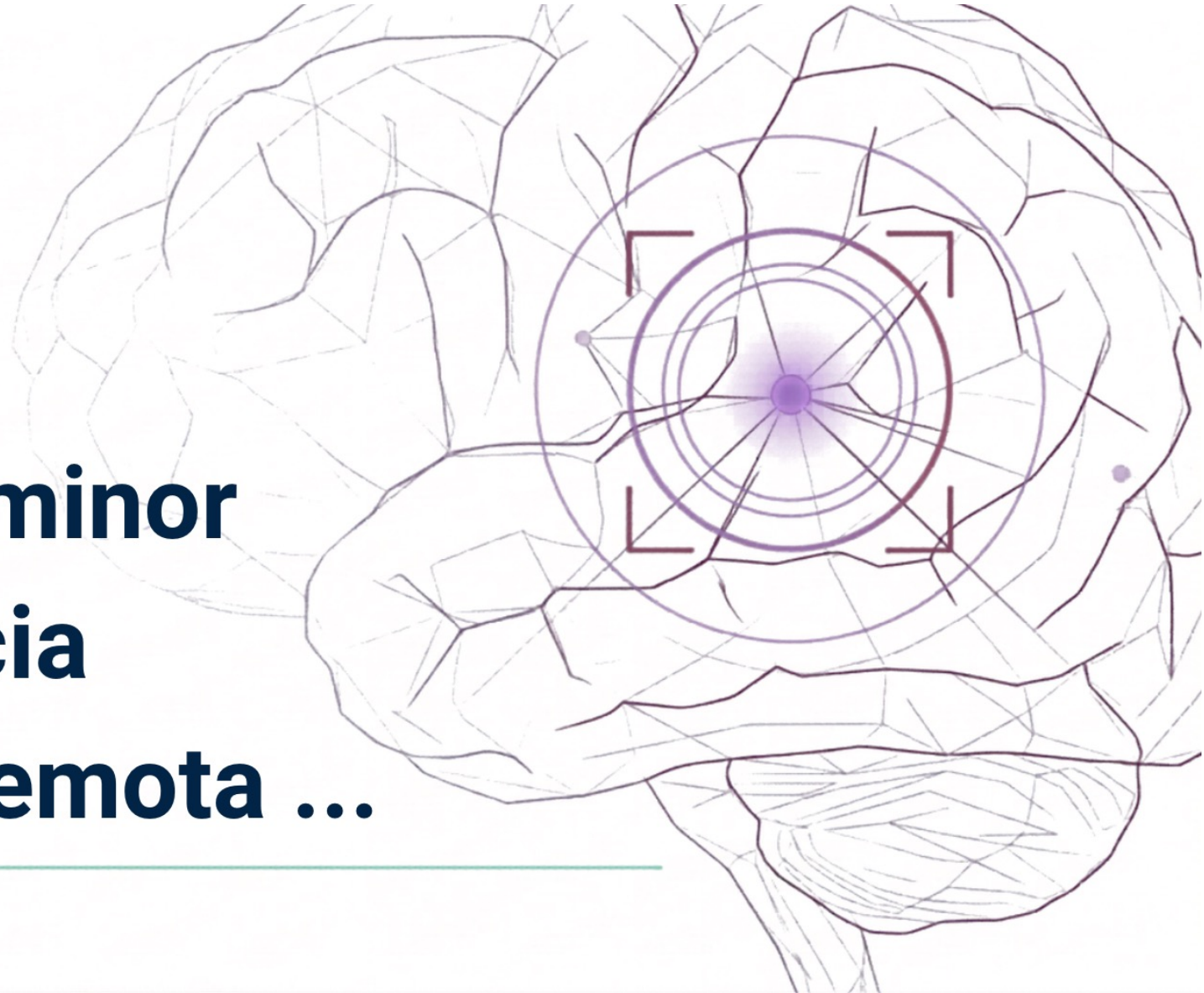


# **... del ictus minor a la tolerancia isquémica remota ...**

Francisco Purroy



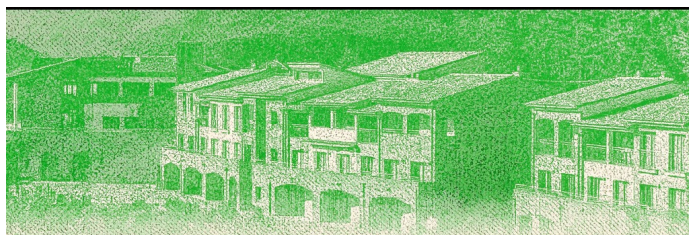
**Diputació de Lleida**

La força dels municipis

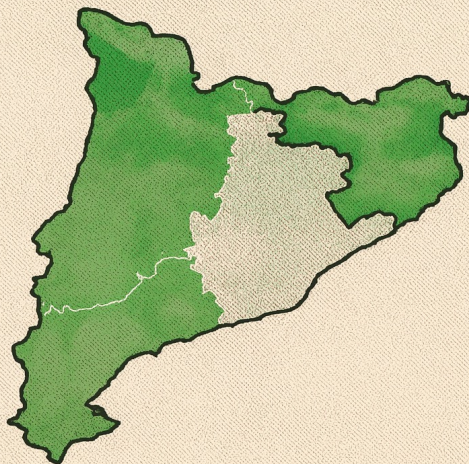


# The Stroke Hinge





*Retreat* Cientific 2018



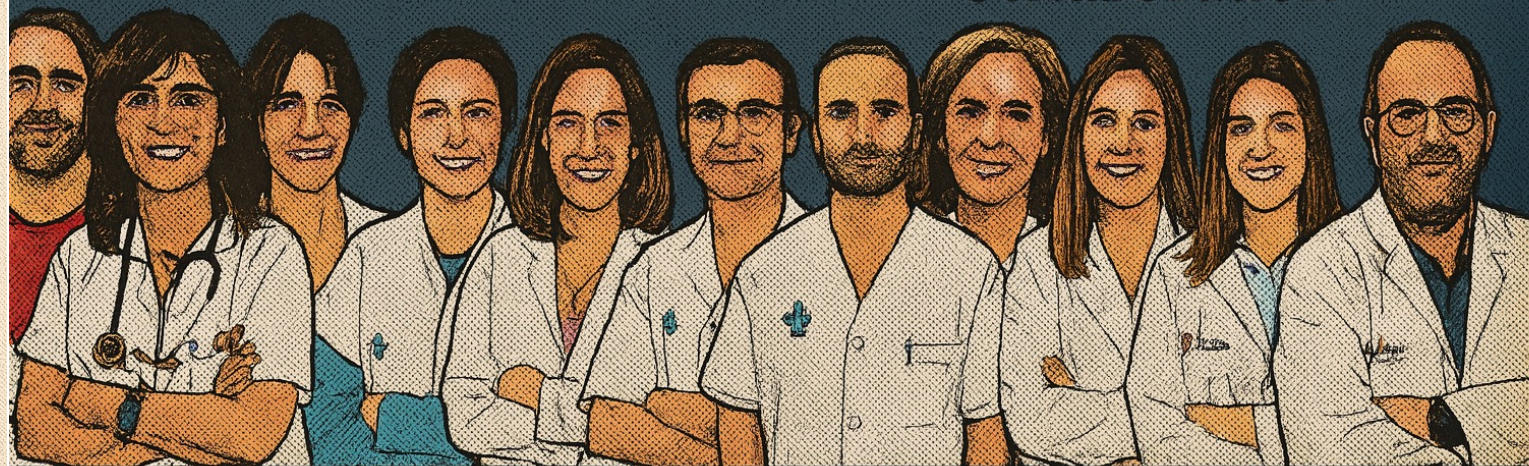
**IISPV**  
INSTITUT D'INVESTIGACIÓ  
SANITÀRIA  
PERE VIRGILI

**IdIB Gi**  
Institut d'Investigació  
Biomèdica  
de Girona  
Dr. Josep Trueta

**IRB Lleida**  
Institut de Recerca Biomèdica

**VALUES:** Singularity  
Multidisciplinary research  
engagement  
perseverance  
perseverance

Applied research  
Social interest  
Translational research  
Collaboration



CLINICAL NEUROSCIENCES GROUP • IRBLleida







CLINICAL NEUROSCIENCE GROUP

# VALUES:

Singularity Responsibility

Multidisciplinary engagement  
research perseverance

Applied research  
Social interest

Translational  
research  
Collaboration





CLINICAL NEUROSCIENCE GROUP

# VALUES:

Singularity Responsibility

Multidisciplinary engagement  
research

perseverance

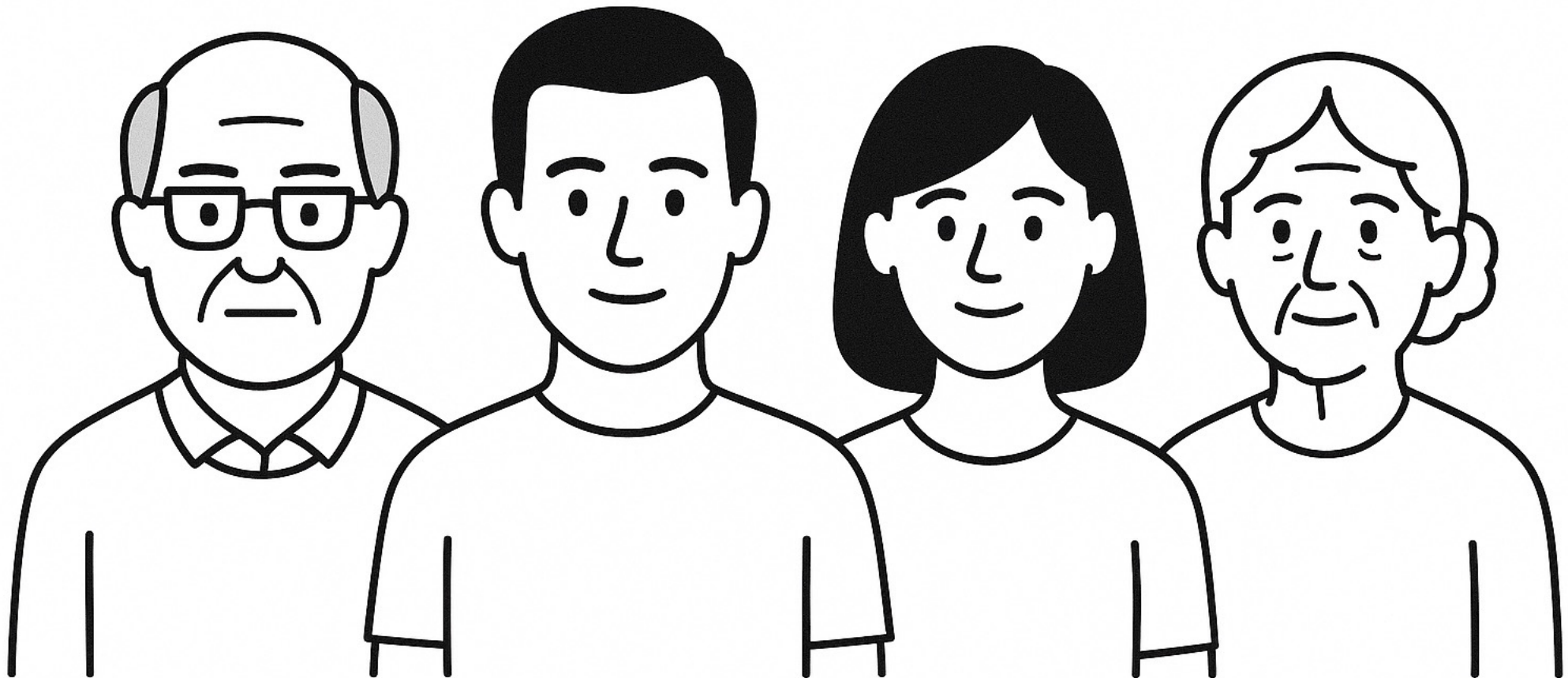
Applied research

Social interest

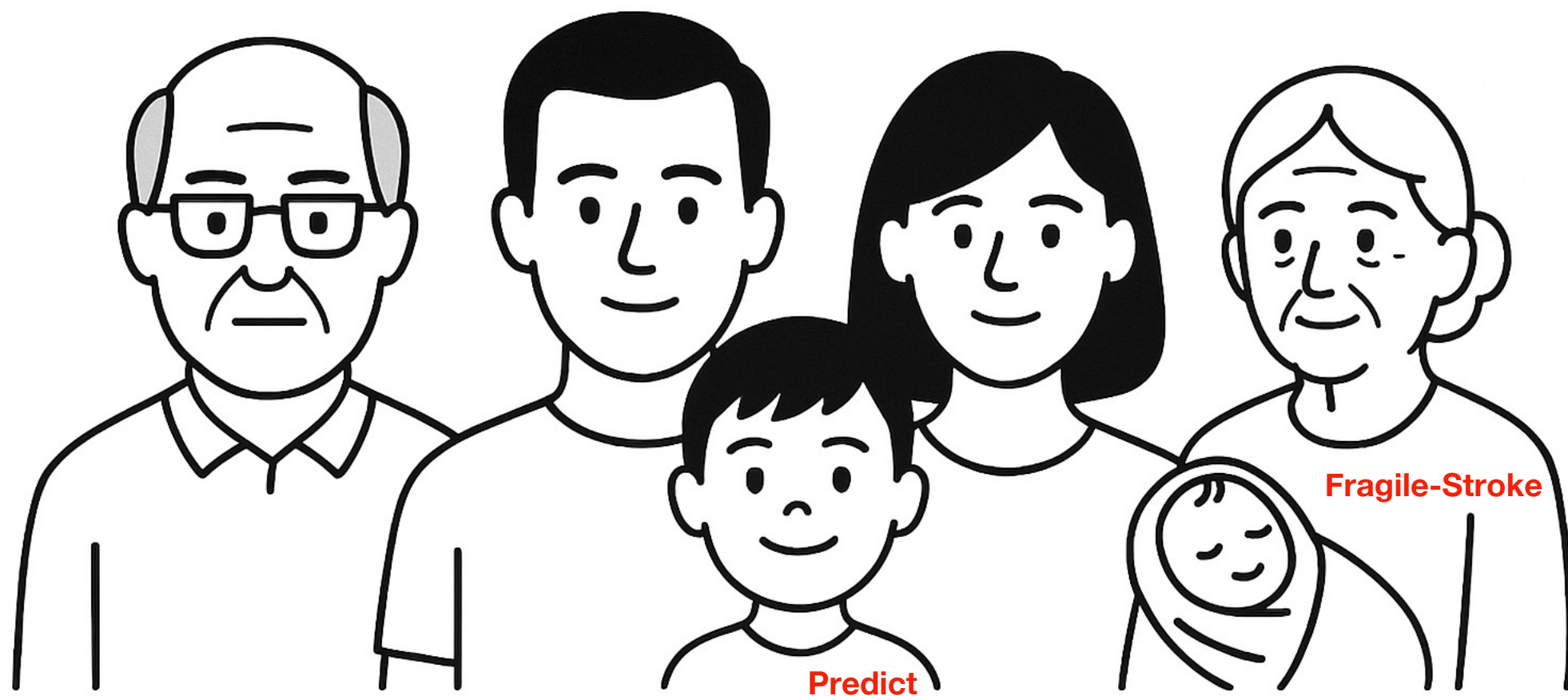
Translationaal  
research

Collaboration





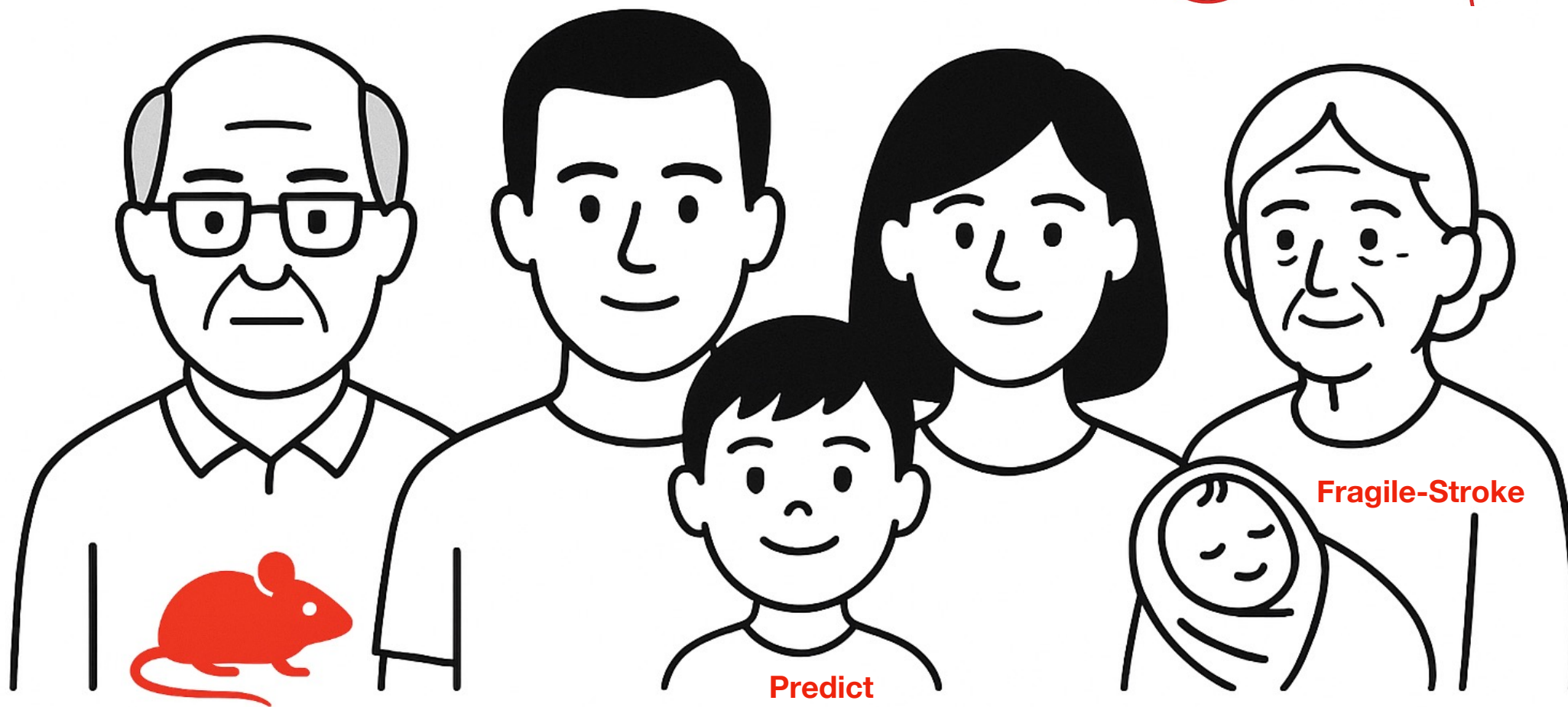




Predict

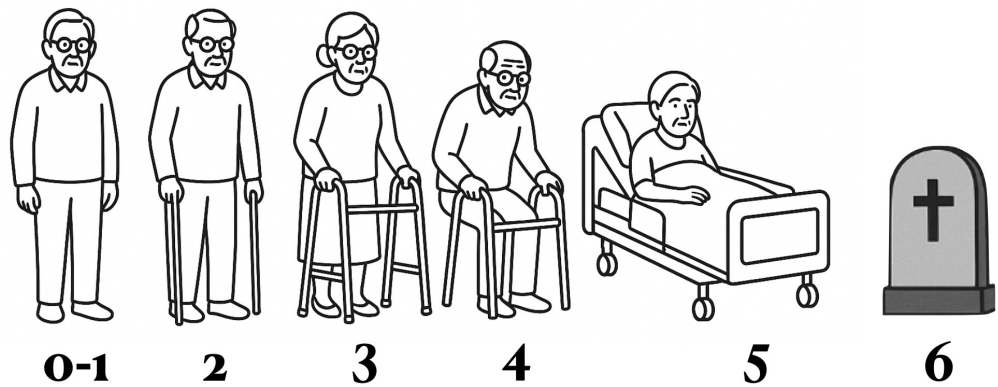
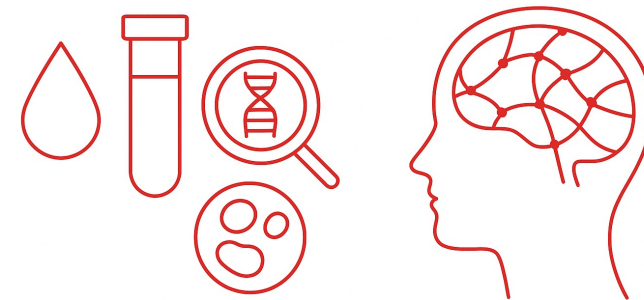
Fragile-Stroke



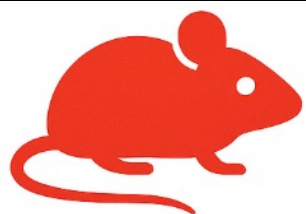
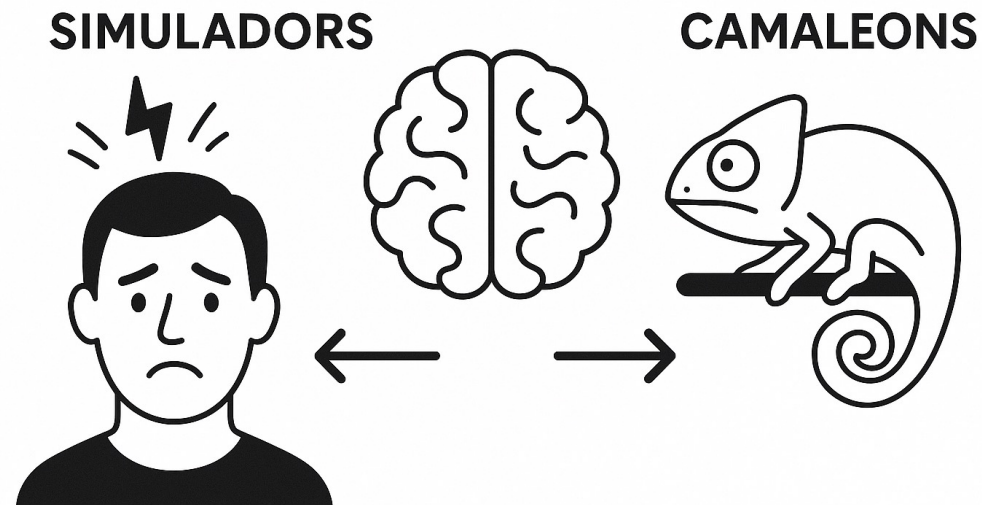


Predict

Fragile-Stroke



Imatge generada amb AI - ChatGPT







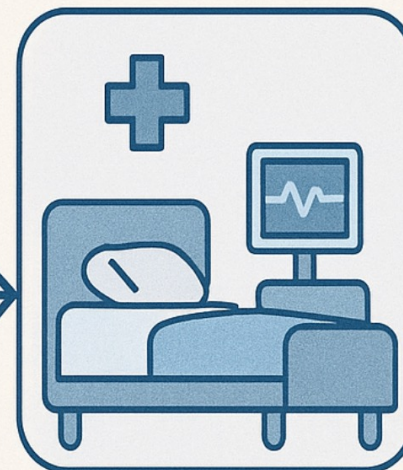
# TRAJECTÒRIA PACIENT AMB ICTUS



AVALUACIÓ  
PREHOSPITALÀRIA



AVALUACIÓ  
A L'HOSPITAL



INGRÉS A  
UNITAT ICTUS



SEGUIMENT  
AMBULATORI

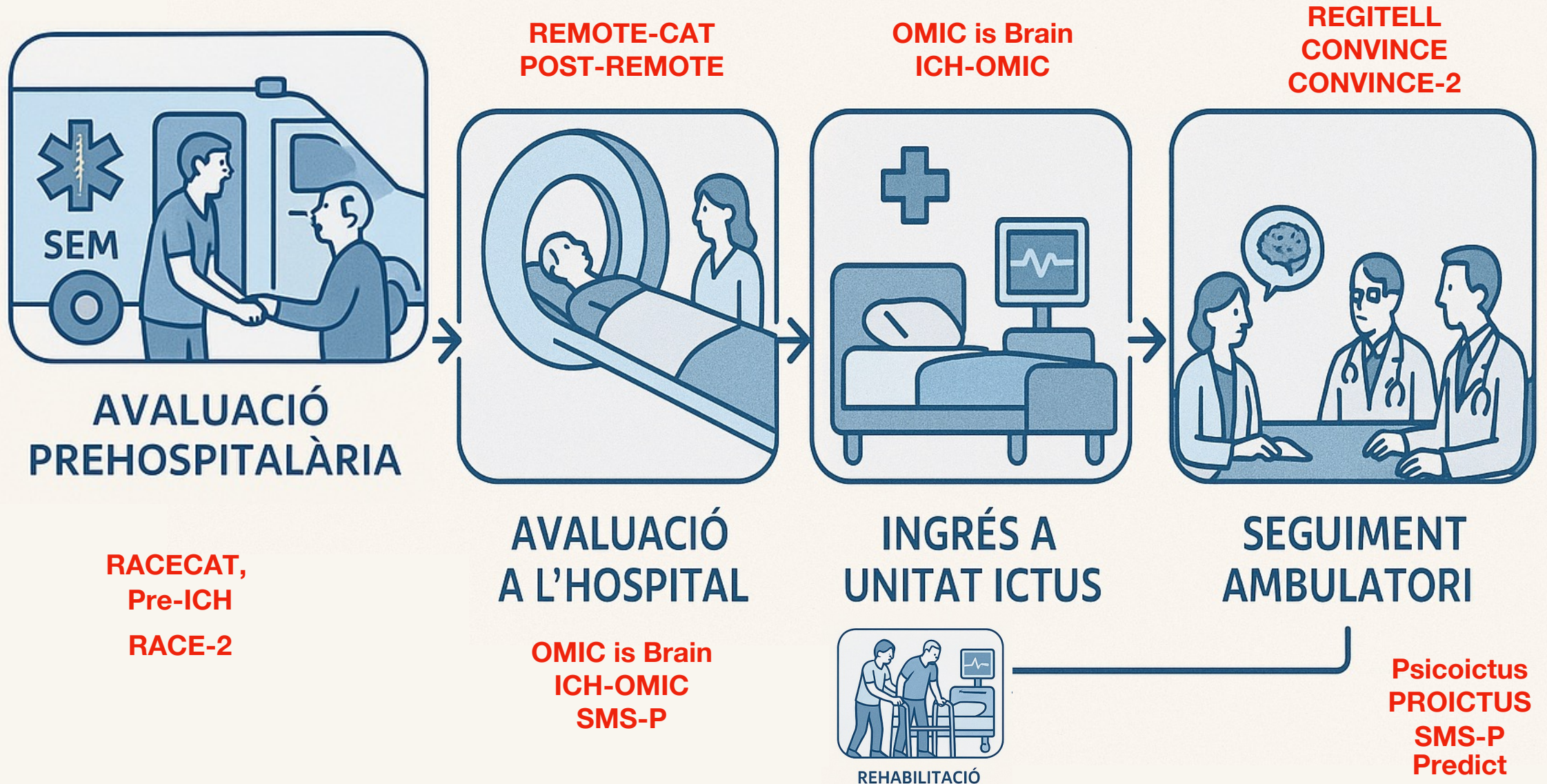


REHABILITACIÓ





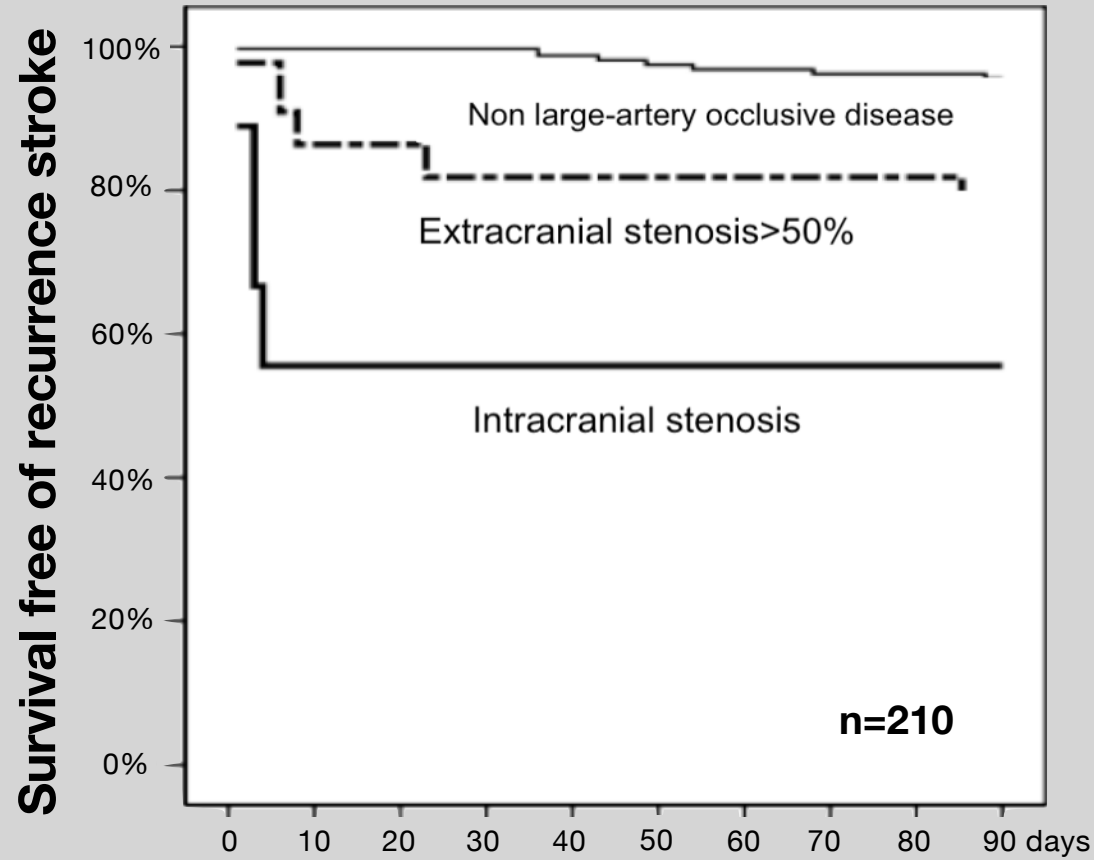
# TRAJECTÒRIA PACIENT AMB ICTUS



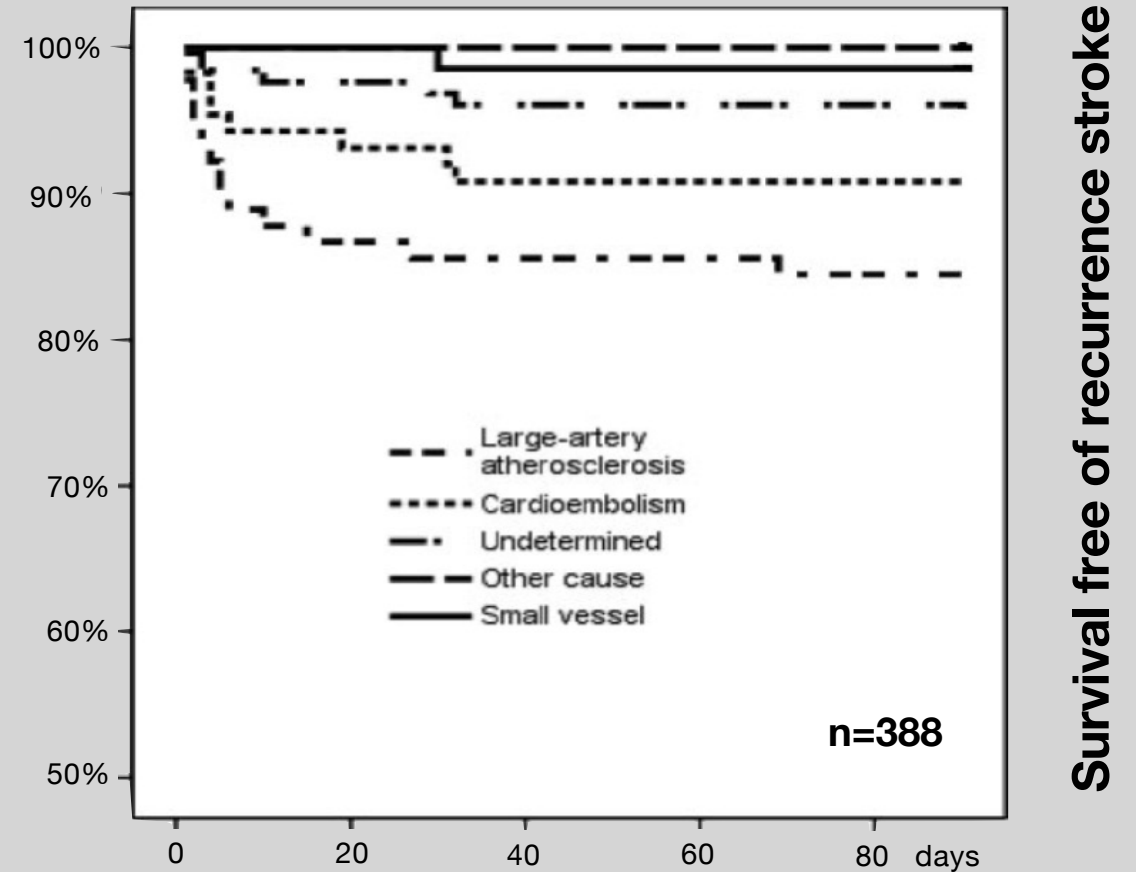




# 90 days



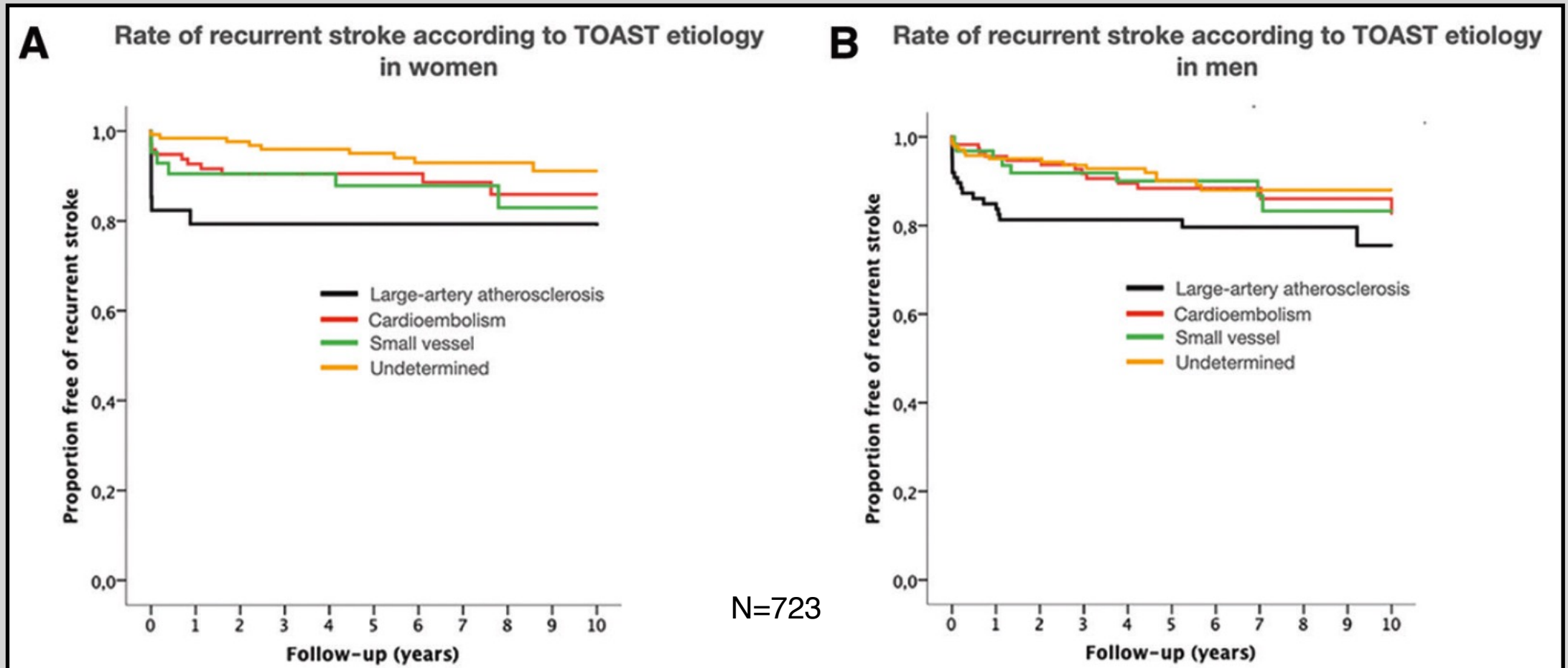
Purroy et al. Med Clin (Barc) 2009;133:283-9.



Purroy et al. Stroke 2007;38:3225-3229



# 10 years of follow-up

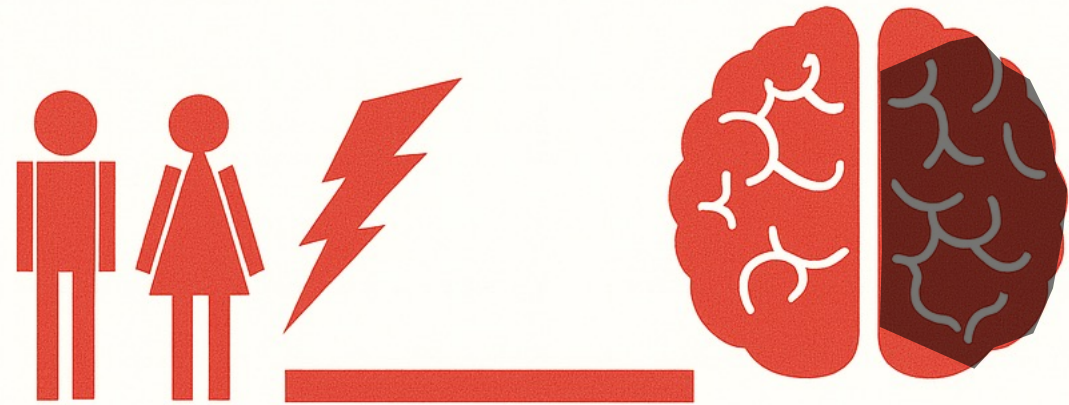






## Preconditioning in real life?

PI14/01574



**Recent previous  
TIA  $\leq 7$   
days**

**CEREBRAL ISCHEMIC  
TOLERANCE**

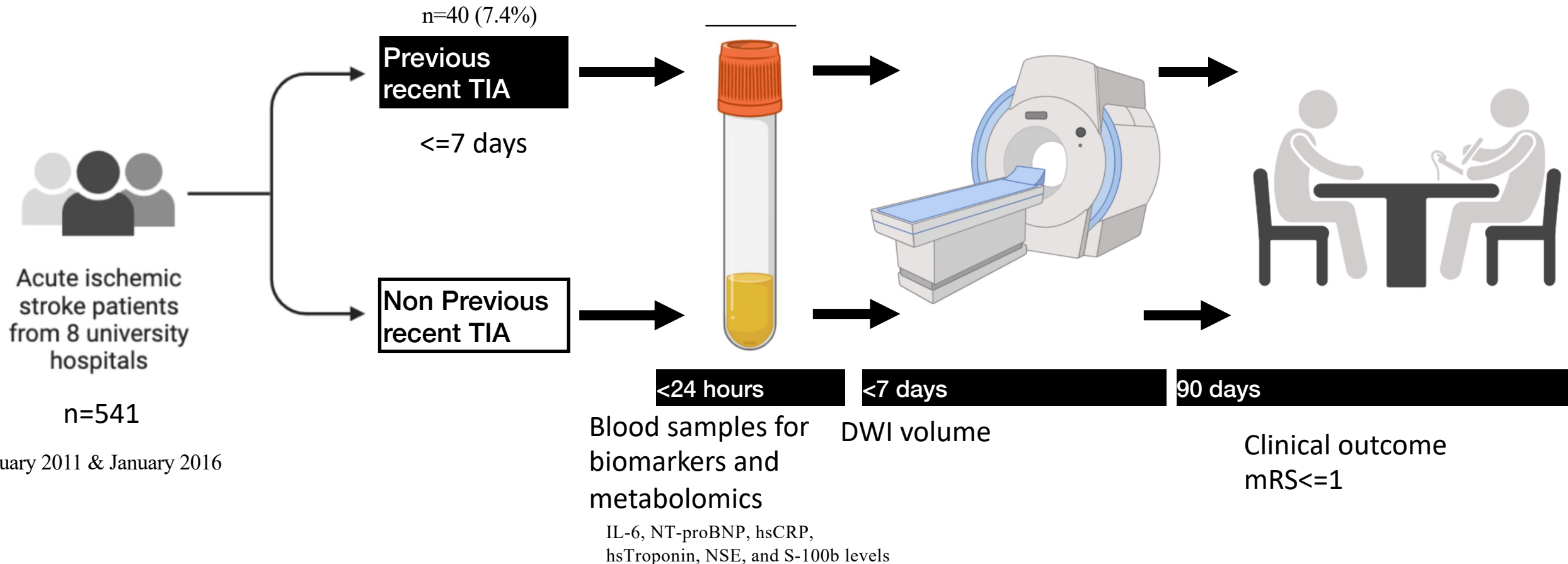
# Ischemia preconditioning induces an adaptive response that defines a circulating metabolomic

Joaquim Sol Ms<sup>1,2,3</sup>. Laura Colàs-Campàs PhD<sup>4</sup>. Gerard Mauri-Capdevila MD-PhD<sup>4,5</sup>. Jessica Molina-Seguin MD-PhD<sup>4</sup>. José Daniel Galo-Licon Ms<sup>1</sup>. Coral Torres-

Querol MsC<sup>4</sup>. Núria Aymerich MD<sup>6</sup>. Ángel Ois MD-PhD<sup>7</sup>. Jaume Roquer PhD<sup>7</sup>. Silvia Tur MD<sup>8</sup>. María del Carmen García-Carreira MD<sup>9</sup>. Joan Martí-Fàbregas

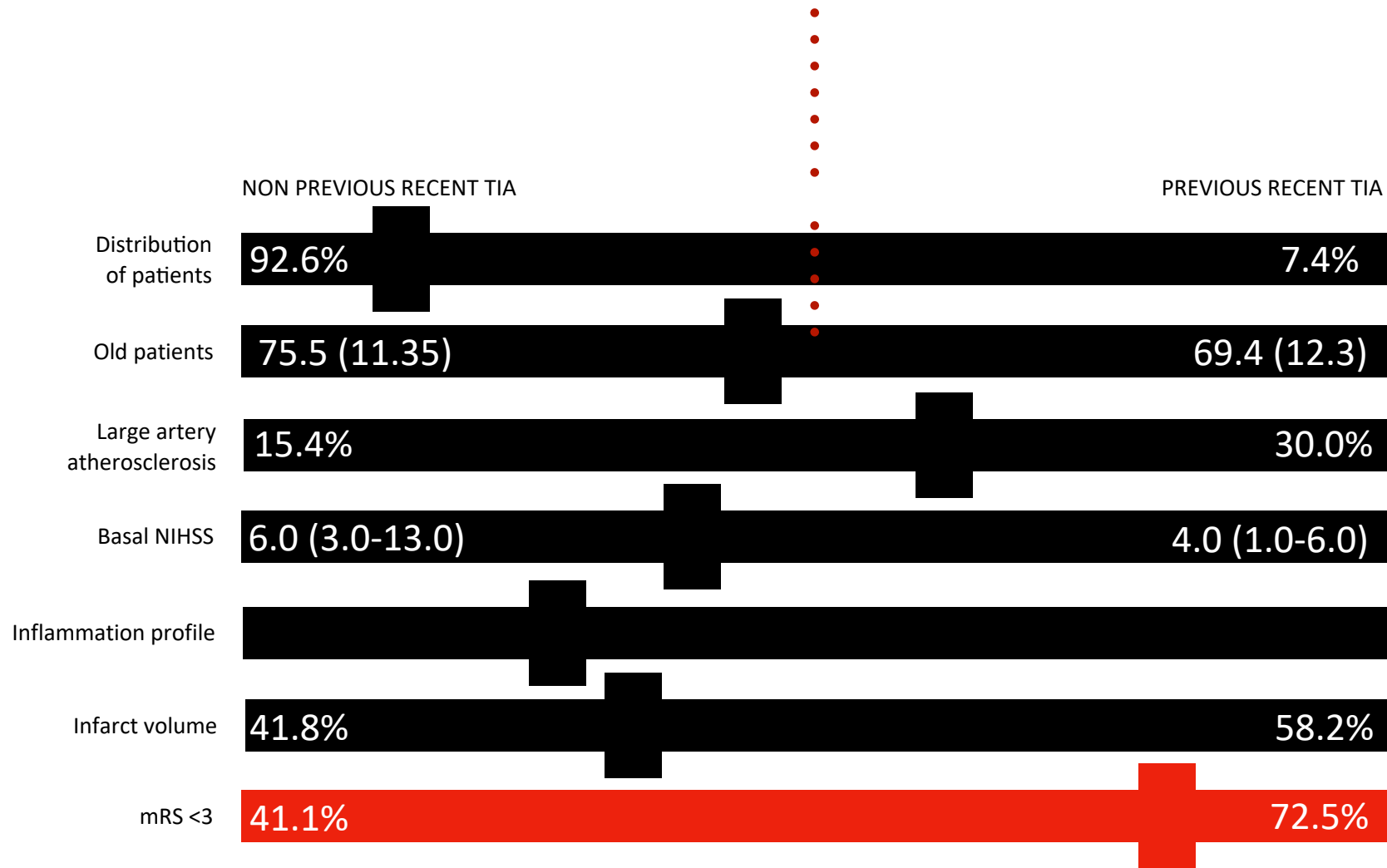
signature in ischemic stroke patients  
MD-PhD<sup>10</sup>. Antonio Guzmán-Cabrera PhD<sup>11</sup>. Tomás Segura MD-PhD<sup>12</sup>. Reinald Pamplona MD-PhD<sup>1</sup>. Manel Portero-Otín MD-PhD<sup>1</sup>. Gloria Arqué PhD<sup>4</sup>. †. Mariona

Jové PhD<sup>1</sup>. †. Francisco Purroy MD-PhD<sup>4,5</sup>. †. \*



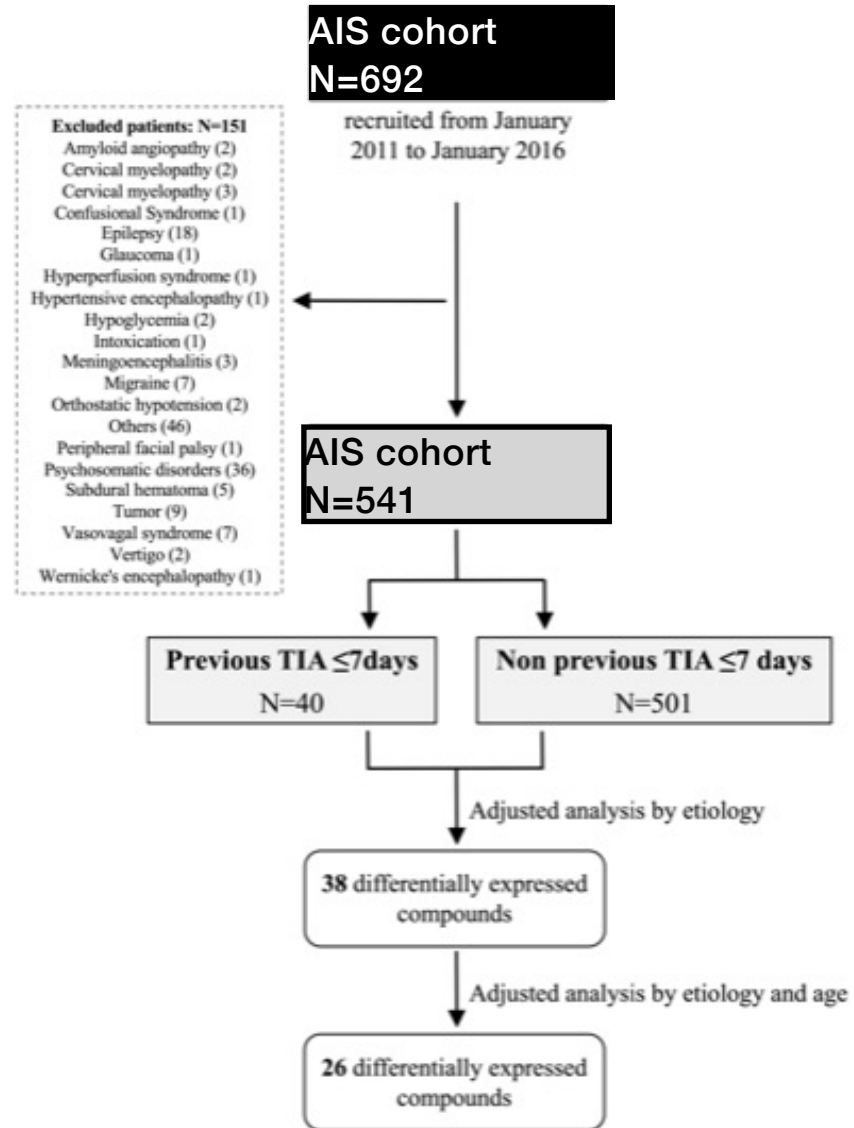
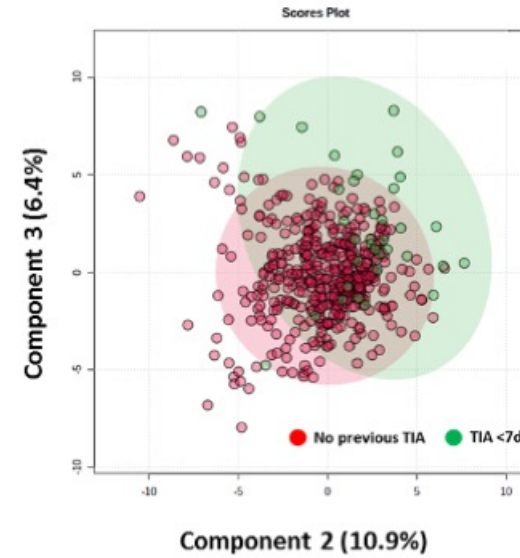
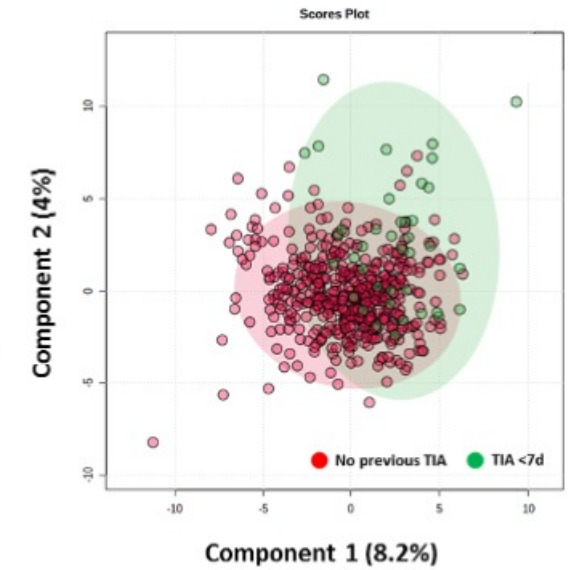
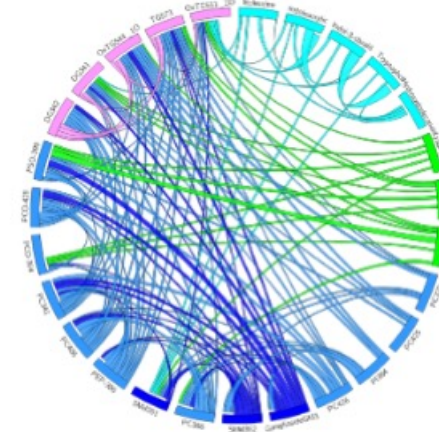
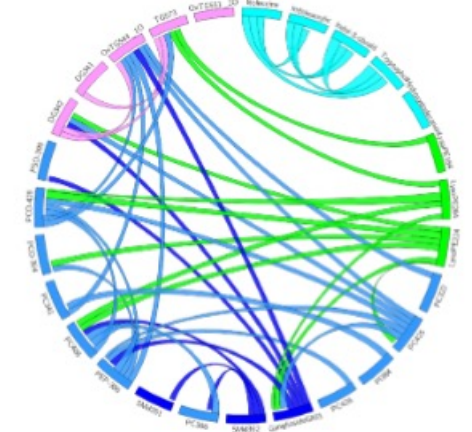


Non Previous recent TIA

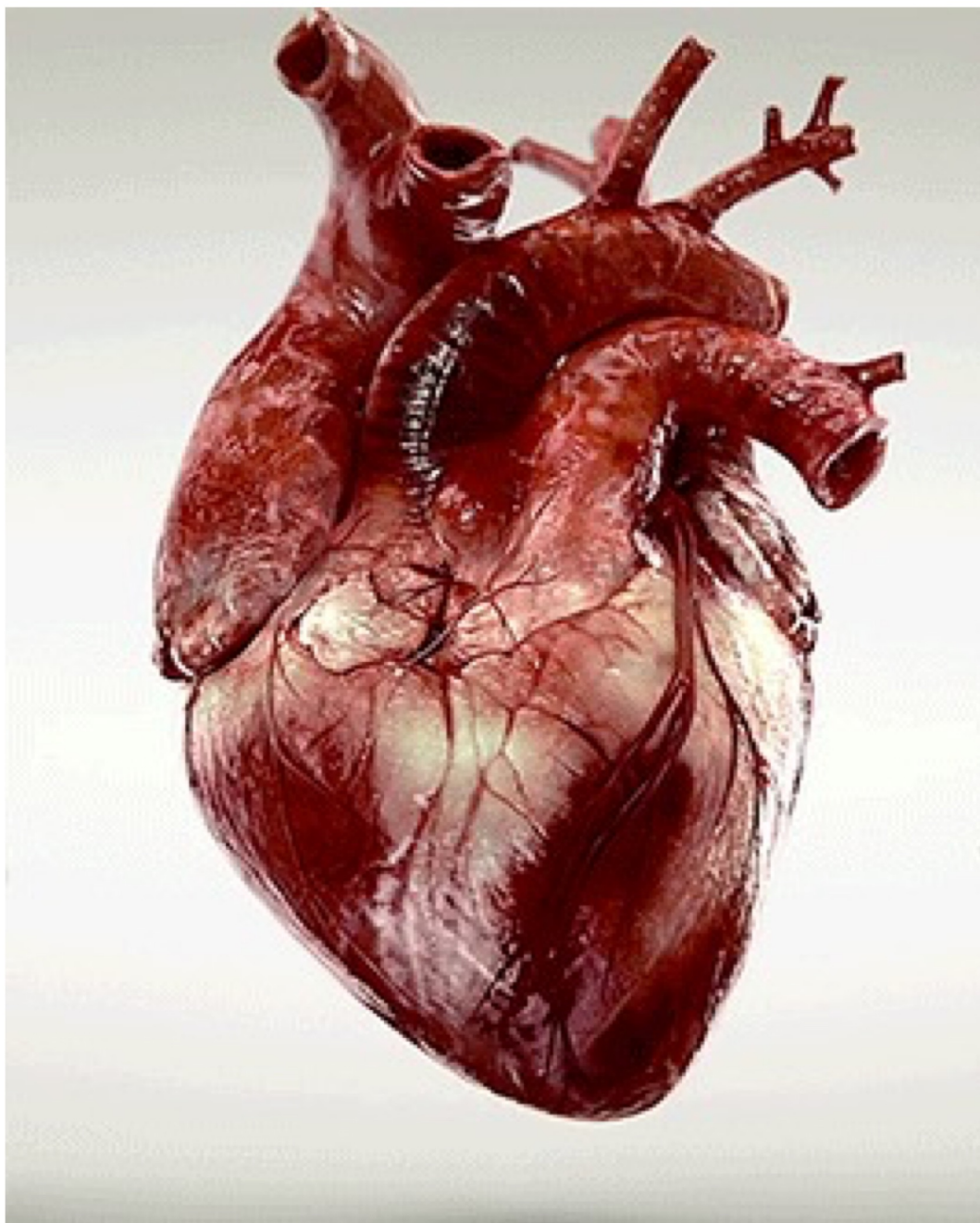


Previous recent TIA

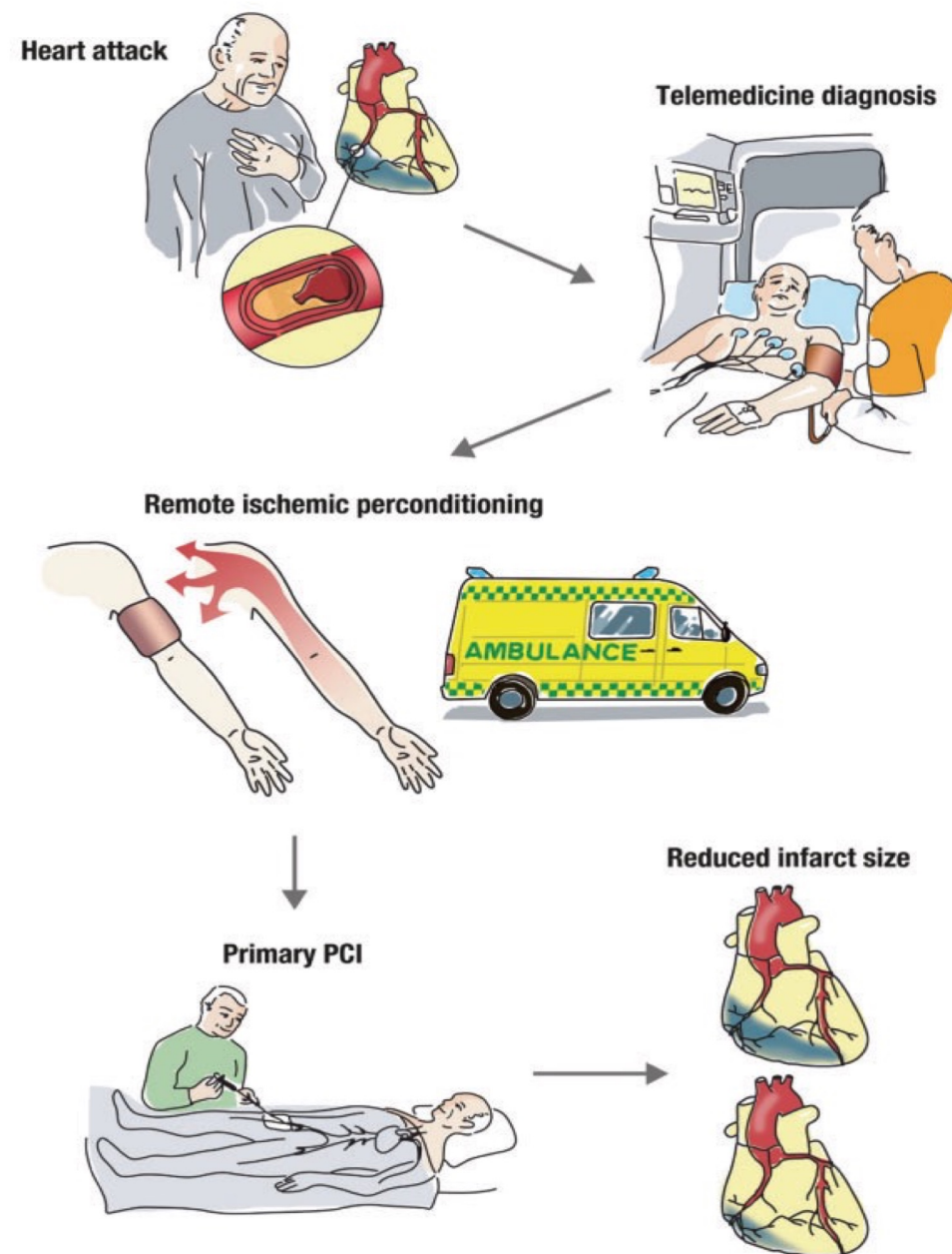
Neutral result

**A****Metabolomics****B****Lipidomics****C****Non previous TIA****D****Previous TIA**





## Remote Ischemic Perconditioning



# Our dream started in 2017...



**we want to improve  
the quality of life for  
ischemic stroke  
patients**





# Our dream started in 2017...



**... not only for those patients  
eligible for fibrinolysis and/or  
thrombectomy but also for all  
acute ischemic stroke  
patients**



# Our dream started in 2017...



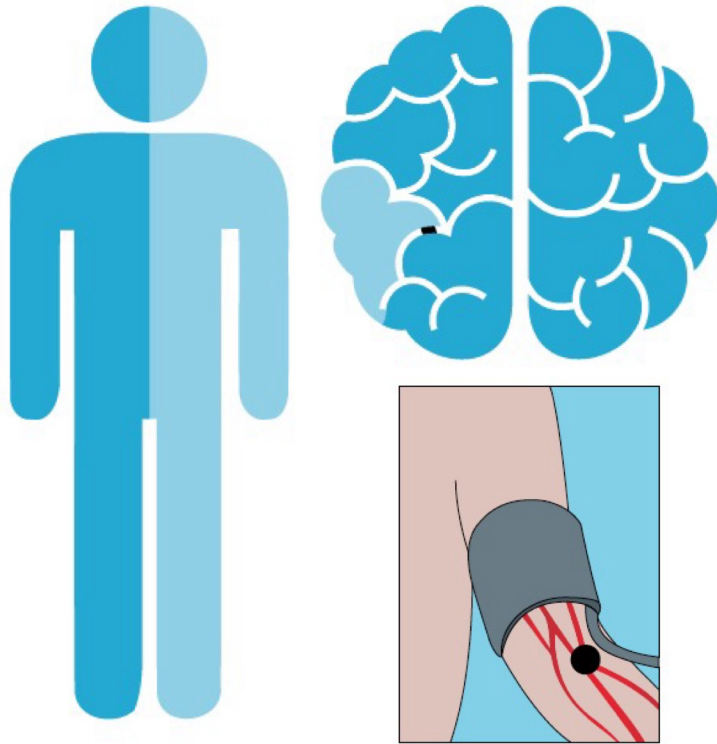
## ... neuroprotective strategy:

- Safe
- Inexpensive
- Easy to implement for prehospital stroke code patients

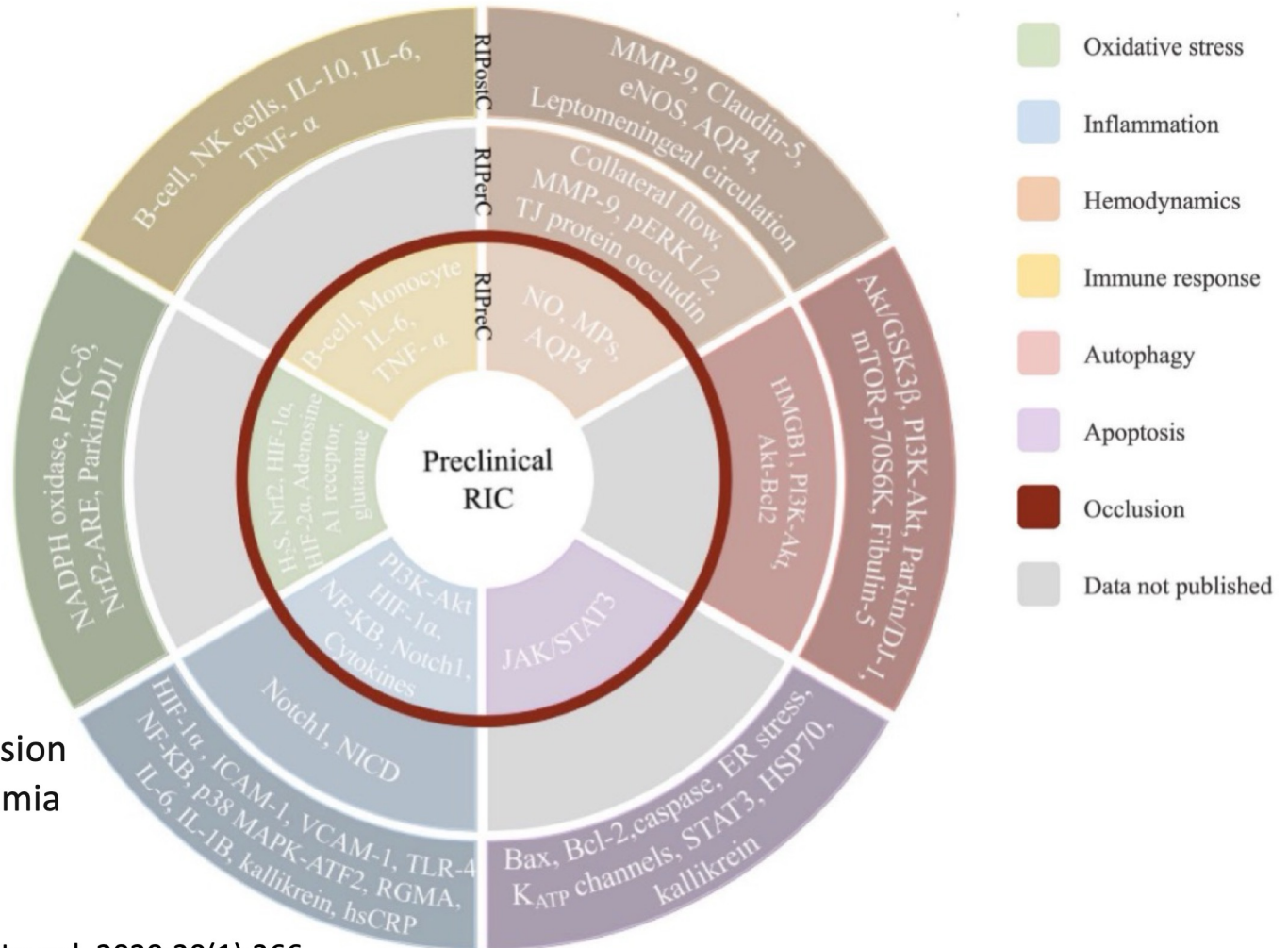




# Remote ischemic preconditioning



RIC consists of short and controlled cycles of ischemia-reperfusion applied to one limb during the establishment of cerebral ischemia

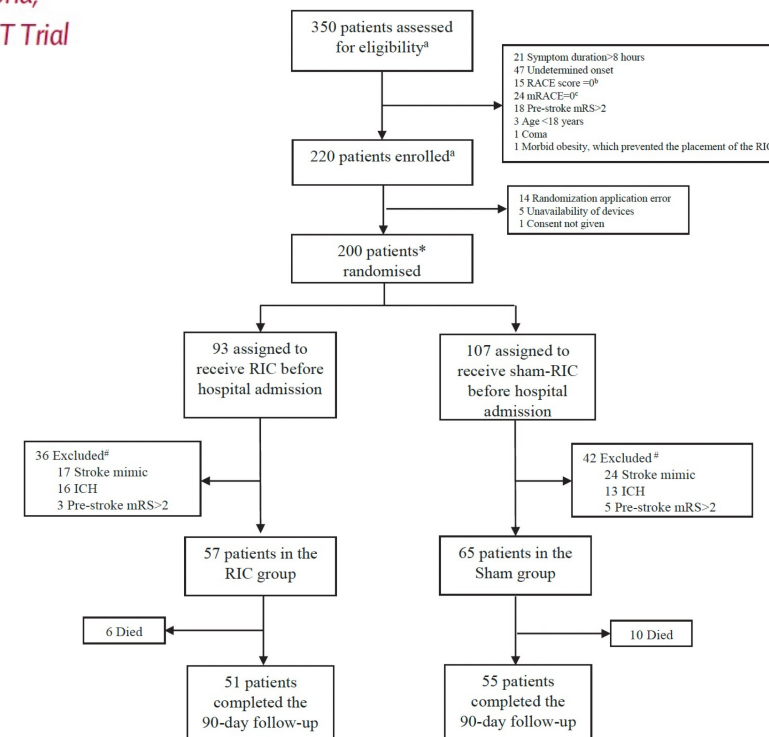
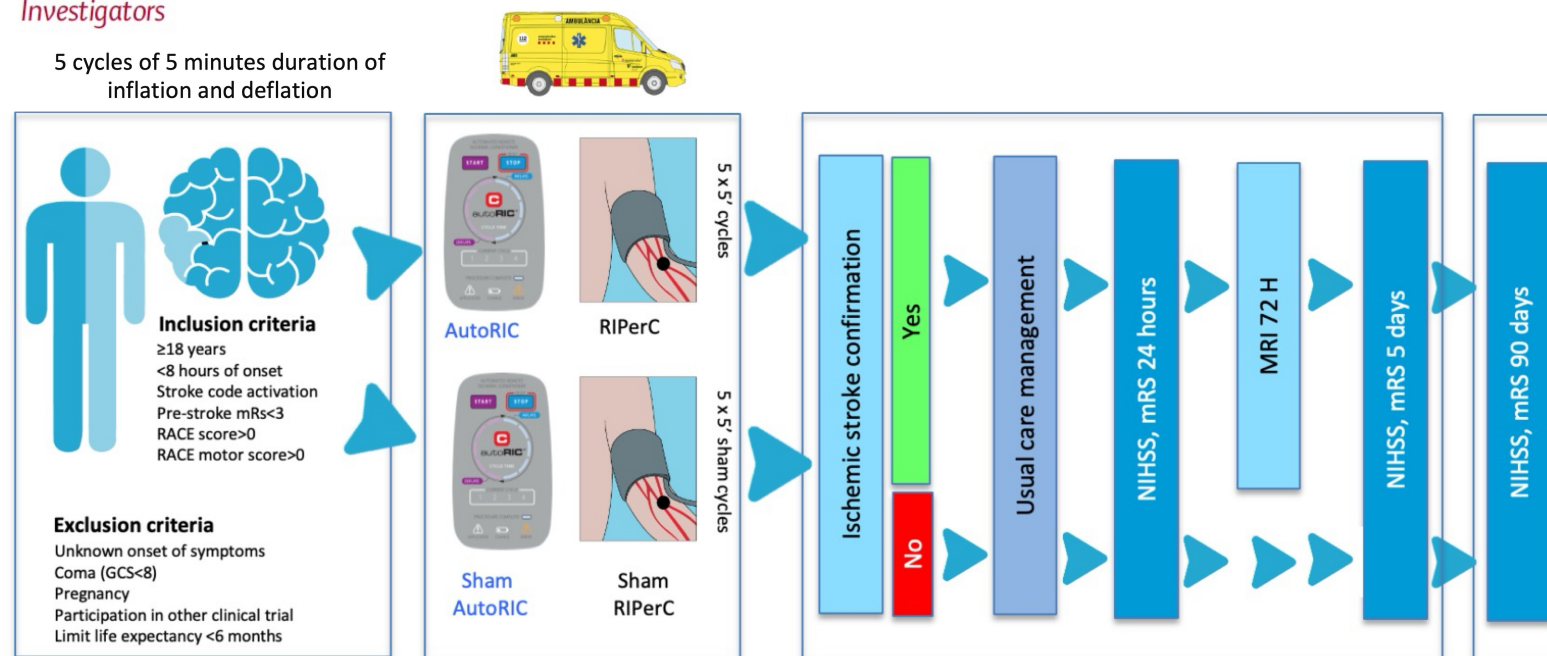


# Prehospital application of remote ischaemic preconditioning in acute ischaemic stroke patients in Catalonia: the REMOTE-CAT clinical trial



eClinicalMedicine  
2025;83: 103208

Francisco Purroy,<sup>a,b,c,\*</sup> Gloria Arqué,<sup>b,c</sup> Xavier Jiménez-Fàbrega,<sup>d</sup> Teresa Subirats,<sup>d</sup> José Ramon Ropero,<sup>d</sup> Mikel Vicente-Pascual,<sup>a,c</sup> Pere Cardona,<sup>e</sup> Manuel Gómez-Choco,<sup>f</sup> Jorge Pagola,<sup>g</sup> Sònia Abilleira,<sup>h</sup> Àlex Rovira,<sup>g</sup> Rafel Cirer-Sastre,<sup>b,i</sup> and Gerard Mauri-Capdevila,<sup>a,b,c</sup> for the REMOTE-CAT Trial Investigators



Multi-center, randomized, sham controlled, double blinded trial  
 Estimated sample size of 572

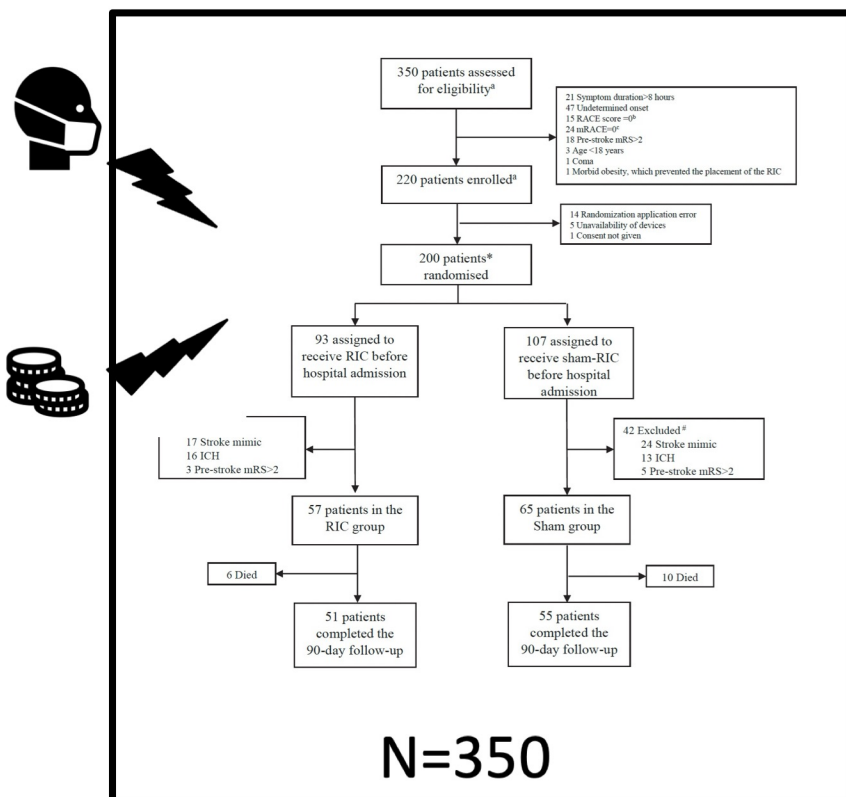


# Prehospital application of remote ischaemic preconditioning in acute ischaemic stroke patients in Catalonia: the REMOTE-CAT clinical trial

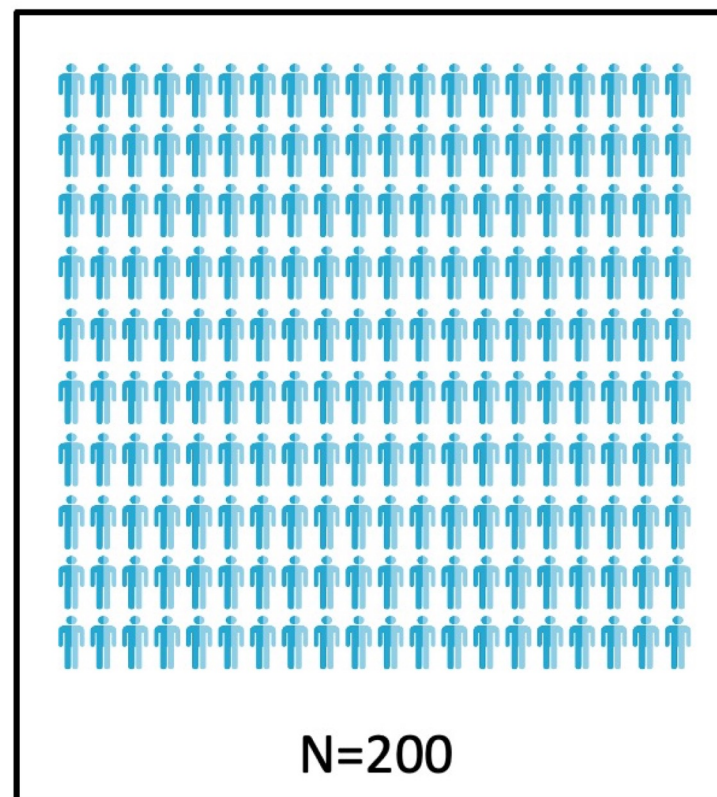


eClinicalMedicine  
2025;83: 103208

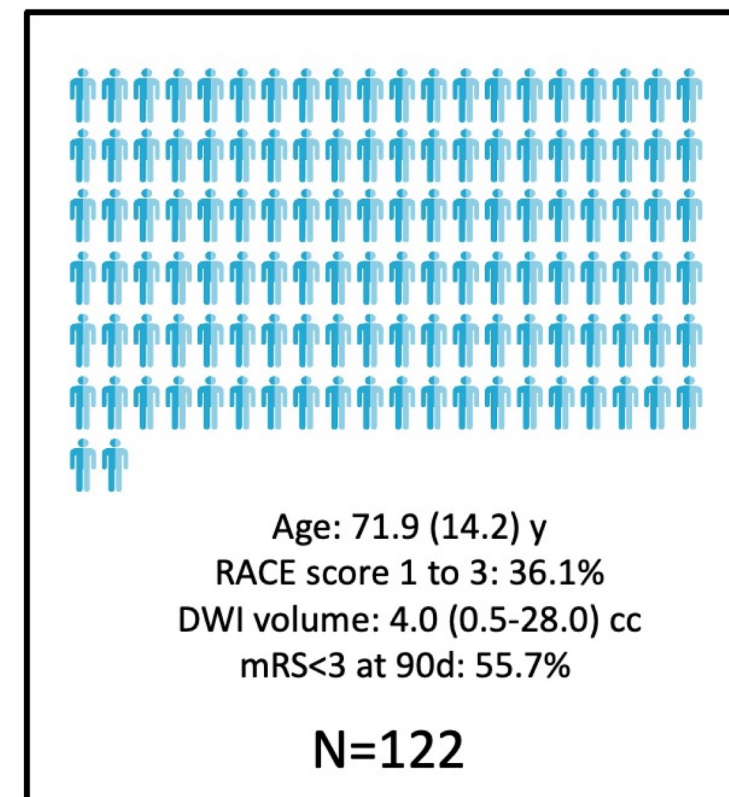
Between August 2019 and December 2023



**Screened patients**



**Randomized patients**



**Primary analysis**

After 78 exclusions (29 haemorrhagic strokes, 41 stroke mimics, and 8 patients with mRS > 3)

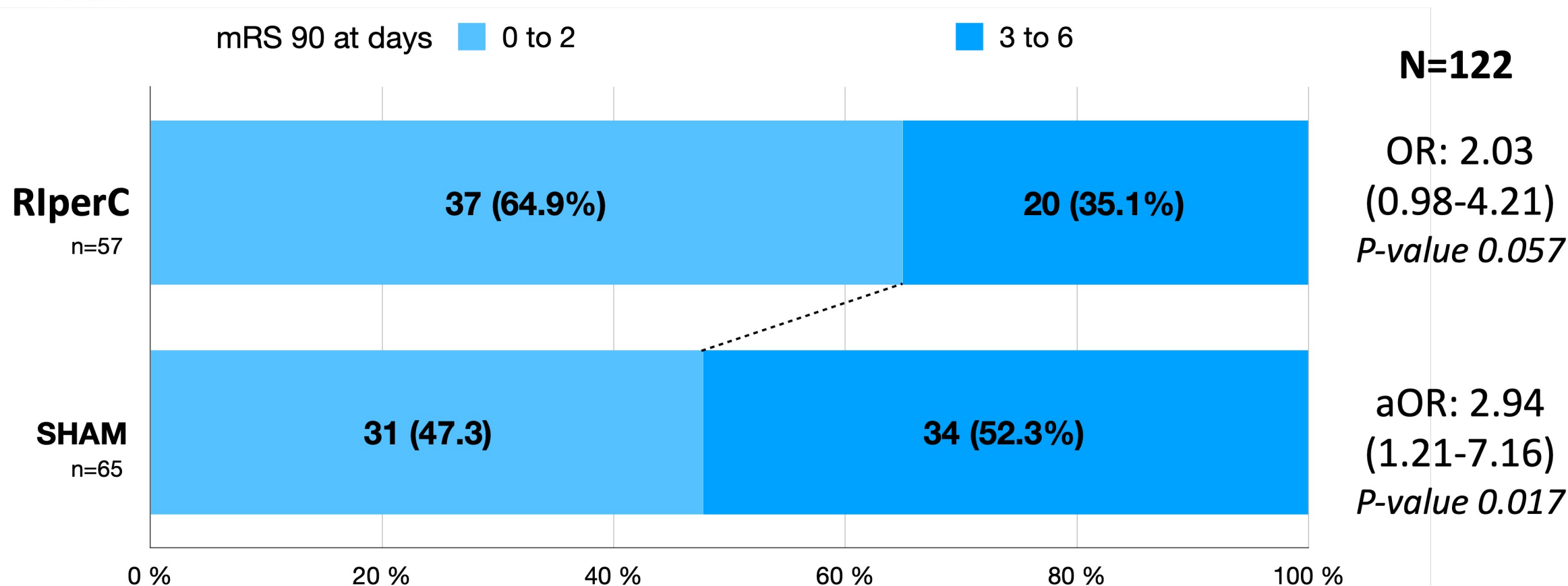
*Estimated sample size of 572 subjects*

# Prehospital application of remote ischaemic preconditioning in acute ischaemic stroke patients in Catalonia: the REMOTE-CAT clinical trial

Francisco Purroy,<sup>a,b,c,\*</sup> Gloria Arqué,<sup>b,c</sup> Xavier Jiménez-Fàbrega,<sup>d</sup> Teresa Subirats,<sup>d</sup> José Ramon Ropero,<sup>d</sup> Mikel Vicente-Pascual,<sup>a,c</sup> Pere Cardona,<sup>e</sup> Manuel Gómez-Choco,<sup>f</sup> Jorge Pagola,<sup>g</sup> Sònia Abilleira,<sup>h</sup> Àlex Rovira,<sup>g</sup> Rafel Cirer-Sastre,<sup>b,i</sup> and Gerard Mauri-Capdevila,<sup>a,b,c</sup> for the REMOTE-CAT Trial Investigators



eClinicalMedicine  
2025;83: 103208



aOR: post-hoc análisis adjusted for age, baseline status (determined by pre-stroke mRS score), and initial stroke severity (measured by baseline RACE score by paramedics)



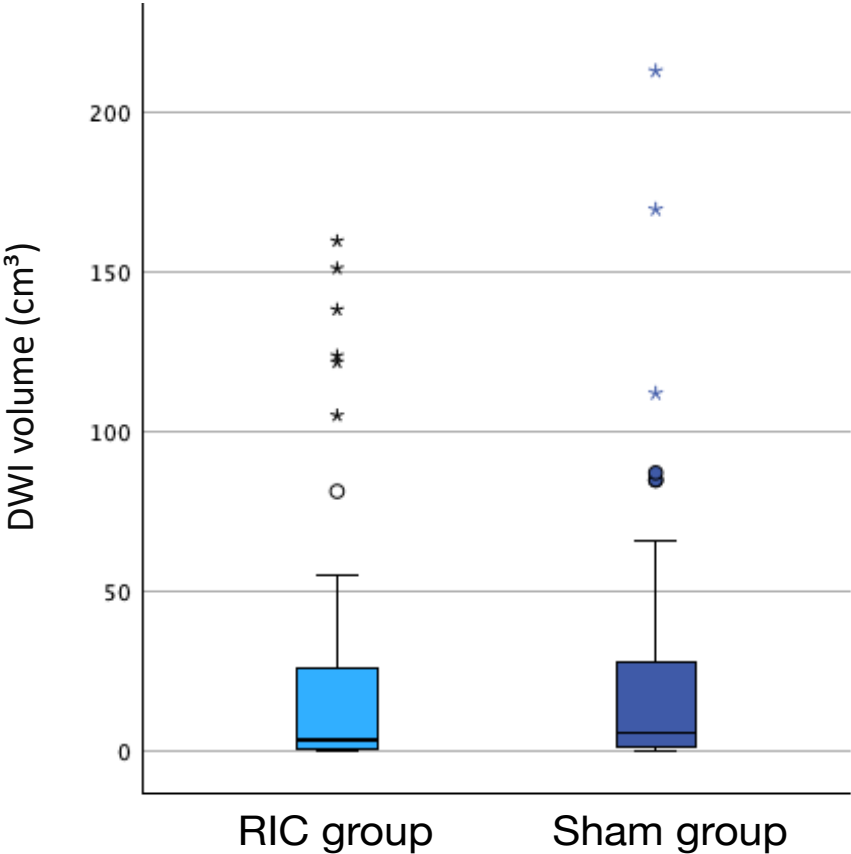
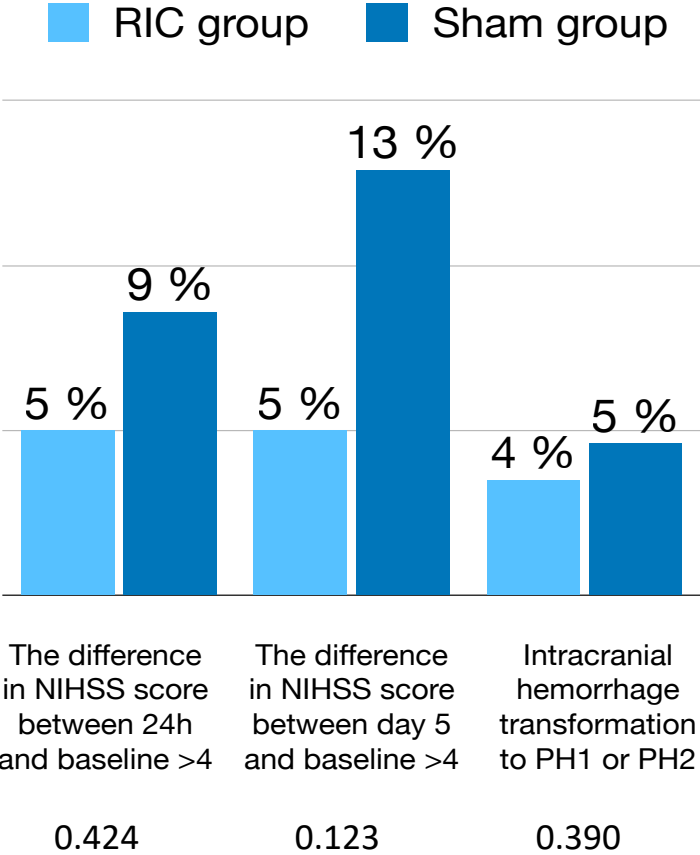
# Results: *Secondary outcomes*

ITT analysis



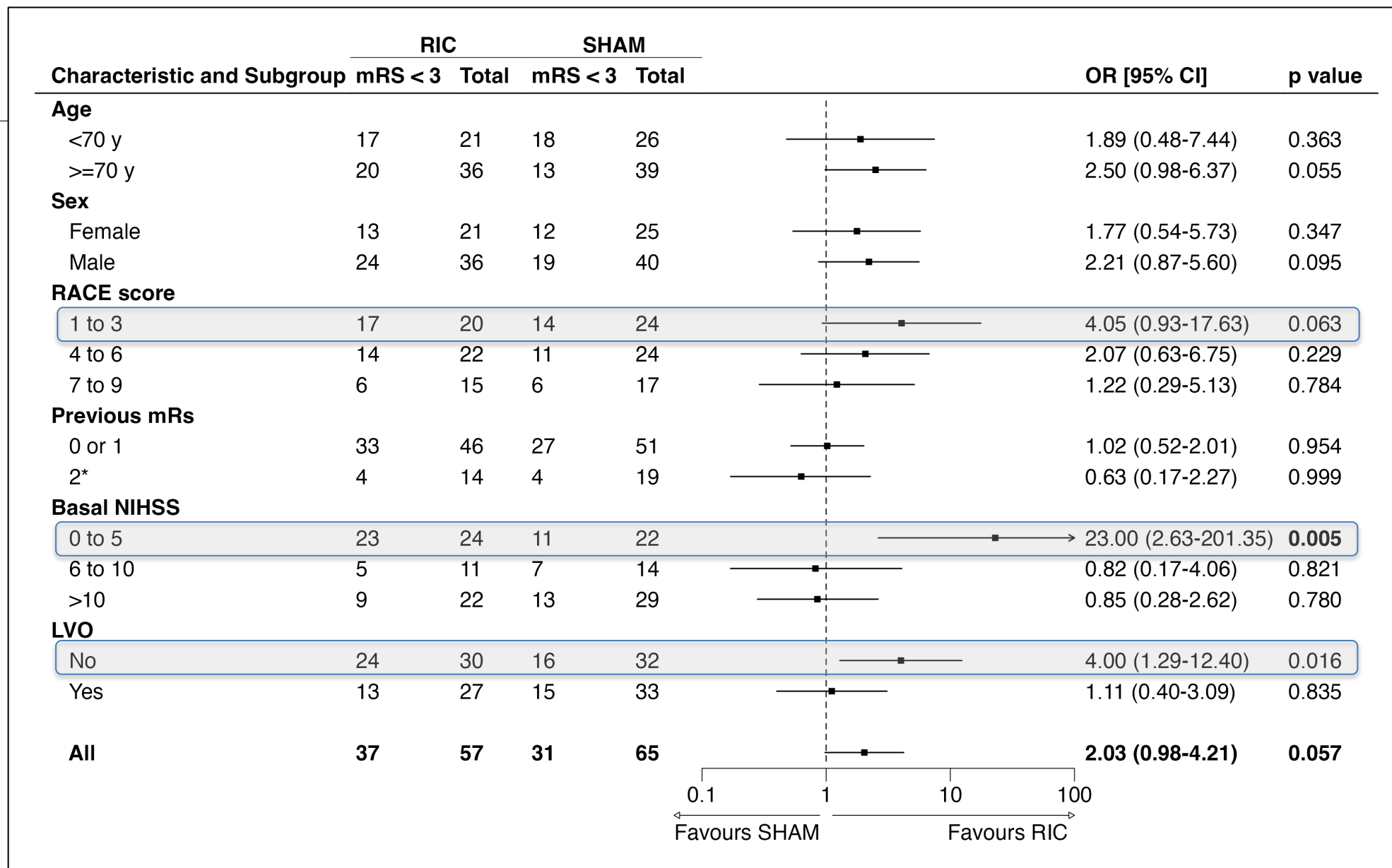
ITT analysis

N=122



N=101 (82.8%)

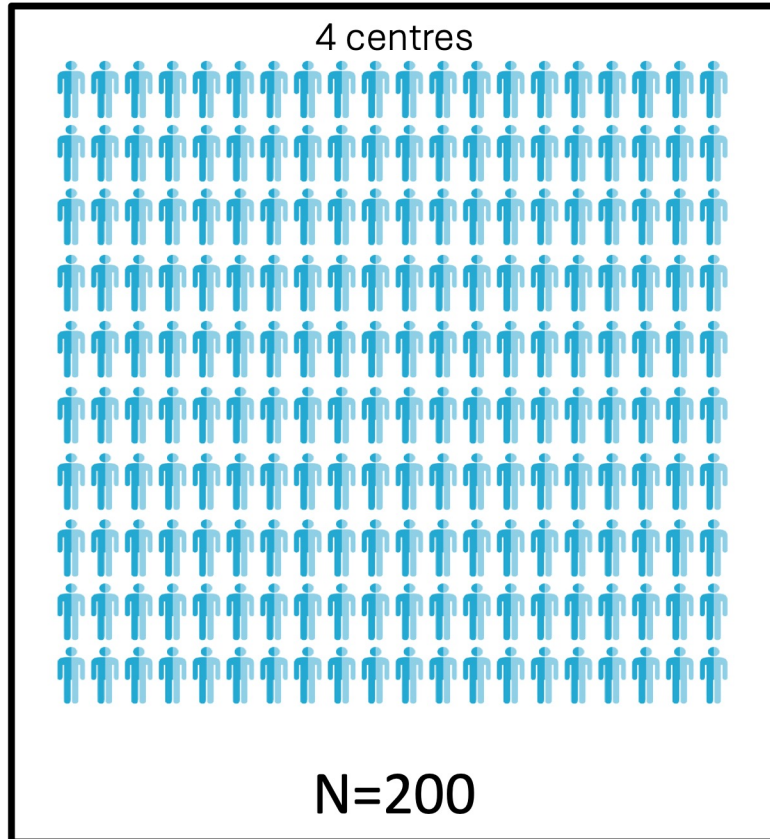
Median (IQR) 2.76 (0.03-25.82) 6.14 (0.88-26.85) P-value 0.184  
cm3



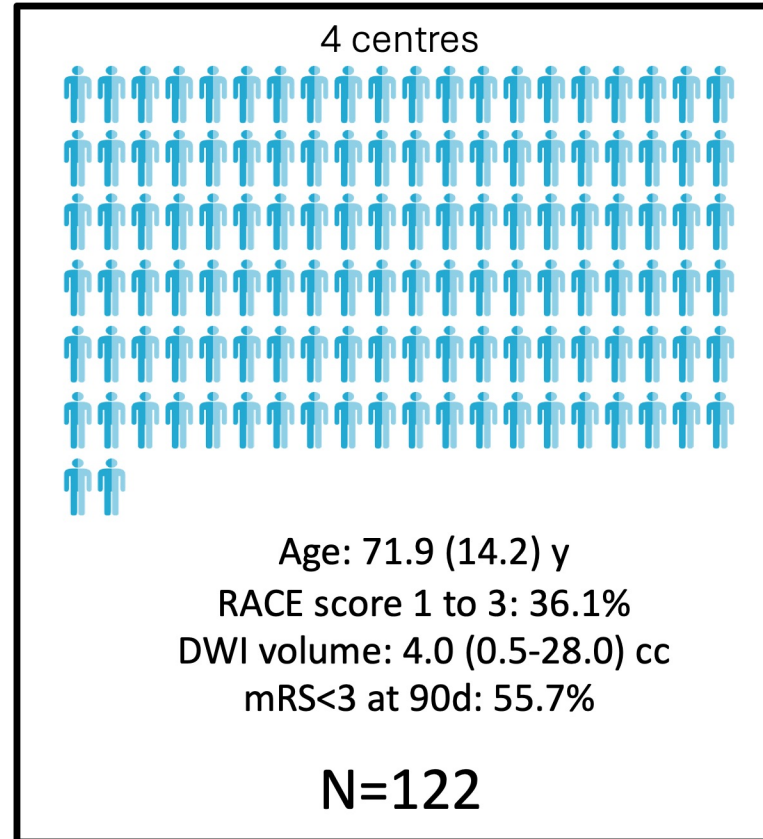


# Results:

*Between August 2019 and December 2023*

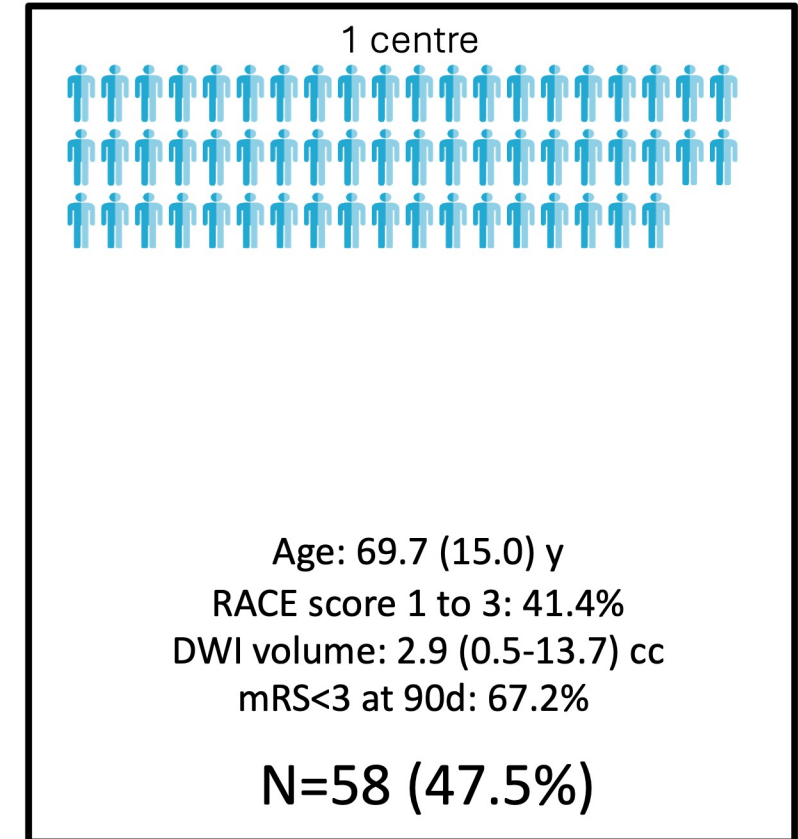


**Randomized patients**



**Primary analysis**

*After 78 exclusions (29 haemorrhagic strokes,  
41 stroke mimics, and 8 patients with mRS  
≥3)*  
eClinicalMedicine 2025;83: 103208



**Cognitive impairment  
subanalysis**



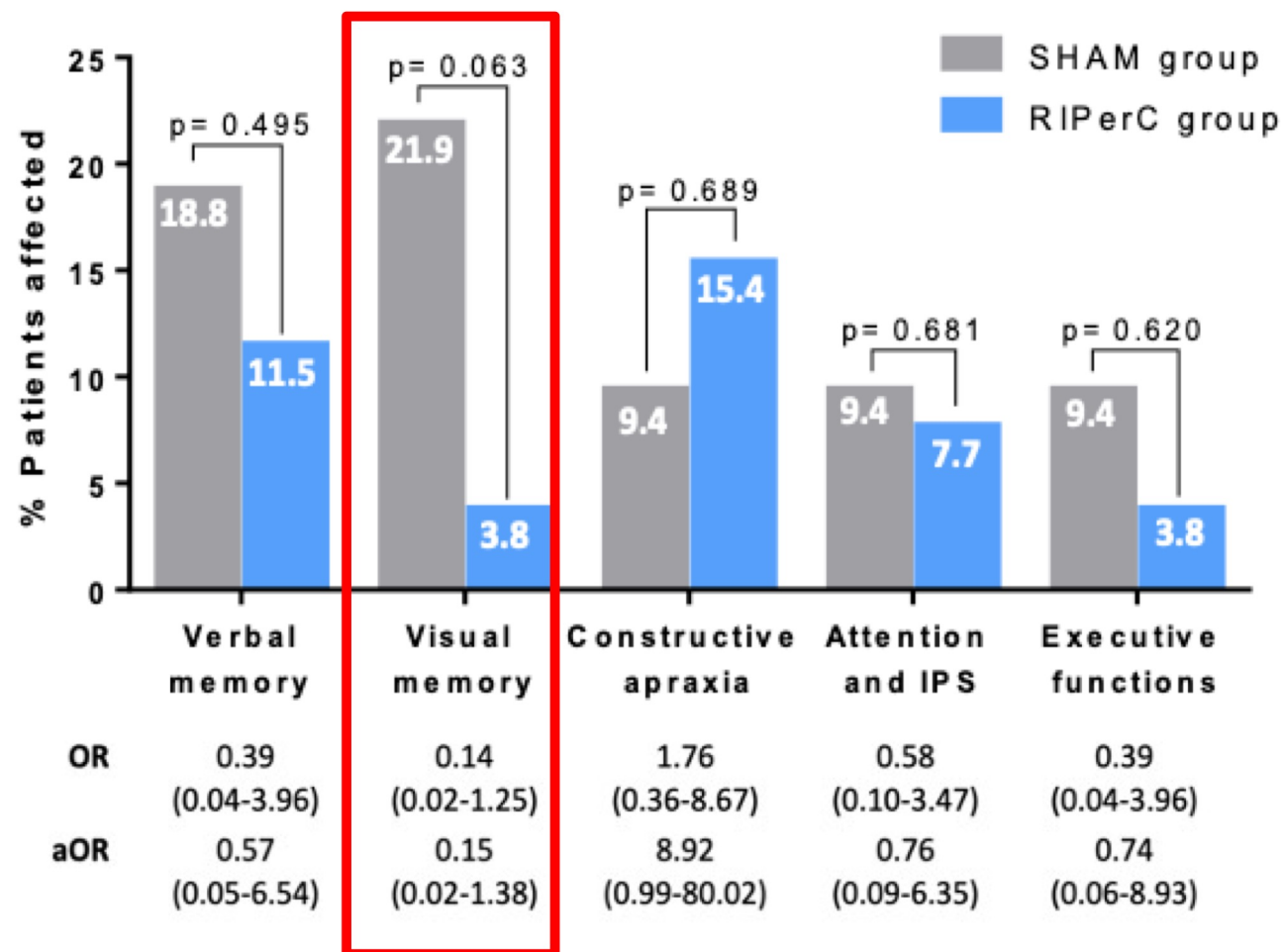
THE VOICE OF STROKE  
IN EUROPE

[eso-stroke.org/esoc2025](https://eso-stroke.org/esoc2025)

# Results:



## Neuropsychological profile



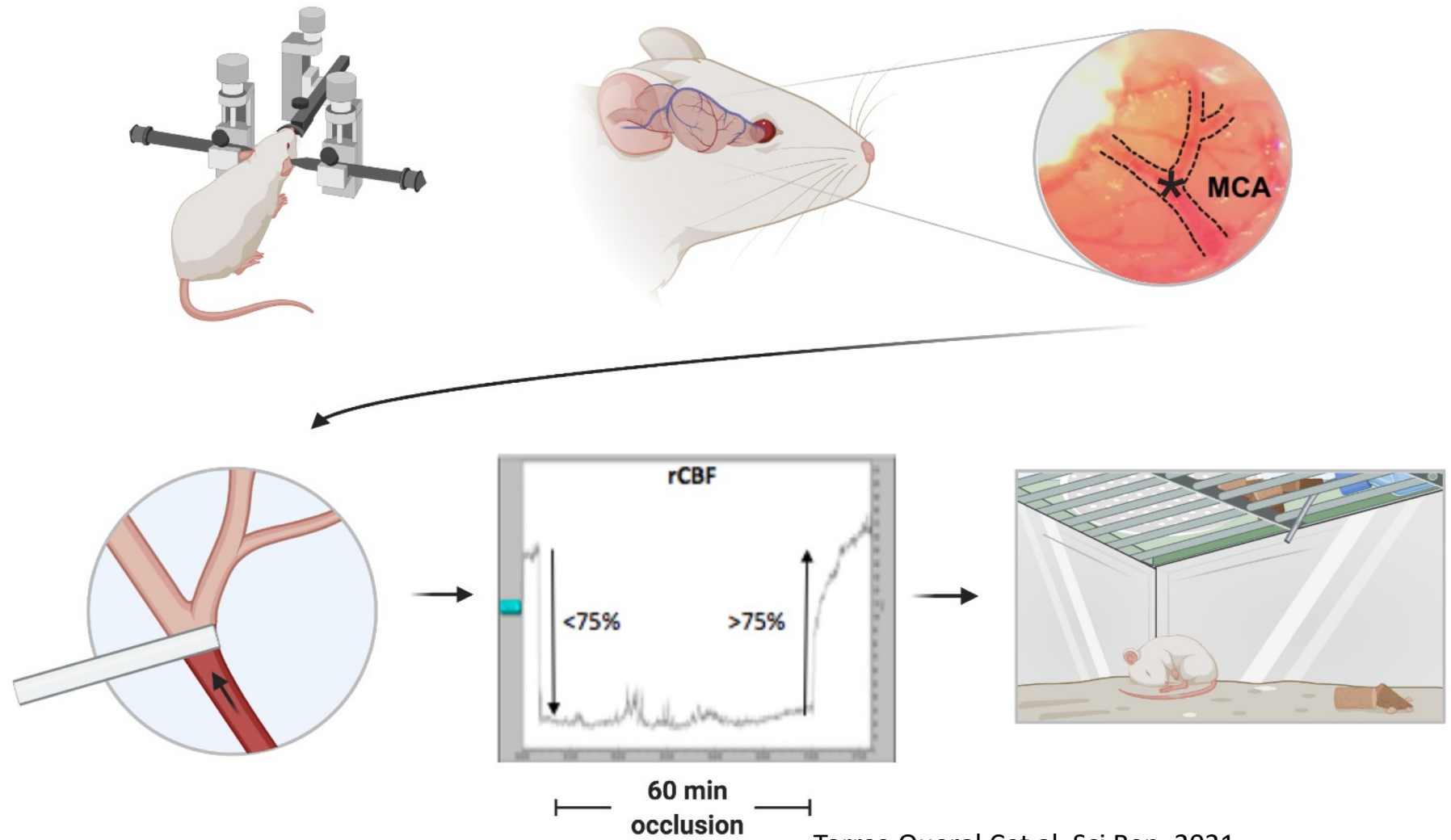


## Staff Scientist



Gloria Arqué, PhD

## Mouse model of transient middle cerebral artery occlusion (tMCAo)



## PhD Student

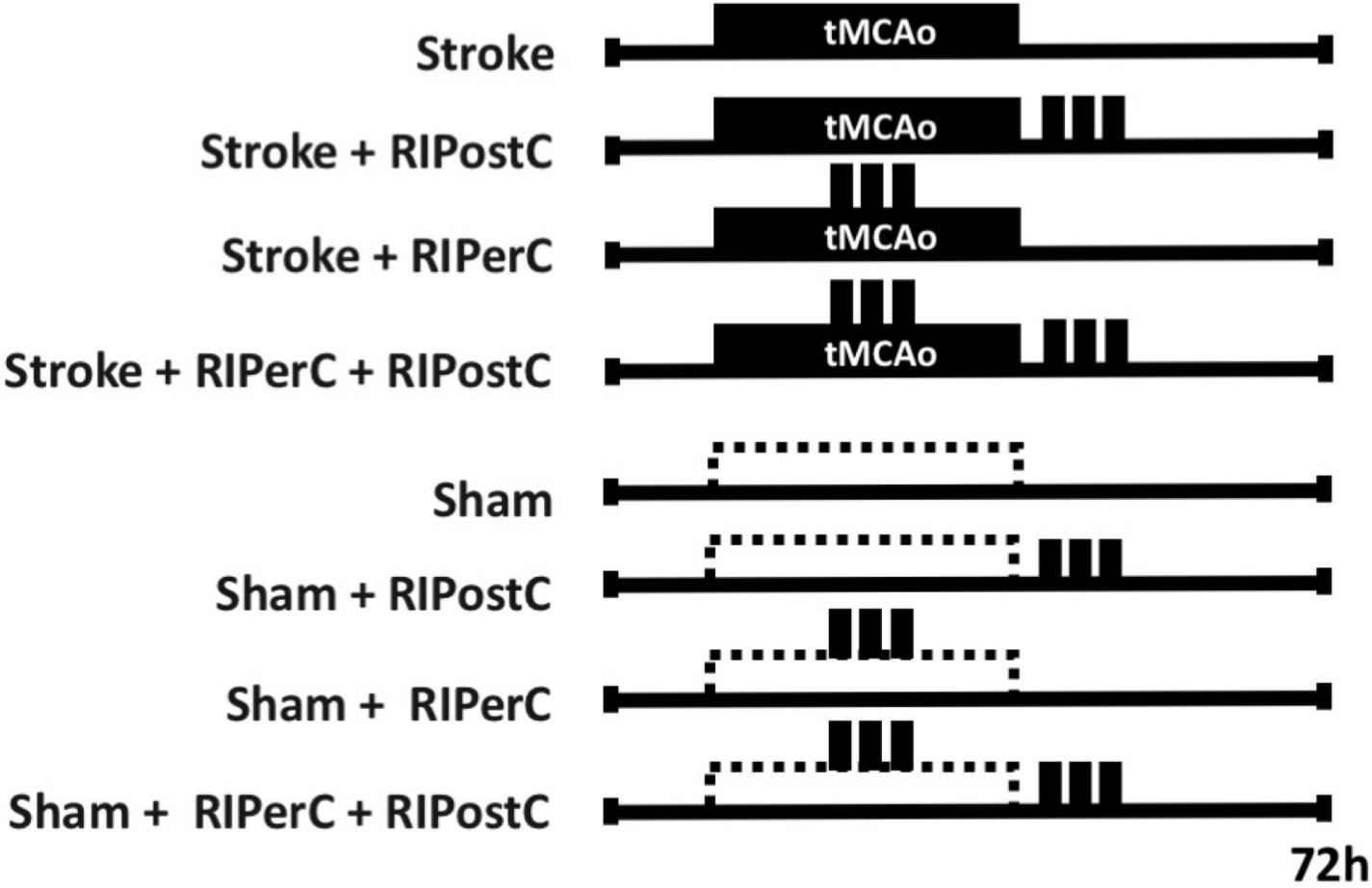


Coral Torres

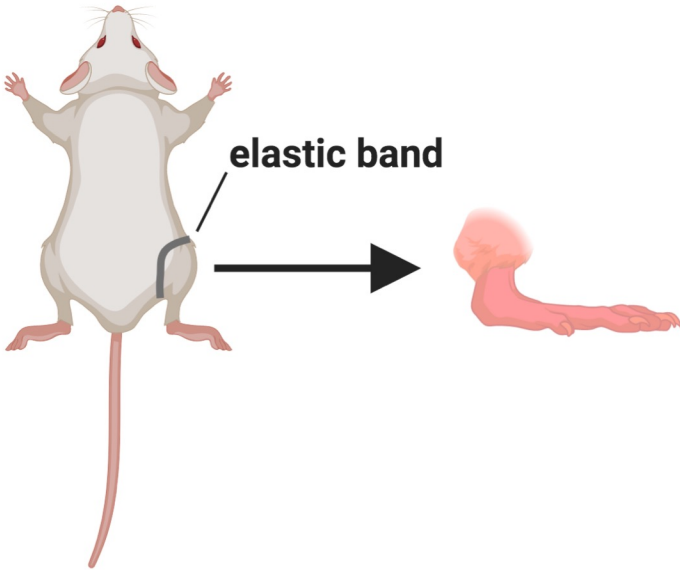
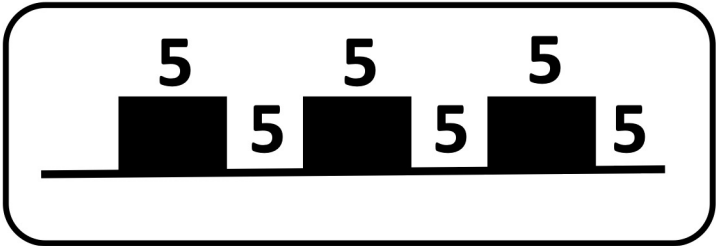
Torres-Querol Cet al. Sci Rep. 2021  
Cambray S, et al. Mol Neurobiol. 2018  
Torres-Querol et al. J Cereb Blood Flow Metab. 2026  
Torres-Querol et al. J Stroke Vasc Neurol. 2025

3. Describe the effect of RIC treatment on infarct volume, neurological function and the histopathological effect induced by ischemic stroke

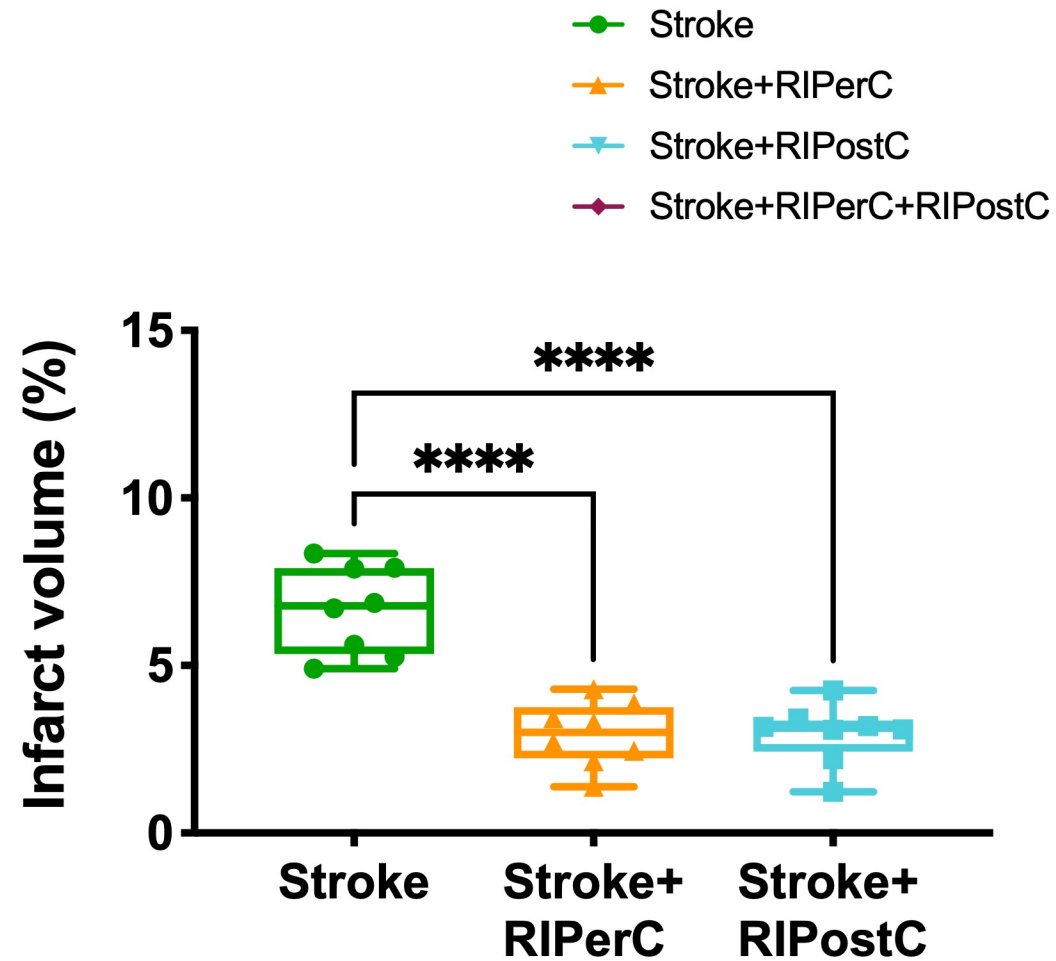
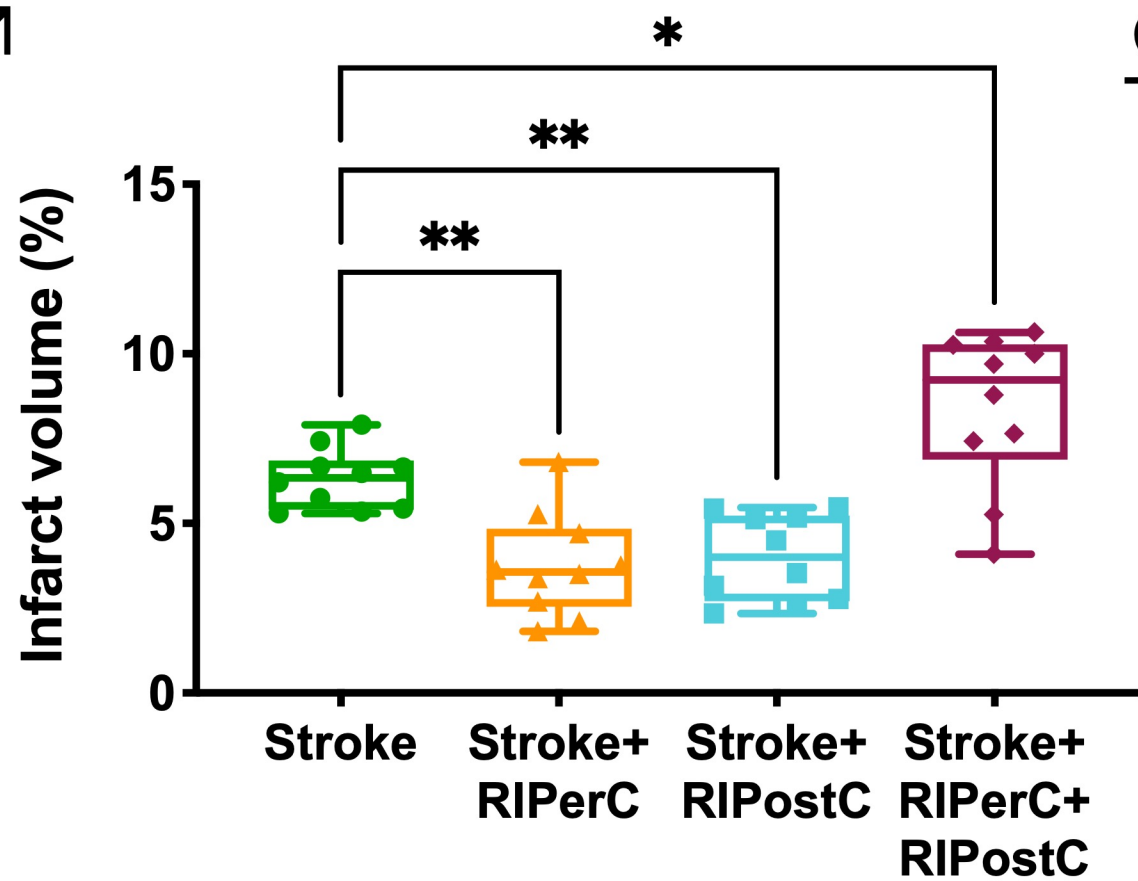
Mice were assigned to 8 different groups:

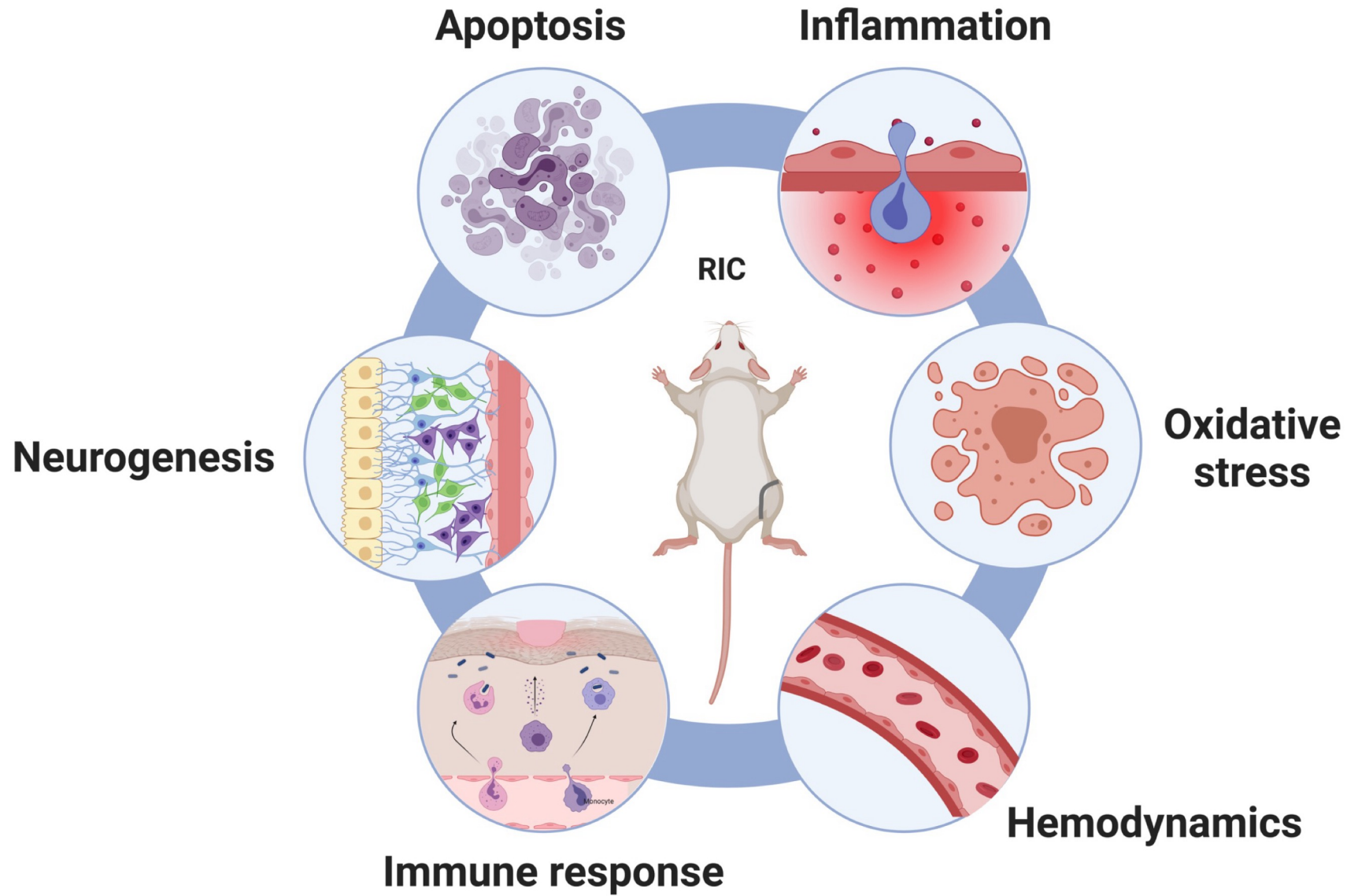


RIC protocol

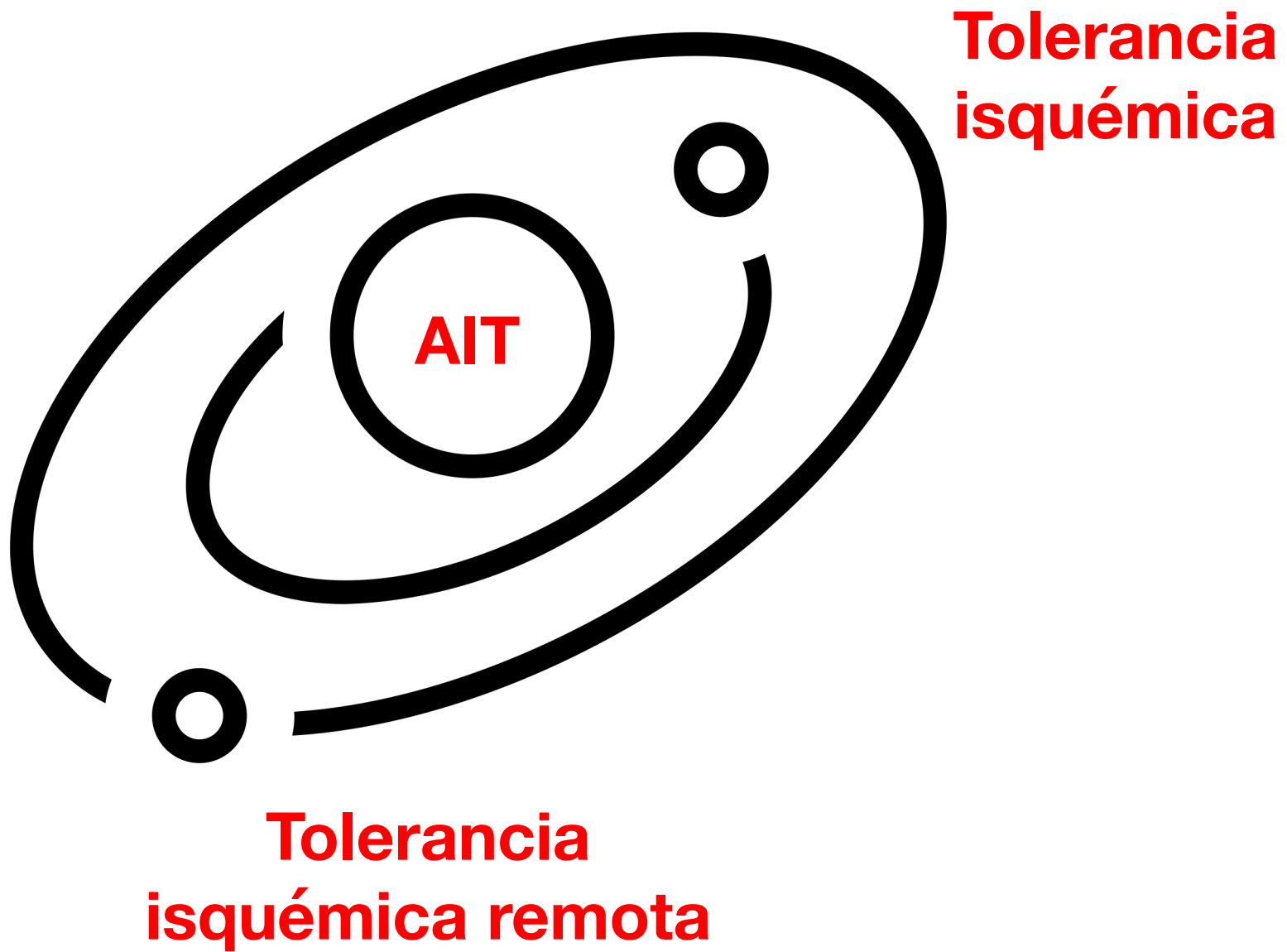














2026





# 2026 REPERFUSION GUIDELINES FOR ACUTE ISCHEMIC STROKE

Summary of 2026 AHA/ASA indications for intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT), including Tenecteplase, expanded windows, and pediatric protocols.

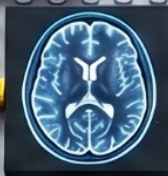
## INTRAVENOUS THROMBOLYSIS (IVT)



**4.5-HOUR WINDOW**



**4.5-9 HOURS**



### EXTENDED WINDOW THROMBOLYSIS

Recommended for select patients with unknown onset using advanced imaging mismatch criteria

### PEDIATRIC IVT CONSIDERATIONS

May be considered for children (28 days to 18 years) with disabling

### PREFERRED AGENTS

**Tenecteplase**  
(0.25 mg/kg bolus)

endorsed alongside Alteplase for adult patients

## ENDOVASCULAR THROMBECTOMY (EVT)



**0-6 HOURS**

### STANDARD WINDOW

Recommended for anterior LVO (ICA/M1) with NIHSS  $\geq 6$  and ASPECTS 3-10



**6-24 HOURS**

### EXPANDED LATE WINDOW

Indicated for LVO patients with salvageable tissue or ASPECTS  $\geq 6$  on advanced imaging

### PEDIATRIC EVT ELIGIBILITY

Effective for children  $\geq 6$  years with LVO and salvageable tissue up to 24 hours.

## QUICK-REFERENCE SELECTION CRITERIA (ADULT ANTERIOR LVO)

| WINDOW     | NIHSS SCORE | ASPECTS  | RECOMMENDATION                  |
|------------|-------------|----------|---------------------------------|
| 0-6 Hours  | $\geq 6$    | 3-10     | COR 1<br>(Strongly Recommended) |
| 6-24 Hours | $\geq 6$    | $\geq 6$ | COR 1<br>(Strongly Recommended) |
| 6-24 Hours | $\geq 6$    | 3-5      | COR 1<br>(In Selected Patients) |

**ASPECTS BRAIN MAP**





**Post-REMOTE**

**Convince 2**

**SMS-p**

**2026**





**Post-REMOTE**

**Convince 2**

**SMS-p**

**2026**

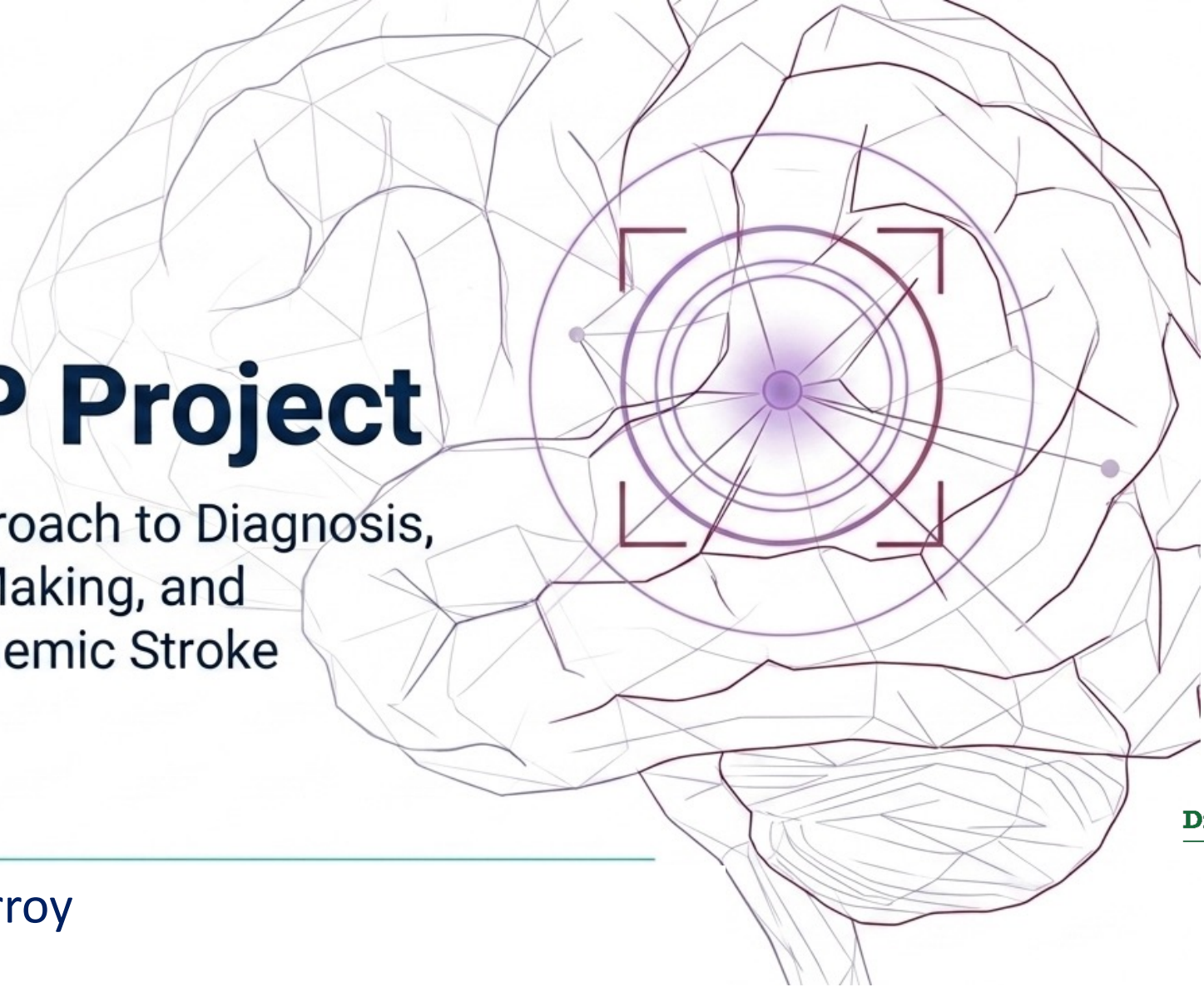


# The SMS-P Project

A Multidisciplinary Approach to Diagnosis,  
Therapeutic Decision-Making, and  
Prognosis in Minor Ischemic Stroke

---

M. Gómez-Choco & F. Purroy



**Diputació de Lleida**

La força dels municipis



# The Minor Stroke Misconception

## The Perception



**25–50%**

of all acute ischemic strokes  
NIHSS 0–5 (Minor Symptoms)

[1] Author et al., Journal. Year;Vol:Pages.

## The Reality



**30%** functional disability  
or death at 90 days

**10–20%** early neurological  
deterioration

[2] Author et al., Journal. Year;Vol:Pages.

**A mild clinical presentation does not  
guarantee a benign outcome.**



# MANAGING THE “NOT-SO-MINOR” STROKE: CLINICAL GUIDANCE FOR NIHSS $\leq 5$

## PHASE 1: ASSESSMENT & DEFINITION



**DEFINITION:** Mild deficits but require careful screening for subtle functional impairments.

**The 30% Disability Risk**  
Up to one-third of MIS patients develop functional disability within 90 days if undertreated.

**NIHSS SCORE  $\leq 5$**

### DISABLING



Deficits like aphasia or hemianopia are “disabling” regardless of a low score.

### NONDISABLING



Isolated sensory loss is usually “non-disabling”.

## PHASE 2: ACUTE TREATMENT PATHWAYS



### DISABLING? Use Thrombolysis.

For disabling symptoms within 4.5 hours, Intravenous Thrombolysis (Tenecteplase preferred) is the standard of care.



### SUPPORTING FACT: THE LVO UNCERTAINTY

If Large Vessel Occlusion is present, the benefit of Endovascular Thrombectomy is still being studied; consider enrollment in clinical trials.

### NONDISABLING? Use DAPT.

For non-disabling, non-cardioembolic cases, Dual Antiplatelet Therapy (Aspirin + Clopidogrel/ Ticagrelor) is superior to thrombolysis.



### RECOMMENDED DRUG REGIMENS

| STROKE TYPE       | RECOMMENDED FIRST-LINE THERAPY                    |
|-------------------|---------------------------------------------------|
| Non-cardioembolic | 21 Days of BAPT (Aspirin + P2Y12 inhibitor)       |
| Cardioembolic     | Early Anticoagulation (initiated within 48 hours) |



# Beyond the Number: The Evaluation of Disability

## The Quantitative Criterion



### NIHSS Score $\leq 5$

It is the most accepted quantitative threshold in clinical trials, although some protocols require  $\leq 3$  or 0 points in the level of consciousness item.

## The Qualitative Criterion (Crucial)



### NON-DISABLING

Deficits that do not prevent basic activities.

**Examples:** Isolated sensory loss, mild central facial paresis.

*\*Definition based on expert consensus and clinical guidelines.\**



### DISABLING

Deficits that, if unresolved, impact autonomy or return to work.

**Examples:** Aphasia, hemianopsia, mild weakness in extremities, gait ataxia.

*\*Definition based on expert consensus and clinical guidelines.\**

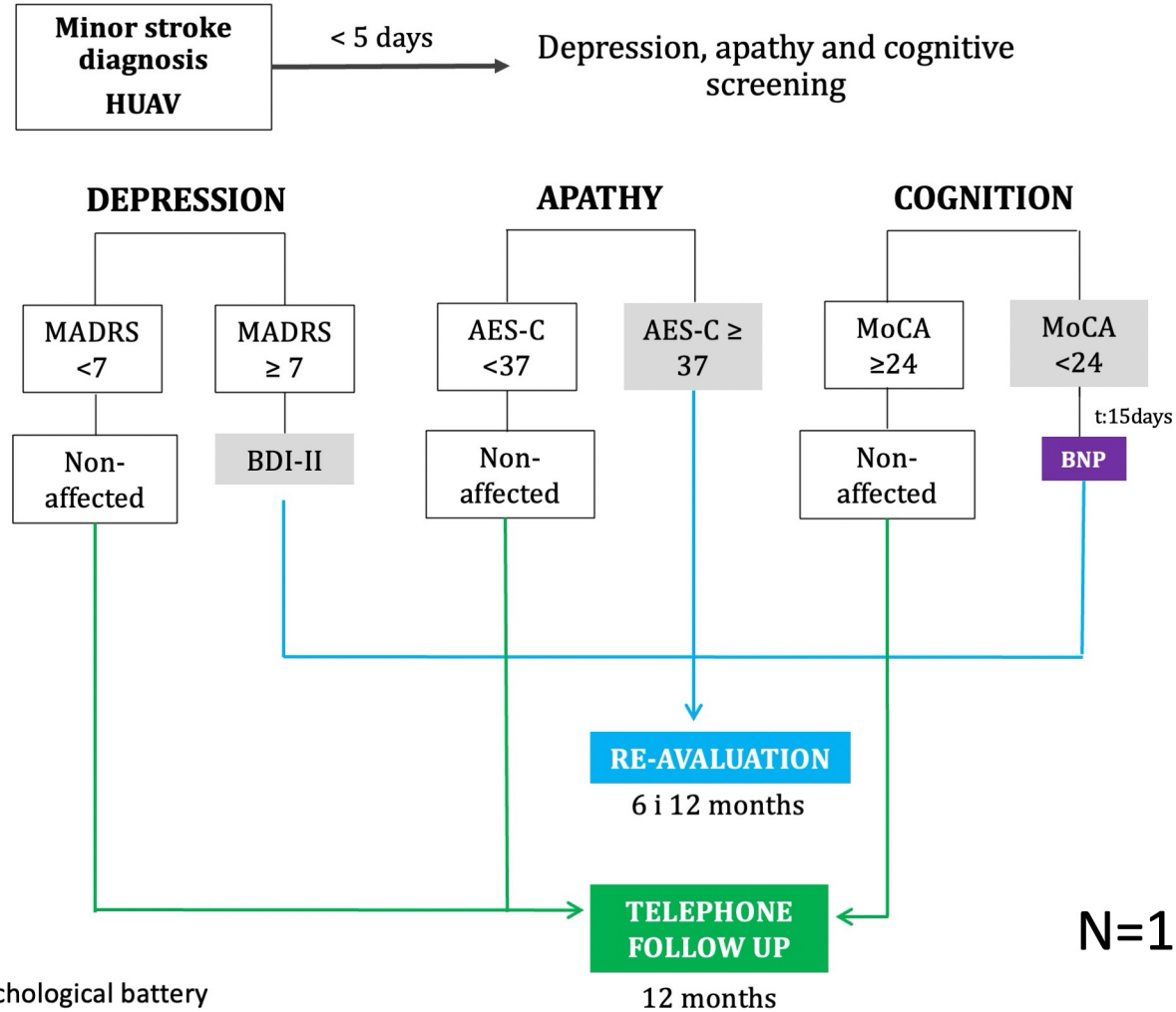


# Evidence in Acute Phase: Intravenous Thrombolysis (IVT)

| Trial   | Intervention              | Patient Profile      | Study Details (N, NIHSS, Window, Endpoint) | Clinical Verdict                                                                  |
|---------|---------------------------|----------------------|--------------------------------------------|-----------------------------------------------------------------------------------|
| PRISMS  | Alteplase vs. Aspirin     | Non-Disabling        | N=313, NIHSS≤5, <3h, mRS 0-1               | No functional benefit, higher risk of symptomatic intracranial hemorrhage (sICH). |
| ARAMIS  | Alteplase vs. DAPT        | Non-Disabling        | N=760, NIHSS≤5, <4.5h, mRS 0-1             | DAPT (Clopidogrel+Aspirin) showed non-inferiority and a safer profile.            |
| TEMPO-2 | Tenecteplase vs. Standard | With Occlusion (LVO) | N=888, NIHSS≤5, <12h, mRS 0-1              | No functional benefit, increased mortality and bleeding.                          |
| PUMICE  | Prourokinase vs. Standard | MIS General          | N=400, NIHSS≤5, <9h, mRS 0-1               | Trial stopped prematurely for futility.                                           |

**Clinical Conclusion:** IVT is not recommended routinely in non-disabling deficits. DAPT is the current standard.

# PSICO ICTUS



\*BNP: neuropsychological battery

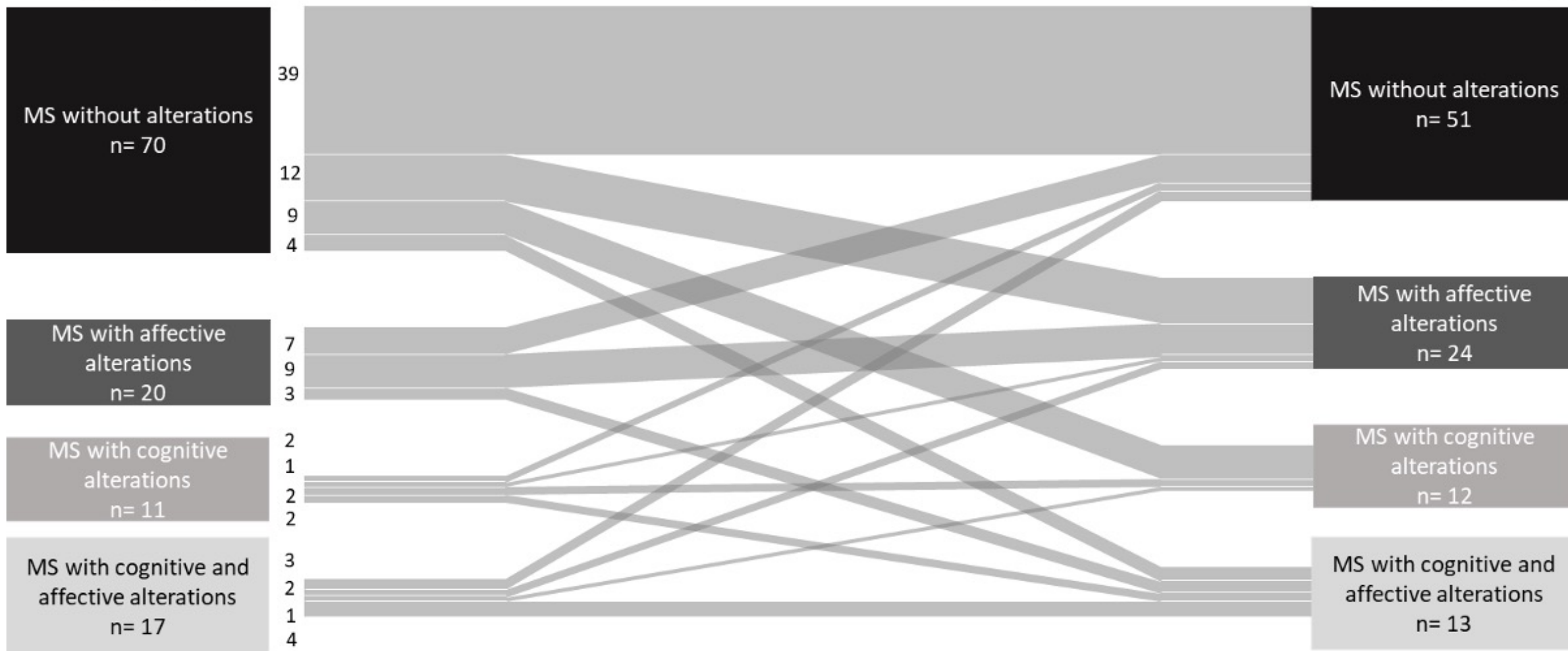
N=118



Cristina Pereira

Baseline

12 months follow-up



Tesis Cristina Pereira



# The Radiological Lens: Multiparametric CT

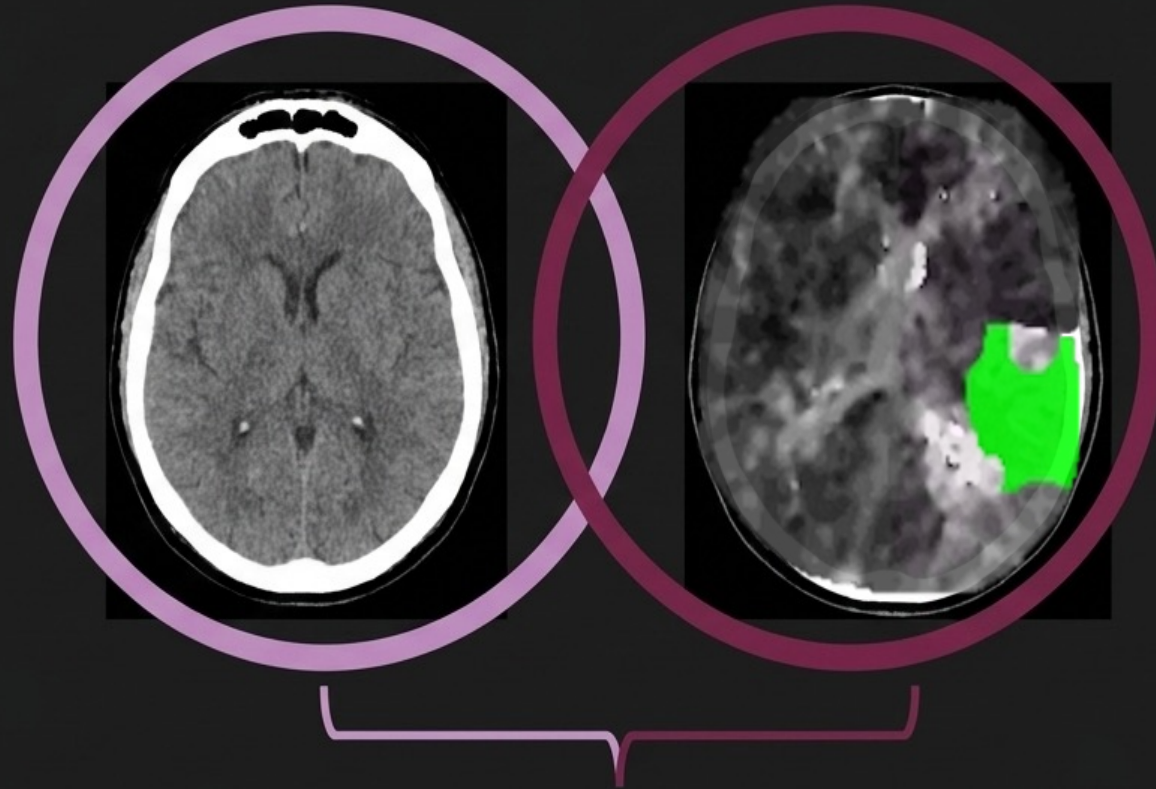
**Intervention:** Systematic application upon hospital arrival

Standard NCCT  
Advanced CTP / CTA

## Key Targets:

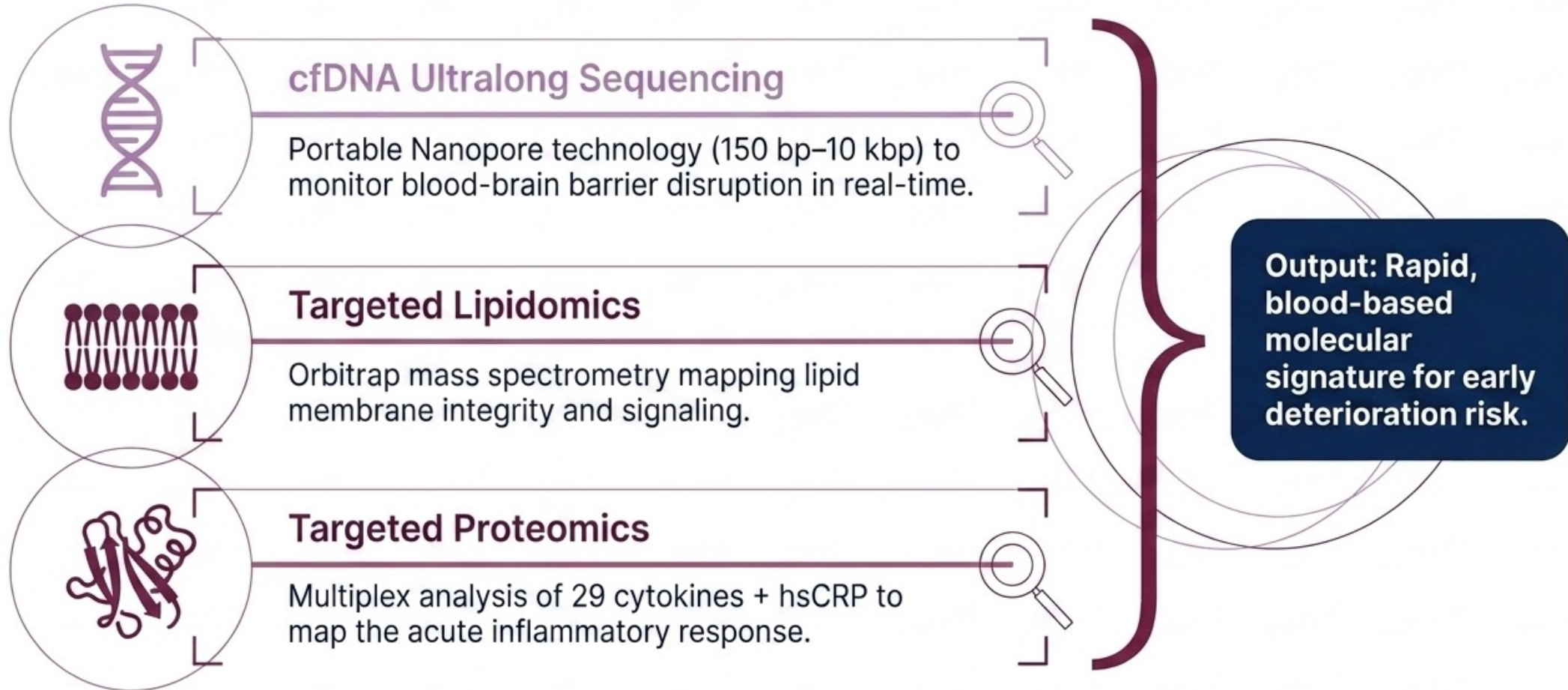
- **Perfusion Deficits (CTP+):**  
Tmax >6s, CBF <30%
- **Large Vessel Occlusions (CTA+):**  
Arterial blockage mapping

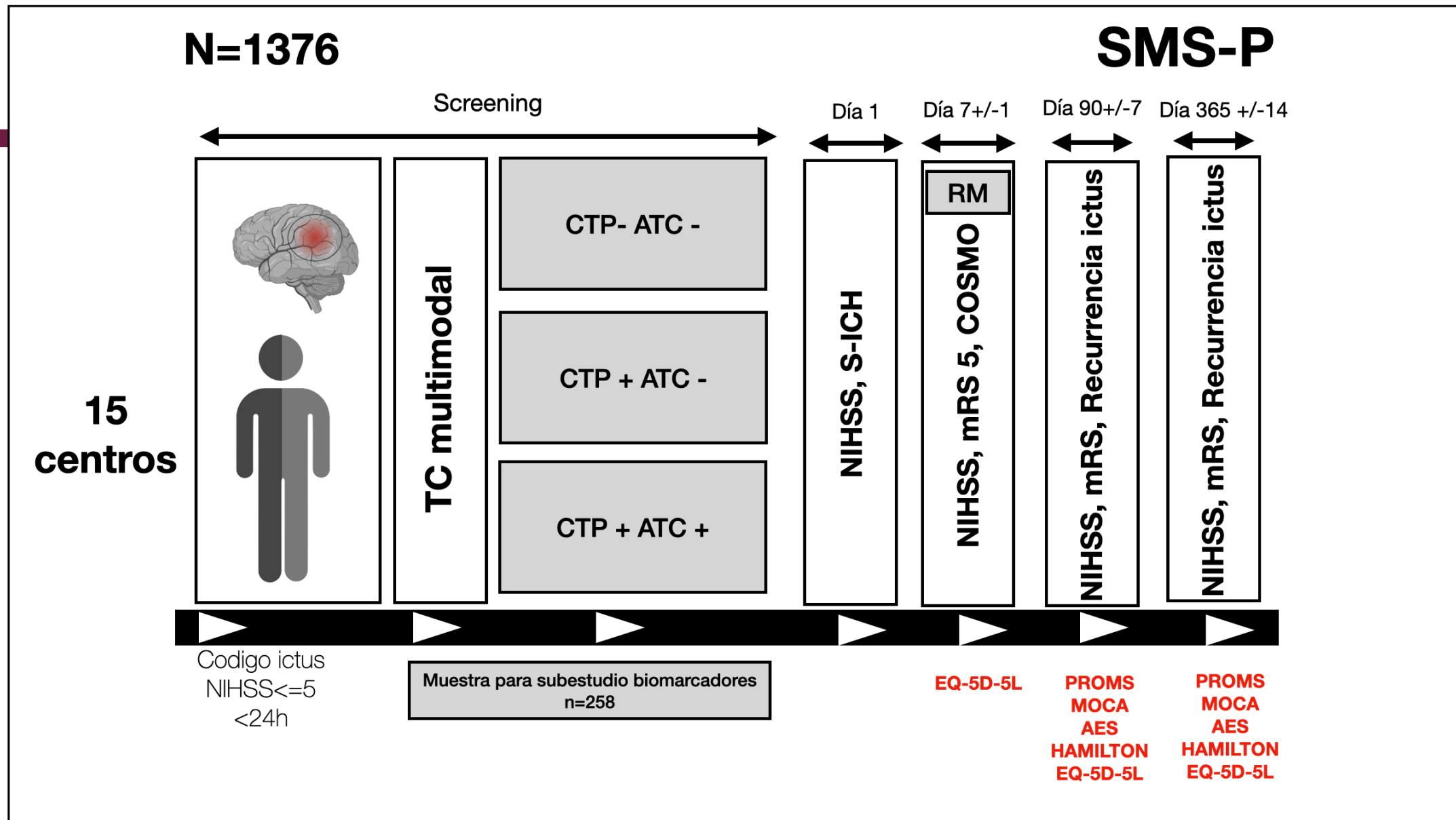
**The Goal:** Establish reliable cut-off values for acute therapeutic decision-making and correlate with 90-day recurrence risk.



Hidden Perfusion Deficit Highlighted

# The Molecular Lens: Real-Time Multi-Omics

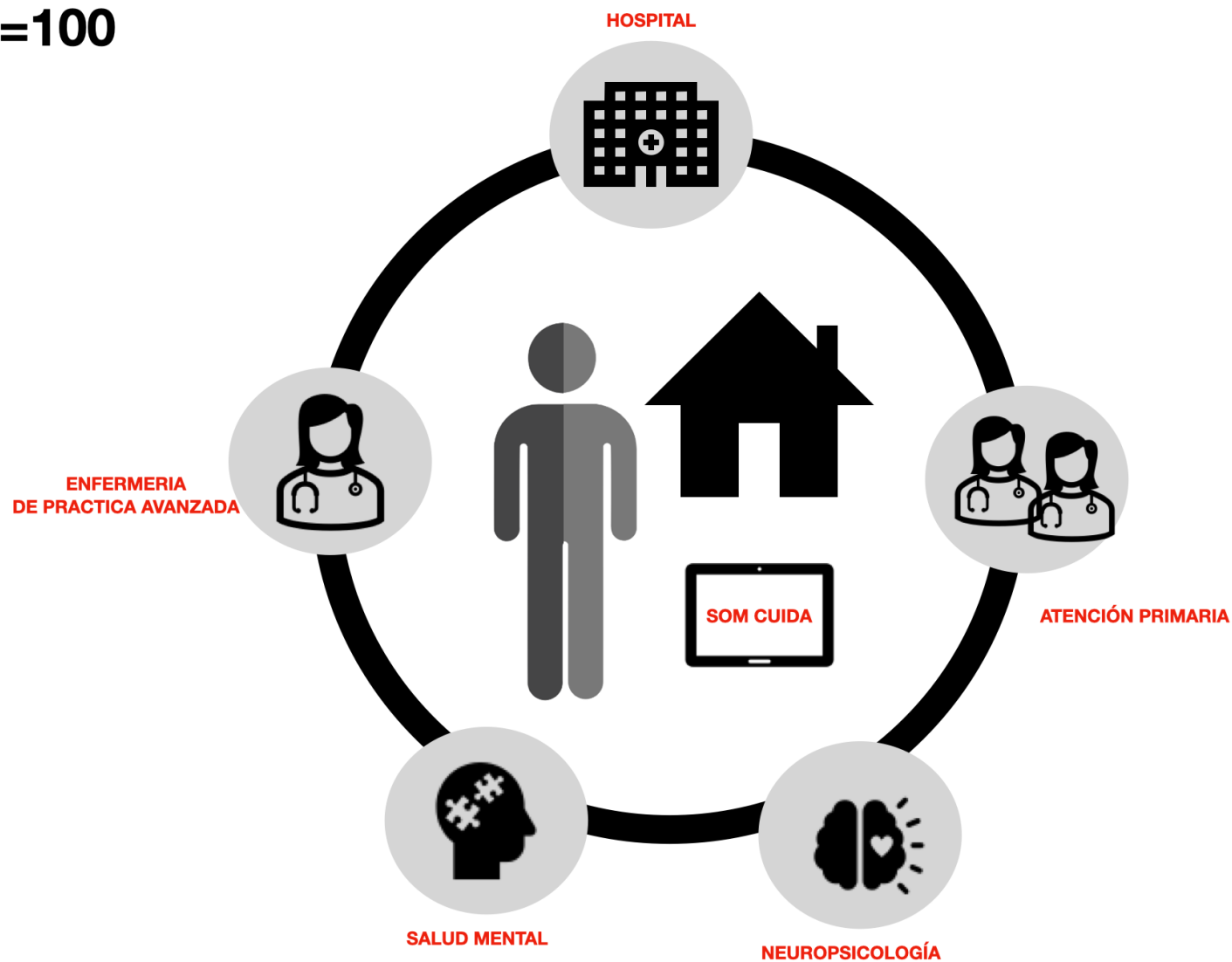






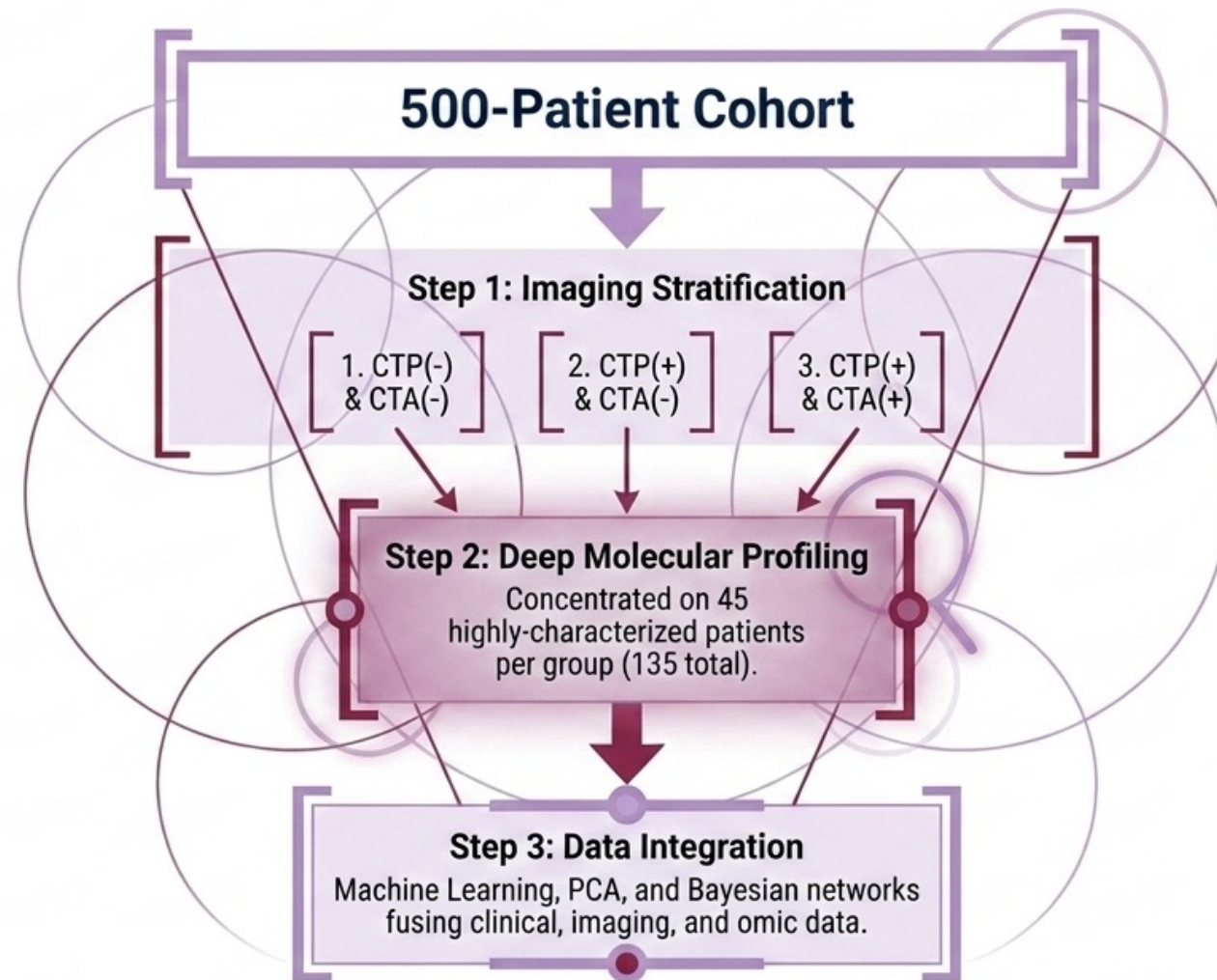


N=100

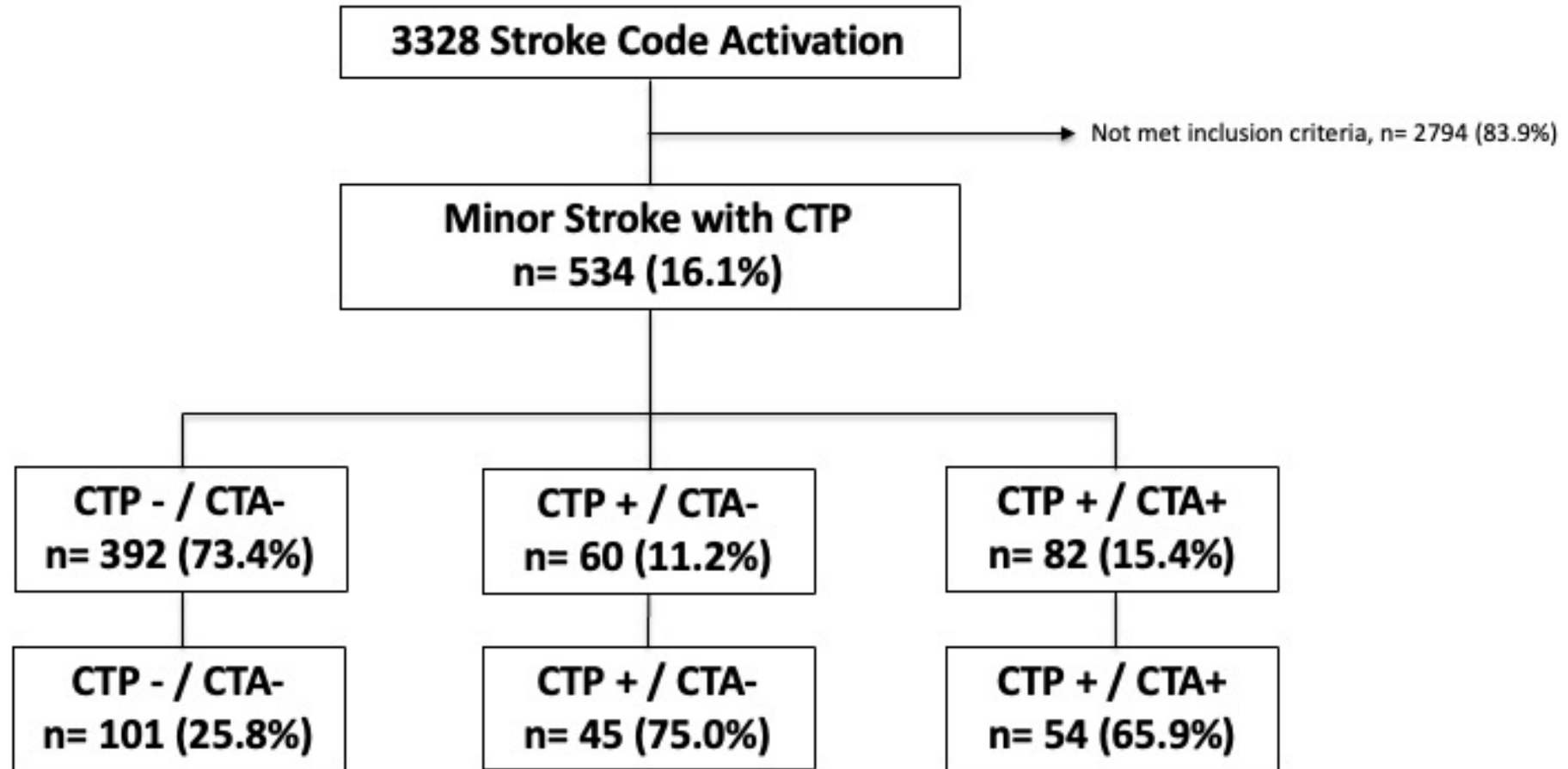




# The Discovery Engine: Targeted Resource Optimization



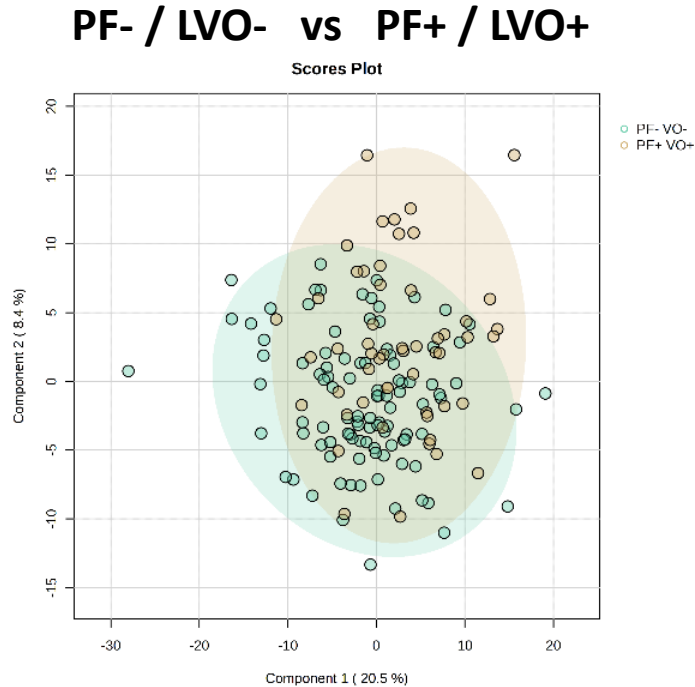




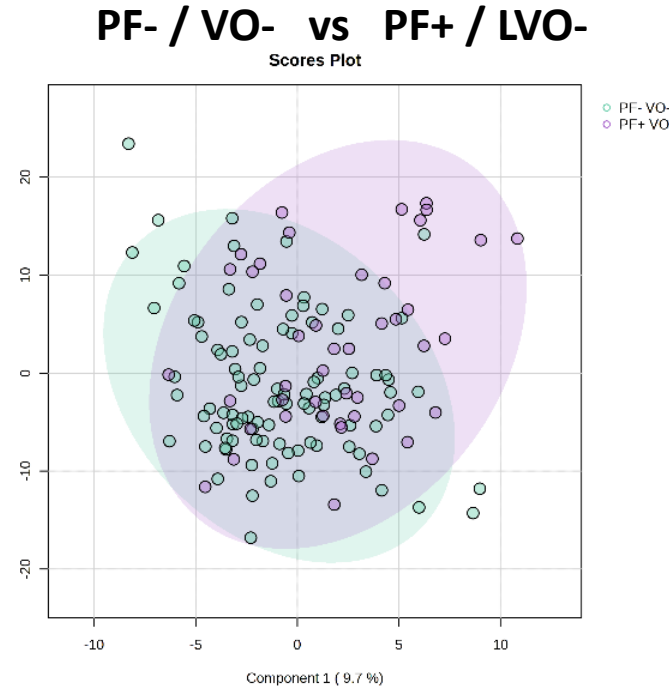
## Targeted Lipidomics - 3 groups analysis

n = 200

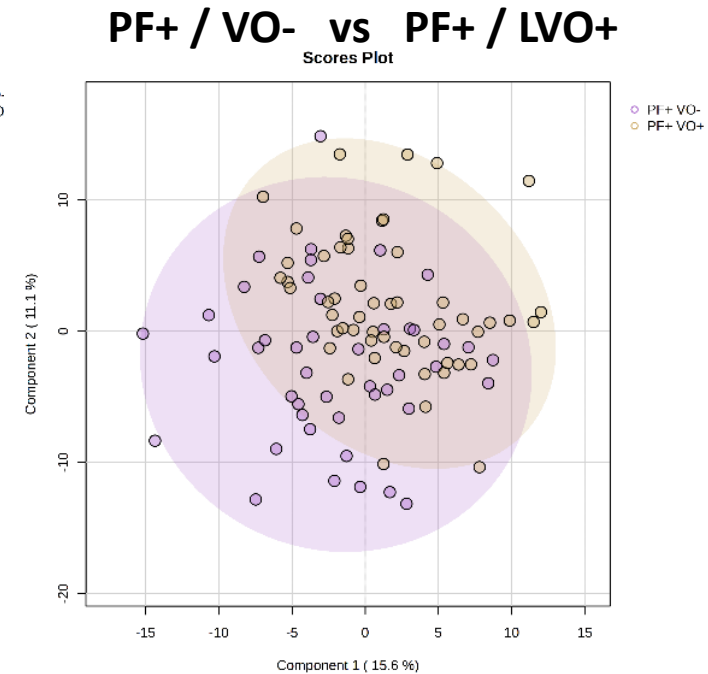
- (0) PF- / LVO-
- (1) PF+ / LVO-
- (2) PF+ / LVO+



**27 significant lipids**



**10 significant lipids**



**5 significant lipids**

**Significant lipids**  
(non parametric raw p.value)

# Scaling for Validation: The RICORS-ICTUS Network

## The Network

8 Comprehensive Stroke Centers across Spain.

## The Target

814 independent validation patients.

## Quality Control

- Centralized REDCap eCRF
- Rigorous remote & on-site monitoring
- Standardized PROMs at 90 & 365 days

**The Value:** Ensures external validity and eliminates single-center selection bias.





# Transforming the Future of Minor Stroke Care



## For the Patient

Personalized acute therapy to prevent permanent disability before deterioration occurs.



## For the Science

First integration of ultra-fast Nanopore cfDNA sequencing with multiparametric neuroimaging in acute stroke.



## For the System

Providing clinical evidence to definitively update International Stroke Guidelines on reperfusion.

Thank you to the Foundation for enabling this paradigm shift in stroke neurology.



**Post-REMOTE**

**Convince 2**

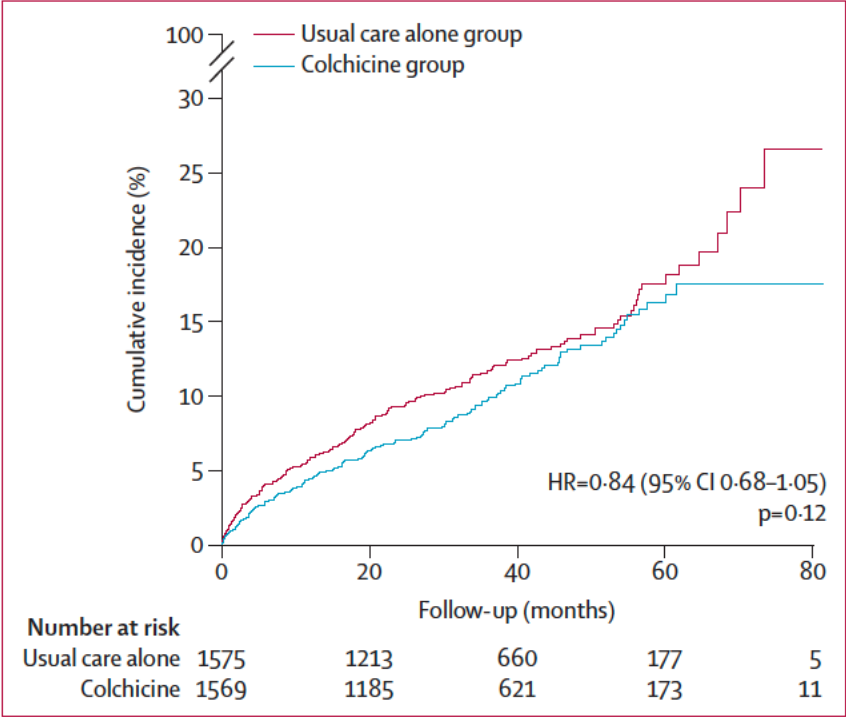
**SMS-p**

**2026**



# Long-term colchicine for the prevention of vascular recurrent events in non-cardioembolic stroke (CONVINCE): a randomised controlled trial

Peter Kelly, Robin Lemmens, Christian Weimar, Cathal Walsh, Francisco Purroy, Mark Barber, Ronan Collins, Simon Cronin, Anna Czlonkowska, Philippe Desfontaines, Adinda De Pauw, Nicholas Richard Evans, Urs Fischer, Catarina Fonseca, John Forbes, Michael D Hill, Dalius Jatuzis, Janika Kõrv, Peter Kraft, Christina Kruuse, Catherine Lynch, Dominick McCabe, Robert Mikulik, Sean Murphy, Paul Nederkoorn, Martin O'Donnell, Peter Sandercock, Bernadette Schroeder, Gek Shim, Katrina Tobin, David J Williams, Christopher Price





# CONVINCE<sup>2P</sup>-BIOSPAIN

Colchicine for Vascular Ischemic Event Prevention  
in Plaque-Positive Non-cardioembolic Stroke/TIA



## STUDY OVERVIEW



**25** centres in Spain



**640** patients expected



Mechanistic study



Multicentre randomised trial



Health economic analysis

Study of the impact on



MACE



PROMS



Quality of life



MOCA

## PARTICIPANT SELECTION



Non-cardioembolic  
Ischaemic Stroke / TIA

Randomisation 1:1



1:1

0.5 mg/day



Atherosclerotic  
plaque present



## OUTCOMES



Blood  
Sample  
Collection



Biomarkers

Known & Novel

Proteomics

Pharmacogenomics



Atherosclerotic Plaque Evolution



Carotid  
Ultrasound



# CONVINCE2p-BIOSPAIN: Building a New Defense Against Stroke Recurrence

## The Challenge: Protecting Stroke Survivors



**The Reality of Residual Risk**  
Many stroke survivors remain at high risk for a second event due to persistent arterial inflammation despite standard treatment.

# 1 in 5

### Patients at Risk

Approx. 20% may experience another major vascular event within five years.



**The Role of "Plaque"**  
Atherosclerosis creates inflamed plaques; rupture causes stroke-causing clots.

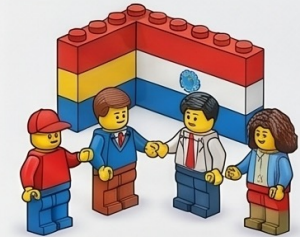
## The Intervention: Low-Dose Colchicine



**A Familiar Tool for a New Job**  
Affordable gout drug repurposed to stabilize arterial plaques.



**Simple Daily Defense**  
One low-dose (0.5 mg) tablet daily on top of standard treatments.



**Global Scientific Collaboration**  
Spain leads part of a 15-country platform evaluating colchicine.

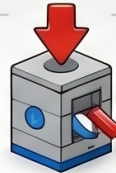
## The Clinical Journey (Methodology)



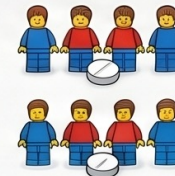
**Step 1: 1-Month Run-In**  
All participants take colchicine for one month to ensure tolerance.

# 640

Spanish participants

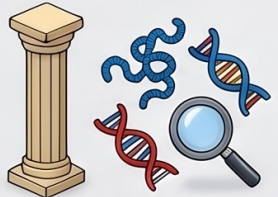


**Step 2: Randomization**  
Randomly assigned 1:1 to colchicine or placebo to prove effectiveness.



**Step 3: Long-term Monitoring**  
Patients followed every 8 months for at least two years to track health, safety, and quality of life.

## The 5 Pillars of BIOSPAIN Research



### Biological Defense

Using Olink proteomics to analyze over 1,000 blood proteins for inflammation reduction.



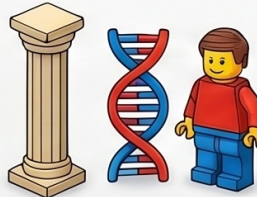
### Advanced Plaque Imaging

Annual ultrasounds track colchicine's effect on careful plaque growth or vulnerability.



### Economic Value

Calculating cost-savings for the Spanish healthcare system by preventing long-term disability.



### Genetic Susceptibility

Exploring individual DNA's effect on colchicine response for personalized medicine.



### Focus on Equity

Analyzing results for women, the elderly, and rural vs. metropolitan areas for equal benefit.

## Social Impact & Patient Involvement



### Patient-Centered Design

Patient associations involved in creating accessible information and sharing results.



### Beyond Survival: Quality of Life

Measuring memory, mobility, and independent living ability, not just survival.

NotebookLM

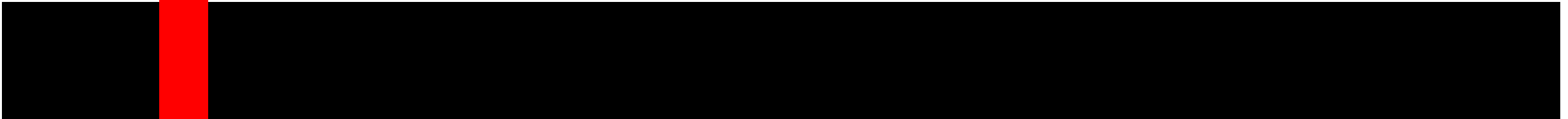
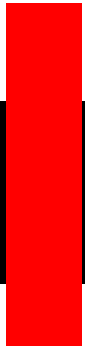
# Post-REMOTE



**Convince 2**

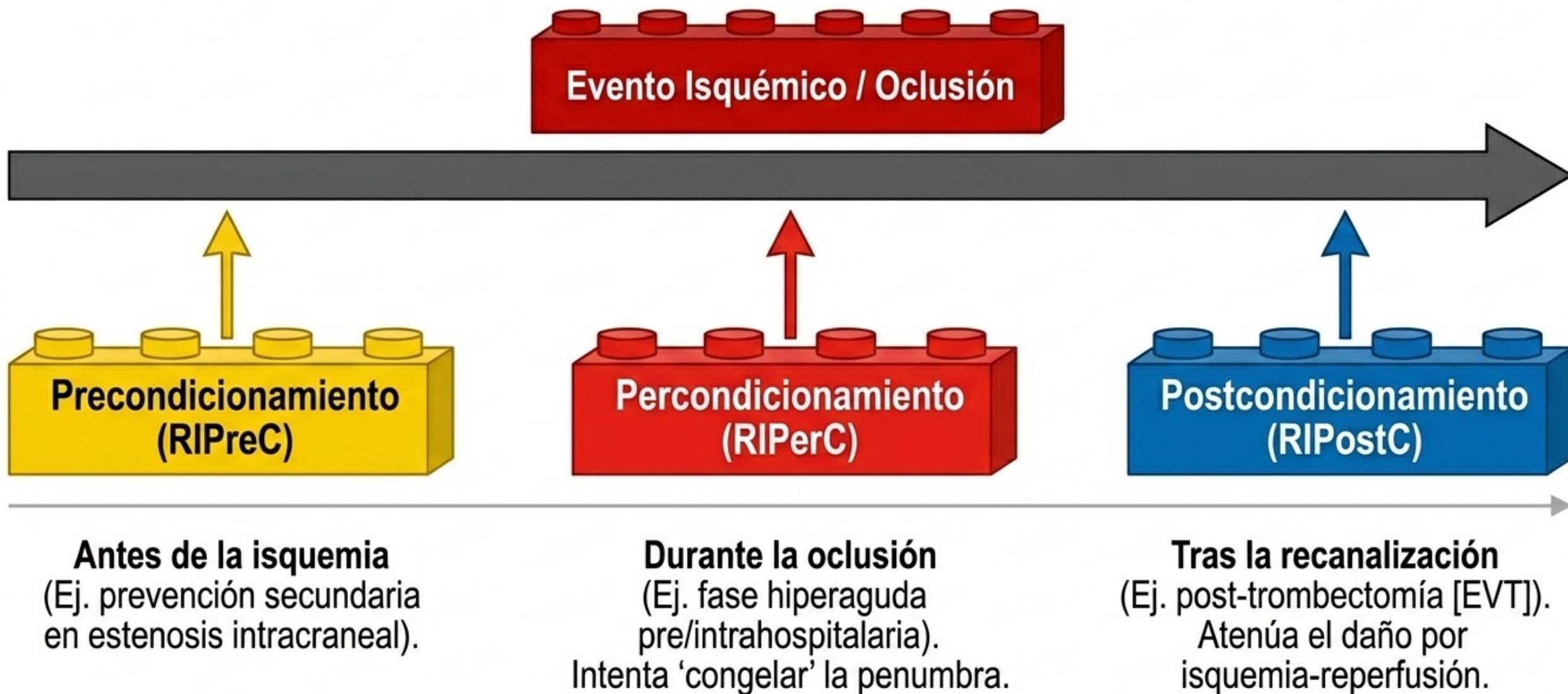
**SMS-p**

**2026**

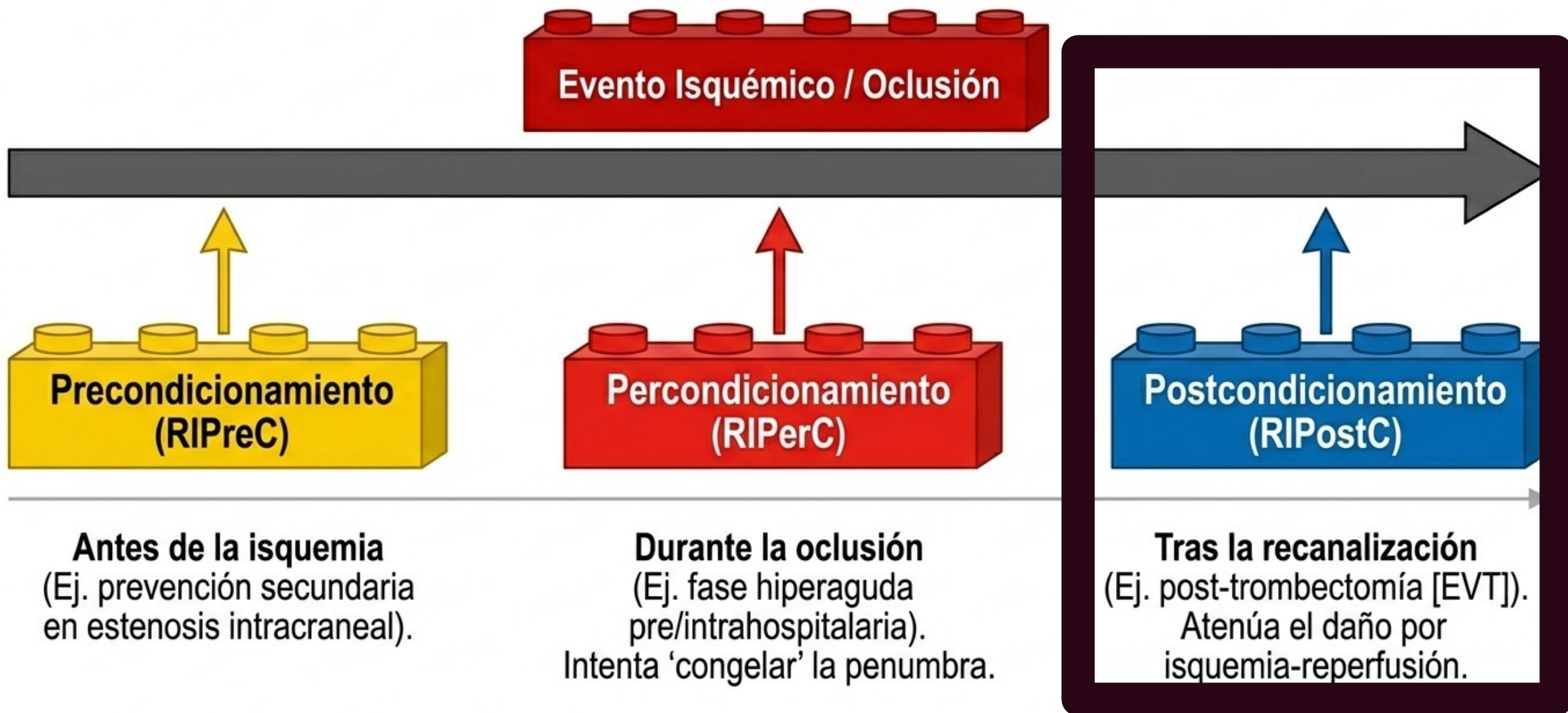




# La arquitectura temporal del RIC



# La arquitectura temporal del RIC





# RIC: A Remote Shield for the Ischaemic Brain

## THE RIC PROTOCOL (THE "TREATMENT")

### 3 CYCLES OF PROTECTION



**5 MIN**  
ISCHAEMIA  
(OCCLUSION)



**5 MIN**  
REPERFUSION  
(BLOOD FLOW)

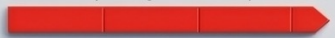


**5 MIN**  
REPERFUSION  
(BLOOD FLOW)



### RIPerC vs. RIPOstC

RIPerC (During Ischaemia)



RIPOstC (10 min after Reperfusion)



### AVOID COMBINATION THERAPY

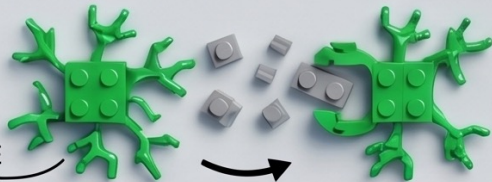


Increased brain damage by ~33%

## THE MICROGLIAL MECHANISM

### MICROGLIAL PHAGOCYTOSIS

PROTECTIVE  
MICROGLIA  
SURVEILLANCE  
PHENOTYPE



INCREASED  
CD68+ ACTIVITY  
clears cellular  
debris

### MORPHOLOGICAL SHIFT



AMEBOID



HYPER-RAMIFIED  
PROTECTIVE

### MICROGLIA-INDEPENDENT BACKUP



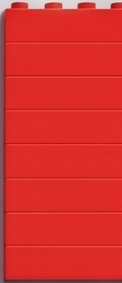
RIC REMAINS  
PROTECTIVE even with  
71% microglia depletion  
(PLX3367 diet)



## IMPACT ON BRAIN DAMAGE & RECOVERY

### FEMALE INFARCT REDUCTION

6.69%



STROKE  
(CONTROL)

**55%**  
REDUCTION



2.95%

RIC

### MALE INFARCT REDUCTION

6.31%



STROKE  
(CONTROL)

**36%**  
REDUCTION



4.00%

RIC

### IMPROVED MOTOR COORDINATION



Strong positive correlation with reduced brain damage

## FUELING NEUROREPAIR

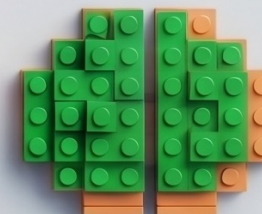
### 100% INCREASE IN NEUROBLASTS

UNTREATED STROKE



DCX+  
IMMATURE  
NEURONS

RIC TREATED



Doubled DCX+ neuroblasts in infarct core & subventricular zone

### ENHANCED CELL PROLIFERATION



Ki67+  
CELL BIRTH

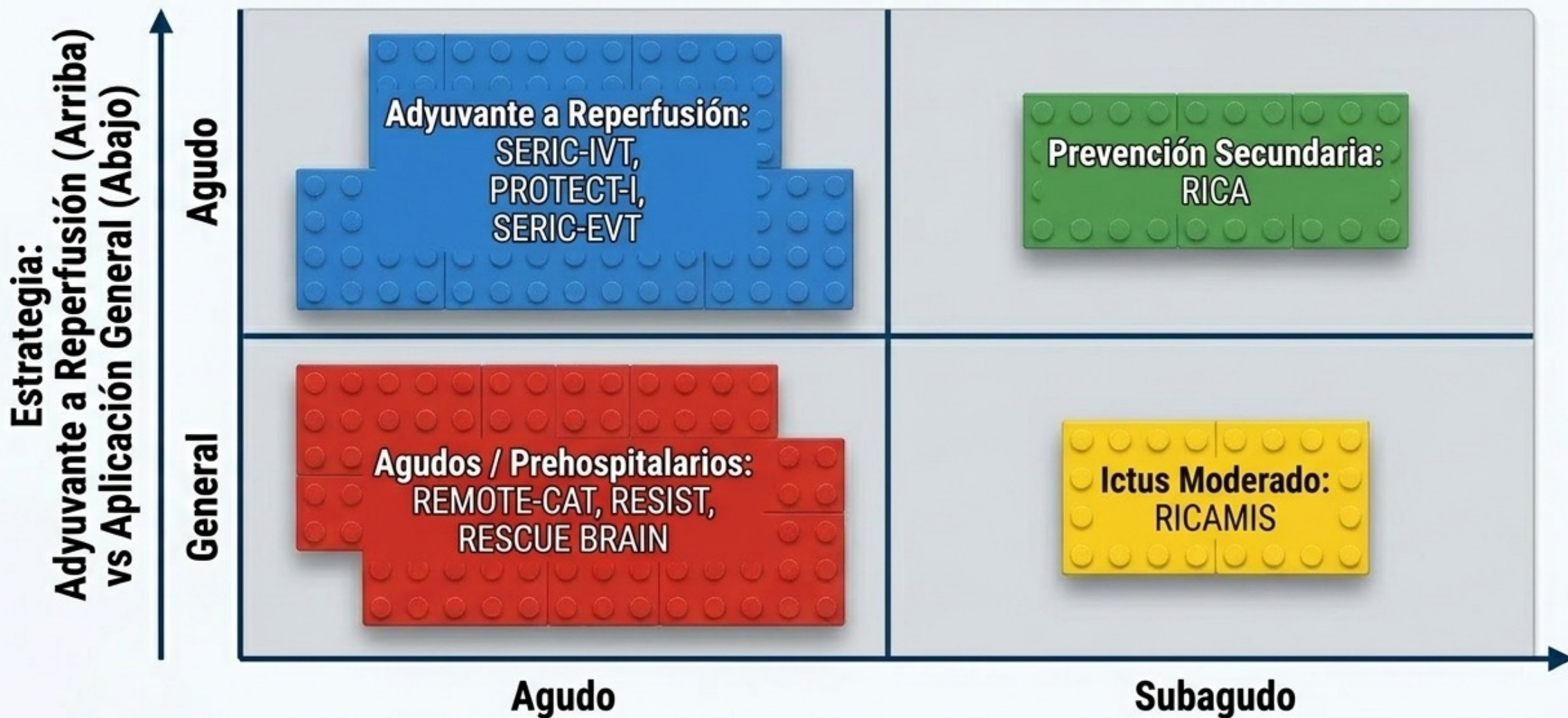
BOOSTED Ki67+ CELL COUNTS  
in hippocampus and subventricular zone

RIC-specific cytoprotective profile mediated by microglia in a mouse model of acute ischaemic stroke.

C. Torres-Querol, G. Arque and F. Purroy Stroke Vasc Neurol 2025



# El paisaje de la evidencia clínica: Mapeo de los grandes ensayos

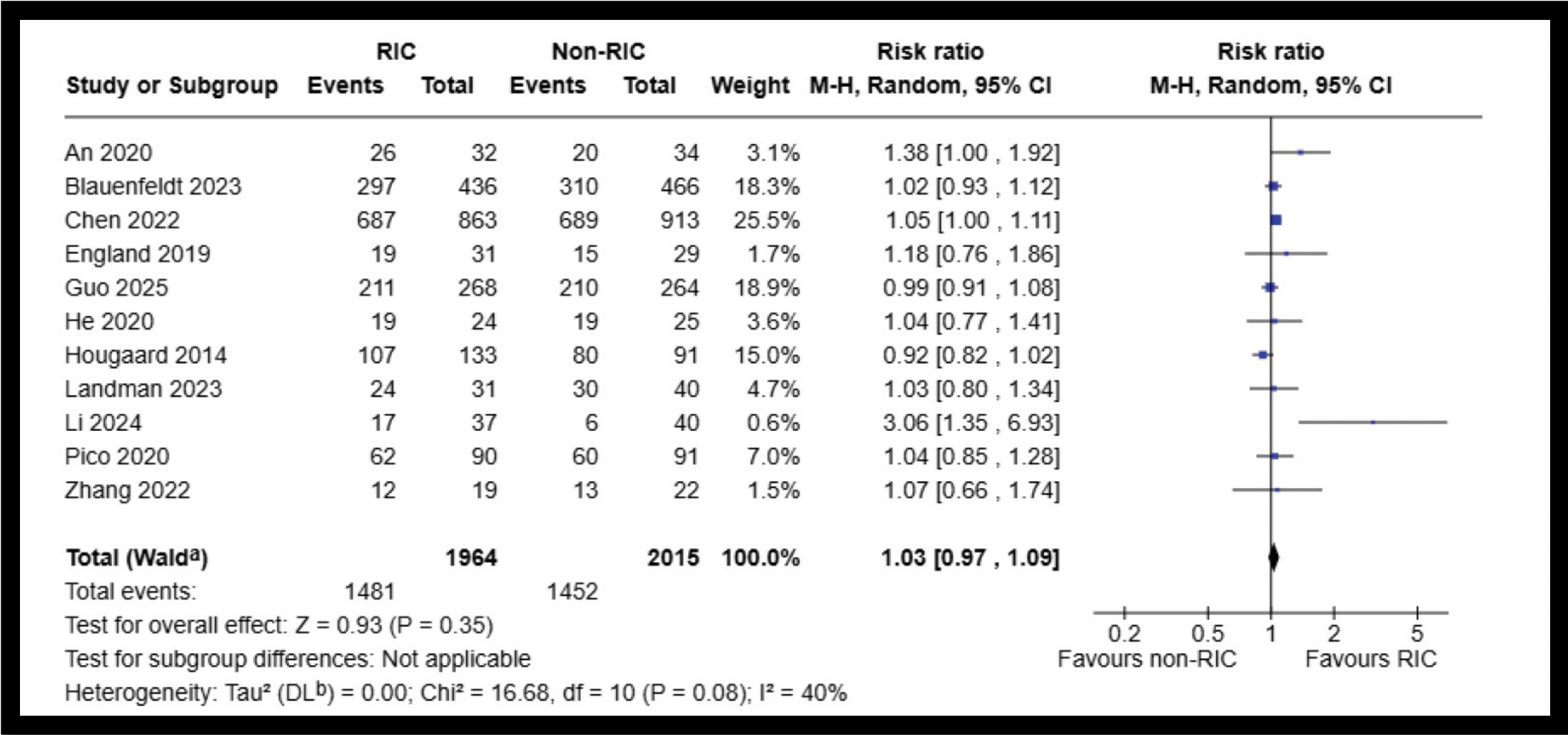


**Ventana Terapéutica:** Prehospitalario → Hospitalario → Crónico

# Análisis de los grandes ensayos en fase hiperaguda

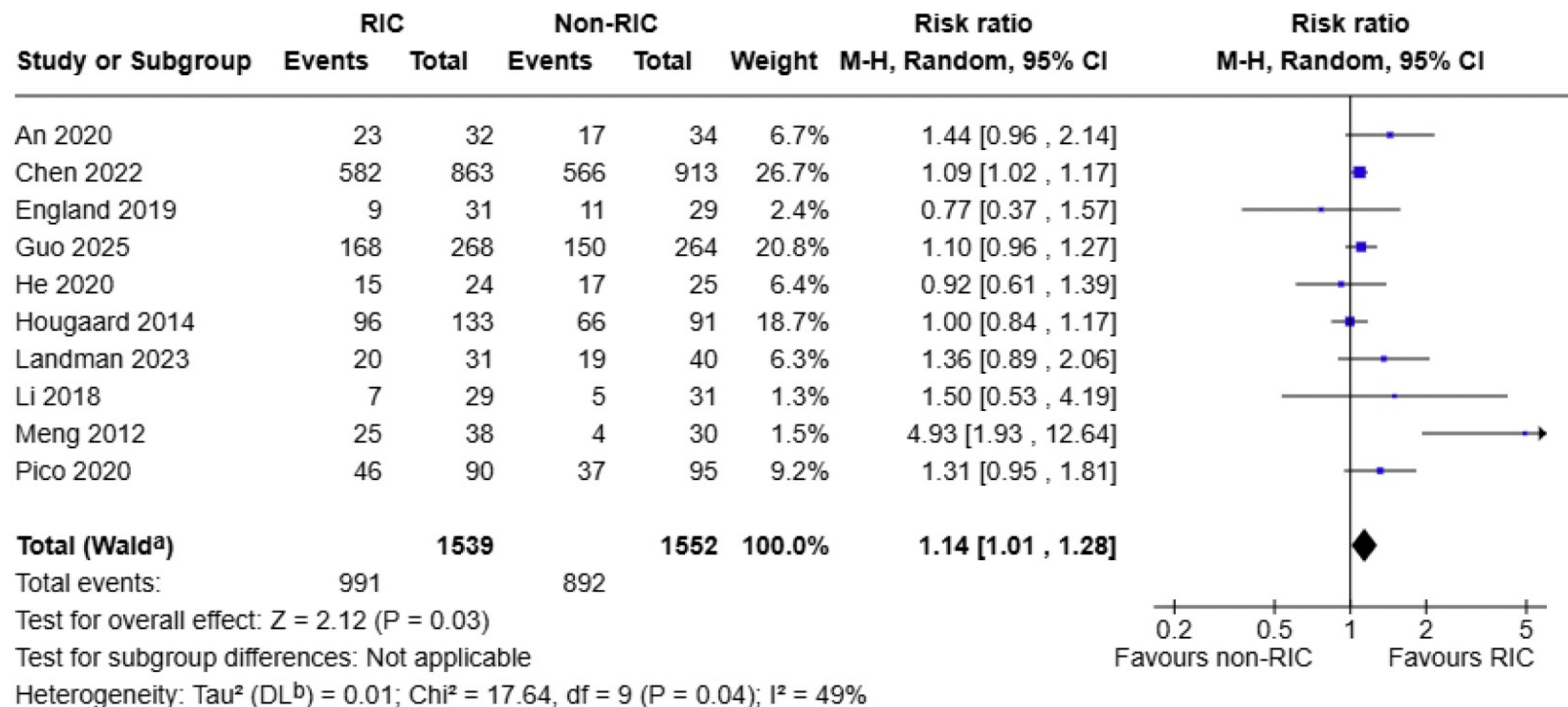
| Parámetro            | REMOTE-CAT (2025)             | RESIST (2023)                  | RESCUE BRAIN (2020)                  |
|----------------------|-------------------------------|--------------------------------|--------------------------------------|
| Escenario            | Prehospitalario (<8h)         | Prehospitalario (<4h)          | Intrahospitalario                    |
| Criterios            | LVO y no-LVO (RACE $\geq 1$ ) | Sospecha de ictus              | RM confirmada                        |
| N incluido           | 122                           | 1500                           | 188                                  |
| Protocolo RIC        | 5 ciclos 5x5                  | 5 ciclos 5x5                   | 4 ciclos 5x5                         |
| Endpoint y Resultado | mRS 0-2 a 90d<br>P=0,057      | mRS ordinal a 90d<br>⚠ NEUTRAL | Crecimiento del infarto<br>⚠ NEUTRAL |

Forest plot of functional independence (mRS 0–2) at 90 days.

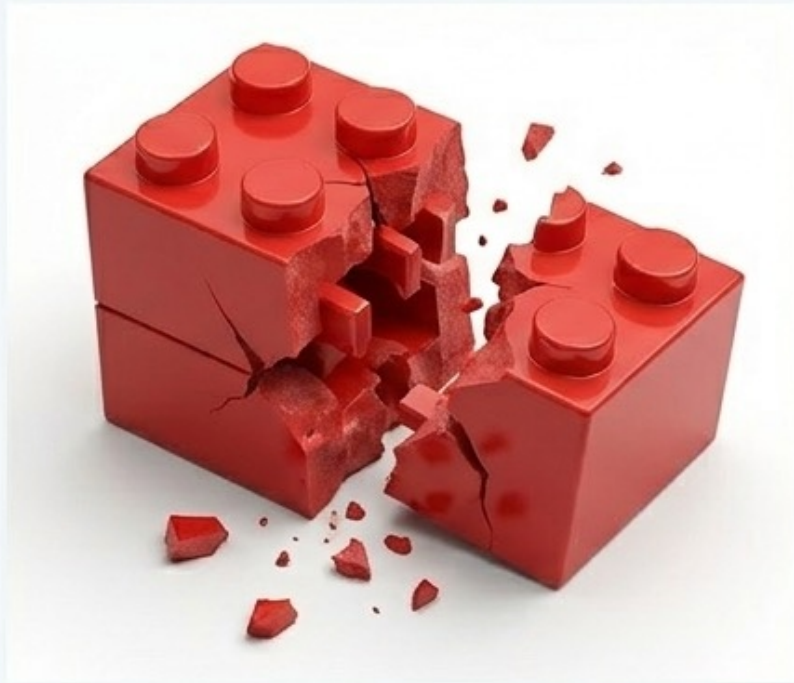




**Figure 6. Forest plot of excellent functional outcome (mRS 0–1) at 90 days.**



# Autopsia de los resultados neutrales: ¿Falló la biología o el diseño?



## Dilución del efecto

Inclusión masiva de ictus menores, AITs o stroke mimics (ej. RESIST). El RIC no tiene margen para demostrar beneficio clínico (efecto techo) en tejido que ya está a salvo.



## Falta de perfusión anatómica

El percondicionamiento puede "congelar" la penumbra isquémica, pero sin recanalización final (apertura del vaso), la necrosis tisular termina ocurriendo inevitablemente.



## Fisiopatología heterogénea

El mecanismo de rescate necesario en un infarto lacunar difiere enormemente del requerido en una oclusión proximal (LVO). El enfoque de "talla única" fracasa.



# El rompecabezas metodológico del RIC: Ruido estadístico

## Timing

Mezcla de RPerC (salvar penumbra) frente a RPostC (prevenir daño por isquemia/reperfusión).  
Ventanas biológicas opuestas.

## Protocolos

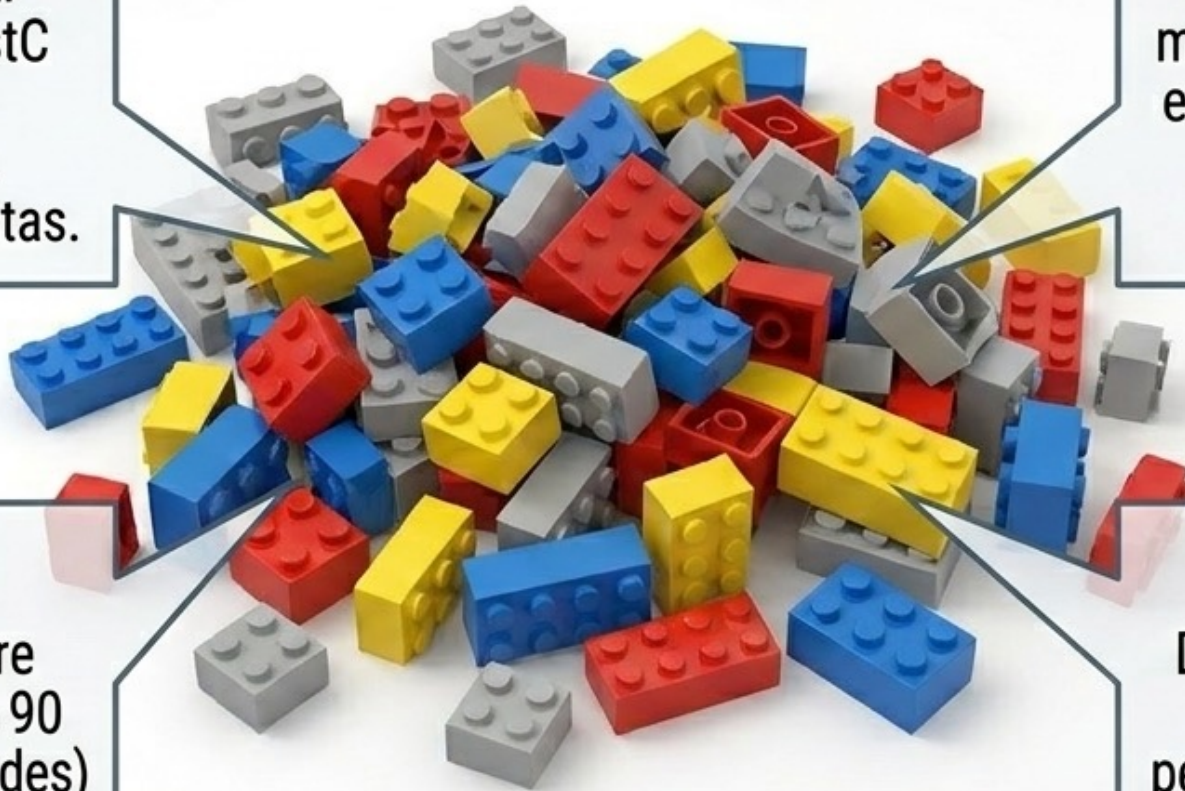
Variabilidad extrema: mezclar dosis agudas únicas en ambulancia con sesiones diarias (CRIC) durante semanas.

## Endpoints

Discordancia masiva entre endpoints clínicos (mRS a 90 días, sensible a comorbilidades) e imagenológicos (volumen del infarto).

## Control Sham

Dificultad intrínseca para el cegamiento: el paciente percibe claramente la presión de 200 mmHg frente a una compresión simulada leve.





# POSTCONDICIONAMIENTO ISQUÉMICO REMOTO

| Estudio          | Año  | Contexto           | Criterios Inclusión       | N   | Protocolo               | Endpoint 1º                                      | Resultados                         | Referencia                                                         |
|------------------|------|--------------------|---------------------------|-----|-------------------------|--------------------------------------------------|------------------------------------|--------------------------------------------------------------------|
| <b>SERIC-EVT</b> | 2025 | EVT / LVO anterior | NIHSS $\geq 6$ , post-EVT | 498 | 4x5 min, 2x/día x 7d    | mRS a 90 días                                    | Eficacia y seguridad en evaluación | SERIC-EVT Trial Group                                              |
| <b>PROTECT-I</b> | 2026 | EVT / LVO anterior | Ictus agudo EVT           | 130 | 4x5 min, brazo, 200mmHg | Volumen final infarto vs perfusión basal (Día 1) | Presentado en ESOC 2026            | Abstract ESOC2026A2328, DOI 10.1093/esj/aaka g023.152, NCT03915782 |



**Ambos ensayos representan el nuevo paradigma: restringir la población a oclusiones de gran vaso y aplicar la terapia post-reperusión.**

# POSTCONDICIONAMIENTO ISQUÉMICO REMOTO

| SERIC-EVT (n=488)                                   |                  | PROTECT-I (n=130)                                               |
|-----------------------------------------------------|------------------|-----------------------------------------------------------------|
| Oclusión de gran vaso (LVO) anterior + EVT [178]    | Población        | Oclusión de gran vaso (LVO) anterior + EVT [231]                |
| Post-EVT [180]                                      | Timing           | Per-EVT [231]                                                   |
| 14 sesiones (Tratamiento sostenido de 7 días) [180] | Intensidad       | 1 sesión única [231]                                            |
| mRS 0-2 a 90 días (61.1% vs 48.9%) [191]            | Métrica de éxito | Volumen de infarto final (% de lesión de perfusión basal) [232] |

# SERIC-EVT trial

European Heart Journal (2025) 00, 1–9

## Study design

### Baseline

Patients



498

Centres



25

China



AIS onset within 24h; anterior circulation large vessel occlusion; undergoing EVT

Randomization

### RIC/sham RIC treatment

RIC group, N = 249



200 mmHg  
consecutive 7 days

Sham RIC group, N = 249



60 mmHg  
consecutive 7 days

### Follow-up



OR



Follow-up at 90 days after EVT was assessed in person or by telephone by the principal centre

## Efficacy outcomes: RIC vs sham

### Primary outcome

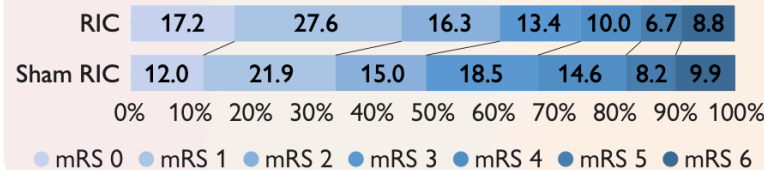
mRS score of 0–2 at 90 days (61.1% vs 48.9%; unadjusted RR, 1.25; 95% CI, 1.06 to 1.47;  $P = 0.009$ )

### Secondary outcomes

mRS score of 0–1 at 90 days (44.8% vs 33.9%; unadjusted RR, 1.32; 95% CI, 1.05 to 1.66;  $P = 0.017$ )

Early neurological deterioration at 7 days (4.2% vs 10.3%; unadjusted RR, 0.41; 95% CI, 0.20 to 0.83;  $P = 0.013$ )

### mRS score distribution at 90 days



## Safety outcomes

- Haemorrhagic transformation within 7d ( $P = 0.573$ )
- Symptomatic intracranial haemorrhage within 7d ( $P > 0.999$ )
- Mortality within 90d ( $P = 0.686$ )
- All adverse events within 90d ( $P = 0.924$ )
- Serious adverse events within 90d ( $P = 0.697$ )
- RIC-related adverse events within 90d ( $P = 0.061$ )



# Neuroprotective Effects of Rapid Local Ischemic Postconditioning in Patients Underwent Successful Endovascular Thrombectomy

**Purpose** To determine the efficacy of RL-IPostC immediately after successful reperfusion in acute ischemic stroke (AIS) patients who undergo endovascular EVT.

## Participants and Methods

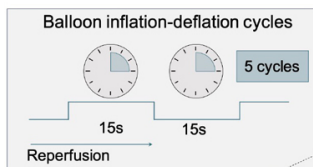
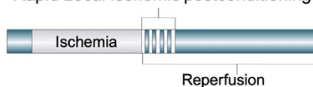


Two independent centers

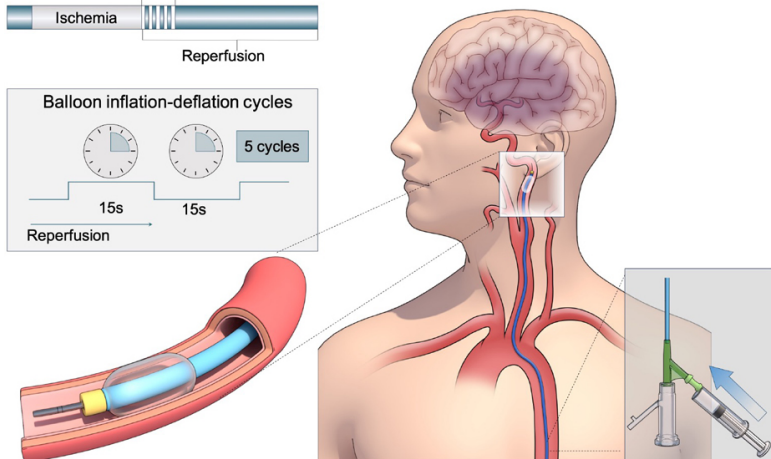


207 participants: 78 in the RL-IPostC group  
129 in the control group  
136 patients were selected after 1:1 PSM

Rapid Local Ischemic postconditioning



Acute Ischemia after Reperfusion



Clinical assessment

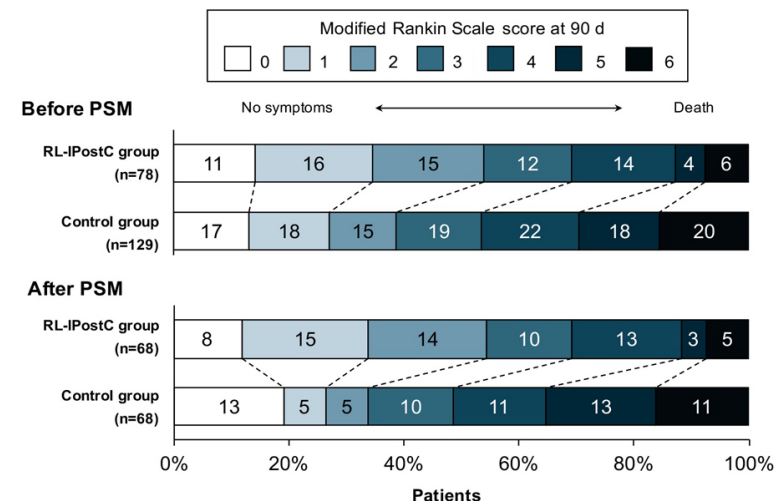
Imaging assessment

Infract lesion analysis

NWU analysis

CSF analysis

## Results



RL-IPostC

Higher functional independence

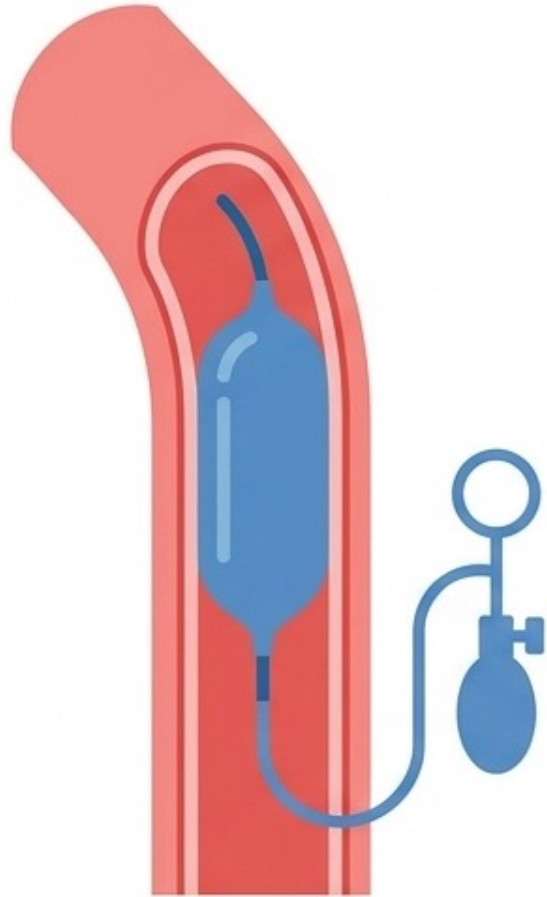
Lower infract volume and growth

Lower NWU and CSF changes

Lower midline shift

## Conclusions

Our findings support that RL-IPostC is safe and effective in carefully selected patients, possibly improving functional independence rates in patients who achieved successful reperfusion.



**Target: Arteria carótida interna ipsilateral**  
(tras recanalización exitosa) [146]

**15 segundos  
de inflado**  
(Isquemia local)  
[154]

**Repetir x 5  
Ciclos**  
[146]

**15 segundos  
de desinflado**  
(Reperusión)  
[154]

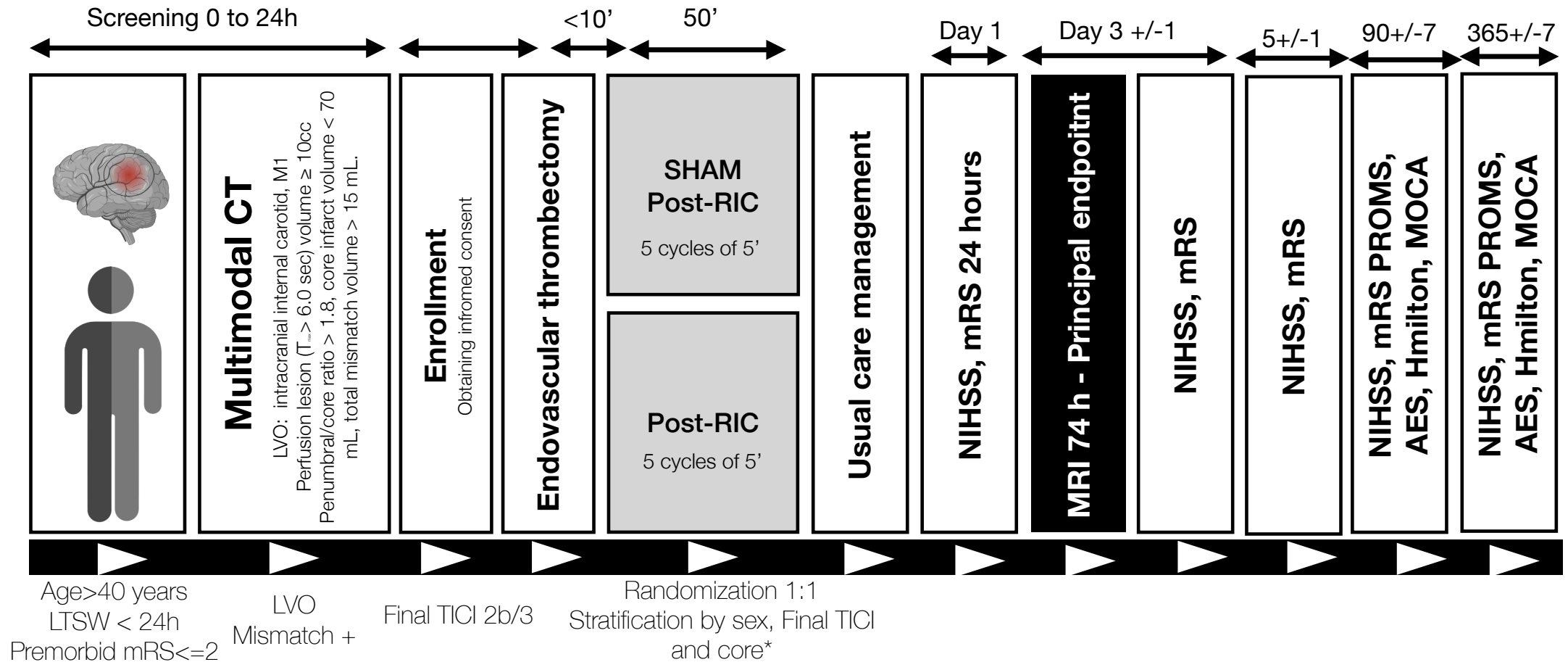
**Intervención de duración ultracorta (<3 minutos  
totales) directamente en la zona de penumbra.**

post - REMOTE

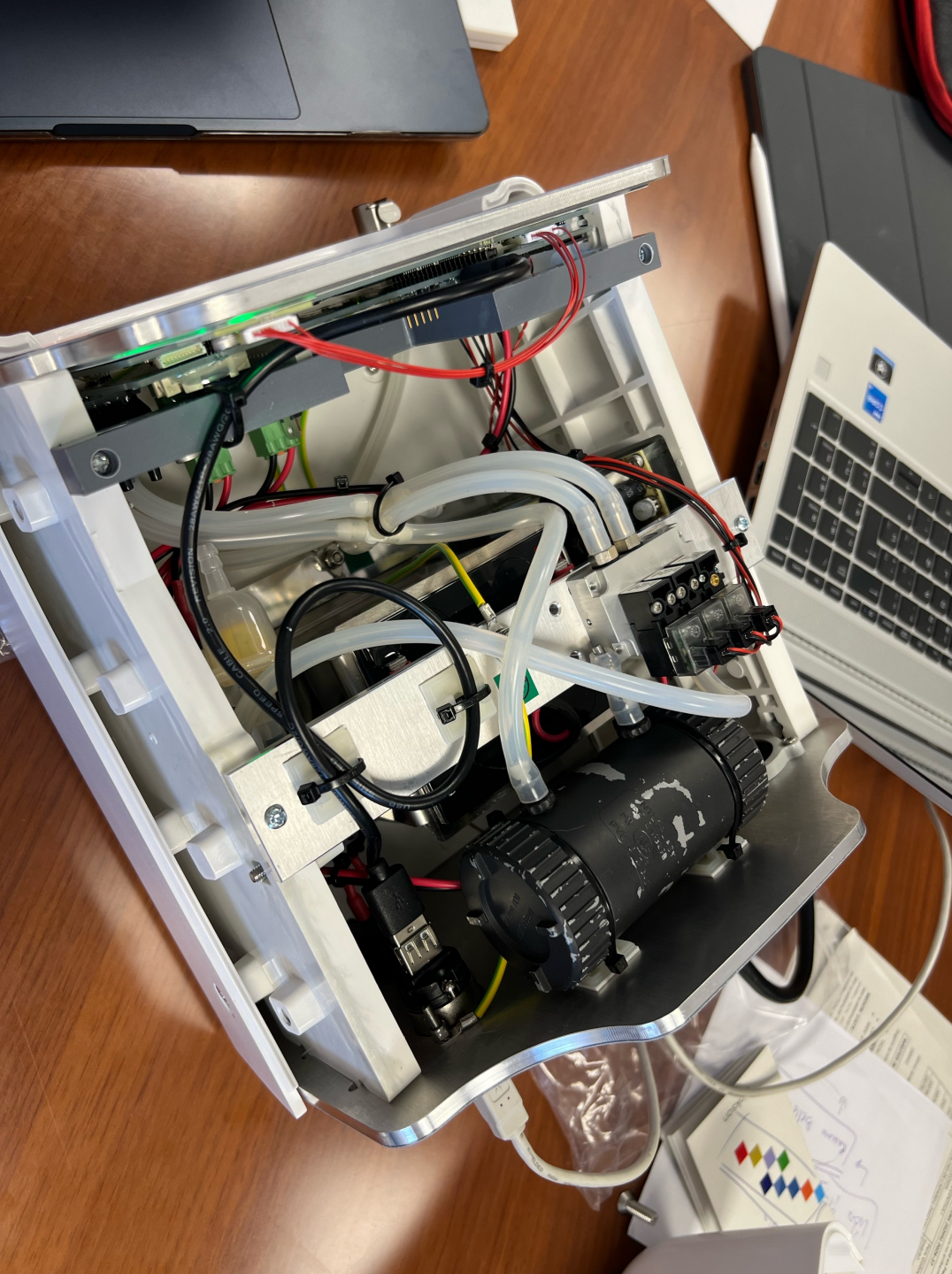


N=180

## POST-REMOTE



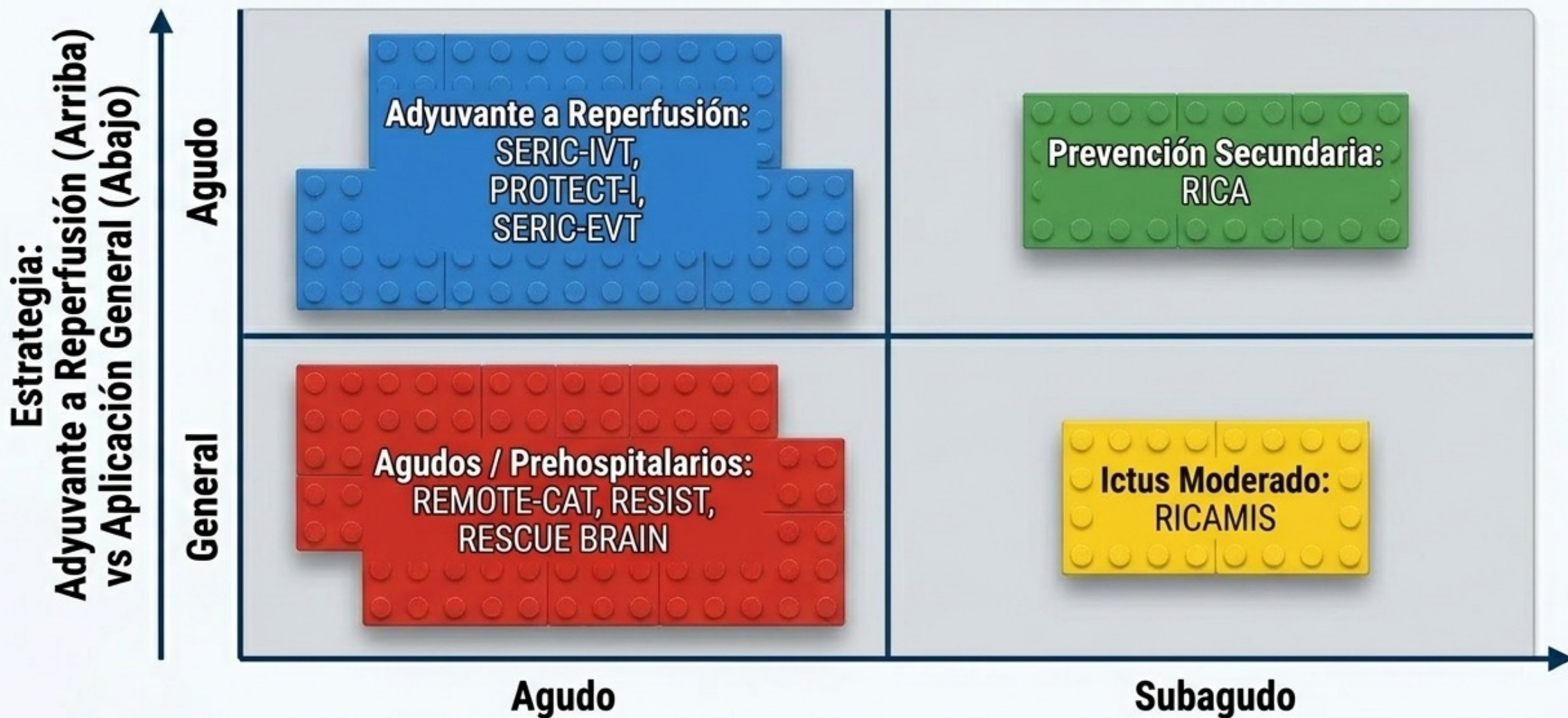
\* FSC volume <30%: ≤ 35cc or >35cc, sex, and by the degree of reperfusion (TICl2b or TICl 3).



**Spengler-Medical**



# El paisaje de la evidencia clínica: Mapeo de los grandes ensayos



**Ventana Terapéutica:** Prehospitalario → Hospitalario → Crónico



**QUESTION** Does remote ischemic conditioning (RIC), which involves repeated occlusion/release cycles on bilateral upper limb arteries, improve neurologic function in patients with acute moderate ischemic stroke?

**CONCLUSION** This randomized clinical trial found that while remote ischemic conditioning was associated with better neurologic function, replication is required before concluding efficacy for this intervention.

## POPULATION

1170 Men  
606 Women



Adults aged 18 years or older with acute moderate ischemic stroke

Mean age: 65 years

## LOCATIONS

55 Hospitals  
in China



## INTERVENTION



1893 Patients randomized  
1776 Patients analyzed

922  
**RIC**

RIC treatment plus guideline-recommended treatment (ie, antiplatelet or anticoagulant medication or statins)

971

**Control**

Guideline-recommended treatment only



## PRIMARY OUTCOMES

Excellent functional outcome at 90 days, defined as a modified Rankin Scale score of 0 to 1

## FINDINGS

© AMA

Patients with excellent functional outcome at 90 days

**RIC**

582 of 863 patients



**Control**

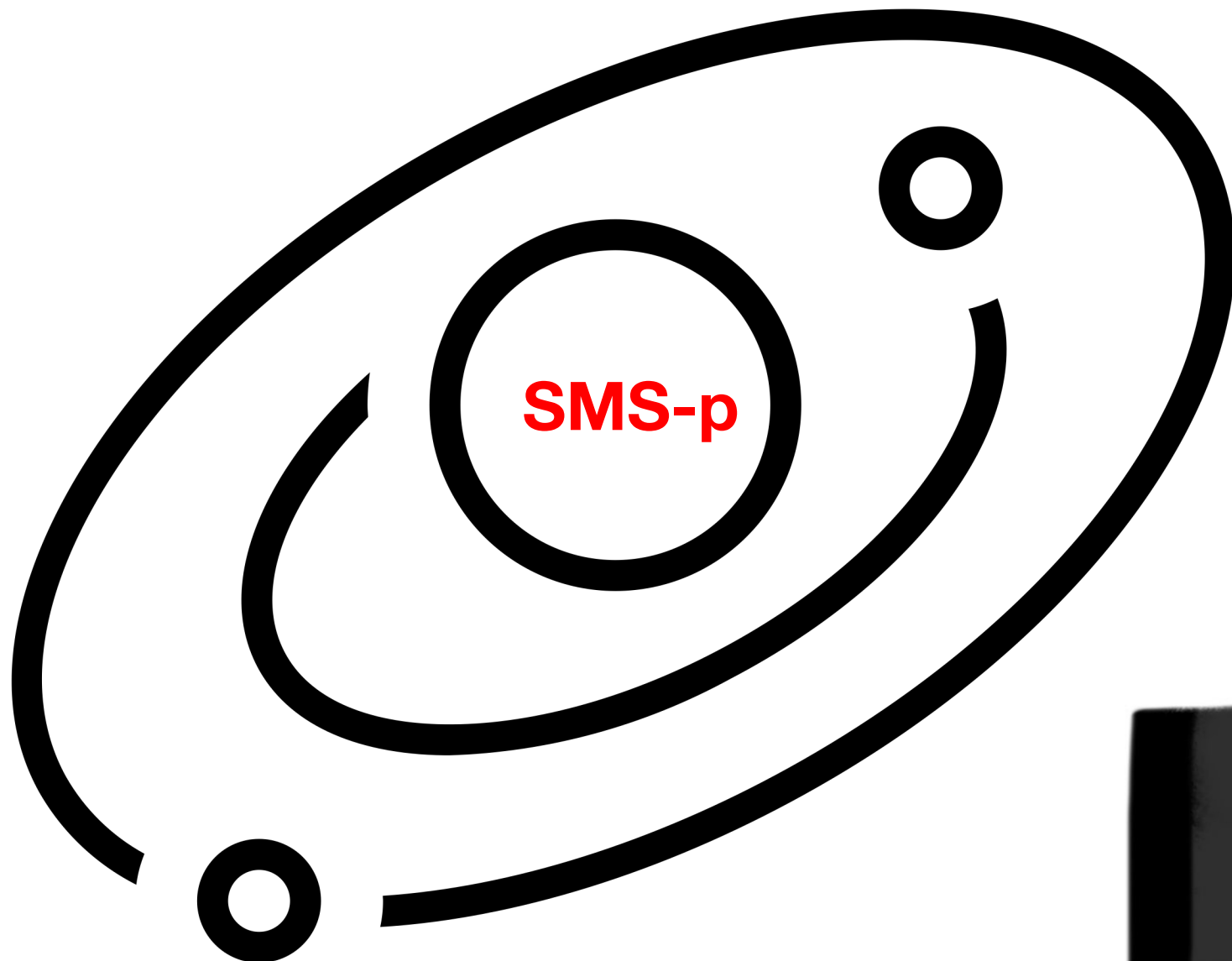
566 of 913 patients



Results were statistically significant:

Risk difference, **5.4%** (95% CI, 1.0% to 9.9%)

Odds ratio, **1.27** (95% CI, 1.05 to 1.54);  $P = .02$



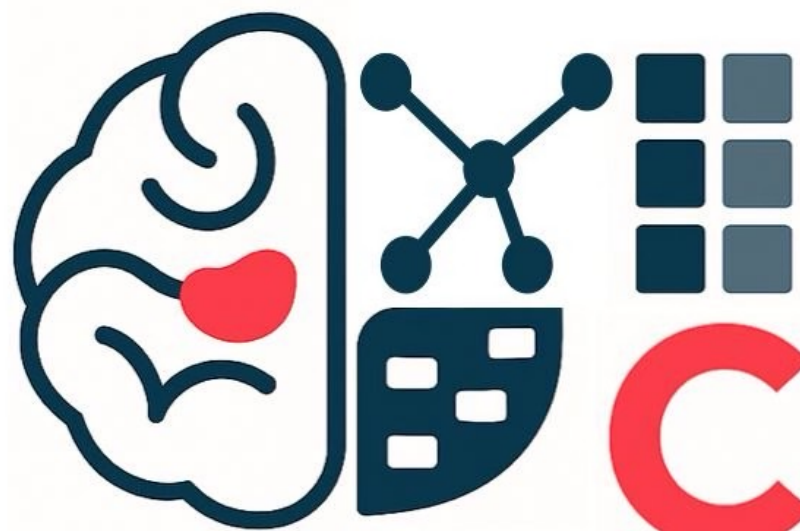
**POST-REMOTE**



**CONVINCE-2**

**2026**

**2031**



**CNG**

**CLINICAL NEUROSCIENCE GROUP**



Francesc Purroy