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An Evaluation of In-Hospital Stroke in Irish Acute Hospitals

By

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Declaration

I declare that this thesis has not been submitted as an exercise for a degree at this or any other university and it is entirely my own work. Ethical approval for this research work was obtained from the St. James's Hospital and Tallaght University Hospital Joint Research Ethics Committee. The need for informed consent was waived given the retrospective study design, anonymisation of the data and data collection was completed under the principles and procedures of the National Office of Clinical Audit. I agree to deposit this thesis in the University's open access institutional repository or allow the Library to do so on my behalf, subject to Irish Copyright Legislation and Trinity College Library conditions of use and acknowledgement. I consent to the examiner retaining a copy of the thesis beyond the examining period, should they so wish (EU GDPR May 2018).

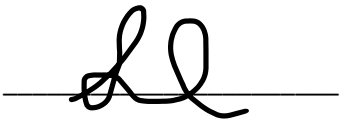

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Table of Contents

List of Figures 9
List of Tables 10
Glossary 11
General Introduction 13
Rationale 13
Aim 14
Objective 14
Abstract 15
Chapter 1. Literature Review 16
1.1 Introduction 16
1.2 Definition of Stroke 16
1.3 Stroke Subtype and Mechanisms 17
1.4 Stroke Diagnosis 18
1.4.1 Clinical Aspects of Diagnosis 18
1.4.2 Imaging Aspects of Diagnosis 19
1.5 Acute Stroke Treatment – Ischaemic Stroke 19
1.5.1 Acute Stroke Treatment – Haemorrhagic Stroke 21
1.6 Care Within the Stroke Unit 21
1.7 Background of In-Hospital Stroke 21
1.7.1 Age 22
1.7.2 Pre-Stroke Function 22
1.7.3 Comorbidity 23
1.7.4 Reason for Hospitalisation 24
1.7.5 Procedures 24
1.7.6 Location at Onset 25
1.7.7 Stroke Subtype and Severity 26
1.7.8 Mimics 27
1.8 In-Hospital Stroke Outcomes 28
1.8.1 Mortality 28
1.8.2 Thrombolysis Rates 29
1.8.3 Thrombectomy Rates 31
1.8.4 Length-of-stay 32
1.8.5 Post Stroke Disability and Discharge Destination 32
1.9 In-Hospital Stroke Quality-of-Care Measures 40
1.9.1 Time-based Intervals in Acute Stroke 40
1.9.2 Time to Stroke Recognition 41

1.9.3 Time to Imaging 42
1.9.4 Time to Reperfusion 42
1.9.5 Location & Time-based Intervals 43
1.9.6 Admission to the Stroke Unit 47
1.10 Summary of Literature Review 48
1.11 Thesis Layout 49
Chapter 2. Single Centre Review of In-Hospital Stroke in St. James's Hospital 50
2.1 Introduction 50
2.2 Aim 50
2.3 Objectives 50
2.4 Methods 51
2.4.1 Study Design & Setting 51
2.4.2 HIPE Data 51
2.4.3 Local Audit Coordinators 52
2.4.4 Current Definition of IHS 52
2.4.5 Inclusion Criteria for Validation 52
2.4.6 Exclusion Criteria for Validation 52
2.4.7 Clinical Validation 53
2.4.8 Cohort Study Variables 54
2.4.9 Statistical Analysis 55
2.5 Results of Clinical Validation Study 56
2.5.1 Validated Stroke Cases 56
2.5.2 Validated IHS Cases 56
2.5.3 Level of Agreement for IHS Cases 58
2.6 Results of Retrospective Cohort Study 60
2.6.1 Demographics and Characteristics 60
2.6.2 Outcome Variables 61
2.6.3 Quality-of-Care Variables 63
2.7 Discussion of Clinical Validation Study 67
2.8 Discussion of Retrospective Cohort Study 69
2.9 Conclusions 71
Chapter 3. Methods of National In-Hospital Stroke Review 72
3.1 Study Design 72
3.2 Background of Core Clinical Dataset in INAS 72
3.3 Data Access 73
3.5 IHS Case Definition 73
3.6 COS Case Definition 74

3.7 Cohort Selection 74
3.8 Data Variables 78
3.8.1 Time-based Quality-of-Care Measures 78
3.8.2 Stroke Subtype 79
3.8.3 LOS 80
3.8.4 Hospital Model and PCI Centres 80
3.8.5 Reasons for Non-Admission to Stroke Unit 82
3.8.6 In-Hospital Mortality 84
3.9 Statistical Analysis 84
Chapter 4. Results: Demographics 85
4.1 IHS Rate 85
4.2 Sex and Age 87
4.3 Stroke Subtype 87
4.4 Admission Source 89
4.5 Pre-Stroke Modified Rankin Score 89
4.6 Principal Diagnosis at Admission 90
4.7 Critical Care Bed Admissions 91
4.8 COVID-19 Co-Diagnosis 91
4.9 Specialty of Care at Discharge 91
Chapter 5. Results: Quality-of-Care Measures 94
5.1 Stroke Unit Admission 94
5.2 Swallow Screening 97
5.3 Health and Social Care Professionals' Assessments 98
5.4 Carotid Disease 98
5.5 Antithrombotic Therapy 100
5.6 Atrial Fibrillation 101
5.7 Interval to Stroke Symptom Onset 102
5.8 Time to Medical Review 103
5.9 Time to Brain Imaging 105
5.10 Time to Thrombolysis 106
5.11 Summary of Performance on Time-based Intervals 108
Chapter 6. Results: Outcomes 109
6.1 Length-of-Stay 109
6.2 Thrombolysis Rates 109
6.3 In-Hospital Mortality 111
6.4 Modified Rankin Score at Discharge 114
6.5 Discharge Destination 117

Chapter 7. Discussion: Demographics and Quality-of-Care Measures 119
7.1 IHS Rate 119
7.2 Demographic Profile of the IHS Cohort 120
7.3 MDT-Led Care 125
7.4 Performance on Time-Based Stroke Measures 126
Chapter 8. Discussion: Outcomes 130
8.1 Rates of Reperfusion Therapy 130
8.2 In-Hospital Mortality Rates 131
8.3 Post-Stroke Disability & Discharge Outcomes 132
8.4 Limitations 133
Chapter 9. Conclusions 136
9.1 Final Conclusions 136
9.2 Recommendations 139
References 141
Appendix 1: Data Variables from the Irish National Audit of Stroke 148
Appendix 2: Time-Based Intervals Data Elements 152
Appendix 3: Details of Missing and Erroneous Time-Based Data Variables 153

List of Figures

Figure 1.1: Image of the American Heart Association Stroke Definition (Sacco et al., 2013) ……17
Figure 1.2: Visual Representation of Differences in Time-based Intervals between IHS and COS Cohorts …..41
Figure 2.1: Flowchart of Clinical Validation Methods and Excluded Cases (n=34) ……54
Figure 2.2: Venn Diagram of IHS Case (n=88) Identification by HIPE & Audit Coordinator ……57
Figure 2.3: Post Stroke Disability Using Modified Rankin Scores by Stroke Cohort (IHS: n=88; COS n=475)…63
Figure 2.4: Specialty at Discharge for IHS Cohort (IHS n=88) ……66
Figure 3.1: Cohort Selection with Breakdown by Data Scenario ……77
Figure 4.1: Per Hospital Rate of IHS (IHS n=618) ……85
Figure 4.2: Percentage of Stroke Patients by Age and Cohort (COS n=10163; IHS n=618) ……87
Figure 4.3: Pre-Stroke Modified Rankin Scores by Cohort, (IHS n=618, COS n=10163) ……89
Figure 4.4: Principal Diagnosis Coded Using ICD-10-AM for IHS Cases (n=618) ……90
Figure 5.1: Stroke Unit Admission Rates by Cohort, IHS n=618, COS n=10,163 ……94
Figure 5.2: Reasons for Stroke Unit Non-Admission by Cohort, (IHS n=345; COS n=3027) ……96
Figure 5.3: Antithrombotic Therapy Amongst Ischaemic Strokes by Cohort, IHS n= 520, COS n=8680 ……100
Figure 5.4: Atrial Fibrillation Amongst Ischaemic Strokes by Cohort, IHS n= 520, COS n=8680 ……101
Figure 5.5: Box and Whisker Plot of Time to Medical Review from Stroke Symptom Onset (IHS n=276) or Hospital Arrival (COS n=8496) ……104
Figure 5.6: Time to Medical Review from Stroke Symptom Onset for IHS Cases (n=276) or Hospital Arrival for COS Cases (n=8496) ……104
Figure 5.7: Box and Whisker Plot of Time to Brain Imaging from Stroke Symptom Onset (IHS n=285) or Hospital Arrival (COS n=9264) ……105
Figure 5.8: Time to Brain Imaging from Stroke Symptom Onset for IHS Cases (n=285) or Hospital Arrival for COS Cases (n=9264) ……106
Figure 5.9: Box and Whisker Plot of Time to Thrombolysis from Stroke symptom Onset (IHS n=30) or Hospital Arrival (COS n=827) ……107
Figure 5.10: Distribution of Time to Thrombolysis from Stroke Symptom Onset (n=30) or Hospital Arrival (COS n=827) ……107
Figure 6.1: Proportion of Ischaemic Strokes Receiving Thrombolysis by Cohort……111
Figure 6.2: Modified Rankin Score at Discharge by Cohort (IHS n=618; COS n=10163) ……115
Figure 6.3: Discharge Destination by Cohort, (IHS n=618; COS n=10163) ……118
Figure 9.1: Summary of Main Findings of Retrospective Cohort Study Comparing IHS and COS……138

List of Tables

Table 1.1: Key Quality Indicators from the Irish National Audit of Stroke (NOCA 2023c) ……19

Table 1.2: Summary of Charateristics and Outcomes of Reviewed Studies ……34

Table 1.3: Summary of Time-based Results for Reviewed Studies ……44

Table 2.1: Components of Two-Step Clinical Validation ……53

Table 2.2: Data Entry Permutations & Outcomes for Validation Sample (n=169) ……58

Table 2.3: Sensitivity, Specificity, κ Calculations for IHS Cases (n=88) ……59

Table 2.4: Characteristics of IHS (n=88) and COS (n=475) Cohorts ……61

Table 2.5: Outcomes Reported by Stroke Cohort, (IHS n=88, COS n=475) ……62

Table 2.6: Time-Based Quality-of-Care Outcomes of IHS (n=88) and COS (n=475) Cohorts ……64

Table 2.7: Quality-of-Care Outcomes of IHS (n=88) and COS (n=475) Cohorts ……65

Table 3.1: Criteria for IHS in the INAS ……74

Table 3.2: Data Scenarios (n=16) for Stroke Audit Data Recorded 2020 & 2021 ……75

Table 3.3: Hospital Models and PCI Centres for Hospitals Participating in the INAS ……81

Table 3.4: Re-Categorisation of Reasons for Non-Admission to SU ……83

Table 4.1: Total COS and IHS Cases Per Hospital (IHS n=618; COS n=10,163) ……86

Table 4.2: Demographic Results by Cohort (IHS n=618; COS n=10163) ……88

Table 4.3: Stroke Cases by Speciality at Discharge by Cohort (IHS n=615; COS n= 10148) ……93

Table 5.1: Stroke Unit Admission by Cohort (IHS n=618; COS n= 10163) ……95

Table 5.2: Predictors of Stroke Unit Admission ……96

Table 5.3: Swallow Screening by Cohort (IHS n=618; COS n= 10163) ……97

Table 5.4: Health and Social Care Professionals' Assessments by Cohort (IHS n=618; COS n= 10,163) ……99

Table 5.5: Availability and Correctness of Time-based Data Variables by Cohort ……103

Table 5.6: Summary of Time-Based Intervals Performance by Cohort ……108

Table 6.1: Comparison of Median Length of Stay by Cohort ……109

Table 6.2: Subgroup Analysis of Thrombolysis Rates (IHS n=520; COS n=8675) ……110

Table 6.3: In-Hospital Mortality by Cohort (IHS n=618; COS n=10163) With Subgroup Analysis ……112

Table 6.4: Binary Logistic Regression for In-Hospital Mortality for Total Cohort ……113

Table 6.5: Binary Logistic Regression for In-Hospital Mortality by Cohort ……114

Table 6.6: Modified Rankin Score at Discharge by Cohort, (IHS n=618, COS n=10163) ……115

Table 6.7: Binary Logistic Regression for Modified Rankin Score at Discharge for Total Cohort ……116

Table 6.8: Binary Logistic Regression for Modified Rankin Score at Discharge by Cohort ……117

Glossary

AF	Atrial Fibrillation
AHA	American Heart Association
AHP	Allied Health Professional
BP	Blood Pressure
CCF	Congestive Cardiac Failure
CCU	Coronary Care Unit
CGA	Comprehensive Geriatric Assessment
CI	Confidence Interval
CNS	Central Nervous System
COS	Community-onset Stroke
CT	Computed Tomography
ED	Emergency Department
EPR	Electronic Patient Record
EVT	Endovascular Thrombectomy
FAST	Face Arm Speech Time
G45	Transient Ischaemic Attack
H34	Retinal Artery Occlusion
HADx	Hospital Acquired Diagnosis
HDU	High Dependancy Unit
HIPE	Hospital Inpatient Enquiry
HPO	Healthcare Pricing Office
HSCP	Health and Social Care Professionals
HSE	Health Service Executive
I60	Subarachnoid Haemorrhage
I61	Nontraumatic Intracerebral Haemorrhage
I63	Cerebral Infarction
I64	Stroke, not specified as haemorrhage or infarction
IBM	International Business Machines
ICD-10-AM	International Classification of Diseases, Tenth Revision, Australian Modification
ICH	Intracerebral Haemorrhage
ICU	Intensive Care Unit
IHS	In-hospital Stroke
INAS	Irish National Audit of Stroke
IQR	Interquartile Range
IVT	Intravenous Thrombolysis
KQI	Key Quality Indicator
LOS	Length-of-stay
LTC	Long Term Care
LVO	Large Vessel Occlusion
MDT	Multidisciplinary Team
MI	Myocardial Infarction
MRI	Magnetic Resonance Imaging
mRS	modified Rankin Score
MSW	Medical Social Work
NIHSS	National Institutes of Health Stroke Scale

NOCA	National Office for Clinical Audit
NS	Not Statistically Significant
OT	Occupational Therapist
OR	Odds Ratio
PCI	Percutaneous Coronary Intervention
QI	Quality Improvement
SAH	Subarachnoid Haemorrhage
SALT	Speech and Language Therapist
SD	Standard Deviation
SSNAP	Sentinel Stroke National Audit Programme
SU	Stroke Unit
TIA	Transient Ischaemic Attack
TOAST	Trial of ORG 10172 in Acute Stroke Treatment
TPA	Tissue Plasminogen Activator
WHO	World Health Organisation

General Introduction

In-hospital stroke (IHS) is defined as a stroke occurring while in hospital for another diagnosis (Nouh et al., 2022). Approximately one in twenty strokes in the United Kingdom in 2023 had their onset in hospital (Healthcare Quality Improvement Partnership 2023). Nationally in Ireland, 9% of strokes recorded by the Irish National Audit of Stroke (INAS) in 2020 were IHS cases (NOCA 2022a). Community-onset strokes (COS) are more commonly encountered and are characterised by the onset of stroke symptoms before admission to hospital. The literature presented will emphasise that the IHS cohort represents a distinct subgroup of stroke patients. As well as the differing location at the onset of stroke symptoms, IHS cases contrast with COS cases in terms of baseline demographics, outcomes and performance on process and quality-of-care measures in clinical stroke. IHS are associated with, and sometimes caused by, comorbid diagnoses, treatments, and procedures. In Ireland, clinical data on stroke is collected annually from public hospitals delivering acute stroke care in the INAS (NOCA 2023c, NOCA 2023a, NOCA 2022a). Since 2020, clinical data has been gathered on IHS cases however prior analysis on the Irish IHS subgroup has been limited (NOCA 2022a).

Rationale

By analysing the IHS group, future quality improvement (QI) initiatives can be targeted at this distinct stroke cohort. QI is an ongoing, continuous process and without dedicated analysis of IHS, targets for improvement cannot be identified. The importance of QI is underlined by the Health Service Executive (HSE) in Ireland and a suggested framework for the implementation of QI initiatives has been published (Health Service Executive 2016). Indeed, the INAS annual report devotes a chapter to successful QI initiatives undertaken for stroke nationally (NOCA 2023c, NOCA 2023a).

Aim

The aim of this research is to compare IHS cases with COS counterparts in terms of demographics, outcomes, and performance on stroke quality-of-care measures in an Irish context.

Objective

The objective is to conduct a retrospective cohort study comparing cases of IHS and COS from January 1st 2020, to December 31st 2021 in terms of demographics, outcomes and quality-of-care measures using data gathered as part of the INAS.

Abstract

Introduction

Between 1 and 17% of strokes occur in-hospital in patients hospitalised for another reason. In-hospital strokes are associated with worse outcomes and poor performance on quality-of-care measures of acute stroke care.

Methods

A retrospective multi-centre cohort study comparing in-hospital and community-onset strokes was conducted using stroke data collected for the purposes of the Irish National Audit of Stroke from the 1st of January 2020 to the 31st of December 2021.

Results

Of 10,781 stroke cases, 618 occurred in patients in-hospital stroke equating to 5.7% of strokes. In-hospital stroke patients were older (Median age 76 years [IQR 67 to 84 years] versus 74 years [IQR 64 to 82 years] of community-onset stroke). Patients with an in-hospital stroke were more likely to have an ischaemic stroke (90.0% versus 85.4%; p=0.002, pre-stroke disability (modified Rankin score of 3 to 5 30.6% versus 14.3%; p<.001), atrial fibrillation (40.6% versus 29.8%; p<.001) than community-onset stroke patients. The median [IQR] length-of-stay was longer for in-hospital stroke (14 [6-30] versus 8 [4-16] days) and admission to the stroke unit was less frequent (44.2% versus 70.2% of community-onset strokes; adjusted odds ratio 0.46 95% CI 0.38-0.56; p<.001). Longer median [IQR] times to medical assessment (20 [5-84] versus 12 [0-100] minutes; p<.001) and thrombolysis (90 [63-135] versus 54 [37-80] minutes; p<.001) were observed for patients with an in-hospital onset compared with community-onset stroke. Thrombolysis rates were lower amongst ischaemic stroke patients with in-hospital onset (8.7%) versus community-onset stroke (9.9%; p=0.36). One in four (27.2%) in-hospital onset stroke cases die in-hospital compared with one in ten (10.4%) community-onset strokes (adjusted odds ratio 2.98 [2.37-3.75]; p<.001). Favourable functional ability was less likely at discharge for in-hospital onset stroke cases (28.9% versus 52.3% of community-onset strokes; adjusted odds ratio 0.38 [0.30-0.48]; p<.001).

Conclusions

The Irish cohort of in-hospital stroke patients reflect a distinct stroke subgroup. Longer delays to medical assessment and thrombolysis, poorer functional outcomes and increased in-hospital mortality were observed highlighting opportunities to improve care for patients with in-hospital stroke onset.

Chapter 1. Literature Review

1.1 Introduction

Firstly, key definitions and clinical aspects specific to acute stroke care are presented to put later chapters into context. Standards in the quality of stroke care are also detailed and are informed by the National Clinical Guideline for Stroke published in 2023 (Intercollegiate Stroke Working Party 2023) and the designated key quality indicators (KQIs) from the INAS. This is followed by details on the IHS cohort itself including demographics, stroke subtype and mechanisms, pre-stroke disability, inpatient context at the time of stroke onset including location, comorbid diagnoses, and associated procedures. Literature on process and outcome indicators for the IHS cohort including mortality, length-of-stay (LOS), rates of thrombolysis and thrombectomy, post-stroke disability and discharge destination, are then presented. Finally, process and quality-of-care measures of stroke for IHS cases are examined. This includes the time taken to undergo brain imaging and to receive therapeutic interventions. Admission rates to the stroke unit (SU) are also explored.

1.2 Definition of Stroke

The definition of stroke varies depending on the source used. The World Health Organisation (WHO) definition stated that "stroke is rapidly developing clinical signs of focal (or global) disturbance of cerebral function, with symptoms lasting 24 hours or longer, or leading to death, with no apparent cause other than of vascular origin" (Warlow, 1998). The American Heart Association (AHA) broadened its definition to include symptom and/or pathology and imaging criteria (Sacco et al., 2013) (Figure 1.1). Firstly, central nervous system (CNS) infarction is defined as cell death of tissue of the brain, spinal cord, or retina due to ischaemia. The definition of infarction can be based upon pathology, imaging, other objective evidence of ischaemia in a vascular distribution or clinical features of ischaemic injury which last more than 24 hours. Thus, an ischaemic stroke is defined as an episode of neurological dysfunction due to focal cerebral, spinal, or retinal infarction. This means that stroke can include cases with clinical signs of lasting greater than 24 hours with or without objective infarction and can also be a silent event

without any neurological symptoms if infarction is identified on imaging. The definition of transient ischaemic attack (TIA) is focal arterial ischaemia with symptoms lasting less than 24 hours without evidence of infarction on pathology or imaging.

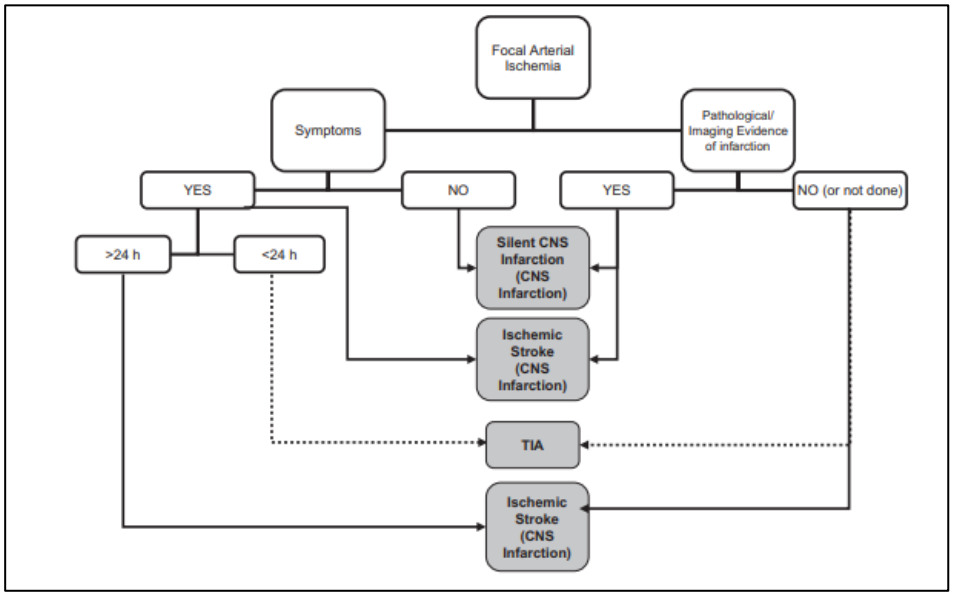

Figure 1.1: Image of the American Heart Association Stroke Definition (Sacco et al., 2013)

Stroke due to intracerebral haemorrhage (ICH) causes neurological dysfunction due to a focal collection of blood in the brain tissue or ventricles which is not due to trauma. Bleeding into the subarachnoid space also leads to neurological dysfunction or headache which is defined as a stroke. The mainstay of treatment for subarachnoid haemorrhage (SAH) is neurosurgical intervention. For this reason, stroke cases due to SAH are sometimes excluded from registry and audit datasets. For instance, SAH is excluded from INAS and the Sentinel Stroke National Audit Programme (SSNAP) which collects data for England, Wales, and Northern Ireland. As a result, SAH cases are not presented in this research.

1.3 Stroke Subtype and Mechanisms

Ischemic stroke is more common than haemorrhagic stroke. Geographical variances in stroke subtype were observed in a large global observational study with higher proportions of ischaemic stroke observed in higher income countries (O'Donnell et al.,

2016). The proportion of ischaemic stroke was 93% in Western Europe, Northern America, and Australia. Various mechanisms cause an ischaemic stroke with subclassification facilitated using the Trial of ORG 10172 in Acute Stroke Treatment (TOAST) criteria. The TOAST criteria defines five mechanisms of ischaemic stroke: large-artery atherosclerosis, cardioembolic, small-vessel occlusion, stroke of other determined aetiology, and stroke of undetermined aetiology (Adams et al., 1993). Mechanisms for ICH include hypertensive angiopathy, cerebral amyloid angiopathy, arteriovenous malformations and cavernous angiomas (Magid-Bernstein et al., 2022).

1.4 Stroke Diagnosis

Rapid diagnosis of an acute stroke is required to ensure necessary investigations are completed so that time sensitive treatments can be initiated. Specifically there should be "no delays in diagnosis and treatment" (Intercollegiate Stroke Working Party 2023).

1.4.1 Clinical Aspects of Diagnosis

Different tools have been developed to facilitate stroke recognition with varying sensitivity and specificity in detecting stroke (Rudd et al., 2016). Ultimately the tool chosen to detect stroke needs to reflect the purpose and the clinical setting. One tool to detect early signs of stroke is the face arm speech time (FAST) test (Harbison et al., 2003). Its implementation amongst paramedics assists in the rapid pre-hospital recognition of acute stroke and facilitates transfer to an acute stroke hospital. Public awareness campaigns have also attempted to educate the public on recognising stroke symptoms using the FAST test. These measures aid pre-hospital recognition of COS cases to a greater degree than IHS events. The National Clinical Guideline for Stroke advises that staff in clinical areas where inpatients are high-risk for acute stroke (cardiothoracic, cardiology, and nephrology wards are specifically mentioned) should have good awareness of acute stroke recognition, the time-critical nature of an acute stroke, pathways to imaging and stroke specialist review (Healthcare Quality Improvement Partnership 2023). The National Institutes of Health Stroke Scale (NIHSS) is an 11-item scoring system used to assess severity of a stroke (National Institutes of Health 2024). It is also used to

standardise the clinical assessment of an acute stroke which facilitates the application of evidence-based guidelines which often employ the use of the NIHSS.

1.4.2 Imaging Aspects of Diagnosis

Cerebral imaging is essential to differentiate between ischaemic and haemorrhagic stroke and identify those patients with ischaemic stroke who are appropriate for reperfusion interventions like intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT). Without imaging, clinicians cannot progress to the appropriate treatment steps. Whilst haemorrhagic stroke is not amenable to IVT or EVT, prompt imaging for these patients still has benefits namely initiation of blood pressure management, reversal of anticoagulants and identifying patients with haemorrhage that should be considered for neurosurgical intervention. Acute stroke patients should receive brain imaging with computed tomography (CT) at most within one hour of arrival at hospital (Intercollegiate Stroke Working Party 2023). The INAS also incorporates this recommendation as one of its KQIs, specifically KQI 4 (Table 1.1) (NOCA 2023c). Furthermore, the National Clinical Guideline for Stroke recommends CT angiogram from aortic arch to skull vertex should be completed for those ischaemic stroke patients who are potentially eligible for thrombectomy. CT perfusion should be utilised for those with a delayed presentation or unknown onset time who might benefit from reperfusion therapies (Intercollegiate Stroke Working Party 2023).

Table 1.1: Key Quality Indicators from the Irish National Audit of Stroke (NOCA 2023c)

KQI	KQI Definition	Target
1	The proportion of patients admitted to a stroke unit	**90%**
2	The proportion of admission spent in a stroke unit	**90%**
3	The proportion of patients with ischaemic stroke who received thrombolysis	**12%**
4	The median time between hospital arrival time and brain imaging time	**60 mins**
5	The median time between hospital arrival time and time of thrombolysis	**60 mins**
6	The rate of swallow screening	**90%**
7	The proportion of patients with swallow screen completed within 4 hours	**90%**

1.5 Acute Stroke Treatment – Ischaemic Stroke

The time-sensitive nature of acute stroke care is related to the limited window to perform reperfusion therapy in acute ischaemic stroke. Reperfusion therapy includes IVT – the intravenous administration of a medication to dissolve or break up a clot (thrombus) and EVT – an endovascular procedure performed to remove or extract a clot from a cerebral blood vessel. Patients with acute ischaemic stroke in whom treatment can be started within 4.5 hours of stroke symptom onset, should be considered for thrombolysis (Intercollegiate Stroke Working Party 2023). Additionally, by using CT perfusion to identify still salvageable brain tissue, thrombolysis can sometimes be started between 4.5 and 9 hours of symptom onset. The INAS has two KQIs targeting thrombolysis. KQI 3 indicates a target of 12% for the proportion of patients with an ischaemic stroke who receive thrombolysis. KQI 5 designates a median time from hospital arrival to thrombolysis of 60 minutes (NOCA 2023c). Internationally, a faster median time from arrival to thrombolysis of 45 minutes has been targeted in QI initiatives (Xian et al., 2022).

Thrombectomy is used for patients with ischemic stroke when a thrombus or large vessel occlusion (LVO) is identified on CT angiogram imaging. Depending upon factors such as pre-stroke function, NIHSS score and the location of occlusion, thrombectomy is indicated in ischaemic stroke patients where the procedure can begin within 6 hours of symptom onset but is even performed in some cases up to 24 hours from last known well. Advanced imaging such as CT perfusion plays an important role in deciding if patients with delayed presentations or unknown onset time are amenable to reperfusion with EVT. Two EVT stroke centres operate in Ireland – Beaumont Hospital and Cork University Hospital (NOCA 2023c). Given that most acute stroke hospitals in Ireland do not provide thrombectomy on site, transfer to the EVT stroke centre is required. In 2022, 75% of thrombectomy cases were transferred from another primary hospital to an EVT stroke centre with the remaining 25% presenting directly to an EVT centre. The time delay to transfer to an EVT stroke centre for thrombectomy varies based upon geographic location and distance from an EVT stroke centre. It further underlines the absolute requirement for rapid diagnosis and imaging in suspected acute strokes.

1.5.1 Acute Stroke Treatment – Haemorrhagic Stroke

Although management of ICH differs from ischaemic stroke, timely diagnosis is still beneficial. ICH patients can deteriorate quickly and admission to a SU helps to facilitate specialist assessment and observation. Treatment includes reversal of anticoagulants, blood pressure (BP) control, neurosurgical interventions such as external ventricular drain (Intercollegiate Stroke Working Party 2023).

1.6 Care Within the Stroke Unit

The definition of the SU is the organised care for stroke patients in hospital under a multidisciplinary team (MDT) who specialise in stroke management (SUTC 1997). A Cochrane review demonstrated significant benefits of organised SU care, specifically reduced mortality, levels of dependence and rates of institutionalisation when compared with alternative models of care for stroke patients (Langhorne et al., 2020). In the meta-analysis, receiving organised SU care equated to two more stroke patients alive, six more living at home and six more living independently for every 100 patients. The importance of the coordinated care delivered within the SU is reflected by INAS in two national KQIs (NOCA 2023c). KQI 1 sets 90% as the target for the proportion of stroke inpatients admitted to the SU. KQI 2 aims that of those stroke inpatients admitted to the SU, 90% of their total admission should be spent in the SU.

1.7 Background of In-Hospital Stroke

IHS accounts for 1% to 17% of all strokes (Intercollegiate Stroke Working Party 2023, Gu et al., 2023, Liu et al., 2022, Akbik et al., 2020, Lu et al., 2019, Emmett et al., 2019, Schürmann et al., 2016, Saltman et al., 2015, Briggs et al., 2015, Cumbler et al., 2014, Dulli and Samaniego, 2007, Kimura et al., 2006). It is recognised that the incidence of IHS is lower in large registry datasets likely owing to under-reporting of IHS (Nouh et al., 2022, Akbik et al., 2020). Within the large, multicentre registry datasets, the rate of IHS was reported as 1.1% by Gu et al. (2023), 2% by Cumber et al. (2014), 3% by Akbik et al. (2020), and 5.9% by Ben-Shabat et al. (2023). This contrasts with the higher rates of IHS reported within single centre studies – 17% by Dulli and Samaniego (2007), 17% by Liu at

el. (2022) and 9% by Schürmann et al. (2016). At a single centre level, the rate of IHS in one centre may not be easily generalisable to another centre owing to variations in specialty case-mix, patient populations and staff expertise or training (Nouh et al., 2022).

1.7.1 Age

Some studies noted IHS patients tended to be older than COS equivalents (Schürmann et al., 2016, Saltman et al., 2015, Kimura et al., 2006). Saltman et al. (2015) utilised the Ontario stroke registry to compare 973 IHS cases with 28,837 COS cases. Whilst no significant difference was noted in median age between the two groups, the proportion of patients aged greater than 65 years was higher (72%) amongst the IHS cohort compared with the COS cohort (67%; $p<.001$). Work on the South London Stroke Registry over a 10-year period from 1995 to 2015 by Emmett et al. (2019) revealed changes over time in the average age between IHS and COS cohorts. In the earliest analysis from 1995 to 2001, average age was 70.6 years and 74.2 years for COS and IHS cohorts respectively ($p<.001$). However, by the 2009 to 2015 time period, average age was not significantly different at 67.6 years and 69.8 years for COS and IHS cohorts respectively ($p=0.15$). A reason for this fall in age over time was not suggested by the authors.

1.7.2 Pre-Stroke Function

Pre-stroke disability has been shown to reliably predict poorer outcomes post stroke such as LOS, discharge destination, mortality, (de Berker et al., 2021, Garcia-Ptacek et al., 2018, Quinn et al., 2017). Evidence suggests that IHS patients tend to have greater functional disability prior to the onset of stroke when compared with COS patients (Naldi et al., 2023). Of 21, 349 IHS cases, Cumbler et al. (2015) found 83% were independently ambulating prior to stroke onset compared with 90% of COS cases ($p<.0001$). The modified Rankin Score (mRS) is frequently used in stroke populations to compare pre and post stroke levels of disability. A score of zero indicates no disability and one indicates mild disability. One single centre study demonstrated that half (56%) of IHS had a pre-stroke mRS score of zero or one compared with 81% of the COS comparator (Caparros et al., 2017). In a retrospective review of 192 IHS stroke alerts, double the proportion of the IHS cohort (15%) had an mRS score of four, indicating moderately

severe disability, compared with the COS cohort (7%; p<.001) (Chukwudelunzu et al., 2023).

1.7.3 Comorbidity

The burden of cardiovascular comorbidity such as atrial fibrillation (AF), diabetes, myocardial infarction (MI) and congestive cardiac failure (CCF) is greater amongst the IHS group than COS group (Chukwudelunzu et al., 2023, Naldi et al., 2023, Akbik et al., 2020, Saltman et al., 2015, Cumbler et al., 2014, Park et al., 2009). Some studies reported higher proportions of hyperlipidaemia amongst IHS groups (Lu et al., 2019, Saltman et al., 2015, Cumbler et al., 2014) whereas other studies demonstrated a trend towards less hyperlipidaemia amongst IHS groups (Park et al., 2009, Dulli and Samaniego, 2007, Kimura et al., 2006). Additionally, cancer, chronic kidney disease and coagulopathy are also present at greater proportions amongst IHS populations (Qiu et al., 2022, Lu et al., 2019, Saltman et al., 2015, Moradiya and Levine, 2013, Vera et al., 2011). Cancer is associated with an increased risk of stroke (Rogers, 1994, Lindvig et al., 1990, Graus et al., 1985). Stroke (ischaemic and haemorrhagic) in cancer patients can be caused by a variety of factors including direct tumour effects, hyperviscosity, coagulopathy, marantic endocarditis, as well as therapy factors be that related to procedures, radiation or chemotherapy itself (Grisold et al., 2009). The increased risk of stroke driven by hypercoagulability is evidenced by studies finding raised d-dimer levels in stroke patients with cancer and less associations with conventional vascular risk factors (Schwarzbach et al., 2012, Kim et al., 2010). Furthermore, incident cancer is more likely following the onset of the first stroke event particularly amongst younger patients (Verhoeven et al., 2023, Vaz et al., 2023) and cryptogenic strokes (Rioux et al., 2021). Verhoeven et al. (2023) demonstrated that the risk of new cancer diagnosis in a young stroke population was 3 to 5-fold higher than the general population during the first year following stroke. The rate of cryptogenic or stroke of undetermined aetiology observed is higher in cancer patients with half of strokes reported as cryptogenic subtype in two studies (Navi et al., 2014, Schwarzbach et al., 2012). Cryptogenic stroke in cancer patients is associated with increased mortality. In a study of 263 patients with ischaemic stroke and cancer, the median survival in cryptogenic stroke patients was 57 days compared with 147 days in patients with a known aetiology for their stroke (p=0.01) (Navi et al., 2014). A large

retrospective review of acute ischaemic stroke in the USA found 3.7% (n=50553) had a solid organ malignancy, most commonly lung cancer. Acute ischaemic strokes with an associated malignancy were more likely to have intraparenchymal bleeding, die in hospital and to be discharged to a destination other than home (Garg et al., 2022). This emphasises how comorbid diagnoses like cancer not only increase the risk of stroke but also have the potential to impact outcomes like mortality.

1.7.4 Reason for Hospitalisation

The most common reason for original admission to hospital amongst IHS cases is a cardiac indication. Schürmann et al. (2016) found half of IHS patients had originally been admitted to hospital due to cardiac disease whilst Vera et al. (2011) noted 40.1% of IHS patients had been admitted due to cardiac disease and cardiovascular surgery combined. In a single-centre Irish study, the diagnosis at admission coded using the International Classification of Diseases, Tenth Revision, Australian Modification (ICD-10-AM) for 88 IHS admissions was reviewed. The most common admission diagnosis coded was circulatory in one-third (35.2%) of IHS cases followed by stroke in one-quarter (23.9%) and neoplasm in one-fifth (19.3%) of cases (Chapman et al., 2023b). A registry-based Swedish review including 72 hospital sites found similar ICD-10 coding practices with the top five ICD-10 codes applied to IHS at discharge being: stroke (42%), circulatory (22%), injuries (9%), neoplasm (5%) and respiratory (4%). However, it is worth highlighting that discharge coding practices vary. In the Irish setting, the principal discharge diagnosis assigned is the diagnosis which was primarily responsible for resulting in the episode of inpatient care (HPO 2022). In Sweden the cause of admission should be coded as the main discharge diagnosis but on occasion if a condition that arises during the hospitalisation consumes more resources it may be recorded as the main diagnosis at discharge. This reflects a limitation of using coding derived information to ascertain the original presentation diagnosis for an IHS.

1.7.5 Procedures

Many cases of IHS are associated with a procedure (surgical, endovascular, or endoscopic). One case-control study found a mere 3.5% of IHS events were not related to

a surgical procedure (Nadav et al., 2002). Overall, IHS occurring following a procedure ranges from 25% to 77% depending on the time period chosen for review (Chapman et al., 2023b, Ben-Shabat et al., 2023, Cummings et al., 2022, Schürmann et al., 2016, Briggs et al., 2015, Vera et al., 2011, Park et al., 2009, Farooq et al., 2008). For instance, of 97 IHS cases reviewed by Cummings et al. (2022), 77% had a procedure during the period of hospitalisation prior to stroke onset. However, only 13% had stroke onset on the same day of procedure. Likosky et al. (2003) reported 42% of perioperative strokes occurred on the first postoperative day. A German study of IHS noted the median time between procedure and stroke onset was two days (Schürmann et al., 2016). Notably, a significant proportion (59.5%) of IHS in this study had onset of stroke symptoms in an intermediate care ward or an intensive care unit (ICU) setting. Thus, the median time of two days from procedure to stroke onset may be reflective of delays in recognition of stroke symptoms in sedated patients.

The strongest preoperative risk factor for perioperative stroke amongst 16, 184 cardiac surgery cases was a history of cerebrovascular disease (Bucerius et al., 2003). Periprocedural or perioperative stroke rates vary according to the procedure completed. Selim (2007) completed a comprehensive review of perioperative stroke reporting rates for different surgical specialty procedures: isolated valve surgery (4.8-8.8%), carotid endarterectomy (5.5-6.1%), head & neck cancer surgery (4.8%), coronary artery bypass grafting (1.4-3.8%) and general surgery (0.08-0.7%). In a large European review of IHS, the most common procedure types prior to IHS onset were cardiovascular (13.5%), minimally invasive procedures (10.5%), orthopaedic (8.1%) and endoscopic (6.5%) (Ben-Shabat et al., 2023). In a multi-centre statewide study over 6 months, 68% (n=121) of IHS had a procedure prior to the onset of stroke symptoms (Farooq et al., 2008). The most common procedures were cardiovascular (24%), vascular neurology or neurosurgery (16%) and orthopaedic (7%).

1.7.6 Location at Onset

Studies vary in the way the patient location at the time of stroke symptom onset is classified. Furthermore, the nature of specialty work at a hospital site will also influence the location at onset. As a result, the location at stroke onset reported ranges greatly and

may not be easily generalisable from one hospital to another. Overall, cardiology and cardiac surgery clinical areas feature prominently as the location at the time of stroke onset during a hospitalisation. Cardiology wards were the location at onset in 15-32% (Chapman et al., 2023b, Schürmann et al., 2016, Saltman et al., 2015, Cumbler and Simpson, 2015) of IHS cases and cardiac surgery services in 13 to 58% of IHS events (Chapman et al., 2023b, Cummings et al., 2022, Schürmann et al., 2016, Saltman et al., 2015, Cumbler and Simpson, 2015). Stroke onset does occur on general medical wards at reasonable frequencies ranging from 32 to 50% (Chapman et al., 2023b, Emmett et al., 2019, Saltman et al., 2015, Cumbler and Simpson, 2015). Emmett et al. (2019) found that 14% of IHS cases in the South London Register were in the ICU or high dependency unit (HDU) at onset. Whereas a German study reported that 60% of IHS cases were in ICU or an intermediate care ward (Schürmann et al., 2016).

Regarding the stroke onset and its timing within an admission, evidence is limited. Park et al. (2009) reviewed 111 IHS cases and reported that 60% occurred within seven days of admission to hospital. Amongst 193 cases of IHS, Liu et al. (2022) found the median time from admission to stroke onset was five days (IQR 7 days). A large registry based review of 12, 551 IHS cases in Sweden noted the median time elapsed from admission to stroke onset was 1 day with an interquartile range (IQR) of 0 to 4 days and 90% of IHS had occurred by the ninth day of hospitalisation (Ben-Shabat et al., 2023).

1.7.7 Stroke Subtype and Severity

Regarding stroke subtype, Saltman et al. (2015) demonstrated that ischaemic stroke is significantly more likely amongst the IHS cohort when compared with the COS cohort (89% versus 71%; $p<.001$). The mechanism of stroke amongst IHS cases tends to be more often cardioembolic or undetermined aetiologies with lower rates of large artery atherosclerotic stroke reported (Topiwala et al., 2020, Schürmann et al., 2016, Vera et al., 2011). Research on perioperative strokes specifically suggests that an embolic aetiology is more likely than other mechanisms such as hypoperfusion (Selim, 2007, Likosky et al., 2003).

Stroke severity measured using the NIHSS is greater amongst IHS when compared with COS events (Lu et al., 2019, Schürmann et al., 2016, Cumbler and Simpson, 2015, Cumbler et al., 2011, Kimura et al., 2006). This may be linked to the observed higher rates of cardioembolic mechanism as AF is a predictor of severe stroke in ischaemic stroke (Kimura et al., 2005). One study also found that LVO rates are higher amongst IHS cases with LVO in 80% of IHS cases compared with 51% of COS cases (p=0.001) (Schürmann et al., 2016). Rates of no occlusion on imaging were also lower amongst the IHS cohort. A higher proportion (14.2%) of posterior circulation location for arterial thrombus was observed in the IHS cohort compared with the COS cohort (9.8%) in an Italian observational study (p=0.005) (Naldi et al., 2023).

1.7.8 Mimics

Stroke mimics are clinical syndromes which are suggestive of stroke but are not actually caused by an ischaemic event (Dupre et al., 2014). In a narrative review of 79 studies examining stroke mimics, the median rate of stroke mimics found in the pre-hospital stroke group was 27% with seizures and migraine the most common underlying aetiology for the stroke mimic presentation (McClelland et al., 2019). Stroke mimics are more common in an in-hospital context. When 93 inpatient stroke alerts were compared with 204 emergency department (ED) stroke alerts, one-quarter (27%) of inpatients had an actual stroke or TIA compared to one-half (51%) of the ED stroke alert group (p<.0001) (El Husseini and Goldstein, 2015). Analysis of in-hospital stroke alert calls in different studies have revealed stroke mimic rates of 46% (Cumbler and Simpson, 2015), 48% (Chukwudelunzu et al., 2021), 63% (Del Brutto et al., 2019, El Husseini and Goldstein, 2015) and 64% (Topiwala et al., 2020).

Altered mental status as a presenting symptom was found to be a predictor for stroke mimics (El Husseini and Goldstein, 2015) and non-focal neurological deficits are more likely (Del Brutto et al., 2019) on stroke alerts amongst inpatients. The hospital environment gives rise to clinical presentations that mimic stroke for instance anaesthetic or sedation, seizures, delirium particularly hypoactive delirium. The most common diagnoses presenting as a stroke mimic amongst hospitalised inpatients include seizure,

encephalopathy due to systemic illness or infection, medication side effects, syncope and hypotension (Del Brutto et al., 2019, Cumbler and Simpson, 2015).

1.8 In-Hospital Stroke Outcomes

1.8.1 Mortality

Some studies reported mortality at designated time points following stroke, at one month (Lu et al., 2019), at 30 days (Saltman et al., 2015), at three months (Naldi et al., 2023, Caparros et al., 2017) and at 90 days (Qiu et al., 2022) but the majority reported in-hospital mortality. All studies demonstrated increased mortality amongst the IHS group compared to the COS group (Table 1.2). Of the studies that did not restrict inclusion to reperfusion stroke populations, unadjusted mortality rates reported ranged from 5.7% (Gu et al., 2023) to 31.4% (Schürmann et al., 2016) for IHS and from 1.7% (Liu et al., 2022) to 18% (Saltman et al., 2015) for COS. Unadjusted mortality rates tended to be significantly higher in studies focusing specifically on reperfusion (EVT with or without IVT) stroke populations (Akbik et al., 2020, Caparros et al., 2017, Moradiya and Levine, 2013). Across these studies unadjusted mortality ranged from 19.3% to 23.4% for IHS and 13.8% to 15.1% for COS. Other smaller (all single-centre) studies on EVT populations reported non-statistically significant increased mortality rates for IHS patients compared with COS patients (Qiu et al., 2022, Suyama et al., 2022, Sano et al., 2020, Matsubara et al., 2020, Bulwa et al., 2020b, Lu et al., 2019, Mönch et al., 2018). A meta-analysis examining patients who underwent EVT, which included four of these smaller single-centre studies, found that the pooled mortality at follow up for IHS was higher at 26.3% compared to 18.1% of COS cases with reported odds ratio (OR) of 1.65 and 95% Confidence Interval (CI) between 1.33-2.04; $p<0.01$ (Amoukhteh et al., 2024). However, issues were noted as the observed effect size was largely attributed to a single study (Naldi et al., 2023) and larger studies such as Akbik et al. (2020) were not included. The corresponding author for Amoukhteh et al. (2024) was contacted directly regarding this and replied that the authors “are currently working on writing a correction to that article to address the concerns.”

The most frequent variables included for adjustment in regression models for adjusted mortality presented in Table 1.2 were age, sex, stroke severity, and comorbidities or comorbid vascular risk factors (Gu et al., 2023, Naldi et al., 2023, Liu et al., 2022, Akbik et al., 2020, Schürmann et al., 2016, Saltman et al., 2015, Cumbler et al., 2014, Moradiya and Levine, 2013). A single study reported no difference in mortality following adjustment (Saltman et al., 2015). The highest reported adjusted OR (aOR) for mortality was 3.62 (95% CI 1.64-8.00; p=0.001) (Liu et al., 2022). This model adjusted for age, sex, hypertension, diabetes, and hyperlipidaemia. Stroke severity using the NIHSS was included by Liu et al. (2022), however, that model was not statistically significant for in-hospital mortality. Cumbler et al. (2014) noted that mortality was almost 3 times as likely for IHS patients (aOR 2.72; 95% CI 2.57-2.88; p<.001). However, when the NIHSS was included within the model, the reported aOR was 1.51 (95% CI 1.39-1.64; p<.001). There was considerable heterogeneity regarding methods of adjustment for comorbidities and vascular risk factors in regression models. Adjustment ranged from the inclusion of variable numbers and combinations of diagnoses like AF, CCF, diabetes, peripheral vascular disease to structured scoring indexes like the Elixhauser comorbidities (Moradiya and Levine, 2013).

1.8.2 Thrombolysis Rates

Rates for thrombolysis generally tended to be lower amongst the IHS cohort (Table 1.2). Of the studies reporting lower IVT rates for IHS patients, IVT rates varied from 1.6% (Liu et al., 2022) to 13.8% (Emmett et al., 2019) for IHS and from 6.0% (Park et al., 2009) to 19% (Saltman et al., 2015) for COS. When studies with inclusion criteria requiring reperfusion therapy (EVT with or without IVT) were reviewed, the reported rates of IVT obviously reflected a greater proportion of both IHS and COS cohorts. For instance, up to 67.2% of IHS and almost all (99.9%) COS patients were thrombolysed in one French single centre study reviewing stroke patients who underwent reperfusion therapy (IVT, EVT or both) (Caparros et al., 2017). However, the patients in this study may not reflect a typical IHS population as 36% of IHS patients were in the SU at stroke symptom onset and 44% were admitted to hospital with either ischaemic stroke or TIA. The rate of IVT prior to EVT still tended to be lower amongst IHS when compared to COS patients in many studies on reperfusion populations (Matsubara et al., 2020, Bulwa et al., 2020a, Sano et al., 2020,

Mönch et al., 2018) with one small case-control trial of strokes that underwent EVT demonstrating a significantly lower rate of IVT amongst IHS patients (13.9%) versus 43.1% of COS patients in the control group (Qiu et al., 2022). A multi-centre Italian cohort study of patients who received EVT reported lower IVT rates prior to EVT for the IHS cohort (Naldi et al., 2023). A meta-analysis focusing on the EVT subgroup yielded a pooled rate of IVT prior to thrombectomy of 15.8% for IHS (Amoukhteh et al., 2024). IHS were less likely to receive IVT prior to thrombectomy when compared with COS cases with a reported OR of 0.26 (95% CI 0.18-0.38; p<0.01). This meta-analysis included Naldi et al. (2023) and other smaller single centre studies (Qiu et al., 2022, Suyama et al., 2022, Bulwa et al., 2020a, Matsubara et al., 2020, Sano et al., 2020, Lu et al., 2019, Mönch et al., 2018) but as mentioned did not include the larger registry-based publication by Akbik et al. (2020) which compared IHS and COS cohorts in an EVT subgroup analysis of n=43,130 cases.

Three large, multi-centre (greater than 1000 hospital sites) studies utilising national stroke registry data reported a higher rate of IVT for IHS patients at 15.3% (Gu et al., 2023), 15.5% (Akbik et al., 2020), and 11.0% (Cumbler et al., 2014) respectively. The IVT rates for the COS group were 8.0%, 9.9% and 6.6% respectively. As discussed previously the epidemiology of IHS reveals variances in the rates of IHS between single and multi-centre studies. The rate of IHS reported in single centre studies tends to be higher than multi-centre studies possibly due to under-reporting of IHS cases in registry data (Nouh et al., 2022). From this literature review, it appears that the rate of IVT reported for IHS tends to be higher in studies using large registry data and lower in single centre studies. Only Akbik et al. (2020) provide a possible reason to account for this finding. It is possible the reporting is biased in data capture within large datasets towards those who received reperfusion interventions. An IHS event is more likely to be recorded if an intervention like IVT or EVT has occurred as these outcomes are usually collected as mandatory structured data within registry datasets. An IHS event without IVT and EVT may be less likely to be reported as the stroke event may be superseded by other acute clinical issues relating to the primary admission. Interestingly, on subgroup analysis of all stroke patients who received EVT, Akbik et al. (2020) found that IHS patients indeed had significantly lower rates of IVT prior to thrombectomy at 25.8% compared with 45.6% of COS (p<.001).

Lower IVT rates amongst IHS patients are attributed to the presence of contraindications to thrombolysis. These contraindications may be driven by or linked to the original reasons for being admitted to hospital including recent surgical procedures, anticoagulation and active bleeding (Liu et al., 2022, Schürmann et al., 2016, Saltman et al., 2015, Vera et al., 2011). Liu et al. (2022) noted that half of IHS cases could not get thrombolysis due to contraindications and a further one-third had exceeded the time window. Another study highlighted the issue of time-window exceedance as over half (58.2%) of IHS patients could not be thrombolysed for this reason (Vera et al., 2011). The greater frequency of contraindications to IVT amongst IHS patients is of concern as thrombolysis is a crucial therapeutic intervention to restore cerebral perfusion. Even amongst patients with LVO, thrombolysis is still considered an important bridging therapy prior to thrombectomy (Turc et al., 2022).

1.8.3 Thrombectomy Rates

The published research clearly demonstrates that thrombectomy rates are higher amongst the IHS cohort when compared with COS equivalents (Table 1.2). Rates for EVT varied from the lowest reported at 3.7% (Akbik et al., 2020) to 10.4% (Liu et al., 2022) amongst the IHS cohort and 1.3% (Gu et al., 2023) to 4.2% (Lu et al., 2019) for the COS group. Two studies included only thrombolysed strokes and the proportion of IHS patients who proceeded to EVT after thrombolysis was still significantly higher than the COS cohort (Caparros et al., 2017, Moradiya and Levine, 2013). Only one study's results on EVT rates differed (Chukwudelunzu et al., 2023). In this single centre study, the outcome for EVT was transfer for consideration of EVT rather than completed EVT which contrasts with the other studies reviewed. Reasons for the higher rate of thrombectomy amongst IHS cases include greater occurrence of LVO which is the primary indication and target for EVT. Contraindications to thrombolysis within an IHS population do not preclude EVT intervention and may further underline its value as a feasible therapeutic intervention in this stroke population.

Rates of symptomatic ICH following thrombolysis or thrombectomy do not appear to vary between IHS and COS groups (Amoukhteh et al., 2024, Suyama et al., 2022, Qiu et al., 2022, Akbik et al., 2020, Matsubara et al., 2020, Lu et al., 2019, Mönch et al., 2018,

Caparros et al., 2017, Schürmann et al., 2016, Cumbler et al., 2014, Moradiya and Levine, 2013). This is of particular importance as the higher mortality for IHS reported in these studies is not due to symptomatic ICH following reperfusion therapy. This highlights the importance of timely diagnosis and therapeutic interventions for this vulnerable stroke subgroup.

1.8.4 Length-of-stay

IHS patients had longer LOS when compared to COS patients (Fluck et al., 2022, Schürmann et al., 2016, Saltman et al., 2015, Park et al., 2009, Farooq et al., 2008). Studies reported the total hospital LOS for IHS cases rather than the LOS since the onset of the stroke event. This will lead to an increased likelihood of longer LOS reported for IHS cohorts when compared with COS. Reported median total hospital stay [IQR] for IHS versus COS group were as follows: 6 days [4-11] versus 4 days [3-6] ($p<0.0001$) (Cumbler et al., 2014), 17 days [10-31] versus 8 days [4-15.5] ($p<.001$) (Saltman et al., 2015) and 8 days [5-14] versus 4 days [3-7] (Farooq et al., 2008).

1.8.5 Post Stroke Disability and Discharge Destination

IHS patients demonstrate greater disability following stroke when compared to COS counterparts (Table 1.2) (Naldi et al., 2023, Fluck et al., 2022, Liu et al., 2022, Akbik et al., 2020, Lu et al., 2019, Mönch et al., 2018, Caparros et al., 2017, Schürmann et al., 2016, Saltman et al., 2015, Cumbler et al., 2014, Farooq et al., 2008). Even when studies adjusted for stroke severity, poorer functional outcomes were still observed (Naldi et al., 2023, Akbik et al., 2020, Caparros et al., 2017, Saltman et al., 2015, Cumbler et al., 2014). Furthermore, in the large Italian registry-based study poorer functional outcome post stroke was maintained even when patients with pre-stroke disability (mRS score greater than 2) were excluded from analysis (Naldi et al., 2023). Poorer functional outcomes are still demonstrated in studies which specifically focused on evidence-based reperfusion interventions. As discussed EVT rates are higher amongst the IHS population but findings from thrombectomy subgroup analysis still do not yield improvement on post stroke functional scores. Therefore, the poorer functional outcome experienced by IHS cannot be attributed solely to pre-stroke function, stroke severity or access to reperfusion

therapy. Time delays in the pathway of stroke processes have been suggested as a potential contributor and typically IHS cases' progress through stroke pathways is slower. However, IHS cases still demonstrate a benefit over COS as they are in hospital at onset of stroke symptoms and pre-hospital delays are not a factor affecting access to imaging and interventions. Naldi et al. (2023) demonstrated this by evaluating the median time from stroke symptom onset to the end of EVT intervention. Even though IHS cases had slower progress through process-based times to imaging and to puncture at EVT, the overall time elapsed from stroke symptom onset to EVT completion was 293 minutes for COS and only 227 minutes for IHS cases. This suggests that poorer functional outcomes may not be fully related to time delays in process-based care. It is reasonable to assume that the burden of preexisting comorbidities and possibly the original reason for admission which are adjusted for in disparate ways across the studies may exert a confounding effect on post-stroke functional outcomes.

Not surprisingly, the proportion of IHS patients discharged home following stroke is lower than COS counterparts. When statistically significant rates were reviewed, discharge to home following stroke occurs from 21.1% to 40.2% of IHS cases and from 27.0% to 63.4% of COS cases (Table 1.2). Higher rates of admission to long term care (LTC) have been reported amongst the IHS cohort (Chapman et al., 2023b, Fluck et al., 2022, Emmett et al., 2019).

Table 1.2: Summary of Charateristics and Outcomes of Reviewed Studies

Author	Study Description	n	NIHSS	IVT	EVT	Mortality	Discharge Destination/Disability
(Akbik et al., 2020)	Multi-centre (n=1355 site) retrospective cohort study comparing IVT and EVT cohorts for IHS and COS using national stroke registry in the USA From 2008 to 2018	IHS: 67,493 COS: 2,170,250 IHS Rate: 3.0%	Median [IQR] IVT group: 8 [4-15] EVT group: 16 [10-21]	**Higher IVT rate for IHS** IHS: 15.5%; COS: 9.9% (Cumbler et al., 2014)	**Higher EVT rate for IHS** IHS: 3.7%; COS: 1.9% Lower rate of IVT before EVT amongst IHS IHS: 25.8%; COS: 45.6% (p<.001)	**Higher in-hospital mortality for IHS** **IVT group:** IHS: 7.9%; COS: 5.9% IHS aOR 1.39; 95% CI [1.29-1.50] (p <.001) **EVT group:** IHS: 20.4%; COS: 13.9% IHS aOR 1.58; 95% CI [1.43-1.75] (p<.001)	**IHS less likely to be discharged home** IVT group: IHS: 40.2%; COS: 47.1%; aOR 0.69 (p<.001) EVT group: IHS: 21.1%; COS: 27.0%; aOR 0.68 (p<.001) **IHS less likely to ambulate independently at discharge** IVT Group: IHS: 45.1%; COS: 48.8%; aOR 0.69 (p<.001) EVT group: IHS: 26.9%; COS: 31.1%; aOR 0.77 (p<.001)
(Assuncao et al., 2021)	Single centre retrospective cohort study comparing stroke alerts in the ED and in-hospital setting in the USA From Jan 2020 to Dec 2020	IHS: 65 (7 haemorrhagic) COS: 92 (13 haemorrhagic)	-	NS lower IVT rate for IHS IHS: 8.6% (5 of 58 ischaemic stroke alerts) COS: 12.7% (10 of 79 ischaemic stroke alerts)	NS higher EVT rate for IHS IHS: 5.2% (n=3); COS: 1.3% (n=1)	-	-
(Bulwa et al., 2020a)[a]	Single centre case-control study comparing IHS:COS in 1:2 ratio who received EVT in the USA From Sep 2012 to Dec 2018	IHS: 14 COS: 28	Median [IQR] IHS: 15 [8-19] COS: 15 [11-18] (p=0.90)	NS lower IVT rate prior to EVT for IHS IHS: 21%; COS: 46% (p=0.18)	-	NS difference in in-hospital mortality IHS: 7%; COS: 11% (p=1.00)	NS difference in proportion discharged home/to rehabilitation IHS: 79%; COS: 61% (p=0.31)

(Caparros et al., 2017)[a]	Single centre retrospective review comparing IHS and COS who received reperfusion therapy (IVT/EVT/or both) in France From Sep 2003 to Sep 2016	IHS: 64 COS: 1,145	Median [IQR] IHS: 12 [6-18.75] COS: 11 [6-17]	Within this study analysing reperfusion therapies, **IVT rate lower amongst IHS** IHS: 67.2%; COS: 99.9% (p<.001)	Within this study analysing reperfusion therapies, **EVT rate was higher for IHS** IHS: 45.3%; COS: 10.4% (p<.001)	**IHS more likely to have died at 3 months post stroke** IHS: 23.4%; COS: 15.1%; aOR 1.34 (95% CI 0.47-3.82)	**IHS less likely to have mRS score of 0-2 at 3 months post stroke** IHS: 40.6%; COS: 57.4%; aOR 0.87 (95% CI 0.35-2.16)
(Chukwudelunzu et al., 2023)	Single centre retrospective case:control study comparing IHS & COS from hospital stroke alert activations in the USA From Jan 2013 to Dec 2019	IHS: 192 COS: 370	Median [IQR] IHS: 7 [2.5-14] COS: 5 [2-12] (p=0.20)	**Lower IVT rate for IHS** IHS: 8.0%; COS: 33.7% (p<.0001)	**Lower rate of transfers for EVT for IHS** IHS: 3.4%; COS: 11.6% (p=.03)	**Higher in-hospital mortality for IHS** IHS: 19.3%; COS: 7.4% (p=0.003)	**IHS less likely to discharge home** IHS: 28.1%; COS: 51.1% (p<.0001)
(Cumbler et al., 2011)	Multi-centre (n=16 sites) retrospective cohort study comparing IHS & COS using statewide registry in the USA From Aug 2005 to Apr 2009	IHS: 116 COS: 4,946 IHS Rate: 2.3%	Mean [SD] IHS: 9.5 [7.3] COS: 7.0 [7.4] (p=0.01)	NS for IVT IHS: 9.7%; COS: 11.7% (p=0.54)	-	-	-
(Cumbler et al., 2014)	Multi-centre (n=1280 sites) retrospective cohort study comparing IHS & COS using national registry data in the USA From Apr 2003 to Apr 2012	IHS: 21,349 COS: 928,885 2.2%	Median [IQR] IHS: 9 [4-17] COS: 4 [2-11] (p<.0001)	**Higher IVT rate for IHS** IHS: 11%; COS 6.6%	-	**Higher in-hospital mortality for IHS** IHS: 13.9%; COS 5.0% (p<.0001) aOR 2.72 (p<.001) aOR 1.51 [1.39-1.64] (NIHSS included) (p<.001)	**IHS less likely to ambulate independently at discharge** IHS: 31.0%; COS 50.4%; aOR 0.42 (p<.0001) **IHS less likely to discharge home** IHS: 27.7%; COS: 49.9% (p<.0001) aOR 0.37 (p<.001)
(Dulli and Samaniego, 2007)	Single centre retrospective cohort study comparing IHS & COS in the USA From Jan 1996 to Oct 2002	IHS: 161 COS: 786 IHS Rate: 17.0%	-	NS difference in IVT IHS: 3.7%; COS: 5.6% (p=0.44)	-	**Higher in-hospital mortality for IHS** IHS: 14.9%; COS: 6.4% (p=0.001)	-

(Emmett et al., 2019)	Multi-centre cohort study using the South London Stroke Register data in the UK comparing IHS & COS cohorts stratified into 3 time intervals (1995–2001; 2002–2008; 2009–2015) From Jan 1995 to Dec 2015	IHS: 552 COS: 4,567 IHS Rate: 10.8%	% NIHSS >16: *2002-2008*: IHS: 44.2%; COS: 27.0% *2006-2015* IHS: 27.1% COS: 17.7%	**Lower IVT rate for IHS** *2002-2008:* IHS: 5.1%; COS: 10.0% *2006-2015* IHS: 13.8% COS: 17.8%	-	**Higher in-hospital mortality for IHS** *1995–2001:* IHS: 56.9%; COS: 34.1% *2002–2008:* IHS: 44.3%; COS: 19.7% *2009–2015*: IHS: 26.7%; COS: 13.7%	**IHS more likely to require nursing care at discharge** *1995–2001*: IHS: 26.4%; COS: 13.5% *2002–2008:* IHS: 30.1; COS: 10.4% *2009–2015:* IHS: 17.4%; COS: 6.2%
(Farooq et al., 2008)	Multi-centre (n=15) prospective study comparing IHS & COS cohorts in the USA From May 2002 to Nov 2002	IHS: 177 COS: 2,566 IHS Rate: 6.5%	-	NS higher weighted IVT rate for IHS IHS: 8.6%; COS: 2.6% (p=0.28)	-	**Increased case fatality rate for IHS** IHS: 14.6%; COS: 6.9% (p=0.04)	**Higher rate of mRS score 4 or more at discharge for IHS** IHS: 61%; COS:36% (p<.001) **IHS less likely to discharge home** IHS: 23%; COS: 52% (p<.01)
(Fluck et al., 2022)	Multi-centre (n=4 sites) retrospective cohort study comparing IHS & COS in the UK From Jan 2014 to Feb 2016	IHS: 272 COS: 3,037 IHS Rate: 8.2%	% NIHSS >16: IHS: 7.0% COS: 6.8% (p=0.93)	**Lower IVT rate for IHS** IHS: 8.8%; COS: 17.1% (p=0.001)	-	**Higher in-hospital mortality for IHS** IHS: 26.6%; COS: 13.6% (p<.001)	**IHS more likely to have mRS score of 4 or above post stroke** IHS: 45.6% COS: 28.5% (p<.001) **IHS more likely to be require nursing home care** IHS: 10.7%; COS 4.9% (p<0.001)
(Gu et al., 2023)	Multi-centre (n=1476 sites) retrospective cohort study comparing IHS & COS using national registry data in China From Aug 2015 to Dec 2022	IHS: 14,948 COS: 1,366,898 IHS Rate: 1.1%	Median [IQR] IHS: 4 [2-9] COS: 3 [2-6]	**Higher IVT rate for IHS** IHS: 15.3%; COS: 8.0%	**Higher EVT rate for IHS** IHS: 4.2%; COS: 1.3%	**Higher mortality for IHS** IHS: 5.7%; COS: 2.5%; aOR 1.51 95% CI [1.40-1.62] *EVT Subgroup:* IHS: 12.2%; COS: 7.1%; aOR 1.44 95% CI [1.30-1.58]	No significant difference in disability at discharge IHS: 41.1%; COS: 33.1%; aOR 0.99 95% CI [0.88-1.11]
(Kimura et al., 2006)	Multi-centre (n=156 sites) prospective cohort study	IHS: 694 COS: 15, 121	Median [IQR] IHS: 13	-	-	**Higher in-hospital mortality for IHS**	**of mRS score 0-2 amongst IHS**

	comparing IHS & COS using registry data in Japan From May 1999 to April 2000	IHS Rate: 4.4%	COS: 5 (p<.0001)			IHS: 19.2%; COS: 6.8% (p<.0001)	IHS: 28.5%; COS: 59.9% (p<.001)
(Liu et al., 2022)	Single centre retrospective review comparing IHS & COS in China From Jun 2012 to Jan 2022	IHS:193 COS: 969 IHS Rate: 16.6%	Median [IQR] IHS: 5 [8] COS: 4 [6] (p=0.05)	**Lower IVT rate for IHS** IHS: 1.6%; COS: 7.2% (p=0.003)	**Higher EVT rate for IHS** IHS: 10.4%; COS: 2.0% (p<.001)	**Higher in-hospital mortality for IHS** IHS: 6.2%; COS: 1.7% (p<.001) aOR 3.62; 95% CI [1.64-8.00] (p=0.001)	**Lower rate of mRS score 0-2 amongst IHS** IHS: 51%; COS: 61% (p=0.006) aOR 0.67 0; 95% CI [49-0.93] (p=0.02)
(Lu et al., 2019)	Single centre retrospective review comparing IHS & COS in Taiwan. Subgroup analysis of EVT population conducted on IHS (n=24) & COS (n=105). From Jan 2015 to Dec 2017	IHS: 336 COS: 2,477 IHS Rate: 11.9%	Median [IQR] IHS: 15 [6-25] COS: 4 [2-10] (p=0.01)	**Lower IVT rate for IHS** IHS: 3.6%; COS: 7.3% (p=0.01)	**Higher EVT rate for IHS** IHS: 7.1%; COS: 4.2% (p=0.01)	**Higher mortality at 1-month for IHS** IHS: 28.3%; COS: 4.5% (p=0.01) *EVT Only Group:* NS difference in mortality at 1-month for IHS IHS: 16.7%; COS: 12% (p=0.58)	**Higher median [IQR] mRS at 3 months amongst IHS** IHS: 5 [3-6]; COS: 2 [1-4] (p=0.01)
(Matsubara et al., 2020)[a]	Single centre retrospective cohort study comparing IHS and COS who received EVT (including patients with IHS transferred from another hospital) in Japan From Jan 2016 to May 2019	Other hospital IHS: 8 Own hospital IHS: 17 COS: 18	Mean [SD]: Other IHS: 14.4 [6.6] Own IHS: 12.8 [4.3] COS: 14.9 [5.3]	Other hospital IHS: 25% (n=2) Own hospital IHS: 12% (n=2) COS: 22% (n=4)	-	NS difference between the groups in terms of mRS score 5-6 at discharge Other IHS: 25% Own IHS: 29% COS: 22%	NS difference between the groups in terms of mRS score 0-2 at discharge Other IHS: 12%; Own IHS: 30%; COS: 23%
(Mönch et al., 2018)[a]	Single centre case-control study comparing IHS:COS in 1:2 ratio who received EVT in Germany From Jan 2010 to Dec 2017	IHS: 27 COS: 54	Median [min; max]: IHS: 18 [6;26] COS: 16 [6;36] (p=0.89)	NS lower IVT rate prior to EVT for IHS IHS: 22%; COS: 38% (p=0.096)	-	NS higher in-hospital mortality for IHS IHS: 19%; COS: 13% (p=0.75)	**IHS less likely to be independent (mRS 2 or less) at discharge** IHS: 7%; COS: 33% (p=0.03)

(Moradiya and Levine, 2013)[a]	Multi-centre (n=~1000 sites) retrospective cohort study comparing IHS and COS who received IVT using national registry from the Nationwide Inpatient Sample in USA From 2005 to 2010	IHS: 1,020 COS: 10,730	-	-	Within this study analysing thrombolysed strokes, **higher EVT rate for IHS** IHS: 30.5%; COS: 18.8%	**Higher inpatient mortality for IHS** *Total Study Group:* IHS: 15.7%; COS: 9.6% (p<.001); aOR: 1.59 95% CI [1.32-1.92] (p<.001) *IVT Only:* IHS: 14.1%; COS: 8.6% (p<.001) *EVT+IVT:* IHS: 19.3%; COS: 13.8% (p=0.01)	**IHS less likely to discharge home** IHS: 22.8%; COS: 30.0% (p<.001) aOR: 0.79 95% CI [0.67-0.93] (p=0.005)
(Naldi et al., 2023)	Multi-centre (n=61 sites) retrospective cohort study comparing IHS and COS who received EVT using national registry data in Italy From Jan 2015 to Dec 2019	IHS: 406 COS: 5,213	Median [IQR] IHS: 17 [11-20.5] COS: 16 [11-20] (NS)	**Lower rate for IVT prior to EVT for IHS** IHS: 15.2%; COS: 51.1% (p<.001)	-	**Higher mortality at 3-months for IHS** (unadjusted) IHS: 30.1%; COS: 19.6% (p<.001) aOR 1.77; 95% CI [1.33-2.35] (P<.001)	**IHS less likely to score mRS 0-2 at 3-months** IHS: 39%; COS: 48.5% (p<.001)
(Park et al., 2009)	Single centre retrospective review comparing IHS & COS in Korea From Jan 2002 to Dec 2006	IHS: 111 COS: 1,907 IHS Rate: 5.8%	-	**Lower IVT rate for IHS** IHS: 2.7%; COS: 6.0%	-	**Higher in-hospital mortality for IHS** IHS: 19%; COS: 2% (p<.001)	-
(Qiu et al., 2022)[a]	Single centre retrospective case-control study comparing IHS:COS in 1:2 ratio who received EVT in China From Jan 2015 to Jul 2019	IHS: 36 COS: 72	Mean [SD] IHS: 16.9 [7.5] COS: 18 [8.4] (p=0.48)	**Lower IVT rate prior to EVT for IHS** IHS: 13.9%; COS: 43.1% (p=0.002)	-	Higher all cause mortality at 90 days for IHS IHS: 25.0%; COS: 20.8% (p=0.62)	NS in mRS score of 0-2 at 90 days IHS: 30.6%; COS: 41.7% (p=0.26)

(Saltman et al., 2015)	Multi-centre (n=11 sites) retrospective cohort study comparing IHS & COS using regional stroke registry data in Canada From Jul 2003 to Mar 2012	IHS:973 COS: 28,837 IHS Rate: 3.3%	-	**Lower IVT rate for IHS** IHS: 12%; COS: 19% (p<.001)	-	**Higher mortality at 30 days for IHS** (unadjusted) IHS: 22%; COS: 18% (p<.001) **No difference in adjusted mortality at 30 days**: aOR 0.89; 95% CI [0.74-1.07]	**IHS more likely to be dead or disabled (mRS score 3-5) at discharge** IHS: 77%; COS 65%; (p<.001) aOR 1.64 95% CI [1.38-1.96] **IHS less likely to discharge home** IHS: 35%; COS: 44%; (p<.001) aOR 0.76; 95% CI: [0.64-0.90]
(Sano et al., 2020)[a]	Single centre retrospective cohort study comparing IHS & COS who received EVT in Japan From Sep 2015 to Jun 2018	IHS: 19 COS: 154	Median [IQR] IHS: 21 [16-23] COS: 21 [14-26] (p=0.92)	NS lower IVT rate for IHS IHS: 26%; COS: 49% (p=0.07)	-	NS higher 90-day mortality for IHS IHS: 15.8%; COS: 12.3% (p=0.67)	NS in mRS score of 0-2 at 90 days IHS: 36.8%; COS: 35.1% (p=0.88)
(Schürmann et al., 2016)	Single centre retrospective review comparing IHS & COS in Germany From Jan 2010 to Dec 2014	IHS: 331 COS: 3,175 IHS Rate: 9.4%	Median [IQR] IHS: 15.5 [7.3-21] COS: 10 [5-18] (p=0.005)	**Lower IVT rate for IHS** IHS: 4.5%; COS: 16.3% (p<.001)	**Higher EVT rate for IHS** IHS: 9.4%; COS: 3.1%	**Higher in-hospital mortality for IHS** IHS: 31.4% ; COS: 8.0% (p<.001); aOR 3.11 95% CI [1.09-8.88] (p=0.03)	**Higher median [IQR] mRS at discharge amongst IHS** IHS: 4 [4-5.8]; COS: 3 [2-5] (p=0.02) **IHS less likely to discharge home** IHS: 29.6%; COS: 63.4% (p<.001)
(Suyama et al., 2022)[a]	Sinlge centre retrospective cohort study comparing IHS and COS who received EVT in Japan From Jan 2017 to Dec 2019	IHS: 17 COS:87	Median [IQR] IHS: 12 [7-18] COS: 20 [14-25] (p=0.06)	**Lower IVT rate prior to EVT for IHS** IHS: 11.8%; COS: 50.6% (p<.01)	-	NS difference in mortality IHS: 23.5%; COS: 14.9% (p=0.47)	NS difference in median mRS score at discharge IHS: 4 [2-5]; COS: 4 [2-5] (p=0.55)

[a] Studies with inclusion criteria based upon reperfusion therapy (IVT or EVT) being administered. Standard Deviation (SD); Not Statistically Significant (NS)

1.9 In-Hospital Stroke Quality-of-Care Measures

1.9.1 Time-based Intervals in Acute Stroke

Time to imaging and to reperfusion therapy (time to needle for IVT and time to puncture for EVT) evaluate hospital processes on the clinical stroke care pathway. The targets which are outlined in Section 1.4.2 aim for imaging within 60 minutes and thrombolysis within 60 minutes of hospital arrival. These time-based performance measures are traditionally based upon COS populations. COS cases' time interval starts from hospital arrival time. However, IHS cases are already admitted to hospital at the time of stroke onset so the hospital arrival time is rendered redundant as it predates stroke onset. In order to assess IHS cases' performance on time-based process measures, the time interval starts at the time of symptom onset or recognition of the stroke symptoms within the hospital setting (Figure 1.2). Some studies directly compare IHS and COS cohorts using the interval from stroke symptom onset to imaging and to intervention for both groups. For COS cases, this interval includes the pre-hospital time and disproportionately favors IHS cases to perform better on time-based quality-of-care measures. This may lead to the perception that less improvement is needed for the IHS cohort on time-based markers of quality-of-care in the clinical stroke pathway. Given that IHS patients first experience their stroke symptoms in a hospital setting, they should in theory be able to access the stroke pathway without any delay and avail of timely diagnosis to identify those who can obtain evidence-based reperfusion therapy. Studies which compared COS and IHS directly using stroke symptom onset time are highlighted in Table 1.3. In the analysis of reperfusion subgroups, the time elapsed from symptom onset to IVT or EVT is useful as it indicates the overall ischaemic time experienced by comparably treated stroke patients. This may provide insights into variances observed on functional and mortality outcomes as highlighted previously in Section 1.8.5.

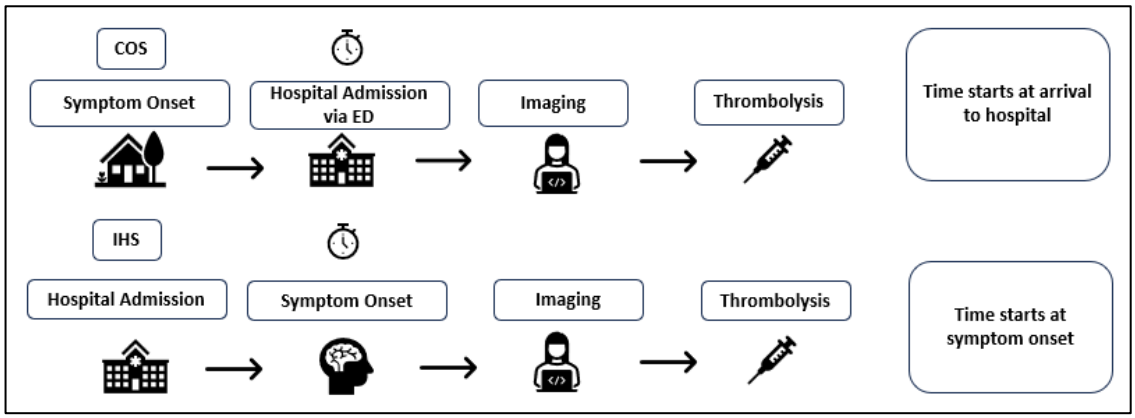

Figure 1.2: Visual Representation of Differences in Time-based Intervals between IHS and COS Cohorts

The reliance on symptom onset for time-based intervals in IHS cases does create data quality issues. The INAS report for 2022 highlighted the variability in recording of symptom onset date and time ranging from 35% to 68% at its highest (NOCA 2023c). It was recommended that every effort should be made to document the symptom onset variable. On the contrary, hospital arrival time for COS cases was recorded in 100% of cases. The date and time of symptom onset is not only important for IHS cases as it is used to identify pre-hospital delays for COS cases which can be reduced using public health campaigns on stroke recognition. Missing data reported by Akibik et al. (2020) show that poor data quality impacts IHS to a greater extent than COS cohorts. In the IVT subgroup, data for the variable of time from stroke presentation to imaging was missing in 22.4% of IHS cases. The comparable variable for the COS cohort of time from hospital arrival to imaging was missing in only 2.4%. Similarly, the proportion of missing data for the same variables in the EVT cohort analysis were 15.6% for IHS and 1.9% for the COS cohort.

1.9.2 Time to Stroke Recognition

It would be assumed that recognition of stroke symptoms would be rapid in a hospital context, however, evidence suggests significant delays in stroke identification occur (Nouh et al., 2022). Up to one-third of IHS patients had delayed recognition of stroke symptom onset in one study (Schürmann et al., 2016) and almost one-third (31.6%) IHS events were unwitnessed in another (Vera et al., 2011). Certain aspects of the hospital environment complicate the detection of stroke symptoms. These include co-existent

diagnoses such as delirium, the postoperative effects of sedation and anaesthesia, reduced consciousness when intubated as well as out-of-hours (Saltman et al., 2015)presentations (Cummings et al., 2022, Mello et al., 2019, Schürmann et al., 2016). A retrospective chart review of 97 IHS cases in a hospital with a dedicated in-hospital stroke protocol reported delays in stroke symptom recognition and stroke team review. The median time from last seen well to stroke team alert generation was 11.4 hours (IQR 2.7-34.2 hours) (Cummings et al 2022). The major time interval contributing to this delay was the time elapsed from last seen well to stroke symptom recognition (Median 5.1 hours; IQR 1.0-19.7 hours). This highlights a degree of ambiguity that exists for time-based intervals for IHS cases when discussing the difference between stroke onset time and stroke recognition time. In some cases of IHS, the stroke onset time may be the same as the recognition time. In other cases, there may be a lag between stroke onset and stroke recognition where a patient may notice the onset of a stroke symptom but it is not recognised by a healthcare professional until a later time point. In other cases, the stroke onset time remains unknown such as wake-up stroke events and the time of stroke recognition is the first available time point.

1.9.3 Time to Imaging

The majority of studies reported that COS cases were imaged sooner than IHS cases (Table 1.3). One study which reported a significantly faster time to imaging (Qiu et al., 2022), utilised symptom onset time for the time-based interval to imaging for both cohorts conferring an advantage to IHS cases. Median times to imaging ranged from 32 minutes (Sano et al., 2020) to 270 minutes (Saltman et al., 2015) for the IHS cohort. The COS cohort's median time to imaging ranged from 11 minutes (Sano et al., 2020) to 72 minutes (Saltman et al., 2015).

1.9.4 Time to Reperfusion

Times to IVT and EVT were generally faster amongst the COS compared to the IHS group (Table 1.3). Two studies reported faster median time to EVT for the IHS cohort with one of the studies utilising symptom onset for both cohorts (Caparros et al., 2017). The other study included a very small sample (IHS: n=6; COS: n=38) and the data presented were

sourced from an online supplement (Lu et al., 2019). Median times to IVT ranged from 69 minutes (Sano et al., 2020) to 120 minutes (Saltman et al., 2015) for IHS cases and from 30 minutes (Sano et al., 2020) to 76 minutes for COS cases. The median times to EVT ranged from 87 minutes (Sano et al., 2020) to 165 minutes (Akbik et al., 2020) for IHS and from 50 minutes (Sano et al., 2020) to 119 minutes (Lu et al., 2019) for the COS studies.

1.9.5 Location & Time-based Intervals

Quality-of-care time-based intervals for IHS can vary according to the clinical location at the onset of stroke symptoms. Saltman et al. (2015) showed that the median time from symptom onset to imaging for an IHS event was shortest when onset occurred in the angiography suite (114 minutes), longest on the cardiac surgery ward (426 minutes) and intermediate on medical wards (186 minutes). The rates of thrombolysis mirrored this finding as clinical areas with longer median times to imaging had lower thrombolysis rates. IVT rates were 28%, 16% and 3% in the angiography suite, medical ward and cardiac surgery wards respectively. In a study comparing 138 IHS events which occurred in the SU and 214 IHS events occuring at any other in-hospital location, IHS events in the SU had faster median times to imaging and thrombectomy (Marto et al., 2022). The influence of the SU location on time-based intervals was also highlighted by Caparros et al. (2017). The median time from onset to IVT differed significantly by location - 64 minutes in the SU, 111 minutes in ED and other clinical areas 138 minutes ($p<.001$). The IHS population of Caparros et al. (2017) was discussed previously as one-third (36%) of the IHS patients were admitted in the SU at stroke symptom onset. This is important as it was one of the few studies to report faster times to EVT for IHS cases compared to COS cases and this finding could be influenced by the clinical location of the IHS population at stroke onset.

Table 1.3: Summary of Time-based Results for Reviewed Studies

Author	Details on Time Intervals	Time to Imaging Median [IQR]	Time to IVT/EVT Median [IQR]
(Akbik et al., 2020)	Time from "presentation" equated to stroke onset recognition for IHS and time of arrival to the ED for COS. Variables used were from presentation to cranial imaging, to IVT bolus and to EVT	**Slower time to imaging for IHS in both IVT and EVT subgroups** *IVT subgroup:* IHS: 33 mins [18-60]; COS: 16 mins [9-26] (p<.001) *EVT group:* IHS: 38 mins [22-69]; COS: 15 mins [9-26] (p<.001)	**Slower time to IVT and EVT for IHS** *Time to IVT*: IHS: 81 mins [52-125]; COS: 60 mins [45-84] (p<.001) *Time to EVT:* IHS: 165 mins [113-245]; COS: 138 mins [96-202] (p<.001)
(Assuncao et al., 2021) [b]	Time-based interval used was from the activation of hospital stroke alert to imaging and to IVT. Times are reported as mean time [95% CI].	**Slower time to imaging for IHS** IHS: 24.99 mins [18.9-31.9] COS: 9.01 mins [5.74-12.3] (p=0.04)	Non statistically significant slower time to IVT for IHS IHS: 100.66 mins [93.7-108] COS: 61.75 mins [54.8-68.7] (p=0.17)
(Bulwa et al., 2020a)	Time-based interval used is from activation of hospital stroke alert to EVT.	-	Non statistically significant slower time to EVT for IHS IHS: 160 mins [77-215]; COS: 146 mins [113-195] (p=0.66)
(Caparros et al., 2017) [a c]	Time-based intervals in the main text start from symptom onset for both IHS & COS favouring the finding of faster times in the IHS.	-	**Faster time to IVT in IHS who also received EVT** IHS: 128 mins [68.75-145]; COS: 145 mins [115-186] (p<.001) **Faster time to IVT in IHS who received IVT only** IHS: 130 mins [78-145]; COS: 145 mins [115-188] (p=0.002)
(Chukwudelunzu et al., 2023)	Time-based intervals started at hospital arrival time for COS and symptom recognition for IHS.	**Slower time to imaging for IHS** IHS: 41 mins [26-67]; COS: 12 mins [8-19] (p=0.001)	Non statistically significant slower time to IVT for IHS IHS: 96 mins [34-149]; COS: 55 mins [44.5-67.5] (p=0.22)
(Cumbler et al., 2011)	Time from recognition of symptoms by hospital staff to brain imaging	Non statistically significant slower time to imaging for IHS IHS: 54 mins; COS: 43 mins (p=0.13)	-
(Cumbler et al., 2014)	From time of symptom recognition time for IHS and time of admission for COS to IVT	-	**Slower time to IVT for IHS** IHS: 100 mins; COS: 76 mins (p<.0001)
(Lu et al., 2019) [a]	Time-based intervals in the main text start from symptom onset for both IHS & COS. However, the online supplement provides intervals from assessment to imaging and assessment to puncture which provides a comparable starting time for IHS & COS. However, negative value noted for IQR for IHS cohort from assessment to imaging suggesting data quality issues.	**Slower time from assessment to imaging for IHS** IHS: 32 mins [-30-55]; COS 56 mins [37-70] (p=0.01)	**Faster time from assessment to EVT for IHS** IHS: 92 mins [42-115]; COS: 119 mins [96-153] (p=0.01)

(Matsubara et al., 2020) [a] [b]	Intervals presented start from both symptom recognition and from hospital arrival thus allowing real-world comparison between IHS & COS cohort. Reported p values are not presented as statistical comparison was performed on time-based intervals that don't facilitate direct comparison i.e. from symptom onset for IHS and COS. Query regarding calculations provided as the time from symptom recognition to recanalisation should equal the time from symptom recognition to puncture time + time from puncture to recanalisation time.	-	Slower time to EVT for IHS *Mean [SD] time from stroke recognition (IHS) or hospital arrival (COS) to EVT* Other Hospital IHS: 212 mins [74] Own Hospital IHS: 166 mins [80] COS: 155 mins [76]
(Mönch et al., 2018) [a] [c]	Time-based intervals in the main text start from symptom onset for both IHS & COS favouring the finding of faster times in the IHS.	Non statistically significant slower time to imaging for IHS IHS: 107 mins [21]; COS: 206 mins [47] (p=0.07)	Non statistically significant faster time to EVT for IHS IHS: 177 mins [106] COS: 232 mins [98] (p=0.18)
(Naldi et al., 2023) [a]	Time-based intervals from symptom onset for both IHS & COS and from arrival time for COS are provided. Time intervals presented are from symptom onset for IHS and from arrival time "door" for COS.	**Slower time to imaging for IHS** IHS: 60 mins [33.7-106]; COS: 29 mins [20-44] (p<.001)	**Slower time to EVT for IHS** IHS: 150 mins [105-220]; COS: 113 mins [84-151] (p<.001) -Onset to the end of EVT for COS: 293 [230-370] -Onset to end of EVT for IHS: 227 [164.5-303.5]
(Qiu et al., 2022) [a] [b] [c]	Time-based intervals in the main text start from symptom onset for both IHS & COS favouring the finding of faster times in the IHS.	**Faster time to imaging for IHS** IHS: 113.9 mins [73.7]; COS: 251.4 mins [191.1]; (p<.001)	Non statistically significant faster time to EVT for IHS IHS: 186.1 mins [86.1]; COS: 198.8 mins [88.5]; (p=0.62)
(Saltman et al., 2015)	Stroke presentation defined as symptom recognition for IHS and ED arrival for COS. Variables reported are from presentation to neuroimaging and to thrombolysis time (Door-to-needle time)	**Slower time to imaging for IHS** IHS: 4.5 hrs [1.5-17.3]; COS 1.2 hrs [0.5-3.0] (p<.001)	**Slower time to IVT for IHS** IHS: 2 hrs [1.4-2.7]; COS 1.2 hrs [0.9-1.6] (p<.001)
(Sano et al., 2020)	Time-based interval starts from stroke detection for IHS and from hospital arrival time "door" for COS	**Slower time to imaging for IHS** IHS: 32 mins [13-41] COS: 11 mins [7-14] (p<.01)	**Slower time to IVT for IHS** IHS: 69 mins [57-93] COS: 30 mins [24-40] (p<.01) **Slower time to EVT for IHS** IHS: 87 mins [60-146] COS: 50 mins [40-68] (p<.01)
(Schürmann et al., 2016)[a]	Time-based intervals *in-table* start from symptom onset for both IHS & COS. However, the times presented here are *in-text* results providing intervals to imaging, to IVT and to angiography for EVT from symptom onset for IHS and from arrival to clinic for COS.	**Slower time to imaging for IHS** IHS: 73.3 mins; COS: 30.9 mins (p<.001)	**Slower time to IVT and EVT for IHS** *Time to IVT:* IHS: 84.9 mins; COS: 37.9 mins (p<.001) *Time to EVT:* IHS: 124.2 mins; COS: 91.8 mins (p=0.008)

	It is assumed times presented *in-text* are median times as the IHS times presented *in-table* are median; IQR; SD		
(Suyama et al., 2022)	Time-based interval used was from arrival time to hospital "door" for COS and stroke recognition time for IHS.	**Slower time to imaging for IHS** IHS: 36 mins; COS: 14 mins (p<0.01)	Non statistically significant slower time to IVT for IHS *Time to IVT:* IHS: 119 mins; COS: 63 mins (p=0.23) **Slower time to EVT for IHS** *Time to EVT:* IHS: 135 mins; COS: 117 mins (p=0.02) Of note, no difference in time from CT to EVT for IHS or COS. Additional delays to EVT for IHS occured between stroke recognition and imaging. *Time from CT to EVT:* IHS: 104 mins; COS: 104 mins (p=0.47)

[a] Details of time intervals presented in section titled "Details on Time Intervals" [b] Mean rather median was reported as measure of central tendency [c] Time-based intervals in the main text start from symptom onset for both IHS & COS. This favours the finding of faster times in the IHS group due to the time between symptom onset in the community to hospital arrival being included for COS cases whereas IHS cases are in hospital already at symptom onset.

1.9.6 Admission to the Stroke Unit

IHS patients are less likely to be admitted to the SU than COS patients (Fluck et al., 2022, Emmett et al., 2019, Briggs et al., 2015, Saltman et al., 2015) Competing medical interests during their hospitalisation, for instance, the requirement for care in specialised clinical areas such as ICU, HDU and the coronary care unit (CCU) contribute to lower SU admission rates (Chapman et al., 2023b). Consequently, swallow screening rates are lower amongst the IHS cohort (Gu et al., 2023, Fluck et al., 2022, Emmett et al., 2019, Saltman et al., 2015, Cumbler et al., 2014). An Australian observational study is the first to analyse the outcomes amongst IHS patients admitted to the SU compared to those admitted on other wards (Cadilhac et al., 2019). IHS patients admitted to the SU have lower in-hospital mortality 13% versus 26% of IHS patients admitted on other wards ($p<.001$). After adjusting for age, sex, stroke severity and stroke type, IHS patients managed in the SU were less likely to die at 7 days (Hazards Ratio 0.47; 95% CI [0.28-0.77]; $p=0.003$) and 30 days (Hazards Ratio 0.56; 95% CI [0.39-0.81]; $p=0.002$). These results could be influenced by the type of IHS patient who is more likely to get admitted to the SU. IHS patients that are too unstable to be admitted to the SU may be more likely to die whether due to the stroke itself or perhaps more likely, due to the original reason for admission to hospital. IHS patients with admission to the SU were statistically more likely to receive aspirin within 48 hours of stroke, antithrombotic therapy at discharge, swallow screening and thrombolysis (14% versus 6%) than IHS equivalents admitted on other wards. Some authors now suggest that lower SU admission rates amongst the IHS group could be contributing to the poorer functional outcomes observed compared to COS patients (Akbik et al., 2020).

Some studies included other markers of quality-of-care such as post stroke investigations and risk factor modifications. Dedicated angiogram imaging of head and neck vessels were less likely amongst IHS patients (Gu et al., 2023, Chukwudelunzu et al., 2023). Statin therapy were less likely to be initiated amongst IHS patients (Chukwudelunzu et al., 2023, Cumbler et al., 2014) Interestingly, Saltman et al. (2015) found IHS patients were more likely to be prescribed antithrombotic therapy at discharge and another study found anticoagulant prescribing for AF was better at discharge amongst IHS patients (Gu et al., 2023).

1.10 Summary of Literature Review

The rate of IHS varies between 1% and 17%. Higher rates of IHS are reported in single-centre studies compared with large registry datasets. IHS have a greater degree of pre-stroke functional impairment. A cardiac aeitology is the most common reason for admission to hospital for IHS cases (Chapman et al., 2023b, Schürmann et al., 2016, Vera et al., 2011). Procedures are associated with IHS in 25% to 77% of events, with cardiac procedures featuring as the most common procedure (Ben-Shabat et al., 2023, Farooq et al., 2008). IHS events tend to occur early in the course of hospital admission. For example, one study reported the median time from admission to stroke onset was one day with 90% of IHS events having occurred by the ninth day (Ben-Shabat et al., 2023). Strokes in an IHS context tend to be more severe and one study found higher rates of LVO (Schürmann et al., 2016). The hospital environment adds further complexity to inpatient stroke alerts as stroke mimic rates are higher when compared with COS population presenting as a stroke alert to the ED. This higher rate of stroke mimics is due to factors like delirium, post-operative anaesthetic or sedation and alternative aetiologies such as seizure, encephalopathy, syncope, hypotension.

Outcomes for IHS patients are poorer when compared with COS counterparts. Mortality is higher and post-stroke disability is greater. LOS is longer and rates of discharge to home are lower. Thrombolysis rates tended to be lower except in three large registry-based datasets which reported higher IVT rates amongst the IHS cohort (Akbik et al., 2020) (Gu et al., 2023, Cumbler et al., 2014). Rates of thrombectomy are higher amongst IHS cases and EVT reflects a critical reperfusion therapy in a cohort of patients with greater contraindications to thrombolysis. Contraindications to thrombolysis and time delays due to poor recognition or slow progress through acute stroke clinical pathways have been cited as possible reasons for lower thrombolysis rates. Overall, mortality rates and post-stroke disability are higher amongst the IHS cohorts, even when adjusted for age, severity and pre-stroke disability. Poor functional outcomes persist even amongst those IHS populations who are treated promptly and receive reperfusion therapies. Thus, poorer functional outcomes are possibly driven by combiditites or the original reason prompting hospital admission.

Review of IHS cases' performance on quality-of-care measures reveals that IHS cases generally are slower to receive brain imaging, thrombolysis and thrombectomy in spite of being in a hospital at the time of stroke symptom onset. Research suggests that location at the time of stroke onset may impact these time-based quality-of-care measures. IHS occur in varied locations across a hospital which poses a challenge to design a clear protocolised pathway for acute stroke care for IHS. Admissions to the SU are also lower amongst the IHS cohort in spite of the demonstrated mortality benefit of care being managed in the SU for this stroke subgroup (Cadilhac et al., 2019).

1.11 Thesis Layout

Informed by the literature review presented here, a single-site retrospective review of IHS at St. James's Hospital was performed to provide knowledge at an institutional level prior to work at a national level. This work is detailed in Chapter 2. The later chapters of this thesis are then devoted to the review of IHS nationally in Ireland. The chapters include the methodology (Chapter 3), analysis in terms of demographics (Chapter 4), quality-of-care measures (Chapter 5), and outcomes (Chapter 6). Discussion of results is included within Chapters 7 and 8 respectively. The final conclusions and recommendations from this research are presented in Chapter 9.

Chapter 2. Single Centre Review of In-Hospital Stroke in St. James's Hospital

2.1 Introduction

As explored in Chapter 1, IHS represents a distinct stroke cohort when compared with the COS group in terms of demographics, outcomes, and performance on process-based stroke pathways. It was hypothesised that dedicated analysis of the IHS subgroup at an institutional level could gather information on demographics and outcomes for IHS patients as well as identify areas for improvement in the clinical stroke pathway. Additionally, the INAS register identifies IHS cases using two linked data sources – via the Hospital Inpatient Enquiry (HIPE) system which assigns stroke diagnoses by HIPE coders at discharge and/or via local stroke audit coordinators who work clinically in stroke teams and input additional stroke specific clinical data. This data definition has never been previously validated, so a clinical validation study was also conducted to assess the accuracy of the IHS definition within INAS. It was hypothesised that the clinical difficulties and nuances of diagnosing IHS as well as the use of two data sources for its definition may impact the quality and accuracy of the definition of IHS.

2.2 Aim

To compare IHS and COS cases at St. James's Hospital in terms of demographics, outcomes and performance on quality and process-based stroke measures and to clinically validate the current definition of IHS within INAS.

2.3 Objectives

The main objectives were:

a) To conduct a single-site retrospective cohort study comparing IHS and COS groups using stroke data collected annually for the national stroke registry, the INAS.
b) To conduct a clinical validation study of the diagnostic accuracy of IHS identification in the stroke data collected at a large teaching hospital. This also ensured accuracy in the cases selected for the IHS cohort.

2.4 Methods

2.4.1 Study Design & Setting

A retrospective clinical validation of IHS diagnoses was completed for a 2-year period from January 1st 2020 to December 31st 2021 in a large urban teaching hospital. This clinical validation study informed a retrospective cohort study comparing IHS and COS cases. The hospital is a 900-bed teaching hospital which is a referral centre for cardiothoracic, cardiology, haematology, and oncology specialities. The annual number of stroke discharges is approximately 250-300 cases. Clinical validation was used as the gold standard to determine the level of agreement between HIPE and audit coordinator IHS cases.

2.4.2 HIPE Data

HIPE is a national, standardised, computer-based system designed to collect demographic, clinical and administrative data on hospital discharges in Ireland (HPO 2022). It utilises the ICD-10-AM classification to assign coded diagnoses to each episode of inpatient care. HIPE data is collected by trained administrative staff who review inpatient records following discharge. The ICD-10-AM coded stroke diagnoses which are included annually for the INAS are: nontraumatic intracerebral haemorrhage (I61), cerebral infarction (I63) and stroke, not specified as haemorrhage or infarction (I64). Importantly, SAH (I60), retinal artery occlusion (H34) and TIA (G45) are not reported in INAS (NOCA 2023a).

HIPE defines the *principal* diagnosis as the diagnosis which is chiefly responsible for resulting in the episode of inpatient care, whilst an *additional* diagnosis is any non-principal diagnoses coded for an episode of care (up to a maximum of 29 diagnoses). IHS cases are defined during the HIPE coding process by assigning a *hospital acquired diagnosis* (HADx) flag to any coded additional (non-principal) diagnosis. A HADx is one that arises during the course of an episode of care and was not present at admission (HPO 2022).

2.4.3 Local Audit Coordinators

The INAS audit coordinators are typically specialist nurses working as part of stroke teams at a hospital site. These coordinators record further clinical stroke data in structured data entry fields within the HIPE stroke audit portal. The question “Did the stroke occur while the patient was in hospital for treatment of another condition?” allows local audit coordinators to indicate if the stroke was an IHS event. This field has been mandatory for completion since 2020.

2.4.4 Current Definition of IHS

The INAS defines IHS as any stroke case that the local audit coordinator has indicated was an IHS event during stroke audit data entry and/or an additional stroke (I61, I63, I64) diagnosis with an HADx flag assigned during HIPE coding. A COS case was one with a principal diagnosis of stroke (I61, I63, I64), no further additional stroke diagnosis recorded, and the audit coordinator indicated it was not an IHS event.

2.4.5 Inclusion Criteria for Validation

Cases for validation were identified using a HIPE-generated list of stroke audit records from this period that were reported to the INAS. Inclusion criteria for validation were a) the local audit coordinator indicated an IHS event during audit data input and/or b) the principal diagnosis coded by HIPE was not a stroke diagnosis (suggesting stroke was not the primary reason for that hospital admission).

2.4.6 Exclusion Criteria for Validation

Cases were not clinically validated if there was a principal diagnosis of stroke (I61, I63, I64), no further additional stroke diagnosis recorded, and where the local audit coordinator indicated it was not an IHS event. The assumption was that these cases were highly likely to reflect COS events.

2.4.7 Clinical Validation

Clinical validation was completed by three researchers – the author, D.B. and J.H. D.B and J.H. are stroke consultants. Clinical validation was completed independently, and cases were randomly assigned to each researcher in a ratio of 2:1:1 for LC:JH:DB. Complex cases (n=26) where the researcher could not come to a final validation conclusion were discussed at a consensus meeting with all three researchers to finalise the case definition. In all other instances, cases were validated on a single researcher's review. The clinical validation process reviewed radiology imaging, radiology reports, and multidisciplinary documentation from the hospital electronic patient record (EPR). Each case was validated in a 2-step process using a checklist proforma under structured headings (Table 2.1).

Table 2.1: Components of Two-Step Clinical Validation

Description of documented stroke symptoms
Imaging modality used - Magnetic Resonance Imaging (MRI) Brain or CT Brain
Description of imaging findings
Presence of symptom-imaging correlation
Categorisation of stroke by AHA criteria
Presence of haemorrhagic transformation (If ischaemic subtype)
In-hospital stroke event (Step 2) – Were stroke symptoms present at admission

The first step of validation used the AHA stroke definition to verify the diagnosis of stroke. Further exclusion criteria were applied following this to eliminate cases that were not stroke, e.g., mimics, duplicate entries, subdural or traumatic bleeds. At this point, cases consistent with TIA, SAH and retinal artery occlusion were also excluded as these cases are not reported by INAS (Figure 2.1).

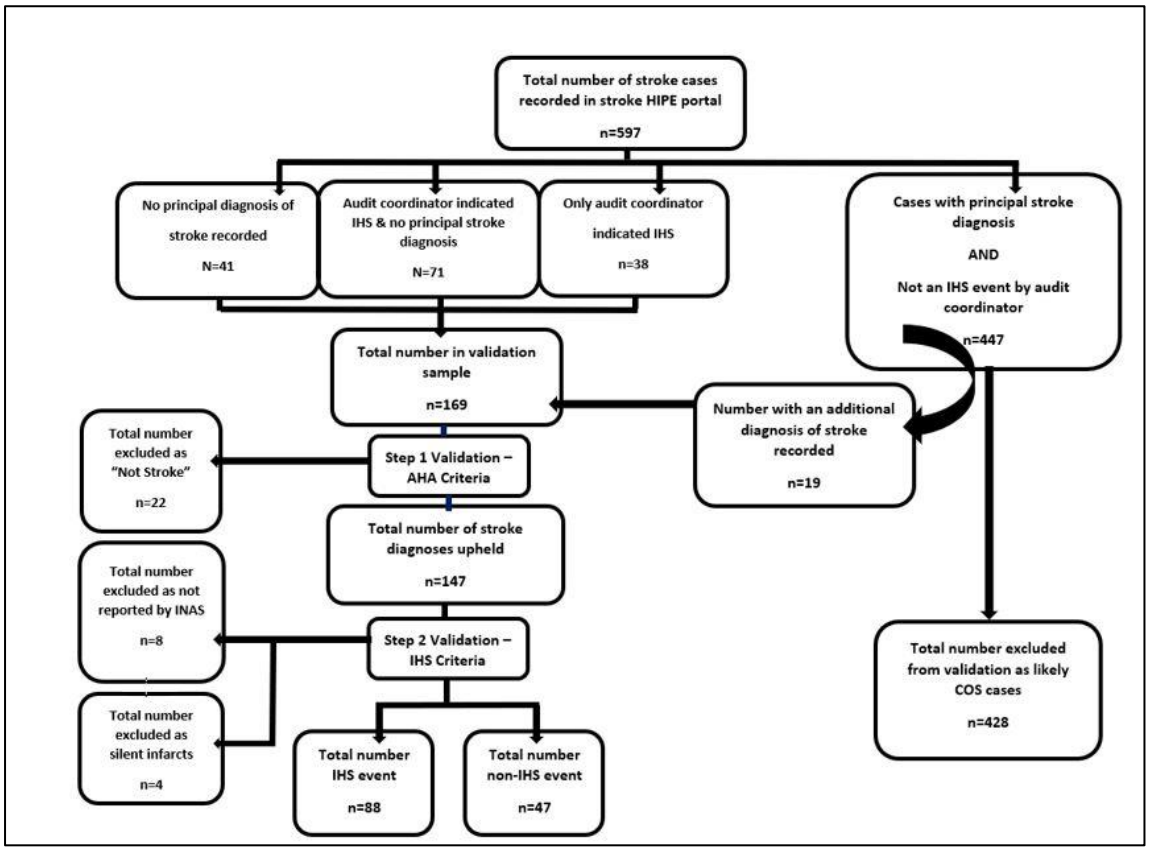

Figure 2.1: Flowchart of Clinical Validation Methods and Excluded Cases (n=34)

The second step of validation considered whether the stroke case reflected an IHS event. To be considered an IHS event, stroke symptoms must not be present at admission and had to develop during the inpatient episode of care.

2.4.8 Cohort Study Variables

Patient characteristics sourced from HIPE included age, sex, admission source, pre and post stroke functional status using the mRS, specialty responsible for care, duration of critical care bed (ICU, HDU or CCU) stay, COVID-19 diagnosis during admission and principal coded diagnosis. Further data was collected for the IHS cohort alone from the EPR. This included NIHSS at stroke onset, emergency stroke code activation (termed a "FAST Call") at stroke onset, symptoms at recognition, procedures during inpatient stay and comorbid active cancer diagnoses.

The clinical data collected by audit coordinators for INAS focuses on quality-of-care and outcome measures required for national reporting on identified KQIs. All variables

collected for the INAS by HIPE (n=35), and audit coordinators (n=17) are published (NOCA 2023c, NOCA 2023a, NOCA 2022a) and available in Appendix 1. The primary outcome measures reported in this cohort study are in-hospital mortality, thrombolysis and thrombectomy rates, discharge destination, LOS, and ambulatory status at discharge using the mRS. The primary quality-of-care outcomes reported are SU admission, swallow assessment and allied health professional (AHP) review. Time-based quality-of-care measures reported include time to medical assessment, time to imaging and time to thrombolysis (if applicable). The initial date and time used for the time-based intervals differs between the cohorts owing to the different locations at the time of stroke symptom onset as previously discussed in Chapter 1, Section 1.9.1. For COS cases, date and time of arrival to hospital is used whereas for IHS cases, date and time of stroke symptom onset is used. For the purposes of reporting results, the term, "recognition time" refers to the arrival to hospital for COS cases and stroke symptom onset for the IHS cases.

2.4.9 Statistical Analysis

The diagnosis obtained through clinical validation was considered the gold standard and was used to assess the performance of IHS diagnosis by the audit coordinator and by the HADx flag HIPE process. Standard definitions of sensitivity and specificity as well as an unweighted Cohen's kappa were calculated to assess the accuracy of IHS diagnosis. Percentages for sensitivity and specificity are presented with exact binomial 95% CI. For the cohort study, descriptive proportions were calculated for each cohort. Comparisons between IHS and COS cohorts for categorical variables was completed using Chi Square analysis. Median times with IQR are reported for time-based quality-of-care measures. Continuous variables were compared using Mann-Whitney U Test. Statistical significance was reported as p value <0.05. International Business Machines (IBM) Statistical Package for the Social Sciences (SPSS) Version 27 was used for statistical analysis.

2.5 Results of Clinical Validation Study

2.5.1 Validated Stroke Cases

There were 597 cases in the HIPE generated stroke audit report during the two-year period. The median age of the population was 72 years with 55% (n =326) of strokes occurring in males. In total, 169 cases (28%) met the research validation criteria (Figure 2.1). Seven cases had a blank field for IHS by the local audit coordinator. To address these blank data fields, the local audit coordinator performed a retrospective completion. These seven cases were automatically included into validation. In the first step of validation, the diagnosis of stroke was upheld against AHA criteria in 87% (n=147) of these cases. The median age of the 147 cases validated as stroke was 74 years. An ischaemic subtype accounted for 86% (n=127) of strokes. The majority (71%) of validated cases had MRI and CT brain imaging performed with the remainder CT alone. Symptoms correlated with imaging findings in 78% (n=115) of cases.

Cases judged not to be stroke by AHA criteria (n=22) were excluded, including TIA cases (n=5). A further eight cases were excluded as they had diagnoses not reported by INAS - SAH (n=6) and retinal artery occlusion (n=2). Four stroke cases could not be categorised as IHS or COS by the researchers (Step 2 of validation). These four cases were all silent CNS infarctions by the AHA stroke definition and had brain MRI demonstrating acute infarction. Given the absence of clinical neurological deficits, the timing of this infarction relative to their admission to hospital was impossible to define. At the time, the WHO stroke definition was routinely used in the hospital.

2.5.2 Validated IHS Cases

Clinical validation revealed that 88 cases were consistent with an IHS event. An IHS diagnosis was specified by the audit coordinator in 86% (n=76) of cases (Figure 2.2). HIPE coding using the HADx flag identified 55% (n=48) cases.

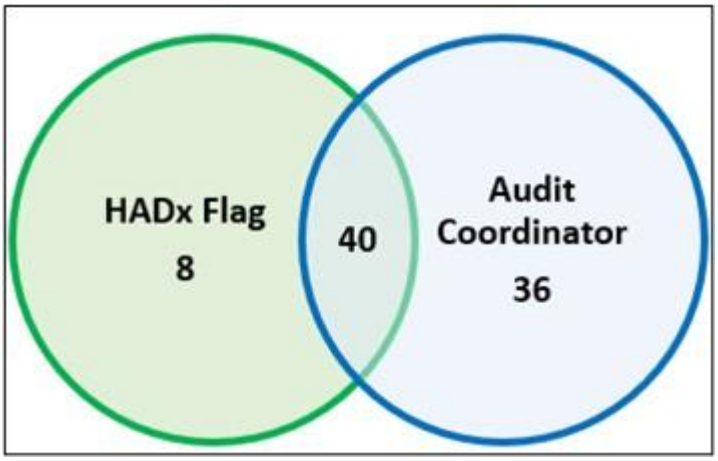

Figure 2.2: Venn Diagram of IHS Case (n=88) Identification by HIPE & Audit Coordinator

The data entry permutations (scenarios) for validated cases with the corresponding validation outcome (Stroke, IHS, Excluded) are summarised in Table 2.2. Almost half (n=40) of IHS cases were identified by both the audit coordinator and HIPE coding using the HADx flag (Scenario 4). Cases correctly identified as IHS from both data sources were more often undergoing a procedure (65% versus 41%; p=0.03), had a primary cardiac reason for admission (50% versus 27%, p=0.03) and were more likely to have been in a critical care bed during admission (65% versus 41%; p=0.03), when compared with cases that were identified as an IHS event by either the audit coordinator or HIPE coding. A further 20% (n=18) of IHS was identified by the audit coordinator with HIPE coding assigning a principal stroke diagnosis (Scenario 10). As evidenced by Scenario 3, 17% (n=15) of IHS identified by the audit coordinator had an additional stroke diagnosis coded with no associated HADx flag.

Table 2.2: Data Entry Permutations & Outcomes for Validation Sample (n=169)

Scenario	Principal Diagnosis of Stroke	Additional Diagnosis of Stroke	Additional Diagnosis & HADx Flag	Audit Coordinator IHS event	Total (n)	Stroke Cases (n)	IHS Cases (n)	Excluded Cases (n)
1.	No	Yes	No	No	**12**	**10**	**3**	**2**
2.	No	Yes	Yes	No	**11**	**9**	**7**	**2**
3.	No	Yes	No	Yes	**21**	**19**	**15**	**2**
4.	No	Yes	Yes	Yes	**42**	**40**	**40**	**2**
5.	No	No	No	Yes	**5**	**2**	**2**	**3**
6.	No	No	No	No	**21**	**9**	**0**	**12**
7.	Yes	Yes	No	No	**16**	**15**	**0**	**1**
8.	Yes	Yes	Yes	No	**1**	**1**	**1**	**0**
9.	Yes	Yes	No	Yes	**1**	**1**	**1**	**0**
10.	Yes	No	No	Yes	**32**	**28**	**18**	**4**
11.	Yes	No	No	No	**7**	**1**	**1**	**6**
Total					**169**	**135**	**88**	**34**

2.5.3 Level of Agreement for IHS Cases

Sensitivity and specificity calculations for IHS diagnosis by audit coordinator and HIPE coding process are shown in Table 2.3. The local audit coordinator identified IHS events with greater sensitivity (86% versus 55%). However, HIPE coding was highly specific at diagnosing IHS cases at 96% (95% CI 85% to 99%) versus 70% (95% CI 55%-83%). Both audit coordinator and HIPE diagnostic processes demonstrated only moderate diagnostic agreement κ=0.57 and κ =0.42 respectively when compared with the clinical gold standard. However, when both data sources were combined, the level of agreement improved to substantial (κ =0.65; p <.001). Combining the data sources also resulted in improved sensitivity to 95% (95% CI 89% to 99%).

Of the IHS cases, 93% (n=82) had an ischaemic subtype confirmed during AHA stroke criteria validation. As local audit coordinators do not record data on stroke subtype, only HIPE coding could be compared against the gold standard in analysis of stroke subtype. The sensitivity of the HIPE process to accurately code an ischaemic (I63) subtype for IHS was 93% (95% CI 85% to 97%) with 83% specificity (95% CI 34% to 96%). The degree of agreement demonstrated by κ was moderate 0.55 (p<.001). Haemorrhagic subtype HIPE

coding was highly specific (98%) and displayed a substantial level of agreement (κ=0.64) with the gold standard.

Table 2.3: Sensitivity, Specificity, κ Calculations for IHS Cases (n=88)

Variables	Sensitivity, % (95% CI)	Specificity, % (95% CI)	Cohen's Kappa K [a]
IHS Diagnosis Audit Coordinator	86 (77-93)	70 (55-83)	0.57 (p<.001)
IHS Diagnosis HIPE Coding HADx Flag	55 (44 to 65)	96 (85-99)	0.42 (p<.001)
IHS Diagnosis Combined Coordinator & HADx Flag	95 (89-99)	66 (51-79)	0.65 (p<.001)
Ischaemic Subtype Diagnosis	93 (85-97)	83 (34-96)	0.55 (p<.001)
Haemorrhagic Subtype Diagnosis	67 (22-96)	98 (91-99)	0.64 (p<.001)

[a] **κ** interpreted as follows: 0.41-0.60 Moderate agreement; 0.61–0.80 substantial agreement; 0.81–1.00 almost perfect agreement.

2.6 Results of Retrospective Cohort Study

2.6.1 Demographics and Characteristics

The median age of patients with IHS was 73 years compared to 72 years for COS cases. The cohorts were evenly matched in terms of age (Table 2.4) with similar proportions aged over 65 years, 67.0% of the IHS cohort and 65.7% of the COS cohort. During the 2-year period, 88 IHS cases occurred yielding an IHS rate of 15.6%. Ischaemic stroke accounted for a greater proportion of the IHS cohort compared with the COS cohort (93.2% versus 85.7%; p=0.06). The vast majority (97.9%) of COS were admitted to hospital from home compared with only 77.3% (n=68) of IHS events. COS patients were more likely to have no pre-stroke disability recorded when compared with IHS patients (47.2% versus 29.5%, p=0.006). Over half (52.3%; n=46) of IHS patients were admitted to a critical care bed during their hospital admission compared with a minority of COS (5.3%; p=<.0001). Co-diagnosis with COVID-19 was more common amongst IHS than COS (9.1% versus 1.3%, p=0.0003).

Of those that experienced IHS, the principal diagnosis by ICD-10-AM coding was circulatory (35.2%; n=31), followed by stroke (I61, I63, I64 codes) (23.9%; n=21), neoplasm (19.3%; n=17), and respiratory (5.7%; n=5). EPR review revealed that approximately one quarter (26.1%; n=23) had an active oncology diagnosis during the admission. The median NIHSS score was nine and was recorded in just over half (n=46) of IHS cases. The date and time of symptom onset was not recorded in 28.4% (n=25) of IHS cases and 42.0% (n=37) occurred during on-call hours. Approximately half (52.3%; n=46) of IHS events had an emergency code activation (“FAST Call”) alert. The most common symptom documented at onset was limb weakness (48.9%) followed by confusion or delirium (19.3%) and aphasia (12.5%). A doctor recognised stroke symptoms most frequently (40%), followed by a nurse (33%). At symptom-onset, the most common service caring for IHS cases was general medicine (39.8%; n=35), followed by cardiology (20.5%; n=18) and cardiothoracic surgery (19.3%; n=17). One quarter (n=22) of IHS patients had undergone a procedure in the 24 hours preceding stroke symptom onset.

Table 2.4: Characteristics of IHS (n=88) and COS (n=475) Cohorts

Characteristic	N (%)	N (%)	Statistic	P value
	IHS (n=88)	COS (n=475)		
Age				
Median (IQR), years	73 (63-81)	72 (62-81)	-0.03[a]	.98
> 65 years	59 (67.0)	312 (65.7)	0.06	.81
> 80 years	26 (29.5)	149 (31.3)	0.12	.73
Female	43 (48.9)	211 (44.4)	0.59	.44
Stroke Subtype				
Ischaemic	82 (93.2)	407 (85.7)	3.66	.06
Haemorrhagic	6 (6.8)	68 (14.3)		
Pre-Stroke disability (modified Rankin Scale)				
0 (None)	26 (29.5)	224 (47.2)	7.52	**.006**
1 & 2 (Mild)	49 (55.7)	193 (40.6)	9.51	**.002**
3, 4 & 5 (Mod-Severe)	7 (8.0)	49 (10.3)	0.3	.58
Unknown	6 (6.8)	9 (1.9)		**.02[b]**
Critical care admission	46 (52.3)	25 (5.3)	148.88	**<.0001**
Co-diagnosis COVID-19	8 (9.1)	6 (1.3)		**.0004[b]**

P values <.05 are shown in bold. [a] Mann Whitney U test calculation used. [b] Fisher exact probability test calculation used.

2.6.2 Outcome Variables

The proportion of IHS patients with ischaemic stroke receiving thrombolysis was less than the COS cohort at 7.3% (n=6) and 12.0% (n=49) respectively (Table 2.5). A greater proportion of IHS patients underwent thrombectomy (9.8% versus 6.6% of COS), however neither thrombolysis nor thrombectomy rates reached statistical significance (p=0.22 and p=0.32) respectively. The reported in-hospital mortality was higher amongst IHS cases at 12.5% (n=11) compared with 7.6% (n=36) of the COS cohort.

Table 2.5: Outcomes Reported by Stroke Cohort, (IHS n=88, COS n=475)

Outcome	**n (%)**	**n (%)**	**Statistic**	**P value**
	IHS (n=88)	COS (n=475)		
IHS Rate	88 (15.6)			
Thrombolysis [b]	6 (7.3)	49 (12.0)	1.52	.22
Thrombectomy [b]	8 (9.8)	27 (6.6)	1.00	.32
In Hospital Mortality	11 (12.5)	36 (7.6)	2.35	.13
mRS </= 2 at discharge	37 (42.0)	294 (61.9)	10.24	**.001**
Discharge destination: Home Nursing home	 45 (51.1) 6 (6.8)	 303 (63.8) 11 (2.3)	 5.04	 **.02** **.04**[a]
LOS Median (IQR), d	23 (10-54)	5 (3-9)	-10.14	**<.001**
Antithrombotic therapy [b]	57 (69.5)	327 (80.3)	2.79	.09
Atrial fibrillation	26 (29.5)	101 (21.2)	3.35	.07
With AF and on anticoagulation	22 (84.6)	71 (70.3)	3.03	.08

P values <.05 are shown in bold. [a] Fisher exact probability test calculation used. [b] Ischaemic subtype only used for analysis (IHS n=82; COS n=407).

Figure 2.3 depicts the better functional outcomes post stroke for COS cases with 61.9% (n=294) scoring mRS 0-2 at discharge compared with only 42.0% (n=37) of the IHS group. Similarly, the median (IQR) mRS at discharge for IHS and COS cohorts were 3 (2-4) and 2 (1-3) respectively (p=0.001).

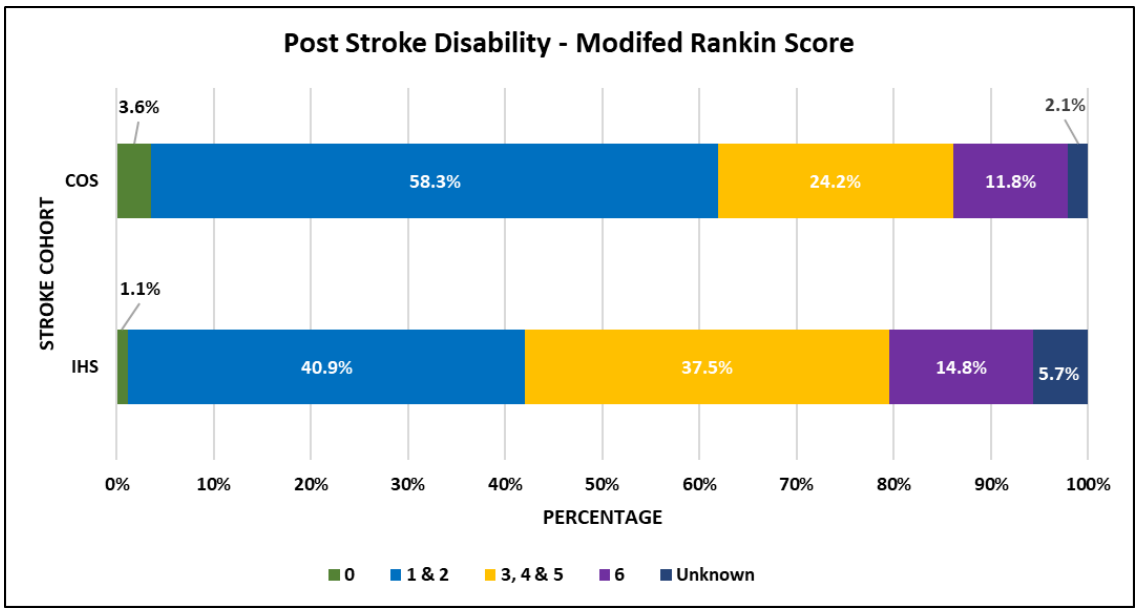

Figure 2.3: Post Stroke Disability Using Modified Rankin Scores by Stroke Cohort (IHS: n=88; COS n=475)

At 23 days (10-54), the median (IQR) LOS documented for IHS patients was significantly longer than COS counterparts (5 days [3-9]; p=<.001). The proportion discharged to LTC was greater amongst the IHS cohort 6.8% versus 2.3% of COS (p=0.04) whereas discharge home was observed more often amongst COS cases (63.8%) compared with IHS cases (51.1%; p=0.02).

2.6.3 Quality-of-Care Variables

The median (IQR) time from recognition of stroke symptoms to medical assessment was significantly faster in the IHS cohort at 28 minutes (5-18) compared with 115 minutes (15-321) in the COS cohort (p<.001) (Table 2.6). Median (IQR) time from recognition to imaging was six minutes faster in the IHS cohort compared with the COS cohort. However, the proportion of COS patients receiving imaging within 30 minutes of stroke symptom recognition was significantly higher at 24.6% (n=112) versus a mere 9.8% (n=5; p=0.02) of the IHS cohort. The median (IQR) time to thrombolysis for IHS cases at 105 minutes (92-113) was significantly longer than COS cases at 66 minutes (49-92); p=0.03.

Table 2.6: Time-Based Quality-of-Care Outcomes of IHS (n=88) and COS (n=475) Cohorts

Time-Based Quality of Care Variables	**median (IQR)/ n (%)**	**median (IQR)/ n (%)**	**Statistic**	**P value**
	IHS (n=88)	COS (n=475)		
From Recognition to Assessment				
Interval from Recognition to Assessment, Median (IQR), mins [a]	28 (5-81)	115 (15-321)	-4.50	**<.001**
Assessment Within 30 mins [a]	27 (51.9)	146 (32.1)	8.17	**.004**
Assessment Within 60 mins [a]	37 (71.2)	192 (42.2)	15.8	**<.0001**
From Recognition to Imaging				
Interval from Recognition to Imaging Median (IQR), mins [b]	72 (39-179)	78 (9-222)	-0.30	0.76
Imaging within 30 mins [b]	5 (9.8)	112 (24.6)	5.63	**.02**
Imaging within 60 mins [b]	23 (45.1)	196 (43.0)	0.08	.78
From Recognition to Thrombolysis				
Interval from Recognition to Thrombolysis Median (IQR), mins [c]	105 (92-113)	66 (49-92)	-2.12	**.03**
Thrombolysis within 45 mins [c]	0 (0.0)	10 (21.3)		.34[d]
Thrombolysis within 60 mins [c]	1 (16.7)	17 (36.2)		.42[d]

[a] Time variables available and correct for analysis in IHS n=52, COS: n=455. [b] Time variables available and correct for analysis in IHS n=51; COS n=456. [c] Time variables available and correct for analysis in IHS n=6; COS n=47. [d] Fisher exact probability test calculation used.

Admission to the SU was much more likely amongst COS cases (78.5%) with only 43.2% (n=38; p<.0001) of the IHS group being admitted to the SU during their inpatient stay (Table 2.7). The requirement of a specialty bed was cited in 75.5% (n=37) of IHS cases as the reason for not being admitted to the SU. In contrast, the lack of an available bed in the SU was the most common reason (67.3%; n=68) accounting for non-admission to the SU amongst COS cases. Three in every four (75.6%) COS patients had swallow screening performed compared with one in every two (48.9%) IHS patients (p<.0001).

Table 2.7: Quality-of-Care Outcomes of IHS (n=88) and COS (n=475) Cohorts

Quality of Care Variables	n (%)	n (%)	Statistic	P value
	IHS (n=88)	COS (n=475)		
Admission to Stroke Unit	38 (43.2)	373 (78.5)	46.01	**<.0001**
Median Stroke Unit Stay (IQR), days	4.5 (3)	4 (4)	-1.687	.09
Swallow Screen Completed	43 (48.9)	359 (75.6)	24.7	**<.0001**
Multidisciplinary assessments:				
Allied Health Professional Required	87 (98.9)	448 (94.3)		.10[a]
Physiotherapy	84 (96.6)	420 (93.8)	1.05	.31
Occupational Therapy	69 (79.3)	411 (91.7)	12.21	**.0005**
Speech & Language	61 (70.1)	315 (70.3)	0	1.0
Dietician	52 (59.8)	113 (25.2)	40.76	**<.0001**
Social Work	39 (44.8)	102 (22.8)	18.27	**<.0001**
Mood Assessment	9 (10.2)	58 (12.2)	0.28	.60
Specialist Stroke Nurse	59 (67.0)	329 (69.3)	0.19	.66
Under Stroke Team at Discharge	20 (22.7)	333 (70.1)	71.26	**<.0001**

P values <.05 are shown in bold. [a] Fisher exact probability test calculation used.

Other variations in assessment by members of the AHP team between the two cohorts were observed (Table 2.7). For instance, IHS cases were more often reviewed by the dietician (59.8% versus 25.2%; p<.0001) and social worker (44.8% versus 2.8%; p<.0001) whereas COS cases were reviewed by occupational therapy (91.7%) significantly more than IHS cohort (79.3%; p=0.0005). At the point of discharge, IHS inpatients were less likely to be under the care of the stroke team than COS inpatients (22.7% versus 70.1%; p<.0001). The proportions by specialty caring for IHS patients at discharge is demonstrated in Figure 2.4. Only one-fifth (22.7%) were under the care of the stroke team at discharge.

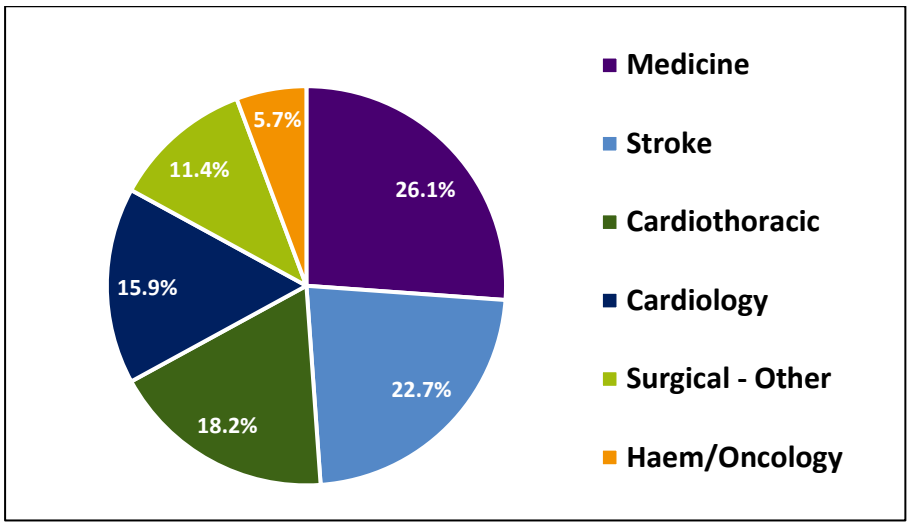

Figure 2.4: Specialty at Discharge for IHS Cohort (IHS n=88)

2.7 Discussion of Clinical Validation Study

The quality of data from administrative sources has previously been highlighted as a key consideration within stroke registers specifically (Baldereschi et al., 2018, Soderholm et al., 2016, Porter et al., 2016, Johnsen et al., 2002). There is a dearth of research validating the definition of IHS applied within stroke registries. A valid definition of IHS within a stroke register is a prerequisite for accurate analysis of this stroke subgroup. The varied permutations in coding and validation outcomes presented in Table 2.2 underline the complexity of the administrative coding process at discharge and the challenges faced by stroke registries to accurately identify and define IHS cohorts.

This clinical validation study demonstrates a moderate level of agreement between the clinical gold standard and either of the recording methods studied for IHS cases (HADx flag assignment during coding and audit coordinator recording). The audit coordinator demonstrated greater sensitivity (86% versus 55%) in the identification of IHS with a level of agreement that approached a substantial level. This may be explained by the audit coordinator's clinical experience as a specialist stroke nurse working routinely in the delivery stroke care. When HIPE and audit coordinator data sources were combined, the sensitivity of IHS identification increased to 95% and the level of agreement improved to a substantial level (κ=0.65). This underlines the strength of linking clinical and administrative data sources in the definition of IHS cases within a stroke register.

There are limitations to this clinical validation study. Firstly, it is acknowledged that IHS cases could have been omitted from validation if they were neither identified by the HIPE coding process nor by the audit coordinator and thus would not have been recorded within INAS data during that period. A prospective methodology would address this limitation. Furthermore, we assumed that cases with a principal stroke diagnosis and which the audit coordinator indicated were not an IHS event (n=447) were highly likely to be COS events. To address this limitation, within this group any cases with an additional diagnosis of stroke (n=16) were included in validation. These cases are represented in scenario 7 in Table 2.2 and reassuringly no IHS cases were found during validation. Future research should include specific clinical validation of this assumed COS group to validate COS cases as well identifying potentially missed IHS events. Finally, this does reflect a

relatively small stroke service including a small number of cases for the clinical validation study, thus its findings may not be directly generalisable to other hospital sites.

2.8 Discussion of Retrospective Cohort Study

At 15.6%, the IHS rate at our hospital is high. This may be reflective of the specialty case-mix at the hospital site which includes interventional cardiology, cardiothoracic surgery and oncology which are all sources of IHS. The hospital is a tertiary referral teaching centre in an urban location, and this may contribute to the higher rate of IHS and may not be typical of other sites. Indeed, the principal diagnosis coded for over half (54.5%) of IHS patients was either a circulatory (35.2%) or an oncology (19.3%) diagnosis. Furthermore, it has been previously acknowledged that IHS rates tend to be higher in single centre studies (Section 1.7).

This study reflects the first comprehensive review of IHS cases in an Irish context utilising national standardised reporting outcomes. It confirms that IHS patients within an Irish tertiary hospital have longer length of hospitalisation, greater disability at discharge, are more often discharged to a LTC facility and are less likely to be discharged home than COS counterparts. Patients with IHS were more likely to die (12.5% versus 7.6%) and less likely to receive thrombolysis (7.3% versus 12%), although these outcomes did not reach statistical significance. A trend towards increased rates of thrombectomy was also observed.

Even though IHS patients are hospitalised at the onset of stroke symptoms, we found that more than one quarter (28.4%) had no recorded symptom onset time, and a "FAST Call" was alerted in only half (52.3%) of stroke events. Education on stroke recognition and acute stroke pathways across the organisation may be of benefit.

In addition, median times from recognition to medical assessment and to imaging were faster amongst IHS patients. However, these early gains in the acute stroke pathway did not equate to faster times to thrombolysis. The median time to thrombolysis for IHS cases was 105 minutes compared with 66 minutes for COS cases (p=0.03). Process-based pathways in stroke care traditionally have been focused upon COS presenting via the ED and these pathways may not transfer to an in-hospital context. The challenges and delays encountered with thrombolysis specifically may be explained by the difficulty initiating thrombolysis on a general or non-specialty ward. A "FAST-Call" pathway specifically for IHS may be of value to improve these findings.

Optimal stroke care is delivered in a dedicated SU, but only 43.2% of IHS patients were admitted to the SU. This had related impacts on swallow screening with less than half (48.9%) of IHS patients receiving the recommended swallow screening compared with 75.6% of COS patients. Care tailored to the post-stroke period may also be influenced as the majority (77.3%) of IHS patients are not under the care of the specialised stroke team at discharge.

There are limitations to this retrospective cohort study. Firstly, the sample of IHS cases is small (n=88) as available data for IHS was limited as collection has only been mandatory in INAS since 2020. This may have impacted on reported outcomes like thrombolysis, thrombectomy and mortality which did not reach statistical significance. Secondly, the findings on IHS in this centre may not be directly transferrable to other hospitals owing to variations in subspecialties and case-mix. Future analysis of IHS data at a national level would help to address limitations by increasing the sample size for analysis and the inclusion of a broader mix of hospitals. Finally, data analysis is limited to the in-hospital period and does not include post-discharge follow-up.

2.9 Conclusions

The combination of ICD-10-AM coded discharge diagnoses with data input by a clinical stroke audit coordinator facilitates identification of IHS cases to a substantial level of agreement with expert clinical validation. The findings may guide future strategies to improve the accuracy of IHS case identification and emphasise the need for validation studies to ensure data quality and accuracy is maintained within stroke registers.

The IHS rate (15.6%) at St. James's Hospital is high. The hospital's specialty case-mix may influence this which include interventional cardiology, cardiothoracic surgery and oncology specialities which are all sources of IHS. Indeed, the principal diagnosis coded for over half (54.5%) of IHS patients was either a circulatory (35.2%) or an oncology (19.3%) diagnosis. IHS patients have worse outcomes than COS with longer length of hospitalisation, greater disability at discharge, are more often discharged to LTC facility and less likely to be discharged home. Outcomes on thrombolysis and thrombectomy rates and mortality rates were not statistically significant. Times to thrombolysis were significantly slower than COS counterparts.

Suggested quality improvement initiatives may include the development of a dedicated acute stroke "FAST Call" pathway for strokes occurring in-hospital so that IHS patients are swiftly identified and progress through the steps of the acute stroke pathway rapidly. Post-stroke care must be adapted as it is acknowledged that IHS patients have competing medical needs and are less likely to be in the specialised SU or under the care of the stroke team at discharge. Further research on larger IHS samples in an Irish context is required.

Chapter 3. Methods of National In-Hospital Stroke Review

3.1 Study Design

A retrospective multi-centre (n=24 hospitals) cohort study comparing IHS and COS cases from the 1st of January 2020 to the 31st of December 2021 was conducted using stroke data collected for the purposes of the annual INAS.

3.2 Background of Core Clinical Dataset in INAS

Aspects of the methodology discussed in Section 2.4 apply to the national analysis, but an overview will be provided here to provide a clear understanding for this analysis of IHS. The core clinical dataset for INAS originates from two linked data sources in the stroke audit portal – HIPE data and stroke-specific data input by local audit coordinators (NOCA 2023a). The HIPE extract of data with pseudonymised cases is sent to the National Office for Clinical Audit (NOCA) from the Healthcare Pricing Office (HPO). Each hospital has a clinical lead and an audit coordinator who leads stroke service governance within the hospital. The audit coordinator in each hospital submits the stroke-specific data for each case via the stroke audit portal. The list of cases eligible for inclusion is identified by running a HIPE discharge report within the stroke audit portal. Additional cases may be identified manually. Data are generally recorded retrospectively. Twenty-four acute public hospitals contribute to the INAS annually (Table 3.3, Section 3.8.4). Patients are included in the INAS report if they have a stroke in any one of these hospitals once the hospital has admitted more than 25 stroke cases that year and the patient is aged 17 years and above. The collection of clinical data on IHS cases became mandatory in 2020. Since 2020, IHS cases are reported in the total number of stroke cases at each hospital. However, further analysis has been limited. It is important to highlight that without the work of HIPE coders and the local audit coordinators at each hospital site, this analysis would not be possible.

3.3 Data Access

Ethical approval was obtained from the St. James's Hospital and Tallaght University Hospital Joint Research Ethics Committee, Application Reference Number: 2296 on February 13th, 2023. A formal data access request was submitted to NOCA, and approval was communicated on the 27th of March 2023. The data access request facilitated row level data presentation from HIPE and INAS core dataset sources during the two-year reporting period. To ensure pseudo anonymisation, the discrete age value was presented as a grouped age category (17-49 years, 50-64 years, 65-79 years and >80 years). Variables which collect specific dates and times were presented as aggregate time data. For example, rather than providing the date and time of arrival to hospital (DD/MM/YYYY and HH:MM) and date and time of medical assessment (DD/MM/YYYY and HH:MM), the interval between arrival to hospital and medical assessment was provided in minutes. Furthermore, in instances where there are five cases or less, values must be suppressed to prevent disclosure. Regarding data completeness, all responses including unknowns were provided.

3.4 Data Coverage

Total coverage was 93% in 2020 and 95% in 2021, as defined in the published INAS report (INAS, 2022).

3.5 IHS Case Definition

As detailed in Section 2.4.4, the definition of IHS cases by the INAS is based upon the HADX flag being assigned during HIPE coding and/or local audit coordinators indicating the case was an IHS event during audit data entry. A case fulfils the definition of an IHS event if either one or both (**and/or basis**) of the criteria are present (Table 3.1).

Table 3.1: Criteria for IHS in the INAS

Case Example	**Audit Coordinator:** In-Hospital Stroke field 1=Yes	**HIPE:** Additional Stroke (I61, I63, I64) Diagnosis with HADx Flag	**IHS Case**
1	✓	✓	**Yes**
2	✓	×	**Yes**
3	×	✓	**Yes**
4	×	×	**No**

3.6 COS Case Definition

A COS case is defined as a case coded with a principal stroke diagnosis (i61, I63 or I64) by HIPE **and** the audit coordinator indicates it is not an IHS event. Stroke symptoms should be present at the start of the episode of care for COS cases. The existing definition of COS cases within INAS does not assess whether there are any further additional stroke diagnoses coded for cases with a principal coded stroke diagnosis.

3.7 Cohort Selection

Firstly, all potential data scenarios for stroke cases recorded using the stroke audit portal during the reporting period (January 1st 2020 to December 31st 2021) were reviewed (Table 3.2). The existing definition of IHS utilised by INAS was not automatically applied as selection of true IHS and true COS cases was deemed to be of great importance given that this is the first national review of IHS. Each scenario was discussed at a consensus meeting with L.C., J.H. and two core members of the INAS team. During this period, 12, 591 stroke cases were recorded. There were 137 cases excluded as the audit coordinator either did not know if a case reflected an IHS event or left the variable blank. Sixteen data scenarios were discovered as multiple stroke diagnoses (up to 29 additional diagnoses) can be coded for an episode of care. As specified by the INAS dataset data dictionary, the date and time of arrival to hospital are recorded by audit coordinators only for COS cases in the stroke audit portal (NOCA 2023c). Consequently, the percent of cases per scenario with an arrival date and time recorded was also reviewed to act as a surrogate data marker for COS cases.

Table 3.2: Data Scenarios (n=16) for Stroke Audit Data Recorded 2020 & 2021

	Audit Coordinator	HIPE	HIPE	HIPE			Audit Coordinator
Scenario	Audit Question 4: In-Hospital Stroke	Principal Stroke Diagnosis	Additional Stroke Diagnosis Without HADx Flag	Additional Stroke Diagnosis With HADx Flag	Cohort Selected	Cases (n)	Hospital Arrival Date Recorded (%)
1	No	Yes	No	No	COS	9710	100%
2	No	Yes	Yes	No	COS	453	100%
3	Yes	No	Yes	Yes	IHS	~	33%
4	Yes	No	No	Yes	IHS	361	1%
5	Yes	No	Yes	No	IHS	114	2%
6	Yes	No	No	No	IHS⁺	78	13%
7	Yes	Yes	No	No	IHS⁺	354	9%
8	Yes	Yes	Yes	No	IHS⁺	20	11%
9	Yes	Yes	No	Yes	IHS⁺	6	33%
10	No	No	Yes	Yes	IHS⁺	~	100%
11	No	No	No	Yes	Unclear	71	100%
12	No	Yes	Yes	Yes	Unclear	~	100%
13	No	Yes	No	Yes	Unclear	62	100%
14	Yes	Yes	Yes	Yes	n/a	0	n/a
15	No	No	Yes	No	Exclude	197	98%
16	No	No	No	No	Exclude	1021	100%
Total						12454	

⁺Cases were subject to further data caveats prior to inclusion into the IHS cohort. ~ Denotes five cases or fewer.

COS

IHS

Unclear for cohort selection/Excluded

The data recorded for scenario 1 (n=9710) and scenario 2 (n=453) were consistent with COS cases as a principal diagnosis of stroke was recorded with no criteria for IHS and 100% of cases had an arrival date recorded.

Scenarios 3, 4 and 5 were deemed to reflect IHS cases. Scenario 3 and scenario 4 fulfilled both IHS criterion with HADx flag and audit coordinator identification and had low percentages of arrival date completion at 33% and 1% respectively. Scenario 5 (n=114) fulfilled the criterion of audit coordinator identification alone but had a secondary diagnosis of stroke recorded without a principal diagnosis. Only 2% of these cases had an arrival date recorded. Interpretation of this data scenario suggested that the audit

coordinator deemed this to be an IHS event. Crucially coding of a principal diagnosis of stroke was absent and arrival date recording was low. The presence of an additional stroke diagnosis, albeit without a HADx flag, supported the assumption this scenario comprised IHS events where the HADx flag was omitted during the coding process.

A further data quality caveat was applied within scenarios 6, 7, 8 and 9 prior to inclusion within the IHS cohort. Scenario 6 (n=78) fulfilled one criterion for IHS (audit coordinator identification). To ensure true cases of IHS were selected, only cases where the date of stroke symptom onset occurred after the admission date were included, equating to 40 cases of the total 78 cases in this data scenario (Figure 3.1).

A principal diagnosis of stroke was recorded in scenarios 7, 8 and 9 as well as at least one inclusion criterion for IHS cases reflecting conflicting criteria for cohort selection. Again, only cases where the date of stroke symptom onset occurred after the hospital admission date were included into the IHS cohort. This equated to 92 cases from scenario 7 (n=354) and seven cases from scenario 8 (n=20) and 9 (n=6) combined.

Scenario 10 and scenario 11 (n=71) fulfilled only one criterion for IHS (HADx flag) without a principal diagnosis of stroke coded. A prior clinical validation exercise to assess the diagnostic accuracy of in-hospital stroke definition in collected stroke audit data at a single hospital site (Chapman et al. 2023b), determined the audit coordinator identified IHS events with higher sensitivity (86%; 95% CI 77%-93%) whereas the HADx flag was more specific at 96% (95% CI 85% to 99%). This finding initially favoured inclusion of these scenarios into the IHS cohort. However, the stroke symptom onset time for these cases were reviewed to assess data quality. Only six cases in scenario 11 had a stroke symptom onset date after admission which would suggest an IHS event. This scenario was deemed to be too unclear to be included within the IHS cohort given the degree of potential data inaccuracy. Regarding scenario 10, the number of cases was small, and no case had a stroke symptom onset date that was before admission thus this scenario was included within the IHS cohort.

Scenarios 12 and 13 were not included into cohort selection as they had conflicting data recording with arrival dates recorded in 100% of cases and a principal stroke diagnosis

coded in conjunction with an assigned HADx flag. Traditionally these cases in INAS would be automatically deemed to reflect a COS event as they have a principal diagnosis of stroke coded.

Scenarios 15 and 16 were excluded as they don't reflect either COS or IHS cases. These cases are likely consistent with TIAs that have clinical data entered by local audit coordinators.

From the total 12, 454 stroke cases available in the stroke audit portal for the two-year reporting period, 1,673 were excluded from cohort selection (Figure 3.1).

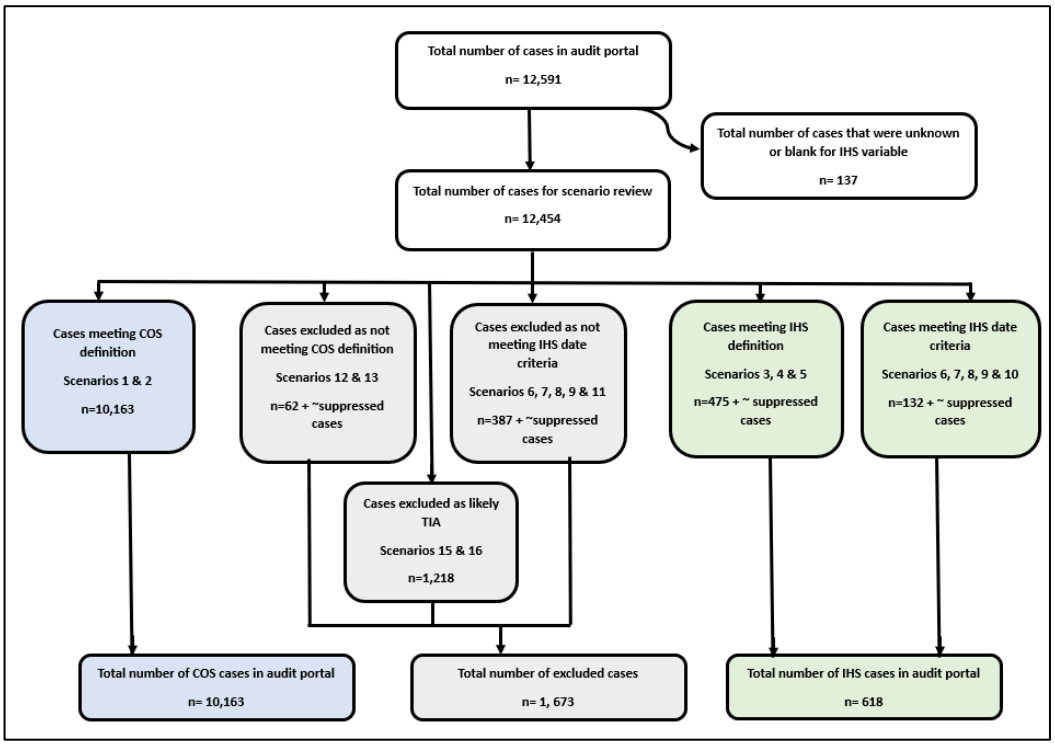

Figure 3.1: Cohort Selection with Breakdown by Data Scenario

~ Denotes five cases or fewer.

3.8 Data Variables

Full details of the data variables used in the core clinical dataset from HIPE and audit coordinator sources are available (Appendix 1). This thesis will present results under three headings – demographics (Chapter 4), quality-of-care measures (Chapter 5) and outcomes (Chapter 6). The demographic results presented are largely HIPE-derived data variables on age, sex, admission sources, ICD-10-AM coded principal diagnosis, stroke subtype, and specialty at discharge. However, pre-stroke functional disability using mRS is sourced from the audit coordinator data entry. The quality-of-care measures presented are sourced from local audit coordinator data entry including time-based intervals (time to assessment, imaging, and thrombolysis), SU admission rates, swallow screening, rates of AHP assessment, antithrombotic therapy, and anticoagulation in AF. The outcome variables presented vary in data source (indicated in brackets after each variable). They include in-hospital mortality (HIPE), thrombolysis rate (Audit coordinator), post-stroke functional disability using mRS (Audit coordinator), LOS (HIPE) and discharge destination (HIPE).

Analysis of thrombectomy data for IHS cases was not possible due to anonymisation of data and the inability to link the data sources for further analysis. This represents a limitation of this report given the importance of thrombectomy in acute stroke care. A further limitation is that the INAS does not include a variable such as NIHSS to assess stroke severity. Certain data variables (time-based quality-of-care measures, stroke subtype, reasons for non-admission to the stroke unit, hospital) demanded further categorisation in the context of IHS specifically. The methodological approaches applied to these variables are discussed below.

3.8.1 Time-based Quality-of-Care Measures

If available, the stroke onset date and time is recorded for all strokes in the stroke audit portal. However, the date and time of arrival to hospital is only recorded for COS cases. As discussed previously in Section 1.9.1, to evaluate performance of the acute stroke clinical pathway for COS cases, time-based quality-of care measures calculate the time elapsed from the date and time of arrival to hospital to medical assessment, brain imaging and interventions (thrombolysis or thrombectomy). Given that IHS cases have their onset in

an hospital setting, the arrival date and time to hospital will precede the onset of stroke symptoms. To evaluate performance of the acute stroke clinical pathway for IHS cases, the time elapsed from the date and time of stroke symptom onset to medical assessment, brain imaging and interventions (thrombolysis or thrombectomy) is used for IHS cases.

Time intervals were subject to data quality measures which are outlined in Appendix 3 and detail the frequency of missing data and negative values which reflect erroneous data entry. Time-based intervals also have certain time cut-offs applied by INAS to improve data quality which are outlined in Appendix 4 of the critical review of stroke from 2013 to 2021 (NOCA 2023a). Data was excluded if the interval between arrival to hospital for COS cases (or stroke symptom onset for IHS cases) and imaging was more than a month. If the interval from arrival to hospital for COS cases (or stroke symptom onset for IHS cases) and thrombolysis was more than 24 hours, data was also excluded.

3.8.2 Stroke Subtype

Stroke subtype is defined according to the ICD-10-AM code reported by HIPE. In line with prior INAS methods, stroke diagnoses coded as I64 are defined as ischaemic stroke. Subarachnoid haemorrhage (I60) and subdural haemorrhage (I62) are not included in the INAS annually (NOCA 2022a).

The stroke subtype for COS cases is easily defined by using the ICD-10-AM code assigned as the principal diagnosis i.e., if the principal diagnosis coded is I63 the stroke subtype is ischaemic. Most strokes within the IHS cohort (n=455) had a single additional stroke diagnosis coded by HIPE for that episode of care. In these instances, the subtype was defined by the ICD-10-AM code of that additional diagnosis, irrespective of whether a HADx flag was present or absent, as it represented the only coded stroke diagnosis for that case. A principal diagnosis of stroke, without any recorded additional stroke diagnoses, was coded for 92 cases within the IHS cohort. In these cases, the ICD-10-AM code of the principal diagnosis defined the stroke subtype. Two additional stroke diagnoses were coded for 24 cases within the IHS cohort. The presence of a HADx flag and secondarily, the coding hierarchy of the diagnoses were employed to define the stroke subtype. If a HADx flag was assigned to one coded stroke diagnosis, this defined the

stroke subtype. If both additional diagnoses had a HADx flag assigned, the coded diagnosis appearing first in the coding hierarchy defined the subtype. If neither had a HADx flag, the coded diagnosis appearing first in the coding hierarchy defined the subtype. A smaller number (n=7) of IHS cohort cases had a principal and an additional stroke diagnosis coded. If the additional stroke diagnosis had a HADx flag this defined the subtype. If the additional diagnosis did not have a HADx flag, the principal diagnosis defined the subtype. Forty cases in the IHS cohort had no ICD-10-AM coded stroke diagnosis and subtype was impossible to define.

3.8.3 LOS

As previously discussed in Section 1.8.4 typically the total hospital LOS is presented. However, to accurately compare LOS as a stroke outcome between COS and IHS, comparison should be between the total hospital LOS for COS cases and the hospital LOS following the onset of stroke symptoms in IHS cases. For this reason, the total hospital LOS and the LOS following stroke will be calculated for the IHS cohort. LOS following stroke is derived by the following equation: Total hospital LOS (days) – [Symptom Onset Date – Hospital Admission Date (days)] = LOS in-hospital following stroke event.

3.8.4 Hospital Model and PCI Centres

In Ireland, there are four models of hospital care based on the type of activity that is provided. These models were originally defined within the National Acute Medicine Programme published in 2010 (HSE, 2010). They not validated or based upon international categorisation. Model 3 hospitals provide acute surgery, acute medicine, and critical care 24 hours per day, every day of the year. Model 4 hospitals are like model 3 hospitals but also provide tertiary care and, in certain locations, supra-regional care (HSE, 2013). A list of the 24 acute public hospitals participating in the INAS with their corresponding hospital model is available in Table 3.3. Given the association between IHS and cardiac presentations and interventions, IHS rates are later presented for hospital centres which are designated percutaneous coronary intervention (PCI) centres. In total, 10 hospitals are PCI centres and are also listed in Table 3.3 (NOCA 2023b).

Table 3.3: Hospital Models and PCI Centres for Hospitals Participating in the INAS

Hospital	Model*	PCI-Centre
Bantry General Hospital	3	No
Beaumont Hospital	4	Yes**
Cavan General Hospital	3	No
Connolly Hospital	3	No
Cork University Hospital	4	Yes
Letterkenny University Hospital	3	Yes
Mater Misericordiae University Hospital	4	Yes
Mayo University Hospital	3	No
Mercy University Hospital	3	No
Naas General Hospital	3	No
Our Lady of Lourdes Hospital Drogheda	3	No
Portiuncula University Hospital	3	No
Regional Hospital Mullingar	3	No
Sligo University Hospital	3	No
St James's Hospital	4	Yes
St Luke's General Hospital, Carlow/Kilkenny	3	No
St Vincent's University Hospital	4	Yes**
Tallaght University Hospital	4	Yes**
Tipperary University Hospital	3	No
University Hospital Galway	4	Yes
University Hospital Kerry	3	No
University Hospital Limerick	4	Yes
University Hospital Waterford	4	Yes***
Wexford General Hospital	3	No

* Model 3 hospitals provide acute surgery, acute medicine, and critical care 24 hours per day, every day of the year. Model 4 hospitals are like model 3 hospitals but also provide tertiary care and, in certain locations, supra-regional care (HSE, 2013).

PCI service 9am to 5pm Monday to Friday. * UHW participated in the national heart attack audit since 1 January 2022. The primary PCI service increased from 8.00am to 5.00pm, Monday to Friday to 8.00am to 8.00pm, Monday to Friday, in September 2022.

3.8.5 Reasons for Non-Admission to Stroke Unit

If a patient is not admitted to the SU, a reason for this non-admission is collected by the INAS. The structured answers for non-admission to the SU include: “No Stroke Unit”, “Bed Not Available”, “Infection Control Risk” and “Other”. If “Other” is selected, a free text reason can be input. On review of this data variable, it was noted that a high proportion (67%) of the IHS cohort had “Other” listed as the reason for non-admission to the SU. As a result, a full review of the free text fields for “Other” in both IHS and COS cohorts was performed. Qualitative categorisation was initially completed using sixteen reasons (Table 3.4). The reason “COVID” was combined with the existing structured answer “Infection Control Risk”. Certain reasons occurred with low frequency (3% or less) in both IHS and COS cohorts. Given the low occurrence of these category answers, they were combined into the category “Other”. As a result, there were nine final structured answers reported for non-admission to the SU.

Table 3.4: Re-Categorisation of Reasons for Non-Admission to SU

Original Reasons for SU Non-Admission	Initial SU Non-Admission Categories	Amalgamated Yes/No	Final Reasons for SU Non-Admission
No Stroke Unit	No Stroke Unit	No	No Stroke Unit
Bed Not Available	Bed Not Available	No	Bed Not Available
Infection Control Risk	Infection Control Risk	No	Infection Control Risk
Other	Other	No	Other
	Specialty Bed Required	No	Specialty Bed Required
	COVID	Yes, Infection Control Risk	
	Not Under Stroke Team/Not Stroke Initially	No	Not Under Stroke Team/Not Stroke Initially
	Palliative/RIP	No	Palliative/RIP
	Minor Stroke/SU Not Required	No	Minor Stroke/SU Not Required
	Transfer	Yes, Other	
	Not Referred/Unaware to Stroke	Yes, Other	
	Discharged/Not Admitted	Yes, Other	
	Symptoms Too Severe/Too Unwell	Yes, Other	
	Patient Refused/Self-discharged	Yes, Other	
	Needed 1:1 Special/Confusion	Yes, Other	
	Unknown Reason	No	Unknown Reason

3.8.6 In-Hospital Mortality

Mortality can be reflected by an mRS score=6 which is entered during clinical stroke data entry by audit coordinators. However, in-hospital mortality is calculated using HIPE as the data source. The INAS reports mortality annually using the HIPE data source because there is mandatory completion of this data variable by HIPE coders on every episode of care which ensures no missing data.

3.9 Statistical Analysis

Numeric counts and proportions in percent are presented. Differences for categorical variables were tested using the Pearson $\chi 2$ test. Fisher's exact probability test was used when less than 80% of cells had an expected frequency less than five. Continuous variables (e.g., time-based variables) reflected a skewed population so the median and IQR are reported, and differences were tested using the Mann-Whitney U test. Both unadjusted and adjusted OR for mortality and favourable functional level at discharge were calculated. Mortality was adjusted for age, sex, stroke subtype, SU admission, AF, COVID-19 and pre-stroke functional disability. Favourable functional level at discharge was defined as an mRS score of 0 to 2 and was adjusted for age, sex, stroke subtype, SU admission, AF, pre stroke functional disability. As no variable for stroke severity is collected in the INAS, adjustment for stroke severity was not possible. CI are reported at 95%. Statistical significance was reported as p value less than 0.05. IBM's SPSS Version 27 was used for statistical analysis.

Chapter 4. Results: Demographics

4.1 IHS Rate

Of the 10, 781 cases available in the stroke audit portal for the 2-year reporting period, 618 were IHS events and 10,163 were COS events yielding a national IHS rate of 5.7% (Table 4.1). The highest IHS rate by hospital was at St. James's Hospital 14.3% (n=74) and the lowest IHS rate was 1.7% at Wexford General Hospital (Figure 4.1). A greater proportion of the IHS cohort were admitted in a model 4 hospital (65.2%) than the COS cohort (57.3%; p<.001) (Table 4.1). St. James's Hospital and University Hospital Waterford accounted for 28.1% of the IHS cases admitted in a model 4 hospital. When comparison was made between the 10 designated PCI centres and the 14 non-PCI centres, the IHS rate was significantly higher amongst PCI centres at 6.3% (n=417) compared with 4.8% (n=201) in non-PCI centres (p<.001).

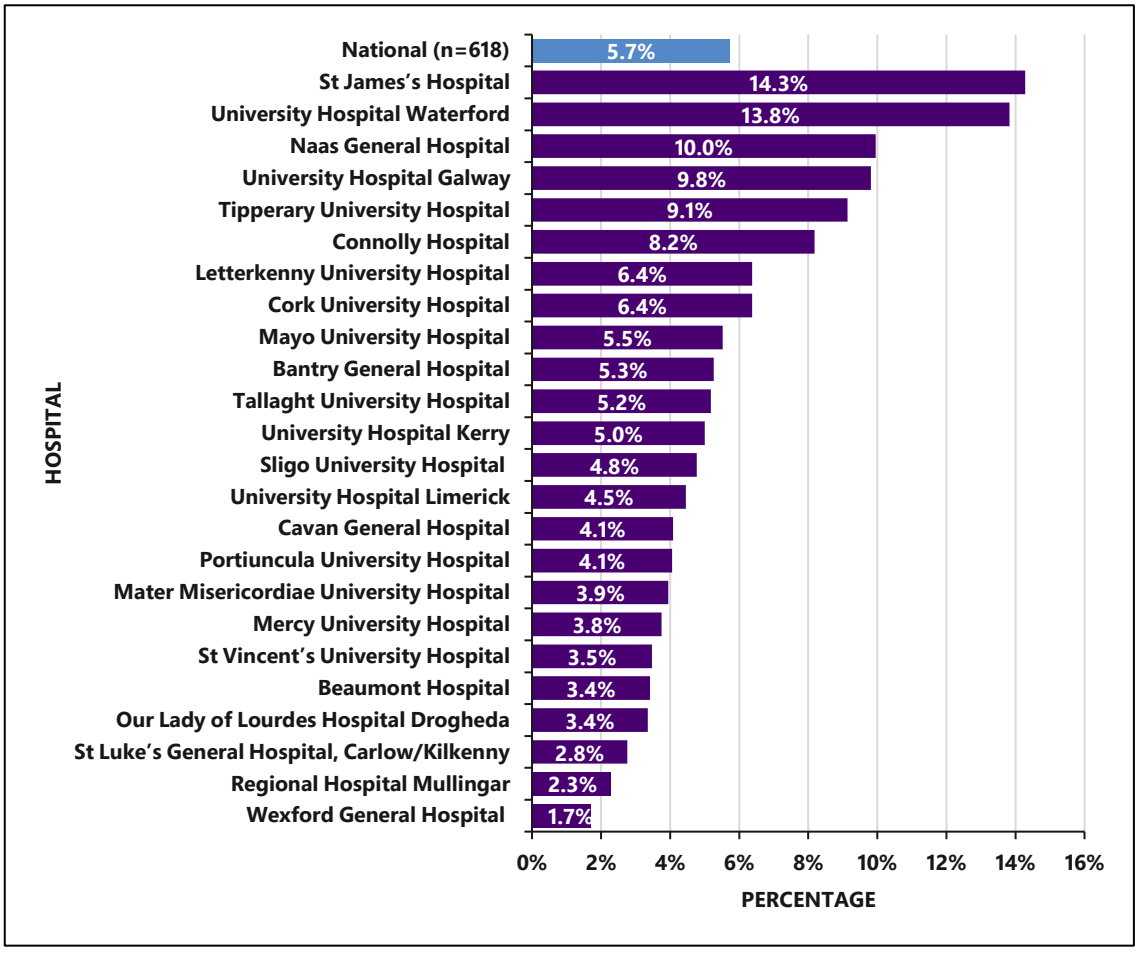

Figure 4.1: Per Hospital Rate of IHS (IHS n=618)

Table 4.1: Total COS and IHS Cases Per Hospital (IHS n=618; COS n=10,163)

Hospital	COS (n)	IHS (n)	Total	COS (%)	IHS (%)	Total
Bantry General Hospital	144	8	152	94.7%	5.3%	100.0%
Beaumont Hospital [a, b]	933	33	966	96.6%	3.4%	100.0%
Cavan General Hospital	282	12	294	95.9%	4.1%	100.0%
Connolly Hospital	415	37	452	91.8%	8.2%	100.0%
Cork University Hospital [a, b]	1013	69	1082	93.6%	6.4%	100.0%
Letterkenny University Hospital [a]	341	14	355	93.6%	6.4%	100.0%
Mater Misericordiae University Hospital [a, b]	599	35	634	96.1%	3.9%	100.0%
Mayo University Hospital	359	14	373	94.5%	5.5%	100.0%
Mercy University Hospital	190	21	211	96.2%	3.8%	100.0%
Naas General Hospital	346	12	358	90.0%	10.0%	100.0%
Our Lady of Lourdes Hospital Drogheda	512	22	534	96.6%	3.4%	100.0%
Portiuncula University Hospital	*	~	*	95.9%	4.1%	100.0%
Regional Hospital Mullingar	301	7	308	97.7%	2.3%	100.0%
Sligo University Hospital	379	19	398	95.2%	4.8%	100.0%
St James's Hospital [a, b]	444	74	518	85.7%	14.3%	100.0%
St Luke's General Hospital, Carlow/Kilkenny	247	7	254	97.2%	2.8%	100.0%
St Vincent's University Hospital [a, b]	806	29	835	96.5%	3.5%	100.0%
Tallaght University Hospital [a, b]	549	30	579	94.8%	5.2%	100.0%
Tipperary University Hospital	199	20	219	90.9%	9.1%	100.0%
University Hospital Galway [a, b]	496	54	550	90.2%	9.8%	100.0%
University Hospital Kerry	266	14	280	95.0%	5.0%	100.0%
University Hospital Limerick [a, b]	686	32	718	95.5%	4.5%	100.0%
University Hospital Waterford [a, b]	293	47	340	86.2%	13.8%	100.0%
Wexford General Hospital	*	~	*	98.3%	1.7%	100.0%
Total	10163	618	10781	94.3%	5.7%	100.0%

~ Denotes five cases or fewer. *Further suppression required to prevent disclosure of five cases or fewer. [a] Designated PCI centres. [b] Model 4 hospital.

4.2 Sex and Age

Males and females were represented similarly between IHS and COS cohorts (Table 4.2). Just over one-half of stroke cases were male with 57.3% (n=5825) in the COS cohort and 56.5% (n=349) in the IHS cohort. IHS patients were older than COS counterparts. The median age of the IHS cohort was 76 years (IQR 67 to 84 years) compared to 74 years (IQR 64 to 82 years) for the COS cohort. Around four-fifths (80.1%) of the IHS cohort were aged 65 years and above compared with three-quarters (73.5%) of the COS cohort (p<.001) (Figure 4.2).

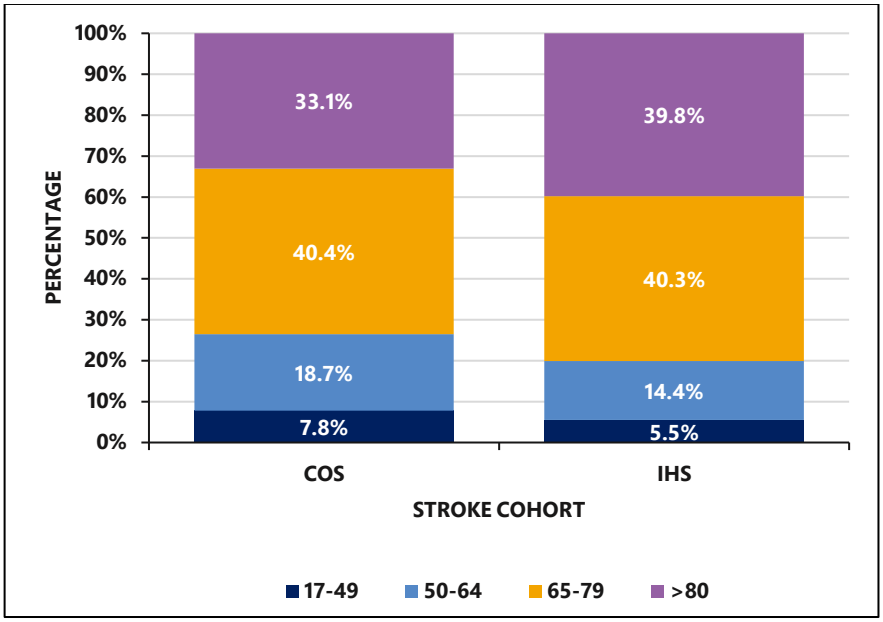

Figure 4.2: Percentage of Stroke Patients by Age and Cohort (COS n=10163; IHS n=618)

4.3 Stroke Subtype

The methodology for the definition of stroke subtype is detailed in Section 3.8.2. Of the 618 IHS cases, forty cases (6.5% of IHS cohort) had no ICD-10-AM coded stroke diagnosis and the stroke subtype was impossible to define. Hence the total available data for this variable for the IHS cohort was n=578. Ischaemic stroke subtype was more commonly recorded amongst IHS cases in 90.0% (n=520) compared with 85.4% (n=8680) of COS patients (p=0.002) (Table 4.2).

Table 4.2: Demographic Results by Cohort (IHS n=618; COS n=10163)

Variable	IHS n (%) (n=618)	COS n (%) (n=10163)	Pearson statistic [a]	P value
Sex				
Male	349 (56.5%)	5825 (57.3%)	0.17	0.68
Age Grouping				
17 – 49 years	34 (5.5%)	795 (7.8%)	17.73	<.001
50 – 64 years	89 (14.4%)	1899 (18.7%)		
65 – 79 years	249 (40.3%)	4106 (40.4%)		
> 80 years	246 (39.8%)	3363 (33.1%)		
Age </> 65 years				
Aged > 65 years	495 (80.1%)	7469 (73.5%)	13.17	<.001
Aged < 65 years	123 (19.9%)	2694 (26.5%)		
Stroke Subtype				
Ischaemic	520 (90.0%)	8680 (85.4%)	9.24	0.002
Haemorrhagic	58 (10.0%)	1483 (14.6%)		
Missing	40 (6.5%)	0 (0.0%)		
By Hospital Model				
Model 3	215 (34.8%)	4344 (42.7%)	15.10	<.001
Model 4	403 (65.2%)	5819 (57.3%)		
By PCI Centre				
PCI Centre	417 (67.5%)	6160 (60.6%)	11.54	<.001
Non-PCI Centre	201 (32.5%)	4003 (39.4%)		
Admission Source				
Home	523 (84.6%)	9047 (89.0%)	13.14[a]	0.004
LTC/Convalescent or long-stay	21 (3.4%)	318 (3.1%)		
Acute Hospital	72 (11.7%)	763 (7.5%)		
Other	2 (0.3%)	35 (0.3%)		
Critical Care Admission				
Critical Care Admission	246 (39.8%)	1390 (13.7%)	308.99	<.001
Critical Care LOS, days mean (SD)	4.7 (11.8)	0.8 (3.6)	-18.5[b]	<.001
COVID-19 Co-Diagnosis				
COVID-19	49 (7.9%)	224 (2.2%)	77.36	<.001
Pre-stroke mRS				
mRS 0-2	372 (60.2%)	7911 (77.8%)	125.34	<.001
mRS 3-5	189 (30.6%)	1460 (14.3%)		
Missing	57 (9.2%)	792 (7.8%)		

[a] Fisher's exact test used. [b] Mann-Whitney U test for continuous variables.

4.4 Admission Source

More patients with COS (89.0%) were living at home prior to their stroke than IHS patients (84.6%; p=0.004) (Table 4.2). Slightly more IHS patients (3.4%) were admitted from a nursing or convalescent home or other long-stay accommodation compared to 3.1% of the COS group.

4.5 Pre-Stroke Modified Rankin Score

Prior to stroke onset, the majority of COS cases had good functional ability as defined by mRS 0 to 2 (77.8%; n=7911) compared with the only two-thirds (60.2%) of the IHS cohort onset (p<.001) (Table 4.2). Further breakdown by mRS score including missing values is displayed in Figure 4.3.

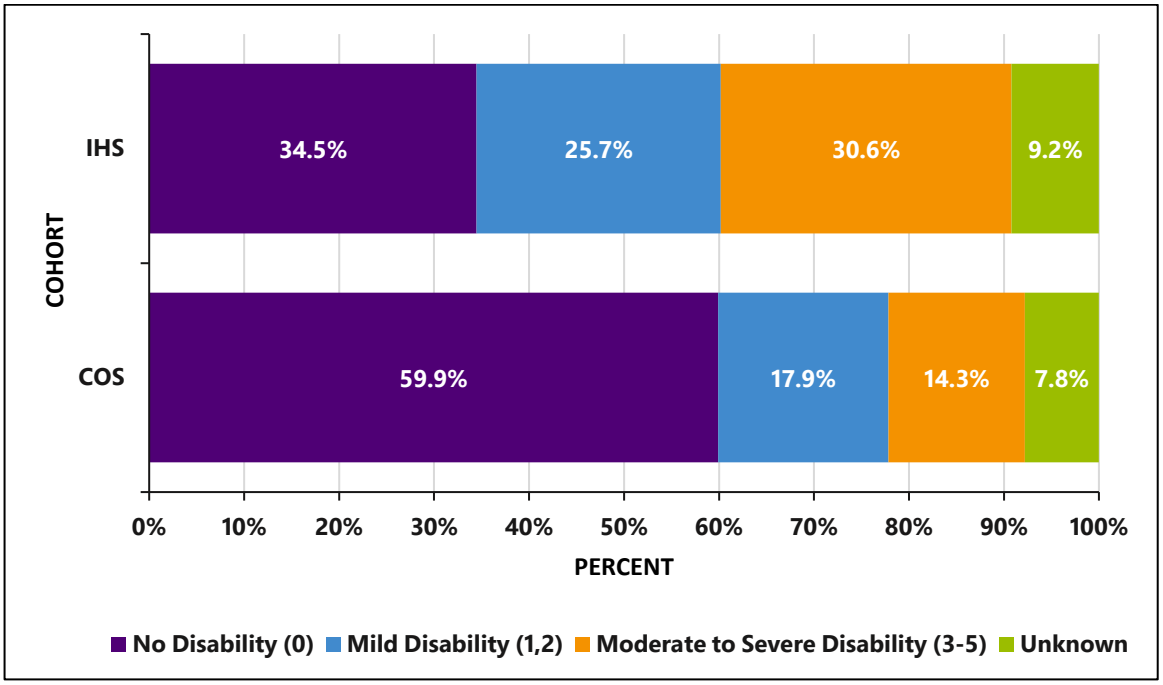

Figure 4.3: Pre-Stroke Modified Rankin Scores by Cohort, (IHS n=618, COS n=10163)

4.6 Principal Diagnosis at Admission

IHS patients are originally admitted to hospital for another reason. Figure 4.4 presents the ICD-10-AM codes assigned as a principal diagnosis for the IHS cohort (n=618). One in every five patients (22.3%, n=138) with IHS had a principal diagnosis coded as diseases of the circulatory system. Ischaemic stroke (I63) was the next most frequent principal diagnosis code at 14.4% (n=89). Injury, poisoning and other consequences of external causes accounted for 13.8% (n=85) of principal diagnoses followed closely by diseases of the respiratory system (12.8%; n= 79).

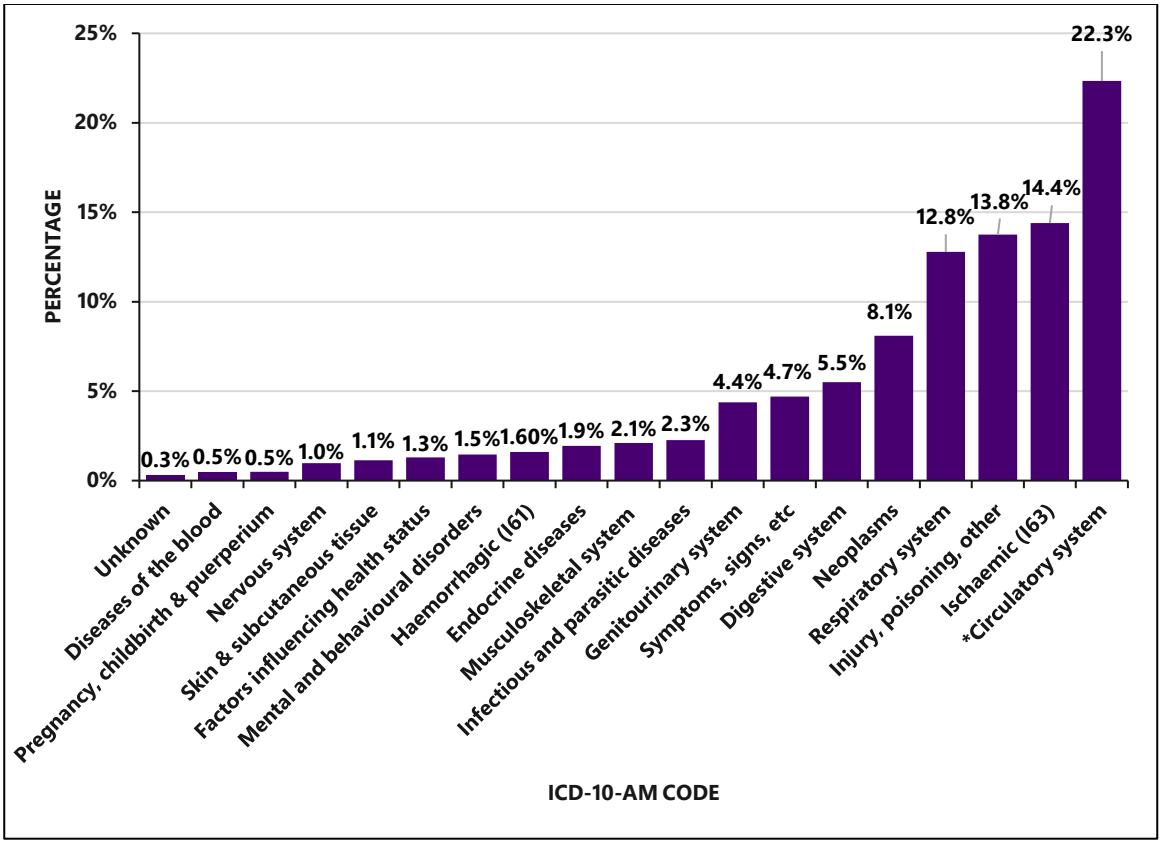

Figure 4.4: Principal Diagnosis Coded Using ICD-10-AM for IHS Cases (n=618)

*****Stroke coded diagnoses I61 and I63 were separated from the ICD-10-AM coded group diseases of the circulatory system

4.7 Critical Care Bed Admissions

Admission to a critical care bed (ICU, HDU or CCU) at any time during a hospital admission is recorded by HIPE. A greater proportion of IHS patients (39.8%, n=246) were admitted to a critical care bed during their inpatient admission compared with 13.7% (n=1390) of COS patients (p<.001). The average LOS in a critical care bed for IHS cases was 4.7 days compared with 0.8 days for COS (p<.001) (Table 4.2). It is not possible from HIPE records to know whether these admissions to critical care level beds were due to the original non-stroke presenting complaint, due to a procedure, or due to the IHS event itself.

4.8 COVID-19 Co-Diagnosis

Patients with IHS were more likely to have a COVID-19 diagnosis during their admission, 7.9% (n=49) compared with merely 2.2% (n=224) of the COS cohort. Differences were observed between cases in 2020 and 2021. In 2020 (n=5265 cases), COVID-19 co-diagnosis occurred in 4.8% (n=15) of IHS and 1.3% (n=62) of COS cases (Fisher's exact test p<.001). In 2021 (n=5516 cases), COVID-19 co-diagnosis was observed at greater frequencies, being recorded in 11.2% (n=34) of IHS and 3.1% (n=162) of COS cases (Pearson 54.67; p<.001).

4.9 Specialty of Care at Discharge

HIPE assigns a speciality at discharge, allowing categorisation as either medical or surgical specialty. Intensive Care (n=17) and ED (n=1) were not categorised resulting in available cases of n=615 and n=10148 for IHS and COS cohorts respectively.

The vast majority (99.1%, n=10069) of COS patients were under a medical specialty at discharge. Whereas 79.9% (n=494) of IHS patients were under the care of a medical specialty at discharge. The breakdown of IHS and COS cases by specialty is presented in Table 4.3. Stroke speciality care can be provided under any one of these three specialities - general medicine, geriatric medicine, or neurology teams - depending on local practices. The majority (94%, n=9548) of COS cases were under the care of either general medicine, geriatric medicine, or neurology teams at discharge. In contrast, just over one-half (59.4%, n=367) of IHS patients were under the care of any one of these three specialities

at discharge. The top five non-stroke specialities at discharge for IHS patients were: Cardiology 7.9% (n=49), Cardiothoracic 5.8% (n=36), General Surgery 4.2% (n=26), Orthopaedics 3.7% (n=23) and Oncology 2.8% (n=17).

Table 4.3: Stroke Cases by Speciality at Discharge by Cohort (IHS n=615; COS n= 10148)

Specialty	Category	Total (n)	COS (n)	IHS (n)	COS (%)	IHS (%)
General Medicine	Medicine	5125	4924	201	48.5%	32.5%
Geriatric	Medicine	3943	3796	147	37.4%	23.8%
Cardiology	Medicine	73	24	49	0.2%	7.9%
Cardio-Thoracic Surgery	Surgery	37	1	36	0.0%	5.8%
General Surgery	Surgery	34	8	26	0.1%	4.2%
Orthopaedics	Surgery	25	2	23	0.0%	3.7%
Neurology	Medicine	847	828	19	8.1%	3.1%
Oncology	Medicine	48	31	17	0.3%	2.8%
Respiratory Medicine	Medicine	130	114	16	1.1%	2.6%
Vascular Surgery	Surgery	32	20	12	0.2%	1.9%
Gastro-Enterology	Medicine	93	84	9	0.8%	1.5%
Endocrinology	Medicine	114	106	8	1.0%	1.3%
Rheumatology	Medicine	70	62	8	0.6%	1.3%
Nephrology	Medicine	56	49	7	0.5%	1.1%
Urology	Surgery	8	1	7	0.0%	1.1%
Infectious Diseases	Medicine	29	23	6	0.2%	1.0%
Haematology	Medicine	10	5	5	0.0%	0.8%
Neurosurgery	Surgery	49	44	5	0.4%	0.8%
Otolaryngology (ENT)	Surgery	4	1	3	0.0%	0.5%
Intensive Care	NC	17	14	3	0.1%	0.5%
Obstetrics/Gynaecology	Surgery	2	0	2	0.0%	0.3%
Plastic Surgery	Surgery	2	0	2	0.0%	0.3%
Breast Surgery	Surgery	2	0	2	0.0%	0.3%
Diabetes Mellitus	Medicine	1	0	1	0.0%	0.2%
Gynaecology	Surgery	2	1	1	0.0%	0.2%
Gastro-Intestinal Surgery	Surgery	2	1	1	0.0%	0.2%
Hepato-Biliary Surgery	Surgery	1	0	1	0.0%	0.2%
Radiotherapy	Medicine	2	1	1	0.0%	0.2%
Psychogeriatric Medicine	Medicine	21	21	0	0.2%	0.0%
Emergency Department	NC	1	1	0	0.0%	0.0%
Palliative Medicine	Medicine	1	1	0	0.0%	0.0%
Total		10781	10163	618	100%	100%

NC – Not Categorised

Chapter 5. Results: Quality-of-Care Measures

5.1 Stroke Unit Admission

Admission to the SU was less likely amongst the IHS cohort compared with the COS cohort (44.2% versus 70.2%; p<.001) (Figure 5.1). Haemorrhagic strokes were less likely to be admitted to the SU when compared with ischaemic strokes (Table 5.1). Only one-third (32.8%) of haemorrhagic strokes occurring in-hospital were admitted to the SU compared with almost two-thirds (64.4%) of haemorrhagic strokes with community-onset (p<.001). The median LOS in the SU was longer for IHS cases at 10 days versus 7 days (p<.001). Both cohorts fell below the target KQI of 90% of cases spending 90% of their hospital stay on the SU. Just over half (57.9%) of COS spent 90% of their hospital stay admitted on the SU compared with one-fifth (19.5%) of the IHS group (p<.001).

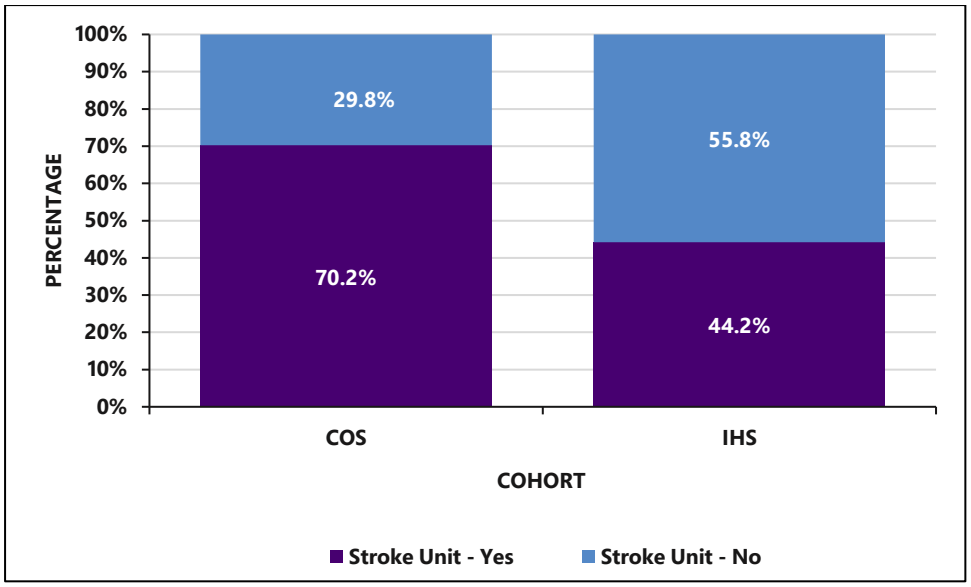

Figure 5.1: Stroke Unit Admission Rates by Cohort, IHS n=618, COS n=10,163

Table 5.1: Stroke Unit Admission by Cohort (IHS n=618; COS n= 10163)

Variable	IHS n (%) (n=618)	COS n (%) (n=10163)	Pearson statistic [a]	P value
SU Admission				
Admitted to SU	273 (44.2%)	7136 (70.2%)	183.80	<.001
Not Admitted to SU	345 (55.8%)	3027 (29.8%)		
Missing	0 (0%)	0 (0%)		
SU Admission by Subtype				
Haemorrhagic				
Admitted to SU	19 (32.8%)	958 (64.6%)	24.39	<.001
Not Admitted to SU	39 (67.2%)	525 (35.4%)		
Ischaemic				
Admitted to SU	242 (46.5%)	6178 (71.2%)	141.22	<.001
Not Admitted to SU	278 (53.5%)	2502 (28.8%)		
Missing	40 (6.5%)	0 (0.0%)		
SU Admission Duration				
SU Stay >90% Admission	52 (19.5%)	4056 (57.9%)	154.87	<.001
SU Stay <90% Admission	215 (80.5%)	2944 (42.1%)		
Missing	5 (1.8%)	43 (0.6%)		
Erroneous % (>100%)	1 (0.4%)	93 (1.3%)		
SU LOS, median days (IQR)	10.0 (5.0-19.75)	7.0 (4-14)	-5.02[a]	<.001
Missing	5 (1.8%)	43 (0.6%)		

[a] Mann-Whitney U test for continuous variable

Binary logistic regression to predict SU admission for the study sample was completed (Table 5.2). The following variables were included in the model: thrombolysis, COVID-19 during admission, specialty at discharge (medicine or surgery), stroke subtype, critical care admission, and stroke cohort (IHS or COS). IHS patients were 50% less likely to be admitted to the SU (OR 0.46; p<.001). Surgical patients (OR 0.15; p<.001) and those with COVID-19 during hospitalisation (OR 0.76; p=0.04) were also less likely to be admitted to the SU. Admission to the SU was twice as likely for thrombolysed patients (OR 2.39; p<.001) and more likely with an ischaemic subtype (OR 1.24; p<.001). When the model

was restricted to the IHS cohort alone, ischaemic strokes were twice as likely to be admitted to the SU (OR 1.96; 95% CI [1.08-3.56]; p=0.03).

Table 5.2: Predictors of Stroke Unit Admission

Variable	OR (95% CI)	p value
Thrombolysis	2.39 (1.99-2.89)	<.001
COVID-19	0.76 (0.59-0.99)	0.04
Specialty (Medicine=0/Surgery=1)	0.15 (0.10-0.22)	<.001
Stroke Subtype (Haemorrhagic=0/Ischaemic=1)	1.24 (1.10-1.39)	<.001
Critical Care Admission	1.07 (0.95-1.22)	0.27
Stroke Cohort (COS=0/IHS=1)	0.46 (0.38-0.56)	<.001

Reasons for non-admission to the SU are displayed in Figure 5.2. Amongst COS cases, the most common reason for non-admission to the SU was due to bed availability (40.2%). The requirement for another specialty bed (29.6%) was the most common reason amongst IHS cases. Of the IHS cases requiring a specialty bed (n=332), three-quarters (73.5%) required an ICU or HDU bed and a further 17.2% (n=52) required a CCU bed. Similar proportions of each cohort could not be admitted to the SU due to infection control risks.

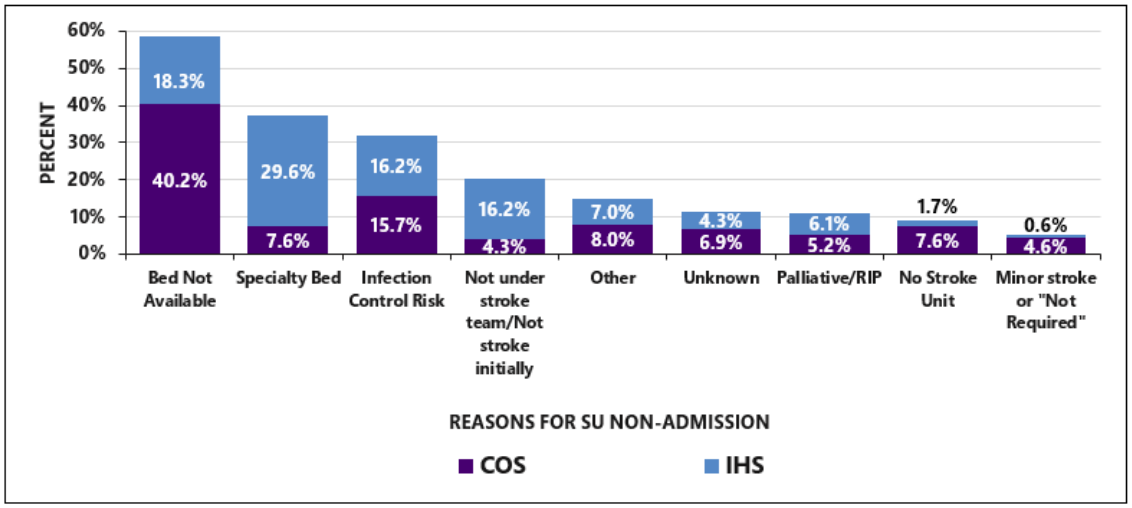

Figure 5.2: Reasons for Stroke Unit Non-Admission by Cohort, (IHS n=345; COS n=3027)

Reasons for non-admission to the SU were also reviewed by stroke subtype given the lower rates of SU admission amongst haemorrhagic strokes compared with ischaemic strokes. Firstly, admission in a neurosurgical unit is not counted by INAS as an admission to the SU which will exert a greater impact on SU admission rates for haemorrhagic strokes compared to ischaemic strokes. This is supported by the data which revealed that amongst haemorrhagic strokes not admitted to the SU, 20.9% (n=118) was due to the requirement of a specialty bed (critical care bed which includes the neurosurgical HDU) compared with just 7.5% (n=209) of ischaemic strokes. Analysis revealed another possible reason that haemorrhagic cases are less likely to be admitted to the SU. 18.3% (n=103) of haemorrhagic stroke cases could not be admitted to the SU as they were palliative or had already died compared with a mere 2.6% (n=72) of the ischaemic stroke cohort. Thus, non-admission to the SU for haemorrhagic strokes could be related to factors specific to haemorrhagic strokes such as complexity of care required and increased mortality leading to earlier death.

5.2 Swallow Screening

There were no significant differences in the proportions receiving swallow screening between IHS (68.2%) and COS (70.3%) groups (p=0.28) (Table 5.3). However, of the patients admitted to the SU, a greater proportion of the IHS cohort (88.4%; n=236) had swallow screening compared with 79.9% (n=5560) of the COS group (Pearson statistic 11.6; p<.001).

Table 5.3: Swallow Screening by Cohort (IHS n=618; COS n= 10163)

Variable	IHS n (%) (n=618)	COS n (%) (n=10163)	Pearson statistic	P value
Swallow Screening				
Swallow Screen Performed	409 (68.2%)	6914 (70.3%)	1.19	0.28
Missing	18 (2.6%)	323 (3.2%)		
Swallow Screen Within 4 hours [a]	180 (45.5%)	2981 (44.6%)	0.12	0.73
Missing	13 (3.2%)	225 (3.3%)		

[a] Swallow screening within 4 hours only calculated for those who had initial swallow screening performed (IHS n=409; COS n=6914)

5.3 Health and Social Care Professionals' Assessments

Similar proportions of the IHS and COS cohorts were reviewed by a health and social care professionals (HSCP) (Table 5.4). A significantly greater proportion of the IHS versus the COS cohort were reviewed by a physiotherapist (96.4% versus 93.8%; p=0.04), speech and language therapist (SALT) (77.0% versus 67.7%; p<.001), dietician (59.2% versus 31.7%; p<.001), and medical social work (MSW) (36.2% versus 24.2%; p<.001). However, a smaller proportion of IHS patients were reviewed by an occupational therapist (OT) (85.0% versus 89.6%; p<.001) or a specialised nurse (70.1% versus 79.8%; p<.001) than COS counterparts. Discussion at a dedicated MDT meeting occurred with lower frequency for IHS patients (63.8%) than COS patients (73.3%; p<.001). Mood screening occurred at low rates in general, but the IHS group had lower observed rates of mood assessment compared to COS patients (28.0% versus 29.5%; p<.001).

5.4 Carotid Disease

There was no significant difference in the proportion of carotid stenosis recorded in the ischaemic stroke subtype between the IHS and COS groups at 7.9% (n=35) and 7.8% (n=638) respectively (p=0.92). A greater proportion of COS cases with carotid stenosis were referred for carotid endarterectomy or carotid stenting (62.5%; n=399) compared with 45.7% (n=16) of IHS cases. However, this did not reach statistical significance on Fisher's exact test (p=0.06).

Table 5.4: Health and Social Care Professionals' Assessments by Cohort (IHS n=618; COS n= 10,163)

Variable	IHS n (%) (n=618)	COS n (%) (n=10163)	Pearson statistic	P value
HSCP Assessment				
HSCP Assessment	535 (87.3%)	8978 (88.4%)	0.76	0.38
Missing	5 (0.8%)	11 (0.1%)		
Physiotherapy [a]				
Physio Assessment	514 (96.4%)	8397 (93.8%)	6.36	0.04
Not Indicated/Assessed	11 (2.1%)/8 (1.5%)	272 (3.0%)/280 (3.1%)		
Missing	2 (0.3%)	29 (0.3%)		
Occupational Therapy [a]				
OT Assessment	452 (85.0%)	7996 (89.6%)	14.67	<.001
Not Indicated/Assessed	43 (8.1%)/37 (7.0%)	415 (4.7%)/513 (5.7%)		
Missing	3 (0.5%)	54 (0.5%)		
Speech & Language Therapy [a]				
SALT Assessment	409 (77.0%)	5998 (67.7%)	20.78	<.001
Not Indicated/Assessed	79 (14.9%)/43 (8.1%)	1733 (19.6%)/1130 (12.8%)		
Missing	4 (0.6%)	117 (1.2%)		
Dietician [a]				
Dietician Assessment	314 (59.2%)	2795 (31.7%)	173.29	<.001
Not Indicated/Assessed	113 (21.3%)/103 (19.4%)	3576 (40.6%)/2440 (27.7%)		
Missing	5 (0.8%)	167 (1.6%)		
Medical Social Work [a]				
MSW Assessment	191 (36.2%)	2130 (24.2%)	46.18	<.001
Not Indicated/Assessed	133 (25.2%)/203 (38.5%)	3195 (36.3%)/3479 (39.5%)		
Missing	8 (1.3%)	174 (1.7%)		
Psychology [a]				
Psychology Assessment	28 (5.4%)	510 (5.8%)	5.50	0.06
Not Indicated/Assessed	145 (28.0%)/345 (66.6%)	2853 (32.7%)/5373 (61.5%)		
Missing	17 (2.8%)	242 (2.4%)		
Specialised Nursing Review				
Nursing Review	431 (70.1%)	8065 (79.8%)	32.95	<.001
Not Assessed	184 (29.9%)	2047 (20.2%)		
Missing	3 (0.5%)	51 (0.5%)		
Mood Screening				

Mood Assessed	159 (28.0%)	2857 (29.5%)	15.26	<.001
Not Indicated/Assessed	177 (31.2%)/231 (40.7%)	3619 (37.4%)/3203 (33.1%)		
Missing	51 (8.3%)	484 (4.8%)		
Multidisciplinary Meeting				
MDT Meeting	372 (63.8%)	7309 (73.3%)	32.67	<.001
Not Indicated/Assessed	58 (9.9%)/153 (26.2%)	948 (9.5%)/1711 (17.2%)		
Missing	35 (5.7%)	195 (1.9%)		

[a] These variables are only completed during audit data entry, if HSCP assessment is answered as yes (IHS n=535; COS n=8978)

5.5 Antithrombotic Therapy

The prescription of antithrombotic therapy was greater amongst the COS cohort (90.7%; n=7764) compared to the IHS cohort (73.9%; n=369; p<.001) (Figure 5.3). Contraindications to antithrombotic therapy were more frequently reported amongst the IHS group at 11.4% (n=57) versus 3.7% (n=319) of the COS group.

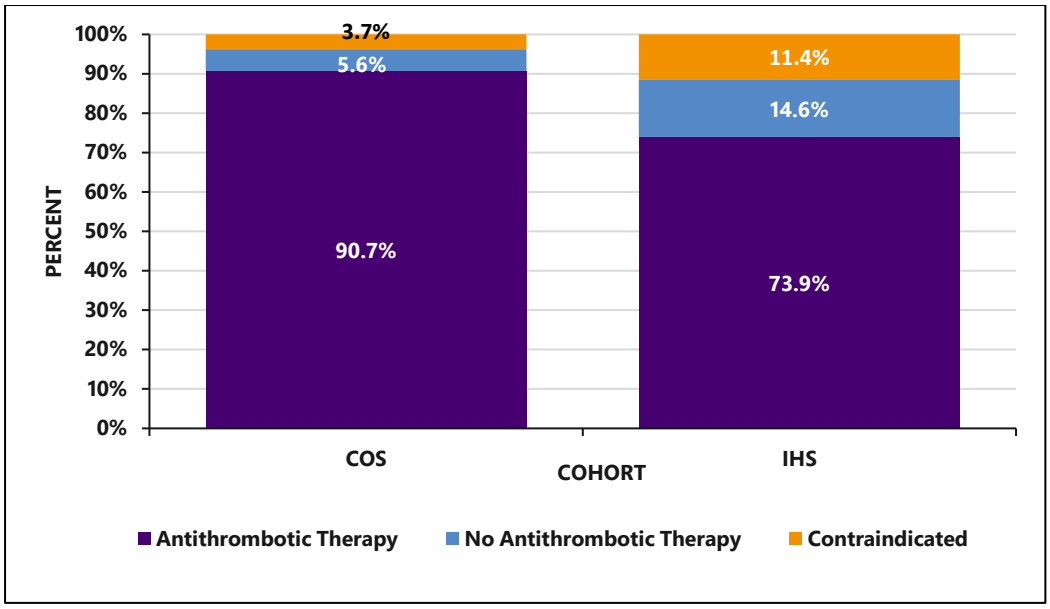

Figure 5.3: Antithrombotic Therapy Amongst Ischaemic Strokes by Cohort, IHS n= 520, COS n=8680

5.6 Atrial Fibrillation

AF was reported significantly more often amongst the IHS cohort (40.6%; n=198 versus 29.8% n=2386; p<.001) (Figure 5.4). Missing data rates were notably high at 7.8% (n=715) for this variable owing to unknown answers and investigations for AF pending at the point of discharge. Of those with AF, 81.6% (n=1849) of the COS cohort were anticoagulated compared with 73.0% (n=135) of the IHS cohort (p=0.004). The most common reasons cited for not anticoagulating the remaining patients with AF included severe illness (34.0% of IHS versus 28.3% of COS), frailty (26.0% of IHS versus 20.1% of COS), major bleeding (18.0% of IHS versus 25.9% of COS) with no reasons given in 18.0% of IHS and 19.9% of COS. The remaining lower frequency reasons reported included poor compliance, falls and liver disease which when combined accounted for 4.0% of IHS and 5.7% of COS cases.

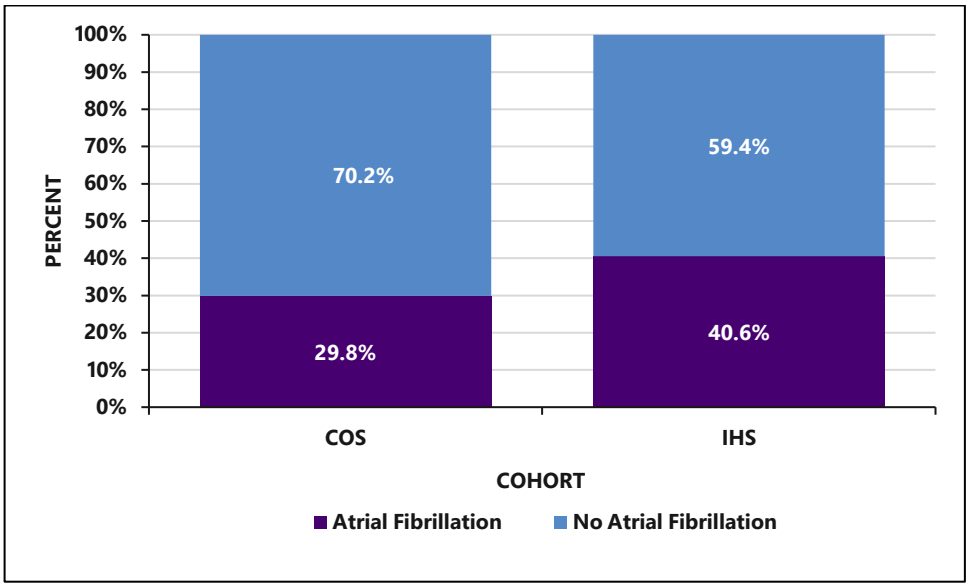

Figure 5.4: Atrial Fibrillation Amongst Ischaemic Strokes by Cohort, IHS n= 520, COS n=8680

5.7 Interval to Stroke Symptom Onset

Analysis of the IHS cohort revealed that the average time spent in hospital prior to the onset of stroke symptoms was 16 days (SD 43 days). The median time in hospital prior to stroke onset was 6 days (IQR 2-14 days). One-quarter (25.4%, n=126) of IHS cases had onset within the first two days of hospitalisation with a further one-third (33.4%; n=166) occurring between day 3 and 7 of admission. Overall, 90.1% (n=448) of IHS events occurred within 30 days of admission to hospital. Of the 618 IHS patients, data variables of admission date and stroke symptom onset date were recorded and correct for 80.4% (n=497).

During the two-year period for this report, 47.4% (n=2808) of COS patients presented within 3 hours of symptom onset to hospital. The median interval between onset and hospital arrival was 3 hours and 20 minutes (IQR 1 hour and 40 minutes to 10 hours and 30 minutes). Just over half (58.3%; n=5924) of the COS cohort had available and correct entries for the data variables of stroke symptom onset date and hospital arrival date required for this data variable (Table 5.5).

Table 5.5: Availability and Correctness of Time-based Data Variables by Cohort

Time-Based Intervals; IHS Cohort (n=618)	**Available n (%)**	**Missing n (%)**	**Entry Error n (%)**
From Hospital Admission Date to Stroke Symptom Onset Date (days)	497 (80.4%)	46 (7.4%)	75 (12.1%)
From Stroke Symptom Onset Date & Time to Medical Review (mins)	276 (44.7%)	328 (53.1%)	14 (2.3%)
From Stroke Symptom Onset Date & Time to CT Imaging [a] (mins)	285 (46.1%)	316 (51.1%)	17 (2.8%)
From Stroke Symptom Onset Date & Time to Thrombolysis [b] (mins)	30 (66.7%)	13 (28.9%)	2 (4.4%)
Time-Based Intervals; COS Cohort (n=10163)	**Available n (%)**	**Missing n (%)**	**Entry Error n (%)**
From Stroke Symptom Onset Date to Hospital Arrival Date (hours)	5924 (58.3%)	4169 (41.0%)	70 (0.07%)
From Hospital Arrival Date & Time to Medical Review (mins)	8496 (83.6%)	1533 (15.1%)	134 (1.3%)
From Hospital Arrival Date & Time to CT Imaging [c] (mins)	9264 (91.2%)	746 (7.3%)	153 (1.5%)
From Hospital Arrival Date & Time to Thrombolysis [d] (mins)	827 (96.4%)	10 (1.2%)	21 (2.4%)

[a] Of the n=316 missing values, n=16 had no CT performed. [b] n=45 cases were ischaemic strokes and received thrombolysis. [c] Of the n=746 missing values, n=649 had no CT performed. [d] n=858 were ischaemic strokes and received thrombolysis.

5.8 Time to Medical Review

The total cases available for analysis for this variable assessing time to medical review were 276 cases (44.7%) and 8496 cases (83.6%) for the IHS and COS cohorts respectively (Table 5.5). The IHS cohort had a median time to medical review of 20 minutes (IQR 5 to 84 minutes) (Figure 5.5). The median time to medical review was significantly shorter in the COS cohort at 12 minutes (IQR 0 to 100 minutes; p<.001).

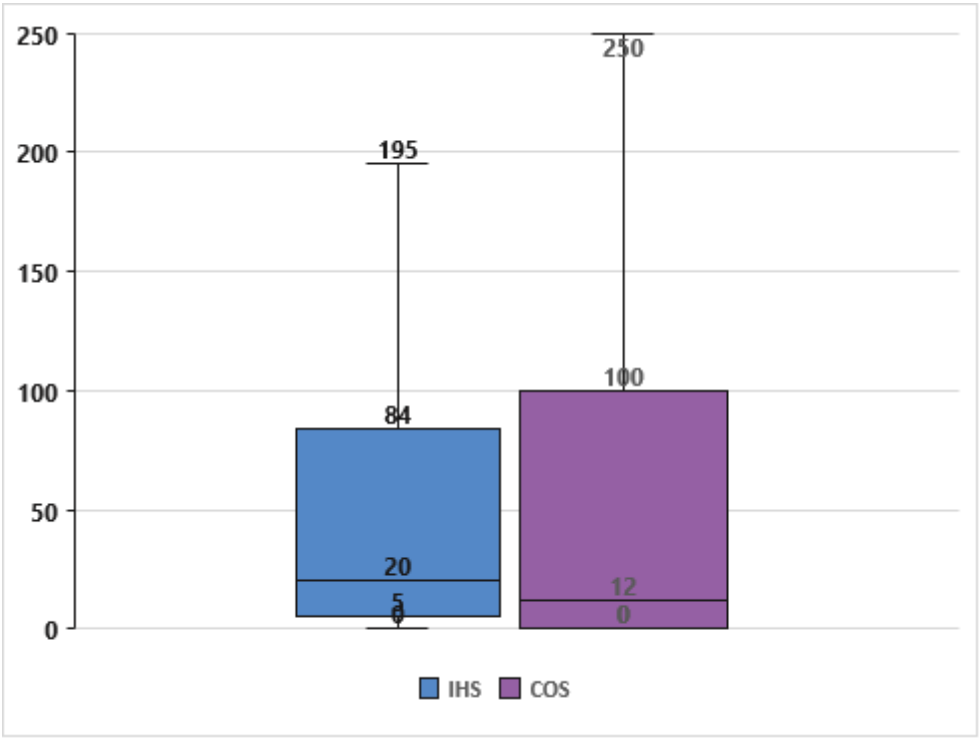

Figure 5.5: Box and Whisker Plot of Time to Medical Review from Stroke Symptom Onset (IHS n=276) or Hospital Arrival (COS n=8496)

Overall, the proportion of IHS patients medically reviewed within 30 minutes (65%, n=180) was slightly more than the COS cohort at 61% (n=5157) (Figure 5.6).

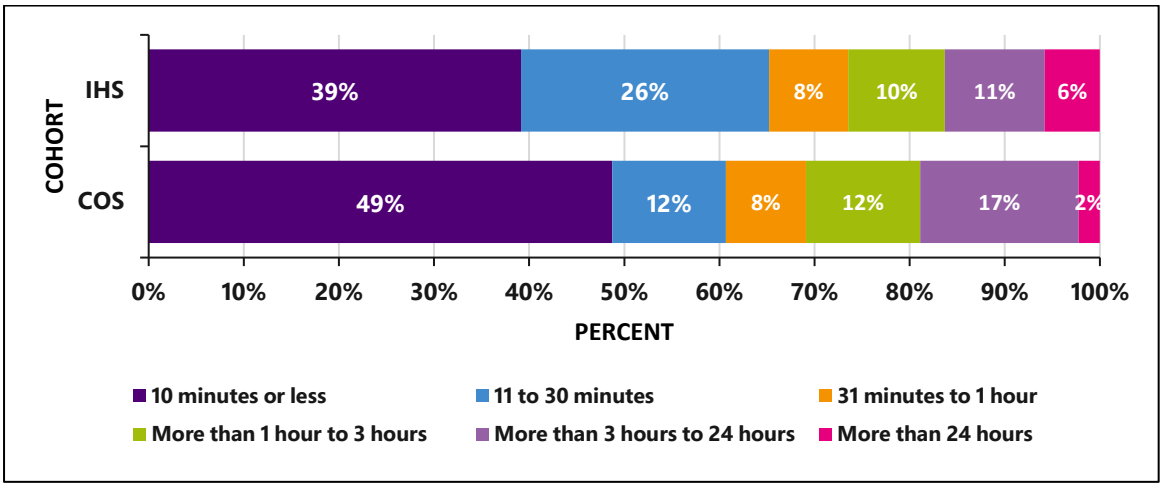

Figure 5.6: Time to Medical Review from Stroke Symptom Onset for IHS Cases (n=276) or Hospital Arrival for COS Cases (n=8496)

5.9 Time to Brain Imaging

In total, 98.1% (n=606) of IHS and 93.6% (n=9514) of COS patients had CT or MRI scan. The audit coordinator indicated that imaging happened pre-admission or transfer in 1.3% (n=8) of IHS cases and in 6.0% (n=604) of COS cases. No imaging was completed in 0.5% (n=3) and 0.3% (n=35) of IHS and COS cases respectively. In eleven cases it was unknown if imaging had occurred. The cases available for analysis were n=285 and n=9264 of the IHS and COS cohorts respectively (Table 5.5). The median time to brain imaging was similar between the two cohorts at 64 minutes (IQR 27 to 248 minutes) and 66 minutes (IQR 35 to 156 minutes) for COS and IHS patients respectively (p=0.49) (Figure 5.7).

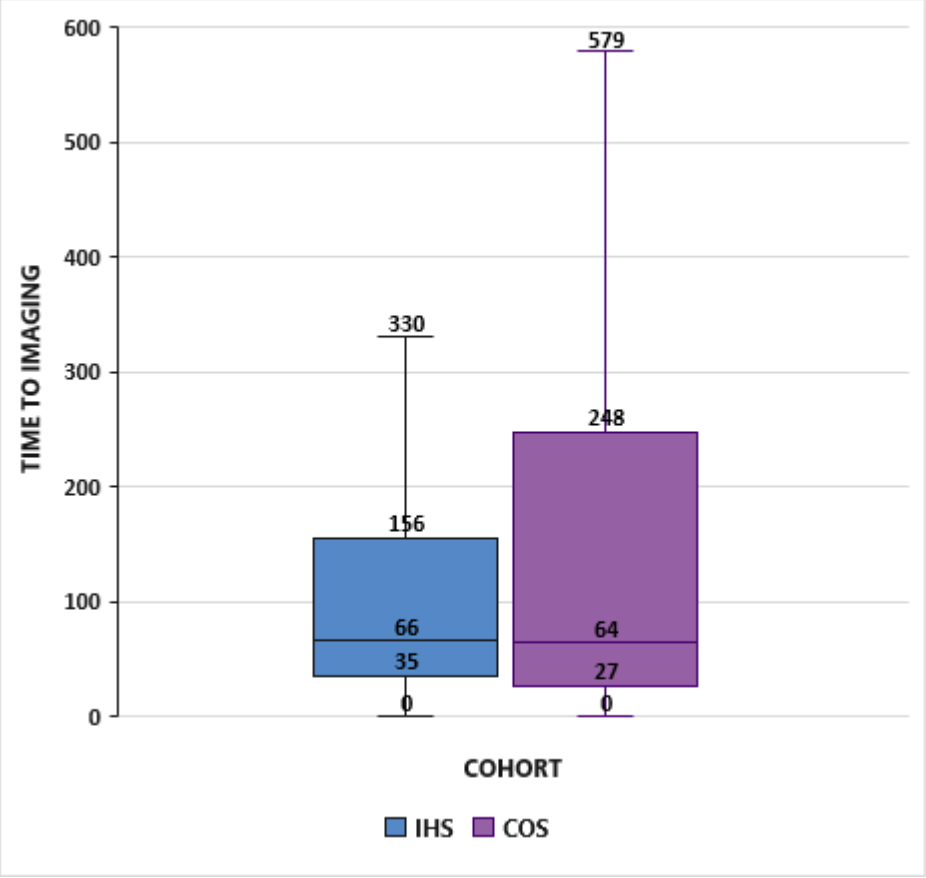

Figure 5.7: Box and Whisker Plot of Time to Brain Imaging from Stroke Symptom Onset (IHS n=285) or Hospital Arrival (COS n=9264)

The proportion of patients receiving brain imaging within 1 hour of hospital arrival (COS) or stroke symptom onset (IHS) was comparable at 48.7% (n=4516) and 47.4% (n=135) of COS and IHS cohorts respectively (Figure 5.8).

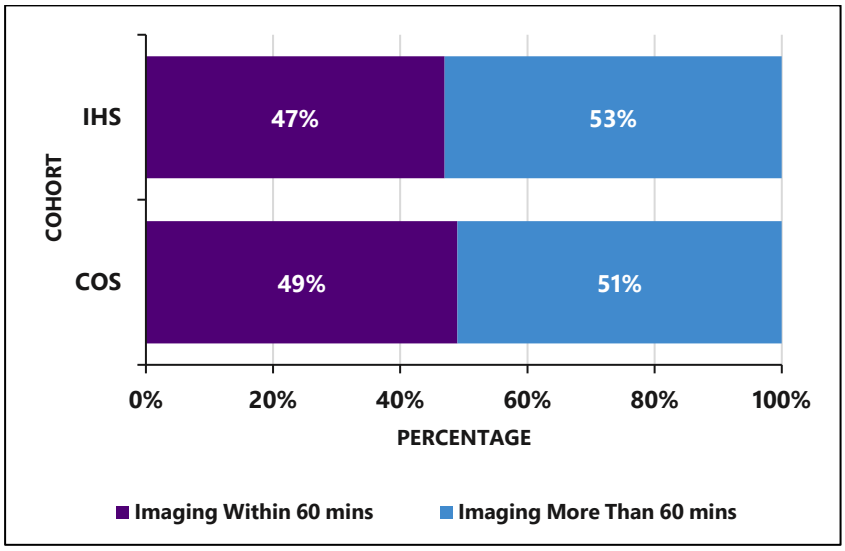

Figure 5.8: Time to Brain Imaging from Stroke Symptom Onset for IHS Cases (n=285) or Hospital Arrival for COS Cases (n=9264)

5.10 Time to Thrombolysis

The median time to thrombolysis amongst the IHS cohort was substantially longer (90 minutes, IQR 63 to 135 minutes) than the COS cohort (54 minutes, IQR 37 to 80 minutes; p<.001) (Figure 5.9).

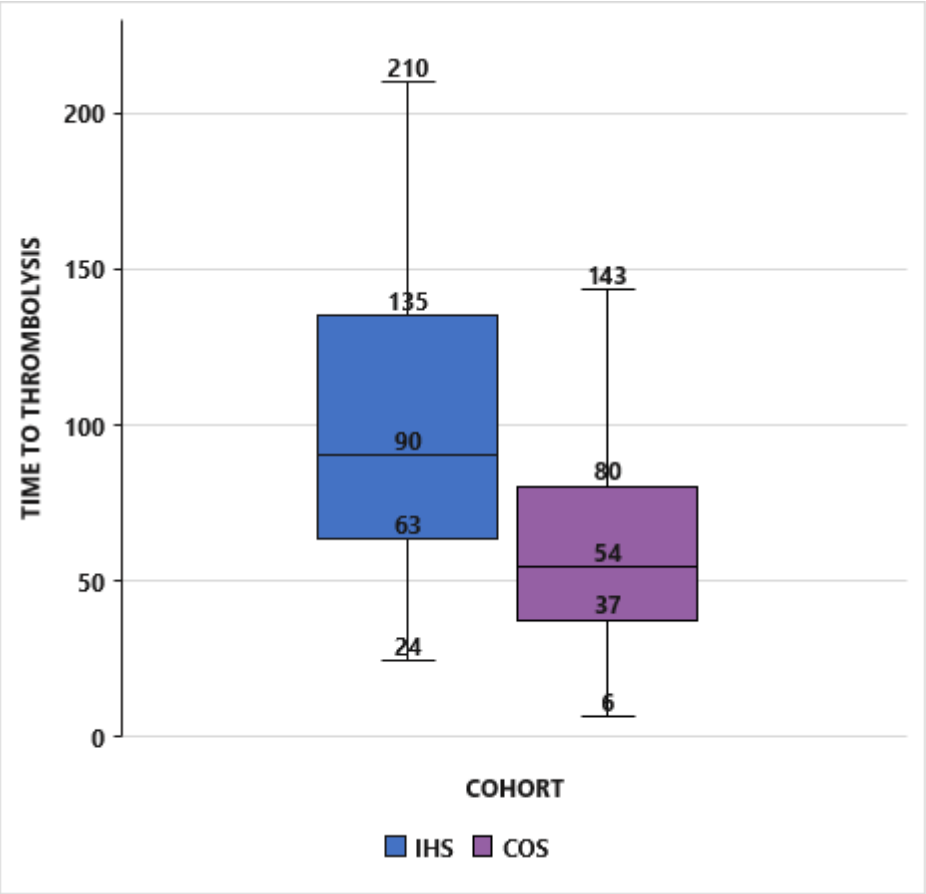

Figure 5.9: Box and Whisker Plot of Time to Thrombolysis from Stroke symptom Onset (IHS n=30) or Hospital Arrival (COS n=827)

Over one-half (58.2%; n=481) of COS patients received thrombolysis within 1 hour at compared with just 23.3% (n=7) of IHS patients (Figure 5.10). The majority (76.7%, n=23) of IHS patients received thrombolysis more than 60 minutes after the onset of stroke symptoms.

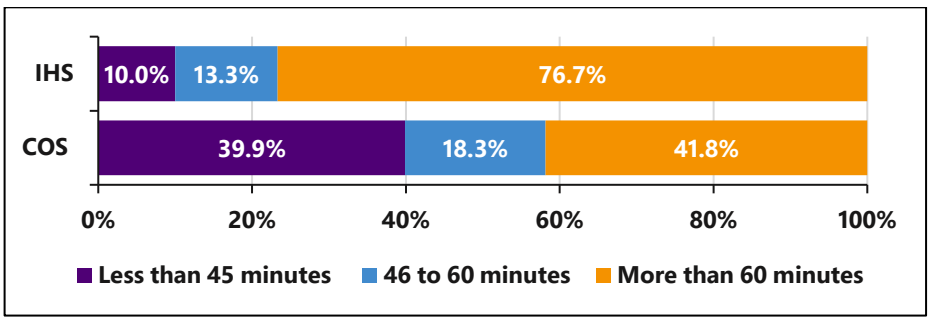

Figure 5.10: Distribution of Time to Thrombolysis from Stroke Symptom Onset (n=30) or Hospital Arrival (COS n=827)

5.11 Summary of Performance on Time-based Intervals

Overall, COS patients were reviewed by a doctor more swiftly than IHS patients, 12 minutes versus 20 minutes. Whilst there were no comparable differences in times to brain imaging between the two cohorts, times to thrombolysis were significantly longer amongst IHS cases (Table 5.6).

Table 5.6: Summary of Time-Based Intervals Performance by Cohort

	IHS Median Time (mins)	COS Median Time (mins)	Mann-Whitney Z Score	p value
Time to Medical Review	20	12	-3.75	<.001
Time to Brain Imaging	66	64	-0.69	0.49
Time to Thrombolysis	90	54	-4.55	<.001

Chapter 6. Results: Outcomes

6.1 Length-of-Stay

Firstly, total hospital LOS between the two cohorts was compared. This revealed a significantly longer median LOS for the IHS group (22 days) compared with the COS group (8 days; p<.001) (Table 6.1). However, as noted in Section 1.8.4, to facilitate fairer comparison between IHS and COS groups the total length of stay for COS was compared directly with the LOS following stroke for the IHS. Median LOS in hospital following a stroke event was still longer amongst the IHS cohort compared with COS equivalents. The median LOS following stroke remained significantly longer at 14 days for the IHS patients and maintained statistical significance when compared with COS equivalents' total hospital LOS (Mann-Whitney U test statistic -9.20; p<.001).

Table 6.1: Comparison of Median Length of Stay by Cohort

Cohort	Variable	Median (days)	IQR (Days)	Total Bed Days	Mann-Whitney Z Score	p value
COS (n= 10163)	Total Hospital LOS	8	4 – 16	152269		
IHS (n=618)	Total Hospital LOS	22	11 – 42	22185	-20.82	<.001
IHS (n=536) [a]	LOS Following Stroke	14	6 – 30	13882	-9.20	<.001

[a] Missing data variables render IHS cohort n=536 for LOS following stroke. Unknown symptom onset date n=46, incorrect negative values on subtraction to yield interval from admission to onset n=23, incorrect negative values on subtraction to yield interval from admission to onset from total LOS n=13.

6.2 Thrombolysis Rates

Overall, the proportion of ischaemic strokes (8.7%) that received thrombolysed in the IHS cohort was slightly less than the COS cohort (9.9%), although this did not reach statistical significance (p=0.36). Thrombolysis rates amongst ischaemic strokes admitted under the care of a medical specialty were comparable between the two cohorts (9.5% for IHS versus 9.9% for COS). A trend towards higher rates of thrombolysis amongst IHS patients

was observed in model 3 hospitals (Table 6.2). The inverse trend was seen in model 4 hospitals where lower rates of thrombolysis were recorded amongst the IHS group (6.6%) when compared with the COS group (10.8%). This trend towards lower thrombolysis rates in model 4 hospitals was statistically significant (p=0.02).

Table 6.2: Subgroup Analysis of Thrombolysis Rates (IHS n=520; COS n=8675)

Subgroup	IHS n (%) (n=520)	COS n (%) (n=8675) [a]	Statistic	P value
Total Cohort				
Thrombolysed	45 (8.7%)	858 (9.9%)	0.85	0.36
Missing	0 (0.0%)	5 (0.09%)		
Pre-stroke mRS 0-2 (n=7118)				
Thrombolysed	35 (11.1%)	733 (10.8%)	0.03	0.87
Missing	0 (0.0%)	3 (0.04%)		
Pre-stroke mRS 3 or more (n=1368)				
Thrombolysed	8 (5.1%)	86 (7.1%)	0.92	0.34
Missing	0 (0.0%)	1 (0.07%)		
Medical Specialty (n=9046)				
Thrombolysed	39 (9.5%)	855 (9.9%)	0.08	0.78
Missing	0 (0.0%)	5 (0.06%)		
Model 3 Hospital (n=3956)				
Thrombolysed	23 (12.2%)	327 (8.7%)	2.79	0.10
Missing	0 (0%)	4 (0.1%)		
Model 4 hospital (n=5244)				
Thrombolysed	22 (6.6%)	531 (10.8%)	5.78	0.02
Missing	0 (0%)	1 (0.02%)		

[a] Total number of ischaemic strokes in COS cohort was n=8680. However, n=5 cases had no data entry for thrombolysis variable, hence total n=8675

Per hospital thrombolysis data is not presented within the body of this report as prior INAS publications have reported on per hospital thrombolysis rates for 2020 (NOCA, 2022b) and 2021 (NOCA, 2023). Furthermore, given the small numbers of thrombolysed cases (n=45) within the IHS cohort, data presentation would be impacted by the requirement for case suppression for five or less cases. Finally, the proportion of

ischaemic strokes not receiving thrombolysis due to a contraindication was the same between the two cohorts (Figure 6.1).

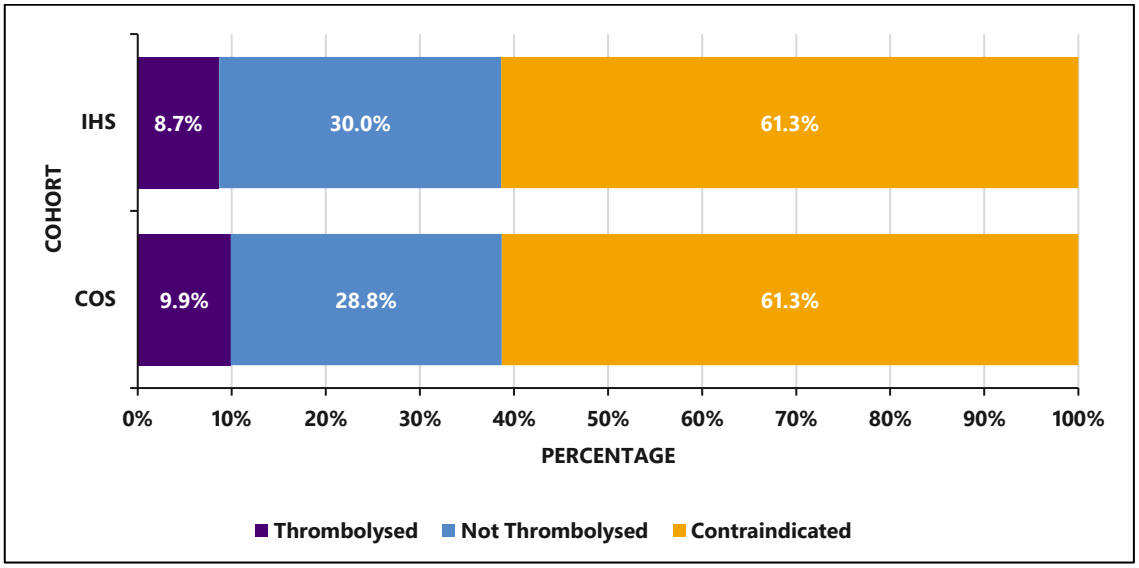

Figure 6.1: Proportion of Ischaemic Strokes Receiving Thrombolysis by Cohort, (IHS n=520; COS n=8675)

6.3 In-Hospital Mortality

The proportion of IHS patients that died in-hospital was higher amongst IHS patients. Overall, about one in four cases (27.2%) of IHS died in-hospital following a stroke compared with one in ten (10.4%) cases of COS (p<.001) (Table 6.3). The mortality rate for haemorrhagic stroke is higher than ischaemic strokes. One in two haemorrhagic strokes (56.9%) died in the IHS cohort compared to 28.7% of the COS cohort. Patients with greater disability (mRS of 3 or more) prior to stroke onset also demonstrated significantly higher mortality rates at 43.4% and 21.8% for IHS and COS groups respectively.

Table 6.3: In-Hospital Mortality by Cohort (IHS n=618; COS n=10163) With Subgroup Analysis

Subgroup	IHS n (%)	COS n (%)	Statistic	P value
Total Cohort	n=618	n=10163		
Mortality	168 (27.2%)	1056 (10.4%)	163.26	<.001
Ischaemic Subtype	n=520	n=8680		
Mortality	130 (25.0%)	630 (7.3%)	203.78	<.001
Haemorrhagic Subtype	n=58	n=1483		
Mortality	33 (56.9%)	426 (28.7%)	21.18	<.001
Thrombolysis Subgroup	n=45	n=858		
Mortality	7 (15.6%)	74 (8.6%)	2.52	0.11
No Thrombolysis Subgroup	n=475	n=7817		
Mortality	123 (25.9%)	554 (7.1%)	211.25	<.001
Age < 65 years	n=123	n=2694		
Mortality	26 (21.1%)	148 (5.5%)	49.68	<.001
Age > 65 years	n=495	n=7469		
Mortality	142 (28.7%)	908 (12.2%)	110.82	<.001
Pre-Stroke mRS 0-2	n=372	n=7911		
Mortality	72 (19.4%)	613 (7.7%)	63.09	<.001
Pre-Stroke mRS >3	n=189	n=1460		
Mortality	82 (43.4%)	318 (21.8%)	42.52	<.001

The unadjusted OR for mortality revealed that IHS patients had 3-fold higher in-hospital mortality (3.22 95% CI 2.67 to 3.89; p<.001) than COS counterparts (Table 6.4). Binary logistic regression was performed on the total cohort to predict mortality with a model including predictor variables. Age, stroke subtype, SU admission, COVID-19, pre-stroke disability, atrial fibrillation, and stroke cohort, were statistically significant predictors of mortality. Specifically, in-hospital mortality remained 3-fold higher for the IHS cohort with aOR of 2.98 (95% CI 2.37 to 3.75; p<.001) and patients with COVID-19 during their hospitalisation were more than twice as likely to die (aOR 2.43; 95% CI 1.72 to 3.43; p<.001). On the other hand, ischaemic subtype (aOR 0.20; 95% CI 0.17 to 0.24), SU admission (aOR 0.56; 95% CI 0.49 to 0.65) and favourable pre-stroke function (aOR 0.37; 95% CI 0.31 to 0.43) were associated with decreased odds of in-hospital mortality.

Table 6.4: Binary Logistic Regression for In-Hospital Mortality for Total Cohort

Variable	Unadjusted OR (95% CI)	aOR (95% CI)	p value
Sex	0.84 (0.74-0.94)	1.07 (0.92-1.23)	0.37
Age >65 years	2.31 (1.95-2.73)	1.88 (1.52-2.31)	<.001
Stroke Cohort (COS=0/IHS=1)	3.22 (2.67-3.89)	2.98 (2.37-3.75)	<.001
COVID-19	2.85 (2.16-3.76)	2.43 (1.72-3.43)	<.001
Stroke Subtype (Haemorrhagic=0/Ischaemic=1)	0.21 (0.19-0.24)	0.20 (0.17-0.24)	<.001
SU Admission	0.49 (0.43-0.55)	0.56 (0.49-0.65)	<.001
Pre-Stroke mRS 0-2	0.28 (0.25-0.32)	0.37 (0.31-0.43)	<.001
Atrial Fibrillation	1.64 (1.44-1.87)	1.50 (1.29-1.75)	<.001

When binary logistic regression analysis was conducted separately for the IHS and COS groups (Table 6.5), only pre-stroke disability (aOR 0.37; 95% CI 0.24-0.57), stroke subtype (aOR 0.23; 95%CI 0.12-0.44), and SU admission (aOR 0.46; 95% CI 0.30-0.72) remained significant predictors of mortality amongst the IHS cohort.

Table 6.5: Binary Logistic Regression for In-Hospital Mortality by Cohort

Variable	OR (95% CI)	p value
COS Cohort		
Sex	1.07 (0.92-1.25)	0.40
Age >65 years	1.95 (1.56-2.44)	<.001
COVID-19	2.66 (1.81-3.92)	<.001
Stroke Subtype (Haemorrhagic=0/Ischaemic=1)	0.20 (0.17-0.24)	<.001
SU Admission	0.58 (0.49-0.68)	<.001
Pre-Stroke mRS 0-2	0.37 (0.31-0.43)	<.001
Atrial Fibrillation	1.52 (1.29-1.79)	<.001
Variable	**OR (95% CI)**	**p value**
IHS Cohort		
Sex	1.08 (0.70-1.66)	0.72
Age >65 years	1.34 (0.75-2.42)	0.33
COVID-19	1.66 (0.80-3.46)	0.18
Stroke Subtype (Haemorrhagic=0/Ischaemic=1)	0.23 (0.12-0.44)	<.001
SU Admission	0.46 (0.30-0.72)	<.001
Pre-Stroke mRS 0-2	0.37 (0.24-0.57)	<.001
Atrial Fibrillation	1.40 (0.89-2.19)	0.15

6.4 Modified Rankin Score at Discharge

Greater post-stroke disability is reported for the IHS cohort (Figure 6.2). Just over one-half (52.3%) of COS compared with just over one-quarter (28.9%) of IHS had a favourable mRS 0-2 at discharge. Even when analysis excluded patients with poorer pre-stroke disability (mRS score of 3 or above), IHS patients still demonstrated greater disability at discharge than COS equivalents (Table 6.6). A greater burden of disability is carried by the haemorrhagic subtype amongst IHS cases with moderate to severe disability at discharge in 90.2% of haemorrhagic IHS cases compared with 70.5% of COS cases (p=0.002).

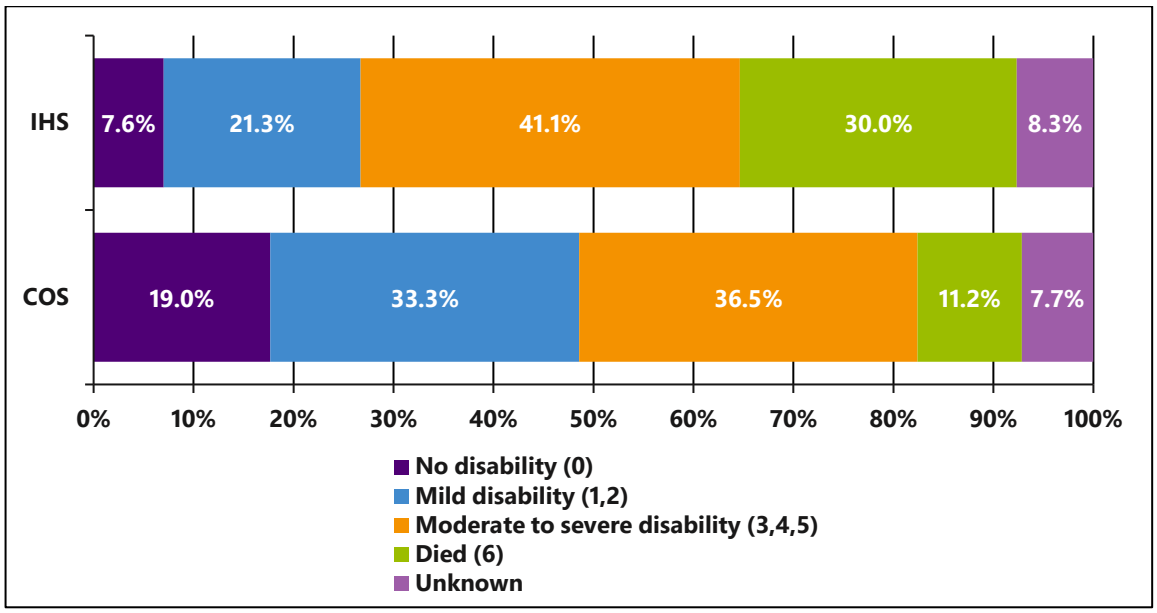

Figure 6.2: Modified Rankin Score at Discharge by Cohort (IHS n=618; COS n=10163)

Table 6.6: Modified Rankin Score at Discharge by Cohort, (IHS n=618, COS n=10163)

	IHS n (%)	COS n (%)	Statistic	P value
Total Cohort	n=618	n=10163		
mRS 0-2 at discharge	164 (28.9%)	4907 (52.3%)	116.88	<.001
mRS 3-6 at discharge	403 (71.1%)	4476 (47.7%)		
Missing	51 (8.3%)	780 (7.7%)		
Excluded Pre-Stroke mRS >3	n=372	n=7911		
mRS 0-2 at discharge	160 (44.7%)	4862 (62.8%)	47.67	<.001
mRS 3-6 at discharge	198 (55.3%)	2879 (37.2%)		
Missing	14 (3.8%)	170 (2.1%)		
Ischaemic	n=520	n=8680		
mRS 0-2 at discharge	147 (30.6%)	4493 (56.2%)	121.52	<.001
mRS 3-6 at discharge	334 (69.5%)	3485 (43.7%)		
Missing	39 (7.5%)	702 (8.1%)		
Haemorrhagic	n=58	n=1483		
mRS 0-2 at discharge	5 (9.8%)	414 (29.5%)	9.28	0.002
mRS 3-6 at discharge	46 (90.2%)	991 (70.5%)		
Missing	7 (12.1%)	78 (5.3%)		

Binary logistic regression was performed on the total cohort to predict variables associated with an mRS of 0-2 at discharge (Table 6.7). An IHS case was 62% less likely to be discharged with an mRS 0-2 (aOR 0.38 95% CI 0.30–0.48; p<.001). The strongest predictor of a favourable mRS at discharge was the pre-stroke mRS recorded. A pre-stroke mRS of 0-2 was associated with an almost 100-fold increase in the likelihood of an mRS of 0-2 at discharge (aOR 99.59 95% CI 65.05-152.48; p<.001). Ischaemic subtype had an aOR of 3.74 (95% CI 3.24-4.30; p<.001) for mRS score 0-2 at discharge.

Table 6.7: Binary Logistic Regression for Modified Rankin Score at Discharge for Total Cohort

Variable	Unadjusted OR (95% CI)	aOR (95% CI)	p value
Sex	1.56 (1.48-1.73)	1.19 (1.08-1.31)	<.001
Age > 65 years	0.31 (0.28-0.34)	0.49 (0.43-0.55)	<.001
Stroke Cohort (COS=0/IHS=1)	0.37 (0.31-0.45)	0.38 (0.30-0.48)	<.001
Stroke Subtype (Haemorrhagic=0/Ischaemic=1)	3.00 (2.66-3.40)	3.74 (3.24-4.30)	<.001
SU Admission	0.81 (0.74-0.88)	0.58 (0.53-0.67)	<.001
Pre-Stroke mRS 0-2	113.89 (75.28-172.31)	99.59 (65.05-152.48)	<.001
Atrial Fibrillation	0.46 (0.42-0.51)	0.60 (0.53-0.67)	<.001

Binary logistic regression exclusively on the IHS cohort revealed that age above 65 years, atrial fibrillation, stroke subtype and pre-stroke mRS remained significant predictors of mRS 0-2 at discharge (Table 6.8). Ischaemic subtype had a 5-fold likelihood of better functional outcome at discharge for the IHS stroke cohort. A good pre-stroke functional level was strongly influential on better functional outcomes at discharge for the IHS cohort with an aOR of 115.09 (95% CI 15.85-835.44). Admission to the SU had no impact on mRS reported at discharge.

Table 6.8: Binary Logistic Regression for Modified Rankin Score at Discharge by Cohort

Variable	OR (95% CI)	p value
COS Cohort		
Sex	1.20 (1.09-1.33)	<.001
Age >65 years	0.49 (0.44-0.55)	<.001
Stroke Subtype (Haemorrhagic=0/Ischaemic=1)	3.72 (3.22-4.29)	<.001
SU Admission	0.56 (0.50-0.63)	<.001
Pre-Stroke mRS 0-2	99.26 (64.16-153.56)	<.001
Atrial Fibrillation	0.60 (0.53-0.67)	<.001
Variable	**OR (95% CI)**	**p value**
IHS Cohort		
Sex	0.95 (0.59-1.52)	0.82
Age >65 years	0.41 (0.24-0.70)	0.001
Stroke Subtype (Haemorrhagic=0/Ischaemic=1)	5.25 (1.88-14.66)	0.002
SU Admission	0.99 (0.62-1.57)	0.95
Pre-Stroke mRS 0-2	115.09 (15.85-835.44)	<.001
Atrial Fibrillation	0.58 (0.35-0.96)	0.03

6.5 Discharge Destination

Discharge home was less likely amongst IHS with an aOR of 0.39 (95% CI 0.32 to 0.47; p<.001) when adjusted for age, sex, subtype, pre-stroke disability and SU admission. 60.3% (n=6067) of the COS cohort were discharged home either directly or with an early supported discharge (ESD) programme compared with 37.3% (n=228) of the IHS cohort (p<.001) (Figure 6.3). One in ten patients (10.6%; n=65) with IHS were discharged to LTC compared with 6.0% (n=607; p<.001).

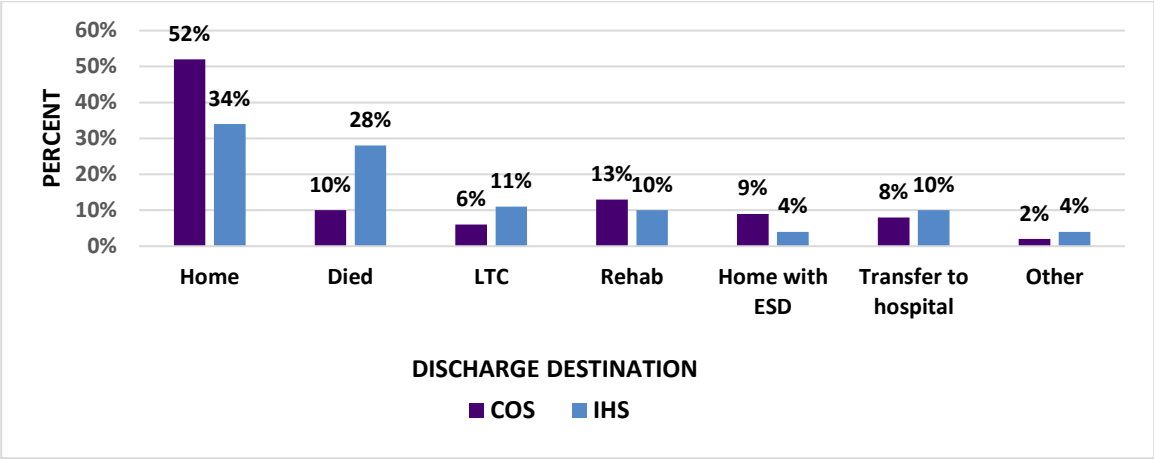

Figure 6.3: Discharge Destination by Cohort, (IHS n=618; COS n=10163)

Chapter 7. Discussion: Demographics and Quality-of-Care Measures

7.1 IHS Rate

There were 618 IHS cases and 10,163 COS cases yielding a national IHS rate in Ireland of 5.7% for the two-year reporting period. This falls within the range of 1% and 17% reported in the IHS literature (Section 1.7). Multi-centre registry datasets tend to yield lower overall rates of IHS when compared with studies at a single site (Nouh et al., 2022, Akbik et al., 2020). IHS rates of between 1.1% and 5.9% were reported amongst four large registry-based studies which all included more than 10,000 IHS cases. When three studies with similarly sized IHS cohorts to this retrospective cohort study were reviewed, the rate of IHS was slightly higher at 3.3% (n=973) (Saltman et al., 2015), 4.4% (n=694) (Kimura et al., 2006), and 10.8% (n=552) (Emmett et al., 2019). Overall, the IHS rate of 5.7% or 1 in every 17 strokes is consistent with the published literature.

The rate of 5.7% may under represent cases of IHS in an Irish context for a few reasons. Firstly, as already explained IHS cases tend to be under-reported during data entry input to stroke registers. Secondly, the incorporation of IHS case reporting into INAS is still relatively recent, being mandatory only since 2020. Chapter 2 explained the clinical validation study of the definition of IHS within an Irish context. One of the major findings was the heterogeneity in the potential permutations from HIPE coding and audit coordinator data sources. Feedback on hospital site specific rates of IHS may facilitate local audits to identify any reasons or practices leading to underreporting. The discussion and dissemination of research in this area for this stroke subgroup could potentially improve case reporting within the INAS audit portal. Thirdly, the cohort selection for this study was relatively cautious using not only the IHS definition criteria but also applying further data quality caveats to certain cases (Figure 3.1). The main aim of the cohort selection was to prioritise accuracy within each cohort as this reflected the first study on IHS in an Irish context. However, true IHS cases may have been excluded from cohort selection potentially reducing the reported IHS rate.

IHS rates were higher amongst the model 4 hospitals. This is explained by model 4 hospitals' provision of tertiary level care which may be associated with greater clinical

complexity. Complexity may be manifested in a patient population with greater comorbidity or resulting from the sub-speciality's case-mix e.g., cardiac, oncology, surgical, endoscopic, or interventional procedures. One prior review demonstrated that IHS following a procedure was more likely amongst university hospitals underlying the link between IHS and the case-mix of a hospital site (Ben-Shabat et al., 2023). In addition, almost all model 4 hospitals are designated PCI centres generating greater volumes of patients with cardiac pathology, a recognised source of IHS. The three highest rates of IHS amongst model 4 hospitals were St. James's Hospital (14.3%), University Hospital Waterford (13.8%) and University Hospital Galway (9.8%). It is worth highlighting the distribution of acute PCI interventions across PCI centres. St. James's Hospital and the Mater Misericordiae University Hospital received approximately one-quarter of all PCI admissions annually from 2017 to 2021 (NOCA 2023b, NOCA 2022b). This greater burden of acute PCI admissions due to the optimal reperfusion service protocol likely contributes to the observed high rate of IHS at St. James's Hospital. However, the rate of IHS reported for the Mater Misericordiae University Hospital (3.9%) would appear incongruous with its acute PCI caseload. Furthermore, its cardiac caseload is notably complex as it delivers the Heart and Lung Transplantation Programme and the Ventricular Assist Programme. Other designated PCI centres with lower rates of IHS like St. Vincent's University Hospital (3.5%) and Beaumont Hospital (3.4%) account for only 1% of the acute PCI admission nationally per annum. The availability of per hospital rates of IHS in an Irish context will facilitate local audit of practices for IHS case reporting. Furthermore, awareness of the hospitals with high rates of IHS is important when interpreting stroke outcomes for that hospital site in general as the IHS cohort tends to have poorer outcomes than COS counterparts.

7.2 Demographic Profile of the IHS Cohort

The median time spent in an Irish hospital before the onset of an IHS event was 6 days (IQR 2-14 days). Over half (58.9%) of strokes occurred within one week of admission. Park et al. (2009) similarly reported that of 111 IHS cases reviewed, 60% occurred within the first week of hospitalisation. A median interval between admission and stroke onset of one day was reported by a Swedish cohort study (Ben-Shabat et al., 2023). In general, it appears that most IHS events generally occur sooner after admission to hospital rather than later. This temporal association between IHS onset and admission to hospital is

worthy of future exploration. Some possible reasons for this could be that the original pathology at admission plays a role in the occurrence of an IHS event, for instance being admitted for a cardiac procedure which ultimately leads to an IHS event. It could also reflect clinically unrecognised cases of COS which were not identified as stroke diagnoses at the point of admission. This can occur as stroke symptoms can be misdiagnosed for example vertigo can be due to inner ear pathology or a posterior circulation stroke or a patient can present with many simultaneous pathologies and a non-stroke problem can initially be to the forefront of clinical management.

The most common principal diagnoses coded for IHS cases were circulatory disorders (22.3%) (Figure 4.4). Review of the literature confirms the interplay between cardiac pathology and IHS. The risk of stroke with cardiac procedures is well documented. Selim et al (2007) highlighted the incidence of stroke following cardiac surgery reporting rates as high as 8.8% following valvular surgery. In a prospective review of 16, 184 cardiac surgeries the overall incidence of stroke was 4.6% (Bucerius et al., 2003). This influences the location or clincial service at stroke onset in hospital too. Whilst this data is not collected by INAS, in the single-site review at an Irish hospital in Chapter 2, almost 40% of IHS were under the care of either cardiology or cardiothoracic surgery (Chapman et al., 2023b).

The next most frequent ICD-10-AM coded diagnosis was ischaemic stroke accounting for 14.4% of the IHS cohort. This most likely reflects a coding issue. The principal diagnosis in HIPE coding is the diagnosis responsible for the hospitalisation. An IHS by definition occurs during a hospital stay and stroke symptoms are not present at the time of admission. There is the potential situation where a patient is originally admitted with a stroke and later develops another stroke which is an IHS event by definition. However, in this situation as per HIPE coding practices, this admission should be coded with a stroke diagnosis as the principal diagnosis and another stroke diagnosis as an additional diagnosis with a HADx flag to record the later IHS event. A similar pattern on ICD-10-AM coded discharges in a Swedish study was observed with 42% of IHS cases having stroke coded as the original reason for hospital admission (Ben-Shabat et al., 2023). However, in a Swedish setting, the principal diagnosis coded can be open to interpretation. If an IHS event occurred and consumed much of the resources and activities of the hospital stay

and eclipsed the principal reason for admission it can be recorded as the principal diagnosis. In an Irish setting, however, the coding definitions do not allow for this degree of flexibility. This highlights the need to assess and evaluate coding practices given the important role it plays for the definition of IHS. Cases of stroke coding can be complicated and challenging. In Chapter 2 during IHS case clinical validation, 26 IHS cases required expert consensus deliberation to facilitate two-step validation. Four of these cases could not be designated as either principal stroke or an IHS. All were silent infarctions, and the timing of the stroke event was impossible to define.

It is suggested that a coding review is undertaken of IHS cases coded with a principal diagnosis of ischaemic stroke (n=89) to validate these cases are true IHS cases. If they are in fact COS cases, this would have implications on data analysis for outcomes such as stroke unit admission, thrombolysis, and mortality. A possible mechanism to ensure ongoing review of stroke coding practices would be routine engagement between stroke clinicians and coders to examine complex cases and conduct regular audits on a selection of stroke admissions. It is suggested that a coding review is undertaken of IHS cases coded with a principal diagnosis of ischaemic stroke (n=89) to validate these cases are true IHS cases. If they are in fact COS cases, this could have implications on data analysis for outcomes such as stroke unit admission, thrombolysis, and mortality.

Injury, poisoning and other consequences of external causes accounted for a reasonable proportion of IHS principal diagnosis at 13.8%. This ICD-10-AM category includes any injury or trauma sustained including fractures and emphasises the interaction between surgical colleagues and IHS. The interchange between malignancy and stroke risk is elaborated in Section 1.7.3 and is emphasised by the finding that one in twelve (8.1%) IHS patients are admitted due to a primary malignancy diagnosis. However, an active malignancy diagnosis is likely to be present in a much higher proportion. These patients may be originally admitted with issues not directly coded as neoplasm such as infection and a malignancy diagnosis could be coded in an additional diagnosis. Up to 29 additional diagnoses can be coded for each admission so the detail required for further analysis of neoplasm coding was beyond the scope of this review.

The IHS patient cohort in Irish acute hospitals are older, suffer more ischaemic strokes, have greater pre-stroke disability, are less likely to be admitted from home and more

likely to be admitted from a LTC facility than the COS cohort (Section 4.3). From an age perspective, IHS and COS cohorts actually had similar proportions of patients aged from 65 to 79 years (40.3% versus 40.4%). Specifically it was the proportion of patients in the age band of 80 years or above which drove the age difference between the two groups (39.8% of IHS versus 33.1% of COS). The variation in patterns of admission sources between IHS and COS groups may be related to this older age profile. The proportion of IHS patients admitted from a LTC facility was slightly higher at 3.4% versus 3.1% of COS cases (p=0.004) (Section). A mere 0.7% of Irish adults aged between 65 and 69 years reside in LTC facilities (BDO 2014). However, the proportion residing in LTC facilities increases exponentially with age, for example, 17.0% of those aged from 85 to 89 years reside in LTC facilities in Ireland.

Ischaemic strokes were more common amongst IHS patients, and relevant to this, AF was reported at greater frequency amongst the IHS cohort (40.6% in IHS versus 29.8% in COS; p<.001). The frequency of comorbid cardiac diagnoses amongst IHS cases is a likely contributor to the ischaemic subtype predominance. It was not possible to ascertain if IHS patients in Ireland suffer strokes of greater severity consistent as the NIHSS is not collected as part of the INAS annually. Given that AF-related strokes are associated with greater severity (Kimura et al., 2005), it could be suggested, although not proven, that this IHS cohort may suffer strokes of greater severity in keeping with the literature. To complete the demographic profile on IHS and to facilitate fair comparison between COS and IHS cases, the inclusion of the NIHSS as a marker of stroke severity within INAS would be useful.

The IHS cohort has a greater burden of disability prior to the onset of their IHS event. IHS patients were twice as likely as COS patients to have moderate to severe disability (mRS score 3-5) prior to their stroke (Section 4.5). This has important implications on stroke outcomes including greater likelihood of post-stroke disability. Pre-stroke functional disability was the strongest predictor of post-stroke discharge disability (aOR 99.59; 95% CI [65.05-152.48]; p<.001) (Table 6.7). Pre-stroke functional impairment renders stroke patients inelligible for reperfusion therapy with EVT. Major trials on EVT in acute stroke typically specifiy that no significant pre-stroke functional impairment should exist for stroke patients being considered for thrombectomy (Albers et al., 2018, Nogueira et al.,

2018, Jovin et al., 2015, Saver et al., 2015, Campbell et al., 2015). Furthermore, in the general older adult population, disability is not inoccuous and is itself associated with increased mortality (Fried et al., 1998), hospitalisation and rates of admission to LTC (Stuck et al., 1999).

Thus the profile of the IHS patient as an older person with greater disability, higher burden of comorbidity especially cardiovascular, and higher rates of institutional care, builds a picture of a distinct stroke subgroup that already harbours greater physical vulnerability prior to the impact of their stroke. The overlapping and complex interactions between comorbidity, disability and frailty have been highlighted (Fried et al., 2004). These factors interact in a dynamic and synergistic fashion to cause and exacerbate one another. If a stroke event then occurs, it is occuring in a person in an already disadvantaged state. Comorbidity, frailty and disability increase with age (Hernandez et al., 2019, Collard et al., 2012, Adams et al., 1999). Comorbidity creates clinical difficulties as treatment of one condition may destabilise, exacerbate or even provoke another condition. This dynamic is crystallised within an IHS population. Patients are admitted to hospital for one condition, and then suffer a stroke which can be related to or precipitated by the original reason for admission. Coexisting acute illness e.g. bleeding impacts the appropriateness of treatment options such as thrombolysis. Frailty is a state of diminished reserve or increased vulnerability to a stressor (Clegg et al., 2013). In an Irish population, one in every five patients aged over 65 years is frail (TILDA 2018). Similar to disability, frailty also predisposes to adverse outcomes such as falls, hospitalisation, LTC admissions and even mortality (Fried et al., 2004).

Whilst this research does not formally assess frailty in the IHS population, it is likely given the features of increased comorbidity, age and disability, that frailty is present. This is important as clinical frailty has been shown to be independently associated with increased 28-day mortality in acute ischaemic stroke (Evans et al., 2020). Frailty was also associated with diminished improvement on the NIHSS following thrombolysis. The most important intervention for assessment and treatment of frail patients remains the application of a comprehensive geriatric assessment (CGA) (Ellis et al., 2011). The CGA is a coordinated and holistic approach demanding the resources and skills from across the MDT. In many ways, the CGA intersects with the principles of SU coordinated, MDT-led

care. A Japanese cohort study demonstrated lower in-hospital mortality and rates of prolonged hospitalisation in older stroke patients who received CGA during their admission (Hosoi et al., 2020). The lower rates of care under a specialist stroke team, which often are led by geriatricians in an Irish context, potentially may impact the provision of this coordinated management approach which is just as, if not more important, to this stroke subgroup. For instance, one in every five IHS patients (19.2%) were under the care of a surgical team at the point of discharge. Approximately 60% of IHS patients in Irish acute hospitals were under the care of either of the three specialities that can provide specialist stroke care general medicine - geriatric medicine, or neurology - compared with the majority (94%) of COS patients. Stroke specific, MDT-led care is likely to be more complicated to deliver across an entire hospital when IHS patients are being cared for by and on varied teams and wards.

7.3 MDT-Led Care

MDT review of the IHS cohort in general was in keeping with the COS cohort (Section 5.3). In fact, a greater proportion of IHS patients were reviewed by physiotherapy, SALT, dieticians, and MSW. However, efforts to coordinate care such as case discussion at an MDT meeting were significantly lower for IHS cases, as was specialised stroke nurse review. Admission within the SU plays a central role in the delivery of coordinated MDT care for stroke patients. The IHS cohort were less likely to be admitted to the SU when compared with the COS cohort (44.42% versus 70.2%; OR 0.46 [0.38-0.56] p<.001). Although the median time spent by an IHS in the SU was longer (10 days versus 7 days; p<.001), only one in every five IHS patients spent 90% of their hospital stay in the SU compared with one in two of COS patients. An important point to highlight was the finding that haemorrhagic strokes are less likely to be admitted to the SU and this is more prominent amongst the IHS cohort. Indeed, the IHS cohort were less likely to be prescribed antithrombotic therapy or be anticoagulated if they had AF when compared with the COS cohort. These measures of care quality are often linked with SU admission as it facilitates the delivery of evidence-based care.

Competing medical treatment and care needs during hospitalisation contributed to the lower SU admission rates as the most common reason cited for non-admission amongst

IHS cases was the requirement for a specialty bed. Given the research by Cadilhac et al. (2019) which emphasised that IHS patients admitted to the SU have lower in-hospital mortality, strategies to promote SU admission amongst the IHS cohort are essential. This may require ongoing input and review by stroke specialists on a consult-basis as initially care within the SU may not be possible if other medical issues demand an alternative location. The role of the SU in stroke care cannot be underestimated and Akbik et al. (2020) who conducted a large cohort study using the AHA Get With The Guidelines Stroke register suggested that reduced SU admission rates could be an under recognised factor contributing to poorer outcomes for IHS patients.

It is important however to mention that whilst this analysis found an association between SU admission and reduced mortality rates, this may be influenced by selection bias. If the requirement for a specialty bed is the most common reason an IHS patient is not admitted to the SU, this indicates a patient cohort with complex care needs that may not be met within the SU. The requirement for a critical care level bed in the ICU or HDU will also be associated with increased mortality. Rather than SU admission being associated with reduced mortality, it may the case that IHS patients who do not get admitted to the SU reflect a stroke subgroup with inherently greater, more complex care needs and consequently higher mortality.

7.4 Performance on Time-Based Stroke Measures

Time-based measures of stroke care facilitate review of the performance of the acute stroke pathway. Interestingly, the proportion of IHS patients (65%) reviewed within 30 minutes of stroke symptom onset was slightly more than the proportion of COS (61%) reviewed within 30 minutes of arrival to hospital. Neither cohort achieved the INAS KQI of median time to imaging of 60 minutes. The major outcome from times-based variables was the finding that IHS patients eligible for thrombolysis do not receive it as promptly as COS counterparts. There were noteworthy delays in the median time to thrombolysis for the IHS cohort at 90 minutes compared to 54 minutes for the COS cohort ($p<.001$). Only 23.3% of IHS patients received thrombolysis within 60 minutes of stroke symptom onset.

Potential challenges for the IHS cohort to receive thrombolysis in a timely fashion compared with the COS cohort have been highlighted including confounding medical illnesses, distance to the radiology department, less efficient processes of acute stroke care on wards compared with the rapid response culture of the ED (Assuncao et al., 2021, Cumbler et al., 2010). In an Irish context, the longer time to thrombolysis is not accounted for by delays in the preceding steps of the acute stroke pathway. Whilst the median time to medical review of IHS patients was significantly longer (20 minutes versus 12 minutes; $p<.001$), more IHS patients were reviewed within 30 minutes. Both cohorts had very similar median times to imaging, 66 minutes and 64 minutes for IHS and COS cohorts, respectively. The proportions of IHS patients who had brain imaging within 60 minutes was also comparable. At the time of medical review, imaging and thrombolysis COS patients are in the ED. The acute stroke pathway for strokes arriving to the ED is well-practised, and often is primed to react thanks to pre-hospital alerts of an inbound acute stroke. The acute stroke pathway that serves COS as they arrive to the ED does not serve patients already admitted on a ward. Thrombolysis administration requires trained staff familiar with the medication. The ED is a source of nurses trained in thrombolysis administration and who also provide the close clinical observation which is required during and after thrombolysis. In contrast, IHS patients may be on any ward across the hospital. General wards do not have the scope or specialty training to administer thrombolysis. Indeed, these wards typically do not stock tissue plasminogen activator (TPA). As a result, time may be spent trying to organise transfer to a suitable clinical location for an IHS patient to receive thrombolysis creating significant delays in its initiation.

Further delays may be encountered within the IHS cohort that are not as apparent in the COS cohort. For instance, decisions regarding thrombolysis may be more challenging owing to the original non-stroke diagnosis. This may require discussion between different specialities to weigh up the possible benefits and risks of thrombolysis or thrombectomy in an already unwell, hospitalised patient who has now developed a stroke. Furthermore, discussion with relatives around previously expressed wishes or views on treatment may be required as inpatients may not be able to express their opinions due to in-hospital factors affecting capacity such as delirium or reduced consciousness in the perioperative or intubated patient.

Efforts have been made at hospitals to improve the stroke protocol dedicated to IHS (Koge et al., 2017, Kassardjian et al., 2017, Yoo et al., 2016, Cumbler et al., 2010). These QI initiatives incorporate some form of education and training of staff to identify stroke symptoms and activate the IHS protocol. For any IHS protocol to work effectively, staff need to recognise an acute stroke and know how to trigger the IHS protocol into action. Educational activities utilised in the studies included ward or department-based educational presentations, workshops, posters, and intranet postings. The IHS protocols themselves then varied from a mobile stroke team with a TPA administration kit (Koge et al., 2017), to a rapid response inpatient stroke team (Cumbler et al., 2010) to an algorithmic approach to contact existing neurology staff (Kassardjian et al., 2017). One study focused only on areas of high-risk for IHS e.g. cardiac wards and utilised functionality from the existing EPR (Yoo et al., 2016).

An IHS protocol must identify a dedicated, appropriate location to administer TPA, facilitate access to TPA as well as the staff trained to administer it. It must also enable timely medical review and transfer to the radiology department to imaging. The mobile stroke team complete with TPA administration kit by Koge et al. (2017) provides solutions to the possible causes for delays in an Irish IHS context. The team was composed of an ED nurse, SU senior nurse, neurologist, and the doctor responsible for the patient. The ED nurse brought the TPA kit to the stroke alert as well as the expertise in its administration. To facilitate faster times to thrombolysis in an Irish context, a dedicated IHS protocol is required which addresses the nuances and challenges specific to IHS. Following activation of an acute IHS protocol, medical review and transfer to radiology department are the initial steps. If thrombolysis is indicated, it should start immediately. However, a dedicated clinical location for the IHS patient to receive thrombolysis, be monitored and potentially await transfer to an EVT centre (if indicated), is required. The protocol must incorporate nursing staff trained in the administration of thrombolysis and be available for an IHS patient at any time without delay. It may be particularly difficult to guarantee location and staff availability for a contingency event like IHS given that many hospitals routinely operate above capacity and are understaffed. However, without changes in the

acute stroke pathway dedicated to IHS patients, delays to thrombolysis and indeed, thrombectomy in eligible inpatients will continue.

Finally, it is important to highlight the potential limitations when using time-based data within an IHS population specifically. As outlined in Section 1.9.1, the starting time point in the IHS pathway should be from symptom onset rather than hospital arrival as is the case with the COS group. This facilitates fair comparison between these two distinct stroke cohorts. The literature review highlighted that some studies compared COS and IHS cases using symptom onset time for both groups (Table 1.3) which disproportionately favours IHS cases and could lead to the perception that improvements in the IHS pathway are not required. Researchers in this area should consider carefully the time-based intervals used for comparison to ensure correct conclusions are drawn for clinical care. Furthermore, the accuracy of times recorded within large datasets for stroke care must be questioned. Firstly, times recorded during manual data input can be erroneous and the INAS has data quality criteria applied within its dataset to try to mitigate these risks. Secondly, Section 1.9.1 highlighted that missing data appears to affect the time-based intervals using stroke symptom onset (32-65% missing) to a greater degree than those using hospital arrival time (0% missing). This affects data availability for the IHS cohort to a greater degree than the COS group. Finally, the accuracy of time-based data that is recorded may be subject to greater degrees of error amongst the IHS group owing to the hospital environment itself as explored in Section 1.9.2. For instance, the exact time of stroke onset in an intubated or post operative sedated patient will be very difficult to assign. Other co-diagnoses such as delirium may complicate clinical recognition of stroke symptoms. Inpatients in hospitals are not always under constant supervision and sometimes do not report new symptoms until a later time. There may be a temptation during data collection to record a symptom onset time for IHS cases to facilitate data analysis, but the accuracy of these times relies upon clear clinical documentation and is impacted by the hospital environment itself. These nuances and challenges are specific to time-based intervals for the IHS group. In contrast, the time-based intervals for the COS group typically start at hospital admission or arrival time which tends to be less affected by missing data and tends to be more concrete and subject to less interpretation.

Chapter 8. Discussion: Outcomes

8.1 Rates of Reperfusion Therapy

Thrombolysis was less likely amongst the IHS cohort (8.7% versus 9.9% amongst COS), but this failed to reach statistical significance (p=0.36). The number of strokes that received thrombolysis in the IHS cohort was relatively small n=45 which reflects a limitation of this analysis. Data for IHS cases is only available from 2020 so this review was limited to a 2-year period. Future research on the IHS cohort would benefit from a longer period of review which would provide greater numbers of cases and likely better power to detect statistical significance.

On subgroup analysis of model 4 hospitals, IHS patients were less likely to receive thrombolysis (6.6%) compared with 10.8% of COS patients admitted to a model 4 hospital (p=0.02). A potential explanation for this is that model 4 hospitals are tertiary centres delivering speciality surgical and procedural interventions in complex patient groups. This may lead to greater likelihood of contraindications to thrombolysis owing to the case-mix of the IHS patient population admitted in these tertiary centres.

The literature supports the finding that lower rates of thrombolysis are typically observed amongst IHS cohorts (Section 1.8.2). This is attributed to the presence of contraindications to thrombolysis which occur with admission to hospital e.g. surgical procedures, active bleeding anticoagulation for other comorbid condition (Liu et al., 2022, Schürmann et al., 2016, Saltman et al., 2015, Vera et al., 2011). The reported rate of contraindications to thrombolysis between IHS and COS cohorts was the same (Section 6.2). Further information on these contraindications is not available within INAS. This would be a beneficial data element addition as reasons why a patient is not thrombolysed likely differ between the cohorts. An important point in this regard is the finding by two studies that IHS patients could not be thrombolysed due to exceeding the time-based window for thrombolysis in one-third (Liu et al., 2022) to one-half of cases (Vera et al., 2011). Whilst CT perfusion assists greatly in tissue rather than solely time-based decisions on reperfusion therapy, time delays appear to be an important factor delaying IHS cases' progress through the acute stroke pathway. The longer median time to thrombolysis

observed in this study for IHS cases compared with COS cases, supports this suggestion that time delays are likely to be an important factor impacting thrombolysis rates for the IHS group.

Lower rates of thrombolysis are also observed amongst IHS patients prior to thrombectomy compared with COS counterparts (Amoukhteh et al., 2024, Naldi et al., 2023, Qiu et al., 2022, Akbik et al., 2020). However, a significant limitation of this analysis exists due to the lack of available thrombectomy data due to issues with linkage of the data. The INAS has created a solution for this and the thrombectomy dataset can be linked with the clinical INAS dataset for future analysis. The importance of thrombectomy rates in an IHS population is underlined by the lower rates of thrombolysis, thus thrombectomy offers the only appropriate reperfusion therapy for some patients within this already vulnerable cohort.

8.2 In-Hospital Mortality Rates

Over one in four cases (27.2%) of IHS die in hospital compared with one in ten (10.4%) COS patients (p<.001) and IHS patients are 3 times as likely to die in hospital as COS patients. This is consistent with international literature which reveals that IHS patients are more likely to die than COS patients (Section 1.8.1). Haemorrhagic strokes are associated with greater mortality than ischaemic strokes. For example, the INAS reported a mortality rate of 7.5% for ischaemic stroke and 30% for haemorrhagic stroke in 2022 (NOCA 2023c). The mortality rate for IHS patients with haemorrhagic stroke was even more marked. One in two haemorrhagic strokes (56.9%) die in hospital amongst the IHS cohort compared with one in four haemorrhagic strokes (28.7%) within the COS cohort (p<.001). The odds of dying were significantly reduced for IHS patients with an ischaemic stroke with an aOR 0.20; 95% CI 0.17 to 0.24 (p<.001). Much of the IHS literature reports on mortality associated with ischaemic stroke but this shows that haemorrhagic strokes amongst the IHS population are particularly at-risk for mortality. This is an important finding as it can guide and inform realistic discussion and prognostication with patients and families.

The greater burden of pre-stroke disability was previously highlighted as an important factor in the demographic profile of an IHS. Better pre-stroke functional ability was found

to be associated with reduced mortality. The mortality rate for IHS patients with a pre-stroke mRS score 0-2 was 19.4% compared with 43.4% for IHS patients with an mRS score of 3 or more (Table 6.3, Section 6.3). This was supported by 60% lower odds of death for IHS patients with favourable pre-stroke function (aOR 0.37; 95% CI 0.31 to 0.43; p<.001). This further highlights the impact of the pre-stroke demographic profile of the IHS patient and how it negatively affects stroke outcomes.

Another important finding was the lower odds of death found amongst IHS patients admitted to the SU with an aOR of 0.46 (95% CI 0.30 to 0.72; p<.001). This supports findings by Cadilhac et al. (2019) where patients with IHS admitted to the SU were less likely to die within 30 days. This association may be influenced by selection bias as IHS patients who are admitted to the SU may have less acuity associated with their original reason for admission and less competing medical interests. Thus, IHS patients who do get admitted to the SU may represent a more favourable subgroup within IHS and hence are less likely to die. However, given the clear evidence that SU admission positively aids stroke care and outcomes, it is likely that IHS patients do benefit from their care being managed and centralised in the SU and this should be prioritised where possible during their in-hospital stay.

A limitation in the analysis of mortality and indeed other outcomes, is the lack of an appropriate data variable within the INAS to assess stroke severity such as the NIHSS. This means outcomes cannot be reported or adjusted for stroke severity.

8.3 Post-Stroke Disability & Discharge Outcomes

For the outcome of favourable functional level at discharge, IHS patients were less likely to have an mRS of 0-2 compared with COS patients (28.9% versus 52.3%; aOR 0.38 95% CI 0.30 to 0.48; p <.001). Post-stroke disability amongst the IHS cohort is significantly influenced by pre-stroke functional baseline, stroke subtype, age, and the presence of AF. The strongest predictor for favourable mRS at discharge amongst the IHS cohort was a pre-stroke mRS score of 0-2 (aOR 115.09; 95% CI 15.85 to 835.44) and an ischaemic stroke subtype (aOR 5.25; 95% CI 1.88-14.66). The observed aOR for both predictors was greater amongst the IHS cohort when compared with the observed aOR for the COS

cohort. Favourable functional scores at discharge were 59% less likely with age above 65 years and 42% less likely with the presence of AF amongst IHS patients (Table 6.8, Section 6.4). These findings stress the importance of the impact of the IHS patient profile on outcomes post stroke as they reflect an older population with greater pre-stroke disability and higher burden of AF, which contribute to poorer functional outcomes. Admission to the SU exerted no significant impact on disability post stroke (aOR 0.99; 95% CI 0.62 to 1.57; p=0.95) for the IHS cohort in contrast with the COS cohort. Factors other than coordinated care in the SU, yield better functional outcomes amongst IHS patients. It is not surprising that given the higher level of post-disability amongst the IHS cohort that discharge home was less frequent (37.3% of IHS versus 60.3% of COS; p<.001) and discharge to LTC facility (10.6% versus 6.0%; p<.001) was more frequent.

8.4 Limitations

Firstly, the review period is relatively short at only two years which impacts the number of IHS cases disproportionately as IHS events occur less frequently. This is relevant when analysing cases of thrombolysis as the number of cases for the IHS cohort is very small n=45. This led to insufficient case numbers to reach statistical significance for outcomes such as thrombolysis rates. Future research should include longer time periods for review.

Secondly, this study is retrospective in design which deserves discussion. The data definitions provided by the INAS and the dedicated role in data entry which local audit coordinators provide help to ensure data integrity within the INAS dataset. However, variances in data collection and entry could have introduced bias. Data is generally entered retrospectively by the local audit coordinators following discharge home given the reliance on HIPE-generated discharge data to identify cases. Recall bias can emerge as an issue when using retrospectively entered data that rely on clinical records as the data source. Details on certain variables may be incomplete or missing from the clinical record e.g., time-based data, mRS score. Reliance on paper-based records in Ireland also means audit coordinators face challenges entering data as chart entries may be illegible. Missing case data is also an important point that must be mentioned in relation to retrospective stroke cohorts reviewing IHS populations. Evidence for reporting bias already exists within the published literature as the rate of IHS reported in small-centre studies is higher than

in larger registry based studies (Nouh et al., 2022, Akbik et al., 2020). It is suggested this is due to decreased likelihood to report IHS cases in larger datasets. In an Irish context, an IHS case can be missed during coding as the other medical or surgical complaints that the patient presented with to hospital may dominate the admission. Indeed, HIPE coding has lower sensitivity but higher specificity than audit coordinators for detecting IHS cases in an Irish acute hospital (Chapman et al., 2023a). Reporting bias also exerts an impact within the IHS population as an IHS stroke which undergoes reperfusion therapy is more likely to be captured on stroke registry datasets compared with an IHS event that does not undergo thrombolysis (Akbik et al., 2020). The literature review provides evidence for this reporting bias as higher rates of thrombolysis amongst IHS populations were only reported in the largest stroke register based studies (Gu et al., 2023, Akbik et al., 2020, Cumbler et al., 2014). Although retrospective in design, selection bias is limited as the cohort does reflect a representative sample of stroke patients in an Irish setting. The data is population-based and sourced from the 24 acute public Irish hospitals which report annually to the INAS. Cohort selection for IHS cases was cautious and caveats in addition to the existing definition of IHS were applied. This means that the cases included as IHS cases may reflect an underestimation of the IHS population but are likely to reflect true IHS cases.

Many different healthcare professionals were involved and engaged in the care of IHS which means there will be factors impacting stroke care and outcomes that are not accounted for within the retrospective study design. In a prospective design this limitation would be less evident. However, the varied pattern of care is reflective of the typical hospital course of an IHS patient in Ireland, so it is unlikely to influence outcome results but rather can be seen as an observed outcome of the pattern of care for IHS patients.

As with any retrospective cohort study, the estimated odds ratios can only establish associations and cannot provide causality. This means the exact causes for poorer outcomes such as increased mortality are difficult to define and can at best be inferred from retrospective cohort studies. However, the findings still provide valuable information to guide improvements to care for this stroke population. The lack of a measure of stroke severity means adjustment for this variable was not possible which is a

limitation as in the available literature, stroke severity impacted reported OR in studies which adjusted for it. As mentioned, the lack of available linked thrombectomy data impacts the analysis of outcomes significantly.

Chapter 9. Conclusions

9.1 Final Conclusions

Results from this retrospective cohort study reveal that the national rate of IHS in Ireland was 5.7%. The highest rate of IHS was at St. James's Hospital (14.3%) and the lowest was at Wexford General Hospital (1.7%). The most common primary reason for admission was a circulatory diagnosis (22.3%). The median time spent in hospital prior to stroke symptoms onset was 6 days (IQR 2-14 days) with almost 60% occurring within the first week of hospitalisation. A summary of the main findings is depicted in Figure 9.1. The IHS population exhibited greater comorbidity and complexity with older age (median age 76 years versus 74 years for COS), higher levels of pre-stroke disability, lower rates of living at home on admission (84.6% versus 89.0%), higher reporting of AF (40.6% versus 29.8% of COS), more frequently had a critical care admission (39.8% versus 13.7% of COS) with longer critical care stays (median stay 4.7 days versus 0.8 days for COS) and were less likely to be under the care of a stroke team at discharge (59.4% versus 94% of COS).

IHS did not perform as well on measures of quality of stroke care. Rates of admission to the SU were lower (44.2% versus 70.2% for COS; aOR 0.46; 95% CI 0.38-0.56; p<.001). The reason for non-admission to the SU was the requirement of another specialty bed for IHS cases compared with a lack of bed availability for COS cases. Prescribing of antithrombotic therapy and anticoagulation in patients with AF were lower amongst the IHS cohort. The median time to medical review was longer amongst IHS cases despite being admitted in hospital at the time of stroke onset (20 minutes versus 12 minutes; p<.001). Of particular concern were the delays observed in the median time thrombolysis of 90 minutes for IHS patients compared with 54 minutes for COS cases (p<.001). Discussion of care at a dedicated MDT meeting was less likely amongst IHS patients but higher rates of review by a physiotherapist, SALT, dietician and MSW were observed.

Outcomes for the IHS cohort were generally poorer with longer LOS (14 days versus 8 days for COS; p<.001), lower rates of thrombolysis (8.7% versus 9.9% for COS) albeit non-significantly (p=0.36) and lower rates of discharge home with corresponding higher rates of admission to a LTC facility. One in four (27.2%) IHS cases compared with one in ten

(10.4%) cases of COS died in-hospital following a stroke (aOR 2.98; 95% CI 2.37-3.75; p<.001). Ischaemic subtype, SU admission and lower pre-stroke disability levels were associated with lower odds of in-hospital mortality for IHS cases. No or only mild disability at discharge was less likely to be reported for IHS patients (28.9% versus 52.3% for COS; aOR 0.38; 95% CI 0.30-0.48; p<.001). The strongest predictor of favourable disability levels at discharge for the IHS cohort was lower levels of pre-stroke disability (aOR 115.09; 95% CI 15.85-835.44; p<.001).

The IHS cohort reflects a distinct stroke subgroup with different baseline characteristics and poorer outcomes compared with their COS counterparts. This demands separate and dedicated analysis of outcomes and performance on quality and process-based measures of care. This will facilitate improvements and changes to acute inpatient stroke pathways to provide care tailored to this specific stroke subgroup.

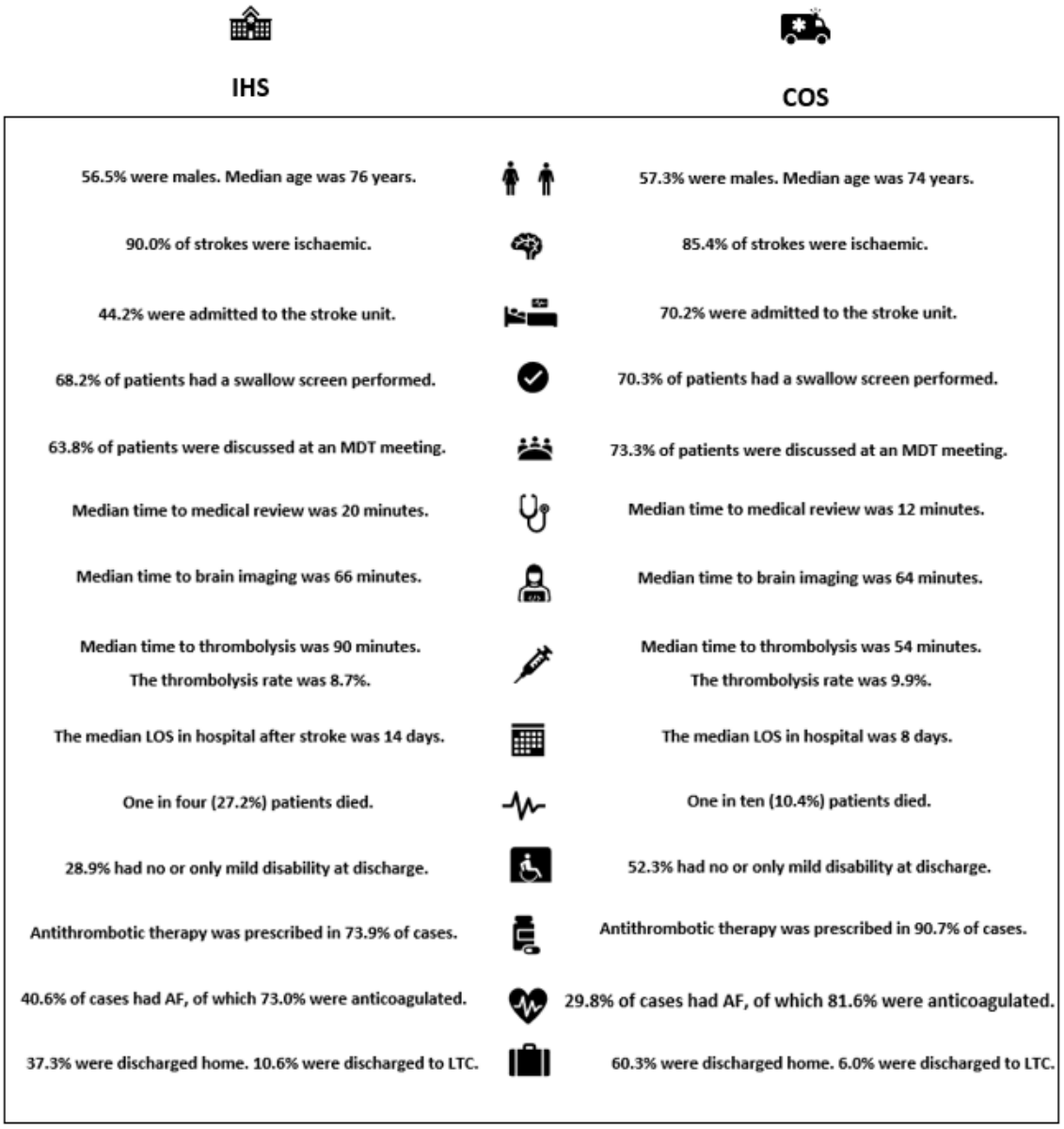

Figure 9.1: Summary of Main Findings of Retrospective Cohort Study Comparing IHS and COS

9.2 Recommendations

Clinical Recommendations

1. A dedicated acute IHS protocol should exist in every hospital. This should facilitate prompt stroke recognition on any ward or clinical area in the hospital and generate activation of an acute FAST call. The protocol should provide a pathway to facilitate rapid medical review and transfer to the radiology department for imaging. Crucially, the protocol should provide access to TPA, a location to deliver thrombolysis and staff trained and familiar with its administration.
2. IHS patients should be prioritised for admission to the SU. If this isn't feasible due to other medical issues, it should be facilitated as soon as it is safe to do so. SU admission of haemorrhagic strokes should be promoted given the lower rates of admission amongst this subtype.
3. It is accepted that some patients with a stroke during their hospital stay will not be admitted to the SU due to other competing medical treatment and care needs. In these cases, a structured protocol of coordinated care involving stroke specialists and dedicated members of the stroke MDT should be provided. Patients may be seen on a consult basis, but this should follow a schedule with an emphasis on the measures of quality stroke care outlined by the INAS. For instance, review by the specialist stroke team might occur at designated time benchmarks to ensure that the aspects central to good quality stroke care are not omitted during the inpatient journey.

Hospital Data Management Recommendations

4. Local hospital audits on existing IHS case detection are required as variances exist in the IHS rates reported per hospital. Clinical interpretation is required to identify IHS cases by audit coordinator and HIPE coders. Involvement of stroke clinicians may help as IHS cases can present as clinically challenging cases to define on occasions. Audits on HADx flag assignment could help to identify IHS cases that may be missed during coding owing to HADx flag omissions.

INAS Data Management Recommendations

5. A measure of stroke severity such as the NIHSS should be incorporated into the INAS clinical dataset.
6. Incorporation of structured reasons for contraindications to thrombolysis should be considered within the INAS clinical dataset. This would inform reasons why patients are not eligible for reperfusion therapy and guide future QI efforts.
7. The linkage of the thrombectomy dataset with the clinical INAS dataset is necessary for future research as thrombectomy is a major evidence-based therapy for stroke patients.
8. The inclusion of a pre-stroke score on frailty e.g., Clinical Frailty Score, may help to contextualise and stratify the IHS cohort as it represents a complex, comorbid, vulnerable stroke subgroup.

Research Recommendations

9. Qualitative investigation may help to map the care processes specific to the IHS cohort. This would provide useful insights to inform the development of an acute IHS pathway and may also highlight potential challenges or obstacles to its implementation.
10. A prospective observational study design using an interrupted time series analysis should be conducted to assess the response and findings following the implementation of clinical recommendations.
11. Once linkage of the thrombectomy and INAS datasets is achieved, prospective observational studies should be conducted to analyse the impact of thrombectomy on the IHS cohort.

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Appendix 1: Data Variables from the Irish National Audit of Stroke

Dataset	Data Element Name	Definition	Codes and values
HIPE	HOSPITAL	NAME OF HOSPITAL	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	MRN_ENC	PATIENT HOSPITAL NUMBER ENCRYPTED	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	ADMDATE	HIPE ADMISSION DATE	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	DISDATE	HIPE DISCHARGE DATE	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	IS DAY CASE	HIPE VARIABLE	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	ADMTYPE	HIPE VARIABLE	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	DischargeCode	HIPE DISCHARGE DESTINATION	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	SEX	GENDER	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	MARRSTATUS	MARITAL STATUS	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	RESID	HIPE VARIABLE IDETIFYING AREA OF RESIDENCE	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	SPECIALITY	HIPE VARIABLE INDICATING MEDICAL SPECIALITY	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	DISSTATUS	HIPE VARIABLE DESCRIBING DISCHARGE STATUS	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	ADMWARD	HIPE VARIABLE ADMISSION WARD	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	DISWARD	HIPE VARIABLE DISCHARGE WARD	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	ADMSOURCE	HIPE VARIABLE SOURCE OF ADMISSION	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	PRIVDAYS	HIPE VARIABLE PRIVATE DAYS	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	PUBDAYS	HIPE VARIBLE PUBLIC DAYS	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	SEMIPRIVDAYS	HIPE VARIABLE SEMI-PRIVATE DAYS	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	ITUDAYS	HIPE VARIABLE ITU LENGTH OF STAY	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	WLIST	HIPE VARIABLE WAITING LIST INDICATOR	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	EMADM	HIPE VARIABLE MODE OF EMERGENCY ADMISSION	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	ADMWEIGHT	HIPE VARIABLE ADMISSION WEIGHT	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	WASINDAYWARD	HIPE VARIBALE WAS IN A DAY WARD	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	DAYWARD	HIPE WARIABLE DAY WARD INDICATOR	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	TRANSINHOSP	HIPE VARIABLE TRANSFER HOSPITAL FROM	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	TRANSOUTHOSP	HIPE VARIABLE TRANSFER HOSPITAL TO	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	LOS	HIPE VARIABLE LENGTH OF STAY	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	AGE	HIPE VARIABLE AGE	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	DRG	HIPE VARIABLE DIAGNOSIS RELATED GROUP	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	MDC	HIPE VARIABLE MAJOR DIAGNOSTIC CATEGORY	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	HASMEDCARD	HIPE VARIABLE HAS MEDICAL CARD	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	HEALTHINSURER	HIPE VARIABLE NAME OF HEALTH INSURER	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	DIAG1	HIPE VARIABLE DIAGNOSIS 1	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	HAD	HIPE VARIABLE Diagnosis 2-30	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	PROC	HIPE VARIABLE PROCEDURE 1-20	http://www.hpo.ie/HIPE_Data_Dictionary.htm
HIPE	PROCDATE	HIPE Variable Procedure date	http://www.hpo.ie/HIPE_Data_Dictionary.htm

INAS	TRANS_HOSP	Which hospital was patient transferred from (if any)	0000 Not Applicable 0941 Childrens Crumlin 0101 St Columcilles 0102 Naas General 0908 Mater Hospital 0910 SVUH 0925 Peamount Hospital 0955 Cappagh Orthopaedic 0940 Temple Street 0947 St Lukes Rathgar 0904 SJH Dublin 0108 Connolly Blanchardstown 0912 Michaels Dun Laoghaire 0950 RVEEH 0960 National Rehabilitation 0930 Coombe Hospital 0932 Rotunda Dublin 0931 National Maternity Hosp 1270 Tallaght Hospital 1762 Josephs Raheny 0954 Clontarf Orthopaedic 1001 Blackrock Hospice 0600 Waterford 0601 St Lukes KK 0605 Wexford 0602 Kilcreene 0607 Clonmel 0705 Finbarrs Cork 0704 Bantry 0913 Mercy Cork 0915 South Infirmary 0703 Mallow 0724 CUH 0726 Kerry 0301 Limerick Maternity 0300 Limerick 0302 Croom Limerick 0918 St Johns Limerick 0305 Ennis 0304 Nenagh 0803 Roscommon 0919 Portiuncula 0800 Galway 0802 Mayo 0801 Merlin Park 0203 Tullamore 0202 Mullingar 0201 Portlaoise 0500 Letterkenny 0501 Sligo 0922 Drogheda 0402 Cavan 0400 Louth County 0404 Monaghan 0403 Navan 8888 Other
INAS	TRANS_REASON	Why was the patient transferred	1 Thrombolysis 2 Thrombectomy 3 Neuro Surgery 8 Other
INAS	TRANS_REASON_OTHER	If other transfer reason, please specify	Freetext
INAS	TRANS_HOSP_OTHER	If other transfer hospital, please specify	Freetext
INAS	ONSET_DATE	Symptom onset date	
INAS	ONSET_TIME	Symptom onset time (enter 9999 if unknown)	
INAS	LAST_TIME_WELL_DATE	If symptom onset time is unknown, what date was the patient last known to be well	
INAS	LAST_TIME_WELL_TIME	If symptom onset time is unknown, what time was the patient last known to be well	
INAS	IN_HOSPITAL_STROKE	Did the stroke occur while the patient was in hospital for treatment of another condition	1 Yes 2 No 9 Unknown
INAS	HOSP_ARR_DATE	If no, date of presentation to hospital	
INAS	HOSP_ARR_TIME	If no, time of presentation to hospital	
INAS	ARR_WITHIN_4_5	If presentation time is unknown, was presentation to hospital within 4.5 hrs of symptom onset	1 Yes, 2 No 9 Unknown
INAS	TEAM_DATE	Medical assessment date	
INAS	TEAM_TIME	Medical assessment time	
INAS	CT_OR_MRI	Brain CT or MRI performed	1 Yes, 2 No 3 Performed pre adm / hosp transfer 9 Unknown
INAS	BRAIN_IMG_DATE	If yes, First Brain Imaging date	
INAS	BRAIN_IMG_TIME	If yes, First Brain Imaging time	
INAS	THROMBOLYSIS	Did the patient receive I.V. Thrombolysis	1 Yes, 2 No 5 Contraindicated
INAS	THROMBOLYSIS_DATE	If yes, enter date	
INAS	THROMBOLYSIS_TIME	If yes, enter time	
INAS	INTRACEREB_BLEED	If yes, was intracerebral bleed seen on scan within 36 hrs	1 Yes, 2 No 9 Unknown
INAS	NEURO_DETER_ASSOC_WITH_BLEED	If intracerebral bleed, was neuro deterioration associated with it	1 Yes, 2 No 9 Unknown
INAS	SWALLOW_SCREEN_PERFORMED	Was a swallow screen completed	1 Yes, 2 No 9 Unknown
INAS	SWALLOW_SCREEN_PERFORMED_WITHIN	If yes, was swallow screen completed within 4 hours of presentation	1 Yes, 2 No 9 Unknown

INAS	PRE_STRK_RANKIN	Modified Rankin Scale pre stroke	0 Zero 1 One 2 Two 3 Three 4 Four 5 Five ~~6 Six~~ 9 Unknown
INAS	ADM_TO_STROKE_UNIT	Admitted to Stroke Unit (Key Performance Indicator)	1 Yes, 2 No
INAS	STROKE_UNIT_ADM_DATE	If yes, date admitted to Stroke Unit (Key Performance Indicator)	
INAS	STROKE_UNIT_DIS_DATE	If yes, date discharged from Stroke Unit (Key Performance Indicator)	
INAS	STROKE_UNIT_NO	If no, reason why	1 No Stroke Unit, 2 Bed Not Available, 5 Infection Control Risk, 6 Repatriated immediately* 8 Other * added in 2024
INAS	STROKE_UNIT_NO_OTHER	If other reason, please specify	Freetext
INAS	AHP_ASSESSMENT	Allied Health Professional (AHP) Assessment	1 Yes, 2 No
INAS	PHYSIO_ASSESSMENT	If yes, Physiotherapy	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	OCCUPATIONAL_ASSESSMENT	If yes, Occupational Therapy	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	SPEECH_ASSESSMENT	If yes, Speech and Language Therapy	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	DIETETICS_ASSESSMENT	If yes, Dietetics	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	MSW_ASSESSMENT	If yes, Medical Social Worker	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	PSYCHOLOGY_ASSESSMENT	If yes, Psychology	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	ASSESSED_SNP	Was the patient assessed by Stroke Nurse Specialist	1 Yes, 2 No, 9 Unknown
INAS	ASSESSED_SNP_NO	If no, reason why	Freetext
INAS	MULTIDISCIP_ASSESSMENT	Multidisciplinary Meeting Case assessment	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	MOOD_ASSESSED	Was an assessment of mood completed and documented by a member of the MDT	1 Yes, 2 No 3 Not Indicated 9 Unknown
INAS	CAROTID_STENOSIS	Does the patient have Symptomatic Carotid Stenosis	1 Yes, 2 No 9 Unknown
INAS	REFER_FOR_CAROTID_ENDARTERECTOMY	If Symptomatic Carotid Stenosis, was the patient referred for Carotid Endarterectomy	1 Yes, 2 No 9 Unknown
INAS	REFER_FOR_CAROTID_STENTING	If Symptomatic Carotid Stenosis, was the patient referred for Carotid Stenting	1 Yes, 2 No 9 Unknown
INAS	ANTITHROMB_THERAPY_FOR_ACUTE_TR	New or Altered Antithrombotic Therapy prescribed for acute treatment	1 Yes, 2 No 3 Contraindicated 9 Unknown
INAS	ANTITHROMB_START_DATE	If yes, Antiplatelet Or Anticoagulant (for acute treatment) start date	
INAS	ATRIAL_FIBRILLATION	Does the patient have Atrial Fibrillation	1 Yes, 2 No 4 Results Pending 9 Unknown
INAS	ATRIAL_FIBRILLATION_KNOWN_PRIOR	If Atrial Fibrillation, was atrial fibrillation known prior to stroke onset	1 Yes, 2 No 9 Unknown
INAS	ANTICOAG_AT_ONSET	If atrial fibrillation known prior to stroke onset, was Antiplatelet And/Or Anticoagulant prescribed prior to Stroke onset	1 Yes, 2 No 9 Unknown
INAS	ANTICOAG_AT_ONSET_YES	If yes, please specify Antiplatelet / Anticoagulant - prior to stroke	0 NOAC 1 Warfarin 5 Aspirin 6 Clopidogrel 7 Other Antiplatelet 8 Dual Antiplatelet Therapy 9 Antiplatelet & Anticoagulant
INAS	WARFARIN_INR_2_3_AT_ONSET	If atrial fibrillation known prior to stroke onset, and on Warfarin, was INR(International Normalised Ratio) 2-3 at Stroke onset.	0 Not applicable 1 Yes, 2 No 9 Unknown
INAS	ANTICOAG_FOR_2ND_PREV	If Atrial Fibrillation, Anticoagulation prescribed for secondary prevention	1 Yes, 2 No 9 Unknown
INAS	ANTICOAG_ON_DISCHARGE	If yes, please specify Antiplatelet / Anticoagulant - on discharge	0 NOAC 1 Warfarin 5 Aspirin 6 Clopidogrel 7 Other Antiplatelet 8 Dual Antiplatelet Therapy 9 Antiplatelet & Anticoagulant

INAS	ANTICOAG_DOC	If no, please enter reason documented	01 No reason documented 02 Major bleeding (prior history) 03 Severe illness (e.g. cancer, dementia) 04 Poor compliance (known or suspected) 05 Patient refused anticoagulation 06 Alcohol excess 07 Falls 08 Extreme frailty 09 Liver disease 10 Will commence anticoagulation as an out-patient.
INAS	ON_DIS_RANKIN	Modified Rankin Scale on discharge	0 Zero 1 One 2 Two 3 Three 4 Four 5 Five 6 Six 9 Unknown
INAS	DISCHARGE_DESTINATION	Discharge destination	1 Home 2 Patient died 3 Discharge to long term care 4 Discharge to off-site rehab 5 Transfer to referring hosp 6 Transfer to other hosp for on-going stroke care 7 Home with ESD 8 Other 9 Unknown
INAS	CASE_COMPLETE	Case complete	1 Yes, 2 No, 9 Unknown

Appendix 2: Time-Based Intervals Data Elements

Cohort	Interval Name	Interval Context	Interval	Data Elements Used	Interval Definition
IHS	Adm_Onset	From Hospital Admission to Onset of Stroke Symptoms	Days	ONSET_DATE	ADMDate Minus ONSET_DATE
				ADMDate	
IHS	Onset_Team	From Onset of Stroke Symptoms to Assessment	Minutes	ONSET_DATE	TEAM_DATE/TIME Minus ONSET_DATE/TIME
				ONSET_TIME	
				TEAM_DATE	
				TEAM_TIME	
IHS	Onset_Brain	From Onset of Stroke Symptoms to Imaging	Minutes	ONSET_DATE	BRAIN_IMG_DATE/TIME Minus ONSET_DATE/TIME
				ONSET_TIME	
				BRAIN_IMG_DATE	
				BRAIN_IMG_TIME	
IHS	Onset_Thrombolysis	From Onset of Stroke Symptoms to Thrombolysis	Minutes	ONSET_DATE	THROMBOLYSIS_DATE/TIME Minus ONSET_DATE/TIME
				ONSET_TIME	
				THROMBOLYSIS_DATE	
				THROMBOLYSIS_TIME	
Both	SU_Days	Time Spent in Stroke Unit	Days	STROKE_UNIT_DIS_DATE	STROKE_UNIT_DIS_DATE Minus STROKE_UNIT_ADM_DATE
				STROKE_UNIT_ADM_DATE	
COS	Onset_Arrival	From Onset of Stroke Symptoms to Arrival in Hospital	Minutes	HOSP_ARR_DATE	HOSP_ARR_DATE/TIME Minus ONSET_DATE/TIME
				HOSP_ARR_TIME	
				ONSET_DATE	
				ONSET_TIME	
COS	Arrival_Team	From Arrival to Hospital to Assessment	Minutes	HOSP_ARR_DATE	TEAM_DATE/TIME Minus HOSP_ARR_DATE/TIME
				HOSP_ARR_TIME	
				TEAM_DATE	
				TEAM_TIME	
COS	Arrival_Brain	From Arrival to Hospital to Imaging	Minutes	HOSP_ARR_DATE	BRAIN_IMG_DATE/TIME Minus HOSP_ARR_DATE/TIME
				HOSP_ARR_TIME	
				BRAIN_IMG_DATE	
				BRAIN_IMG_TIME	
COS	Arrival_Thrombolysis	From Arrival to Hospital to Thrombolysis	Minutes	HOSP_ARR_DATE	THROMBOLYSIS_DATE/TIME Minus HOSP_ARR_DATE/TIME
				HOSP_ARR_TIME	
				THROMBOLYSIS_DATE	
				THROMBOLYSIS_TIME	

Appendix 3: Details of Missing and Erroneous Time-Based Data Variables

Cohort	Interval Name		
IHS	Adm_Onset	Available	497
		Missing Data	46
		Erroneous Values	75
		Total	618
IHS	Onset_Team	Available	276
		Missing Data	328
		Erroneous Values	14
		Total	618
IHS	Onset_Brain	Available	285
		Missing Data	304
		Erroneous Values	16
		Interval > 1 month	1
		Total	606
IHS	Onset_Thrombolysis	Available	30
		Missing Data	13
		Erroneous Values	2
		Total	45
COS	Onset_Arrival	Available	5924
		Missing Data	4169
		Erroneous Values	70
		Total	10163
COS	Arrival_Team	Available	8496
		Missing Data	1533
		Erroneous Values	134
		Total	10163
COS	Arrival_Brain	Available	9264
		Missing Data	97
		Erroneous Values	137
		Interval > 1 month	16
		Total	9514
COS	Arrival_Thrombolysis	Available	827
		Missing Data	10
		Erroneous Values	20
		Interval > 24 hours	1
		Total	858