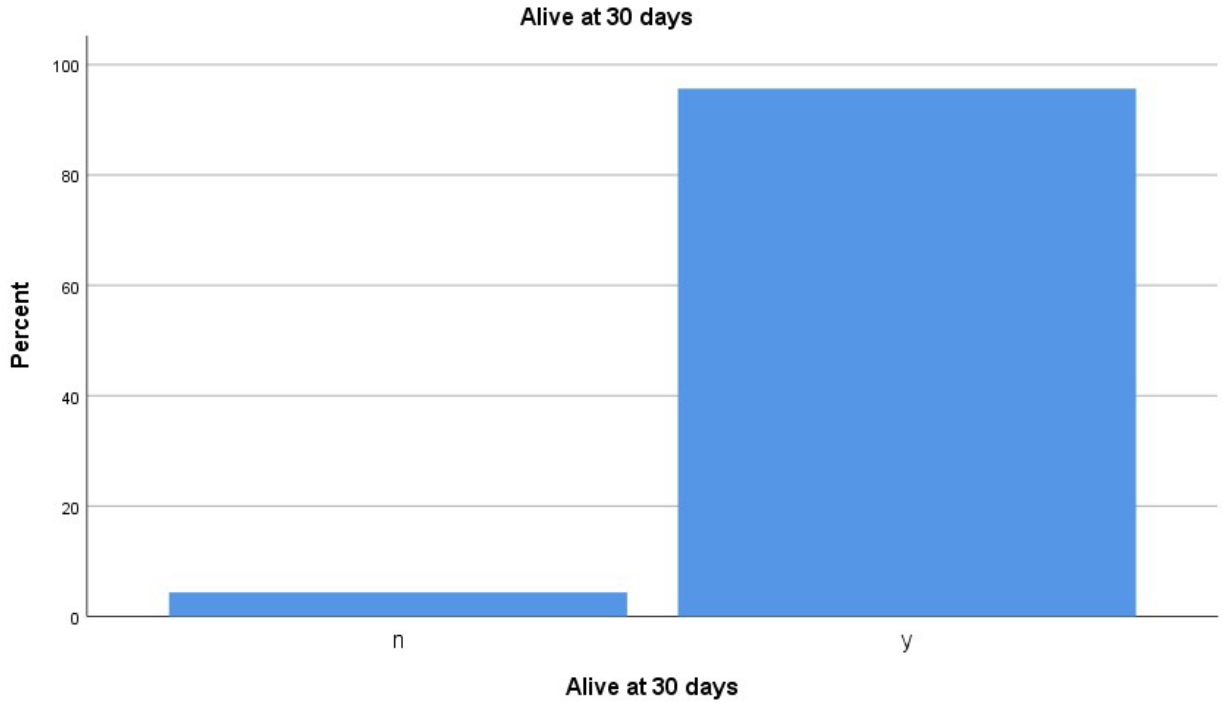
	Frequency	Percent	Valid Percent	Cumulative Percent
No	20	4.3	4.3	4.3
Yes	440	95.7	95.7	100.0
Total	460	100.0	100.0	

4.6.2 Alive at 30 days

Table 4.31 provides information about the survival status of patients 30 days after experiencing a stroke. The frequency table reveals key statistics and insights into the 30-day survival rate among stroke patients. Out of the 460 patients, 440 (95.7%) were alive at 30 days, while 20 (4.3%) were not. The results demonstrate a notably high 30day survival rate among stroke patients, with 95.7% of individuals being alive at the

end of this period. Only 4.3% of patients did not survive the first 30 days following their stroke. The data indicates that the majority of patients, specifically 95.7%, were still alive at 30 days after experiencing a stroke. This is a positive outcome, as it suggests that most patients survived the critical 30-day post-stroke period. On the other hand, 4.3% of patients did not survive up to 30 days following their stroke. While this is a relatively small percentage, it is important to note that stroke can have severe and sometimes fatal consequences. This information is valuable for healthcare providers and researchers as it reflects the short-term mortality rate in the stroke patient population. Further investigation may be needed to understand the factors contributing to patient outcomes and to identify ways to improve care and reduce mortality rates. The data may also prompt a deeper analysis of the specific treatments and interventions provided to patients to determine their impact on survival rates.

Figure 4.6 Bar Chart of Alive at 30 days



4.7 STATISTICAL COMPARISONS OF PATIENTS WHO DIED AND PATIENTS WHO SURVIVED

Table 4.32 Statistics of Student T-Test

Group Statistics

	Alive at 30 days	N	Mean	Std. Deviation	Std. Error Mean
Age	Yes	440	46.92	8.085	.385
	No	20	45.65	8.905	1.991

Table 4.32 displays the group statistics and provide a summary of the age distribution for patients who were alive at 30 days (Yes) and those who died within 30 days (No). The mean displayed the central tendency of the age distribution in each group. The mean age for patients who were alive at 30 days is approximately 46.92 years, while for those who died within 30 days, the mean age is around 45.65 years. Furthermore, the standard deviation measured the amount of variation or dispersion in the dataset. For patients alive at 30 days, the standard deviation is approximately 8.085. This indicates that ages within this group are relatively close to the mean. On the other hand, for patients who died within 30 days, the standard deviation is higher at approximately 8.905. This suggests a wider spread of ages around the mean. A larger standard deviation implies greater variability in ages within the group.

The standard error of the mean (SEM) quantified the variability of sample means around the population mean. For patients alive at 30 days, the standard error mean is approximately 0.385, and for those who died within 30 days, it is approximately 1.991. The standard error mean provided an estimate of how much the sample mean is likely to vary from the true population mean. A higher standard error mean for the group of patients who died within 30 days indicates that the sample mean is less precise and more likely to differ from the true population mean.

4.7.1 The Levene's Test for Equality of Variances

The Levene's Test for Equality of Variances is a statistical test that was used to assess whether the variances of two groups are equal or not. The Levene's Test for Equality of Variances helped to understand whether the spread or variability of the ages between two groups of patients is similar or different. The test was applied to age of the patients under the study to specifically compare those who survived at 30 days (grouped as 'y') and those who did not survive (grouped as 'n'). The Levene's Test produced a significance level which indicated whether there is a significant difference in the variances between the two groups. In the output, there are results for both the assumption of equal variances and the assumption of unequal variances. For the assumption of equal variances, the test statistic (F-ratio) is 0.887 while the p-value associated with the F-ratio is 0.347. For the assumption of unequal variances, the test statistic (F-ratio) is 0.624 while the p-value associated with the F-ratio is 20.449. By general principle, a low p-value (typically less than 0.05) indicates that there is evidence to reject the null hypothesis of equal variances. In this case, for both assumptions (equal and unequal variances), the p-values are higher than 0.05. This signifies that there is no significant difference in the variances of the two groups. This suggests that the assumption of equal variances is reasonable for the variable ages of the patients who survived at 30 days and those who did not. As the p-value value is high (typically above 0.05), it can be concluded that there's no strong evidence to say the variability in ages is significantly different between the groups. In other words, there’s no good reason to believe the ages vary differently between those who survived and those who did not.

4.7.2 T-test for Equality of Means

This statistical test was used to determine if there is a significant difference between the average ages of patients who survived at 30 days and those who did not. The ttest produced a t-statistic, which measured how far the sample mean (average age) is from the population mean, relative to the sample's standard deviation. In this study, it compared the mean ages of the two groups (survived and did not survive) to see if they are significantly different. The 't' value is accompanied by a 'Sig.' (significance) value, which was crucial in interpreting the results. From the table, the Equal

Variances, the 't' value is 0.682, and the 'Sig.' is 0.496. The 'df' (degrees of freedom) is 458. The 'Sig.' value here is greater than the commonly used significance level of 0.05. This implied that that there is no strong evidence to reject the null hypothesis. In other words, there is no significant difference in the average ages between the two groups. So, the t-test, portrayed that the observed difference in average ages between those who survived and those who did not could likely occurred by random chance. Therefore, there is not enough evidence to claim a significant difference in average ages. In conclusion, based on the t-test results, there is no sufficient evidence to claim a significant difference in the average ages between patients who survived at 30 days and those who did not. This implied that age, at least based on this analysis, may not be a critical factor in determining the 30-day survival outcome.

4.7.3 Chi-Square Test

Table 4.33 Independent Samples Test

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Age	Equal variances assumed	.887	.347	.682	458	.496	1.266	1.857	-2.383	4.915
	Equal variances not assumed			.624	20.449	.539	1.266	2.028	-2.959	5.490

Gender Alive at 30 days Cross tabulation

		No	30 days Yes	Total
Gender	Female	11	157	168
	Male	9	283	292
Total		20	440	460

Table 4.34 Gender Alive at 30 days Cross tabulation

The cross-tabulation table examined the relationship between gender and survival outcomes at 30 days. This breakdown provided a gender-specific overview of survival outcomes. Looking at the overall distribution, 20 patients did not survive, and 440 patients did, summing up to the total dataset of 460 patients. Focusing on the female category, 11 patients did not survive within the 30-day period, while 157 individuals did. On the male side, 9 patients did not survive, and 283 others did.

Table 4.35 Chi-Square Tests

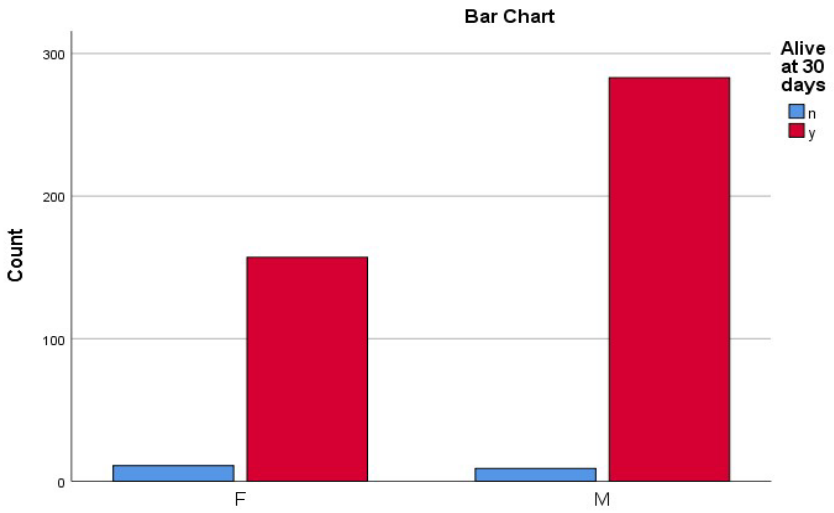
Chi-Square Tests

	Value	df	Asymptotic Significance (2sided)	Exact Sig. (2sided)	Exact Sig. (1sided)
Pearson Chi-Square	3.080[a]	1	.079		
Continuity Correction[b]	2.303	1	.129		
Likelihood Ratio	2.949	1	.086		
Fisher's Exact Test				.097	.067
N of Valid Cases	460				

a. 0 cells (0.0%) have expected count less than 5. The minimum expected count is 7.30.

b. Computed only for a 2x2 table

Figure 4.7: Bar Chart of Patients Alive at 30 days



The chi-square test was used to determine if there is a significant association between categorical variables. it was applied to assess the relationship between gender and the survival status of patients at 30 days. The Pearson Chi-Square statistic had a value of 3.080 with 1 degree of freedom. The associated p-value is 0.079. This p-value is a crucial indicator of whether the observed distribution of data significantly differed from the expected distribution under the assumption of independence between gender and survival status. The Continuity Correction statistic, which is 2.303, also had 1 degree of freedom. The Continuity Correction was applied to adjust the chi-square statistic and improve the accuracy of the test.

The Likelihood Ratio statistic is 2.949 with 1 degree of freedom, and the associated pvalue is 0.086. This statistic is an alternative approach to the Pearson Chi-Square and was particularly useful to improve the accuracy of the Chi-Square Test. More so, the Fisher's Exact Test yielded a p-value of 0.097 for the two-sided test and 0.067 for the one-sided test. The Fisher's Exact Test further supported the lack of evidence for a significant association between gender and survival status. In conclusion, the overall p-values from the Pearson Chi-Square, continuity correction, and likelihood ratio tests are all above the conventional significance level of 0.05. This implied that there is no strong evidence to reject the null hypothesis of independence between gender, age, and survival status at 30 days.

CHAPTER FIVE

Discussion and Conclusion

5.1 Introduction

This research aimed to unravel the enigmatic world of stroke in young adults in Southwest England. The study began with a profound acknowledgment of the shifting paradigm in stroke occurrences, particularly the marked increase among young adults, aged 18 to 55. This demographic shift prompted this investigation into the characteristics, risk factors, clinical presentations, and outcomes of stroke in this often-overlooked age group. The core aims and objectives guiding this research centers on comprehensively characterizing stroke in young adults presenting at the Bristol Royal Infirmary Stroke Unit, Bristol. This was done with the intent of determining the frequency of stroke; the risk factors and prognosis of stroke, as well as the clinical presentation of stroke among the young adults in Southwest England. This chapter synthesizes and summarizes the research findings from Chapter Four.

5.2 SUMMARY OF RESEARCH FINDINGS

5.2.1 Demographic Variables

The age distribution of the young adult stroke patients in this research ranged from 18 to 55 years, with a total of 460 patients in the study population. The mean age of the patients was approximately 46.86 years; this indicated that the average age of young adults experiencing stroke was close to the upper limit of the defined age range (55 years). In addition, the median age was 50.00 years; this indicated a relatively balanced distribution of ages without significant skew towards younger or older patients. The standard deviation of 8.116 indicated some variation in age within the study population and reflected the diversity of age groups affected by stroke among young adults. From the frequency distribution of the patient ages, while the majority of the patients fell within the early 50s, there was a consistent distribution observed across various age groups, and this emphasized the broad spectrum of ages affected by stroke among the young adults.

The sex demographics of the patients revealed a significant imbalance in the occurrence of stroke among the young adults in the study population. Out of the 460 patients included in the study population, 292 (63.5%) were male and 168 (36.5%) were

female. In terms of ethnicity, the study population exhibited a diverse range of ethnic backgrounds among the young adult stroke patients. The majority of the patients (78.6%) identified as British. Other ethnicities represented included African (4.0%), Caribbean (2.8%), and a variety of less frequently represented ethnic backgrounds. Notably, the "not stated" and "unknown" category accounted for 4.7% of the total study population. Besides, the vast majority of the patients (96.2%) were residents of the United Kingdom (UK). A small percentage of the patients originated from other countries, including Belgium, China, France, and Singapore, each representing less than 1% of the total study population. The "Unknown" category accounted for 2.8% of the total study population.

5.2.2 CLINICAL VARIABLES

5.2.2.1 Type of Stroke

The findings revealed valuable insights into the prevalence of ischaemic and haemorrhagic strokes in the study population. The results revealed a prevalence of ischaemic strokes among the young adults, accounting for 88.5% of the total study population. On the other hand, haemorrhagic strokes accounted for 11.5% of the study population. The study by Capriotti and Murphy (2016) noted that approximately 87% of all strokes worldwide are ischaemic. Similar trends are observed in various populations, as highlighted by Katzan (2013) and Hui et al. (2018), further affirming the global predominance of ischaemic stroke.

Studies focusing on older adults also report a high incidence of ischaemic strokes, but the proportion tends to be lower due to an increased occurrence of haemorrhagic strokes in this age group (Capriotti and Murphy, 2016; Alharbi et al., 2019). This distinction suggests that while ischaemic strokes are the most common type across all ages, younger adults may have a higher relative prevalence due to different risk factor profiles, such as a lower prevalence of conditions like atrial fibrillation, which is more common in older adults and contributes significantly to ischaemic stroke risk (Boehme et al., 2017).

Although less common, haemorrhagic strokes are associated with higher morbidity and mortality rates due to the significant brain damage that can result from bleeding (Doria

and Forgacs, 2019; Ojaghihaghighi et al., 2017). This finding is consistent with the literature, which frequently reports a lower incidence of haemorrhagic strokes compared to ischaemic strokes (Montaño et al., 2021). However, it is important to note that the proportion of haemorrhagic strokes may vary with age. Older adults tend to have a higher incidence of haemorrhagic strokes, partly due to age-related factors such as hypertension and amyloid angiopathy, which are less prevalent in younger populations (Gottesman and Seshadri, 2022).

This study's focus on young adults adds a critical dimension to the existing body of knowledge by highlighting the specific characteristics of stroke in this demographic. While stroke is traditionally associated with older age, the increasing incidence among younger adults necessitates a closer examination of the unique risk factors and clinical presentations in this group (Smajlović, 2015). Compared to other studies on young stroke patients, the high prevalence of ischaemic strokes observed here is consistent with findings in different regions and populations, such as the studies by Smajlović (2015) and Alharbi et al. (2019), which also report a predominance of ischaemic strokes in young adults. However, the specific rates and risk factor profiles can vary depending on genetic, lifestyle, and environmental factors (Boehme et al., 2017).

5.2.2.2 Severity of Stroke (NIHSS)

The severity of strokes among the study population was assessed using the National Institutes of Health Stroke Scale (NIHSS). The results showed that the mean NIHSS score was 4.87, this means that the strokes experienced by the study population generally fell within the minor to moderate severity range. It also reflects the level of neurological deficits observed among the patients, from mild impairments to more significant dysfunction. The median NIHSS score of 3.00 further highlights the typical severity level experienced by the patients. It showed that approximately half of the study population had scores of 3 or lower, which points to a trend toward milder stroke presentations. This is an encouraging finding, as lower NIHSS scores are generally associated with better prognoses and greater potential for functional recovery. Additionally, the mode score of 0 indicated minimal or no detectable neurological deficits, and further confirmed that a significant subset of patients presented with very mild symptoms or experienced rapid recovery. These findings are consistent with other

clinical observations found in young stroke patients in past studies (Abbott et al., 2017; Yakhkind et al., 2016). More so, the observed mild to moderate stroke severity aligns with past research on young stroke patients, which generally reports that strokes in younger adults tend to be less severe compared to those in older adults. This is often attributed to younger individuals having fewer comorbidities and better overall vascular health, factors that contribute to less severe neurological outcomes (Lutski et al., 2017; Yousufuddin and Young, 2019).

In contrast, studies focusing on older stroke patients often report higher NIHSS scores, reflecting more severe strokes. Older adults are more likely to have multiple comorbid conditions, such as atrial fibrillation and atherosclerosis, which contribute to both the frequency and severity of strokes in this age group (Bencivenga et al., 2020; Katzan et al., 2014). This difference highlights the importance of age-specific strategies in stroke management, where younger patients might benefit more from early and aggressive rehabilitation, given their higher potential for recovery.

5.2.3 EXPOSURE

5.2.3.1 Traditional Stroke Risk Factors

5.2.3.1.1 Hypertension (HTN)

Hypertension emerged as a significant risk factor for stroke among the young adults in this study, with 38% of the patients diagnosed with hypertension. This high prevalence underscores the crucial role of blood pressure management in stroke prevention, particularly among younger populations. Uncontrolled hypertension is known to cause vascular damage, significantly increasing the risk of both ischaemic and haemorrhagic strokes (Dubow and Fink, 2011). Therefore, effective measures to control hypertension are essential in reducing stroke incidence and its associated disabilities.

The strong association between uncontrolled hypertension and an elevated risk of stroke is well-documented in the literature. Pistoia et al. (2016a) and Wajngarten and Silva (2019) both emphasize that hypertension is a key factor in the development of both ischaemic and haemorrhagic strokes. Globally, hypertension remains one of the leading causes of stroke, as demonstrated by Mills et al. (2020), who found that this risk factor significantly impacts stroke rates across all age groups. The study by

Namaganda et al. (2022) further supports these findings by explaining the persistent burden of hypertension-related strokes worldwide, particularly among younger adults.

It is evident that hypertension is a universal risk factor, but its impact may differ across age groups. While hypertension is a well-known risk factor in older stroke patients, where the prevalence is often higher due to age-related increases in blood pressure and vascular stiffness, the significance of hypertension in younger stroke patients is increasingly recognized. This study's finding that 38% of the patients had hypertension aligns with other research showing that hypertension is becoming more prevalent among younger populations, likely due to lifestyle factors such as poor diet, physical inactivity, and obesity (Mills et al., 2020; Samadian et al., 2016).

In contrast, older stroke cohorts typically exhibit a higher prevalence of hypertension, often exceeding 60% in some studies (Ovbiagele and Nguyen-Huynh, 2011). This difference in prevalence highlights the importance of early detection and management of hypertension in younger individuals to prevent stroke occurrence later in life. The relatively lower prevalence in younger adults suggests a window of opportunity for intervention before hypertension becomes more severe and entrenched.

Furthermore, a comparison of this study's findings to other studies focused on younger stroke patients shows a similar pattern. The study by Ramírez-Moreno et al. (2022) report hypertension as a leading risk factor among young stroke patients, with prevalence rates comparable to those found in this study. This consistency across studies emphasizes the need for targeted public health strategies to address hypertension in younger populations, particularly given the rising rates of hypertension-related strokes among young adults worldwide.

5.2.3.1.2 Atrial Fibrillation (AF)

Atrial fibrillation (AF) was observed in 8.2% of the young adults in the study population, indicating a less prevalent yet significant risk factor for stroke. Although AF was less common in this cohort, its presence is particularly concerning due to its association with severe stroke outcomes. Past studies have shown that AF poses a substantial stroke risk, regardless of age. Studies like those by EscuderoMartinez et al. (2023) and Essa

et al. (2021) have shown that AF is more prevalent among older stroke patients, contributing to a higher incidence of ischaemic strokes in that demographic. Pistoia et al. (2016b) demonstrated through a large-scale cohort study that individuals with AF face a significantly increased stroke risk, with variations depending on age, sex, and comorbidities. This study's findings align with these earlier studies, particularly in recognizing AF as a critical risk factor despite its lower prevalence among young adults. Moreover, the literature suggests that while AF is less common in younger stroke patients, it should not be underestimated. Bencivenga et al. (2020) and Zathar et al. (2019) report that the impact of AF on stroke severity and outcomes is substantial, particularly as patients age. The lower prevalence of AF in younger adults may reflect better overall cardiovascular health in this age group, but the data from this study reinforce the need for targeted AF management strategies, even in younger populations to prevent severe stroke outcomes.

5.2.3.1.3 Smoking

Smoking was also identified as a risk factor among the young adults in the study, with 15% reporting current smoking habits. The adverse effects of smoking on vascular health are well-established, including the promotion of atherosclerosis, endothelial dysfunction, and increased clotting tendencies (Katsiki et al., 2013). Current smokers face a significantly higher risk of stroke; this shows the the critical need for smoking cessation programs and robust tobacco control measures. Additionally, 22.2% of the study population were ex-smokers, and this highlighted the potential benefits of quitting smoking in reducing stroke risk over time.

The prevalence of smoking observed in this study aligns with studies, which consistently emphasizes the negative impact of smoking on vascular health and its strong association with an increased risk of stroke (Gordon and Flanagan, 2016; Shah and Cole, 2010). Pan et al. (2019) conducted a meta-analysis that revealed a dose-response relationship between smoking and stroke risk, showing that current smokers are at the highest risk compared to nonsmokers and former smokers. This finding is consistent with other studies, such as Choudhury et al. (2015), which highlighted smoking as a modifiable risk factor particularly relevant for young and middle-aged adults.

Moreover, the significance of smoking cessation in reducing stroke risk is well-documented. Parikh et al. (2022) and Shigematsu et al. (2023) emphasized on the importance of targeted interventions to help individuals quit smoking, particularly in younger populations where the long-term benefits of cessation can be substantial. A comparison of these findings with older cohorts suggest that while smoking remains a significant risk factor across all age groups, younger stroke patients may benefit more from early cessation interventions. The lower prevalence of smoking in older stroke patients reported in some studies may reflect the cumulative effects of smoking on cardiovascular health over time, leading to earlier strokes in those who continue smoking (Parikh et al., 2022).

5.2.3.1.4 Alcohol (EtOH) Consumption

Although alcohol consumption was relatively low among the young adults in the study population (11.3%), its potential implications for stroke risk warrant attention. Excessive alcohol intake is known to contribute to conditions such as hypertension, atrial fibrillation, and cardiomyopathy, all of which are associated with an increased risk of stroke (Manolis et al., 2019). Interestingly, a significant majority (88.3%) of individuals in the study abstained from alcohol. However, even with a lower prevalence, the impact of alcohol consumption on stroke occurrence cannot be overlooked. Existing literature acknowledges the complex relationship between alcohol intake and stroke risk. While the study found a lower prevalence of alcohol consumption among the young adults, heavy alcohol use has been consistently linked to an elevated stroke risk through various mechanisms. These include its association with hypertension, atrial fibrillation, and other cardiovascular risk factors that contribute to stroke (Giannopoulos et al., 2022; Sano et al., 2014). Figueredo and Patel (2023) also highlighted the detrimental effects of excessive alcohol consumption on blood pressure regulation by emphasizing its role in promoting hypertension which is a major risk factor for stroke.

When comparing these findings with older stroke cohorts, the data suggest that while alcohol consumption remains a risk factor across all age groups, the impact may be more pronounced in older populations where the cumulative effects of alcohol use can exacerbate existing cardiovascular conditions (Piano, 2017; Whitman et al., 2017). In

younger adults, the lower prevalence of alcohol use observed in this study may partly explain the reduced stroke risk in this group, though the potential for harm in those who do consume alcohol heavily remains significant.

5.2.3.1.5 Hypercholesterolemia

Hypercholesterolemia was identified as a less prevalent risk factor among the young adults in the study, with only 3.3% of patients exhibiting this condition. Although the association between cholesterol levels and stroke is debated, hypercholesterolemia is known to contribute to atherosclerosis, which can increase the risk of ischaemic strokes (George, 2020). Despite its lower prevalence in this study, hypercholesterolemia remains an important factor in stroke risk stratification and indicates the need for effective lipid profile management as part of stroke prevention strategies.

The relatively low prevalence of hypercholesterolemia among the young adults in this study may reflect differences in lipid profile management and varying risk factor profiles across different populations (Belete et al., 2023). Previous research indicates that while hypercholesterolemia is a recognized risk factor for atherosclerosis and ischaemic strokes, its impact can vary based on genetic predispositions, lifestyle factors, and underlying health conditions (Boehme et al., 2017; Della-Morte et al., 2012). Comparing these findings to older stroke cohorts, hypercholesterolemia is generally more prevalent and impactful in older patients. For example, studies have shown that young adults may have a different risk profile compared to older populations, where hypercholesterolemia is more prevalent and its role in stroke risk is more pronounced (Adeloye et al., 2020). This discrepancy highlights the importance of differentiating risk factors by age group. In older adults, elevated cholesterol levels often contribute significantly to stroke risk due to longer exposure to high cholesterol and the cumulative effects of atherosclerosis. In younger patients, the lower prevalence of hypercholesterolemia suggests that while it is a factor, its role might be less prominent compared to other risk factors such as hypertension or smoking.

5.2.3.1.6 Diabetes Mellitus

Diabetes mellitus accounted for 2.8% of the young adults in this study population. The association between diabetes and ischaemic stroke risk is well-established, as

demonstrated by Mitsios et al. (2018), whose systematic review and meta-analysis indicated that individuals with diabetes face a markedly higher stroke risk compared to non-diabetic individuals. This elevated risk is attributed to the multifaceted impact of diabetes on vascular health, including endothelial dysfunction, inflammation, and accelerated atherosclerosis (Barbu et al., 2022; Maida et al., 2022). The findings also echo the results of Lowe et al. (2023), who emphasized that diabetes amplifies stroke risk through its detrimental effects on vascular health.

Comparatively, the 2.8% prevalence observed in this study is lower than that reported in studies involving older cohorts of stroke patients, where diabetes prevalence tends to be higher (García-Esquinas et al., 2015). This discrepancy could be attributed to the generally lower incidence of diabetes among younger adults or to differences in the study populations. However, it is essential to contextualize these findings within the broader literature. While diabetes is a well-recognized risk factor for stroke in older populations, the impact of diabetes on stroke risk in younger adults requires further exploration. The relatively lower prevalence of diabetes in younger stroke patients, as observed in this study, highlights the potential differences in risk factor profiles between younger and older populations. Therefore, the findings suggest that while diabetes remains a critical risk factor, its role in younger adults may differ in magnitude or interact with other risk factors in unique ways.

5.2.3.2 RISK FACTORS SPECIFIC TO YOUNG PEOPLE

5.2.3.2.1 Illicit Drug Use

The result revealed that 7.6% of the young adults in the study population admitted to using recreational drugs. This percentage aligns with documented data on the cardiovascular effects of recreational drugs and their association with increased stroke risk (Gan et al., 2021; Huang et al., 2016). Rendon et al. (2023), in a systematic review and meta-analysis, revealed a significant association between cocaine use and the risk of both ischaemic and haemorrhagic strokes among younger individuals. This is a notable finding, as illicit drug use has been associated with various adverse cardiovascular effects, including hypertension, vasospasm, thromboembolism, and atrial fibrillation (Akasaki & Ohishi, 2020; Esse et al., 2011). These effects contribute to an elevated stroke risk, particularly in younger individuals who may not have other

traditional risk factors. Chronic drug use further exacerbates this risk by damaging blood vessels and the heart, increasing the likelihood of stroke (Bachi et al., 2017). It was encouraging that 92.4% of the young adults reported not using illicit drugs. This meant that a significant portion of the studied population is making healthier lifestyle choices by avoiding recreational drugs. This lower prevalence of drug use implies a potentially reduced risk of strokes associated with drug use in this specific demographic. Studies on older cohorts of stroke patients often report higher rates of illicit drug use and a more pronounced impact on stroke risk (Sordo et al., 2014; Gan et al., 2021). This discrepancy suggests that younger adults may either engage in less frequent drug use or experience different patterns of cardiovascular response to drug use compared to older individuals.

5.2.3.2.2 Hormone Replacement Therapy (HRT)

In this study, only 1.3% of the young adults reported using Hormone Replacement Therapy (HRT). The low prevalence of HRT usage in this study population suggests that hormone therapy is not widely adopted among young adults in this cohort. Consequently, HRT may not be a significant contributor to stroke risk within this specific demographic. The findings from this study contrast with the mixed results in existing literature regarding the relationship between HRT and stroke risk. While some studies have reported a slight increase in stroke risk associated with HRT, particularly among postmenopausal women, others have found conflicting results (Cagnacci & Venier, 2019; Demel et al., 2018; Langer et al., 2021). For instance, Gu et al. (2014) conducted a meta-analysis that indicated an increased stroke risk, particularly with combined estrogen-progestin therapy. In contrast, Oliver-Williams et al. (2019) conducted a systematic review that highlighted the variability in findings, suggesting that the association between HRT and stroke risk may depend on several factors, including the timing of initiation, duration of use, and type of hormones administered.

A comparison of the study's findings with those from studies on older cohorts becomes clear that the role of HRT in stroke risk is more pronounced among older women, particularly those undergoing menopause (Prabakaran et al., 2021). The low prevalence of HRT usage in the younger population observed in this study aligns with the notion that HRT is typically more relevant to postmenopausal women, who are older and at a different stage in their hormonal lifecycle.

5.2.3.2.3 Genetics

Genetic factors are known to play a significant role in stroke risk, and this study identified a stroke-related genetic component in approximately 0.8% of the young adults. Among these cases, specific genetic mutations were identified, including CADASIL (Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy) and MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like Episodes). CADASIL is associated with a mutation in the Notch 3 gene, while MELAS is linked to mutations in mitochondrial DNA (Dunn, 2022). These findings align with the broader understanding that strokes in young adults often have a hereditary component, with genetic variants influencing factors such as blood vessel integrity and clotting mechanisms. Although the overall percentage of patients with stroke-related genetic components in this study is low, these cases underscore the complex role of genetics in stroke aetiology among young adults and highlight the importance of considering genetic analysis as part of the diagnostic work-up, particularly when no obvious risk factors are initially identified.

The identification of genetic factors in a subset of the study population corroborates studies that underscores the significant role genetics play in stroke aetiology (Chauhan & Debette, 2016; Korchagin et al., 2016). According to Bersano et al. (2021), genetic conditions such as CADASIL and MELAS are well-documented contributors to stroke pathophysiology. These findings further support the critical importance of genetics in stroke risk assessment and emphasize the need for genetic testing and counseling as part of a comprehensive approach to managing stroke risk, particularly in young adults. When compared with studies on older cohorts, it is clear that the impact of genetic factors in stroke aetiology may vary with age. Studies have shown that in older populations, stroke risk is often more heavily influenced by traditional risk factors such as hypertension, diabetes, and atherosclerosis, with genetic components playing a more background role (Boehme et al., 2017; Corella et al., 2014; Debette and Markus, 2022). In contrast, among younger stroke patients, as demonstrated in this study, genetic factors can be more prominent, sometimes being the primary risk factor in the absence of other traditional causes.

5.2.3.2.4 Migraine

In this study, approximately 12.8% of the young adults reported a history of migraines. However, the majority of the study population (87.2%) did not report a history of migraines, indicating that migraines may not have been a significant factor for most individuals in this cohort. The prevalence of migraines in the study population is consistent with previous studies linking migraine history, particularly migraines with aura, to an increased risk of ischaemic strokes (Øie et al., 2020; Zhang et al., 2017). Martinez-Majander et al. (2021), in a large-scale prospective cohort study, found a significant association between migraines with aura and ischaemic stroke risk, particularly among younger individuals. Similarly, Valecha et al. (2023) emphasized the importance of considering migraine history, particularly aura status, in stroke risk assessment among young adults. Furthermore, Rist et al. (2017) explored the various pathophysiological mechanisms linking migraines to stroke risk, including endothelial dysfunction, cortical spreading depression, and hypercoagulability. When comparing these findings with those from older cohorts, it is evident that while migraines are a recognized risk factor for stroke, their impact may differ with age. In younger populations, migraines, particularly those with aura, seem to play a more prominent role in stroke risk compared to older populations, where traditional cardiovascular risk factors such as hypertension and diabetes often dominate.

5.2.3.2.5 Deep Vein Thrombosis/Pulmonary Embolism (DVT/PE)

In this study, approximately 7% of the young adults reported a history of Deep Vein Thrombosis (DVT) or Pulmonary Embolism (PE). The relatively low prevalence of DVT/PE in this young adult cohort suggests that these conditions may not be common risk factors for stroke in this population. However, the presence of DVT/PE in a subset of patients could indicate an underlying predisposition to thrombotic events or the existence of shared risk factors with stroke, such as genetic clotting disorders or prolonged immobility. This aligns with the understanding that VTE is more common in older populations, where the prevalence of stroke is also higher. According to Spencer et al. (2014), the relationship between DVT/PE and stroke risk is more pronounced in older adults, where the incidence of VTE and related complications increases with age. In older patients, conditions such as atrial fibrillation and heart failure, which are more

prevalent, further elevate the risk of both VTE and stroke, leading to a more substantial overlap between these conditions (Dicks et al., 2024). On the other hand, the presence of DVT/PE in younger adults may indicate more specific underlying risk factors, such as inherited thrombophilias, autoimmune diseases, or conditions like antiphospholipid syndrome, which can significantly influence stroke risk even in the absence of traditional cardiovascular risk factors.

5.2.3.2.6 Non-Haematological Malignancy

Approximately 7% of the young adults in this study reported a history of non-haematological malignancies. Non-haematological malignancies, including various cancers, have a complex and multifaceted relationship with stroke. Certain cancers, particularly brain tumors, have direct effects on blood vessels, potentially increasing the risk of stroke (Dardiotis et al., 2019). Additionally, the prothrombotic effects induced by tumors and the side effects of cancer treatments, such as chemotherapy and radiotherapy, contribute to the heightened susceptibility to stroke in cancer patients (Costamagna et al., 2023).

The relatively low prevalence of non-haematological malignancies in the study population suggests that, within this specific young adult cohort, cancer is not a predominant risk factor for stroke. This finding is consistent with studies that have reported a lower prevalence of cancer-related strokes in younger populations compared to older cohorts, where cancer is a more significant risk factor due to the higher incidence of malignancies with advancing age (Boehme et al., 2017). This implies that in older populations where the incidence of cancer is higher, the association between malignancies and stroke is more pronounced, and cancer-related strokes are more frequent. However, in younger adults, where cancer prevalence is lower, other risk factors, such as genetic predispositions, lifestyle factors, and autoimmune conditions, may play more substantial roles in stroke aetiology.

5.2.3.2.7 Haematological Malignancy

Only 1% of the young adults in the study population had a history of haematological malignancies. The study identified specific types of blood cancers, including leukemia, lymphoma, and myeloma, in a small percentage of patients. Each of these malignancies

has distinct implications for stroke risk. For example, leukemia is associated with a hypercoagulable state, and increases susceptibility to blood clot formation and stroke (Ferro and Infante, 2021). Similarly, lymphoma and myeloma, which affect lymphocytes and plasma cells respectively, have varying impacts on the vascular system; they contribute to stroke risk through mechanisms such as increased clotting propensity and endothelial dysfunction (Bhagat et al., 2023).

The low prevalence of haematological malignancies in the study population suggests that these conditions are not common risk factors for stroke among young adults in this cohort. However, the presence of haematological malignancies in even a small subset of patients indicates the need for careful consideration of these conditions in the context of stroke risk assessment and management. This finding aligns with previous studies that have reported a lower incidence of stroke associated with haematological malignancies in younger populations compared to older cohorts, where the prevalence of these cancers and their associated stroke risk is higher (Khorana et al., 2022). This shows that the relationship between haematological malignancies and stroke is more significant in older adults, where the prevalence of blood cancers and the associated complications are higher. In younger populations, other risk factors, such as genetic predispositions, lifestyle factors, and autoimmune conditions, may have a more prominent role in stroke aetiology.

5.2.3.2.8 Endocarditis

About 7.7% of the young adults reported a history of endocarditis. Endocarditis, characterised by inflammation of the heart valves and endocardium, is a significant contributor to cardiac embolism and is associated with neurological complications, including strokes (Bettencourt and Ferro, 2020). The prevalence of endocarditis in this study population suggests that while it may not be a highly prevalent risk factor for strokes among young adults, it remains clinically significant in those affected. Compared to older cohorts, the role of endocarditis as a stroke risk factor is generally more prominent in older adults because it is often associated with predisposing conditions like prosthetic heart valves, rheumatic heart disease, and immunosuppression (Cao et al., 2019; Miller and George, 2012). However, in younger populations, where such predisposing factors are less common, the occurrence of endocarditis may be linked to

more specific causes such as intravenous drug use, congenital heart disease, or bacteremia from other sources (Erichsen et al., 2016; Wurcel et al., 2016). This distinction highlights the need for a tailored approach to stroke prevention and management in younger adults, taking into account the unique etiological factors that may not be as prevalent in older populations.

5.2.3.2.9 Peripheral Vascular Disease (PVD)

Peripheral Vascular Disease (PVD) was reported by only 1.3% of the young adults in the study population. The low prevalence of PVD in this study suggests that it is not a common risk factor for stroke in young adults. However, the association between atherosclerosis and stroke risk underscores the importance of considering vascular health, even in younger populations where the condition is less prevalent. In older populations, PVD is more commonly seen and is a significant risk factor for both stroke and cardiovascular events due to the widespread nature of atherosclerosis in these age groups (Criqui et al., 2010). The lower prevalence of PVD in younger adults may reflect the lower overall burden of atherosclerotic disease in this demographic, which could be due to fewer traditional risk factors such as hypertension, diabetes, and smoking. However, in younger adults who do present with PVD, it may indicate a more aggressive or early-onset form of vascular disease. A study by Maillet et al. (2017) highlighted that young adults with PVD have an increased risk of stroke, particularly if they have other concomitant risk factors such as smoking or dyslipidemia. This reinforces the need for a comprehensive approach to stroke risk assessment in young adults, even in the presence of seemingly less common conditions like PVD.

5.2.3.2.10 Cervical Artery Dissection

Cervical artery dissection was identified in approximately 5.7% of the young adults in this study. Although cervical artery dissection is a rare cause of stroke in the general population, it is recognized as one of the more common causes of stroke in younger individuals (Jazbec et al., 2021; Robertson and Koyfman, 2016). The relatively low prevalence of cervical artery dissection in this study aligns with its classification as an uncommon cause of stroke. However, its presence in a subset of the population emphasizes the importance of considering vascular abnormalities as significant contributors to stroke, particularly in young adults.

Past studies show that cervical artery dissection is often associated with physical trauma, both minor and major, or with underlying connective tissue disorders, making it a more frequent cause of stroke in younger adults compared to older populations, where atherosclerosis predominates (Engelter et al., 2021; Mihai et al., 2020). This distinction is crucial for clinical practice, as the management of stroke due to cervical artery dissection differs from that of atherosclerotic stroke; it often involves anticoagulation or antiplatelet therapy rather than cholesterol-lowering agents or other treatments typically used for atherosclerosis-related strokes. Other studies on younger stroke patients, such as the one conducted by Lee et al. (2017), confirm the significance of cervical artery dissection as a leading cause of stroke in this demographic, particularly in those without traditional cardiovascular risk factors. The findings of this study, therefore, reinforce the need for healthcare providers to maintain a high index of suspicion for cervical artery dissection in young adults presenting with stroke symptoms.

5.2.3.2.11 Patent Foramen Ovale (PFO)

Patent foramen ovale (PFO) was identified in approximately 10.4% of the young adults in this study. PFO, a common congenital heart defect characterised by an opening between the heart's two upper chambers, is often asymptomatic but has been associated with an increased risk of cryptogenic strokes due to the potential for paradoxical embolism (Homma et al., 2016; Collado et al., 2018). The relatively high prevalence of PFO in this study suggests that it may be a significant risk factor for stroke among young adults. Comparatively, in older stroke patients, the role of PFO is less clear as the stroke aetiology in older adults is more likely to be related to atherosclerosis, atrial fibrillation, or other age-related cardiovascular conditions (Gaspardone and Sgueglia, 2020; Meier et al., 2012). However, in younger populations, where traditional stroke risk factors are less common, PFO's role in cryptogenic strokes is more pronounced. This aligns with findings from Chen et al. (2023), which indicate that PFO is more frequently identified in younger patients with cryptogenic stroke than in older cohorts. This emphasizes the need for thorough cardiac evaluation in younger adults with unexplained strokes.

5.2.3.2.12 Sickle Cell Disease (SCD)

In the study population, only two patients were diagnosed with sickle cell disease (SCD). This genetic disorder predisposes individuals to hemolytic anemia and vaso-occlusive events, including stroke (Usmani and Machado, 2018). While SCD is a well-established risk factor for stroke, it is important to note that sickle cell trait is generally considered a milder condition with a significantly lower risk of stroke. The identification of SCD in the two patients meant that the necessity for genetic counseling and comprehensive stroke risk assessment in individuals with hemoglobinopathies.

Existing literature consistently supports the association between SCD and an increased risk of stroke among younger generation (Talahma et al., 2014). Multiple cohort studies and clinical trials have provided robust evidence linking SCD to elevated stroke risk (Hankins et al., 2018). Notably, observational studies have identified specific risk factors associated with stroke in children with SCD, including a history of transient ischaemic attacks (TIAs), elevated transcranial Doppler (TCD) velocities, and silent cerebral infarcts (SCIs) detected through neuroimaging. These studies confirm that SCD is predominantly studied in pediatric populations, where the risk factors for stroke have been well-documented.

5.2.3.2.13 Other Cardiac Conditions

The results of the study present other cardiac conditions identified as risk factors within the studied population. These conditions comprise a spectrum of structural, congenital, and acquired abnormalities that affect different components of the cardiovascular system. Firstly, aortic stenosis identified in 0.4% of the cases. Other aortic valve diseases, which include a range of abnormalities that affects the aortic valve beyond stenosis, accounted for 0.6% of the cases. These conditions, though relatively rare, represent significant structural defects that can lead to impaired cardiac function and increased risk of adverse cardiovascular events, including strokes (Greeve et al., 2014).

Other cardiac conditions, ventricular septal defect (VSD) and atrial septal defect (ASD) were found in the study population. Both VSD and ASD were identified in 0.2% each of the study population. More so, aortic valve replacement, mitral valve stenosis, and mitral valve disease, each identified in 0.2% to 0.4% of cases. Furthermore, dilated cardiomyopathy (DCM) and hypertrophic cardiomyopathy (HCM), two distinct forms of myocardial dysfunction were identified in 0.2% and 0.6% of cases respectively. Additionally, left ventricular hypertrophy (LVH) and mechanical valve implantation was found in the study population. LVH and mechanical valve implantation were identified in 0.6% and 0.2% of cases, respectively. For Congenital heart disease (CHD), this was identified in 0.2% of the study population. More so, heart block, a conduction disorder impairing electrical signaling within the heart, was identified in 0.4% of the study population.

The identification of these cardiac conditions among the study population are in line with existing literature. Aortic stenosis (AS) and other aortic valve diseases highlights the association between valvular abnormalities and adverse cardiovascular events, including strokes (Thaden et al., 2014). Several mechanisms may contribute to the elevated stroke risk in individuals with AS. Aortic stenosis is often accompanied by other cardiovascular risk factors, such as hypertension, atrial fibrillation, and atherosclerosis, which are independently known to increase stroke risk (Greve et al., 2014). Furthermore, AS can alter cardiac hemodynamics and promote the formation of blood clots. The turbulent blood flow across the stenotic aortic valve can lead to endothelial injury and platelet activation, thereby contributing to thrombus formation (Bańka et al., 2023). In comparison to older cohorts, where aortic stenosis is typically observed in an older population with multiple comorbidities. This finding aligns with the notion that while AS is less common in young adults, its presence warrants careful consideration of stroke prevention strategies.

Other aortic valve diseases, including aortic regurgitation (AR) and bicuspid aortic valve (BAV), are also associated with an increased risk of stroke among younger adults, although to a lesser extent compared to AS. The pathophysiological mechanisms underlying the association between these aortic valve diseases and stroke risk may vary. Past studies show that the regurgitant flow in AR can lead to

turbulence and stasis of blood flow in the ascending aorta and aortic arch to promote thrombus formation and embolic events (Zeng et al., 2016; Parato et al., 2019).

Additionally, chronic volume overload and left ventricular dilation may be associated with atrial enlargement and atrial fibrillation, further increasing the risk of stroke. BAV, the most common congenital heart valve anomaly, is primarily associated with aortic valve stenosis and regurgitation. However, younger individuals with BAV may also be at an increased risk of stroke due to associated cardiovascular abnormalities, such as aortic dilatation, aortic dissection, and aortopathy (Kusner et al., 2023). Furthermore, although ventricular septal defect (VSD) primarily affects cardiac function, existing literature suggests that it may also be associated with an increased risk of stroke, particularly paradoxical embolic strokes (Kim, 2020; Sakharuk et al., 2023). Individuals with VSD are at risk of developing paradoxical emboli due to the presence of a right-to-left shunt. Our findings suggest that while VSD is a less common cause of stroke, its presence in young adults should prompt a thorough evaluation for potential embolic sources, especially in cases of unexplained stroke. This is consistent with earlier studies that emphasize the importance of identifying congenital heart defects as part of a comprehensive stroke workup in younger populations.

In the context of dilated cardiomyopathy (DCM), the findings are consistent with existing literature, which states that individuals with DCM may be at an increased risk of stroke, particularly ischaemic stroke (Arboix, 2015; Kumar, 2015). Several mechanisms may contribute to the elevated stroke risk in individuals with DCM. Impaired left ventricular function and reduced cardiac output in DCM can lead to blood flow stasis in the left atrium and atrial appendage, promoting thrombus formation (Beigel et al., 2014). These thrombi can embolize to the cerebral circulation, causing ischaemic stroke. Additionally, individuals with DCM may have associated cardiovascular risk factors, such as hypertension, dyslipidemia, and diabetes mellitus, which are known to independently increase the risk of atherosclerosis and stroke (Schultheiss et al., 2019).

For congenital heart disease (CHD), past studies show that the disease is associated with an increased risk of stroke, particularly ischaemic stroke aong younger individuals (Pedersen et al., 2019). The increased risk of stroke in individuals with CHD may be attributed to various factors, including altered hemodynamics, abnormal blood flow patterns, and the presence of associated cardiovascular anomalies (Nattel et al., 2017). Heart block, particularly higher degrees of block (e.g., second-degree or third-degree AV block), is associated with an increased risk of stroke, particularly cardioembolic stroke in younger population (Kamel and Healey, 2017). Comparing the findings to older cohorts, where heart block and stroke may be more common due to a higher prevalence of comorbidities, the presence of heart block in younger patients should be considered a significant risk factor for stroke.

5.2.3.3 OTHER INDIVIDUAL STROKE RISK FACTORS IDENTIFIED

The research findings also provide insights into the individual stroke risk factors beyond the commonly recognized ones. These risk factors, although less frequent, play crucial roles in understanding the multifaceted nature of stroke aetiology, particularly in specific patient populations.

5.2.3.3.1 Thrombophilia

In the study population, thrombophilia was identified in only one patient, indicating its relatively low prevalence compared to other stroke risk factors. However, this low prevalence contrasts with some studies that indicate thrombophilia may be more common than previously believed, particularly in young adults with stroke (Mannucci, 2011; Pezzini et al., 2018). The low incidence observed in this study may reflect either an underdiagnosis or a true lower prevalence in this specific population. Therefore, further research and more extensive screening in similar cohorts could provide better insight into the actual role of thrombophilia in stroke risk among young adults.

Emerging studies highlight the role of inherited thrombophilias, such as Factor V Leiden and prothrombin gene mutations, in increasing the risk of thrombotic events. These genetic conditions lead to a hypercoagulable state, elevating the risk of venous thromboembolism and ischaemic stroke (Beye and Pindur, 2017; Campello et al., 2019). For instance, Ng et al. (2011) noted that while thrombophilia is not among the

most prevalent risk factors for stroke, it can still be a significant contributor to thromboembolic events, especially in young adults with no other traditional risk factors.

In older cohorts, thrombophilia is often overshadowed by these more common risk factors, which may explain its lower prevalence in studies involving older populations (Adeloye et al., 2020). While thrombophilia's low prevalence in our cohort aligns with existing literature, it also suggests that this condition could be an important consideration in cases where traditional risk factors are absent.

5.2.3.3.2 Chronic Kidney Disease (CKD)

In the study population, CKD was identified in only seven patients. CKD is widely recognized as a significant risk factor for cardiovascular diseases, including stroke. Despite its relatively low prevalence in the research, the presence of CKD aligns with existing literature that emphasizes its role in stroke risk. Charytan and Kuntz (2019) describe CKD as both a consequence and a predictor of cardiovascular disease, including stroke. Their work highlights the bidirectional relationship between CKD and cardiovascular conditions, suggesting that CKD not only increases the risk of stroke but may also be exacerbated by stroke-related factors. Compared with earlier studies, it is evident that CKD's role in stroke risk is well-established, though it is less commonly emphasized in younger populations. Most research on CKD and stroke focuses on older adults, where CKD often coexists with other age-related risk factors such as hypertension and diabetes (Charytan and Kuntz, 2019). For example, studies involving older cohorts generally find a higher prevalence of CKD among stroke patients, reflecting the cumulative effects of aging and chronic conditions (Kovesdy et al., 2017). While CKD is less common among young stroke patients compared to older individuals, its presence in highlights its potential importance in stroke risk assessment for younger adults.

5.2.3.3.3 Giant Cell Arteritis (GCA)

In the study population, Giant Cell Arteritis (GCA) was rare, with only one patient diagnosed with the condition. The literature suggests that strokes associated with GCA can result from occlusion of the ophthalmic artery or from arteritic anterior ischaemic optic neuropathy (AAION), which can lead to visual loss and severe ischaemic strokes

(Salvarani et al., 2012; Schmidt, 2020). The rarity of GCA among the patients is consistent with findings from other studies that identify GCA as a relatively uncommon risk factor for stroke, particularly in younger individuals (Smith and Swanson, 2014). When comparing to studies involving older populations, the role of GCA as a stroke risk factor becomes clearer. Older studies frequently report a higher incidence of GCA in stroke patients due to its association with more severe vascular complications in aging individuals (Smith and Swanson, 2014). In contrast, GCA's impact on younger stroke patients remains less understood, reflecting its lower prevalence in this demographic a

5.2.3.3.4 Cerebral Venous Sinus Thrombosis (CVST)

The inclusion of (CVST) as a separate cause of stroke is that it was categorized in this manner in the dataset for this study. While it is recognized that CVST can lead to ischaemic or haemorrhagic strokes due to venous infarction or hemorrhage, the dataset distinguished CVST as an independent category. This approach was followed to maintain consistency with the data provided. However, it is acknowledged that CVST can present with ischaemic or haemorrhagic features, and this will be considered in the interpretation of the results.

Cerebral Venous Sinus Thrombosis (CVST) was identified in only two patients, representing 0.4% of the study population. Despite its low prevalence, CVST disproportionately affects young adults and women especially in those with atypical presentations or risk factors (Kumar and McCullough, 2021). The rarity of CVST in this study aligns with existing literature that characterises it as a less common but potentially severe form of stroke. Research indicates that CVST is often associated with risk factors such as thrombophilia, use of oral contraceptives, pregnancy, infections, and inflammatory disorders (Ferro et al., 2017). For instance, genetic mutations like factor V Leiden and prothrombin gene mutation significantly increase the risk of CVST (Ferro et al., 2017). Moreover, hormonal factors, including the use of oral contraceptives and pregnancy, have been linked to a higher risk of CVST. Dentali et al. (2011) found a higher risk of CVST among oral contraceptive users compared to non-users. Additionally, inflammatory conditions such as systemic lupus erythematosus (SLE) and inflammatory bowel disease (IBD) are associated with an increased risk of CVST (Canhão et al., 2013; Ferro et al., 2017). Past studies have shown that the role of CVST

as a stroke risk factor is less prominent in older populations. A higher prevalence of traditional risk factors, such as atherosclerosis and hypertension are less commonly associated with CVST among the elderly (Kumar and McCullough, 2021).

5.2.3.3.5 Gilbert Syndrome

Gilbert Syndrome was identified in only one patient in the study. Although it is not widely regarded as a significant stroke risk factor, emerging research suggests a potential link between Gilbert Syndrome and cardiovascular risks among the younger generation (Cho et al., 2018; Lin et al., 2019). Studies suggest that while Gilbert Syndrome is not a major risk factor for stroke, understanding its broader implications on cardiovascular health could be valuable. When comparing these findings with older cohorts, the role of Gilbert Syndrome in stroke risk is less well-defined. Most studies often focus on more prominent risk factors, such as hypertension and diabetes, which overshadow the impact of Gilbert Syndrome (Joekim et al., 2022).

5.2.3.3.6 Hepatitis

Hepatitis was diagnosed in only two patients, and this reflected its relatively low prevalence in this population. The relationship between hepatitis and stroke risk is complex and not fully understood, with existing literature presenting mixed findings. Chronic hepatitis B virus (HBV) infection has been associated with an increased risk of stroke in some studies. For instance, Kim et al. (2017) reported that younger individuals with chronic HBV infection may have a heightened risk of stroke compared to those without the infection. However, Chen et al. (2019) found no significant association between HBV infection and stroke risk, highlighting the conflicting nature of this relationship. For older adults, hepatitis appears to be less frequently identified as a primary stroke risk factor, with more prominent factors like hypertension and diabetes often being highlighted.

5.2.3.3.7 Hypothyroidism

Eight patients were diagnosed with hypothyroidism, showing its relative presence as a relevant risk factor for stroke. Existing literature on the association between hypothyroidism and stroke presents a range of findings. Some studies suggest that hypothyroidism is linked to an increased risk of stroke, especially ischaemic stroke

among younger adults (Saranya, 2015). Selmer et al. (2019) observed a positive association between hypothyroidism and stroke risk, indicating that thyroid hormone deficiency might contribute to cerebrovascular events. Conversely, other research has reported no significant relationship between hypothyroidism and stroke risk (Singh et al., 2018). These conflicting results may be due to variations in study populations, methodologies, and the control of confounding variables.

5.2.3.3.8 Graves' Disease

In the study population, only two patients were diagnosed with Graves' disease, reflecting its relatively low prevalence as a stroke risk factor. Existing literature indicates that while Graves' disease itself is not commonly identified as a primary stroke risk factor, the associated hyperthyroidism can have significant cardiovascular impacts. Hyperthyroidism is known to increase heart rate, cardiac output, and arterial stiffness, which can contribute to the development of cardiovascular events, including stroke (Brandt et al., 2018). Khochtali et al. (2010) highlight that Graves' disease, due to its association with hyperthyroidism, can be linked to increased cardiovascular morbidity, including stroke, although this association is less frequent compared to more traditional risk factors like hypertension or diabetes.

5.2.3.3.9 Hyperthyroidism

In the study population, only one patient was diagnosed with hyperthyroidism. Hyperthyroidism, characterised by excessive thyroid hormone production, is known to elevate sympathetic activity, induce cardiac arrhythmias, and increase hypercoagulability, all of which can predispose individuals to thromboembolic events, including stroke (Ahmad et al., 2022). Although the incidence of hyperthyroidism in this study was low, the association between thyroid dysfunction and stroke risk is well-established in the literature. Several studies comparing the findings with those from studies focusing on older stroke patients reveals that the prevalence of hyperthyroidism as a stroke risk factor is generally higher in older populations. For example, a study by Leng and Razvi (2019), found that hyperthyroidism was present more in older stroke patients, and this suggests that while hyperthyroidism is less common in younger stroke patients, it may be more prevalent and have a greater impact in older population. This difference may be due to age-related changes in thyroid function and the cumulative

cardiovascular burden that often accompanies aging. In contrast, studies involving younger stroke patients have reported lower incidences of hyperthyroidism, similar to the findings. However, even in younger populations, the presence of hyperthyroidism can significantly alter stroke risk, particularly when combined with other cardiovascular risk factors.

5.2.3.3.10 Thyroid Cancer

The results of this research indicate that only one patient was diagnosed with thyroid cancer. While thyroid cancer itself is not traditionally considered a direct risk factor for stroke, it may be associated with certain cardiovascular risk factors or treatment-related complications that increase stroke risk (Zoltek, 2023). The presence of thyroid cancer in one patient within our study underscores the importance of comprehensive oncologic and cardiovascular risk assessment in cancer survivors to optimize long-term health outcomes. Existing literature generally supports the view that thyroid cancer, particularly differentiated thyroid cancer (DTC), is not a major direct risk factor for stroke. However, treatment-related factors and the long-term management of thyroid cancer can contribute to an increased risk of cardiovascular complications, including stroke. For instance, Liebner and Shah (2011) note that treatments for thyroid cancer, such as thyroidectomy and radioactive iodine therapy, often result in hypothyroidism. When hypothyroidism is not well-managed, it can lead to various cardiovascular issues, including dyslipidemia, hypertension, and increased carotid intima-media thickness, all of which are risk factors for atherosclerosis and ischaemic stroke.

Past studies involving older stroke cohorts reveals similar conclusions. Grani et al. (2019) emphasized that in older patients, the long-term cardiovascular risks associated with thyroid cancer treatment are more pronounced, given the cumulative effects of aging on cardiovascular health. These risks may be less evident in younger patients, which could explain the lower incidence of stroke in this demographic. However, even in younger patients, the potential for treatment-related cardiovascular complications highlights the need for vigilant long-term monitoring. When compared to other studies focusing on younger stroke patients, the findings are consistent with the broader literature. Thyroid cancer is rarely highlighted as a significant risk factor for stroke in younger populations. For example, research by Lin et al. (2017) on young adult cancer

survivors found that while cancer treatments generally increased the risk of cardiovascular events, thyroid cancer specifically was not a major contributor to stroke risk. This suggests that while thyroid cancer should be a consideration in the overall cardiovascular risk profile, it may not be a primary focus in stroke prevention strategies for young adults.

5.2.3.3.11 JAK2 Mutation

In this study, only one patient was diagnosed with a JAK2 mutation. JAK2 mutations are closely associated with myeloproliferative neoplasms, such as polycythemia vera and essential thrombocythemia, which can significantly increase the risk of thrombotic events, including stroke (Vannucchi, 2010). Despite the low incidence in the study population, the connection between JAK2 mutations and thrombophilia shows the importance of genetic testing and risk stratification in patients with hematologic disorders. Existing literature supports the notion that individuals carrying the JAK2 V617F mutation are at a heightened risk for thrombotic events, including stroke. Tefferi et al. (2015) conducted a comprehensive study that established a significant association between the JAK2 V617F mutation and thrombotic events, encompassing both venous and arterial thrombosis, with stroke being a notable manifestation. Similarly, Barbui et al. (2017) reinforced these findings, showing that individuals with the JAK2 V617F mutation face an elevated risk of thrombotic complications, particularly in the context of myeloproliferative disorders.

When comparing the findings with those from studies involving older cohorts, it is apparent that the risk associated with JAK2 mutations is consistent across age groups. However, the manifestation of thrombotic events, including stroke, might be less frequent in younger individuals due to the overall lower baseline cardiovascular risk. Older patients with JAK2 mutations often have additional risk factors such as hypertension or atherosclerosis, which may exacerbate the risk of stroke. In contrast, younger patients may not present with these comorbidities, which could explain the lower incidence of stroke despite the presence of a JAK2 mutation. In the context of younger stroke patients, the study aligns with the broader literature, which suggests that while the JAK2 mutation is a significant risk factor for thrombotic events, including stroke, it may not be the primary cause in this demographic. For instance, research by

Kristiansen et al. (2023) indicated that while young patients with JAK2 mutations are at risk, their overall likelihood of experiencing a stroke is still relatively low compared to older populations. This reinforces the importance of considering the JAK2 mutation within a broader risk profile, rather than as an isolated predictor.

5.2.3.3.12 Loeys-Dietz Syndrome

In the study population, one patient was diagnosed with Loeys-Dietz syndrome, a rare genetic disorder known for its association with arterial tortuosity, aneurysms, and dissections, which can significantly increase the risk of vascular complications, including stroke (Van Laer et al., 2014). The presence of this syndrome in a young stroke patient underscores the importance of identifying rare genetic conditions in stroke aetiology and emphasizes the need for a multidisciplinary approach to management that addresses the unique cardiovascular risks posed by such syndromes. Existing literature on Loeys-Dietz syndrome (LDS) reveals that it is indeed a significant risk factor for stroke, particularly due to its impact on vascular integrity. Studies comparing the findings with older cohorts of stroke patients shows that the impact of Loeys-Dietz syndrome on stroke risk is not limited to younger populations. According to Iqbal et al. (2021), older patients with LDS typically present with more advanced vascular complications, such as widespread aneurysms or severe arterial tortuosity, which can increase the likelihood of stroke as they age. In contrast, younger patients may experience fewer but more acute vascular events, where the singular occurrence of Loeys-Dietz syndrome was still significant given the patient's age.

5.2.3.3.13 Prothrombin Gene Mutation

In the study population, only one patient was diagnosed with a prothrombin gene mutation, specifically the prothrombin G20210A variant. This finding is consistent with the generally low prevalence of prothrombin gene mutations in the general population. Prothrombin gene mutations are associated with elevated prothrombin levels, which can increase thrombotic risk, including the risk of stroke (Jiang et al., 2014). The presence of a prothrombin gene mutation in the study shows the importance of genetic testing for individuals with a high risk of thromboembolic events. Existing literature supports the association between the prothrombin gene mutation and an increased risk of both venous and arterial thrombotic events including ischaemic stroke. The

prothrombin G20210A mutation leads to higher levels of prothrombin, a protein essential for blood clotting, thereby elevating the risk of thrombosis in younger patients (Poudel et al., 2020). Studies comparing the findings from older population on younger patients shows the role of prothrombin gene mutations in stroke risk remains relatively consistent (Li et al., 2017). However, the relatively low prevalence observed in the study reflects the mutation's infrequent occurrence compared to more common risk factors like hypertension or diabetes. This low prevalence may limit the immediate clinical impact of the mutation in the young adult stroke population, but it indicates the importance of considering genetic predispositions in comprehensive stroke risk assessments.

5.2.3.3.14 Ramsay-Hunt Syndrome

In the study population, only one patient was diagnosed with Ramsay Hunt syndrome. The singular case of RHS in the cohort reinforces the need to consider viral infections as potential risk factors for stroke. Existing literature indicates that the relationship between Ramsay Hunt syndrome (RHS) relationship and stroke is complex. Most studies suggest that RHS primarily affects older adults, where the risk of stroke may be exacerbated by comorbid conditions such as hypertension and diabetes (Wagner et al., 2012). In contrast, this study focuses on a younger population, which raises questions about the unique stroke risks associated with RHS in this demographic. For instance, while older patients might experience strokes secondary to vascular factors, younger individuals with RHS may face different underlying mechanisms, such as direct viral effects on the central nervous system.

5.2.3.3.16 Smith-Magenis Syndrome

In the study population, only one patient was diagnosed with Smith-Magenis syndrome (SMS). This rare genetic disorder primarily affects neurodevelopment and behavior, but existing literature suggests that individuals with SMS may also be at an increased risk of cardiovascular complications, including stroke (Smith and Gropman, 2021). Furthermore, individuals with SMS frequently present with comorbidities such as obesity, sleep disorders, and respiratory problems, which are recognized risk factors for stroke (Rinaldi et al., 2022). The combination of these comorbidities and the

neurodevelopmental characteristics of SMS may further elevate the risk of stroke in affected individuals.

While the association between SMS and stroke risk is not extensively documented, it is critical to recognize that individuals with complex neurodevelopmental disorders often exhibit unique cardiovascular risk profiles that require specialized evaluation and management. Samanta et al. (2019) describe SMS as characterised by intellectual disability, behavioral challenges, and craniofacial anomalies. Given the multifaceted nature of this syndrome, the single instance of SMS in our study population emphasizes the rarity of this disorder in the general population, which limits our ability to draw broader conclusions about its prevalence and stroke risk.

A comparison with existing literature shows that that SMS has not been widely studied in the context of stroke risk. Most research on SMS focuses primarily on neurodevelopmental and behavioral outcomes rather than cardiovascular health. However, understanding the potential cardiovascular risks associated with SMS can be essential for developing comprehensive care strategies for affected individuals. Previous studies on neurodevelopmental disorders have highlighted that patients with complex profiles often face higher cardiovascular risks due to their associated comorbidities (Morris et al., 2017). Therefore, it is imperative to include cardiovascular assessment as part of the comprehensive care for individuals with SMS. Moreover, the prevalence of only one patient with SMS in the study raises questions about how these findings may apply to other cohorts, particularly older stroke patients. Previous research indicates that neurodevelopmental disorders may present differently across age groups, and the cardiovascular implications can vary significantly. For instance, older cohorts with similar neurodevelopmental disorders may exhibit distinct risk factors or clinical presentations that could influence stroke outcomes (Smith et al., 2016).

5.2.3.3.17 Sneddon's Syndrome

In the study, Sneddon's syndrome was identified in only one patient, showing how rare it is within the study population. Sneddon's syndrome is a rare vasculopathy characterised by livedo reticularis and ischaemic cerebrovascular events, including stroke (Samanta et al., 2019). Sneddon's syndrome is associated with an increased

risk of ischaemic stroke due to specific vascular abnormalities, including non-inflammatory arteriopathy with intimal proliferation and fibrosis. This pathophysiological mechanism contributes to the recurrent nature of ischaemic strokes observed in these patients (Cleaver et al., 2020). Although the study identified only one patient with Sneddon's syndrome, the findings align with existing literature, which emphasizes the syndrome's association with stroke and the necessity of considering it in differential diagnoses (Bugrul et al., 2021; Wu et al., 2014). This implies that Sneddon's syndrome remains a rare but significant condition associated with stroke risk. In comparison to older cohorts of stroke patients, the prevalence of Sneddon's syndrome in the study is consistent with the rarity reported in other studies. The low frequency of this syndrome among young stroke patients reinforces the importance of recognizing and managing less common vascular disorders.

5.2.3.3.18 Thrombotic Thrombocytopenic Purpura (TTP)

In the study population, only one patient was diagnosed with TTP. Despite this low prevalence, existing literature suggests that TTP is associated with an increased risk of stroke, particularly ischaemic stroke in young patients (Rhee et al., 2010). The limited incidence of TTP in the cohort raises questions about its implications for stroke risk in young adults. While TTP is established as a risk factor for stroke, most existing studies focus on older cohorts or a general population without a specific emphasis on younger patients. For example, research has shown that older patients with TTP often present with more severe neurological symptoms and a higher incidence of cerebrovascular events, which may differ significantly from the clinical presentations observed in younger populations (Prevel et al., 2015).

Additionally, our study's single case of TTP limits the ability to extrapolate findings to broader conclusions about stroke risk among young adults. Previous literature indicates that the pathophysiological mechanisms of stroke in TTP patients can vary by age, with older adults potentially experiencing different complications or risk factors (Scully et al., 2023).

5.2.3.3.19 Systemic Lupus Erythematosus (SLE)

In the study population, only two patients were diagnosed with Systemic Lupus Erythematosus (SLE). This autoimmune disease predominantly affects young to

middle-aged women and is well-documented to increase the risk of various cardiovascular complications, including stroke (Giannelou and Mavragani, 2017). Comparatively, earlier studies highlight that the stroke risk in SLE patients is multifactorial, involving factors such as antiphospholipid syndrome, which is common in SLE and can lead to increased thrombotic events. For example, a comprehensive review by Cervera et al. (2016) emphasizes the need for regular cardiovascular assessment in SLE patients, particularly in younger cohorts who may present with unique profiles of stroke risk. Furthermore, the prevalence of stroke in older SLE cohorts is often reported to be higher, indicating a potential age-related increase in risk factors and comorbidities that may not be as prominent in younger populations. Given that only two patients in our cohort had SLE, the limited size restricts the ability to draw robust conclusions about the unique stroke risk profiles in young adults with SLE. It underscores the necessity for further research focusing on younger patients to better understand how SLE influences stroke risk and informs clinical management strategies in this demographic.

5.2.3.3.20 Monoclonal Gammopathy of Undetermined Significance (MGUS)

In the context of Monoclonal Gammopathy of Undetermined Significance (MGUS), existing literature suggests an increased risk of thrombotic events, including stroke. Several studies have highlighted a significantly elevated risk of venous thromboembolism (VTE) among individuals with MGUS, but the association with arterial thrombosis, such as stroke, remains less well-established (Korde et al., 2011). The study by Gkalea et al. (2023) reported a higher incidence of VTE among MGUS patients compared to the general population, suggesting a potential prothrombotic state linked to MGUS. Moreover, it is crucial to consider how the findings relate to older cohorts of stroke patients. The existing literature predominantly focuses on older populations, which may exhibit a different risk profile for arterial thrombosis than younger patients with MGUS. For example, the study by González-Calle and Mateos (2018) showed that older adults often present with additional cardiovascular risk factors that could influence stroke outcomes. Thus, the study's findings of only two patients with MGUS, reinforces the need for future research specifically examining the unique thrombotic risks in younger individuals.

5.2.3.3.21 Congestive Heart Failure (CHF)

In this study, only 3.1% of young adults reported a history of Congestive Heart Failure (CHF). CHF, characterised by the heart's inability to pump blood effectively, is a known risk factor for stroke due to its association with conditions like atrial fibrillation and low cardiac output, which can lead to thromboembolism (Wang et al., 2017). The low prevalence of CHF in this study suggests that it is not a common risk factor for stroke among young adults. However, in those with CHF, the condition could still be a significant contributor to stroke risk. A comparison of these findings with older populations, shows that CHF is typically a more prevalent risk factor in the elderly, where it is commonly associated with long-standing hypertension, coronary artery disease, and valve disorders (Vader et al., 2015). In contrast, the occurrence of CHF in younger adults often indicates a more severe or rapidly progressing form of heart disease, possibly due to congenital heart defects, cardiomyopathies, or myocarditis (Groenewegen et al., 2020). In the context of other studies on younger stroke patients, the findings align with research by Triposkiadis et al. (2022), which suggests that while CHF is less common in younger individuals, its presence is associated with a significant increase in stroke risk. This supports the conclusion that although CHF is not highly prevalent among young adults, it remains an important risk factor that should be carefully monitored.

5.2.3.3.22 Ischaemic Heart Disease (IHD)

In this study, about 8.9% of young adults had a history of ischaemic heart disease (IHD). IHD is characterised by reduced blood flow to the heart muscle and is associated with a higher risk of cardiovascular events, including strokes (Jensen et al., 2018). The prevalence of IHD in this study suggests that it may be a significant risk factor for stroke among young adults, particularly due to its association with cardioembolic events. In older populations, IHD is a well-established risk factor for stroke, particularly because of the higher prevalence of coronary artery disease, atrial fibrillation, and other related conditions (Go et al., 2013). In contrast, the presence of IHD in younger adults might indicate early-onset coronary artery disease, often linked to genetic factors, metabolic syndrome, or lifestyle factors like smoking and obesity (George et al., 2020; Putaala, 2016). These results emphasize the importance of addressing IHD in stroke prevention strategies tailored for younger adults, who may have different risk profiles and treatment needs compared to older patients.

5.2.4 TREATMENT MEASURES FOR STROKE IN THE STUDY POPULATION

5.2.4.1 Thrombolysis

In the study population, only 10.7% of the young adults received thrombolysis. Thrombolysis was used primarily for acute ischaemic stroke caused by thrombotic or embolic occlusion of cerebral arteries. The administration of thrombolytic agents, such as tissue plasminogen activator (tPA), aims to dissolve the obstructing blood clot and restore blood flow to ischaemic brain tissue. As only 10.7% of the patients who received thrombolysis, this highlighted possible challenges in timely intervention, patient eligibility, and healthcare infrastructure. Delayed presentation to medical facilities, stringent eligibility criteria, and concerns regarding bleeding complications may contribute to the underutilization of thrombolysis in acute stroke management. It is also worthy to note that the low NIHSS score in this dataset with a mode of 0 could be a contributing factor to the low percentage of patients who needed thrombolysis.

5.2.4.2 Thrombectomy

In the study population, only 1.5% of patients underwent thrombectomy. As a minimally invasive endovascular procedure, thrombectomy is used to remove intracranial blood clots causing acute ischaemic stroke in patients with large vessel occlusion. Using specialized catheters and devices, these help to navigate to the site of occlusion and mechanically disrupt or extract the thrombus and restore blood flow to ischaemic brain tissue. The rarity of only 1.5% of patients undergoing thrombectomy raises potential concerns. This may be attributed to several factors including limited access to advanced neurointerventional services or under-recognition of eligible candidates. Challenges in patient triage, transportation logistics, and regional disparities in healthcare infrastructure may also contribute to the underutilization of thrombectomy in the acute stroke care. However, the greater proportion of patients with low NIHSS in this study can also be a contributing factor as thrombectomy is an acute reperfusion treatment modality is often reserved for cases with NIHSS of 6 and above amongst other criteria.

5.2.4.3 Surgical Interventions

In the study population, surgical interventions: hemicraniectomy and cranioplasty, played a critical role in the management of severe ischaemic stroke or intracerebral hemorrhage complicated by increased intracranial pressure (ICP) and cerebral edema. Hemicraniectomy involves the surgical removal of a portion of the skull to alleviate pressure on the brain and prevent herniation, while cranioplasty restores cranial integrity and protects underlying brain tissue (Alexander et al., 2016). In the study population, only 3.0% of the patients underwent surgical interventions for stroke. This low percentage may be attributed to the selective nature of surgical candidacy and the preference for non-invasive treatment modalities in most cases. Surgical decision-making in stroke management is guided by factors such as stroke severity, imaging findings, neurological status, and patient preferences. The limited utilization of surgery may indicate the importance of individualized treatment approaches tailored to the specific needs and clinical characteristics of stroke patients.

5.2.5 TREATMENT OUTCOMES

The results on the treatment outcomes in the study population provide valuable insights into various aspects of stroke care, including the duration of admission, 30day survival rates, and statistical comparisons of patients who survived and those who did not. These findings shed light on the clinical course, prognosis, and factors that influence outcomes among stroke patients.

5.2.5.1 Duration of Admission

The duration of admission is a crucial metric that reflects the length of hospital stay for stroke patients. In the study population, the mean duration of admission was approximately 14.94 days, with a median of 4.00 days. The mode which represents the most common duration, was 2 days. This indicates that while the majority of the patients had relatively short hospital stays, some individuals required significantly longer periods of hospitalization that led to the higher mean duration. The wide variation in the duration of admission, as evidenced by the high standard deviation of

26.857, underscores the heterogeneity in stroke severity, treatment requirements, and patient recovery trajectories.

5.2.5.2 30-Day Survival Rates

The results showed a high 30-day survival rate among the stroke patients, with 95.7% of the young adults being alive at the end of this period. Only 4.3% of the patients did not survive the first 30 days following their stroke. This finding highlights the critical importance of acute stroke care and early interventions in improving patient outcomes and reducing short-term mortality rates. The high survival rate also emphasizes the effectiveness of contemporary stroke management strategies and the need for timely recognition, diagnosis, and treatment of stroke to optimize patient outcomes.

5.2.5.3 Statistical Comparisons of Patients Who Died and Patients Who Survived

Statistical analyses were conducted to compare the demographic and clinical characteristics between the patients who survived at 30 days and those who did not. The independent samples t-test was used to assess differences in the average ages of the two groups. The results indicated no significant difference in the mean ages between patients who survived and those who did not. By general principle, this means that age is not regarded as a critical factor in determining short-term survival outcomes in this study population. Additionally, the chi-square test examined the association between gender and survival status at 30 days. The results revealed no significant association between gender and survival outcomes. This means that gender is not attributed to be a significant predictor of short-term survival following a stroke.

These findings provide valuable insights into the clinical characteristics and outcomes of stroke patients in the study population. The high 30-day survival rate reflects the effectiveness of acute stroke care interventions and highlights the importance of rapid assessment, early intervention, and multidisciplinary management strategies in improving patient outcomes. The lack of significant differences in age and gender between patients who survived and those who did not suggests that factors other than demographic variables may play a more critical role in determining short-term survival outcomes following a stroke. These factors may include stroke severity, comorbidities,

access to timely medical care, treatment modalities, and individual response to therapy.

The findings show the importance of comprehensive stroke care protocols, including timely thrombolysis, thrombectomy, neurocritical care, rehabilitation, and secondary prevention strategies. It is important for clinicians to prioritize early recognition and prompt initiation of evidence-based interventions to optimize patient outcomes and minimize the risk of mortality following a stroke. Moreover, the results emphasize the need for further research to elucidate the complex interplay of clinical, demographic, genetic, and environmental factors influencing stroke outcomes across diverse patient populations.

5.3 COMPARISON OF RESEARCH FINDINGS WITH EXISTING LITERATURE

Chapter four provided results on stroke cases among young adults (aged 18-55) in Southwest (SW) England based on data from the Sentinel Stroke National Audit Programme (SSNAP). To compare these findings with other studies from across the UK and globally, it is important to examine how the demographics, risk factors, and outcomes in this cohort align or diverge from published research in other young cohorts, national data, and older populations.

5.3.1 Demographics and Age Distribution

This study includes 460 patients with an average age of 46.86 years and a median age of 50, which is similar to other young adult stroke cohorts. For instance, a study by Putaala et al. (2012) on ischaemic stroke in young adults (aged 15-49) found the mean age to be around 41 years. The higher mean age in the cohort studied likely reflects the broader age range (up to 55 years) and underscores that stroke, while often considered an older adult condition, affects a considerable number of individuals nearing middle age.

5.3.2 Gender Differences

In the Southwest England cohort, 63.5% of patients were male and 36.5% were female. This male predominance is consistent with many other studies on young stroke populations. For example, in a Finnish study by Putaala et al. (2009), about 60% of the

cohort were men. Similarly, a study from the UK-wide SSNAP data showed higher stroke incidence in men across all ages, though the gender gap narrows with increasing age (Rudd et al., 2017). This gender disparity could be partially explained by higher rates of some stroke risk factors like smoking, hypertension, and alcohol use among men in many populations.

5.3.3 Ethnicity

The ethnic distribution in this study from the Southwest of England is predominantly White British (78.6%), with smaller representations from African, Caribbean, and other ethnic groups. This is reflective of the regional population demographics but contrasts with stroke studies in more ethnically diverse areas. For example, in a study on stroke in London (Douiri et al., 2013), Black and South Asian patients accounted for a larger proportion of cases. The different ethnic composition in the study's cohort may influence the prevalence of certain stroke risk factors (e.g., hypertension and diabetes) which are known to vary by ethnicity (Gunarathne et al., 2009).

5.3.4 Stroke Subtypes

Ischaemic strokes dominated the study cohort, comprising 88.5% of cases, while 11.5% were haemorrhagic strokes. These proportions are broadly similar to national data and other studies of young stroke cohorts. For example, the UK SSNAP data also reports ischaemic stroke as the most common subtype (Bray et al., 2018). This aligns with studies from other countries, such as the Helsinki Young Stroke Registry, where ischaemic strokes constituted about 85% of cases (Putaala et al., 2009). Haemorrhagic strokes are generally less common but more severe, and their slightly higher prevalence in younger populations could be linked to risk factors like hypertension, illicit drug use, or congenital conditions (Giroud et al., 1997).

5.3.5 Risk Factors: Traditional vs. Young-Specific

This study identified traditional stroke risk factors such as hypertension, atrial fibrillation, smoking, and alcohol use, with a notable presence of hypertension (38%) and smoking (15%). These findings align with broader UK and international research, where hypertension remains a leading risk factor for stroke (Boehme et al., 2017). For example, Putaala et al. (2009) reported a 30-40% prevalence of hypertension among

young stroke patients in their cohort. The prevalence of smoking (15%) is also comparable to other UK studies (around 20%), although lower than in some international cohorts (e.g., 30% in Finland) (Putaala et al., 2009).

Unique to younger populations are risk factors like illicit drug use and genetic conditions. In this study, 7.6% admitted to drug use, a figure consistent with studies in young cohorts, where drug use is increasingly recognized as a significant stroke risk (Cantu & Hill, 2010). For instance, a UK-wide analysis found similar rates of drug use in young stroke patients, particularly for stimulants like cocaine and amphetamines (Westover et al., 2007).

This study revealed that 10.4% of young stroke patients had a diagnosis of patent foramen ovale (PFO). In the UK and worldwide, PFO is a well-recognized cause of cryptogenic stroke in younger adults, and several studies suggest it plays a role in up to 25% of the general population (Homma et al., 2016). In contrast, older populations are more likely to experience strokes from atherosclerotic causes, diminishing the relative impact of PFO. In the UK, the NICE guidelines for PFO management after cryptogenic stroke support closure in carefully selected patients, although the long-term benefit remains debated (NICE, 2018). Worldwide, particularly in Europe and North America, studies corroborate these findings, highlighting PFO as a significant cause of stroke in young adults (Saver et al., 2018). Some global studies support closure in young, recurrent stroke patients, with evidence suggesting a reduction in recurrent stroke rates, especially in patients with large shunts (Messe et al., 2020).

Furthermore, 12.8% of young stroke patients in this study reported a history of migraine. Migraine, particularly with aura, is a well-established risk factor for ischaemic stroke in young adults. A UK-based study by Etminan et al. (2005) found that women with migraines, especially those using hormonal contraceptives, had a significantly increased risk of ischaemic stroke. Internationally, studies from the US and Europe corroborate these findings, with meta-analyses showing that women under 45 with migraines have an elevated stroke risk, particularly in combination with other vascular risk factors (Kurth et al., 2008). In contrast, in older populations, migraine-related stroke

risk diminishes, likely due to the increasing prominence of atherosclerotic and embolic risk factors (Sacco et al., 2013).

This study found that 0.8% of the young stroke cohort had monogenic disorders (CADASIL and MELAS) which are associated with early-onset stroke. In the UK, CADASIL is one of the most common hereditary causes of stroke, and its prevalence among young adults suggests that monogenic factors play a critical role in early-onset stroke (Chabriat et al., 2009). Globally, studies from France and other parts of Europe show similar findings, with CADASIL accounting for a significant proportion of young strokes (Terni et al., 2014, Bersano et al., 2021). In contrast, genetic contributions to stroke in older populations are less commonly attributed to monogenic disorders and more often arise from polygenic risk factors, interacting with lifestyle elements such as smoking and hypertension (Bevan et al., 2012).

In the cohort in this study, 5.7% of strokes were attributed to cervical artery dissection (CAD). In the UK, CAD is responsible for about 20% of ischaemic strokes in patients under 50, consistent with findings from global studies (Debette & Leys, 2009, Debette and Markus, 2022). Research from North America and Europe similarly identifies CAD as a major cause of stroke in young adults, often related to minor trauma or spontaneous arterial injury (Lichy et al., 2015).

Furthermore, 7% of patients in this study cohort had a history of non-haematological malignancy and 1% had history of haematological malignancy. In the UK, similar to what is obtained globally, malignancy-related stroke is under-recognized but significant, with cancers such as lung, breast, and gastrointestinal malignancies contributing to stroke via hypercoagulability (Sener and Keser, 2022). Internationally, studies from Europe and the US similarly emphasize the role of malignancy in stroke, especially in younger patients who may not have other traditional risk factors (Dearborn et al., 2014).

Finally, other risk factors such as thrombophilia (0.2%) were relatively uncommon in this study which is similar to the trend worldwide.

5.3.6 NIHSS Scores and Stroke Severity

The study cohort had a mean National Institutes of Health Stroke Scale (NIHSS) score of 4.87, indicating that most patients had minor to moderate stroke severity. This is consistent with other studies in younger patients, where stroke severity tends to be lower compared to older populations (Putaala et al., 2012). Nationally, the SSNAP audit reports higher NIHSS scores on average across all ages, with more severe strokes common in older patients. This difference may be due to younger patients' better overall health and fewer comorbidities, allowing for less severe strokes and better recovery outcomes (Rudd et al., 2017).

5.3.7 Mortality and Outcomes

The 30-day mortality rate in this study was 4.3%, with 95.7% of patients alive at 30 days. This is lower than the national SSNAP average, where mortality rates are generally higher for all age groups, especially among older patients (Rudd et al., 2017). The relatively low mortality in this study aligns with findings from other studies on young stroke patients, where survival rates are generally better than in older populations. For example, in Putaala et al.'s (2012) study of young ischaemic stroke patients, the mortality rate was less than 5% at 30 days. This survival advantage is likely due to younger patients' greater physiological resilience and fewer pre-existing conditions (Putaala et al., 2012).

5.3.8 Treatment Modalities

Thrombolysis was administered to 10.7% of patients in the SW cohort, which is comparable to national figures from SSNAP. However, thrombectomy was less commonly performed (1.5%), which is lower than the national average, possibly reflecting limited access to specialized stroke care in certain regions (Bray et al., 2018). National SSNAP data indicates that thrombectomy is still relatively underutilized across the UK, though its use is increasing in large urban centres (Rudd et al., 2017). The availability of specialized stroke services may explain regional differences in treatment rates, with urban areas typically offering more advanced interventions (Bray et al., 2018).

5.3.9 Comparisons with Older Populations

When compared to older stroke populations in SSNAP, the young patients in this study demonstrates significant differences in risk factor profiles, stroke severity, and outcomes. For instance, older patients are more likely to have multiple comorbidities such as diabetes and atrial fibrillation, which contribute to more severe strokes and poorer outcomes (Rudd et al., 2017). In contrast, younger patients, as seen in this study, are more likely to experience ischaemic strokes with lower NIHSS scores and better recovery prospects. The use of thrombolysis and thrombectomy is also more common in younger patients, who are typically eligible for these treatments due to their less extensive medical histories (Bray et al., 2018).

This study largely reflects broader trends observed in young adult stroke populations both in the UK and internationally, particularly in terms of demographics, stroke subtypes, and risk factors. However, regional variations in ethnicity and access to advanced treatments like thrombectomy highlight the importance of local healthcare infrastructure and population demographics in shaping stroke care. The relatively low mortality and moderate stroke severity in this study compare favorably with national data and emphasize the better prognosis typically seen in younger patients. Differences in the prevalence of certain risk factors, such as drug use and genetic disorders, underscore the need for targeted interventions in young stroke populations. Further research should explore how regional healthcare disparities impact long-term outcomes for young stroke survivors.

5.4 RELEVANCE OF THE FINDINGS TO THE RESEARCH OBJECTIVES

5.4.1 Frequency of Stroke in Young Patients

The study's findings indicate a significant prevalence of stroke cases among the young patients presenting at the Bristol Royal Infirmary stroke unit. An analysis of the results reveals that stroke is not a rare occurrence among the young adults seeking medical attention at the Bristol Royal Infirmary stroke unit. The prevalence of stroke cases, although lower compared to older age groups, signifies that stroke affects individuals across a wide age spectrum, including those traditionally considered less susceptible to stroke-related events. Furthermore, the research elucidates the significance of recognizing stroke as a potential health concern in young adults by dispelling

misconceptions that it primarily affects older individuals. By quantifying the frequency of stroke in this demographic, the study highlights the need for heightened awareness, proactive screening, and targeted prevention strategies tailored to young adults to mitigate the impact of stroke on their health outcomes. The findings also underscore the importance of early detection and prompt medical intervention in managing stroke among young patients. Despite being a relatively younger cohort, the occurrence of stroke cases necessitates timely and effective treatment to minimize the risk of long-term disability, cognitive impairment, and other adverse sequelae associated with stroke events.

5.4.2 Risk Factors and Prognosis of Stroke in Young Patients

The study meticulously examines a wide array of risk factors that contributes to stroke occurrence among young adults. Among the traditional risk factors, hypertension emerged as a prominent contributor, with a significant proportion of the young patients presenting with elevated blood pressure levels. Hypertension, a well-established risk factor for stroke across all age groups, underscores the importance of early detection and management of elevated blood pressure to mitigate stroke risk among young adults. Also, atrial fibrillation emerged as a notable risk factor identified among the young stroke patients. The presence of atrial fibrillation highlights the relevance of cardiac abnormalities in stroke aetiology among young adults and emphasizing the need for comprehensive cardiac evaluations and targeted interventions to address arrhythmias and associated thromboembolic complications. Moreover, the study identifies lifestyle factors such as smoking and alcohol consumption as significant contributors to stroke risk in young patients. The prevalence of these modifiable risk factors emphasizes the importance of promoting healthy behaviors and implementing interventions aimed at smoking cessation and alcohol moderation to reduce the incidence of stroke in this demographic.

Furthermore, genetic factors also play a key role in stroke risk among the young adults, with specific genetic mutations such as CADASIL and MELAS identified in a subset of patients. The presence of stroke-related genetic components highlights the hereditary nature of stroke susceptibility in some cases, necessitating genetic counseling and targeted screening strategies for individuals with familial predispositions to stroke

related conditions. Additionally, the study explores less common risk factors such as illicit drug use, hormone replacement therapy, migraine, and various medical conditions including thrombophilia, antiphospholipid syndrome, and chronic kidney disease. The diverse array of risk factors underscores the complex interplay of genetic, environmental, and lifestyle factors contributing to stroke occurrence in the young adults. These risk factors emphasize the importance of comprehensive risk assessment and personalized management strategies tailored to individual patient profiles.

In addition to assessing risk factors, the research provides insights into the prognosis of stroke among the young patients by providing valuable information on the clinical outcomes and functional status following stroke events. The analysis of NIHSS scores reveals a spectrum of stroke severity among young adults, ranging from mild impairments to severe neurological deficits. The study highlights the heterogeneity of stroke outcomes in young patients, with some individuals experiencing favorable recovery trajectories characterised by minimal residual deficits, while others face significant challenges in functional recovery and rehabilitation. The variation in prognosis underscores the need for individualized treatment approaches and multidisciplinary care interventions aimed at optimizing functional outcomes and enhancing quality of life for young stroke survivors.

Furthermore, the research sheds light on long-term prognostic indicators such as disability scores, cognitive function assessments, and quality of life measures, providing comprehensive insights into the holistic impact of stroke on young patients' health and well-being. By examining both short-term and long-term prognostic factors, the study facilitates a deeper understanding of the trajectory of recovery and rehabilitation following stroke events among young adults, informing clinical decision making and rehabilitation strategies tailored to individual patient needs.

5.4.3 Clinical Presentation of Stroke in Young Patients

The findings of this research provide valuable insights into the clinical presentation of stroke among the young adults and provides a detailed analysis of the diverse manifestations and neurological deficits observed within the study population. One of the key findings of the study is the identification of a spectrum of stroke severity among

the young patients, ranging from minor to severe presentations. The analysis of NIHSS scores reveals varying degrees of neurological impairment and reflects the heterogeneity of stroke manifestations observed within the study population. Some of the young adults present with mild symptoms, characterised by subtle neurological deficits and preserved functional abilities, while others experience more severe presentations marked by significant impairments in motor function, speech, and cognition.

Ischaemic stroke, the most common type of stroke among the young adults, presents with a diverse array of clinical features depending on the affected vascular territory and the extent of cerebral ischemia. The research highlights the clinical diversity of ischaemic stroke presentations in young patients, encompassing focal neurological deficits such as hemiparesis, hemisensory loss, aphasia, and visual disturbances. Additionally, the young adults may present with atypical symptoms or non-localizing signs that pose diagnostic challenges and emphasizing the importance of thorough clinical evaluations and neuroimaging studies to accurately diagnose ischaemic stroke in this demographic.

On the other hand, haemorrhagic stroke, although less common than ischaemic stroke among the young adults carries significant morbidity and mortality, often presenting with acute neurological deterioration and intracranial hemorrhage. The study identifies haemorrhagic stroke cases within the study population and highlights the acute onset of symptoms such as severe headache, altered mental status, focal deficits, and signs of increased intracranial pressure. The clinical presentation of haemorrhagic stroke underscores the urgency of early recognition and prompt intervention to mitigate secondary brain injury and optimize patient outcomes.

5.5 PRACTICAL IMPLICATIONS OF RESEARCH FINDINGS

- The research findings hold significant practical implications for various stakeholders, including healthcare professionals, policymakers, and public health practitioners. Healthcare professionals, particularly neurologists and stroke physicians, stroke specialists, and emergency physicians, can utilize the research findings to refine clinical management and treatment protocols for

young adults presenting with stroke symptoms. The identification of specific risk factors, clinical presentations, and prognostic indicators can aid in early recognition, accurate diagnosis, and prompt initiation of appropriate treatment modalities, including thrombolysis, thrombectomy, and surgical interventions.

- The research findings underscore the importance of targeted risk factor modification and prevention programs aimed at reducing the incidence and burden of stroke in young adults. Healthcare providers can leverage the identified risk factors, such as hypertension, smoking, and genetic predispositions, to develop personalized intervention strategies tailored to the unique needs and characteristics of the patient population. Public health campaigns focusing on lifestyle modifications, including smoking cessation, adoption of healthy dietary patterns, regular physical activity, and management of comorbid conditions like diabetes and hyperlipidemia, can help mitigate modifiable risk factors associated with stroke.
- The research findings can also serve as foundational knowledge for the development of health education and awareness initiatives targeting both healthcare professionals and the public. Educational programs aimed at raising awareness about the signs and symptoms of stroke, especially among young adults, can promote early recognition and timely intervention, thereby reducing delays in seeking medical attention and improving access to acute stroke care services.
- Policymakers and healthcare administrators can use the research findings to inform policy development and resource allocation decisions aimed at strengthening stroke care infrastructure and enhancing healthcare delivery systems. Investments in stroke prevention programs, community-based interventions, and the expansion of stroke rehabilitation services can help address gaps in care and improve access to comprehensive stroke care services, particularly in underserved regions.
- The research findings provide a valuable foundation for future research endeavors aimed at advancing our understanding of stroke pathophysiology, risk stratification models, and innovative treatment modalities tailored to young adults. Translational research initiatives focused on bridging the gap between scientific discoveries and clinical practice can facilitate the implementation of

evidence-based interventions in real-world settings, leading to improved patient outcomes and quality of life. Besides, collaborative research partnerships between academic institutions, healthcare organizations, and community stakeholders can foster knowledge exchange, interdisciplinary collaboration, and the dissemination of research findings to diverse audiences.

5.6 RECOMMENDATIONS

Based on the findings of the study, several key recommendations are proposed:

- It is recommended to launch targeted campaigns to raise awareness among young adults in Southwest Engand about stroke risk factors, warning signs, and the importance of early intervention. These targeted campaigns should focus on lifestyle changes such as quitting smoking, moderating alcohol intake, adopting a healthy diet, increasing physical activity, and regularly monitoring blood pressure.
- It is important to develop and implement stroke prevention and awareness programs in schools, universities, and community centers in Southwest England. These programs should emphasize recognizing stroke symptoms and the need for immediate medical attention.
- It is recommended to establish and support specialised teams, including stroke physicians, neurologists, neurosurgeons, rehabilitation specialists, and psychologists, to provide comprehensive care tailored to young stroke survivors in Southwest England.
- Allocate resources to research the underlying mechanisms, genetic factors, and potential new treatments for stroke in young patients in Southwest England. This research could inform local protocol adjustments to better address the unique needs of this population.
- Advocate for reforms that promote equitable access to stroke care, reduce disparities, and ensure that young stroke patients receive the resources and services they need. Consider adjusting local protocols to reflect the specific epidemiological trends observed in young stroke patients in the region.

5.7 Research Limitations

- The reliance on data from a single centre - the Bristol Royal Infirmary Stroke Unit - limits the generalizability of the findings. This is because the unique characteristics of this centre, including patient demographics, stroke management practices, and available healthcare resources, may not be representative of other stroke centres or community hospitals. Consequently, the findings may not adequately capture the heterogeneity of stroke presentations and outcomes across different geographic regions and healthcare settings.
- Although the sample size is sufficient for a detailed analysis in this study, it may not be large enough to represent the broader population of young stroke patients. The limited sample size may hinder the ability to detect subtle variations in stroke characteristics and outcomes.
- The inclusion criteria and patient selection process may introduce selection bias. This is because the patients admitted to the Bristol Royal Infirmary Stroke Unit may represent a subset with more severe strokes, higher comorbidity burdens, or unique referral patterns, which may not be reflective of the entire spectrum of young stroke patients in the community.
- The method used to collect data in this study may have inherent limitations such as potential inaccuracies in medical records, patient self-reporting errors, missing data, and inconsistencies in data entry. As obtained in the SSNAP datatset, the risk factors were entered individually, and this does not capture the clustering effects of the risk factors.These limitations can affect the reliability and validity of the data used for analysis in this study.
- Some risk factors like lifestyle-related ones may be underreported or inaccurately recorded. Additionally, the study may not capture all relevant risk factors, especially those that are less commonly recognized or more difficult to measure.
- The multifactorial nature of stroke aetiology that includes genetic, environmental, lifestyle, and medical risk factors, poses challenges in disentangling causal relationships. This implies that unmeasured covariates and residual biases may confound observed associations and limit the validity of the inferential analyses in this study.

- The interpretation approach of the study's findings may have introduced some limitations. The observational nature of the study limits the ability to draw causal inferences and affect the robustness of the conclusions.
- The external validity of the study is limited by the specific characteristics of the study population and setting. The findings may not be directly applicable to other populations, particularly those with different demographic, socioeconomic, and healthcare systems.
- The use of data from the Sentinel Stroke National Audit Programme (SSNAP) introduces challenges related to the variability of data quality between different hospitals. Some centres may have more complete and accurate records than others, which can bias research results. This issue can affect the robustness of comparative analyses across multiple stroke units.
- SSNAP data may lack critical confounding variables such as detailed socioeconomic status, specific pre-existing conditions, or granular comorbidity data. Without the ability to adjust for these missing variables, it becomes challenging to draw precise conclusions about stroke outcomes and interventions.
- Although SSNAP provides short-term and acute care data, it has limited scope in assessing long-term outcomes such as quality of life, social reintegration, and mental health. This limitation restricts the study's ability to evaluate the full spectrum of stroke recovery and the long-term impact of stroke interventions.
- Ethical challenges and strict data privacy regulations, such as GDPR, may limit access to certain types of patient-level data in SSNAP. This can restrict the availability of some important data points and limit the depth of analysis and potentially excluding relevant factors that could influence outcomes.

5.8 Recommendations for Future Research

This study has provided a detailed analysis of stroke in young adults in Southwest England. It has identified the key risk factors, common clinical presentations, and treatment outcomes. However, there is still more to uncover. The next step should be to take this research forward in a way that builds directly on these findings. One important step is to conduct a longitudinal study that follows young stroke patients over time. This research was based on a retrospective cohort from 2013 to 2021, using SSNAP data. Although this data has provided useful insights, it did not track individual patients beyond their initial hospital admission. A follow-up study could monitor these

patients for several years to assess the long-term outcomes. By so doing, this would help to answer critical questions like, how many would experience recurrent strokes? What factors predict better recovery? Are there differences in long-term survival based on initial stroke characteristics? These data would be crucial to improve post-stroke care strategies and rehabilitation programs.

Another key direction would be to expand the dataset to multiple hospitals. This study focused on patients treated at the Bristol Royal Infirmary Stroke Unit. Although the findings are significant, they may not reflect the full picture across Southwest England. A national study could compare stroke patterns across different hospitals to better identify variations in outcomes. This would help to determine whether the trends observed in this study hold true across a wider population.

Further research should also explore genetic and biomarker studies in young stroke patients. This study identified unique risk factors such as patent foramen ovale (PFO) and arterial dissection. However, there is growing evidence that genetic predisposition plays a role in young stroke cases. Future studies could analyse genetic markers linked to increased stroke risk in young adults. This would help to determine whether some individuals are more vulnerable due to inherited traits. In addition, blood biomarkers could be studied to predict stroke severity and recovery potential. These findings could eventually lead to personalized treatment approaches.

Another major aspect to analyse is targeted screening and prevention programs. The study focused on risk factors such as illicit drug use, smoking, and excessive alcohol consumption. However, many young adults remain unaware that these behaviors increase their stroke risk. Future research should evaluate the effectiveness of screening programs. Should young adults with migraines or a family history of stroke be screened earlier for cardiovascular issues? Could lifestyle interventions reduce stroke incidence in high-risk groups? Studies that delve into these questions could lead to better prevention efforts and earlier diagnosis for both patients and healthcare providers.

There is also a need for improved treatment strategies for young stroke patients. The study found that young adults receive less aggressive intervention compared to older patients. For instance, thrombectomy and thrombolysis were underused in younger stroke cases. Future studies should investigate why this is happening. Are younger patients presenting with less severe symptoms that leads to delayed intervention? Are there differences in how clinicians approach treatment decisions for younger individuals? A study comparing treatment protocols and outcomes across age groups would help to clarify these issues. If younger patients are missing out on beneficial treatments, guidelines should be revised to ensure they receive optimal care.

Furthermore, the impact of mental health and cognitive function post-stroke in young adults needs further analysis. Many stroke survivors experience depression, anxiety, and cognitive impairment, which affect their ability to return to work and lead independent lives. Unlike older patients, young adults may face greater challenges in resuming careers and maintaining social relationships. A study that focuses on the long-term psychological and cognitive outcomes could provide insights into how to better support young stroke survivors.

Finally, this research should be used to inform policy changes in stroke management. The findings indicate that young adults have different risk profiles and treatment responses compared to older stroke patients. Healthcare guidelines often focus on stroke prevention and management in older populations. However, this study has shown that young adults require tailored approaches. Future research should assess whether current stroke policies address the needs of younger patients adequately. If gaps exist, recommendations should be made for improved screening, earlier intervention, and better post-stroke support services.

5.9 Conclusion

In conclusion, this research has provided a comprehensive examination of stroke in young adults in Southwest England. Through meticulous analysis of data from the Bristol Royal Infirmary Stroke Unit, this study has illuminated various aspects of stroke epidemiology, risk factors, clinical presentations, and outcomes within this demographic. The findings of this research underscore the importance of

understanding the evolving nature of stroke occurrences among young adults and the critical need for tailored prevention, intervention, and management strategies. By elucidating the frequency, risk factors, and clinical manifestations of stroke in young patients, this research contributes valuable insights to the field of stroke medicine and public health. Moreover, the identification of cardiac conditions and other comorbidities associated with stroke highlights the multifactorial nature of this cerebrovascular event and emphasizes the necessity of holistic approaches to stroke care. The implications of these findings extend beyond clinical practice to inform healthcare policies, public health initiatives, and community-based interventions aimed at reducing the burden of stroke and improving outcomes for young adults in Southwest England. This study also serves as a catalyst for ongoing dialogue, innovation, and action in stroke research and healthcare. The findings of this research emphasize the collective responsibility to safeguard the well-being of young adults and promote a healthier, more resilient community. Through collaborative efforts and sustained dedication, healthcare providers can strive towards a future where strokes are preventable, treatable, and ultimately, no longer a leading cause of disability and mortality among young adults.

If I were to start again, I would refine the data collection process to capture a wider range of clinical and lifestyle factors. The dataset relied on SSNAP records; although is very comprehensive, did not include some key variables that could have added depth to the findings. For example, detailed medication history, socioeconomic status, and family history of stroke were not available. These factors would have played a role in stroke risk and outcomes, and their inclusion could have strengthened the analysis. Finally, I would place greater emphasis on qualitative aspects of patient experience. Stroke in young adults has unique psychological and social consequences, including employment challenges, mental health issues, and reduced independence. A mixed-methods approach that combines quantitative analysis with patient interviews, could provide a better understanding of how stroke affects younger individuals beyond clinical outcomes.

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APPENDIX

A. HRA and Health and Care research Wales (HCRW) Approval Letter

Dr Oladotun Abidakun
Consultant Stroke Physician
University Hospitals Bristol & Weston NHS Foundation Trust
Bristol Royal Infirmary
Upper Maudlin Street
Bristol
BS2 8HW

Email: approvals@hra.nhs.uk
HCRW.approvals@wales.nhs.uk

03 August 2022

Dear Dr Abidakun

HRA and Health and Care Research Wales (HCRW) Approval Letter

Study title:	**CHARACTERISTICS OF STROKE IN YOUNG ADULTS IN SOUTHWEST ENGLAND**
IRAS project ID:	**318589**
Protocol number:	**N/A**
REC reference:	**22/HRA/3235**
Sponsor	**University of Hertfordshire**

I am pleased to confirm that **HRA and Health and Care Research Wales (HCRW) Approval** has been given for the above referenced study, on the basis described in the application form, protocol, supporting documentation and any clarifications received. You should not expect to receive anything further relating to this application.

Please now work with participating NHS organisations to confirm capacity and capability, in line with the instructions provided in the "Information to support study set up" section towards the end of this letter.

How should I work with participating NHS/HSC organisations in Northern Ireland and Scotland?
HRA and HCRW Approval does not apply to NHS/HSC organisations within Northern Ireland and Scotland.

If you indicated in your IRAS form that you do have participating organisations in either of these devolved administrations, the final document set and the study wide governance report

(including this letter) have been sent to the coordinating centre of each participating nation. The relevant national coordinating function/s will contact you as appropriate.

Please see IRAS Help for information on working with NHS/HSC organisations in Northern Ireland and Scotland.

How should I work with participating non-NHS organisations?
HRA and HCRW Approval does not apply to non-NHS organisations. You should work with your non-NHS organisations to obtain local agreement in accordance with their procedures.

What are my notification responsibilities during the study?

The *"After HRA Approval – guidance for sponsors and investigators"* document on the HRA website gives detailed guidance on reporting expectations for studies with HRA and HCRW Approval, including:

- Registration of Research
- Notifying amendments
- Notifying the end of the study

The HRA website also provides guidance on these topics and is updated in the light of changes in reporting expectations or procedures.

Who should I contact for further information?
Please do not hesitate to contact me for assistance with this application. My contact details are below.

Your IRAS project ID is **318589**. Please quote this on all correspondence.

Yours sincerely,

Mathew Barnes
Approvals Specialist

Email: approvals@hra.nhs.uk

Copy to: *Dr Kunle Ashaye*

IRAS project ID	318589

Information to support study set up

The below provides all parties with information to support the arranging and confirming of capacity and capability with participating NHS organisations in England and Wales. This is intended to be an accurate reflection of the study at the time of issue of this letter.

Types of participating NHS organisation	Expectations related to confirmation of capacity and capability	Agreement to be used	Funding arrangements	Oversight expectations	HR Good Practice Resource Pack expectations
This is a single research site study.	The single participating NHS organisation of this type is also sponsoring the research. You should work with your sponsor R&D office to make arrangements to set up the study. The sponsor R&D office will confirm to you when the study can start following issue of HRA and HCRW Approval.	No agreement is expected.	No application for external funding has been made.	In line with HRA/HCRW expectations a Principal Investigator should be appointed at participating NHS organisations of this type.	It is not expected that any additional HR arrangements will be necessary.

Other information to aid study set-up and delivery

This details any other information that may be helpful to sponsors and participating NHS organisations in England and Wales in study set-up.
The applicant has indicated that they do not intend to apply for inclusion on the NIHR CRN Portfolio.

List of Documents

The final document set assessed and approved by HRA and HCRW Approval is listed below.

Document	*Version*	*Date*
IRAS Application Form [IRAS_Form_27072022]		27 July 2022
Research protocol or project proposal [Proposal]		01 October 2021
Summary CV for Chief Investigator (CI) [CV]		

B. Sponsorship Letter

University of Hertfordshire UH

University of Hertfordshire
Higher Education Corporation
Hatfield, Hertfordshire
AL10 9AB

Telephone +44 (0) 1707 284000
Fax +44 (0) 1707 284115
Website www.herts.ac.uk

John M Senior
BSc MSc DSc PGCE CEng FIET FRSA FHEA
Professor of Communication Networks
Pro Vice-Chancellor (Research and Enterprise)

Prof Kunle Ashaye/Dr Oladotun Abidakun
Life & Medical Sciences/Health & Social Work

15 December 2022

Dear Prof Ashaye and Dr Abidakun

Re: **UNIVERSITY OF HERTFORDSHIRE SPONSORSHIP IN FULL for the following:**
RESEARCH STUDY TITLE: CHARACTERISTICS OF STROKE IN YOUNG ADULTS IN SOUTHWEST ENGLAND
NAME OF CHIEF INVESTIGATOR (Supervisor): Prof Kunle Ashaye
NAME OF INVESTIGATOR (Student): Dr Oladotun Abidakun
UNIVERSITY OF HERTFORDSHIRE ETHICS PROTOCOL NUMBER: LMS/PGR/UH/05172
HEALTH RESEARCH AUTHORITY REFERENCE: 22/HRA/3235

This letter is to confirm your research study detailed above has been reviewed and accepted and I agree to give full University of Hertfordshire sponsorship, so you may now commence your research.

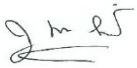
As a condition of receiving full sponsorship, please note that it is the responsibility of the Chief Investigator to inform the Sponsor at any time of any changes to the duration or funding of the project, changes of investigators, changes to the protocol and any future amendments, or deviations from the protocol, which may require re-evaluation of the sponsorship arrangements.

Permission to seek changes as outlined above should be requested from myself before submission and notification to the Health Research Authority (HRA) or University of Hertfordshire Ethics Committee with Delegated Authority (ECDA) as relevant, and I must also be notified of the outcome. It is essential that evidence of any further relevant external permissions is provided as they are received. Copies of annual reports and the end of study report as submitted to the HRA also need to be provided. Please do this via email to research-sponsorship@herts.ac.uk

Please note that University Sponsorship of your study is invalidated if this process is not followed.

In the meantime, I wish you well in pursuing this interesting research study.

Yours sincerely



Professor J M Senior
Pro Vice-Chancellor (Research and Enterprise)

C. Results

Table 4.1a Descriptive Statistics of Age Variable

Descriptive Statistics

Age

Total	**Valid Age**	**460**
	Missing Age	0
Mean		46.86
Median		50.00
Std. Deviation		8.116

Table 4.2a Frequency Distribution of Patient's Age

Age Distribution

		Frequency	Percent	Valid Percent	Cumulative Percent
Age in Ascending Order	17	2	.4	.4	.4
	19	1	.2	.2	.7
	20	1	.2	.2	.9
	21	1	.2	.2	1.1
	22	3	.7	.7	1.7
	24	3	.7	.7	2.4
	25	2	.4	.4	2.8
	26	5	1.1	1.1	3.9
	27	2	.4	.4	4.3
	28	3	.7	.7	5.0
	29	1	.2	.2	5.2
	30	4	.9	.9	6.1
	31	4	.9	.9	7.0
	32	4	.9	.9	7.8
	33	3	.7	.7	8.5
	34	5	1.1	1.1	9.6
	35	3	.7	.7	10.2
	36	7	1.5	1.5	11.7
	37	7	1.5	1.5	13.3

	38	9	2.0	2.0	15.2
	39	5	1.1	1.1	16.3
	40	11	2.4	2.4	18.7
	41	15	3.3	3.3	22.0
	42	5	1.1	1.1	23.0
	43	9	2.0	2.0	25.0
	44	16	3.5	3.5	28.5
	45	12	2.6	2.6	31.1
	46	21	4.6	4.6	35.7
	47	10	2.2	2.2	37.8
48		23	5.0	5.0	42.8
	49	27	5.9	5.9	48.7
	50	33	7.2	7.2	55.9
	51	34	7.4	7.4	63.3
	52	42	9.1	9.1	72.4
	53	48	10.4	10.4	82.8
	54	33	7.2	7.2	90.0
	55	46	10.0	10.0	100.0
	Total	460	100.0	100.0	

Table 4.3a: Frequency Distribution of the Patients Gender

Gender

		Frequency	Percent	Valid Percent	Cumulative Percent
	FEMALE	168	36.5	36.5	36.5
	MALE	292	63.5	63.5	100.0
	Total	460	100.0	100.0	

Table 4.4a: Frequency Distribution of the Patients Ethnicity

Ethnicity

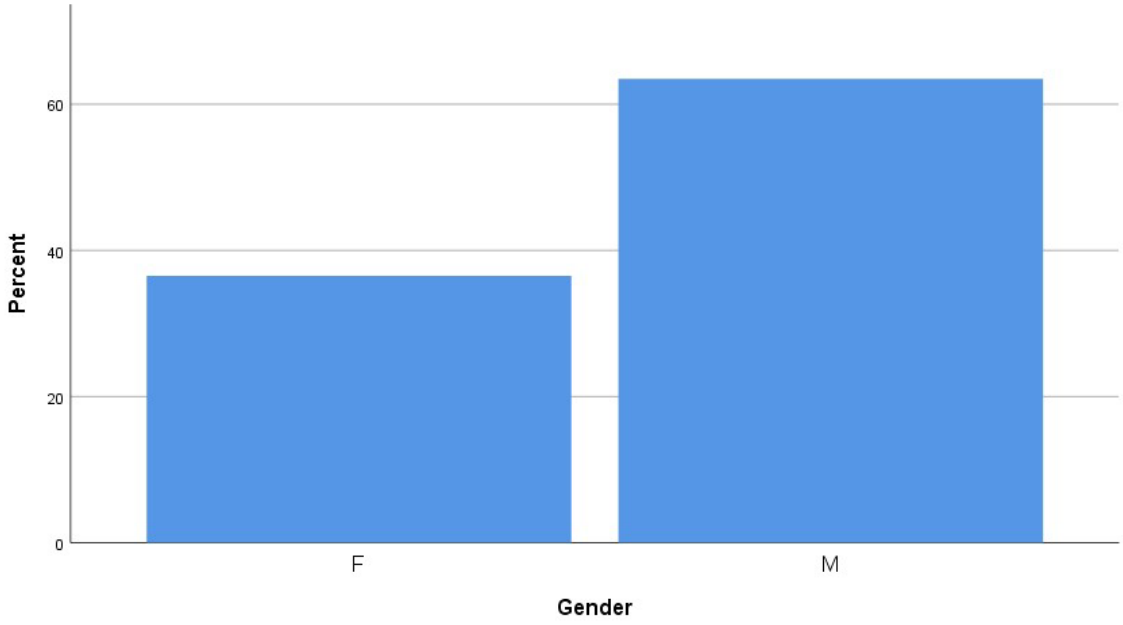
	Frequency	Percent	Valid Percent	Cumulative Percent
African	18	4.0	4.0	2.4
American	1	.2	.2	2.6
Other Ethnic groups	3	.7	.7	3.5
Other Mixed background	1	.2	.2	3.7
Asian	10	2.2	2.2	5.4
Belgian	1	.2	.2	5.7
Black	5	1.1	1.1	6.5
British	365	78.6	78.6	84.6
Bulgaria	1	.2	.2	84.8
Caribbean	13	2.8	2.8	87.2
German	2	.4	.4	87.8
Irish	1	.2	.2	88.3
Italian	1	.2	.2	88.5
Lithuanian	1	.2	.2	89.1
Not Stated and Unknown	22	4.7	4.7	92.4
Peru	2	.4	.4	93.7
Polish	3	.7	.7	94.3
Portuguese	1	.2	.2	94.6
Romanian	2	.4	.4	95.0
Russian	2	.4	.4	95.4
Spanish	3	.7	.7	97.2
Turkish	1	.2	.2	97.4
Ukrainian	1	.2	.2	97.6
Total	460	100.0	100.0	

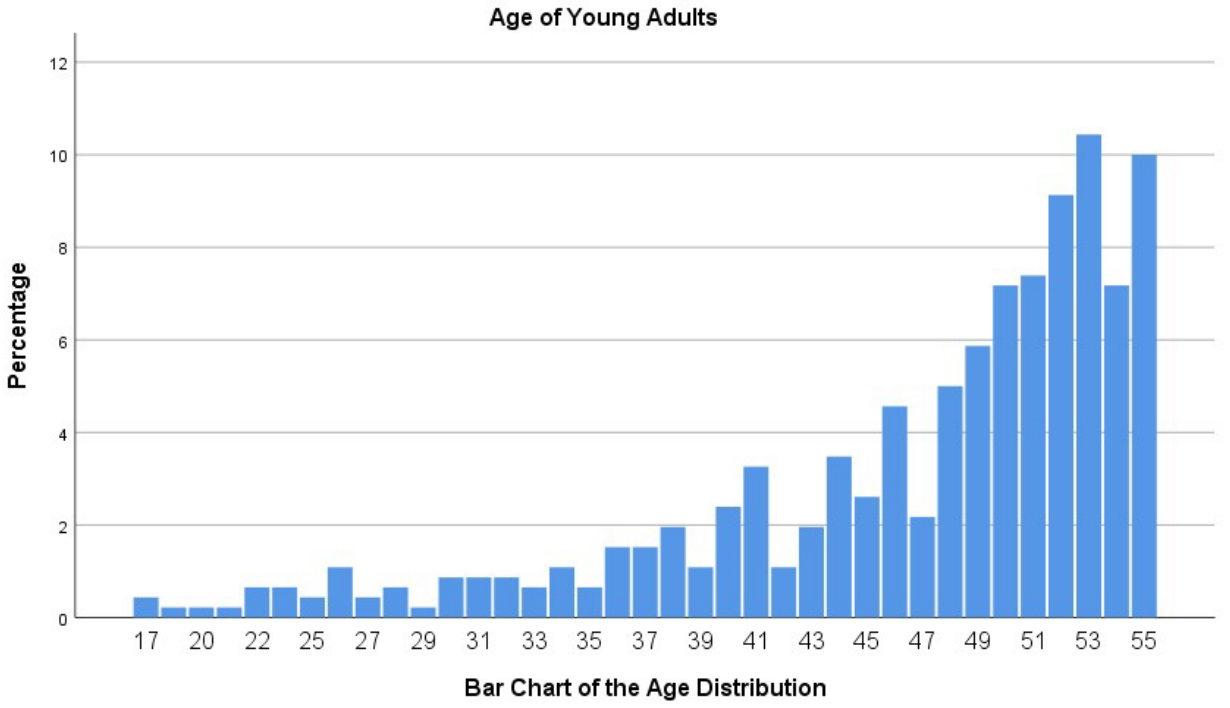
Table 4.5a Frequency Distribution of the Patients Country of Residence

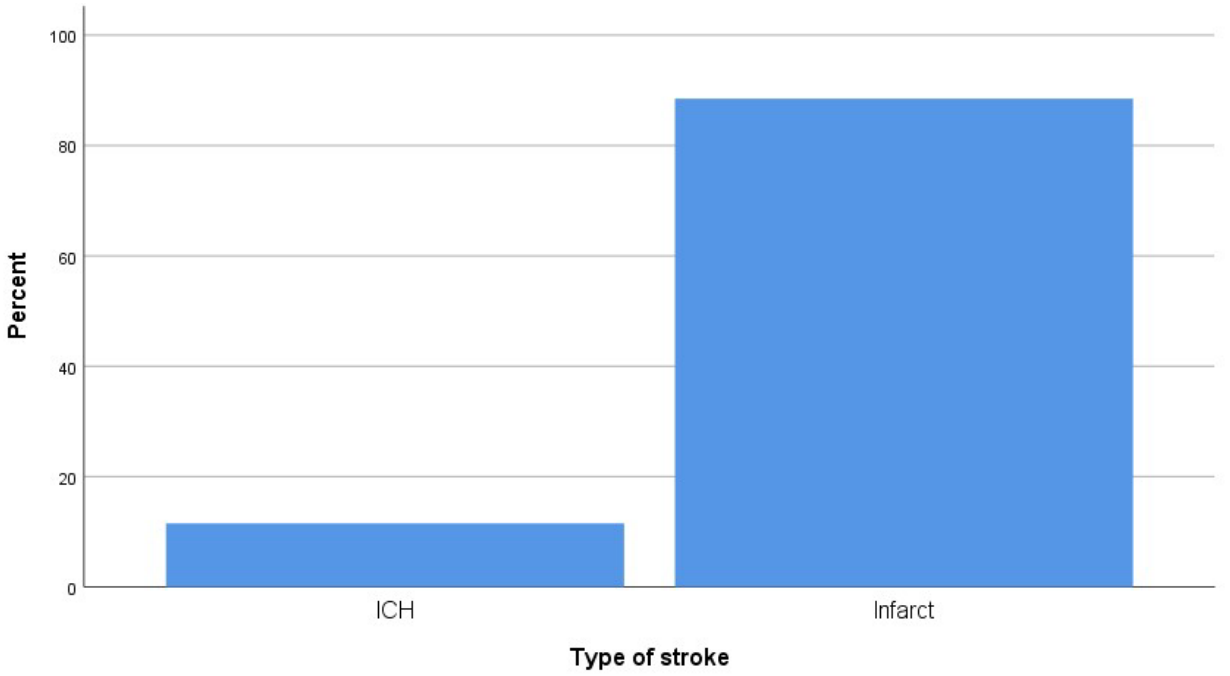
Country of Residence

	Frequency	Percent	Valid Percent	Cumulative Percent
Belgium	1	.2	.2	.4

China	1	.2		.2		.7
France	1	.2		.2		.9
Singapore	1	.2		.2		1.1
UK	442	96.2		96.2		99.5
Unknown	13	2.8		2.8		100.0
Total	460	100.0		100.0		




Age of Young Adults
Percentage
12
10
8
6
4
2
0
17 20 22 25 27 29 31 33 35 37 39 41 43 45 47 49 51 53 55
Bar Chart of the Age Distribution


Percent
100
80
60
40
20
0
ICH
Infarct
Type of stroke

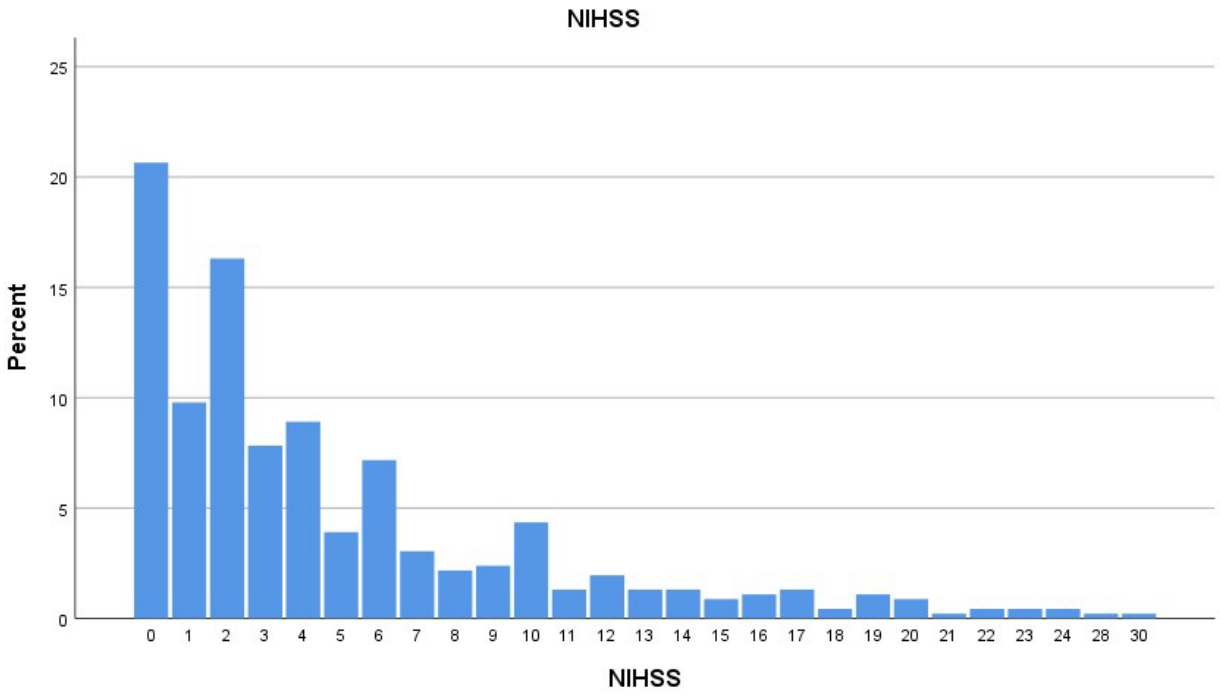

NIHSS
Percent
25
20
15
10
5
0
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 28 30
NIHSS

Table 4.6 Frequency Distribution of the Patients Type of Stroke

Type of stroke

	Frequency	Percent	Valid Percent	Cumulative Percent
ICH	53	11.5	11.5	11.5
Infarct	407	88.5	88.5	100.0
Total	460	100.0	100.0	

Table 4.7 Statistics of the Severity of Stroke (NIHSS)

Statistics

NIHSS

N	**Valid**	**460**
	Missing	0
Mean		4.87
Median		3.00
Mode		0
Std. Deviation		5.478

Table 4.8 Frequency Distribution of the Severity of Stroke (NIHSS)

NIHSS

	Frequency	Percent	Valid Percent	Cumulative Percent
0	95	20.7	20.7	20.7
1	45	9.8	9.8	30.4
2	75	16.3	16.3	46.7
3	36	7.8	7.8	54.6
4	41	8.9	8.9	63.5
5	18	3.9	3.9	67.4
6	33	7.2	7.2	74.6
7	14	3.0	3.0	77.6
8	10	2.2	2.2	79.8
9	11	2.4	2.4	82.2
10	20	4.3	4.3	86.5
11	6	1.3	1.3	87.8
12	9	2.0	2.0	89.8
13	6	1.3	1.3	91.1
14	6	1.3	1.3	92.4
15	4	.9	.9	93.3
16	5	1.1	1.1	94.3
17	6	1.3	1.3	95.7
18	2	.4	.4	96.1
19	5	1.1	1.1	97.2
20	4	.9	.9	98.0
21	1	.2	.2	98.3
22	2	.4	.4	98.7
23	2	.4	.4	99.1
24	2	.4	.4	99.6
				99.8
				100.0

28	1	.2		.2		
30	1	.2		.2		
Total	460	100.0		100.0		

Table 4.9 Frequency Distribution of Hypertension (HTN)

Hypertension (HTN)

		Frequency	Percent	Valid Percent	Cumulative Percent
	No	285	62.0	62.0	62.0
	Yes	175	38.0	38.0	100.0
	Total	460	100.0	100.0	

Table 4.10 Frequency Distribution of Atrial Fibrillation (AF)

Atrial Fibrillation (AF)

	Freque ncy	Percen t	Valid Pe	rcent	Cumulative Percent
No	422	91.8	91.8	91.8	
Yes	38	8.2	8.2	100.0	
Total	460	100.0	100.0		

Table 4.11 Frequency Distribution of Smoking

Smoking

	Frequency	Percent	Valid Percent	Cumulative Percent
Ex-Smoker	102	22.2	22.2	22.2
No	259	62.9	62.9	85.0
Yes	69	15.0	15.0	100.0
Total	460	100.0	100.0	

Table 4.12 Frequency Distribution of ETOH (Alcohol Consumption)

ETOH (Alcohol Consumption)

	Frequency	Percent	Valid Percent	Cumulative Percent
Ex	2	.4	.4	.4
No	406	88.3	88.3	88.7
Yes	52	11.3	11.3	100.0
Total	460	100.0	100.0	

Table 4.13 Frequency Distribution of Hypercholesterolemia

Hypercholesterolemia

	Frequency	Percent	Valid Percent	Cumulative Percent
No	445	96.7	96.7	96.7
Yes	15	3.3	3.3	100.0
Total	460	100.0	100.0	

Table 4.14 Frequency Distribution of Diabetes Mellitus

Diabetes Mellitus

	Freque ncy	Percen t	Valid Pe rcent	Cumulative Percent
No	445	97.2	97.2	97.2
Yes	13	2.8	2.8	100.0
Total	460	100.0	100.0	

Table 4.15 Frequency Distribution of Illicit Drug Use

Illicit Drug use

	Frequency	Percent	Valid Percent	Cumulative Percent
No	426	92.4	92.4	92.4
Yes	35	7.6	7.6	100.0
Total	460	100.0	100.0	

Table 4.16: Frequency Distribution of Hormone Replacement Therapy (HRT)

Hormone Replacement Therapy (HRT)

	Frequency	Percent	Valid Percent	Cumulative Percent
No	451	97.8	97.8	98.5
Yes	9	1.3	1.3	100.0
Total	460	100.0	100.0	

Table 4.17: Frequency Distribution of Genetics

Genetics

	Frequency	Percent	Valid Percent	Cumulative Percent
No	456	99.2	99.2	99.2
Yes	4	0.8	0.8	100.0
Total	460	100.0	100.0	

Table 4.18 Frequency Distribution of Migraine

Migraine

	Frequency	Percent	Valid Percent	Cumulative Percent
No	301	87.2	87.2	87.2
Yes	59	12.8	12.8	100.0
Total	460	100.0	100.0	

Table 4.19 Frequency Distribution of Deep Vein Thrombosis/Pulmonary Embolism (DVT/PE)

Deep Vein Thrombosis/Pulmonary Embolism (DVT/PE)

	Frequency	Percent	Valid Percent	Cumulative Percent
No	428	93.0	93.0	93.0
Yes	32	7.0	7.0	100.0
Total	460	100.0	100.0	

Table 4.20 Frequency Distribution of Non-haematological Malignancy

Malignancy

	Frequency	Percent	Valid Percent	Cumulative Percent
No	427	92.8	92.8	92.8
Yes	33	7.0	7.0	100.0
Total	460	100.0	100.0	

Table 4.21 Frequency Distribution of Haematological Malignancy

	Frequency	Percent	Valid Percent	Cumulative Percent
No	455	99.0	99.0	99.0
Yes	5	1.0	1.0	100.0
Total	460	100.0	100.0	

Table 4.22 Frequency Distribution of Endocarditis

Endocarditis

	Frequency	Percent	Valid Percent	Cumulative Percent
No	443	92.3	92.3	92.3
Yes	17	7.7	7.7	100
Total	460	100.0	100.0	

Table 4.23 Frequency Distribution of Peripheral Vascular Disease (PVD)

Peripheral Vascular Disease (PVD)

	Frequency	Percent	Valid Percent	Cumulative Percent
No	454	98.7	98.7	98.7
Yes	6	1.3	1.3	100.0
Total	460	100.0	100.0	

Table 4.24 Frequency Distribution of Cervical Artery Dissection

Cervical Artery Dissection

	Frequency	Percent	Valid Percent	Cumulative Percent
No	434	94.3	94.3	94.3
Yes	26	5.7	5.7	100.0
Total	460	100.0	100.0	

Table 4.25 Frequency Distribution of Congestive Heart Failure (CHF)

Congestive Heart Failure (CHF)

	Frequency	Percent	Valid Percent	Cumulative Percent
No	446	96.9	96.9	96.9
Yes	14	3.1	3.1	100.0
Total	460	100.0	100.0	

Table 4.26 Frequency Distribution of Patent Foramen Ovale (PFO)

Patent Foramen Ovale (PFO)

	Frequency	Percent	Valid Percent	Cumulative Percent
No	412	89.6	89.6	89.6
Yes	48	10.4	10.4	100.0
Total	460	100.0	100.0	

Table 4.27 Frequency Distribution of Ischaemic Heart Disease (IHD)

Ischaemic Heart Disease (IHD)

	Frequency	Percent	Valid Percent	Cumulative Percent
No	419	91.1	91.1	91.1
Yes	41	8.9	8.9	100.0
Total	460	100.0	100.0	

4.3.2.14 Other Cardiac Conditions

Cardiac Conditions	Frequency	Percent	Valid Percent	Cumulative Percent
Aortic Stenosis	2	0.4	0.4	0.4
Other Aortic Valve Diseases	3	0.6	0.6	1.0
Ventricular Septal Defect	1	0.2	0.2	1.2
Aortic Valve Replacement	1	0.2	0.2	1.4
Dilated Cardiomyopathy	2	0.2	0.2	1.6
Congenital Heart Disease (Unspecified)	1	0.2	0.2	1.8

Heart Block	2	0.4	0.4	2.2
Hypertrophic Cardiomyopathy	2	0.2	0.2	2.4
Left Ventricular Hypertrophy	3	0.6	0.6	3.0
Mechanical Valve	1	0.2	0.2	3.2
Mitral Valve Disease (Unspecified)	2	0.4	0.4	3.6
Mitral Valve Stenosis	1	0.2	0.2	3.8
Valve Replacement (Unspecified)	2	0.4	0.4	4.2
NO	437	95.0	95.0	100
Total	460	100.0	100.0	

The table above shows a spectrum of other cardiac conditions identified in the dataset which cumulatively account for 4.2% of the risk factors.

Table 4.27 Frequency of other individual Stroke Risk Factors identified in the Dataset

Stroke Risk Factor	Frequency	Percent	Valid Percent	Cumulative Percent
Thrombophilia	1	0.2	0.2	0.2
Antiphospholipid Syndrome	3	0.6	0.6	0.8
Systemic Lupus Erythematosus (SLE)	2	0.4	0.4	1.2
CKD	7	1.4	1.4	2.6
DiGeorge Syndrome	1	0.2	0.2	2.8
Giant cell arteritis (GCA)	1	0.2	0.2	3.0
Gilbert Syndrome	1	0.2	0.2	3.2
Graves Disease	2	0.4	0.4	3.6
Hepatitis	2	0.4	0.4	4.0
Hypothyroidism	8	1.6	1.6	5.6
Jak 2 Mutation	1	0.2	0.2	5.8
Cerebral Venous Sinus Thrombosis	2	0.4	0.4	6.2
MGUS	1	0.2	0.2	6.4
Loeys Dietz Syndrome	1	0.2	0.2	6.6
Prothrombin Gene Mutation	1	0.2	0.2	6.8
Ramsay-Hunt Syndrome	1	0.2	0.2	7.0
Sickle Cell Disease	2	0.4	0.2	7.2
Hyperthyroidism	1	0.2	0.2	7.4

Smith-Magenis Syndrome	1	0.2	0.2	7.6
Sneddon's syndrome	1	0.2	0.2	7.8
Thrombotic Thrombocytopenic Purpura	1	0.2	0.2	8.0
Thyroid Cancer	1	0.2	0.2	8.2
NO	417	91.8	91.8	100
Total	460	100.0	100.0	

Table 4.29 Frequency Distribution of Treatment Type: Thrombolysis

Thrombolysis

	Frequency	Percent	Valid Percent	Cumulative Percent
No	411	89.3	89.3	89.3
Yes	49	10.7	10.7	100.0
Total	460	100.0	100.0	

Table 4.30 Frequency Distribution of Treatment Type: Thrombectomy

Thrombectomy

	Frequency	Percent	Valid Percent	Cumulative Percent
No	452	98.3	98.3	98.5
Yes	7	1.5	1.5	100.0
Total	460	100.0	100.0	

Table 4.31 Frequency Distribution of Treatment Type: Surgery

Surgery

	Frequency	Percent	Valid Percent	Cumulative Percent
No	446	97.0	97.0	97.0
Yes	14	3.0	3.0	100.0
Total	460	100.0	100.0	

4.6.1 Duration of Admission

Table 4.30 Statistics of Duration of Admission

		Duration of admission	Alive at 30 days
N	Valid	459	460
	Missing	1	0
Mean		14.94	
Median		4.00	
Mode		2	
Std. Deviation		26.857	

Duration of Admission

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	0	17	3.7	3.7	3.7
	1	66	14.3	14.4	18.1
	2	68	14.8	14.8	32.9
	3	38	8.3	8.3	41.2
	4	48	10.4	10.5	51.6
	5	25	5.4	5.4	57.1
	6	17	3.7	3.7	60.8
	7	14	3.0	3.1	63.8
	8	7	1.5	1.5	65.4

	9	14	3.0	3.1	68.4
	10	9	2.0	2.0	70.4
	11	6	1.3	1.3	71.7
	12	5	1.1	1.1	72.8
	13	9	2.0	2.0	74.7
	14	7	1.5	1.5	76.3
	15	4	.9	.9	77.1
	16	6	1.3	1.3	78.4
	17	8	1.7	1.7	80.2
	18	2	.4	.4	80.6
	19	3	.7	.7	81.3
	20	2	.4	.4	81.7
	21	1	.2	.2	81.9
	22	2	.4	.4	82.4
	23	2	.4	.4	82.8
	24	4	.9	.9	83.7
	25	3	.7	.7	84.3
	26	1	.2	.2	84.5
	27	3	.7	.7	85.2
	28	1	.2	.2	85.4
	29	1	.2	.2	85.6
	30	3	.7	.7	86.3
	31	1	.2	.2	86.5
	32	1	.2	.2	86.7
	33	2	.4	.4	87.1
	34	2	.4	.4	87.6
	35	2	.4	.4	88.0
	36	1	.2	.2	88.2
	38	2	.4	.4	88.7
	39	**2**	**.4**	**.4**	**89.1**
	40	1	.2	.2	89.3
	41	3	.7	.7	90.0
	42	3	.7	.7	90.6
	43	1	.2	.2	90.8
	44	1	.2	.2	91.1
	45	1	.2	.2	91.3
	46	2	.4	.4	91.7
	48	1	.2	.2	91.9

	49	1	.2	.2	92.2
	50	1	.2	.2	92.4
	51	3	.7	.7	93.0
	56	1	.2	.2	93.2
	61	2	.4	.4	93.7
	62	1	.2	.2	93.9
	64	2	.4	.4	94.3
	71	1	.2	.2	94.6
	73	1	.2	.2	94.8
	75	2	.4	.4	95.2
	77	1	.2	.2	95.4
	79	1	.2	.2	95.6
	85	1	.2	.2	95.9
	90	1	.2	.2	96.1
	93	1	.2	.2	96.3
	94	1	.2	.2	96.5
	96	1	.2	.2	96.7
	99	1	.2	.2	96.9
	100	1	.2	.2	97.2
	101	1	.2	.2	97.4
	107	2	.4	.4	97.8
	116	1	.2	.2	98.0
	119	1	.2	.2	98.3
	127	2	.4	.4	98.7
	133	1	.2	.2	98.9
	138	1	.2	.2	99.1
	141	1	.2	.2	99.3
	152	1	.2	.2	99.6
	166	1	.2	.2	99.8
	173	1	.2	.2	100.0
	Total	459	99.8	100.0	
Missing	System	1	.2		
Total		460	100.0		

Table 4.31 Frequency Distribution of Patients Alive at 30 days

Alive at 30 days

	Frequency	Percent	Valid Percent	Cumulative Percent
No	20	4.3	4.3	4.3
Yes	440	95.7	95.7	100.0
Total	460	100.0	100.0	

Table 4.32 Statistics of Student T-Test

Group Statistics

	Alive at 30 days	N	Mean	Std. Deviation	Std. Error Mean
Age	Yes	440	46.92	8.085	.385
	No	20	45.65	8.905	1.991

Table 4.33 Independent Samples Test

Independent Samples Test

		Levene's Test for Equality of Variances		t-test for Equality of Means						
		F	Sig.	t	df	Sig. (2tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference	
									Lower	Upper
Age	Equal variances assumed	.887	.347	.682	458	.496	1.266	1.857	-2.383	4.915
	Equal variances not assumed			.624	20.449	.539	1.266	2.028	-2.959	5.490

Gender * Alive at 30 days Cross tabulation

		No	t 30 days Yes	Total
Gender	Female	11	157	168
	Male	9	283	292
Total		20	440	460

Table 4.34 Gender * Alive at 30 days Cross tabulation