# Revisiting Post-thrombolysis ICH
*How are we doing Post Covid*?

# A retrospective Audit

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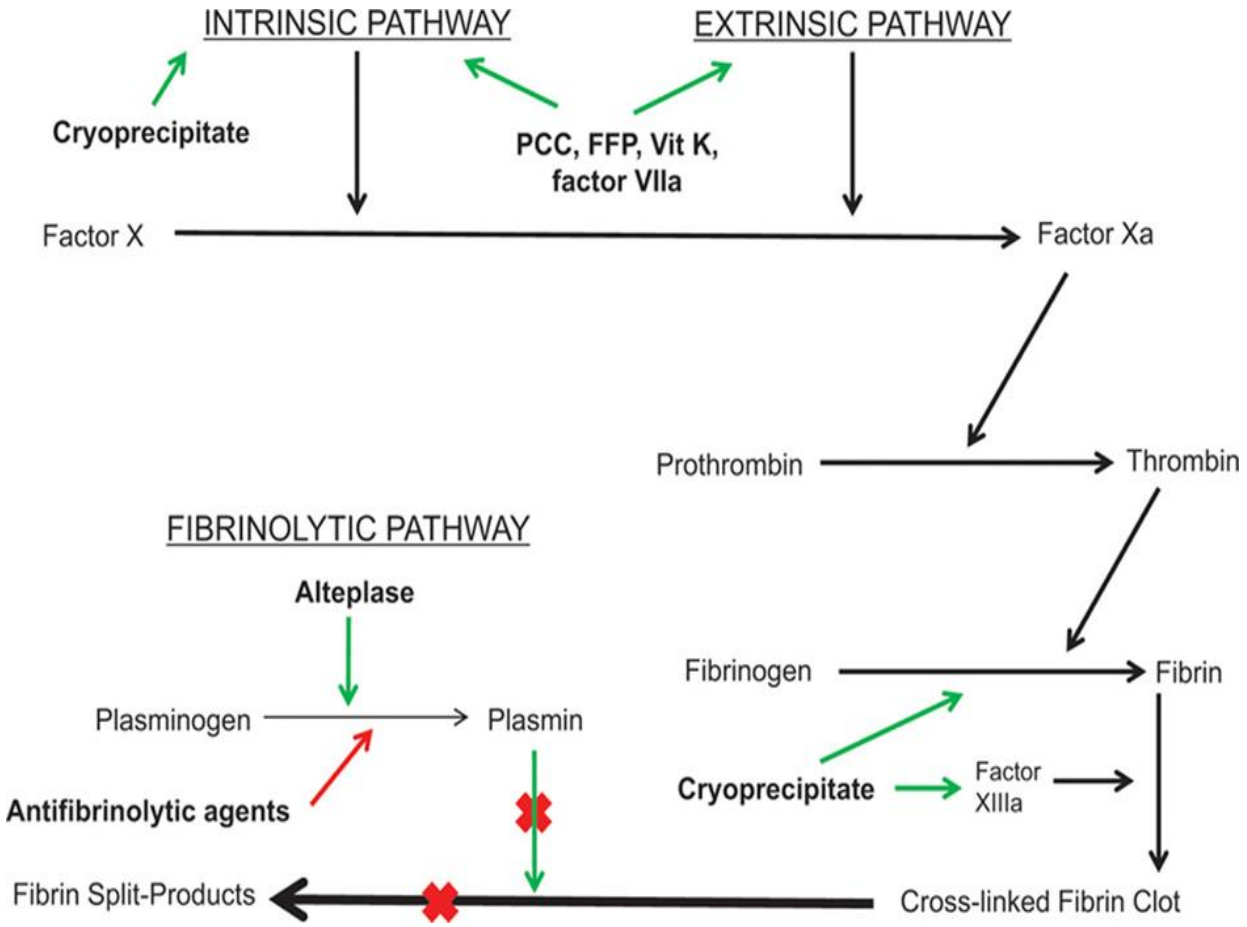
# Pathophysiology of Alteplase-Related Hemorrhagic Transformation




Mechanism of action of alteplase and various treatments in patients with thrombolysis-related hemorrhage. In green: Alteplase promotes plasmin activation, which in turn degrades cross-linked fibrin into fibrin split products and reversal agents, promoting various steps of the coagulation cascade. In red: The antifibrinolytic agents (aminocaproic acid and tranexamic acid) deactivate plasmin formation, which prevents the degradation of cross-linked fibrin

# Some Statistics:

Adverse consequences of immediate thrombolysis-related complications with haemorrhage from a multi-centre registry-based cohort study of acute stroke
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8791861/

- In recent years, the rates of thrombolysis amongst patients admitted with AIS were 11.1% in Sweden and 11–12% in England and Wales
- The average proportion of immediate TRC is around 6.4% observed in various studies in UK and abroad
- The NHS for England set a long-term thrombolysis target of 20% a year (approximately 14,000 patients/year). Assuming that the immediate TRC rate remains unchanged, the number of thrombolysis-related complications is expected to be nearly double the current number (approximately 14,000 × 6.4% = 900 patients/year).

# Post Thrombolysis ICH: What makes the trajectory safer? Considerations

- Correct selection of patients with All Exclusion Criteria being ruled out
- 'Senior Level Decision' in cases with low or borderline NHS
- Time Critical intervention and implication of delayed or prolonged DTN
- Management of Hypertension beyond 185/110 Pre-thrombolysis
- Correct Dose of Alteplase strictly based on Actual Body weight
- Rigorous monitoring of Blood Pressure, every 15 minutes, 30 minutes, hourly and 2 hourly as per agreed protocol with Target BP recorded, over 24 hours post thrombolysis
- Active management of Post Thrombolysis Bleed, as appropriate, as per agreed protocol

Overall, currently available literature suggests that sICH within 24 h of alteplase therapy or with hypofibrinogenemia might be a reasonable indication for treatment.

Although very limited data are available to support treatment of asymptomatic bleeding, the use of reversal agents for any asymptomatic PH occurring within 24 h of alteplase infusion may be considered, particularly in the setting of an ongoing coagulopathy

# Audit Rationale

Symptomatic intracranial haemorrhage (sICH) is the most feared complication of intravenous thrombolytic therapy in acute ischemic stroke. Prompt diagnosis and early correction of the coagulopathy after alteplase have remained the mainstay of treatment.

Aberrance in clinical practice around this dreaded complication within the directorate, identified earlier, led to increased morbidity and mortality

Several areas of concern were identified and addressed in the last 2 audit cycles (Cycle 1: 2013-16; Cycle 2: 2017- 18)

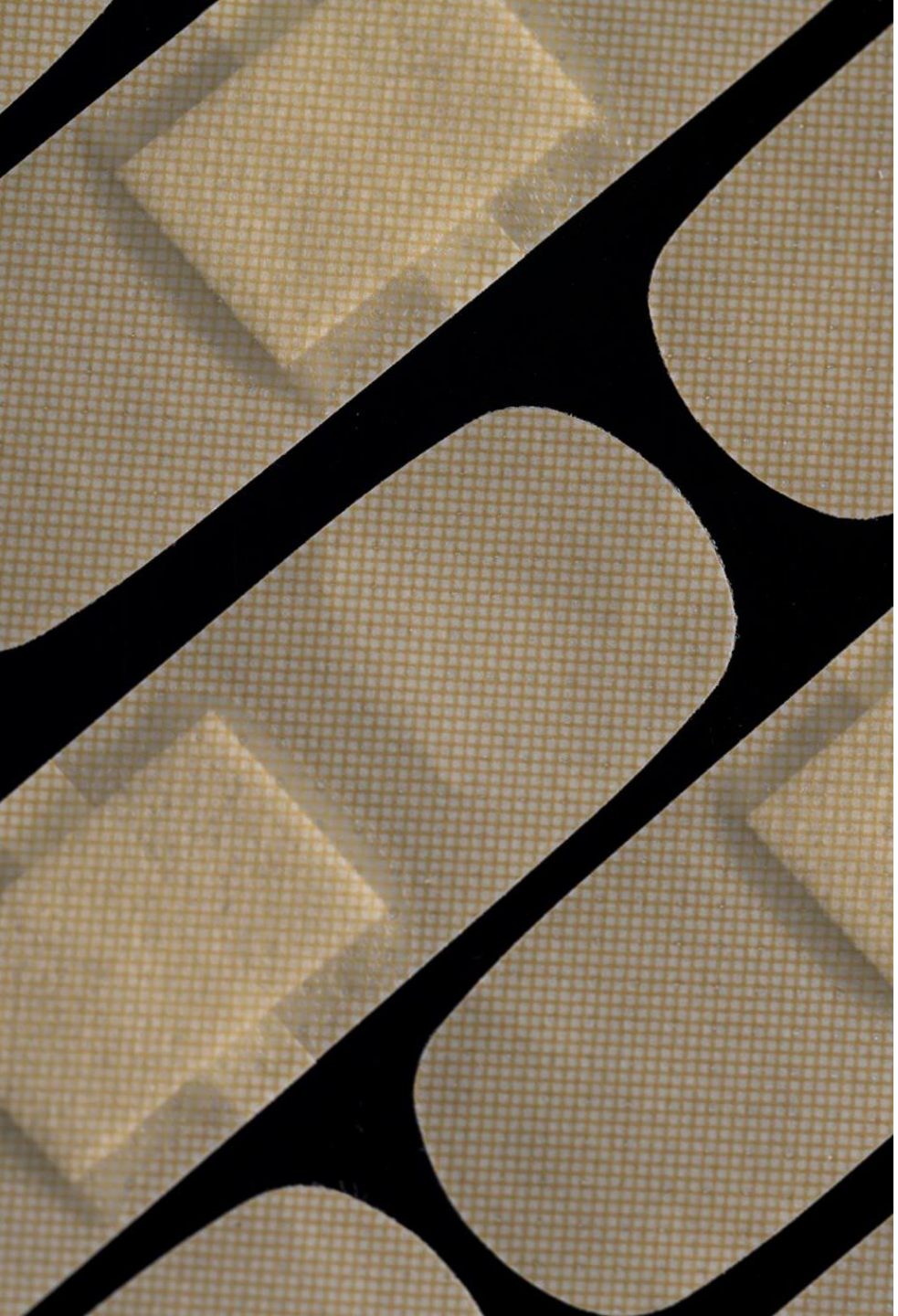
# Brief overview of previous cycles

| Criteria | Std (%) | Result of cycle 1 | Result of cycle 2 | Compliant ? | Risk |
|---|---|---|---|---|---|
| NIH Scoring on admission | 100 % | 100 % | 100 % | 100% | None |
| Management of Blood Pressure in Hyper-acute phase Pre Thrombolysis | 100 % | 100 % | 100 % | 100% | None |
| Management of Blood Pressure in the immediate Post Thrombolysis phase (15 mins) | 100 % | 85% | 60% | X | Major |
| 30 min, 60 min and 2 hourly BP measurements | 100 % | Approx 50% | Approx 50% | X | Major |
| Management of ICH Post thrombolysis within first 24 hours | 100 % | 15% | 15% | X | Major |
| Body weight based Dosing of Alteplase | 100% | 0 % | 0 % | XX | Major |

# Audit Design

Retrospective Study

Measure data from ED records and ward records



# Inclusion Criteria:
## How best to define?
## National /International Standards

1. Symptomatic Vs Asymptomatic Bleed: Does it matter?

2. Size, Location and Volume of bleed: Does it change outcome?

3. Which category of Post- thrombolysis bleed tend to have poorer prognosis?

4. Earlier 2 cycles did not take into account the above variables and as such may not have reflected a true outcome in terms of morbidity or mortality in patients with Post Thrombolysis bleed

# The insight

sICH classification after thrombolytic therapy is based on radiographic appearance and associated neurological deterioration.

→

Traditional classification distinguishes between hemorrhagic infarction and parenchymal hematoma.

→

The Heidelberg Bleeding Classification is a proposed expanded system.

↓

Integrating ICH and neurological deterioration with alteplase is challenging due to varying definitions and other causes of deterioration.

→

Different definitions of sICH impact reported rates and have varying interrater agreement and correlation with mortality.

→

ECASS II has high interrater agreement, while SITS-MOST correlates strongly with mortality.

# The Heidelberg Bleeding Classification

| Table 1. Anatomic Description of Intracranial Hemorrhages | | |
|---|---|---|
| Class | Type | Description |
| 1 | Hemorrhagic transformation of infarcted brain tissue | |
| 1a | HI1 | Scattered small petechiae, no mass effect |
| 1b | HI2 | Confluent petechiae, no mass effect |
| 1c | PH1 | Hematoma within infarcted tissue, occupying <30%, no substantive mass effect |
| 2 | Intracerebral hemorrhage within and beyond infarcted brain tissue | |
| | PH2 | Hematoma occupying 30% or more of the infarcted tissue, with obvious mass effect |
| 3 | Intracerebral hemorrhage outside the infarcted brain tissue or intracranial-extracerebral hemorrhage | |
| 3a | Parenchymal hematoma remote from infarcted brain tissue | |
| 3b | Intraventricular hemorrhage | |
| 3c | Subarachnoid hemorrhage | |
| 3d | Subdural hemorrhage | |

# Defining Clinical Deterioration
## In the context of thrombolysis

- increase of ≥4 points in total NIHSS score at the time of diagnosis compared with immediately before worsening or ≥2 points in 1 NIHSS category,
- Intubation, hemicraniectomy, ventricular drain placement, or other major medical/surgical intervention
- Any haemorrhage
- Absence of alternative explanation for deterioration
- Up to 24-36 h after intervention

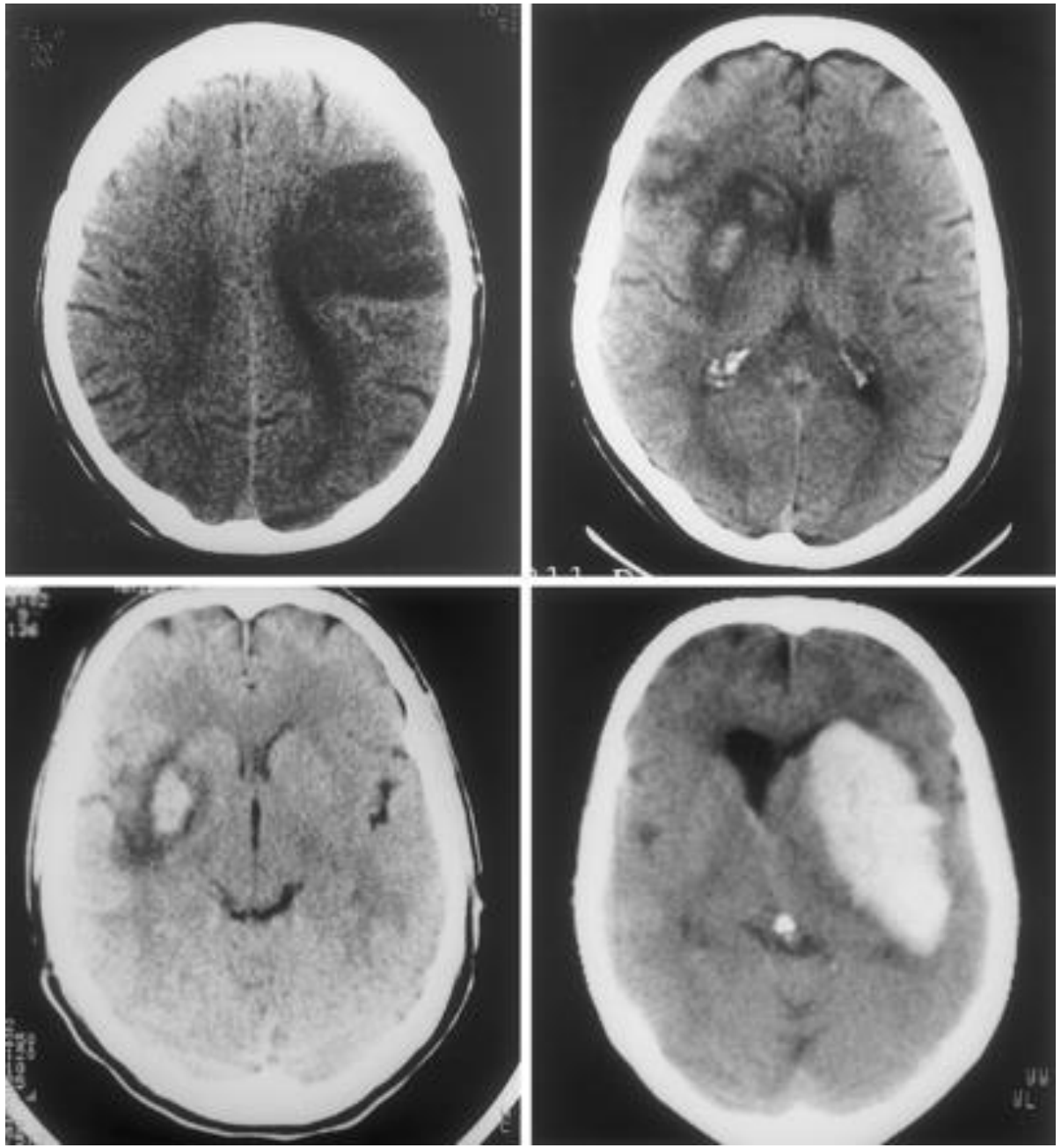
**Subtypes of hemorrhagic transformation:**

HI1 (top left),

HI2 (top right),

PH1 (bottom left),

**PH2 (bottom right)**



# Radiographic Appearance and risk of expansion : Unclear association but PH2 and above appear significant

It is unclear whether type of ICH (HI-1, HI-2, PH-1, PH-2, subarachnoid hemorrhage, or subdural hemorrhage) affects the risk of expansion

Existing studies of hemorrhage expansion after thrombolysis typically include only sICH and thus are weighted toward PH-2

One study considered radiographic type and found that PH-2 represented nearly 2/3, ≈64% of sICH cases

It therefore appears reasonable to look more specifically at Post Thrombolysis Symptomatic ICH patients with PH2 and above in our study cohort to analyse outcome

# Targets and Objectives

| Criteria & Standards | | | | |
|---|---|---|---|---|
| | Criteria | Standard (%) | Exceptions | Source |
| 1 | NIH Scoring on admission | 100 % | none | NINDS Guideline |
| 2 | Management of Blood Pressure in Hyper-acute phase Pre Thrombolysis | 100% | none | AHA Guideline |
| 3 | Management of Blood Pressure in the immediate Post Thrombolysis phase | 100% | none | AHA Guideline |
| 4 | 30 min, 60 min and 2 hourly BP measurements | 100% | none | AHA Guideline |
| 5 | Management of ICH Post thrombolysis | 100% | none | Trust Guideline available in Intranet |
| 6 | Adherence to Current updated Trust Guideline | 100% | none | Current Evidence Based Researches<br>and Outcome of discussions from<br>Seminars and Symposiums from WSC<br>2014 and ESC 2016 |

# Metrics Measured

- Demographic Details
- Modified Rankin Scores
- Blood Pressure Management & Monitoring
- Time delay in detection of bleed
- Management of bleed
- Weight & Alteplase Dose
- Inclusion Criteria for thrombolysis

# Time Period
# January 2022 to April 2023

**1372** patients were diagnosed with ischaemic stroke.

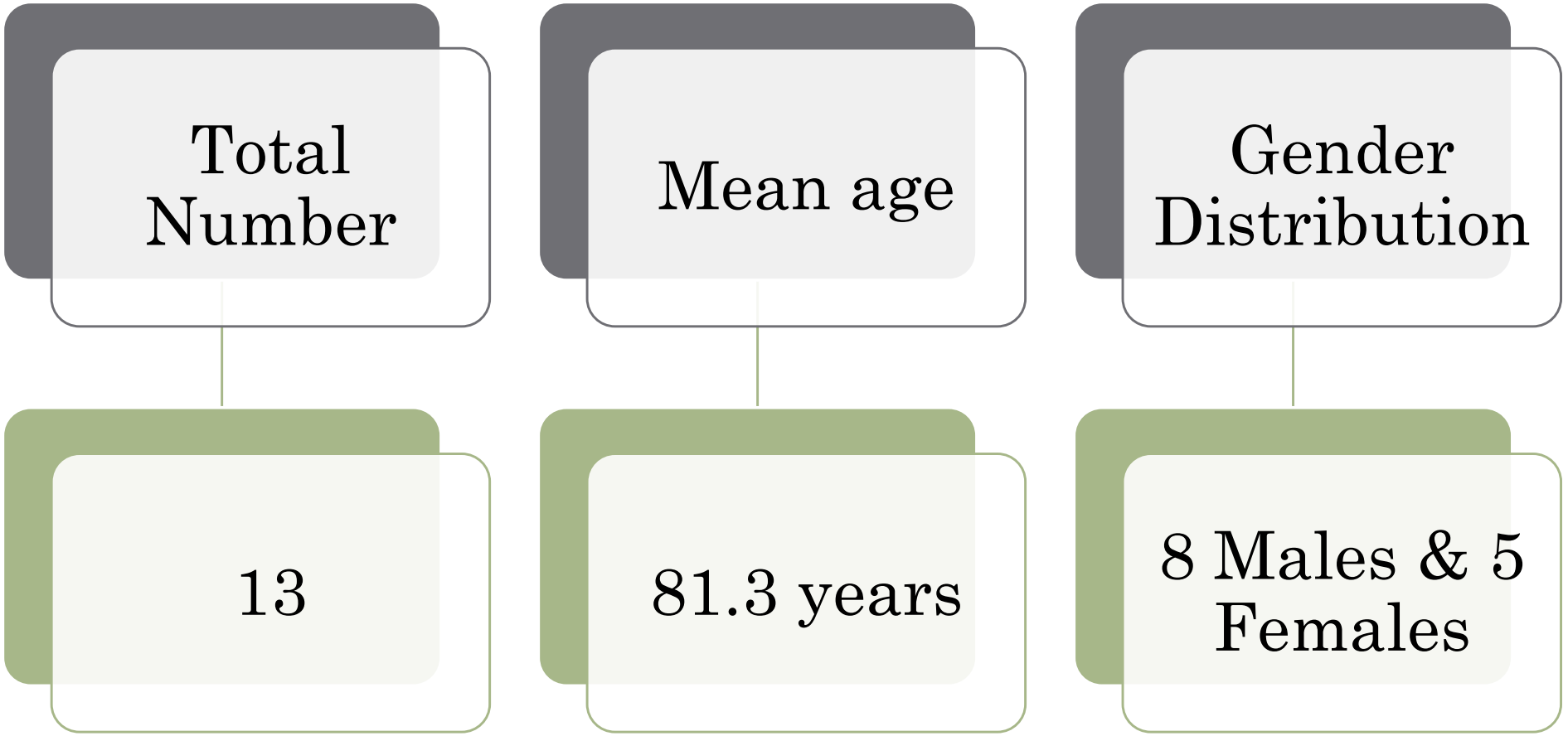
Of these, **168 (12.2%)** patients were thrombolysed.

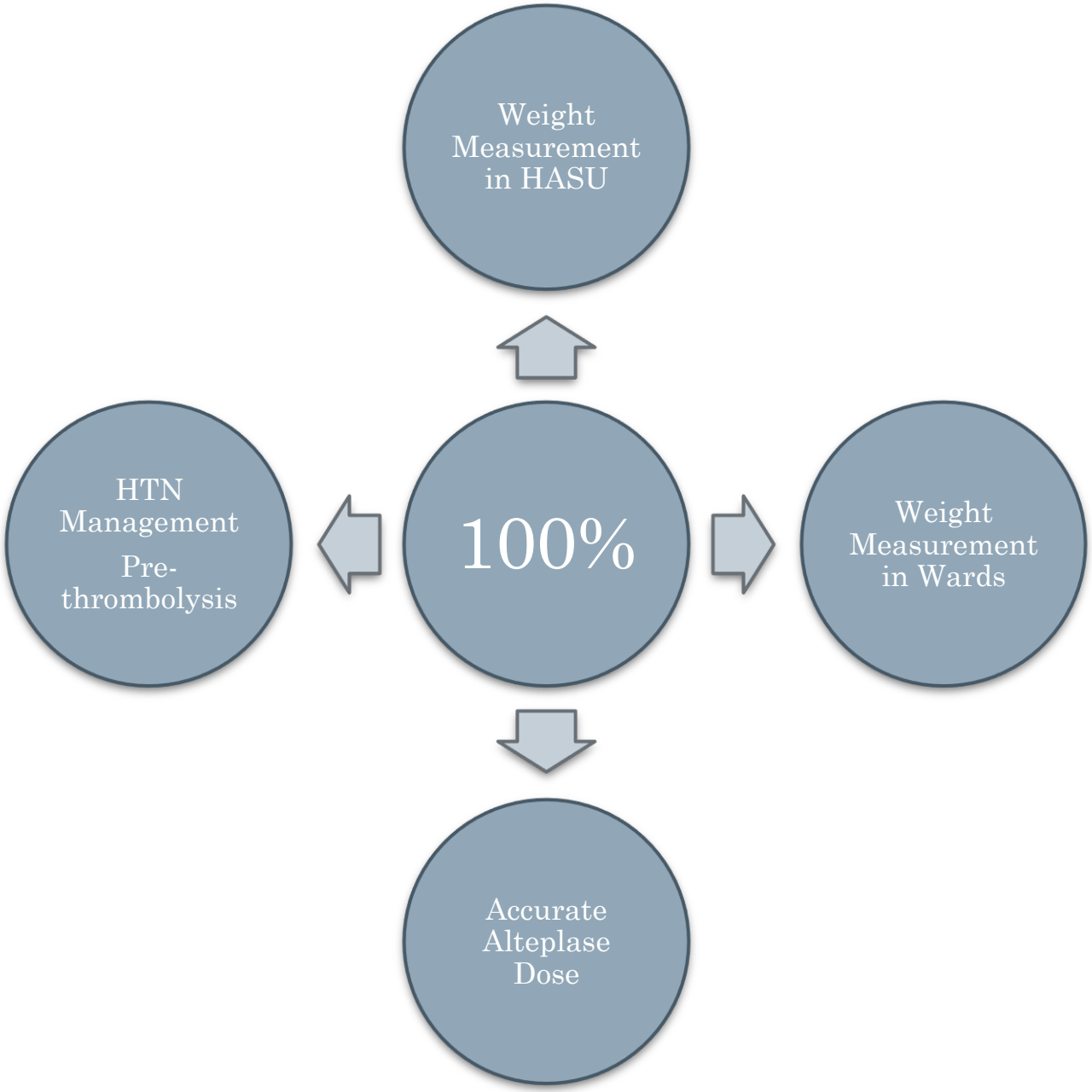
Of the 168, a total of **17 (10.1%)** had post-thrombolysis intracranial hemorrhage.

Of the 17, **13** met the Heidelberg Criteria of the study of PH2 and above (7.73% of total).

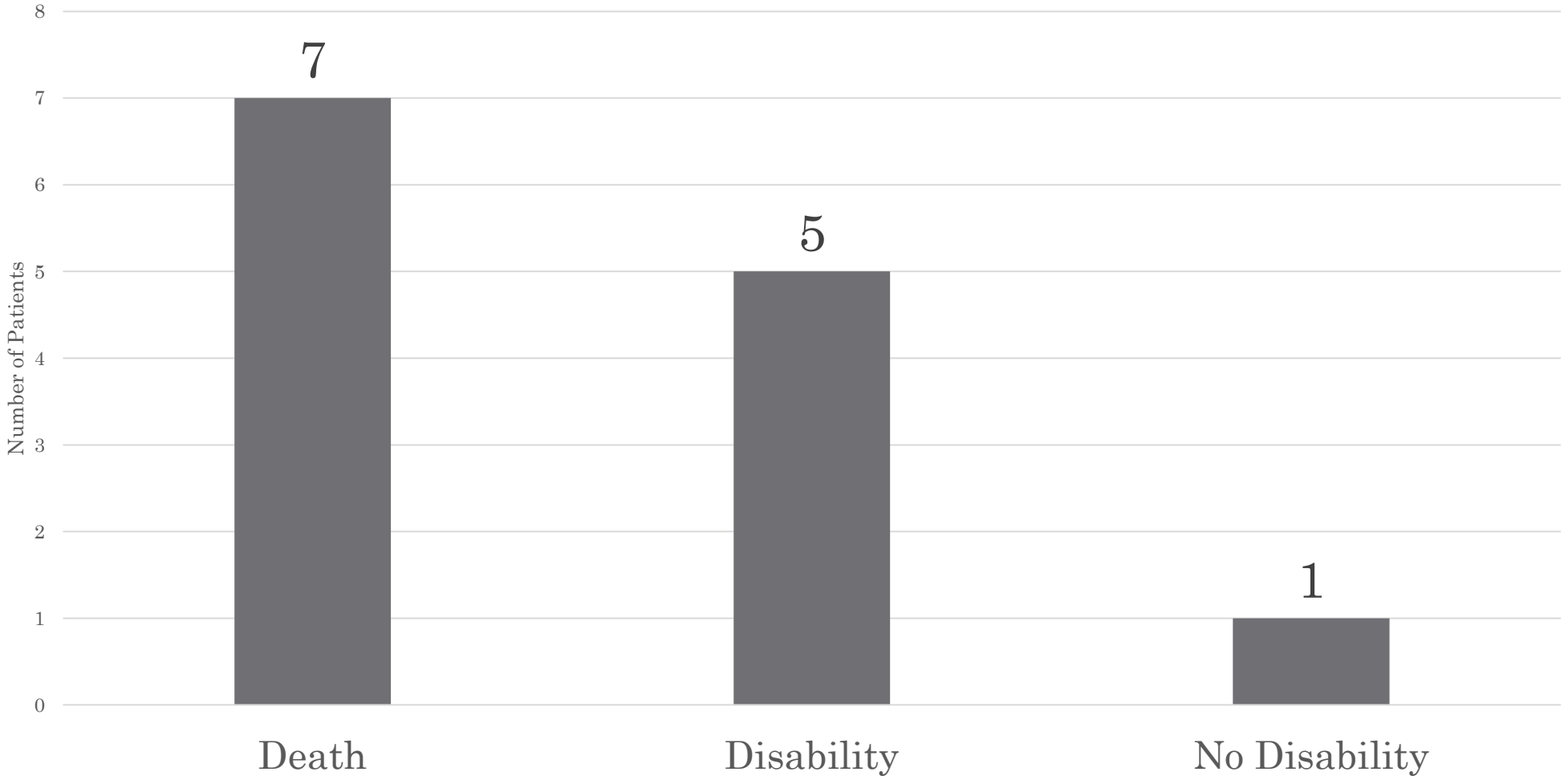
Of the 13, 8 were asymptomatic while **5 (3% of the total)** were symptomatic.

# Demographics



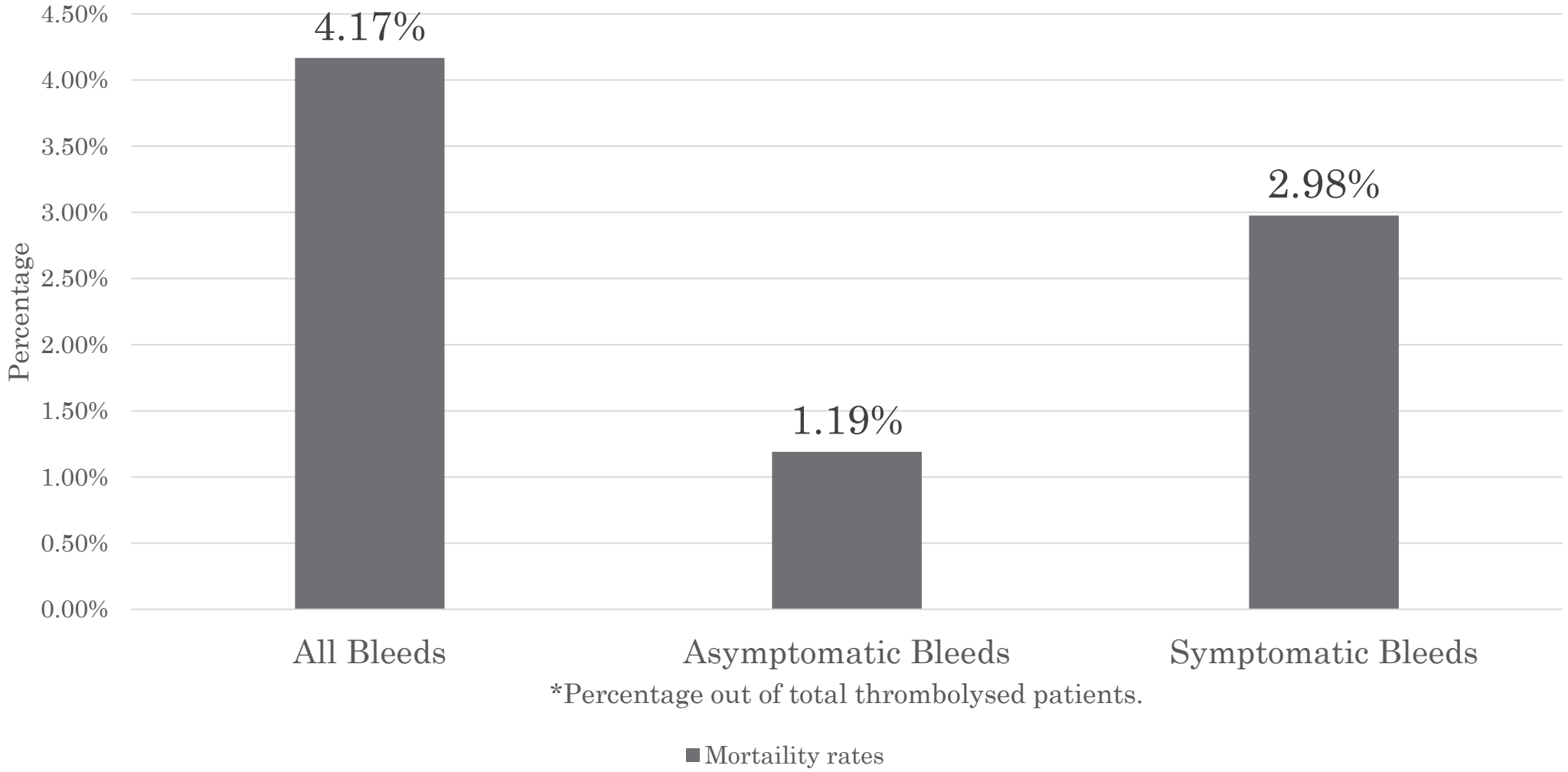

Weight Measurement in HASU
HTN Management Pre-thrombolysis
100%
Weight Measurement in Wards
Accurate Alteplase Dose

# Mortality & Disability Post-thrombolysis ICH

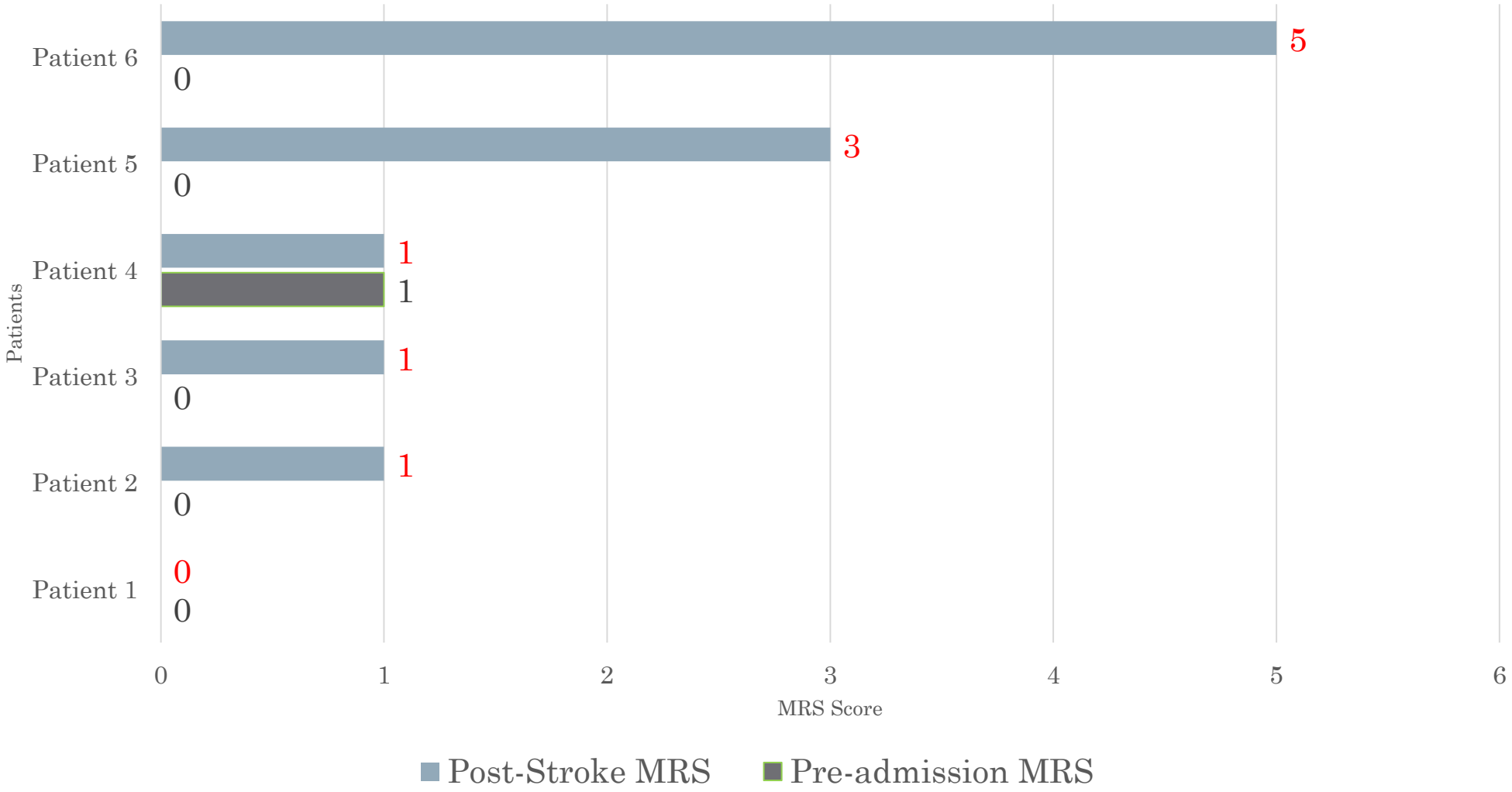



Disability means any increase in MRS score following stroke; No Disability → No change in MRS Pre & Post-stroke

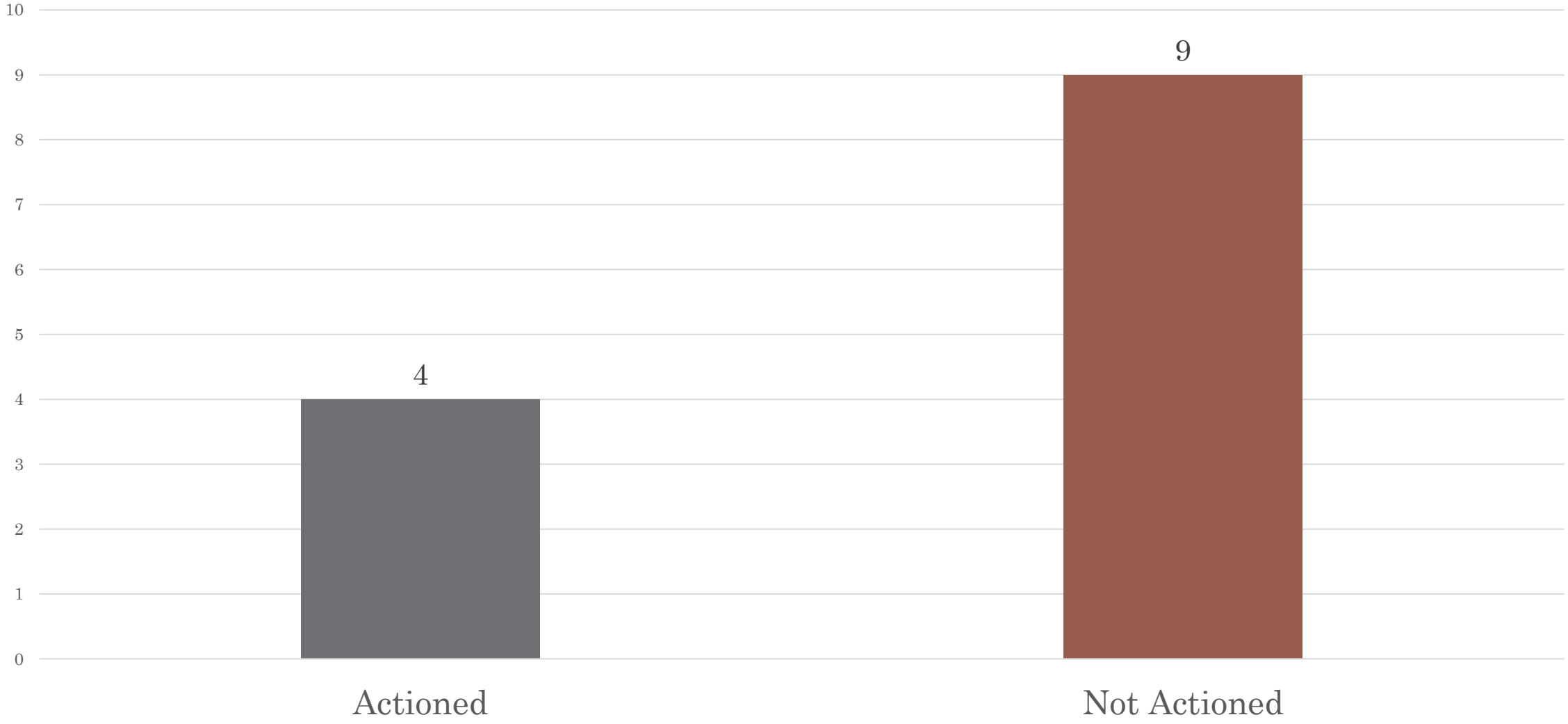
# Mortaility rates



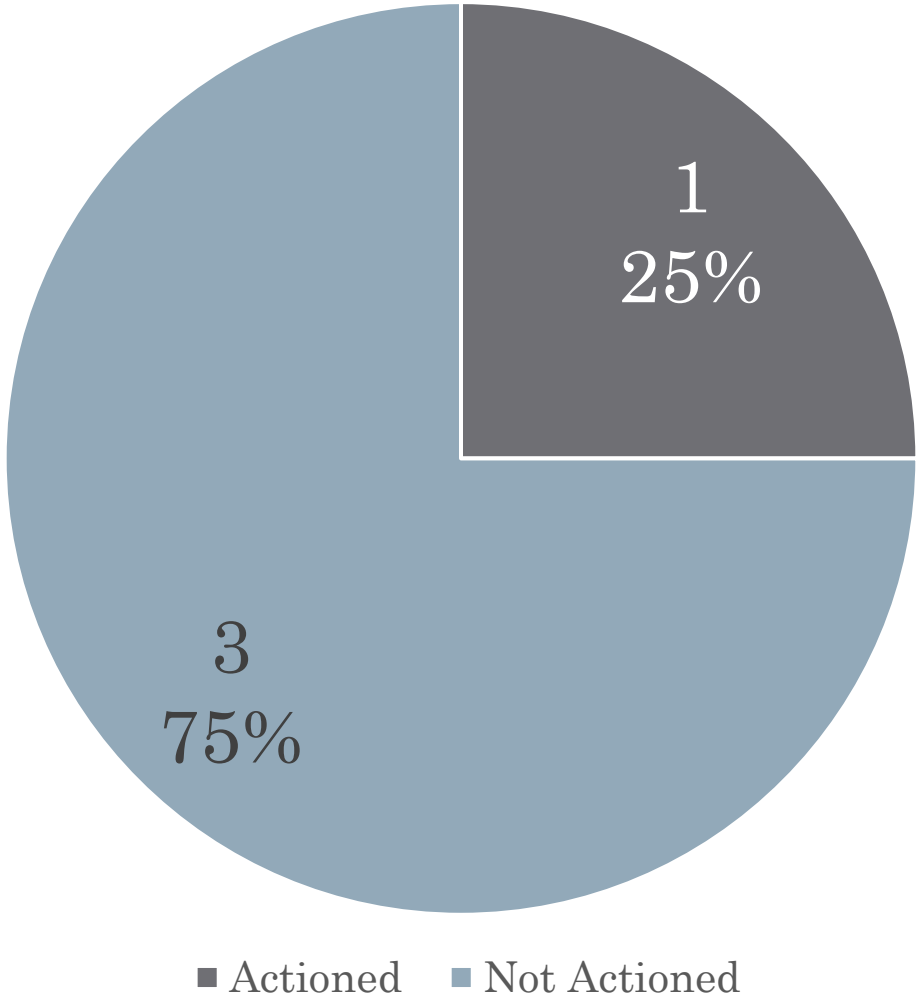
# Patient wise Changes in MRS following Stroke



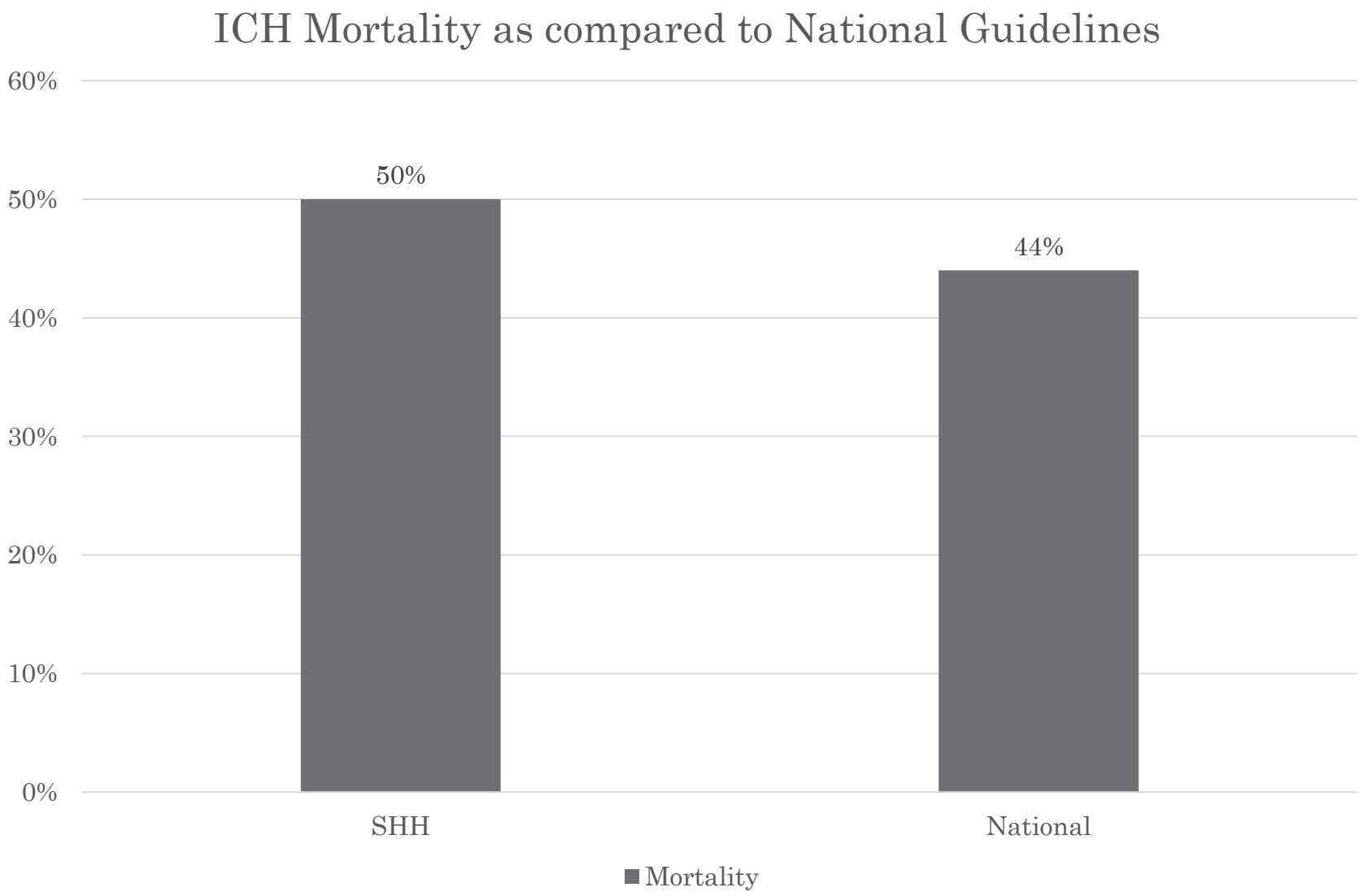
# Action taken in 90 minutes of bleed detection



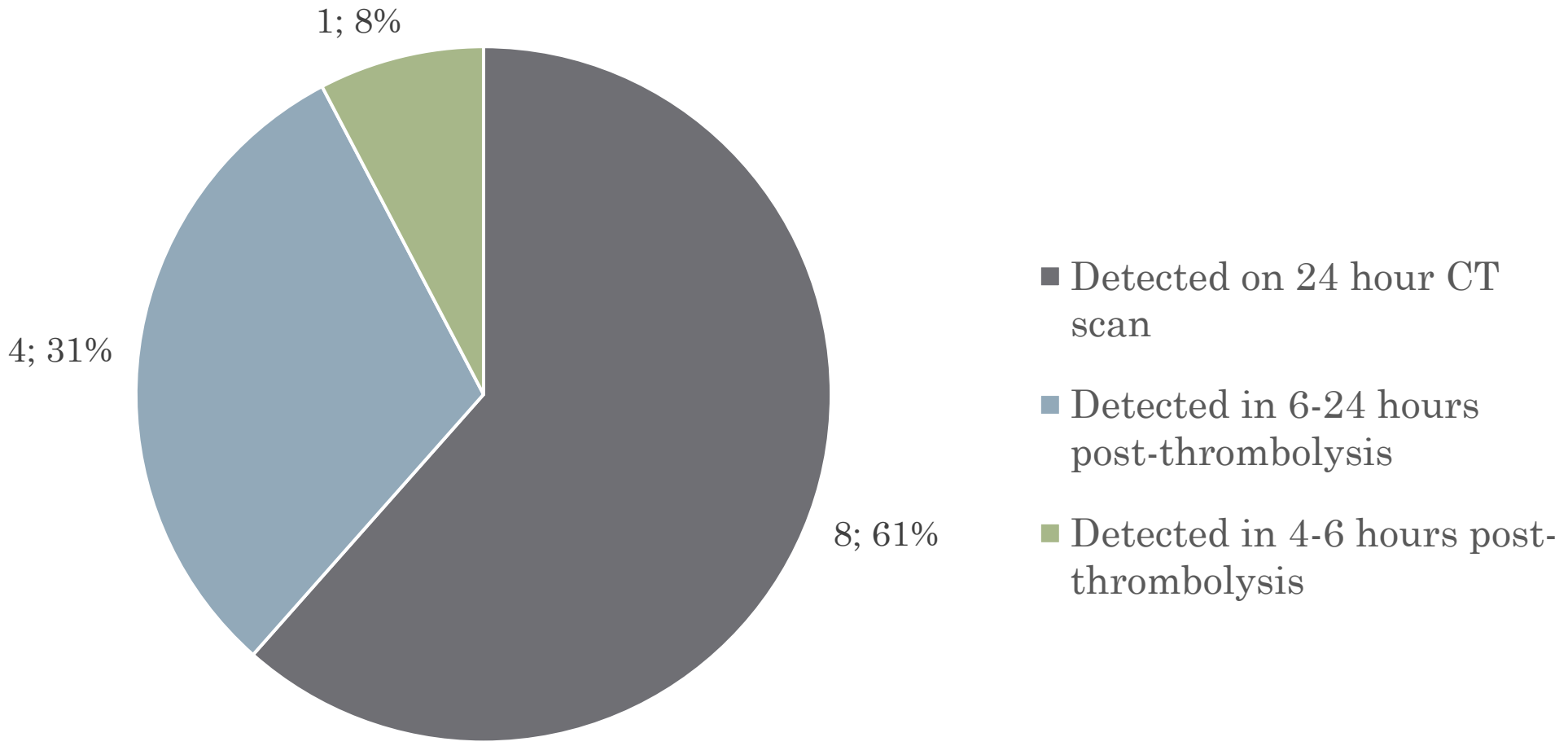
# Fatal Symptomatic Bleed — Actioned within 90 minutes



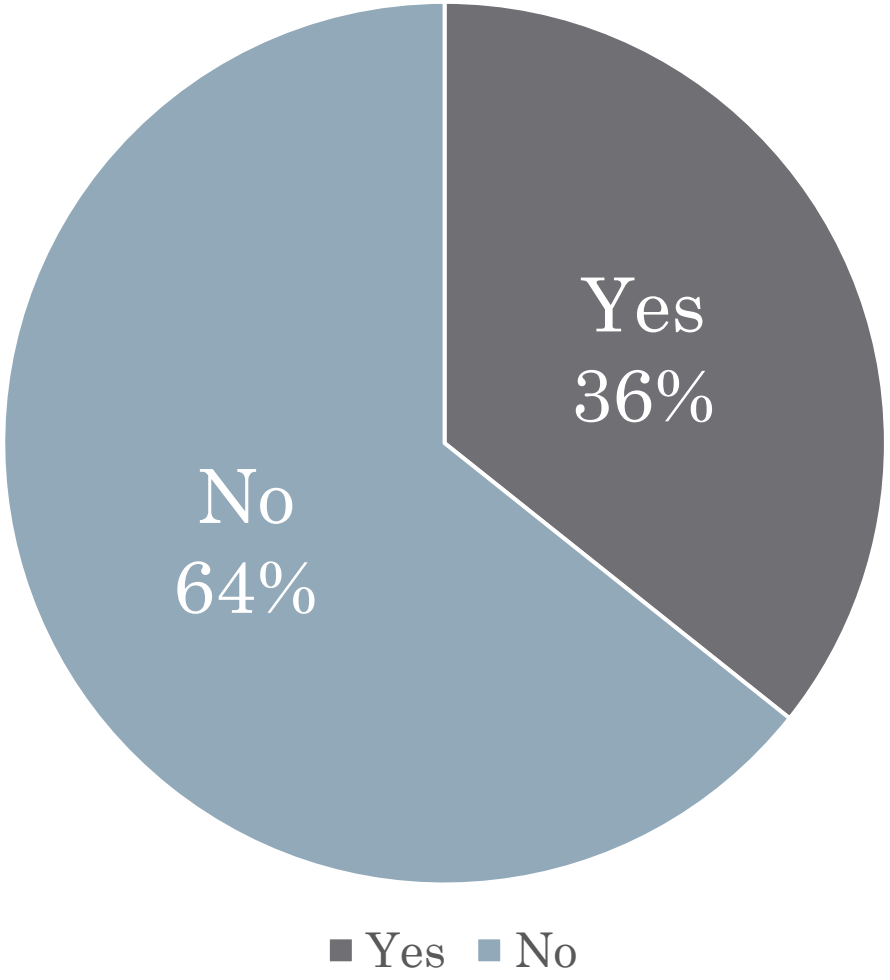

*Note – Number totals to 4, 1 patient was put on End of Life, hence not intervened


ICH Mortality as compared to National Guidelines
60%
50%
40%
30%
20%
10%
0%
50%
44%
SHH
National
Mortality

# Detection of post-thrombolysis bleed



# Identification of Target BP in notes

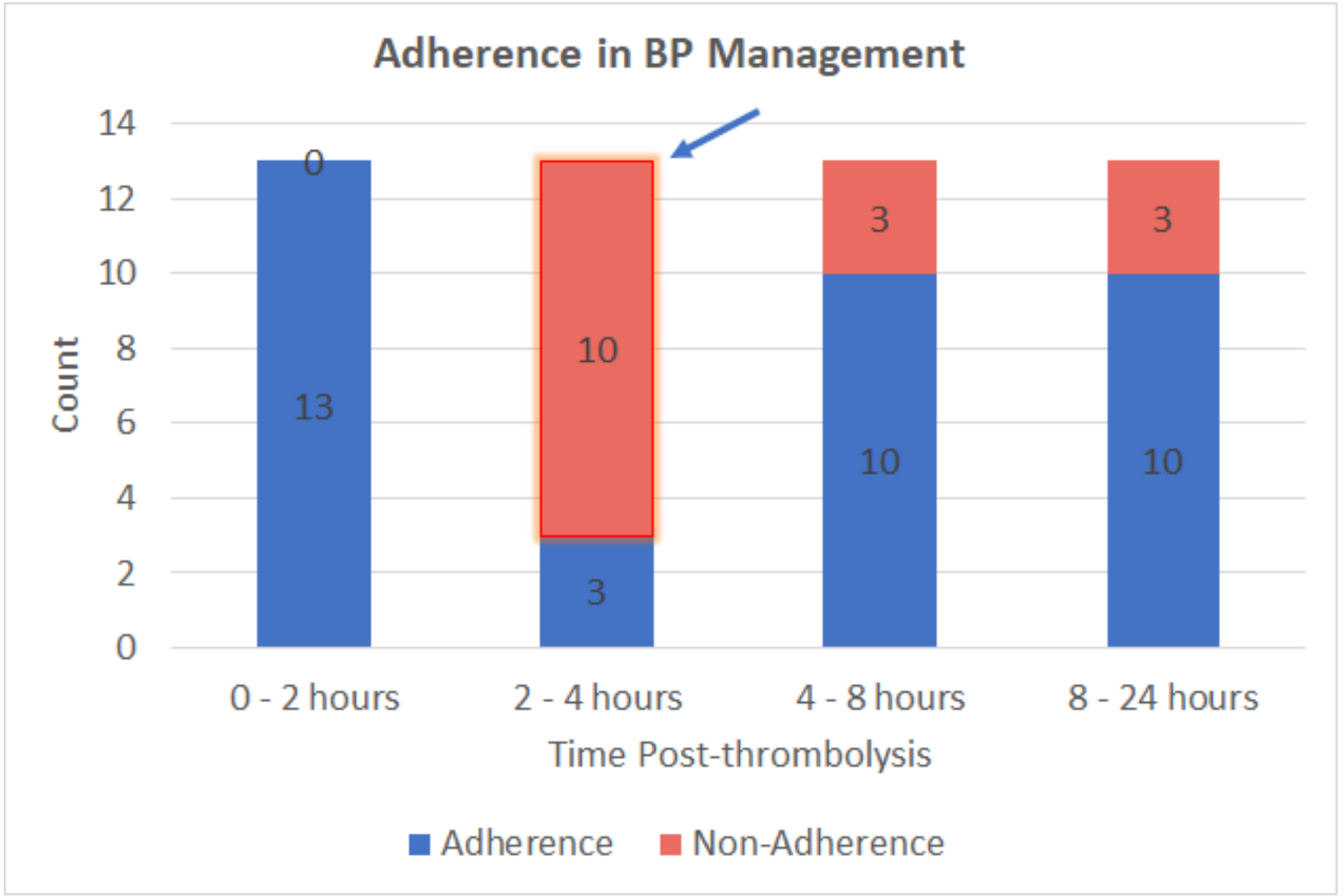


# Blood Pressure Monitoring

| | |
|---|---|
| 0-2 hours | • Every 15 minutes |
| 2-4 hours | • Every 30 minutes |
| 4-8 hours | • Every 60 minutes |
| 8 – 24 hours | • Every 2 hours |

# BP Monitoring — prior Audits

| BP recording | 2013-16 | 2017-18 | 2019-2020 |
|---|---|---|---|
| Every 15 minutes for first 2 hours (0-2 hours) | 85% | 60% | 27% |
| Every 30 minutes for next 2 hours (2-4 hours) | 10% | 50% | 0% |
| Every 60 minutes for next 4 hours (4-8 hours) | 5% | 60% | 73% |
| Every 2 hours until repeat CT Head Scan | 5% | 40% | 91% |

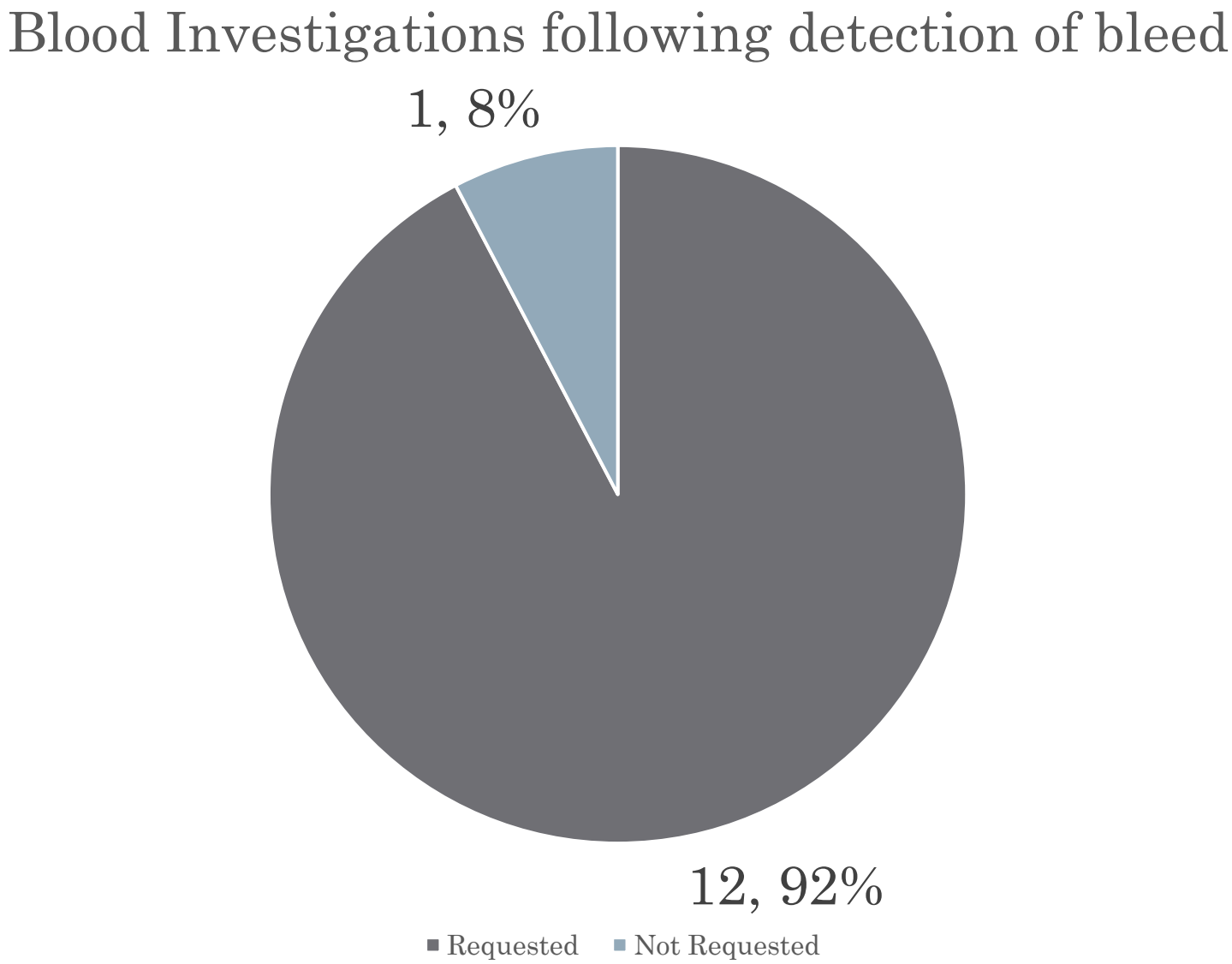

Adherence in BP Management
14
12
10
8
6
4
2
0
Count
0
13
10
3
3
10
3
10
0 - 2 hours
2 - 4 hours
4 - 8 hours
8 - 24 hours
Time Post-thrombolysis
Adherence
Non-Adherence

| 418819711 | 4488513956 | 4306779017 | 4405205000 | 4222336432 |
|---|---|---|---|---|
| **90 years** | 65 | 90 | 77 | 87 |
| **NIH Score 22** | NIH Score 8 | NIH SCORE 14 | NIH Score 13 | NIH Score 5 |
| **Aspect <5** | Aspect 8 | | Aspect 5 | Aspect 9 |
| **GCS 11/15** | GCS 14/15 | GCS 11/15 | GCS 10/15 | GCS 15/15 |
| **Deteriorated 2/12 hours—seen by stroke team—GCS 11—8 & NIH score 22—25, Tier 2** | Deteriorated after 7 ½ hours, Worsening left sided weakness and GCS Dropped from 14—11/15. Seen by Medical team. Tier 2 | Deteriorated after 8 hours, Increasing agitation and Respiratory distress, GCS 10/15, Reviewed by Medical team on call, decided by stroke consultant – not for reversal as deterioration is due to Primary infarction rather haemorrhage. | Deteriorated after 23 hours, GCS DROPPED FROM 10/15—6/15, Seen by stroke team –End of Life care and not for Reversal | Deteriorated after 6 hours, Drop in GCS 15/15—13/15, tier 2 , seen by stroke team, BP at 18:20—236/90 |
| **Fibringoen and FBC requested** | Blood tests requested | Blood tests requested | NA | Blood tests requested |

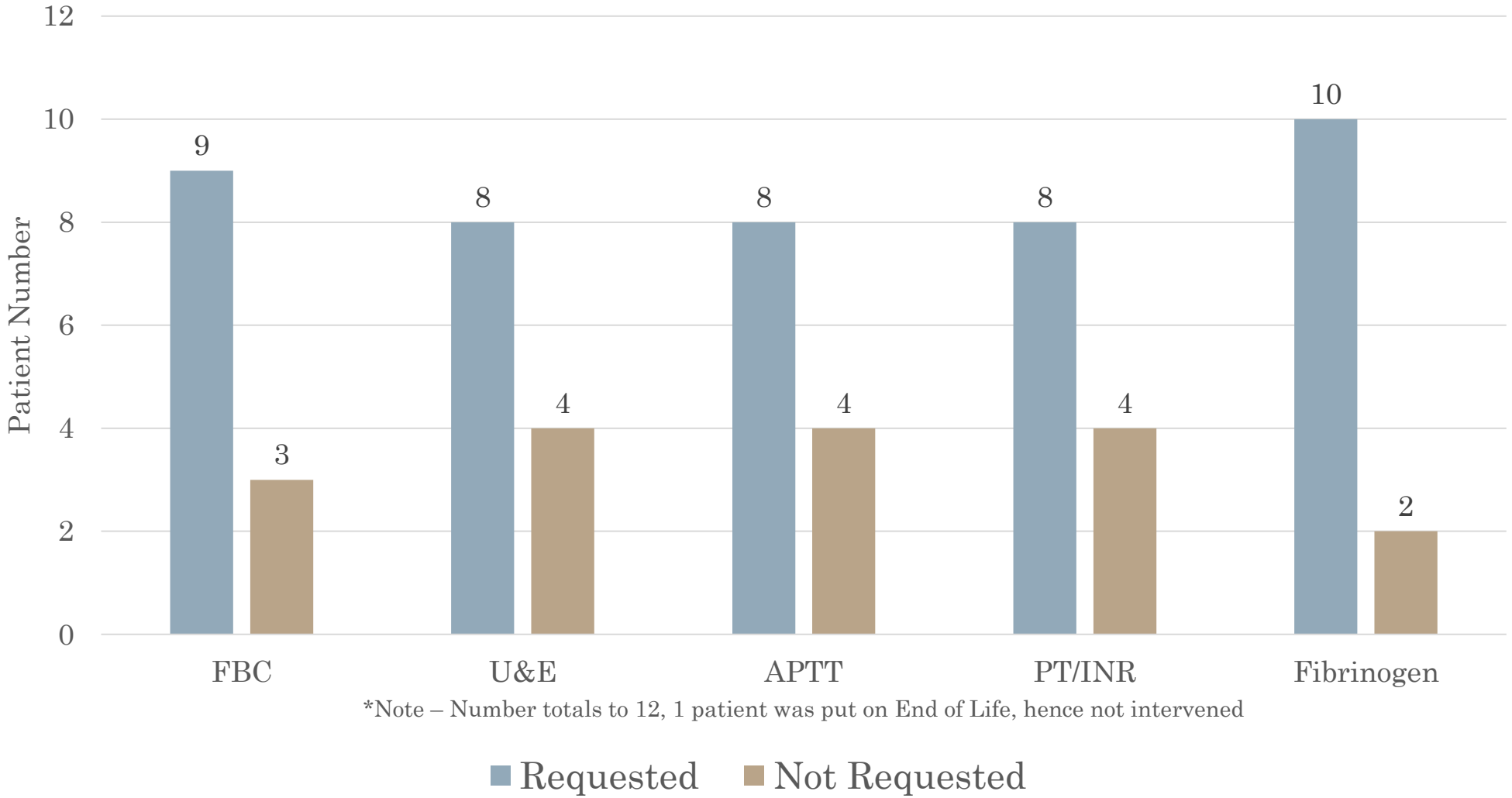
| Blood products given and documentation within 90 minutes | Blood products received but results not documented within 90 minutes | Not documented within 90 minutes | | Blood products given but not documented within 90 minutes | |
|---|---|---|---|---|---|
| **BP Recordings** | BP Recordings | BP Recordings | BP Recordings | BP Recordings | |
| **15:53** | 20:03 | 20:47 | 14:50 | 11:45 | |
| **16:14** | 20:09 | 21:01 | 14:57 | 11:52 | |
| **16:41** | 20:17 | 21:29 | 15:03 | 11:58 | |
| **16:46** | 20:30 | 21:58 | 15:11 | 12:10 | |
| **17:30 ward** | 20:45 | 22:38 ward | 15:24 | 12:17 | |
| **01:39** | 21:01 | 23:40 | 15:41 | 12:34 | |
| **04:15** | 21:33 | 00:14 | 16:09 | 12:59 | |
| **06:18** | 22:03 | 01:33 | 17:04 | 13:03 | |
| **09:57** | 22:40 ward | 02:31 | 17:54 Ward | 13:57 ward | |
| **12:18** | 23:23 | 03:34 | 18:55 | 15:29 | |
| **14:07** | 00:00 | 04:14 | 20:28 | 16:36 | |
| **16:58** | 01:05 | 04:56 | 20:45 | 18:20 | |
| **21:24** | 02:07 | 06:15 | 22:24 | 19:26 | |
| | 03:36 | 07:09 | 22:53 | 21:30 | |
| | 04:20 | 08:37 | 23:17 | 21:47 | |
| | 06:19 | 10:04 | 23:51 | 22:57 | |
| | 07:28 | 11:39 | 00:15 | 23:25 | |
| | 08:48 | 12:44 | 00:44 | 23:50 | |
| | 09:52 | 14:08 | 01:24 | 00:09 | |
| | 11:31 | 15:34 | 02:17 | 00:34 | |
| | 11:40 | 16:48 | 03:04 | 01:39 | |
| | 11:47 | 17:48 | 03:37 | 02:57 | |
| | 11:57 | 18:40 | 04:44 | 03:59 | |
| | 12:08 | 19:53 | 05:44 | 04:53 | |
| | 13:16 | 22:25 | 06:55 | 05:44 | |
| | 13:25 | | 07:38 | 06:51 | |
| | | | 08:02 | 06:51 | |
| | | | 09:18 | 07:43 | |
| | | | 10:23 | 09:04 | |
| | | | 11:31 | 10:35 | |
| | | | 12:49 | 12:36 | |
| | | | 13:37 | | |
| | | | 14:07 | | |
| | | | | | |

# Updated BP Monitoring

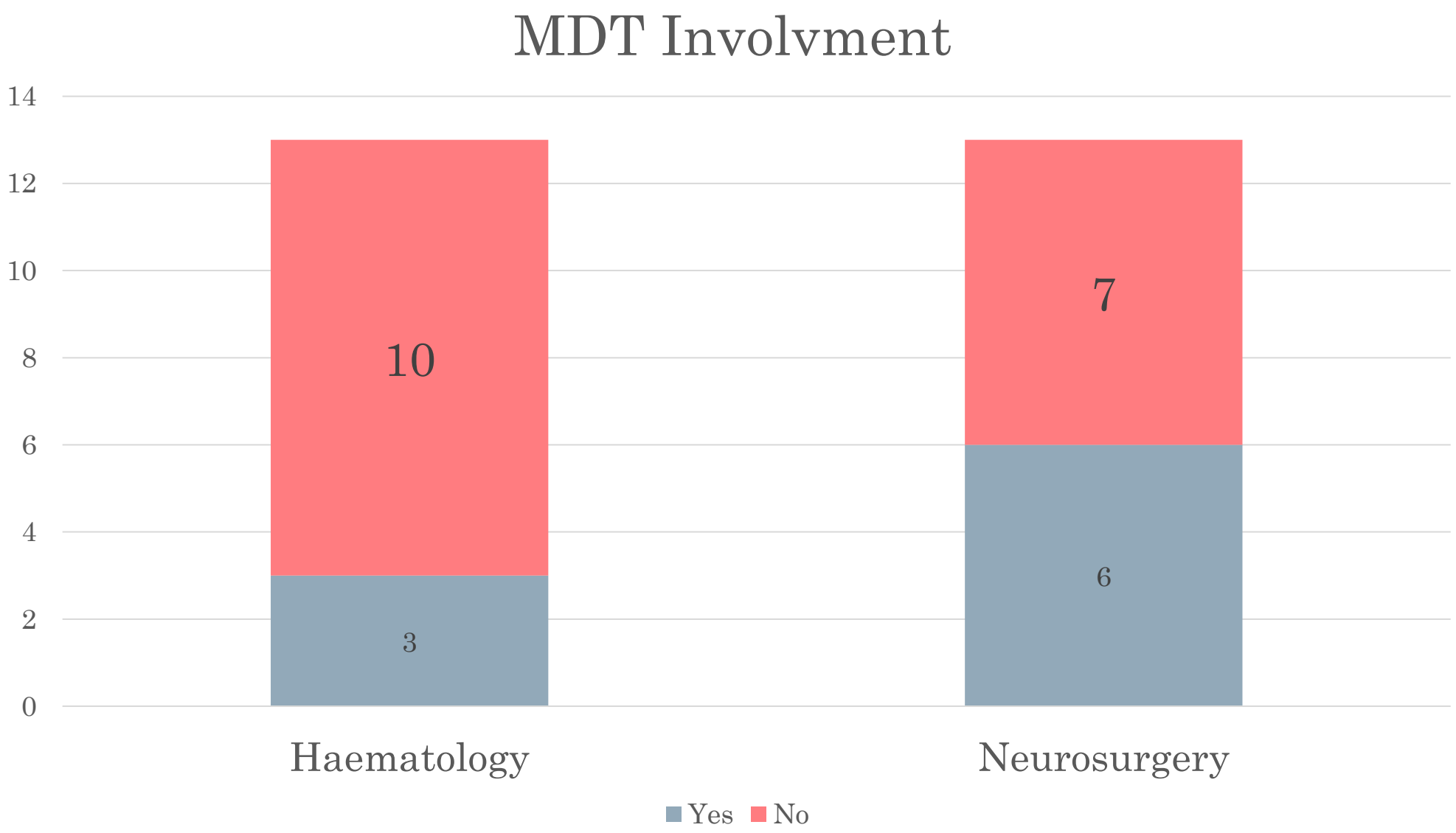
| BP recording | 2013-16 | 2017-18 | 2019-2020 | 2023-24 |
|---|---|---|---|---|
| Every 15 minutes for first 2 hours (0-2 hours) | 85% | 60% | 27% | **100%** |
| Every 30 minutes for next 2 hours (2-4 hours) | 10% | 50% | 0% | **23%** |
| Every 60 minutes for next 4 hours (4-8 hours) | 5% | 60% | 73% | **77%** |
| Every 2 hours until repeat CT Head Scan | 5% | 40% | 91% | **91%** |


Blood Investigations following detection of bleed
1, 8%
12, 92%
Requested
Not Requested

# Breakdown of Blood Requests post bleed detection




*Note – Number totals to 12, 1 patient was put on End of Life, hence not intervened


MDT Involvment
14
12
10
8
6
4
2
0
10
3
7
6
Haematology
Neurosurgery
Yes
No

# Learning Point

- Appropriate BP monitoring and Weight measurement are one of the most cost-effective and efficient methods of preventing post-thrombolysis complications
- We seem to be doing very well now in terms of 'Dosing of Alteplase' based on Body Weight
- Some further improvements required in BP monitoring all-over, and especially in 2—4-hour period post-thrombolysis
- It is difficult to envisage to what extent retrospective entries contributed to a mismatch or deviation from accepted standard
- Focus on real time entries by nursing staff may show improved compliance
- Staffing issues, especially when patients are being transferred to the AIO ASU from HASU may have to be looked at to facilitate better compliance of accepted standard
- Re-Audit in 18-24 months with a larger cohort and with subset analysis of aberrance in monitoring, if any, with time of bleed to see if causal relationships exist

# Action Points

Some further improvements required in BP monitoring all-over, and especially in 2—4-hour period post-thrombolysis : Electronic System does not allow retrospective entry and as such a real time entry to be incorporated on each measurement. Metron Clare Mcquaker to raise awareness and discuss amongst nursing colleagues : Completed

Staffing issues, especially when patients are being transferred to the A1O ASU from HASU may have to be looked at to facilitate better compliance of accepted standard: This can be technically challenging, given current staff shortage and unanticipated sickness. Metron Clare Mcquaker to raise awareness of the Stroke Nurse responsibilities and appropriate hand over to the staff on night shift with further discussion amongst nursing colleagues : Completed

More explicit documentation in notes during various stages of patient's clinical trajectory in the first 24 hours: Clinical Governance Lead Dr Datta to discuss in Quarterly Governance Meeting and raise awareness: Completed

Re-Audit in 18-24 months with a larger cohort and with subset analysis of aberrance in monitoring, if any, with time of bleed to see if causal relationships exist: To be undertaken by Lead, Clinical Governance

# Resources

- https://www.ahajournals.org/doi/full/10.1161/str.0000000000000152