

# CoPrema Study: Cord blood copeptin levels in neonates born preterm: Prognostic factor for fluctuations in natremia in the first 10 days of life?

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## BACKGROUND

- Preterm (PT) birth is associated with extreme and rapid variations of natremia and plasma osmolarity in the first 10 days of life.
- These variations can lead to serious neurological damages; hydro-sodium homeostasis is essential in PT neonates to avoid neurological injuries.
- Hydric homeostasis is regulated in part by vasopressin (ADH).
- The assessment of **Copeptin** levels, a stable pre-pro-hormone of ADH, could help predict natremia in PT neonates in the first 10 days of life.

## Aim 1

To determine the association between cord blood Copeptin level and natremia in the first 10 days of life in PT newborns <37w.

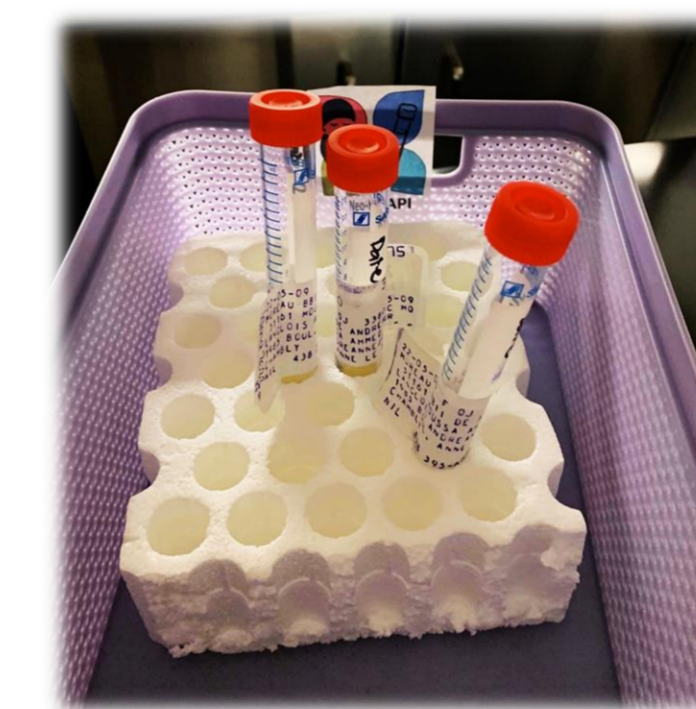
## Aim 2

To examine the association between cord blood copeptin levels and gestational age, birth weight, sex, delivery mode, multiples, maternal factors (gestational hypertension, pre-eclampsia/eclampsia, HELLP syndrome).

## MATERIALS and METHODS

- Study design:** Single-center prospective observational cohort study (Ethics approval 2022-3527).
- Recruitment period:** April 2022-December 2023.
- Study population:** Target sample size of 70 preterm infants.
- Inclusion criteria:** PT neonates <37w and term-born controls, born at CHUSJ.
- Exclusion criteria:** neonates with cerebral anomaly involving the pituitary region or significant congenital renal anomaly.
- Study variables:**

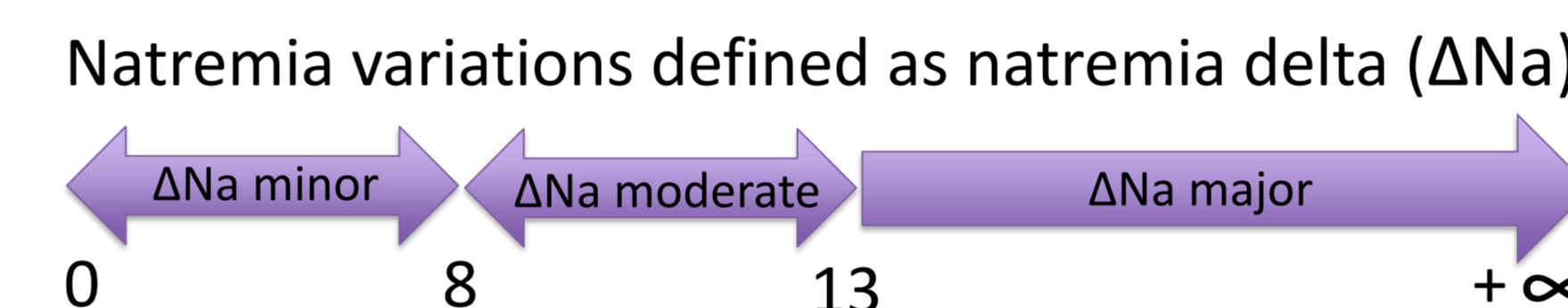
Urine samples collected in the NICU (0,5 ml minimally)



- About the "control" group of full-term (T) newborns :
  - collection of the same variables each day during their stay in the newborn nursery
  - matching 2 PT babies for 1 full-term
  - to compare copeptin values and changes in other study variables, adjusting for potential confounding factors (sex, birth weight, mode of delivery, potential maternal pathologies).

**At Birth** COPEPTIN, measured in cord blood plasma (volume 0.5mL; non-competitive immunofluorescence test – London Health Sciences Center, Ontario).

- From D0 to D10**
- Perinatal data, weight, diuresis → from medical records.
  - Natremia, natriuresis, kaliuresis, urinary osmolarity → from biochemistry department.
  - Plasma osmolarity → measured and calculated =  $[Na^+] \times 2 + [Gly] + [Urea]$ .
  - Natremia variations during the first 10 days classified according to 3 levels.



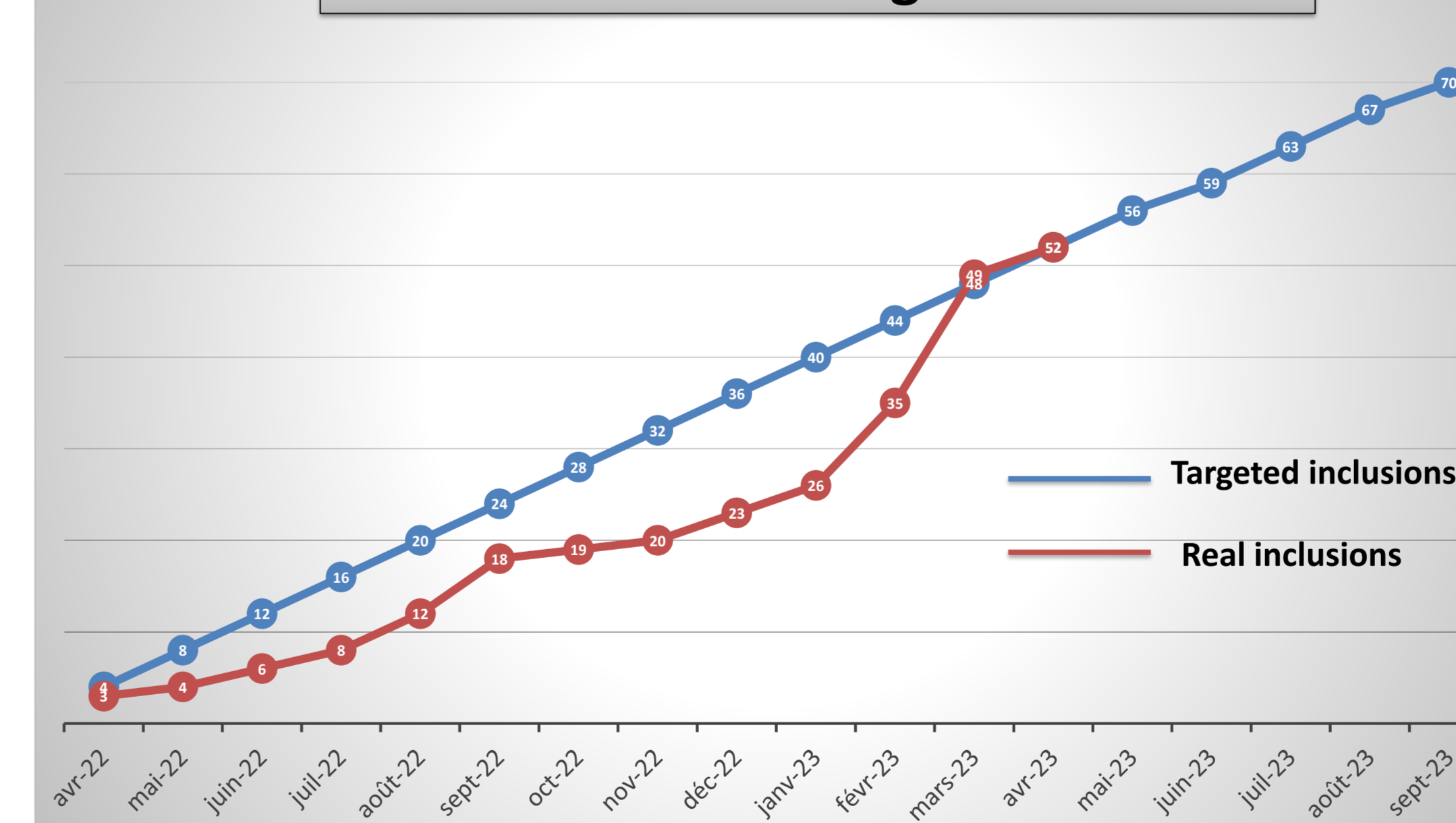
- Statistics:**
  - Descriptive stats: mean (SD), median (IQR), proportions.
  - Relationship between copeptin levels and other co-variate assessed by regression analyses.
  - Between-group comparisons (PT vs T) using regression analyses.

## PRELIMINARY RESULTS (as of 2023/04/18)

### General characteristics of the CoPrema cohort

Neonates included - n (%)	52/70 targeted (74% of target)
Gestational age (weeks + days)	Min : 25w +6/7 Maxi : 36w +6/7
Male sex - n (%)	♂ 28 (54%)
Birth weight (g)	Min : 600 Max : 3180
Copeptin assays - n (%)	12/52 (23%)
Copeptin results (pmol/L)	Min : 8,3 / Max : 930,1 Median : 58,4 (IQR : 145,2) Mean : 173,7 (SD : 267,9)
Urine analysis - n (%)	For all neonates
Death before D10 of life - n (%)	1/52 (2%)

### Real inclusions vs. Targeted inclusions

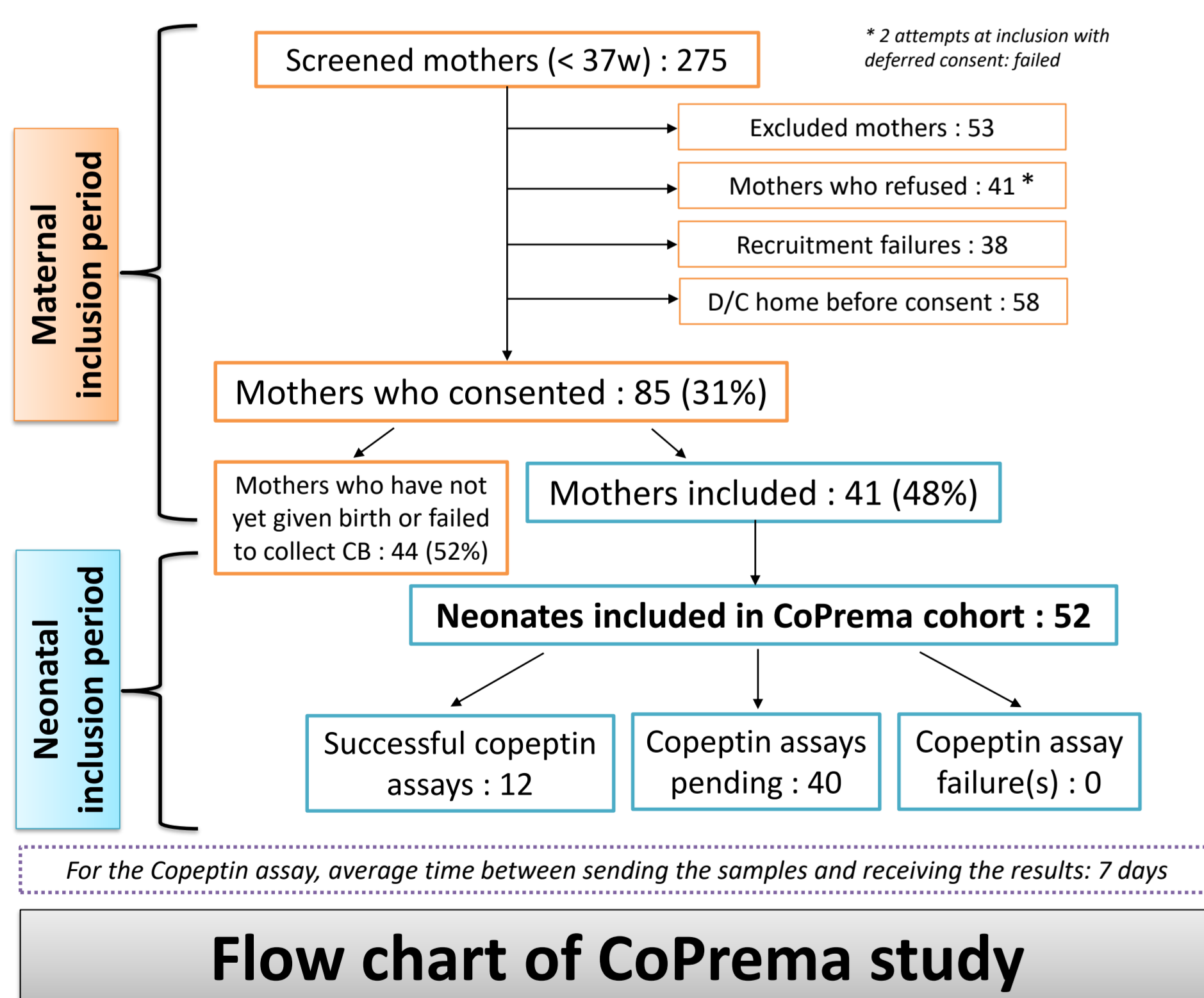


### Study Strengths:

- High consent rate.
- Benefits of copeptin:
  - very stable
  - supports very well freezing and thawing
  - can be measured even in low blood volume.

## CONCLUSIONS AND PERSPECTIVES

- After 1 year of active recruitment, this study demonstrated feasibility;
- The potential link between copeptin cord blood levels and the hydro-sodium control in preterm neonates could pave the way for a predictive biomarker of the hydric status and of neonatal fluid regulation in this vulnerable population;
- Appropriate management of fluid and electrolyte disorders in the first days of life could contribute to prevent the adverse consequences, particularly neurological complications.



### Limitations and challenges:

- Cord blood sampling in extreme PT newborn and severe intrauterine growth retardation is difficult.
- Only PT newborns are included at this point because of the challenges in collecting their cord blood. For full-term newborns we anticipate difficulties in collecting urine during 10 days.
- Increased time and higher costs due to copeptin analysis by an external laboratory.
- Necessity to aliquot plasma sample since plasma osmolarity is accessed at CHUSJ.