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Survival of the littlest: improving preterm outcomes through metabolomics and microsampling

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Stellingen (Propositions)

Behorende bij het proefschrift

Survival of the Littlest:

Improving Preterm Outcomes through Metabolomics and Microsampling

1. A central clinical challenge in preterm neonatal care lies in balancing the iatrogenic risks of unnecessary interventions against the potentially fatal consequences of delayed diagnosis; resolving this dilemma requires population-specific research that enables early and accurate diagnosis, which is ethically contingent upon low-burden sampling approaches. (*this thesis*)
2. The disease-healthy control paradigm limits the clinical relevance of biomarker research in preterm neonatal care, because treatment decisions hinge on distinguishing true pathology from suspicion-driven cases with identical non-specific signs; this distinction must take methodological primacy to achieve translational success. (*this thesis*)
3. Aggregate analyses show biological variation but cannot guide care; stratified analyses by sex, gestational age, clinical phenotype, and risk strata are indispensable for converting population-level data into patient-specific treatment decisions that define precision care in preterm neonates. (*this thesis*)
4. VAMS is a promising alternative to DBS sampling; however, its widespread clinical implementation requires robust standardization of pre-analytical procedures, class-specific analytical validation, demonstrated stability under realistic conditions, predictable concordance with reference matrices, and operator-independent performance. (*this thesis*)
5. To build a more comprehensive molecular profile of sepsis, metabolomics should be integrated with other omics modalities (*Baizhanova et al. Computational and Structural Biotechnology Journal. 2025*). While multi-omics integration may enhance mechanistic understanding, its clinical feasibility in preterm care remains limited; within the constraints of minimal sampling, rapid turnaround, and ethical proportionality, metabolomics tailored to microsampling provides a more pragmatic and cost-effective foundation for timely clinical decision-making.
6. In comparison to DBS, VAMS offers the advantage of overcoming issues related to the haematocrit, the volume of the blood spotted on the filter paper, and the sample homogeneity (*Volani et al. Metabolites. 2023*). By focusing on analytical precision, the DBS-VAMS debate overlooks a fundamental clinical reality: both methods depend on lancet puncture and perpetuate the pain and tissue damage of repeated blood sampling in preterm neonates; integrating VAMS with microneedle-based sampling would represent enhanced clinical utility in preterm care.

7. Some studies reach opposite conclusions with respect to the same metabolites; this may be the result of differing biological fluids, gestational age, populations, or may indicate random variation due to small sample size (*Carter et al. Metabolites. 2019*). However, framing biofluid differences as mere inconsistency conflates biology with noise: distinct matrices interrogate orthogonal metabolic compartments and timescales. Opposing metabolite findings may therefore reflect true physiological context-dependence rather than failed reproducibility.
8. Inhibiting the inflammatory response associated with preterm labor using emerging anti-inflammatory therapeutics shows promise in preventing preterm birth (*Habelrih et al. Cytokine and Growth Factor Reviews. 2024*). However, since parturition itself is an inflammatory process, suppressing inflammation without etiological discrimination may delay birth while masking risks from unresolved upstream drivers.
9. Success is not final, failure is not fatal: it is the courage to continue that counts (*Winston Churchill*)
10. Where there's ruin, there's hope for a treasure (*Rumi*)

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Leiden, 26th February 2026