

# **Intraparenchymal hematoma-Who warrants surgical decompression / minimally invasive evacuation**

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HARVARD MEDICAL SCHOOL  
TEACHING HOSPITAL

# DISCLOSURES

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Medtronic (Consultant)

Pipeline proctor > 100 cases

# ICH Surgical Trials (2004-2023)

| Year | Surgical Trial | Outcome  | Aim  | Evacuation Method           | Patients | Result  |
|------|----------------|----------|--|-----------------------------|----------|---|
| 2004 | STICH          | Failed   | Early surgery vs. Initial Conservative TX for sICH                         | Any method available        | 1033     | Did not achieve primary endpoint  |
| 2005 | STICH II       | Failed   | Early surgery vs. Initial Conservative TX for LOBAR sICH                   | Any method available        | 601      | Signal – not statistically significant  |
| 2013 | MISTIE II      | N/A      | Safety of MIS and rtPA to remove ICH                                       | Intraclot catheter and rtPA | 118      | N/A - Drug safety study, not powered for efficacy   |
| 2019 | MISTIE III     | Failed   | Safety & Efficacy of MIS and rtPA for 3 days to remove ICH vs MM           | Intraclot catheter and rtPA | 506      | Achieved 4% difference, goal was 12%  |
| 2023 | ENRICH         | Positive | Improve functional outcome >97.5% for MIPS over MM at 180 days using UWmRS | MIPS – BrainPath and Myriad | 300      | <b>98.1% posterior probability of superiority of MIPS over MM. Analogous to p-value 0.032</b> |
| 2023 | MIND           | Failed   | Safety and Efficacy of MIS with the Artemis Neuro Evacuation device        | Endoscope – with Artemis    | 236/500  | Stopped by Sponsor  |

# Common Criticism of Early Trials

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## **Poor patient selection**

Heterogenous patients (different hematoma sizes, locations, levels of consciousness). Subgroups may have benefited but were lumped together.

## **Delayed timing of surgery**

STICH trial median time from onset to treatment for early surgery group was 30 hours (interquartile range, 16 to 49 hours)

## **Absence of minimal invasive techniques**

No newer minimally invasive techniques (e.g., stereotactic aspiration, endoscopic evacuation), which may have a different risk-benefit profile.

# Common Criticism of Early Trials

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## **High crossover rates**

STICH TRIAL: Approximately **26%** of patients assigned to initial conservative treatment crossed over to surgery.

## **Outcome measures may have been too crude**

Glasgow Outcome Scale (8-point)

## **Underpowered subgroup analyses**

Underpowered for example for lobar hemorrhage

## **Heterogeneity in surgical expertise**

No strong surgical vetting/credentialing

# WHAT LED TO ENRICH TRIAL?

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## Disappointment with open surgery trials

- The problem might not be *whether* to remove blood
- But *how* and *in whom*

## Recognition of subgroup signals

- Patients with **superficial lobar hemorrhages** (closer to the cortex) might benefit
- Deep hemorrhages (e.g., basal ganglia) did worse with open surgery

# WHAT LED TO ENRICH TRIAL?

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## Rise of minimally invasive techniques

Techniques like tubular retractors and endoscopic evacuation were developed to:

- Reduce surgical trauma to surrounding brain
- technique + execution quality** are critical (MISTIE)

## Importance of early intervention

- Secondary injury (inflammation, edema, toxicity from blood products) evolves quickly
- Waiting too long may negate the benefit of clot removal

# WHAT LED TO ENRICH TRIAL?

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## **Need for pragmatic, real-world applicability**

ENRICH aimed to:

- Standardize a specific minimally invasive approach
- Streamline workflow for rapid treatment
- Focus on outcomes that reflect real clinical recovery

## **Device-driven innovation**

The development of tools like the BrainPath tubular retractor system (used in ENRICH) made it feasible to:

- Consistently perform minimally invasive evacuation



# WHAT LED TO ENRICH TRIAL?

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*If you select the right patients (mainly lobar ICH), operate early, and use minimally invasive techniques, can surgery finally show a clear functional benefit?*

**BUT**

*EMORY LED BUT INDUSTRY SPONSORED  
(NICO Corporation, BRAINPATH)*

# ENRICH TRIAL

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Whether early minimally invasive surgical removal would result in better outcomes than medical management is not known.

# ENRICH TRIAL

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**300 patient, multicenter, randomized, adaptive clinical trial**

## **Primary endpoint o Functional outcome**

Utility-weighted modified Rankin scale (UW-mRS) score at 180 days. Converts the 7-point scale into a continuous variable (0 to 1) o Better reflects patient-centered values about the desirability of an outcome

## **Adaptive trial with location enrichment**

Encouraged by FDA and NIH to modernize clinical trials by improving speed, efficiency and protecting patient safety

## Key Inclusion Criteria:

- Time Window:** Surgery initiated within 24 hours of "last known well".
  - ICH Location:** Spontaneous supratentorial ICH, specifically targeting anterior basal ganglia or lobar locations.
  - Volume:** 30–80 mL, calculated using the ABC/2 method.
- Neurological Status:** GCS 5-14 (mild-to-severe) and NIHSS>5
- Functional Status:** Premorbid mRS of 0 or 1.

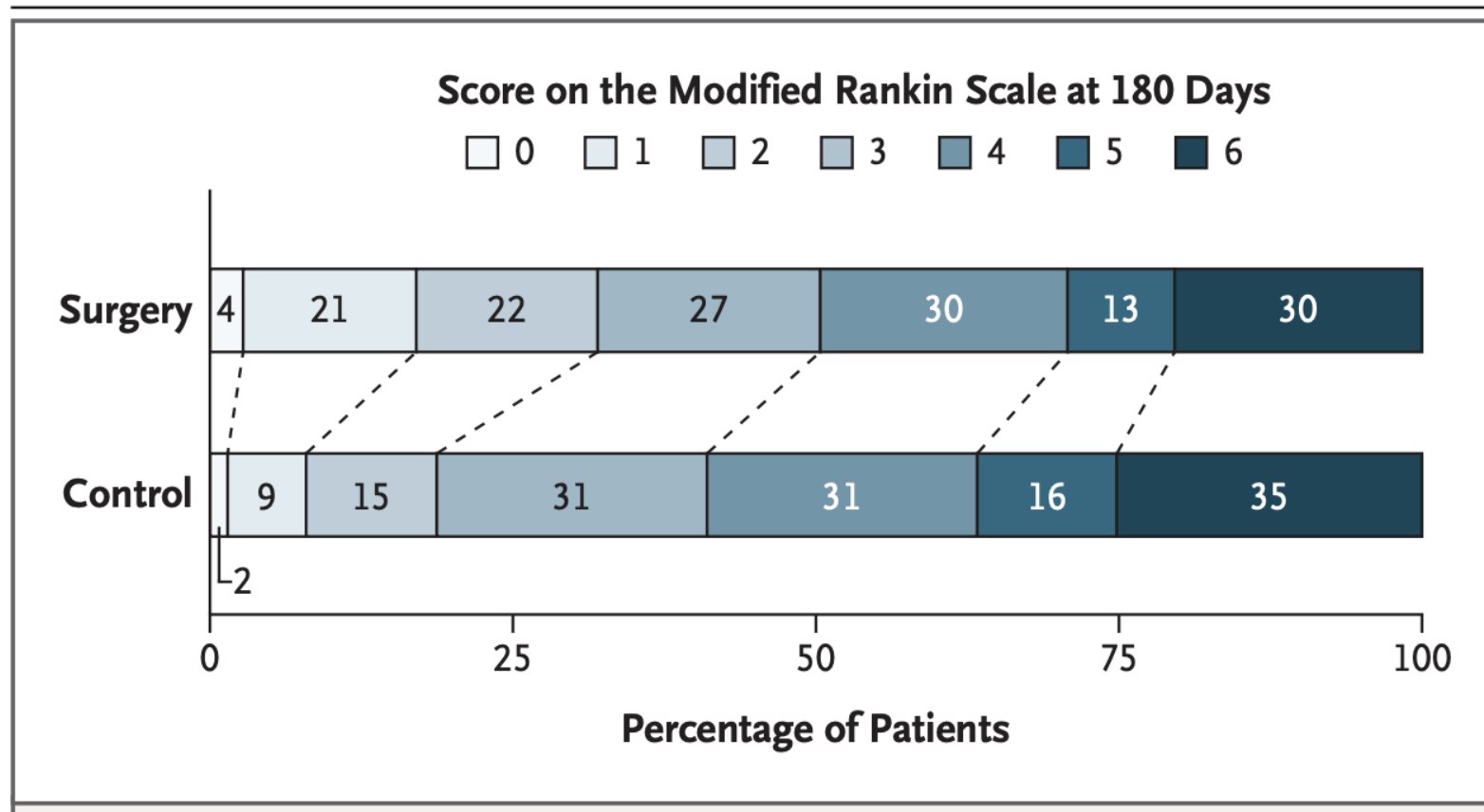
## Key Exclusion Criteria:

- **Secondary Causes:** aneurysms, AVM, tumors etc
- **Location:** Primary thalamic or infratentorial (cerebellar/brainstem) hemorrhages.
- **Severity:** Intraventricular extension  $> 50\%$  of either lateral ventricle.
- **Coagulopathy:** Patients on anticoagulants that cannot be rapidly reversed.

## **Adaptive Enrichment Strategy:**

The trial was initially designed to include both lobar and anterior basal ganglia hemorrhage, but after an interim analysis showed futility for deep hemorrhage, the protocol was adapted to enrich the trial by focusing only on lobar hemorrhages

# ENRICH TRIAL



# ENRICH TRIAL: SURGERY

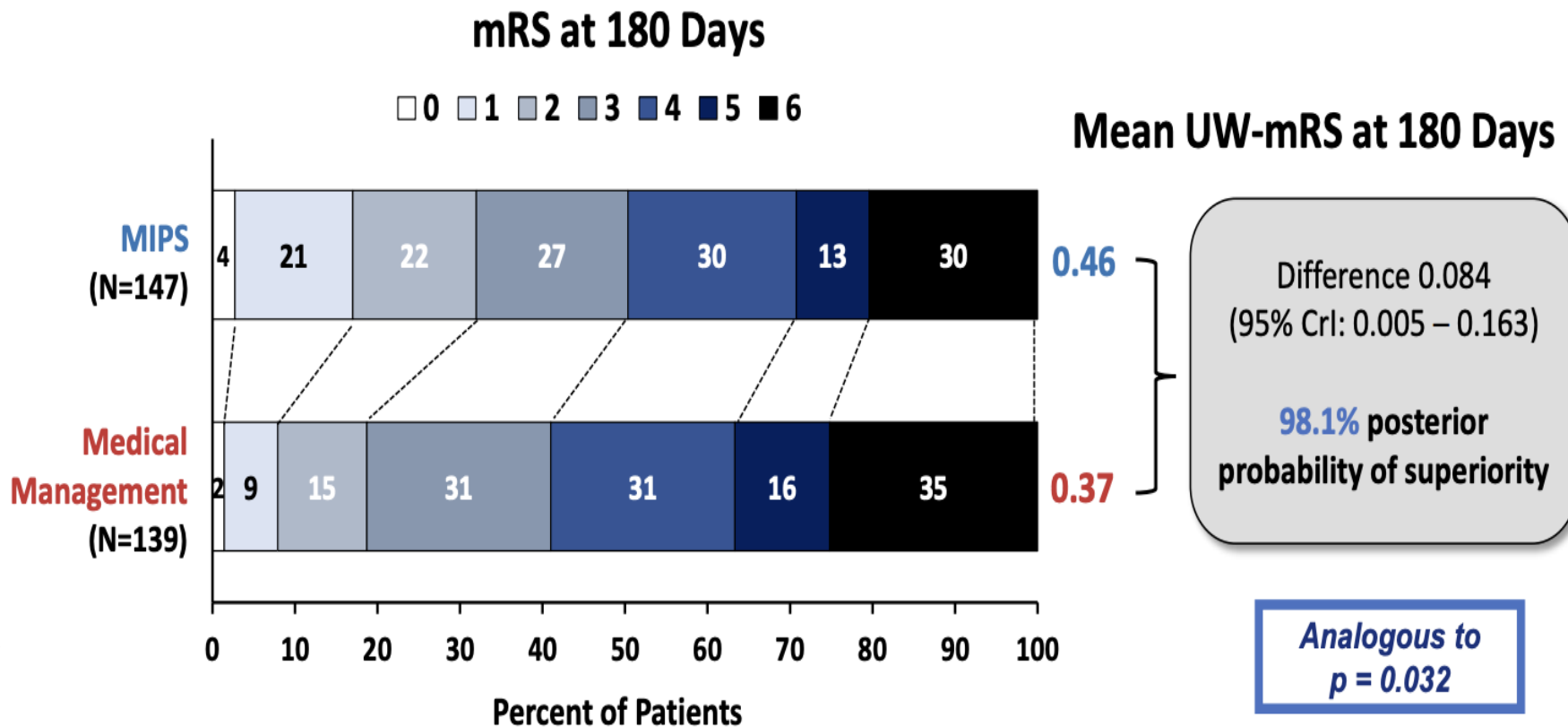
| <b>NIHSS</b>          | 12-22                          |
|-----------------------|--------------------------------|
| <b>GCS</b>            | 9-14 (80% of patients)         |
| <b>ICH LOCATION</b>   | Anterior BG: 30%<br>Lobar: 70% |
| <b>ICH VOLUME</b>     | 40-72 ml                       |
| <b>LKW to SURGERY</b> | 10-21 hours                    |



# ENRICH TRIAL: SURGERY

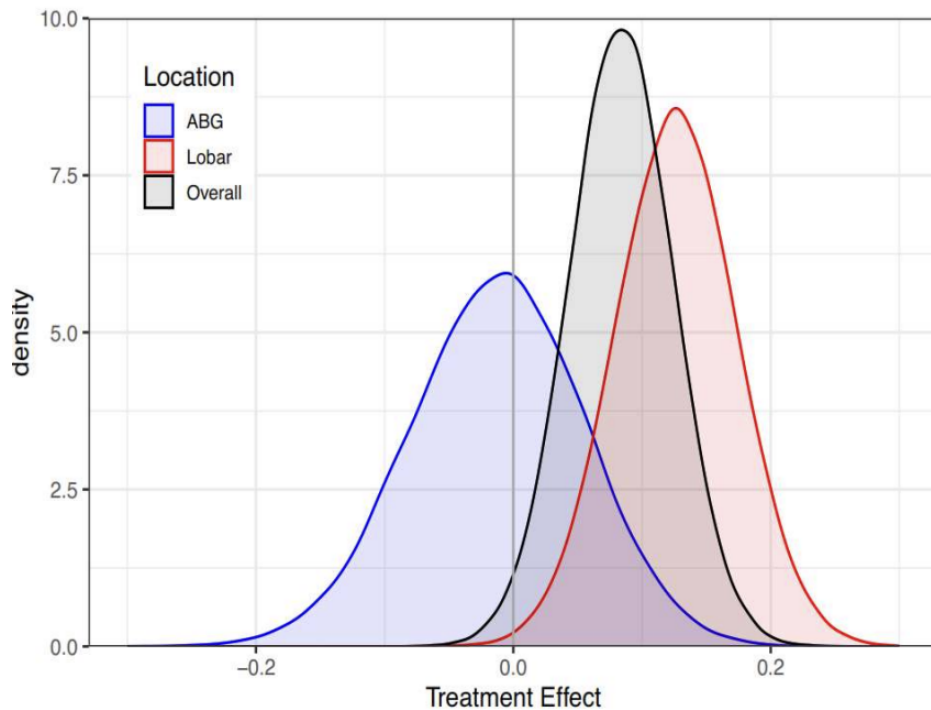
| <b>DOOR TO SURGERY</b>                            | 1-2 hours |
|---|-----------|
| <b>ACCESS DEVICE</b>                              | BrainPath |
| <b>HEMATOMA SIZE<br/>REDUCTION %</b>              | 73%       |
| <b>HEMATOMA SIZE<br/>AFTER SURGERY<br/>(MEAN)</b> | 15ml      |

# ENRICH TRIAL



# ENRICH TRIAL

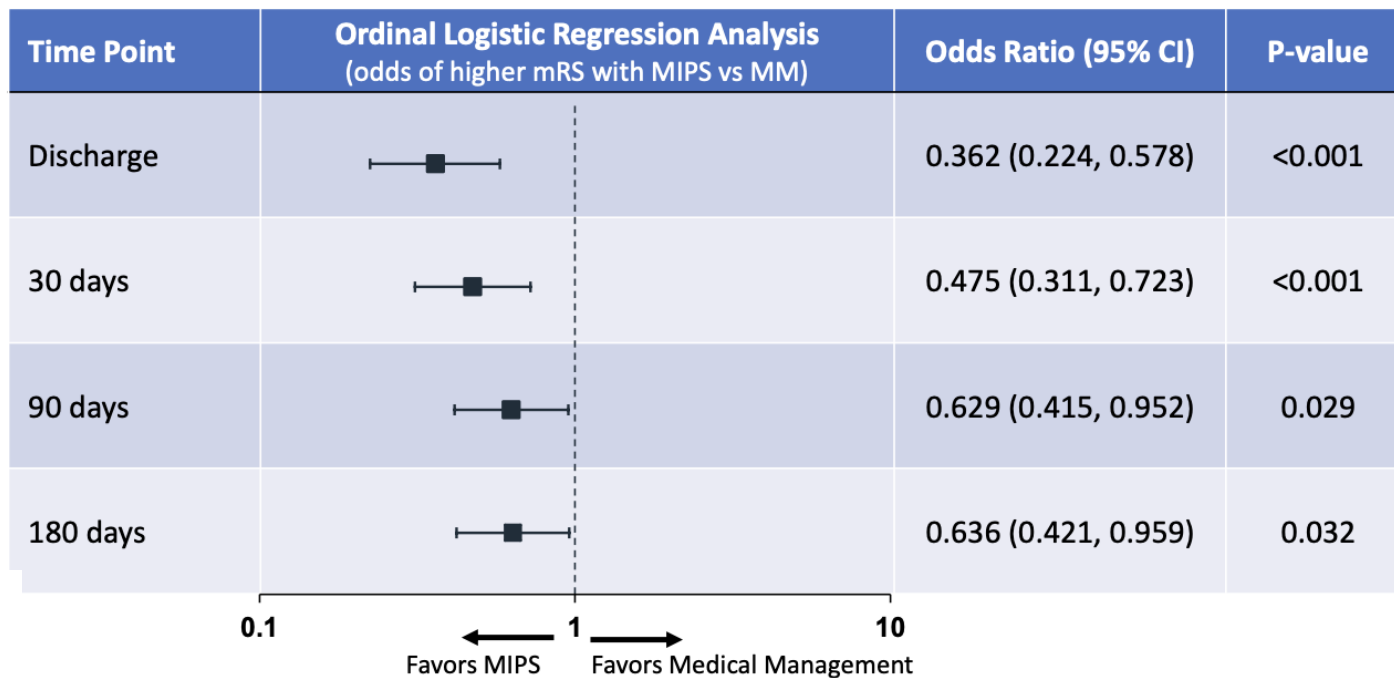
## Posterior Distribution of Treatment Effect



| Location | Estimate (95% CrI)     | Probability of Superiority |
|----------|------------------------|----------------------------|
| ABG      | -0.013 (-0.147, 0.116) | 0.4301                     |
| Lobar    | 0.127 (0.035, 0.219)   | 0.9968                     |
| Combined | 0.084 (0.005, 0.163)   | 0.9813                     |

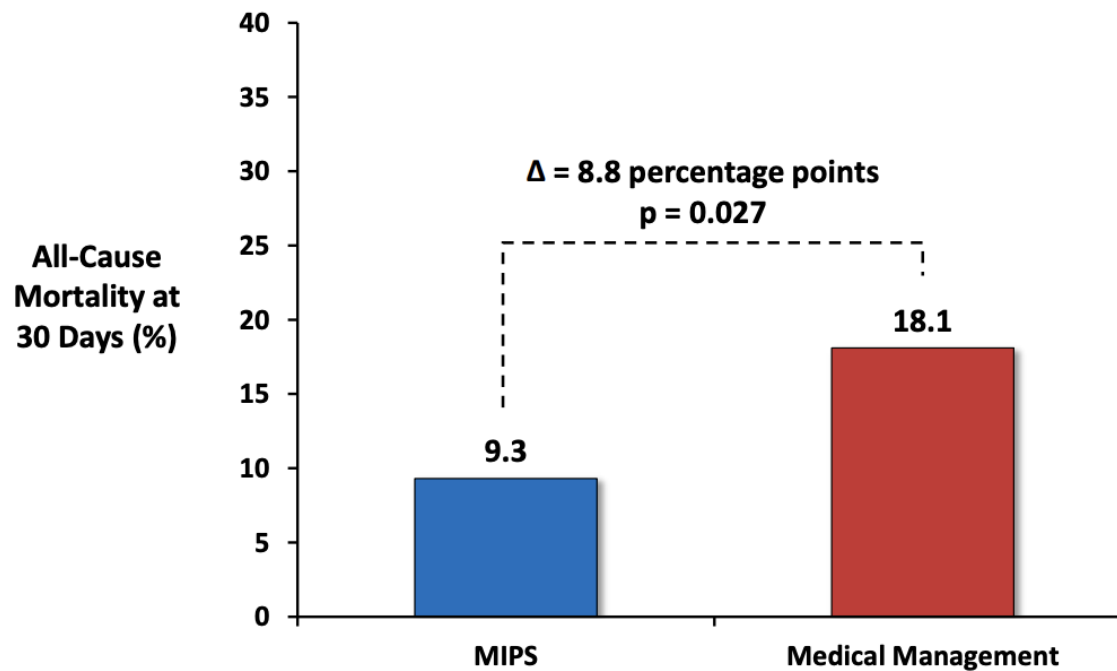
# ENRICH TRIAL

## MIPS Benefits on mRS Observed Early, Consistent Through Follow-up



# ENRICH TRIAL

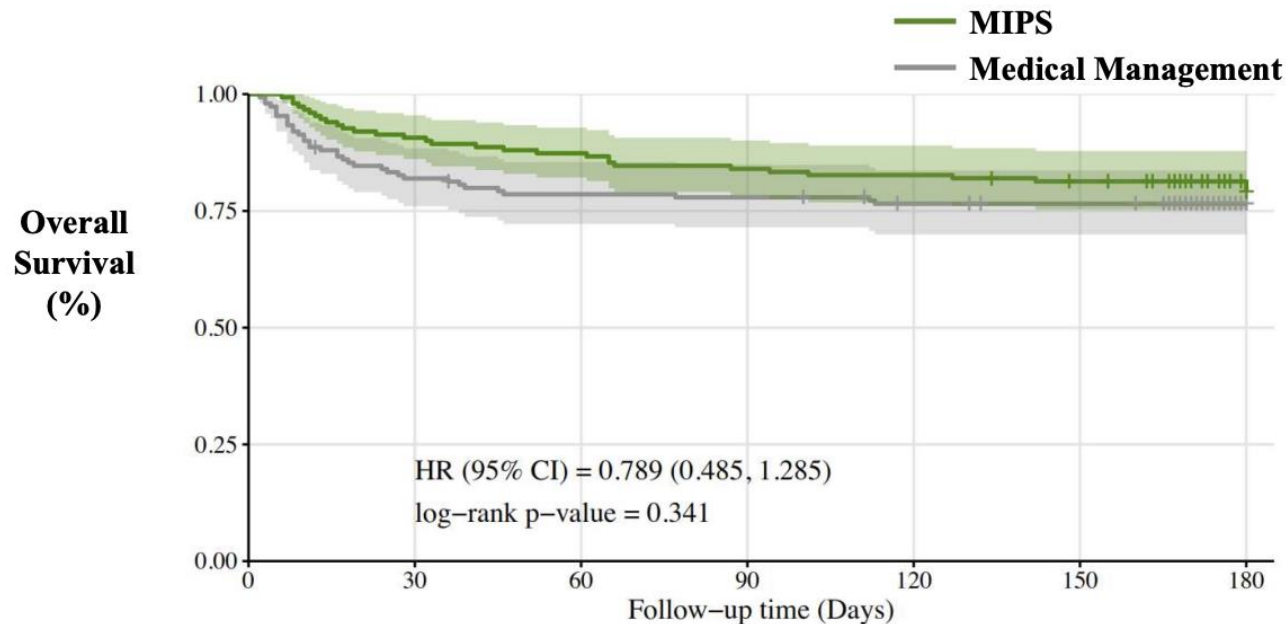
## Lower 30-Day All-Cause Mortality with MIPS



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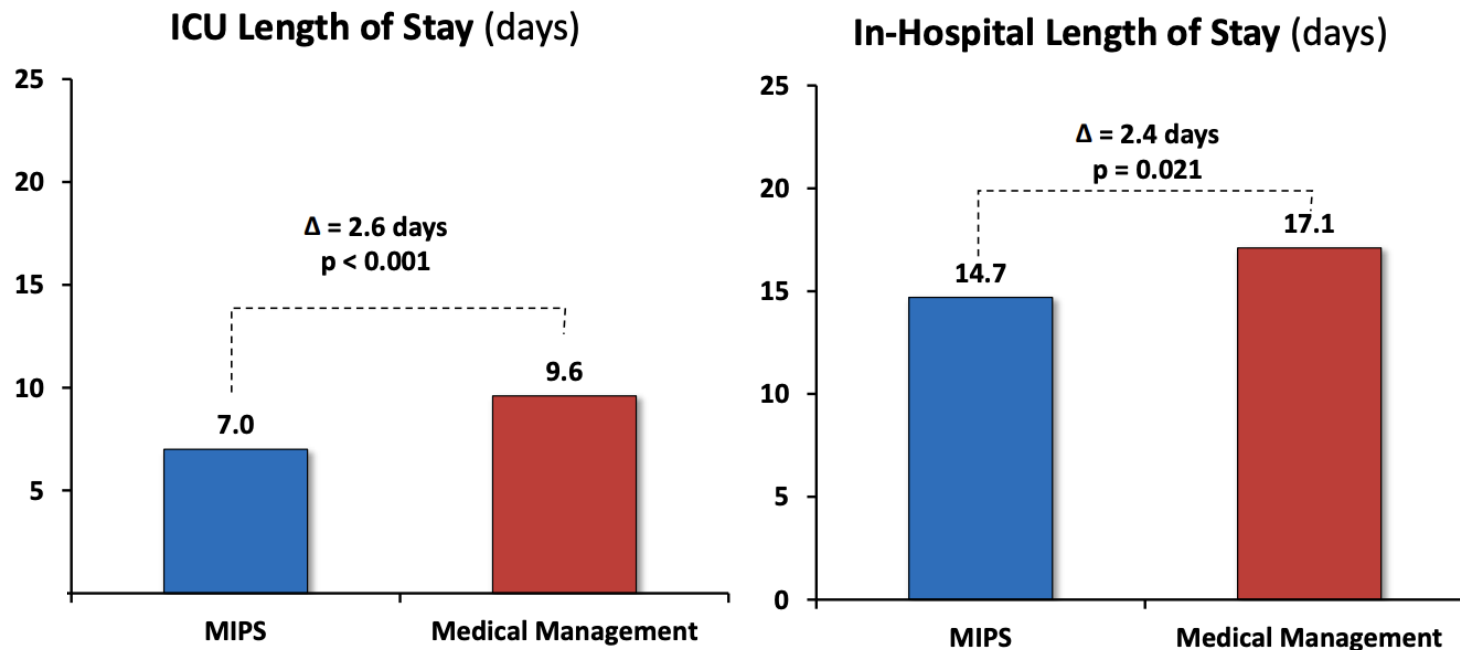
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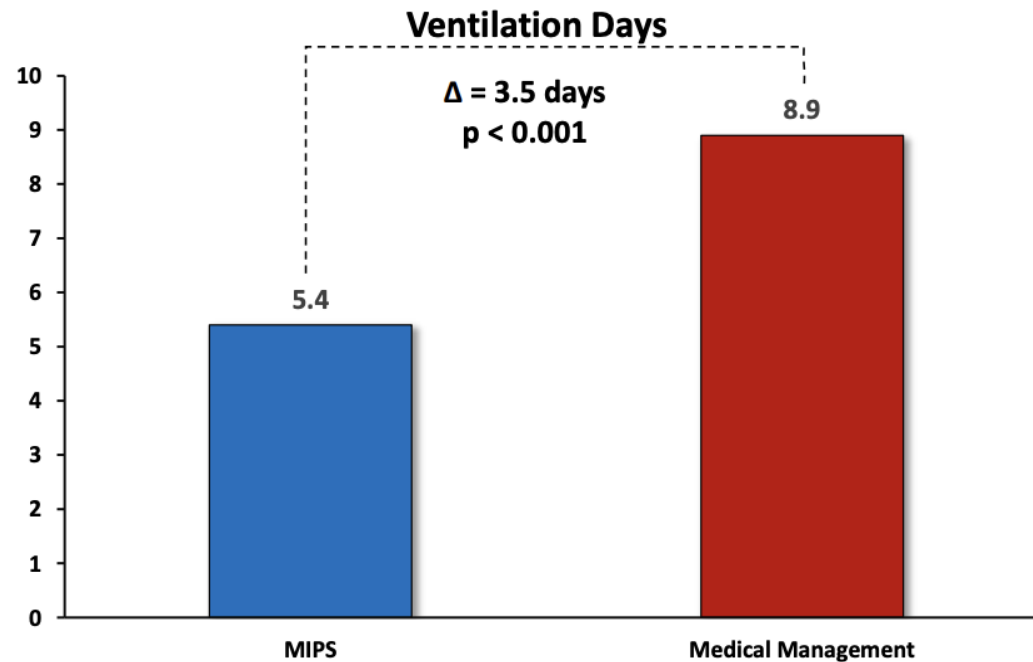
# ENRICH TRIAL

## Significantly Shorter Lengths of Stay in ICU and Hospital



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## Significantly Fewer Ventilator Days with MIPS





# ENRICH TRIAL: WEAKNESSES

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## External validity/Generalizability

- Single country
- Strict exclusion criteria – very specific population in terms of ICH size and location

## Utility weighted mRS:

- The weights chosen have potential to alter outcome
- Not validated in this cohort of patients

# ENRICH TRIAL: WEAKNESSES

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Sponsorship by NICO, the manufacture of the devices used in the trial, although no incentives provided, no involvement in data collection, analysis or trial design

# Conclusion

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- **Early surgical trials (STICH I/II) showed no benefit of surgery for ICH.**
- **Likely this was due delayed surgery and large surgery (large craniotomy)**
- **ENRICH TRIAL is first positive trial for surgical intervention for ICH using a minimally invasive approach**
- **ENRICH trial shows a benefit associated with the intervention for lobar haemorrhage is functionally important**

**MINUTE**

Minimally Invasive Neuroendoscopic Ultra Early Targeted ICH Evacuation Trial

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**MINUTE is a prospective, multi-center, randomized, controlled, blinded assessor, adaptive enrichment design, clinical trial.**

Eligible patients with spontaneous BGH  $\geq 20$  mL will be randomized 1:1 to either minimally invasive endoscopic SCUBA evacuation plus standard medical management or standard medical management alone;

# THANK YOU



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