Cell Population Data (CPD): Neonatal Reference Intervals And Relevance For The Detection Of Sepsis And Necrotizing Enterocolitis

Flavia Ferraro [1]*, Laura Fillistorf [1], Varvara Dimopoulou [1], Lorenzo Alberio [2], Christine Coutaz [2], Sylvain Meylan [3], Raphael Matusiak [4], Jeremy Despraz [4], Eric Giannoni [1]

1 Clinic of Neonatology, Department Woman-Mother-Child, Lausanne University Hospital

2 General Hematology Laboratory, Lausanne University Hospital

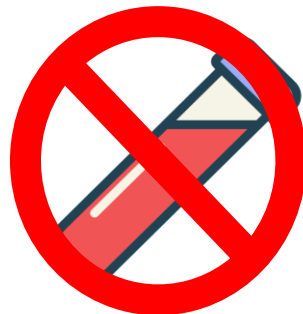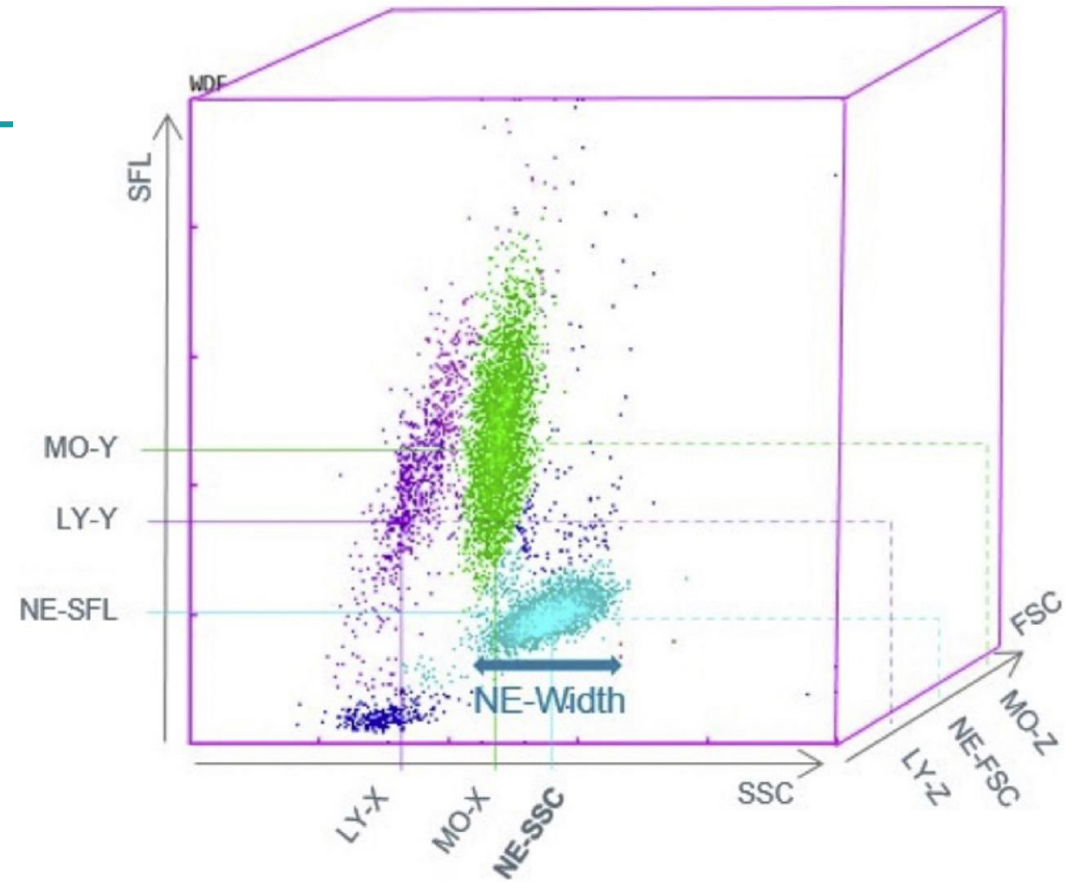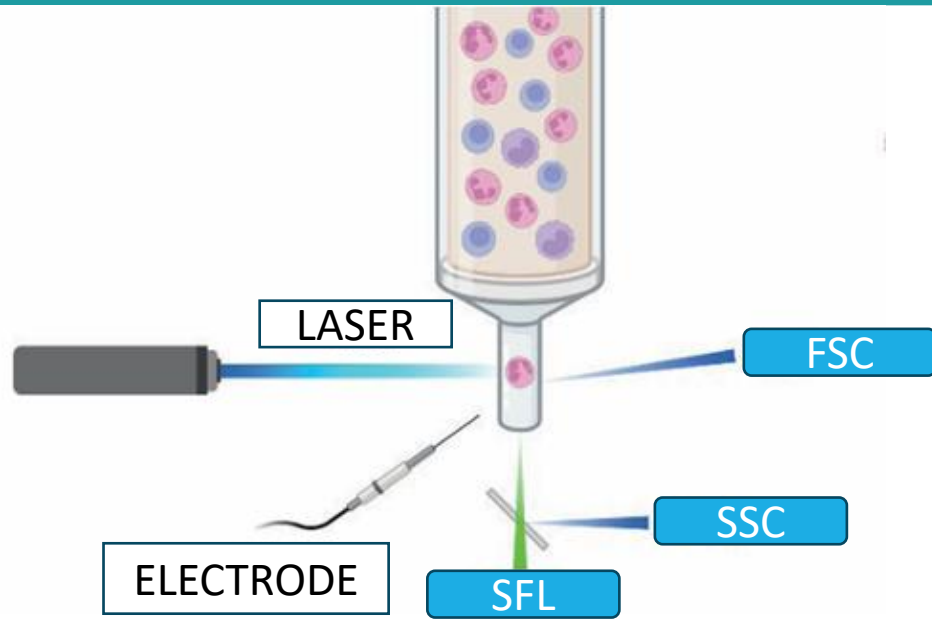3 Infectious Diseases Service, Department of Medicine, Lausanne University Hospital

4 Health Informatics and Data Protection Group, Biomedical Data Science Center, Lausanne University Hospital

CHUV

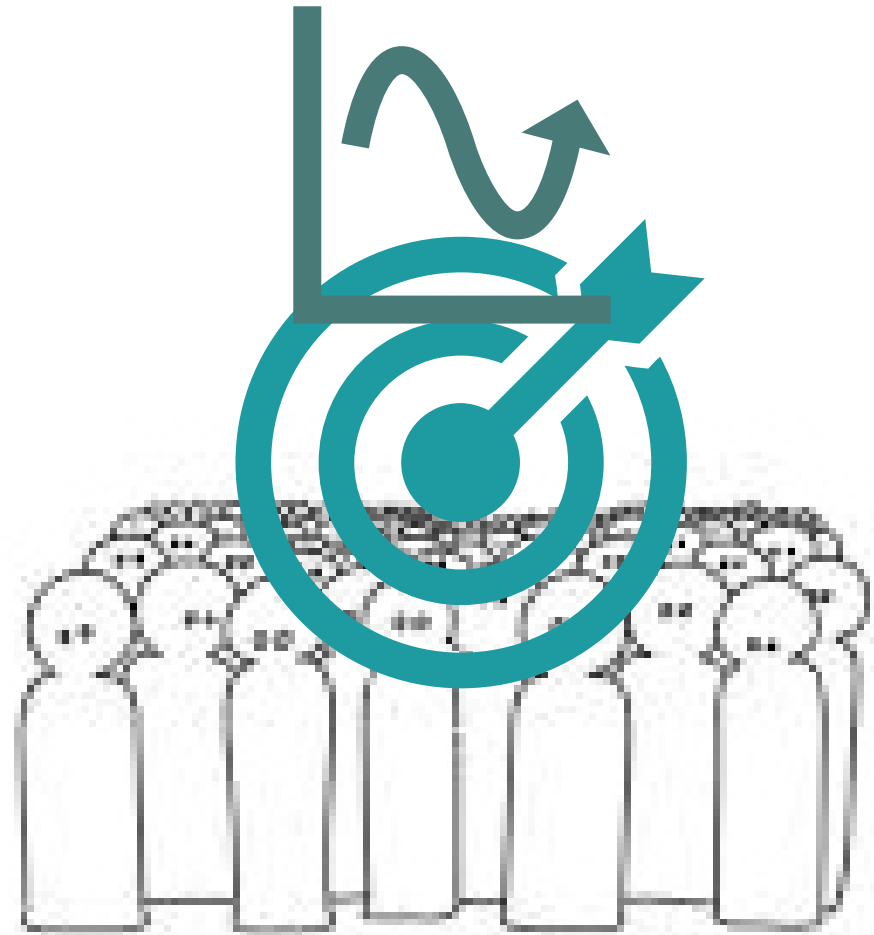UNIL | Université de Lausanne

Background

24-36 hours
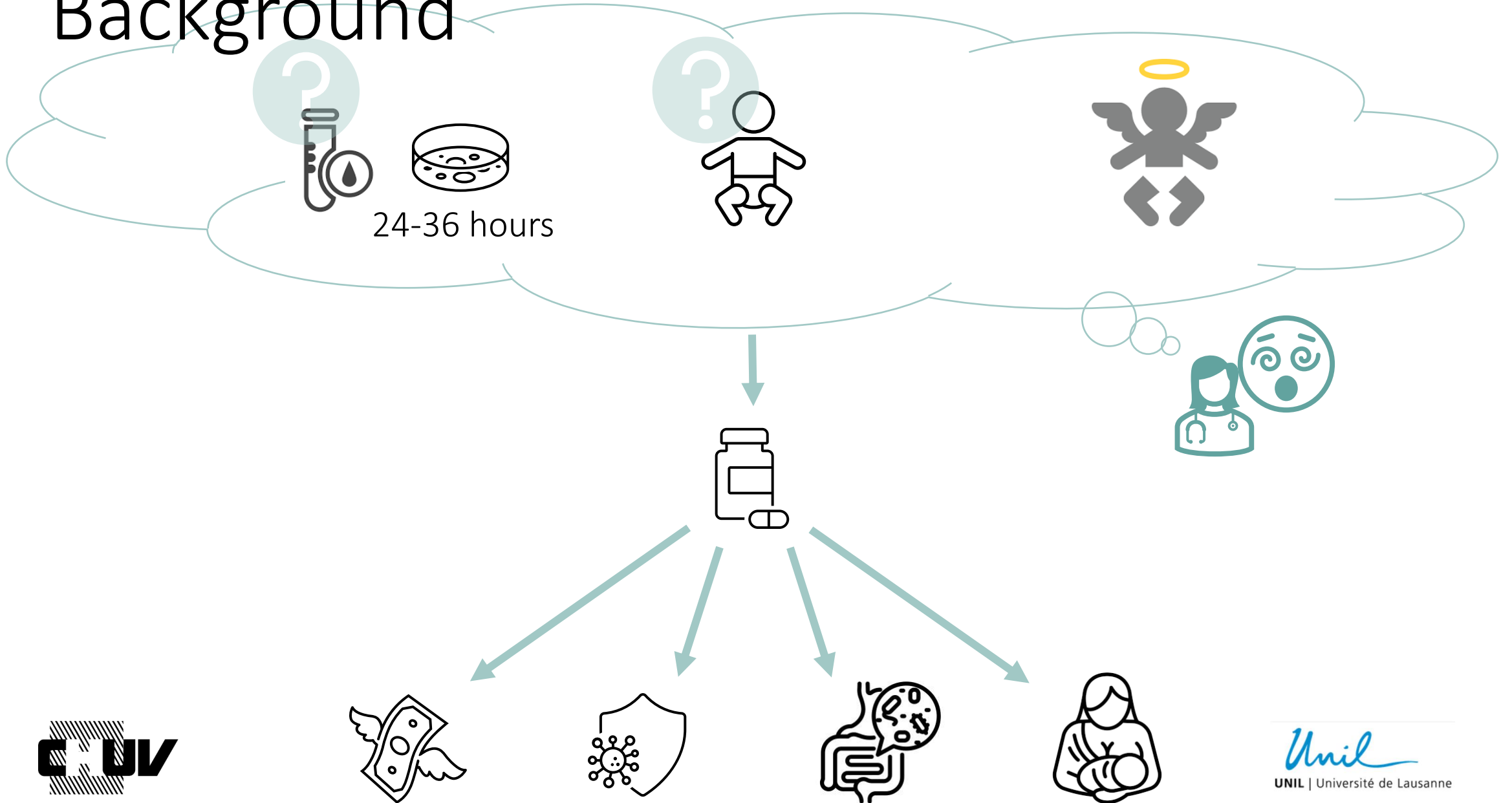
Cell Population Data

Objectives

1. Establish reference intervals for leukocyte CPD in the newborn

2. Explore the potential of CPD as biomarkers of sepsis and necrotizing enterocolitis (NEC)

Methods

Population

- Hospitalized neonates 24-44 weeks of GA; at least one complete blood count (CBC)
- Monocentric retrospective observational study (01.01.2021-30.06.2023)
- Sepsis = positive blood culture, NEC = Bell stage ≥ 2
- Exclusion: focal infection (antibiotics for at least 5 days), denied general consent for research and missing CPD parameters
- Reference population: neonates thought to have minimal disorders relevant to the laboratory test

Indicator

- 18 leukocytes CPD parameters
- Cellular size, complexity, fluorescence intensity and their width of dispersion

Comparison

- Standard CBC parameters
- C-reactive protein
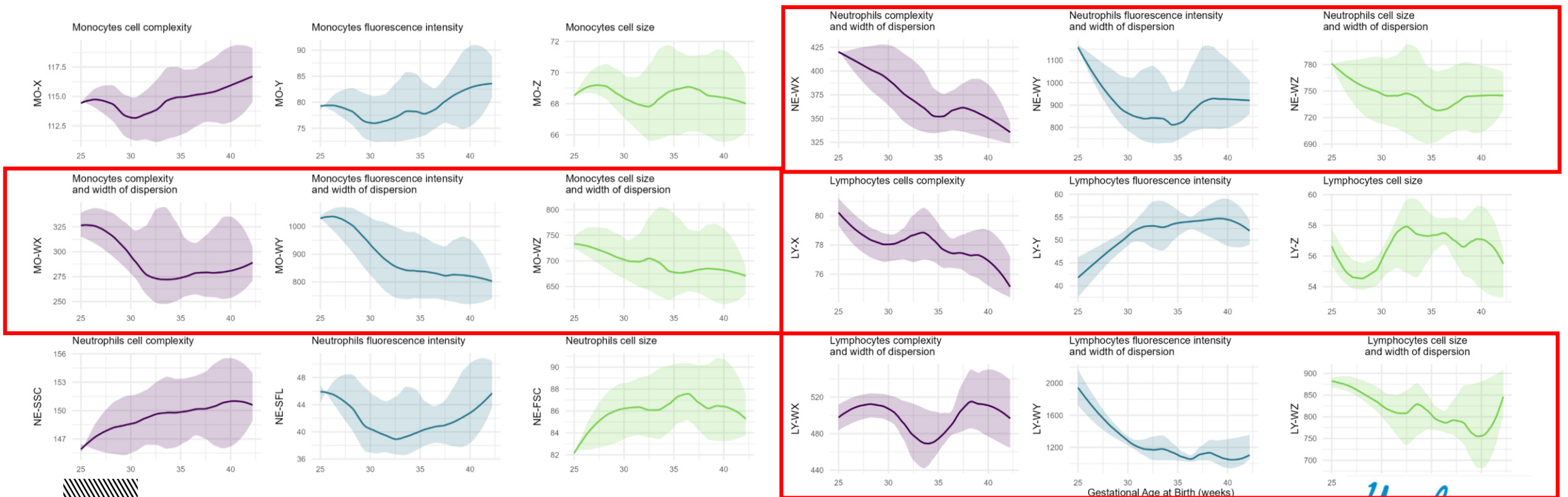
Demographics and clinical characteristics

	Sepsis/NEC group	No sepsis nor NEC	P value
Patients	39 (3.8)	974 (96.2)	----
Age (days)	9 (5.5-20)	----	----
Weight (Kg)	0.92 (0.66-2.05)	2.75 (1.94-3.39)	<0.001
Gestational age (weeks)	28.3 (26.3-34.2)	37.3 (34.0-40.0)	<0.001
Female	23 (58.9)	414 (42.5)	0.06
Culture positive sepsis	34 (87.2)	----	----
Necrotizing enterocolitis	10 (25.6)	----	----

UNIL | Université de Lausanne

Reference intervals on the day of birth according to gestational age

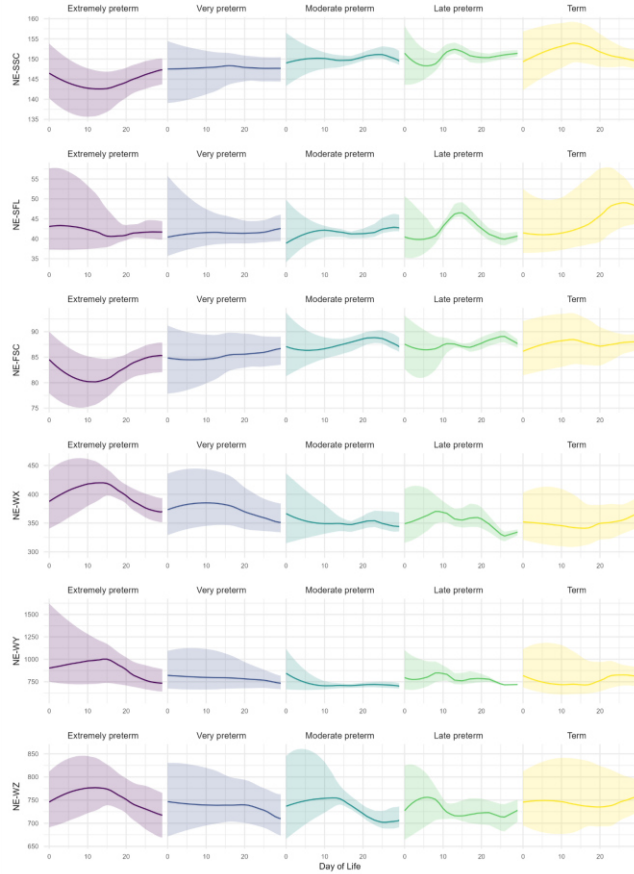**Selection Criteria**: Neonates with minimal or non-impactful disorders for leukocytes tests; N=905.

Range Definition: 5th to 95th percentiles, excluding the outermost 5% values.

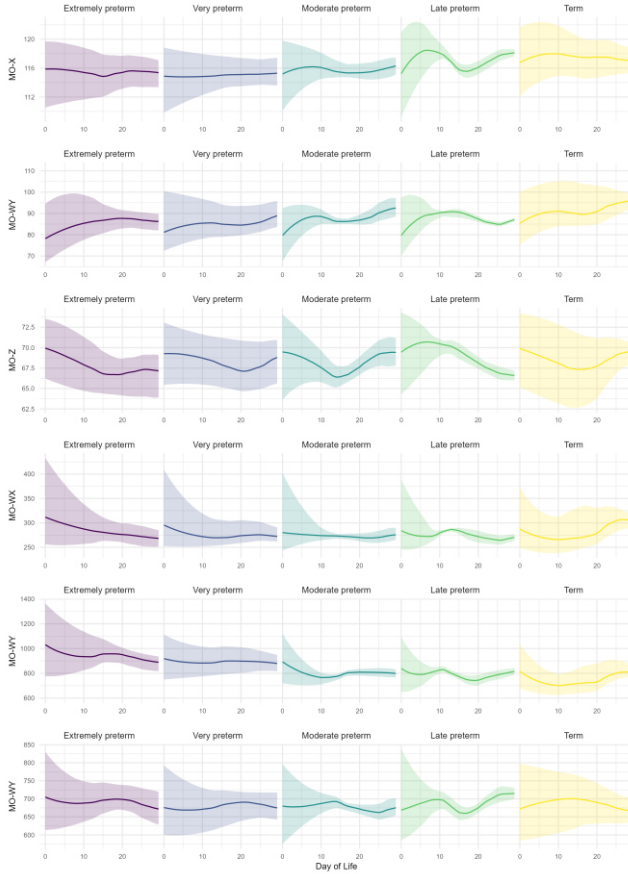**Data Display**: Birth data by gestational age; subsequent changes over weeks/months.

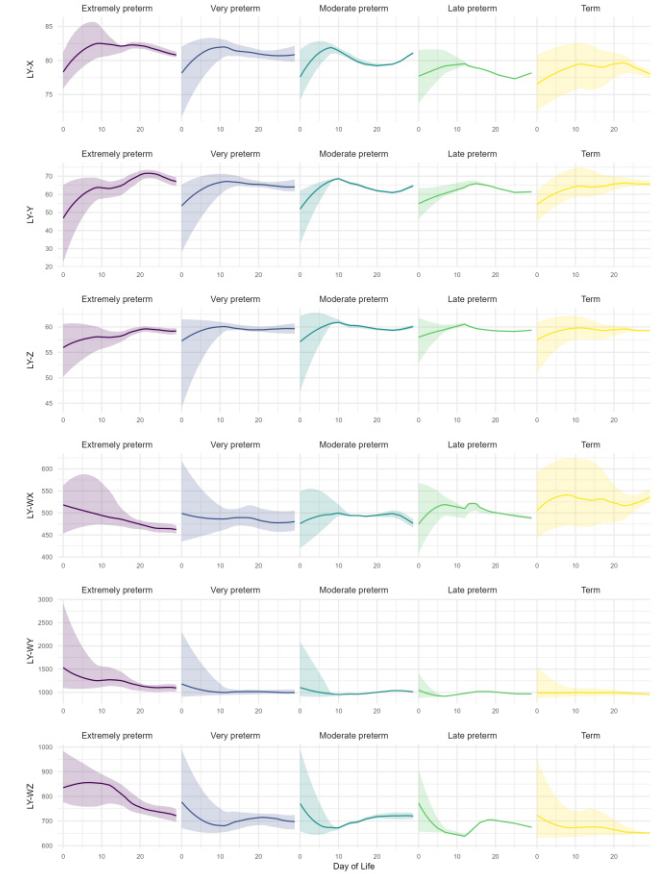# Reference intervals during the first 28 days of life

The lines represent the smoothed median values; the bands represent the 5th to 95th percentile range.

Diagnostic accuracy of CPD vs classical biomarkers

Parameter	AUC	Cut off value	Specificity	Sensitivity	PPV	NPV
NE-SFL (ch)	0.88	49.75	91%	73%	25%	98%
LY-X (ch)	0.81	79.8	84%	42%	10%	97%
CRP (mg/L)	0.72	8.95	86%	64%	16%	98%
Leukocytes (G/L)	0.60	6.35	91%	46%	17%	97%
Neutrophils (G/L)	0.61	3.56	70%	51%	7%	97%
Bands (G/L)	0.67	0.19	44%	87%	6%	98%
I/T ratio (%)	0.77	8.5	86%	56%	14%	97%
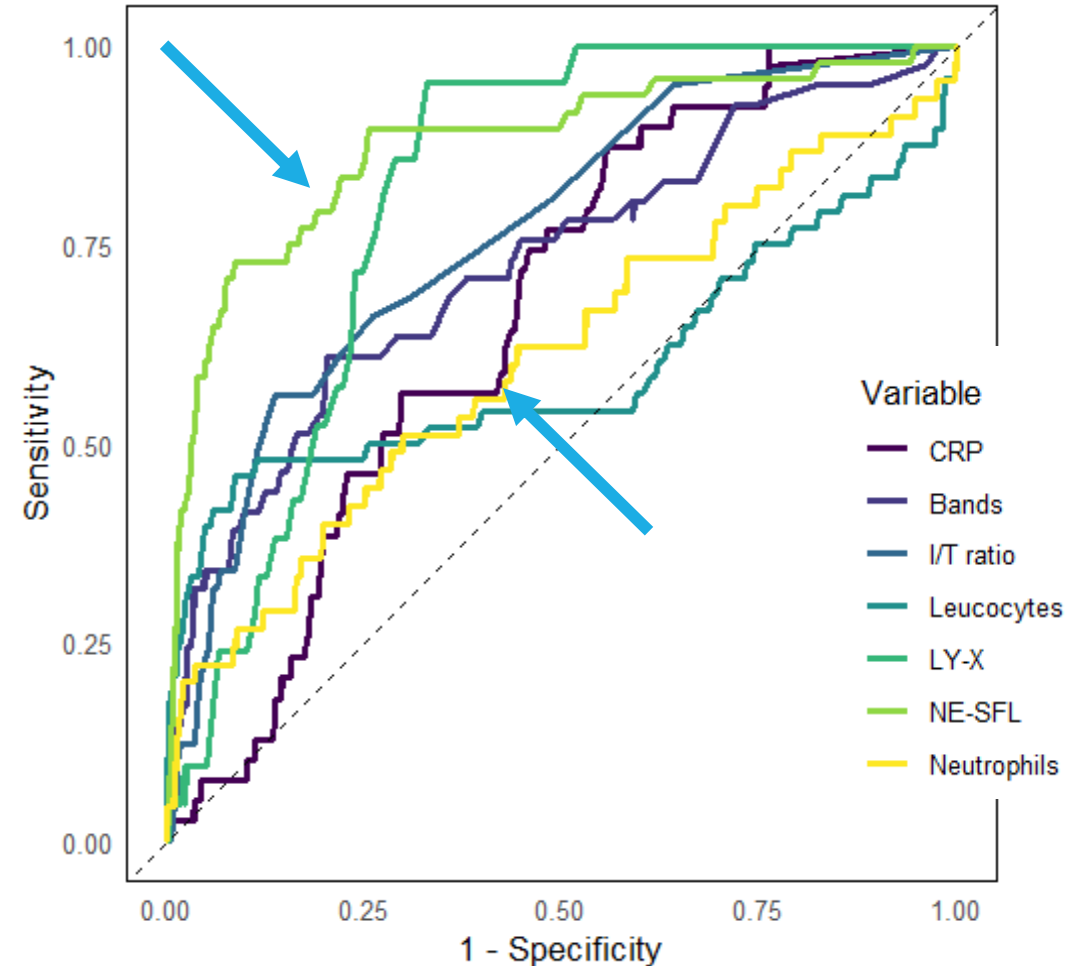
Diagnostic accuracy of a model combining NE-SFL, LY-X and CRP
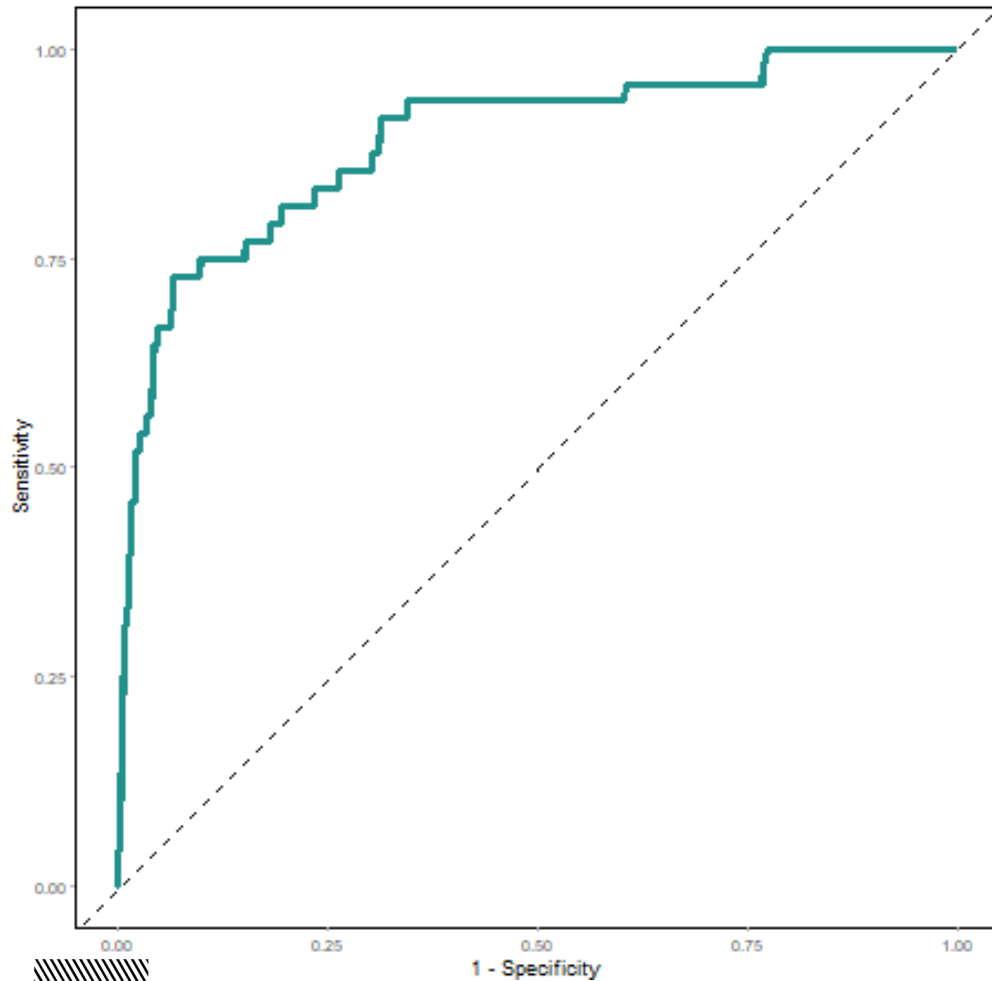
Parameter	AUC	Sensitivity	Specificity	PPV	NPV
NE-SFL (ch)+ LY-X (ch)+ CRP (mg/L)	0.89	73%	93%	31%	99%

Conclusions

This study

establishes reference intervals for Cell Population Data in newborns

identifies NE-SFL as an attractive biomarker candidate to assist clinicians in decision making regarding sepsis

UNIL | Université de Lausanne