

# Necrotizing enterocolitis – growth, bone health and intestinal microbiota during childhood

AKADEMISK AVHANDLING

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademien, Göteborgs universitet kommer att offentligen försvaras i föreläsningssal **Tallen**, Drottning Silvias barnsjukhus, Sahlgrenska Universitetssjukhuset/Östra, den **14 juni 2023**, klockan **13:00**

av Amanda Magnusson

Fakultetsopponent: Tomas Wester, Professor, Karolinska Institutet, Stockholm, Sverige

## Avhandlingen baseras på följande delarbeten

- I. **Magnusson A**, Ahle M, Swolin-Eide D, Elfvin A, Andersson RE. Population-based study showed that necrotizing enterocolitis occurred in space-time clusters with a decreasing secular trend in Sweden. *Acta Paediatr.* 2017;106(7):1097-102.
- II. **Magnusson A**, Ahle M, Andersson RE, Swolin-Eide D, Elfvin A. Increased risk of rickets but not fractures during childhood and adolescence following necrotizing enterocolitis among children born preterm in Sweden. *Pediatr Res.* 2019;86(1):100-6.
- III. **Magnusson A**, Swolin-Eide D, Elfvin A. Body composition and bone mass among five-year-old survivors of necrotizing enterocolitis. *Pediatr Res.* 2023;93(4):924-31.
- IV. **Magnusson A**, Jabbari Shiadeh SM, Ardalan M, Swolin-Eide D, Elfvin A. Intestinal microbiota at five years of age among children born preterm with a history of necrotizing enterocolitis. In manuscript.

**SAHLGRENKA AKADEMIN**  
**INSTITUTIONEN FÖR KLINISKA VETENSKAPER**



# Necrotizing enterocolitis – growth, bone health and intestinal microbiota during childhood

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## **Abstract**

**Necrotizing enterocolitis (NEC)** is a dreaded gastrointestinal disease primarily affecting infants born preterm. Despite extensive research, NEC is still one of the most devastating diseases in neonatal intensive care. Improvements in neonatal care during the last decades have led to increased survival of more preterm infants, and thus, the group at risk to suffer from NEC has increased. Research is limited regarding if NEC in the neonatal period can affect growth, bone mass, body composition, fracture tendency and intestinal microbiota several years after the disease.

**The aim** of this thesis was to clarify if children born preterm with a history of NEC, had altered growth, body composition, bone mass, fracture tendency and intestinal microbiota during their childhood compared to preterm children without a history of NEC. Another aim was to investigate the occurrence of space-time clusters of NEC.

**This thesis** is based on the results of four different studies. Study I and II were retrospective cohort studies based on diagnostic codes from register data from children born between 1987 and 2009. Study I investigated the occurrence of space time-clustering of NEC, showing significant clustering on hospital level with a decreasing trend. Study II examined the risk for fractures and rickets in preterm children with and without a history of NEC, where a history of NEC appeared to increase the risk for rickets but not fractures. Study III and IV were prospective cohort studies of growth, bone mass, body composition and intestinal microbiota in five-year-old children born preterm with and without a history of NEC. Study III showed that NEC-survivors were shorter, had lower weight, affected bone parameters and lower fat mass than matched controls. Study IV revealed significantly lower alpha diversity in the intestinal microbiota in NEC-survivors compared to controls. Significant differences between NEC-cases and controls were seen in relative abundance on both bacterial genus and species level. The differences in microbiota diversity were especially pronounced in the surgically treated NEC group.

**In conclusion**, these studies suggest that a history of NEC may have an impact on growth, bone mass and fat mass several years after the disease. However, a history of NEC does not seem to increase the risk for fractures. The results also indicate that intestinal dysbiosis after NEC is long-lasting, especially if NEC was surgically treated. A decrease of clustering of NEC on hospital level over time may reflect the improved routines in neonatal care to minimize the transmission of contaminants between patients.

**Keywords:** skeleton, preterm, NEC, microbiota

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