

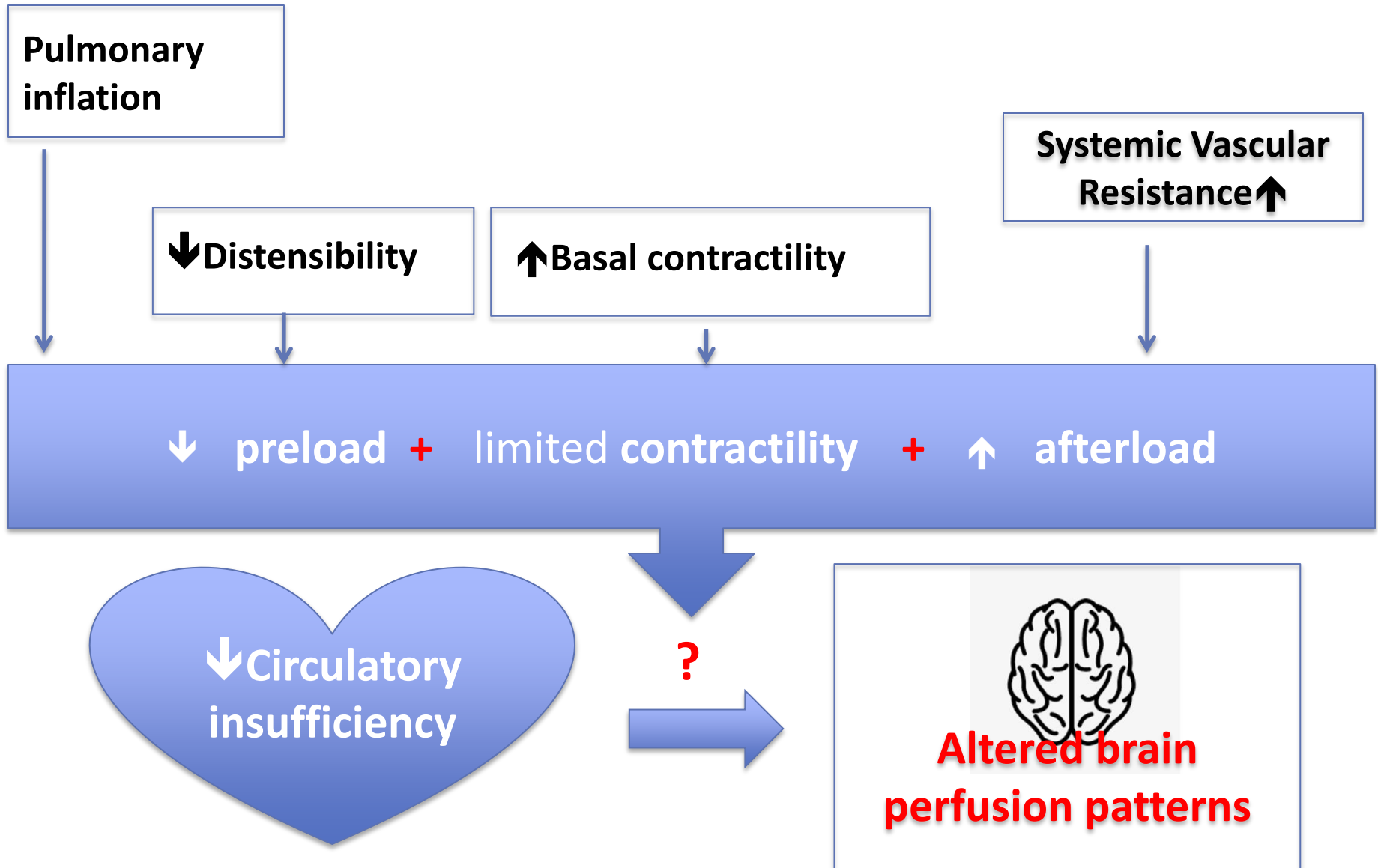
## PROPUESTAS PARA INICATIVAS CONJUNTAS

**Los retos de realizar grandes trials sobre adaptación circulatoria neonatal**

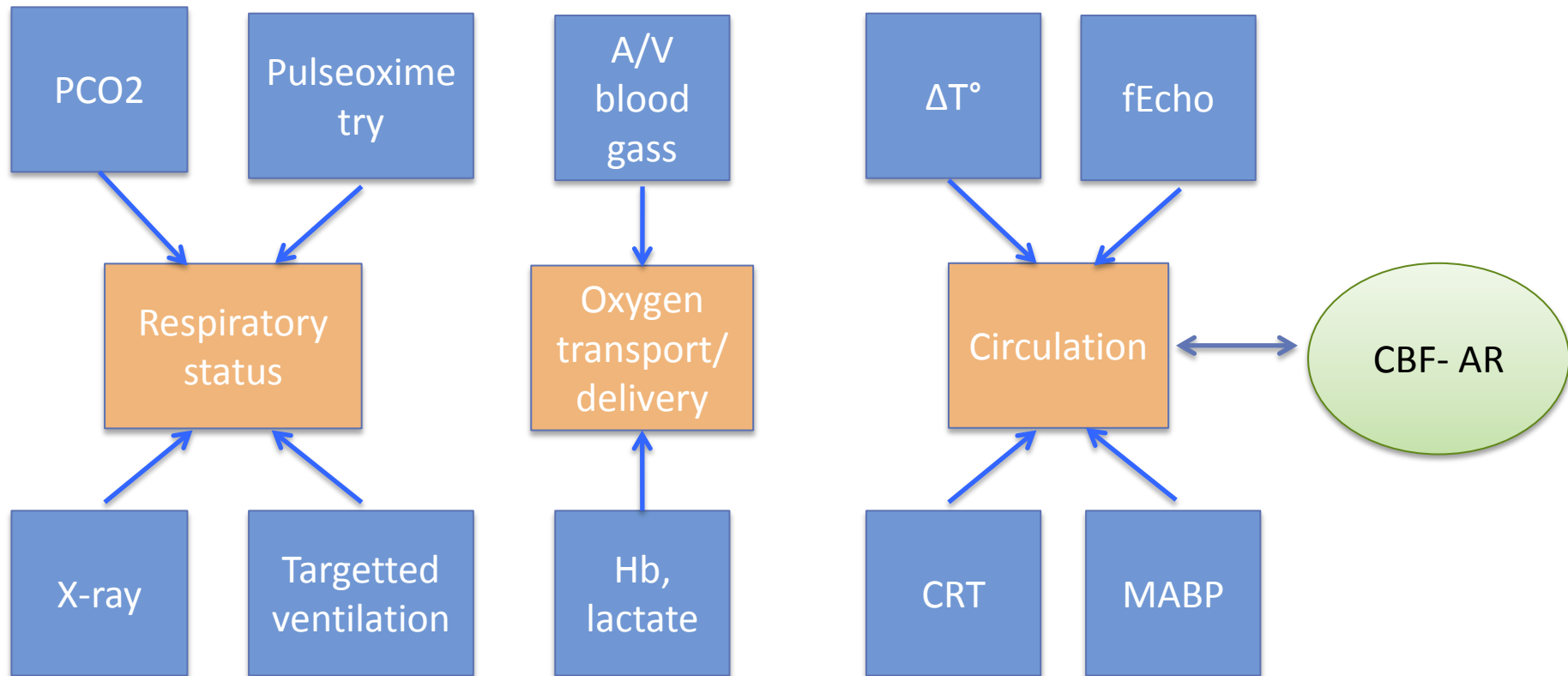
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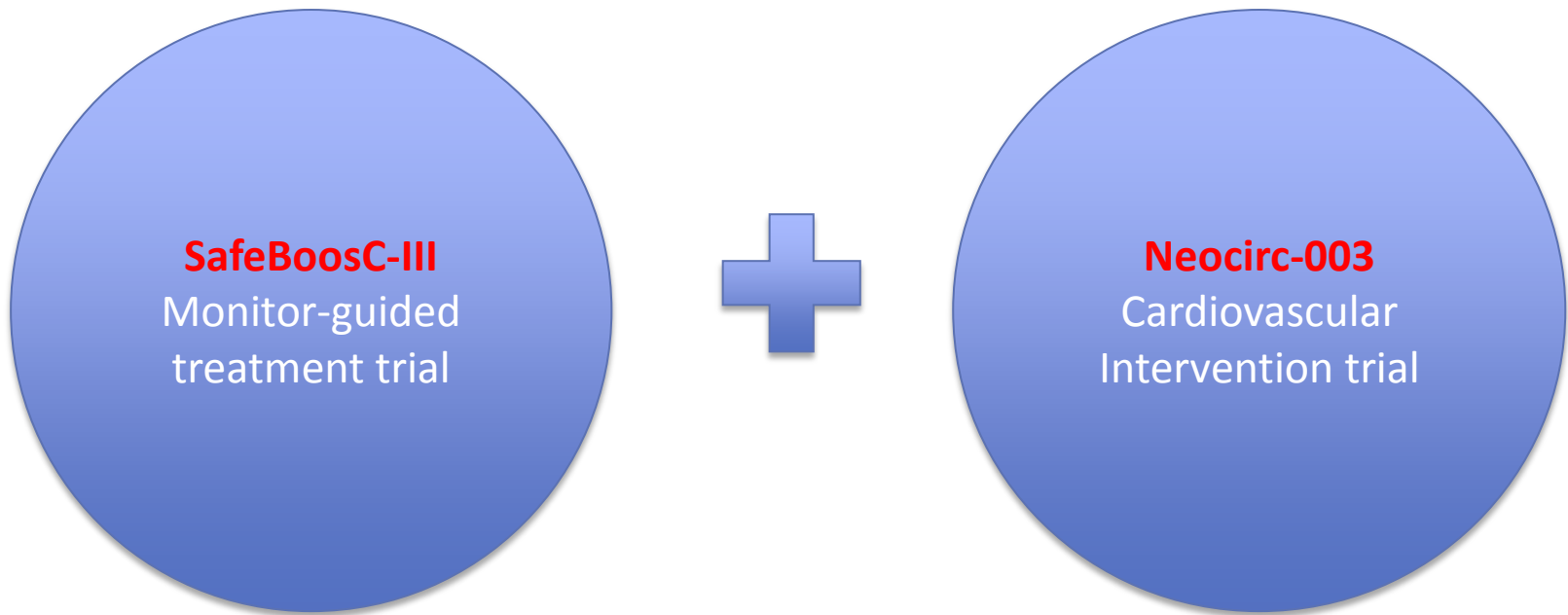
# TRANSITIONAL CIRCULATION



# THE PATHOPHYSIOLOGY



# Getting infants into both RCTs



Questions to address have common pathophysiology

# SafeBoosC phase III trial

# NeoCirc-003

## Enrollment

Assess eligibility

Inclusion criteria

Exclusion criteria

Randomisation

## Allocation

N=1,600

N=800

N=800

### Experimental group

Treatment based on NIRS reading according to evidence-based guideline

**Intervention time: 72**

### Control group

Treatment as usual

## Follow up

Routine series of cranial ultrasounds until week 36 postmenstrual age

## Analysis

Primary outcome: death or severe brain injury at 36 weeks  
Exploratory outcomes: Major neonatal morbidities, NEC, ROP and BPD

Total: 270. Perform screening assessments within 0-72h of birth.

Randomize

Arm 1 (N=90)

Arm 2 (N=90)

Arm 3 (N=90)

Perform baseline assessments.

Treatment initiation: Administer fluid bolus of Normal Saline for 30 min immediately followed by infusion of initial dose of IMP. Perform visit assessments.

Administer IMP according to given dose escalation scheme. Perform visit assessments.  
Arm 1: Dobutamine 2.5-5.0-7.5-10.0 µg/kg/min  
Arm 2: Dobutamine 5-10-15-20 µg/kg/min  
Arm 3: Normal Saline at equal volume

Evaluate PD response to treatment 60 min after start of new IMP infusion (at every dose during up-titration). Perform visit assessments.

Re-evaluate PD response to treatment 120-180 min after start of new IMP infusion. TO CONFIRM SUCCESSFUL DOSES ONLY. Perform visit assessments.

Assess 1<sup>st</sup> co-primary endpoint at 72 h of birth. Perform visit assessments.

Conduct end of treatment assessment at treatment completion. Perform visit assessments.

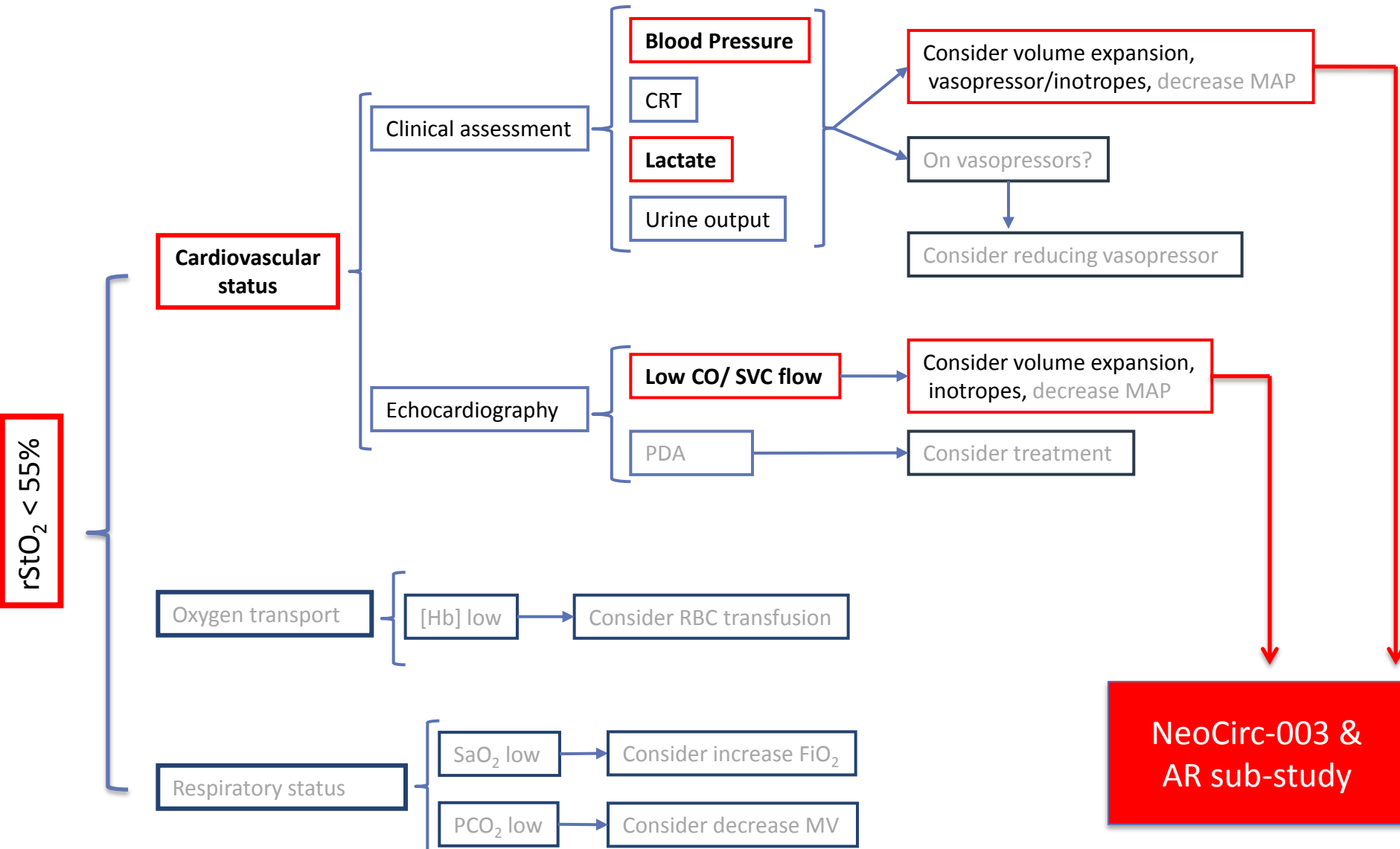
### Final Assessments

**Early-FU:** Repeated cUS-D scans at Days 3, 7, 14 and 35 of life.

**Mid-FU:** cUS-D scan at term equivalent age (TEA) and evaluate 2nd co-primary endpoint. Assess neonatal outcomes at TEA.

**Long-FU:** Assess neurodevelopmental outcome at 24months corrected GA.

# Clinical intervention algorithm in the SafeBoosC phase III trial



# NeoCirculation & CBF-AR sub-studies

- NIRS continuous monitoring
  - Continuous data recording
  - AR studies (invasive blood pressure required)
    - BiAR-COH
    - $PDC_{MABP \gg rStO_2}$
  - rStO<sub>2</sub> is not a criterion for entry or rescue
  - rStO<sub>2</sub> may help in decision-making

# Procedures

- Antenatal informed consent
  - Specific ICF
    - SafeBoosC-III (op-out IC/deferred IC)
    - NeoCirc-003 (deferred ICF)
  - Deferred consent in both trials (approval site-dependent)
- CBF-AR only if SafeBoosC-III experimental group



