



Higher intake of coagulase-negative staphylococci from breast milk promotes gut colonization with *meca*-negative *S. epidermidis* in preterm neonates

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Background

- *S. epidermidis* causing late-onset sepsis in preterm neonates
 - 87-100% are *mecA*-positive (Salgueiro et al. 2017, Soeorg et al. 2017)
 - colonize gut prior to the onset of infection (Soeorg et al. 2013)

Mother's own milk (MOM) of mothers of preterm neonates

- rich in *S. epidermidis* that are mostly *mecA*-negative (MSSE) (Soeorg et al. 2017)
- feeding with MOM → the proportion of MSSE increases in gut of preterm neonates (Soeorg et al. 2017)

Aim

- To determine factors associated with gut colonization of preterm neonates with *mecA*-negative *Staphylococcus epidermidis* strains present in mother's own milk.

Methods

January 2014 – December 2015

Preterm neonates & their mothers (n=49)

- **Hospitalized in the NICU**
- **Started to receive MOM** within the first week of life

Term neonates & their mothers (n=20)

- **Healthy**
- **Exclusively breastfed**

Once a week in the first month of life

- **Stool** from neonates
- **MOM** from mothers

Cultured onto salt-mannitol agar

Incubated at 37 °C for 48 h

5 colonies

MALDI-TOF mass spectrometry

S. epidermidis, *S. haemolyticus*

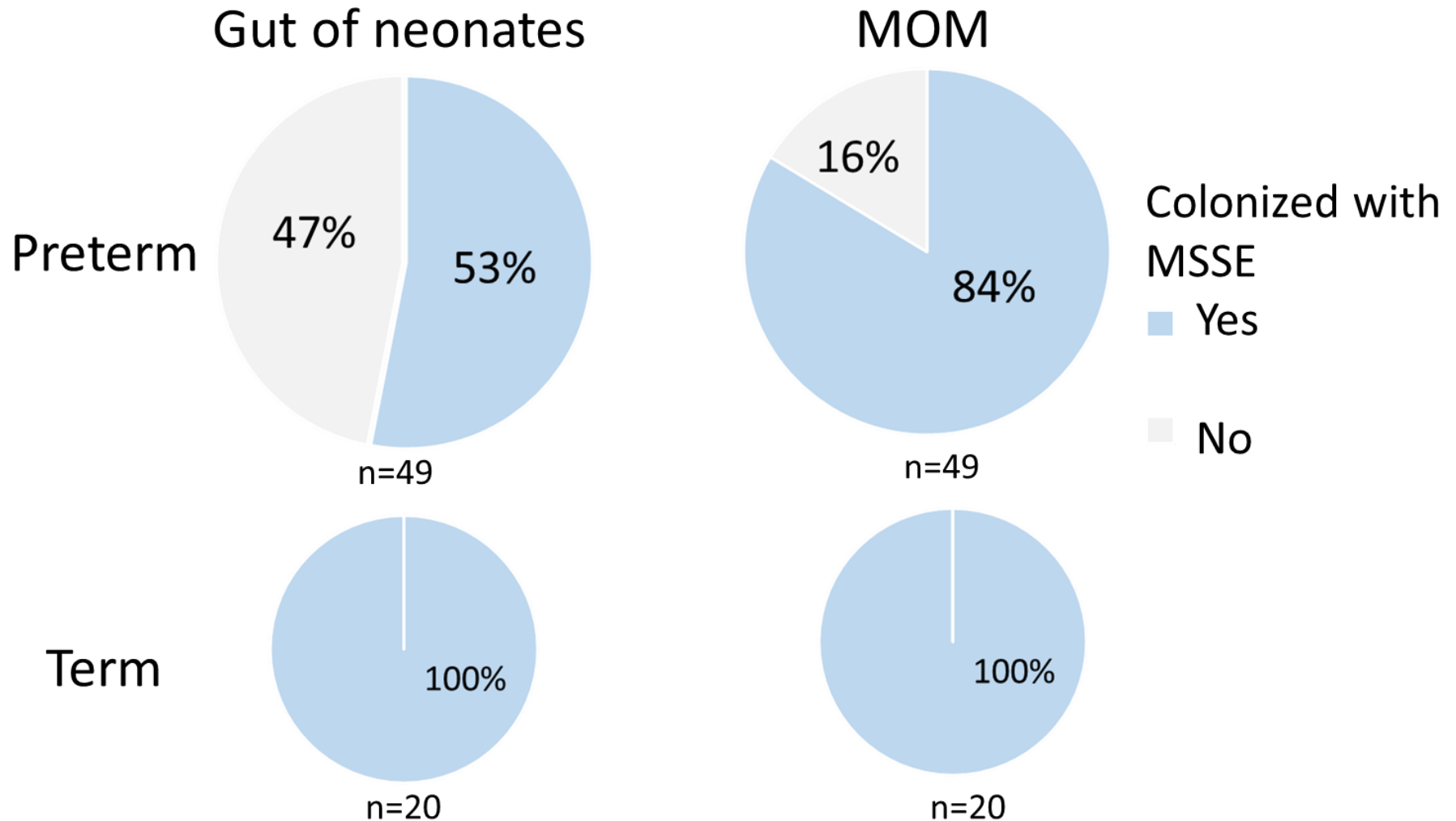
Multilocus variable-number tandem-repeat analysis (**MLVA**)

mecA

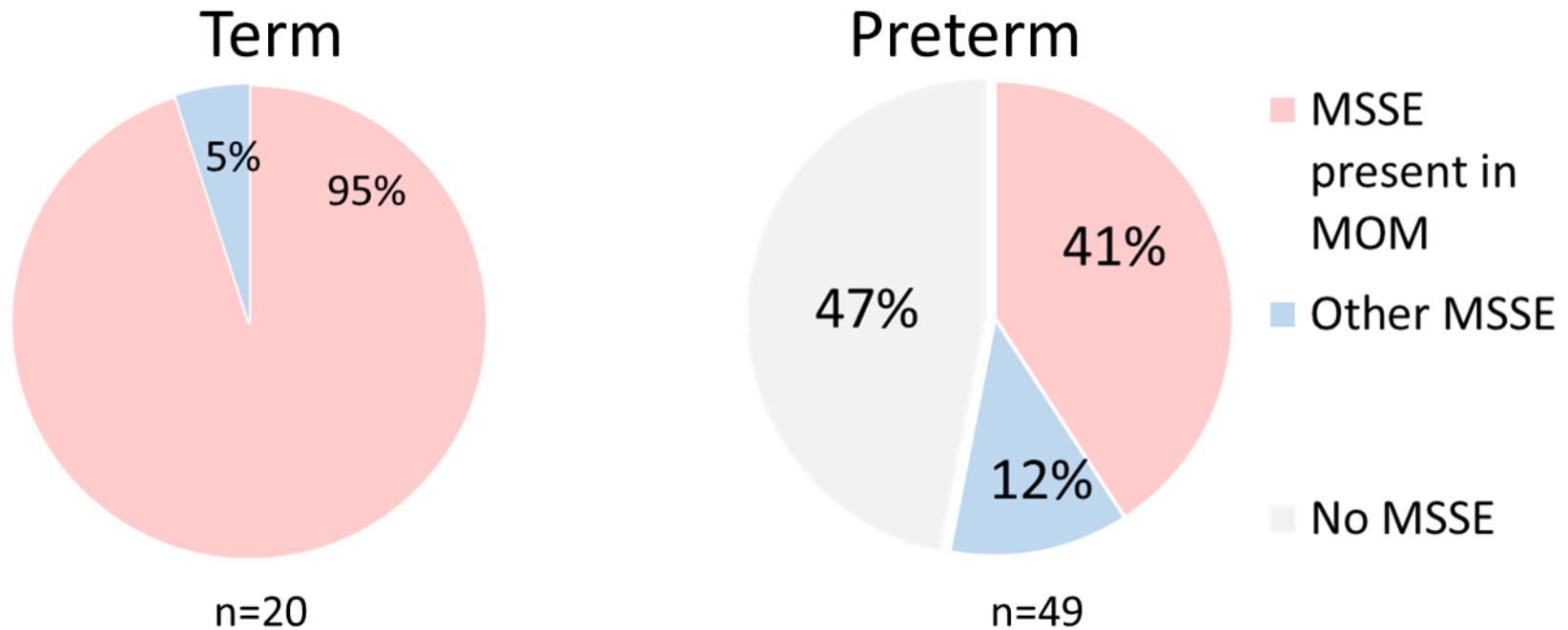
Neonates

	Preterm neonates (n=49)	Term neonates (n=20)
Gestational age (median)	28 weeks	40 weeks
Birth weight (median)	1.15 kg	3.65 kg
Exclusively MOM-fed	6%	100%
Age at initiation of MOM-feeding (median)	2 days	0 days
Cumulative % of MOM of total enteral feeds (median)		
0-3 days	28%	100%
0-7 days	77%	100%
0-14 days	95%	100%
0-21 days	97%	100%

MSSE in neonates & mothers



Colonization of gut of neonates with MSSE present in MOM



Median (IQR) age at colonization with MSSE present in MOM:

2 (1-6) days

vs

15.5 (11-21)

($p < 0.001$)

MOM – mother's own milk

MSSE – *mecA*-negative *S. epidermidis*

Factors associated with gut colonization with MSSE present in MOM in preterm neonates

Cox proportional hazards regression with Firth's penalized likelihood

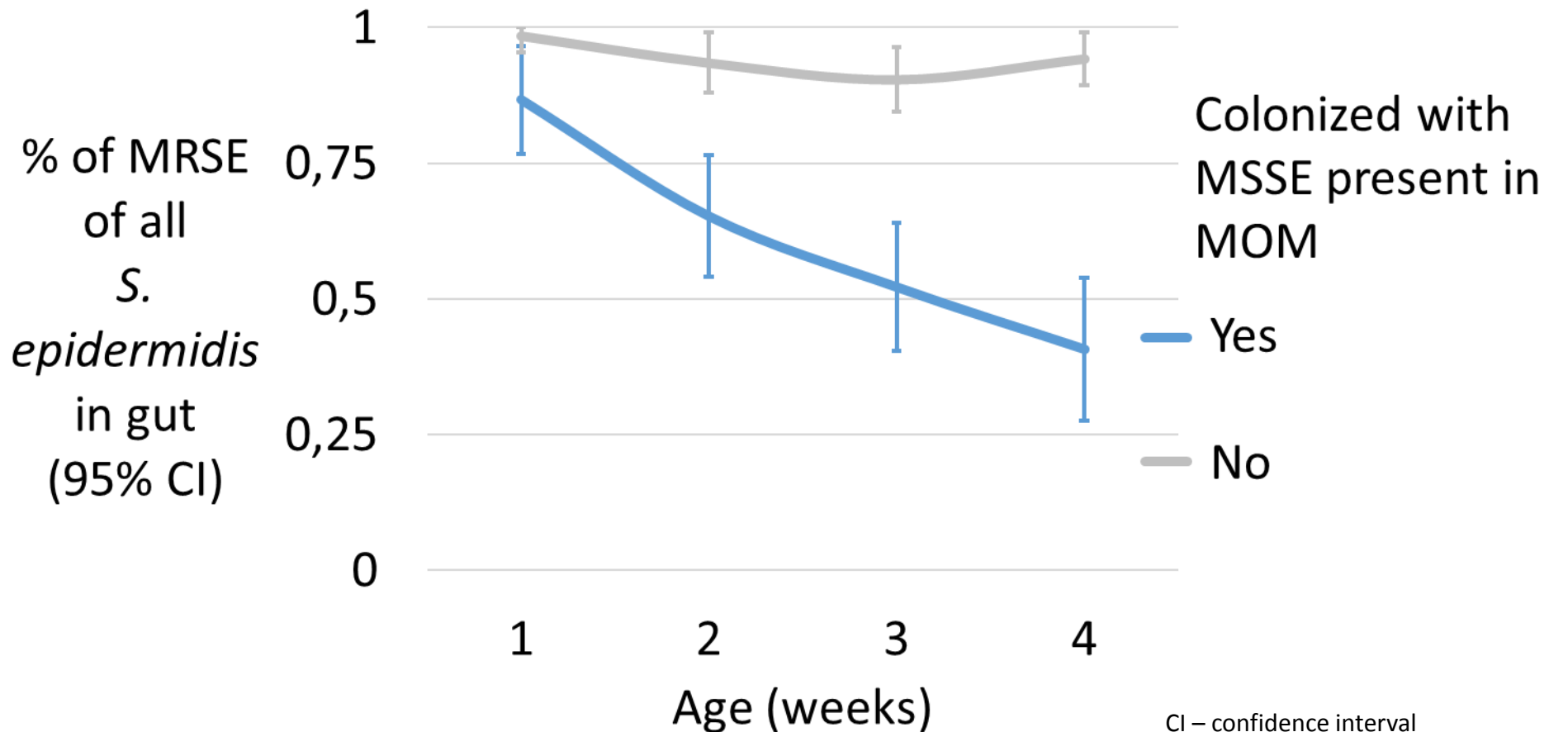
	Hazard ratio (95% CI)	p-value
Daily intake of CoNS from MOM (10^6 cfu)	1.006 (1.00-1.01)	0.049
Proportion of <i>mecA</i> -positive <i>S. epidermidis</i> or <i>S. haemolyticus</i> strains spreading in NICU and causing LOS among all staphylococci in gut	0.09 (0.01-0.49)	0.004

Not associated with gut colonization with MSSE present in MOM

- gestational age, birth weight, delivery mode
- treatment with antibiotics
- amount of enteral feeds (mL)
- count of CoNS in MOM (cfu/mL)

cfu – colony forming unit
CI – confidence interval
CoNS – coagulase-negative staphylococci
LOS – late-onset sepsis
MOM – mother's own milk
MSSE – *mecA*-negative *S. epidermidis*

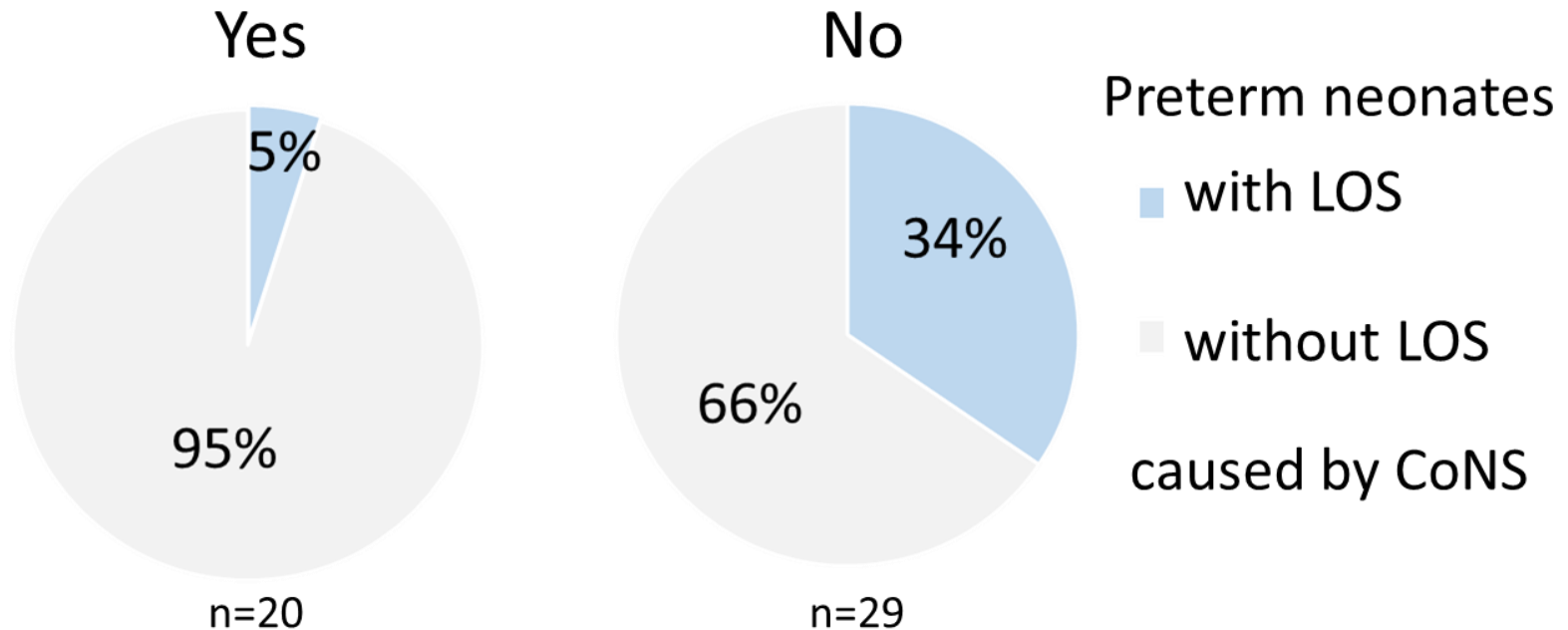
Proportion of MRSE among *S. epidermidis* in gut of preterm neonates colonized with MSSE present in MOM



CI – confidence interval
MOM – mother’s own milk
MRSE – *mecA*-positive *S. epidermidis*
MSSE – *mecA*-negative *S. epidermidis*

Colonization with MSSE present in MOM & late-onset sepsis caused by CoNS

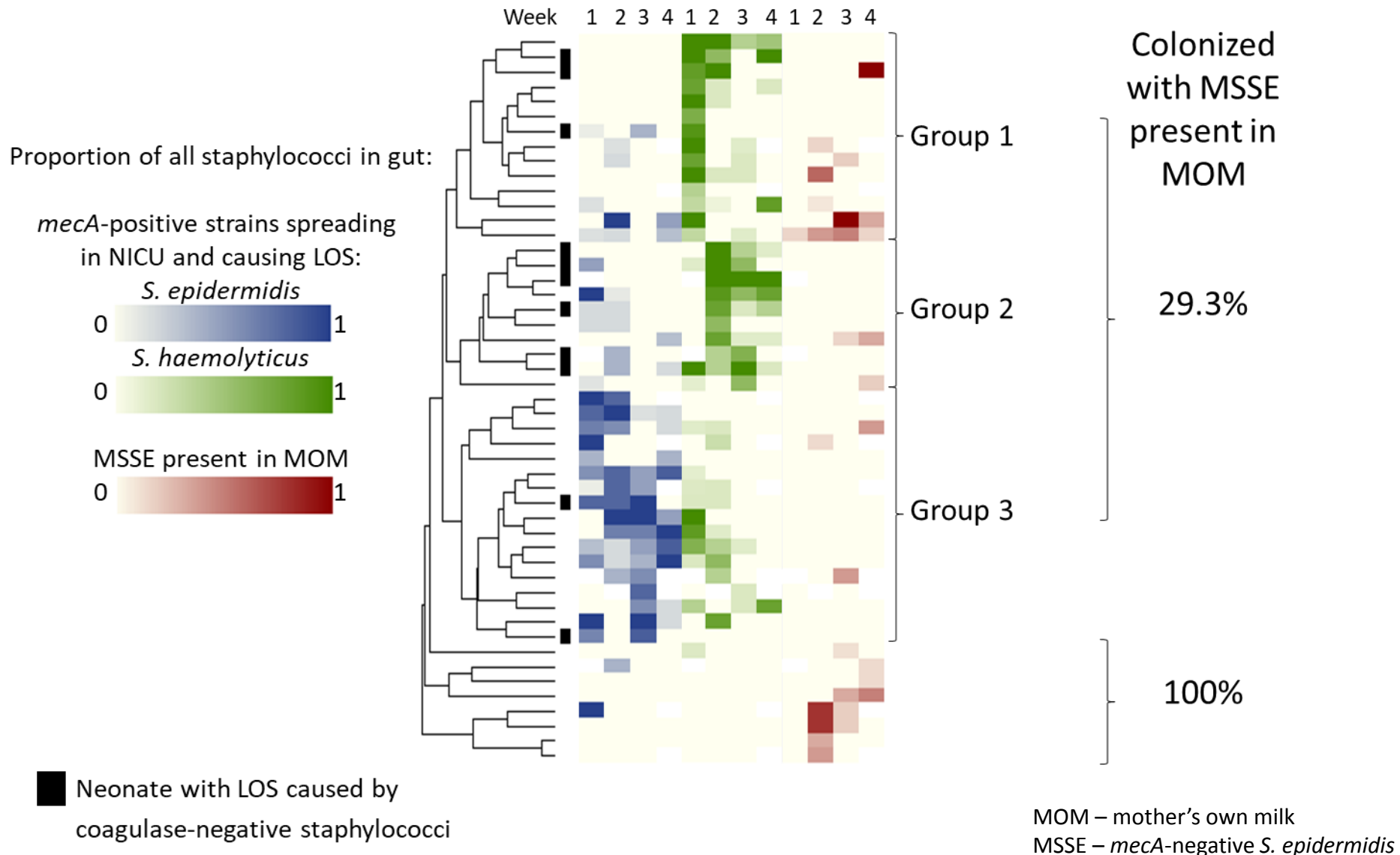
Preterm neonates colonized with MSSE present in MOM:




Median (IQR) at the onset of LOS caused by CoNS 8 (5-14) days.

CoNS – coagulase-negative staphylococci
LOS – late-onset sepsis
MOM – mother's own milk
MSSE – *mecA*-negative *S. epidermidis*

Gut colonization dynamics in preterm neonates



Conclusion

- Larger proportion of unpasteurized MOM in enteral feeds
 - Prevention of colonization of gut with *mecA*-positive staphylococcal strains spreading in NICU
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- Promote gut colonization with MSSE present in MOM
 - Reduce the abundance of MRSE in gut
 - May reduce the risk of late-onset sepsis

MOM – mother's own milk
MRSE – *mecA*-positive *S. epidermidis*
MSSE – *mecA*-negative *S. epidermidis*

Acknowledgements

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