Head Positioning and Mobilization in Acute Stroke: Up, Down…Does it Matter?

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Disclosures

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Zero Degree Positioning is Theoretically Sound

- Early observations described head elevation in acute ischemic stroke as potentially detrimental and associated with neurologic worsening
  - Toole (1968)
  - Caplan and Segay (1976)
- Physiologic mechanisms for blood flow augmentation and clinical improvement/stability with zero degree positioning:
  - Enhance direct gravitational flow through large arteries undergoing vasomotor exhaustion within the ischemic bed
  - Fosters collateralization
  - Viable penumbral tissue will likely respond to abrupt increases or decreases in blood flow; changes in clinical responsiveness cannot be identified without completion of serial clinical exams

Head Positioning Studies Favoring Zero Degrees in LVO

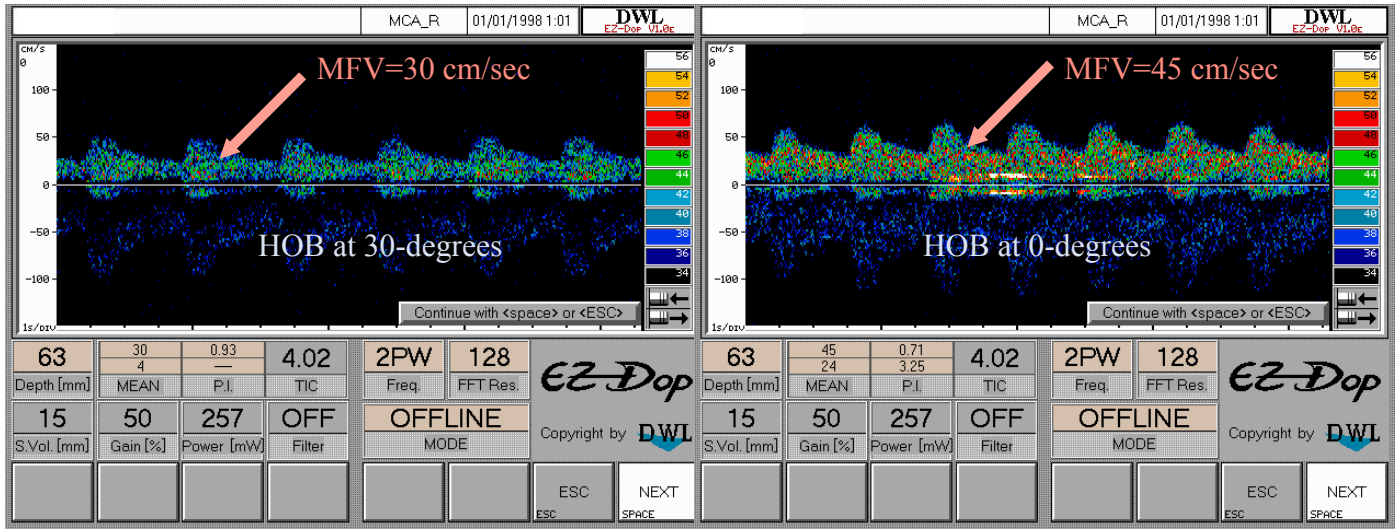
Table Studies evaluating the effect of head of bed (HOB) positioning on different imaging and clinical endpoints

Study	Design	N	Stroke, subtype	Endpoint/outcome	Main finding
Ali et al.[13]	Prospective cohort	5	AIS (LVO)	Neurologic worsening	60% of patients experienced neurologic worsening in upright position
Anderson et al.[1]	RCT	11,093	AIS and ICH	Three-month disability (mRS)	HOB positioning did not affect outcomes
Aries et al.[14]	Prospective case-control	67	AIS	CBFV (TCD), frontal oxygenation (NIRS)	HOB positioning did not affect imaging endpoints
Favilla et al.[9]	Prospective cohort	17	AIS (LVO)	CBF (DCS), CBFV (TCD)	Lower HOB angle was associated with increased CBF and no change in CBFV
Hayashida et al.[4]	Prospective cohort	19	AIS (10 with LVO, 9 with LV stenosis)	CBF (HMPAO-SPECT)	Upright position decreased CBF in LVO patients and did not affect CBF in patients with LV stenosis
Hunter et al.[8]	Prospective cohort	8	AIS (LVO)	CBFV (TCD)	Upright position decreased CBFV in incompletely recanalized LVO patients
Olavarria et al.[10]	Meta-analysis	57	AIS (LVO)	CBFV (TCD)	Flat positioning increased CBFV
Ouchi et al.[5]	Prospective cohort		AIS (LVO)	OEF and rCBF (PET)	Upright position exerted an adverse effect on local perfusion in hemodynamically compromised LVO patients
Palazzo et al.[11]	Retrospective cohort	333	AIS	HAP	HAP was uncommon in AIS patients treated with IVT whose HOB was positioned at 0°
Saqqur et al.[12]	Retrospective case-series	16	AIS/TIA (LVO) with neurologic worsening during postural changes	CBFV (TCD)	Greater reduction in CBFV predicted neurologic worsening during postural changes (upright position)
Schwarz et al.[46]	Prospective cohort	18	AIS (LVO)	CPP (ICP monitoring)	Flat positioning increased CPP
Wojner et al.[6]	Prospective cohort	11	AIS (LVO)	CBFV (TCD)	Flat positioning increased CBFV
Wojner-Alexandrov et al.[7]	Prospective cohort	20	AIS (LVO)	CBFV (TCD)	Flat positioning increased CBFV

Abbreviations: AIS = acute ischemic stroke; CBF = cerebral blood flow; CBFV = cerebral blood flow velocity; CPP = cerebral perfusion pressure; DCS = diffuse correlation spectroscopy; HAP = hospital-acquired pneumonia; HMPAO = Tc-hexamethylpropyleneamine oxime; HOB = head of bed; ICH = intracerebral hemorrhage; ICP = intracranial pressure; IVT = IV thrombolysis; LVO = large vessel occlusion (extracranial or intracranial circulation); mRS = modified Rankin Scale; NIRS = near-infrared spectroscopy; OEF = oxygen extraction fraction; rCBF = regional cerebral blood flow; RCT = randomized controlled clinical trial; TCD = transcranial Doppler.

“Heads Down”

20% increase in mean flow on average in large vessel occlusions (LVO) when HOB lowered from 30 to 0 degrees (effect size for the intervention at three levels = 0.47; *r* = 0.90 and observed power of 0.99)



18% of subjects demonstrated clinical improvement within 30 minutes of placing the head at 0-degrees flat positioning

HeadPoST

- Trial using a simple cluster randomization design, whereby hospitals were randomized to either head up at 30-degrees or head down at 0-degrees for all patients admitted with either ischemic stroke or intracerebral hemorrhage; patients were not consented
- After a hospital had enrolled 50% of their projected admissions they would crossover to the other treatment group for the remaining 50% of enrollments
- No serial evaluations of clinical change tied to head positioning were performed – believed, “Nurses are incapable of performing the NIHSS accurately or reliably” at the majority of sites used; used a 3 month mRS endpoint, yet powered the study with thrombolysis and blood flow data

Conclusions: Head positioning doesn’t matter

Are HeadPoST findings valid?

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VIEWS & REVIEWS

HeadPoST

Rightly positioned, or flat out wrong?

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Head Position in Stroke Trial

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- Broad mix of patients instead of a discreet population known to benefit from pilot work
- Enrollment of:
  - Milder strokes with a median NIHSS score of 4 (IQR 2–8)
  - At later time windows after stroke onset (median 14 hours [IQR 5–35]) with a median time from admission to positioning of 7 hours in both groups
- Intervention fidelity was questionable and not measured (allowed out of bed; ability to maintain head elevation in flat beds unknown)
- No serial monitoring of clinical change
- No pilot data supported use of a 3 month mRS primary outcome; instead they used:
  - TCD mean flow velocity changes, and functional outcome differences in rehabilitation patients and post-thrombolysis outcomes
  - Expected a relative 16% improvement/ shift in death and disability on the 3-month mRS which is unheard of for a positioning intervention
- No imaging confirmation of which patients had LVO or small vessel stroke

ZODIAC

(ZerO Degree head positioning In hyper-Acute large artery ischemiC stroke)

International Trial Investigators: Anne W. Alexandrov, PhD, David Liebeskind, MD, Georgios Tsivgoulis, PhD, MD, Sandy Middleton, PhD, Barbara Brewer, PhD, Michael D. Hill, MD, Andrei V. Alexandrov, MD

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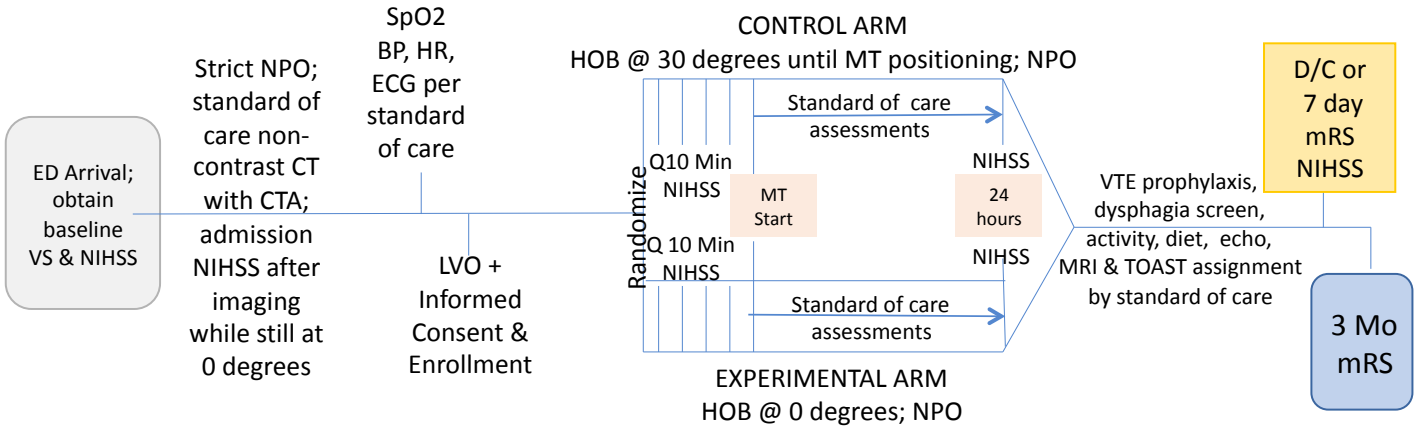

Note: During intervention, NIHSS reassessment should be performed at least every 10 minutes; however, if a patient overtly changes (improvement or deterioration), the NIHSS can be repeated more frequently; repeat one final assessment just prior thrombectomy.

Is there clinical equipoise about head positioning in ICH post HeadPoST?

- Prior to the conduct of HeadPoST, an international survey of 128 clinicians suggested the presence of clinical equipoise for best HOB position in acute ischemic stroke.
- Positioning orders for intracerebral hemorrhage (ICH) patients commonly recommend 30-degree HOB positioning despite HeadPoST findings. Therefore, we aimed to determine whether HOB positioning equipoise still exists in ICH following publication of the HeadPoST study.

Is there clinical equipoise about head positioning in ICH post HeadPoST?

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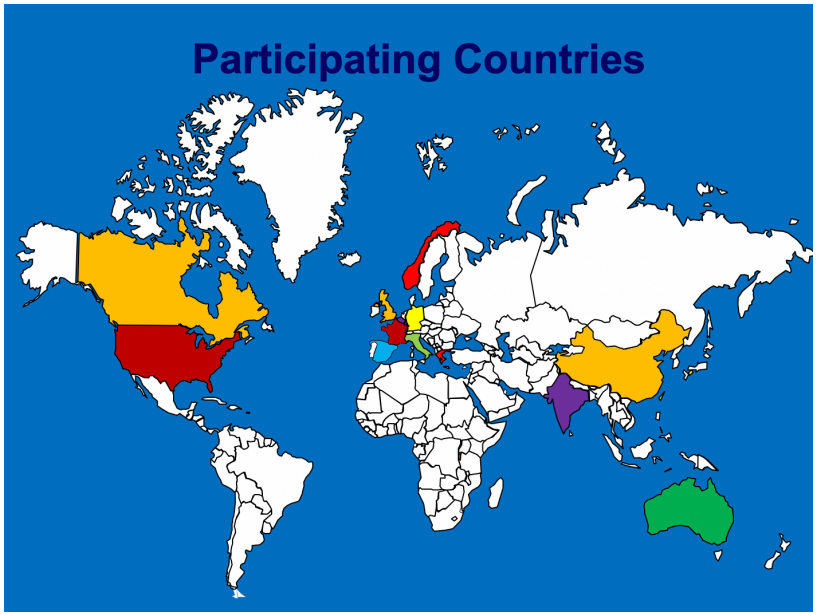
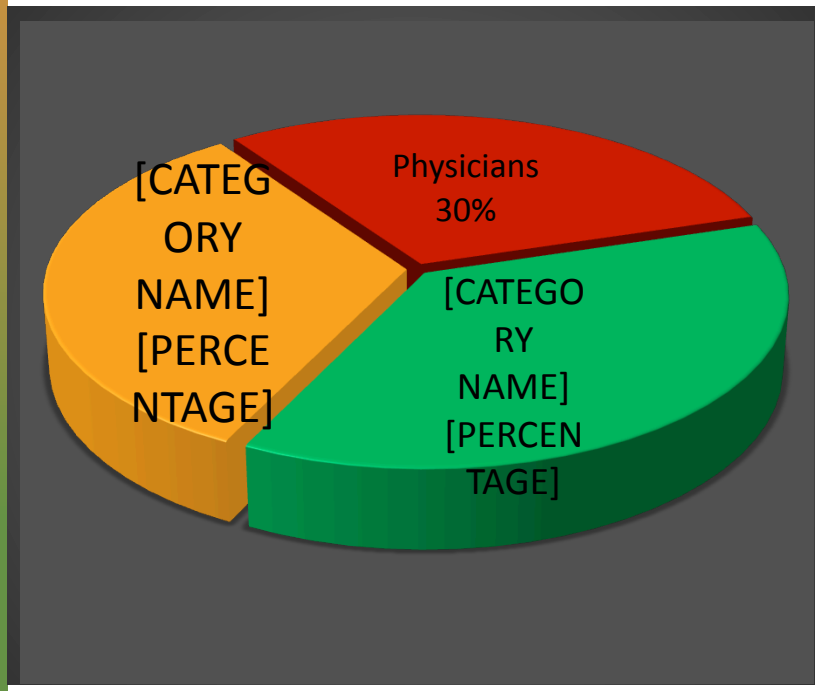
- A 5-question international survey was constructed about ICH HOB positioning for interdisciplinary clinicians.
  - Likert scale: 1=strongly agree, 2=agree, 3=unsure, 4=disagree, 5=strongly disagree
- Items were developed to understand opinions related to the validity of HeadPoST findings, current orders and hospital policies for head positioning in ICH patients, opinions about what constitutes an appropriate primary endpoint in ICH, and beliefs about whether head positioning alone could influence distal 6 month outcomes after ICH.
- Surveys were distributed on stroke-specific listservs targeting physicians, advanced practice providers (APP), and nurses, and e-mailed to practitioners worldwide.

Results

- A total of 181 responses were received from a total of 13 countries across 4 continents
  - 79% North America
  - 11% Europe
  - 7% Australia
  - 3% Asia
- Disciplines responding were 37% registered nurses, 33% APP, and 30% physicians
- Respondents had 8.6 ± 8 (median 7) years experience in acute stroke, with a median 100 {IQR 37.5-200) ICH admissions/year at their hospitals



Results (continued)



- Respondents disagreed {4; IQR:3-4) that HeadPoST provided definitive evidence for ICH HOB practices and agreed {2; IQR:2-3) with the statement, "medical orders at my hospital call for ICH HOB 30-degrees" with no differences by nurse/physician profession.
- Policy/procedures for ICH HOB 30-degrees existed at 54% of hospitals.
- Respondents were unsure {3; IQR:2-3) whether 30-degree HOB alone could influence ICH 6-month outcome.
- 82% believed proximal clinical stability was the most appropriate future trial endpoint; 14% believed longitudinal measures were suitable and 4% felt both proximal/ longitudinal measures were important endpoints.

History of Early Mobilization

- First discussed at a conference on stroke care in Sweden in the 1980's
- In the 1990's Indredavik and colleagues reported a decrease in death and disability when early rehabilitation was compared to general care
- AVERT was the first multisite, international blinded outcome, randomized controlled trial conducted; began in 2004, concluded in 2014 (published 2015)
- Numerous small, single site, biased studies of heterogeneous neurocritical care patients over the past 5 years

How is Early Mobilization Defined?

What is the Dose of Early Mobilization Utilized?

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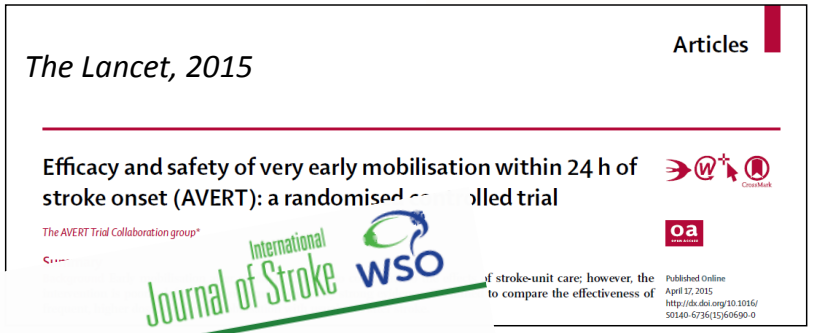
Two High Quality Studies

Publications	Methods	Main Findings
Sundseth A, Thommessen B, Ronning OM. Outcome after mobilization within 24 hours of acute stroke: A randomized controlled trial. Stroke; 2012;43(9): 2389-2394.	PROBE design	Very early mobilization (VEM) patients showed a trend towards poor outcome (OR=2.7), death (OR=5.26), or dependency (OR=1.25); p=ns. (n=56).
The AVERT Trial Collaboration Group. Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): A randomised controlled trial. Lancet. 2015;386:46-55.	PROBE design	Fewer VEM patients had favorable outcome (46%; n=480), compared to usual rested care (50%; n=525; adjusted OR=0.73; p=0.004). Death associated with neurologic deterioration or recurrent stroke in the VEM group totaled 42, compared to 26 in the usual care group; pneumonia as a cause of death occurred in 19 VEM vs. 15 usual care patients. Stroke progression occurred in 72 VEM vs. 56 usual care patients. (n=2104).

The Bottom Line…

- Slower mobilization occurring beyond the first 24 hours is associated with higher favorable outcome (mRS 0-2) at 90 days
- Very early mobilization (within first 24 hours) is associated with a number needed to harm of 25
- In acute stroke, evidence supports a rested approach to care within *at least* the first 24 hours of hospitalization
  - GRADE: Strong recommendation, high quality of evidence
- Similar to acute MI, vascular insufficiency in acute stroke likely warrants a more guarded approach to mobility
- Additional studies are warranted to determine the optimal "dose" and "timing" of exercise/mobility in acute stroke, and whether this differs by stroke subtype and mechanism; stay tuned for AVERT DOSE

AVERT


The Lancet, 2015

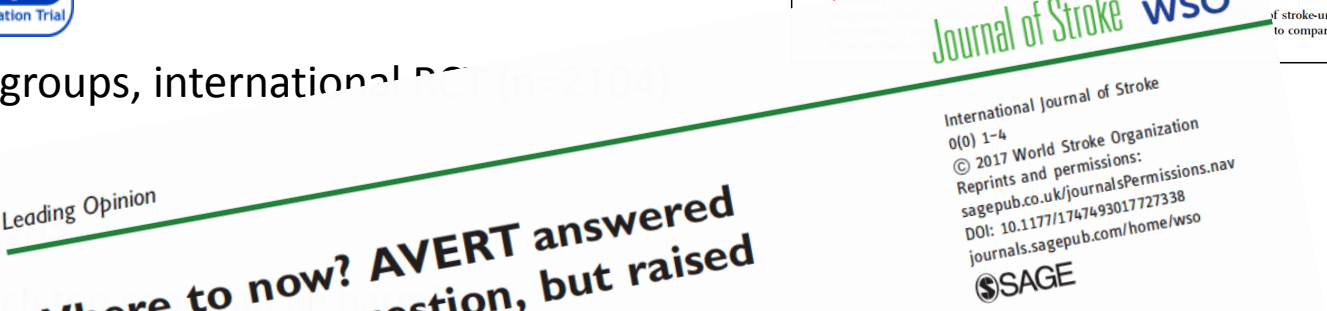
Articles

Efficacy and safety of very early mobilisation within 24 h of stroke onset (AVERT): a randomised c… lled trial

The AVERT Trial Collaboration group*

…f stroke-unit care; however, the … to compare the effectiveness of

Published Online April 17, 2015 http://dx.doi.org/10.1016/S0140-6736(15)60690-0


Leading Opinion

Where to now? AVERT answered an important question, but raised many more

Mark T Bayley[1,2], Audrey Bowen[3], Coralie English[4], Robert Teasell[5] and Janice J Eng[6]

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Large, 2 groups, international RCT (n=2104)

Conclus…

- Too mu…
- Severe s… ICH showed harm
- Dose ana… showed benefit … severely affected …
- Clinicians … don't know what is best. Guidelines to be developed.

Aim and Hypotheses

Aim To define optimal early mobility intervention regimens for people with mild and moderate stroke.

Hypotheses Optimal dose intervention regimen(s) will result in:

- More patients with **no or little disability** at 3 months post stroke, (1° outcome)
- Patients with **fewer and less severe complications**
- Better **quality of life** at 6 months

Cost-effectiveness and a range of sub-studies are included to examine recovery processes.

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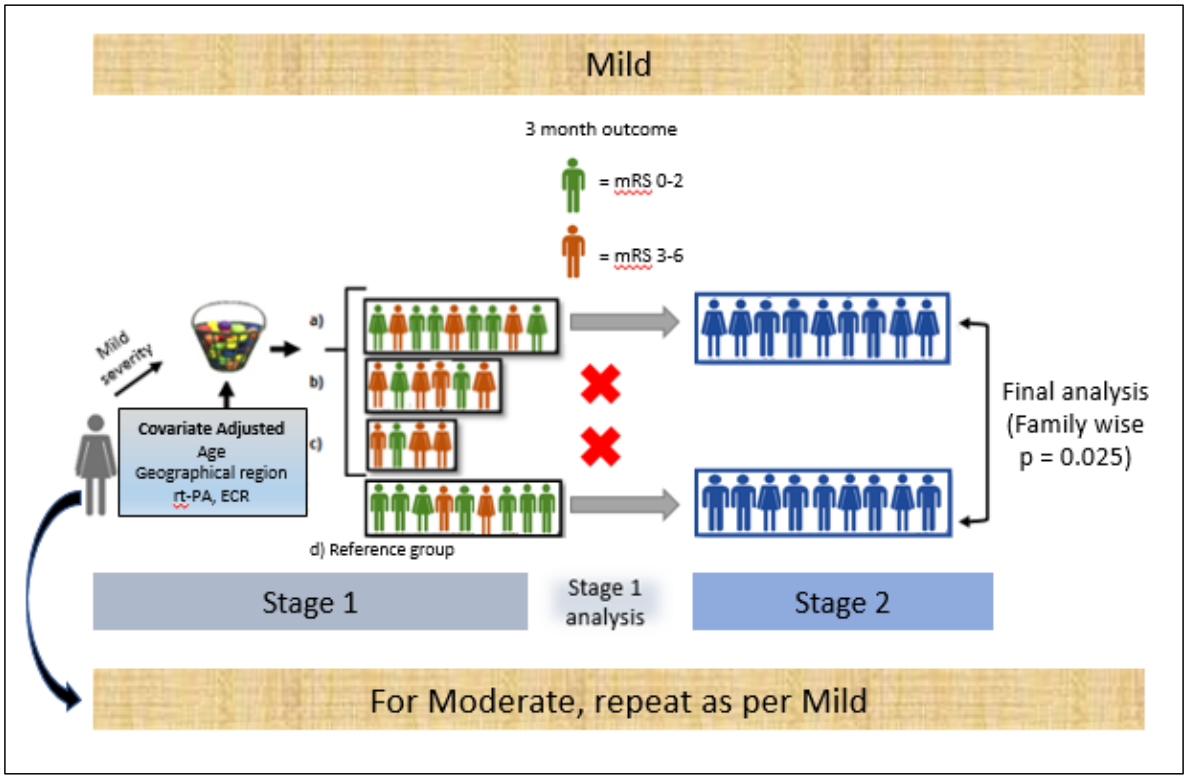
Multi-Arm Multi-Stage (MAMS) Covariate-Adjusted Response-Adaptive (CARA) Randomization Design



DOSE
Varying amount
Varying frequency
Tailored to patient

Number of participants:
n >2,500

Adaptive design differences

Randomized Clinical Trial	AVERT DOSE Adaptive Randomization
Randomization to group is remote, computer generated	Randomization to group is remote, computer generated
Group allocation is concealed	Group allocation is concealed
Randomization is fixed. For four groups, equal allocation would be 1:1:1:1	• One group is allocated as reference group • For the other three groups, randomisation adapts based on 3-month outcomes. • Group with better outcomes adapt to get more patients. • Best group is compared to the reference group after stage 1 analysis
Blinded outcomes at 3 and 6 months	Blinded outcomes at 3 and 6 months

Inclusion/Exclusion Criteria

Inclusion	Exclusion
Patients ≥ 18 years admitted to a stroke unit within 48 hour of onset of stroke with: Ischemic stroke • Mild (NIHSS 0-7) or moderate stroke severity (NIHSS 8 ≤ 16) • Pre stroke mRS of 0 – 2 • Medically stable	• Pre-stroke mRS of 3, 4 or 5 • Hemorrhagic stroke or TIA • Severe stroke (NIHSS > 16) • Co-morbid progressive neurological or coronary conditions or other rapidly deteriorating disease • Palliation or immediate surgery • A lower limb fracture/disability • Patients with no evident mobility problems or expected to be discharged within 3 days post enrolment. • Currently in a drug or other intervention trial

Conclusions

- Head positioning may be one of the most important first steps in the management of acute stroke patients
  - Findings from the HeadPoST trial have not been accepted as definitive evidence of best head position for either LVO or ICH patients
- ZODIAC, AVERT DOSE, and future ICH head positioning trials will build knowledge of positioning best practices…stay tuned!

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