



Infant Vitamin B12 Deficiency



Thanks to

The Infants and Families

The Committee

The Medical Faculty

Vestfold Hospital

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Terje Rootwelt



By Erik Wike Ljungblad

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Images Microsoft PowerPoint



- Background
- Aims
- Overview of methods and results
- Results from four papers
- Summary



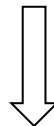
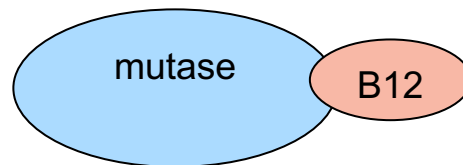
Photos by Linda Wike Ljungblad



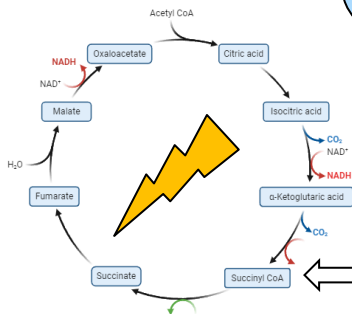
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methylmalonyl-CoA

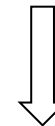
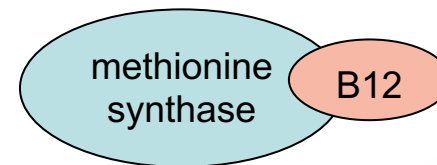
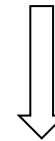


Succinyl-CoA

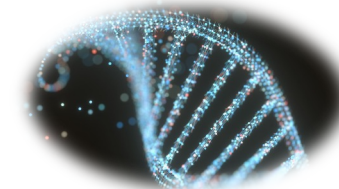
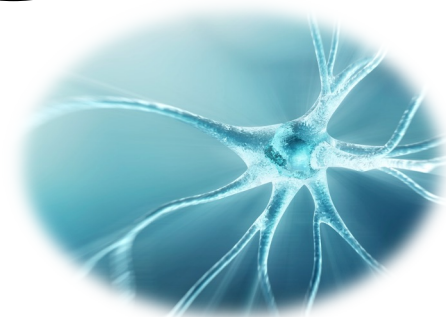


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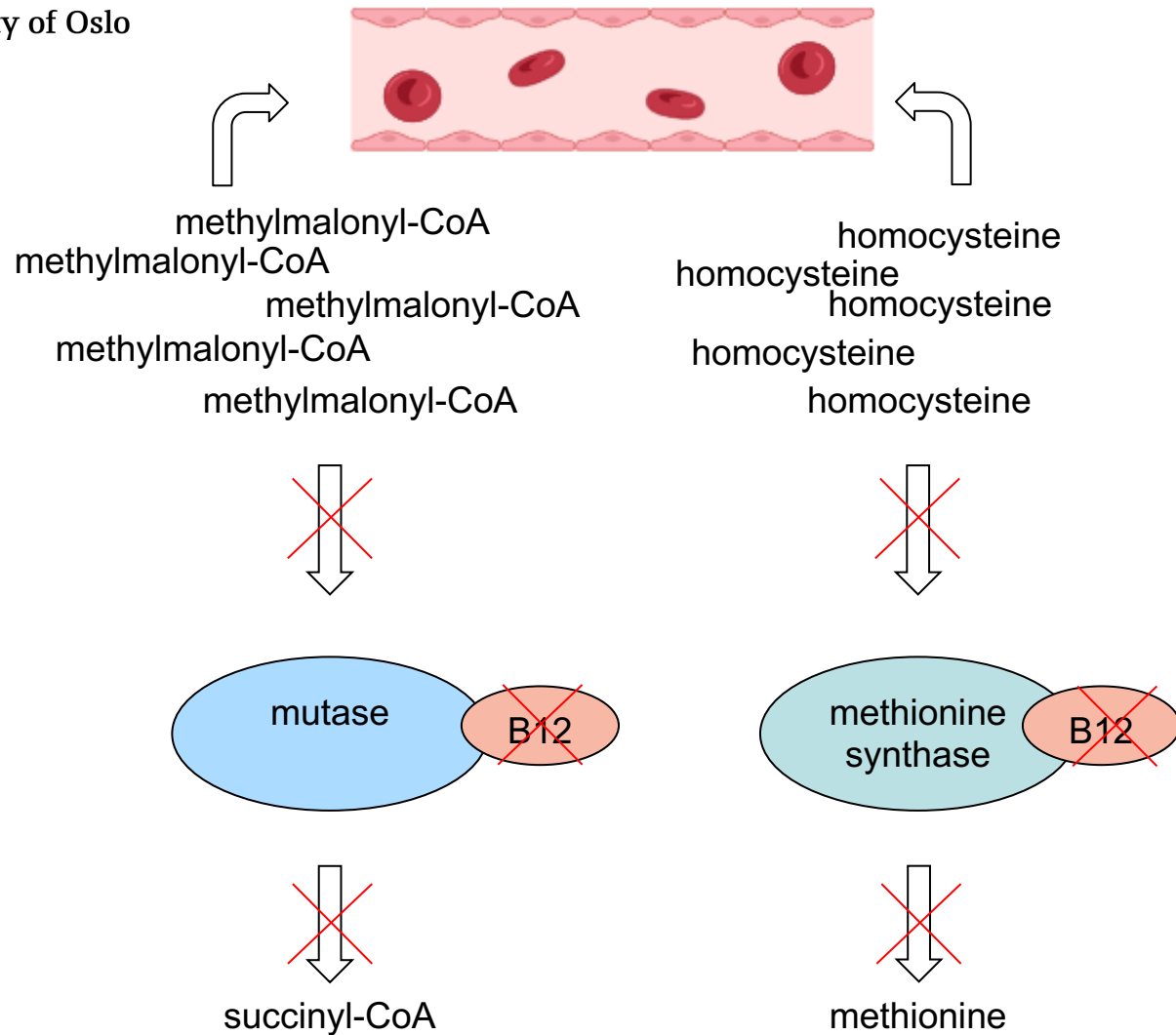
homocysteine

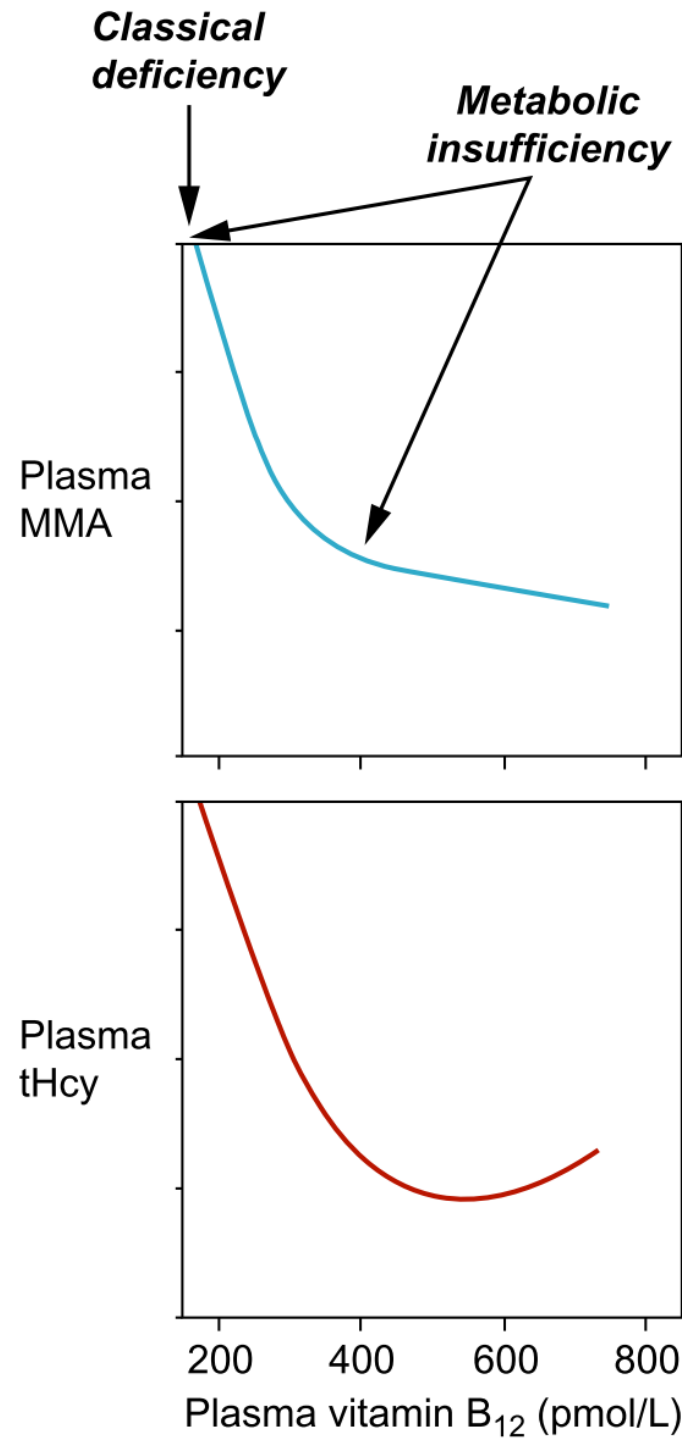
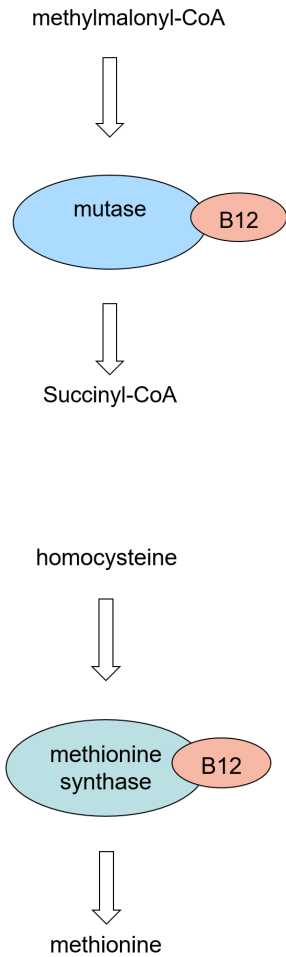


methionine

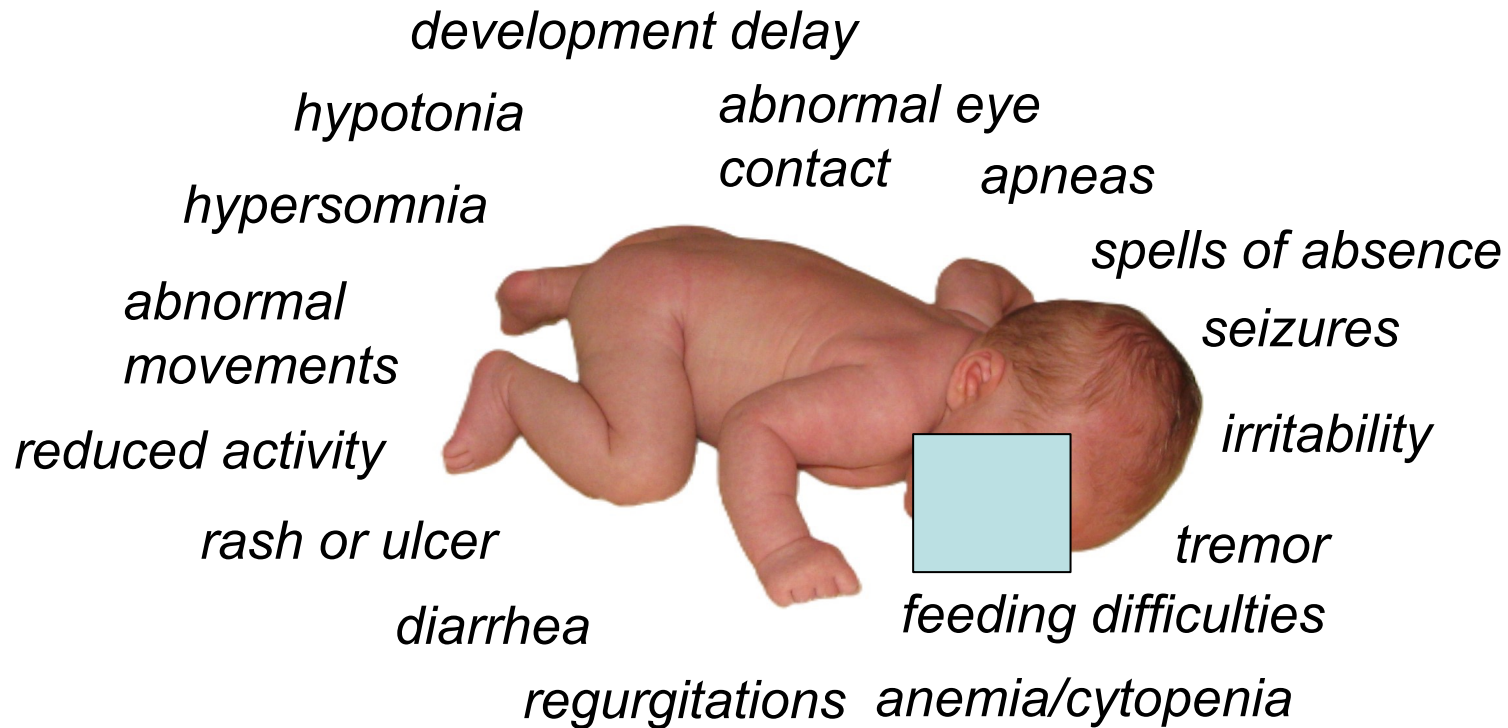


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Smith, Warren et al. (2018), see Figure 4 in the Thesis.



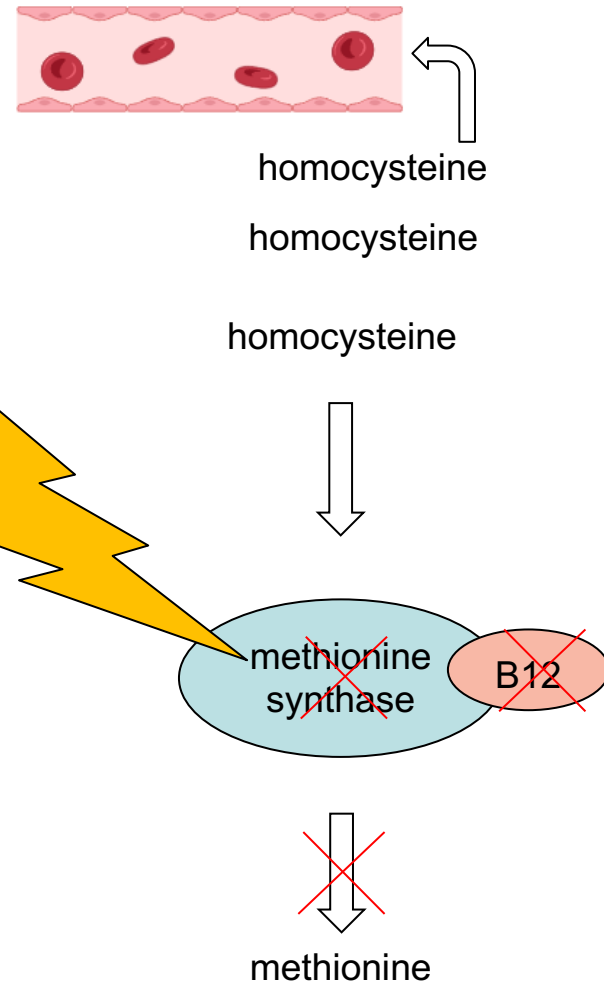
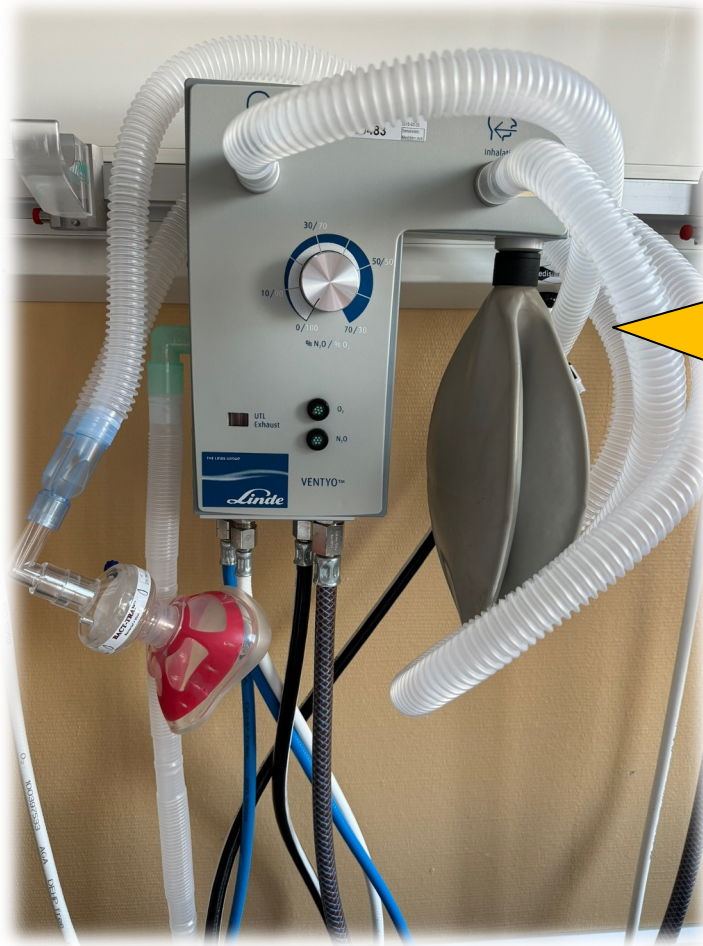
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ACTA PÆDIATRICA
[NURTURING THE CHILD]

Acta Paediatrica ISSN 0803-5253

REGULAR ARTICLE

B12 deficiency is common in infants and is accompanied by serious neurological symptoms

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²Department of Clinical Science, Paediatrics, Umeå University, Umeå, Sweden

Keywords
Apparent life-threatening event, Infant nutrition, Neurological symptoms, Seizures, Vitamin B12 deficiency

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ABSTRACT
Aim: Adverse neurological symptoms have been linked to vitamin B12 deficiency in infants. This explorative study described the clinical presentation associated with vitamin B12 deficiency in this age group.
Methods: The study comprised infants who were born between 2004 and 2012 and were tested for vitamin B12 levels after they were admitted to a hospital with neurological symptoms at less than one year of age. Vitamin B12 deficiency was defined as low cobalamin in serum and/or increased homocysteine and/or increased methylmalonate. It was diagnosed according to the applicable International Classification of Diseases, 10th revision, and recorded as vitamin B12 deficiency in the medical records. All information was retrieved from medical records and compared to symptomatic infants with normal levels.
Results: Of the 121 infants tested, 35 had vitamin B12 deficiency and 86 had normal levels.

NOVEMBER 3, 1962

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VITAMIN-B₁₂ DEFICIENCY IN INDIAN INFANTS

Clinical Syndrome

J. K. G. WEBB
M.A., B.M. Oxon, M.R.C.P.
PROFESSOR OF PÆDIATRICS

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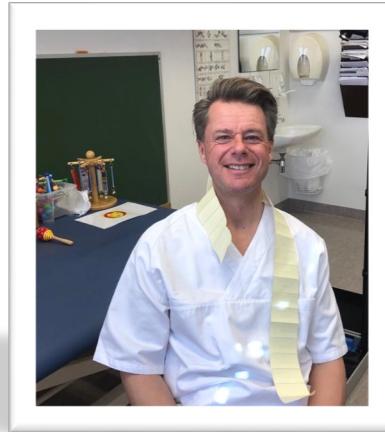
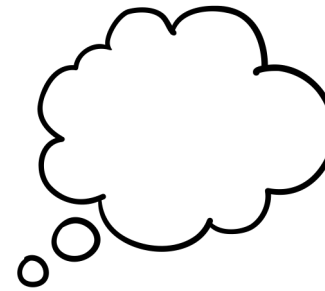
Common Metabolic Profile in Infants Indicating Impaired Cobalamin Status Responds to Cobalamin Supplementation

Anne-Lise Bjørke-Monsen, Ingrid Torsvik, Hege Sætran, Trond Markestad and Per Magne Ueland

Pediatrics 2008;122:83-91
DOI: 10.1542/peds.2007-2716

vitamin-B₁₂ content of breast-milk (Baker et al. 1962). This may lead to frank vitamin-B₁₂ deficiency in breast-fed infants.





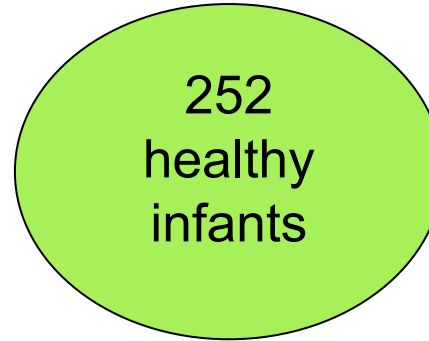
- How common is symptomatic vitamin B12 deficiency in infants?
- What are the symptoms?
- What are the risk factors?
- Can we predict it with newborn screening?



Birth



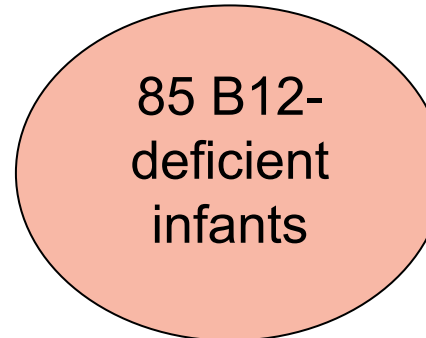
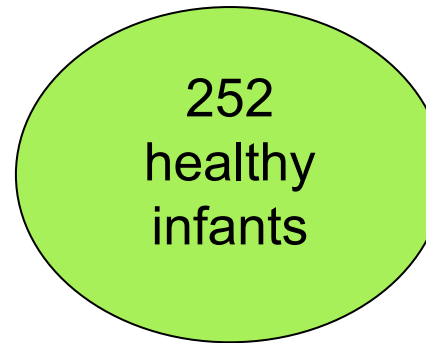
252
healthy
infants



Prospective
observational
study



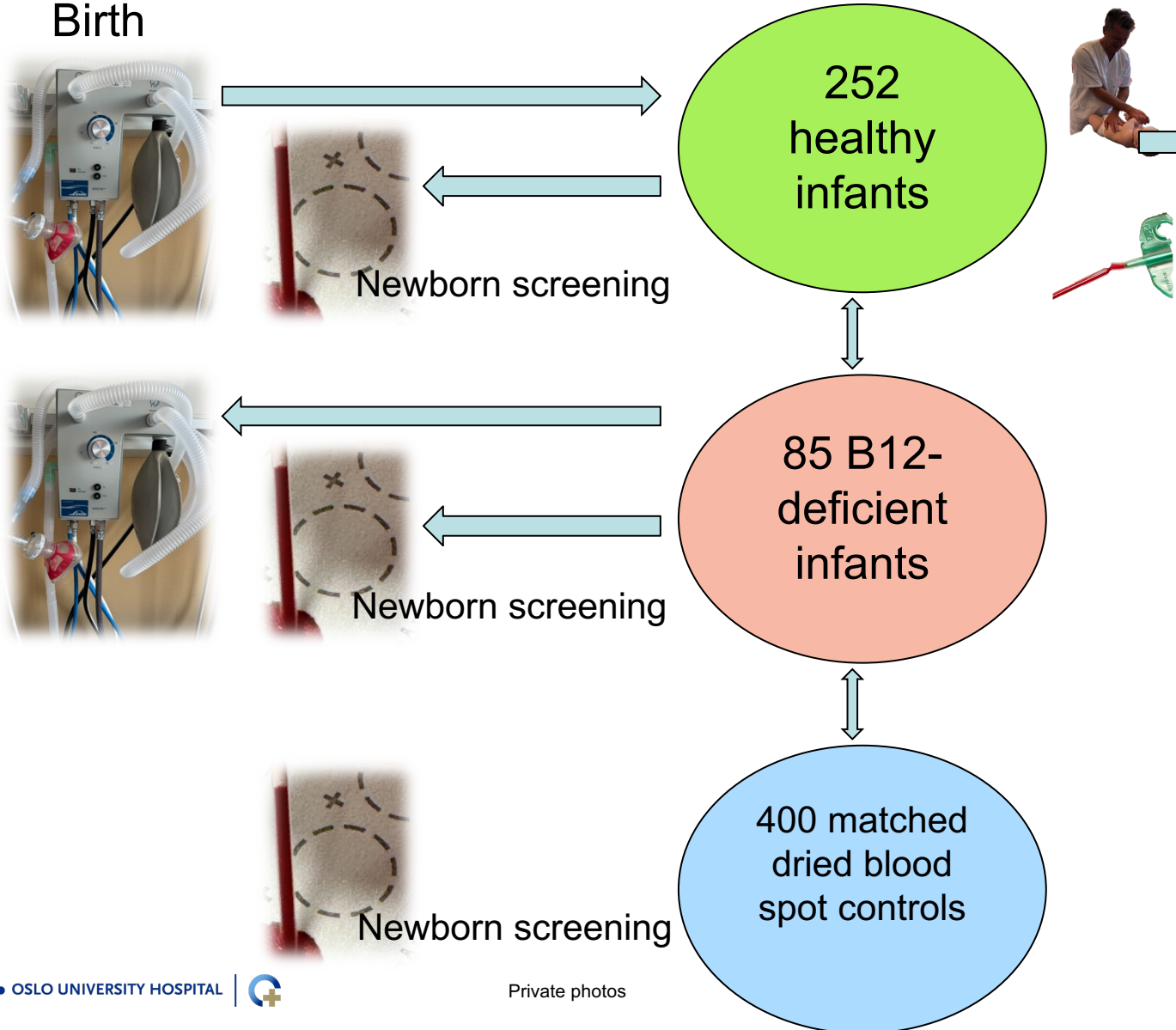
Birth



Case-control
study



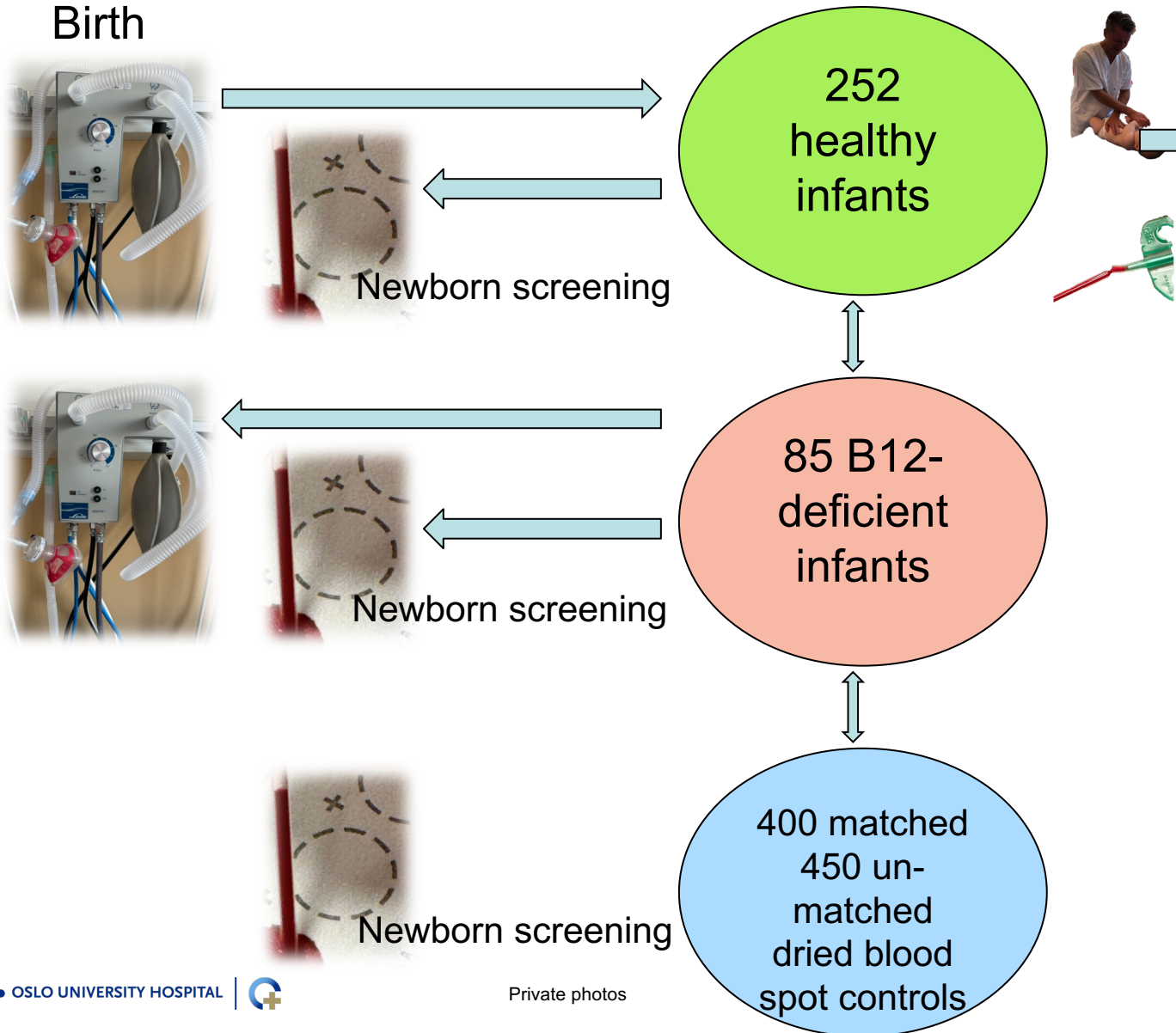
Birth

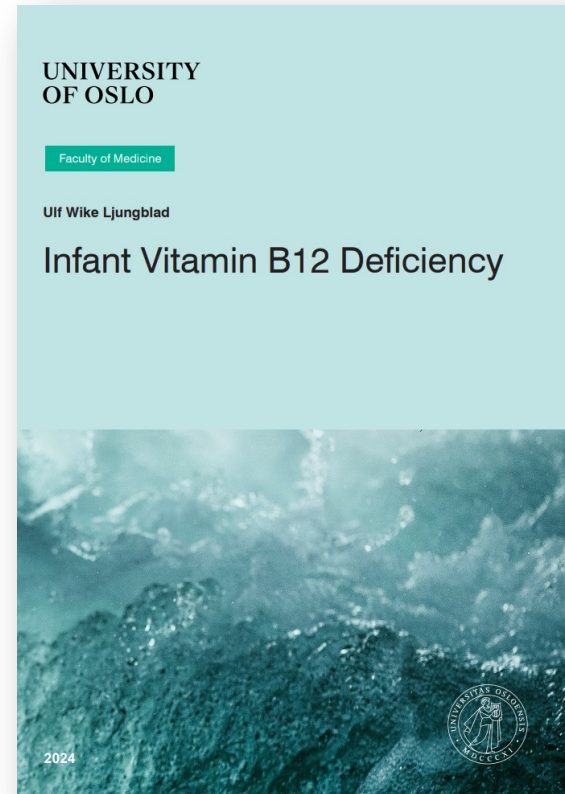
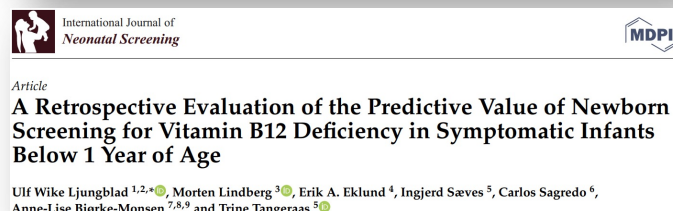
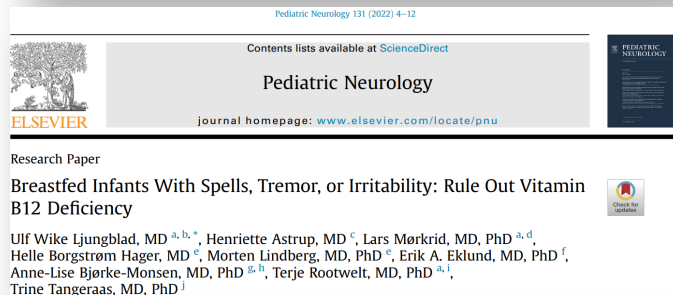
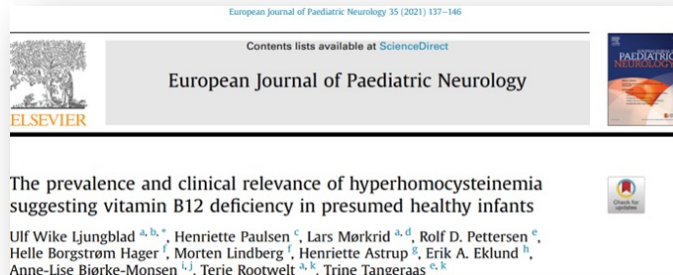


Case-control study



Birth





Paper 1

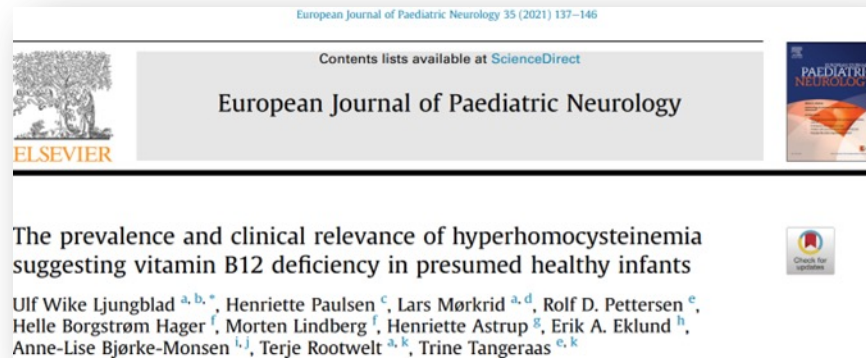
Explorative prospective observational study

252 infants 3-7 months



Photos by Henriette Paulsen

Paper 1



- 46% S-tHcy > 8 µmol/L
- Associations between S-tHcy > 8 µmol/L and tremor, parent-reported excessive sleep
- 10% had clinically relevant S-tHcy > 8 µmol/L suggesting B12 deficiency

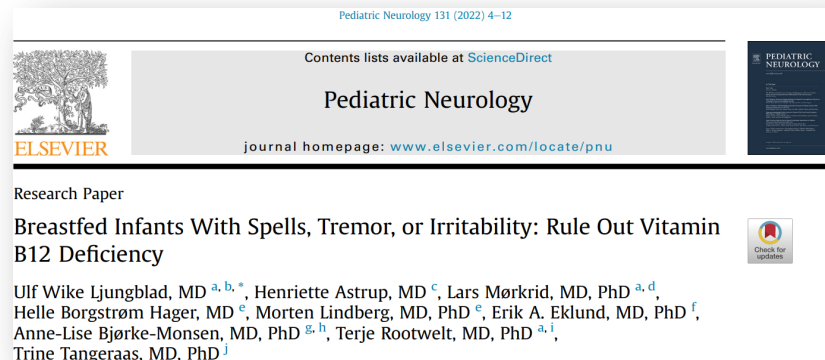


Paper 1

- Exclusive breastfeeding increased the odds three times for tHcy $>8 \mu\text{mol/L}$
- No increased risk for tHcy $>8 \mu\text{mol/L}$ for infants born preterm or small for gestational age



Paper 2



- Retrospective case-control study
- 85 cases
- 252 controls

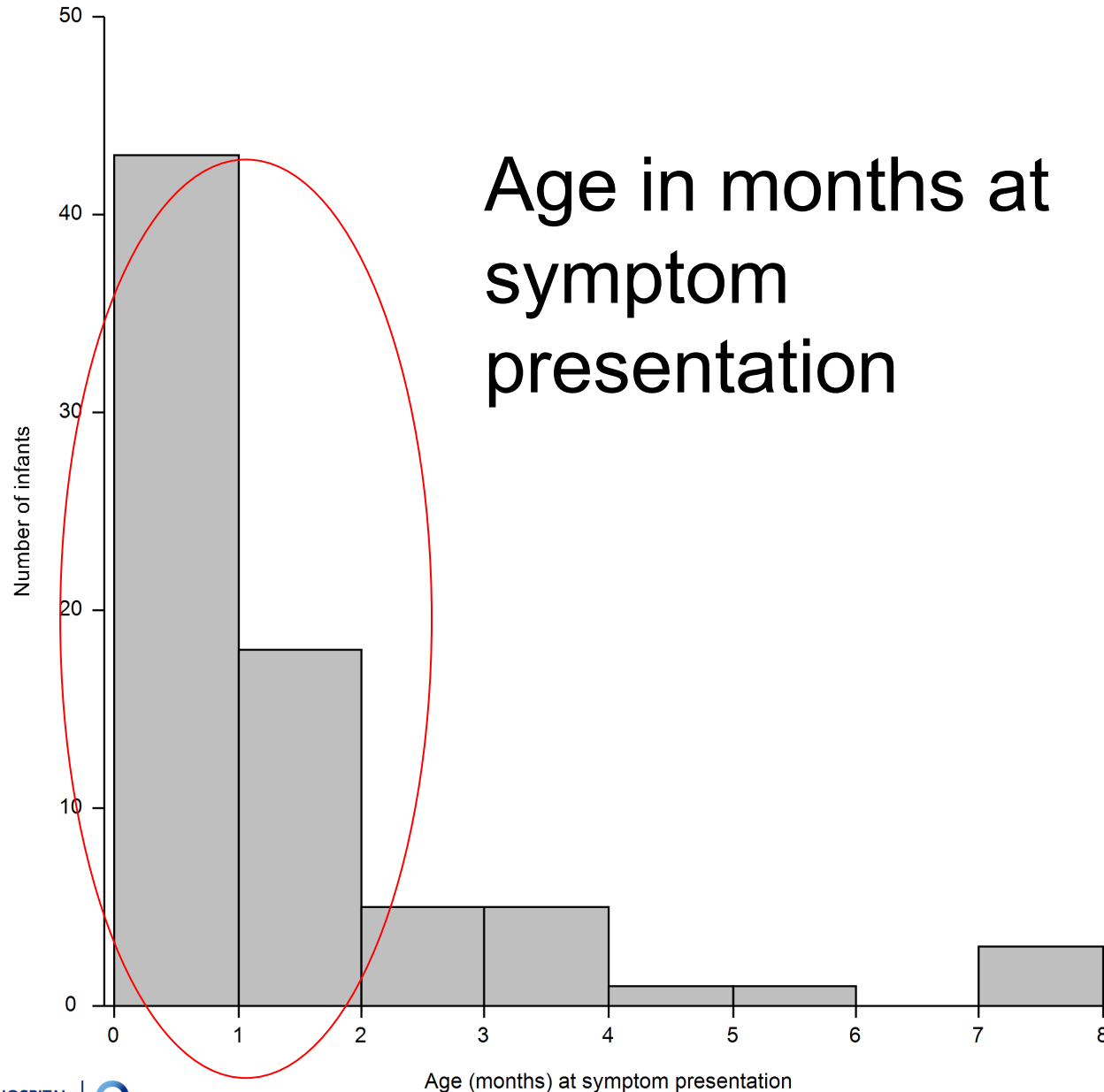
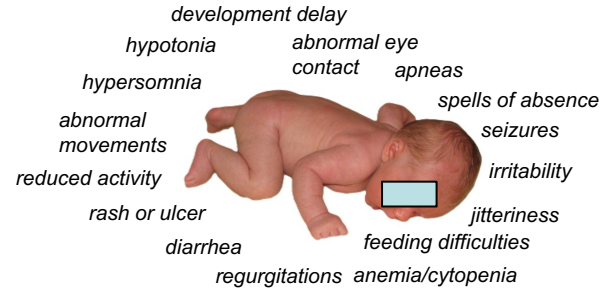


Figure 2 in Paper 2



Symptom or Finding	Cases n=85	Controls n=252	p
Spells (motor seizures, apneas, or absences)	30/76 (39%)	0/250 (0 %)	<0.001
Tremor	21/72 (29%)	13/250 (5.2%)	<0.001
Irritability	12/68 (18%)	19/252 (7.5%)	0.012
Head-lag at pull-to-sit	26/53 (49%)	38/250 (15%)	<0.001
Abnormal eye contact	9/67 (13%)	0/250 (0 %)	<0.001

N=9 infants evaluated after newborn screening test results or due to family history of B12 deficiency are excluded



Paper 2

- No vegetarian mothers
- 25% reported earlier B12 deficiency
- Dose of nitrous oxide associated with tHcy and MMA at diagnosis
- Earlier referral age when the mother received nitrous oxide
- Exclusive breastfeeding a risk factor

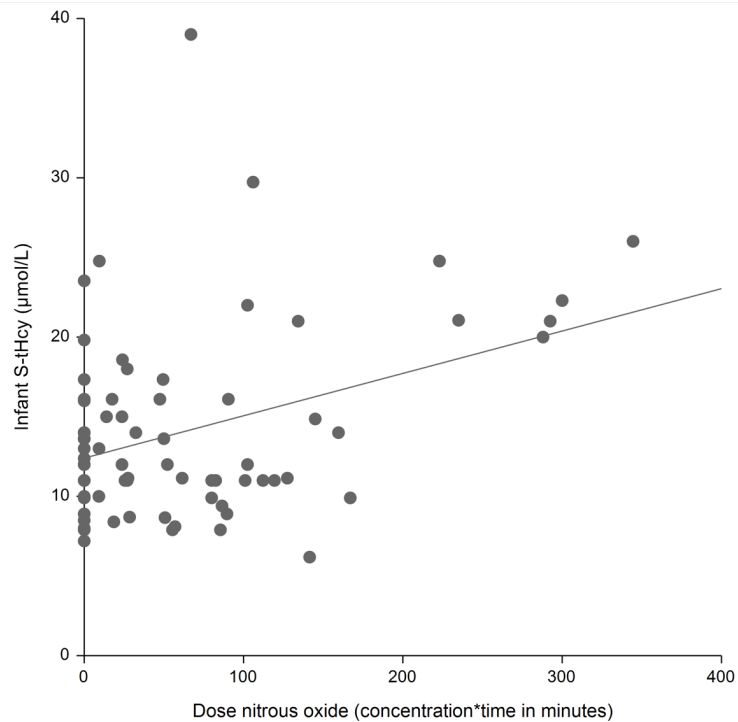


Figure 5 in Paper 2. Photos private.



months later





Paper 3



- Retrospective case-control study
- 85 cases, 252 clinical controls, and 400 dry-blood-spot-controls





Paper 3

- B12 deficient infants had higher markers of B12 deficiency at newborn screening
- The dose of nitrous oxide to the mother in labor was the strongest predictor for total homocysteine



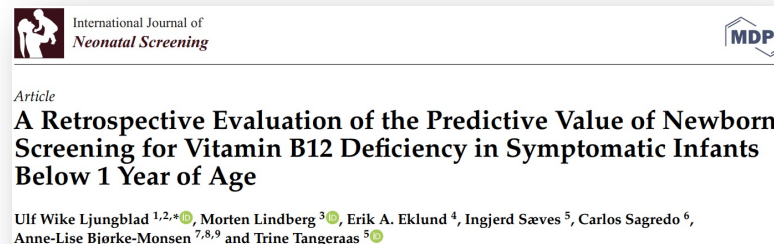
B12 deficient infants



Controls



Paper 4



- Retrospective case-control study
- 70 clinical cases, 646 matched controls and 434 un-matched controls





Paper 4

- Newborn screening failed to identify over 90% of infants with symptomatic B12 deficiency



Symptomatic B12
deficient infants

Controls



Vitamin B12 deficiency is common in infants



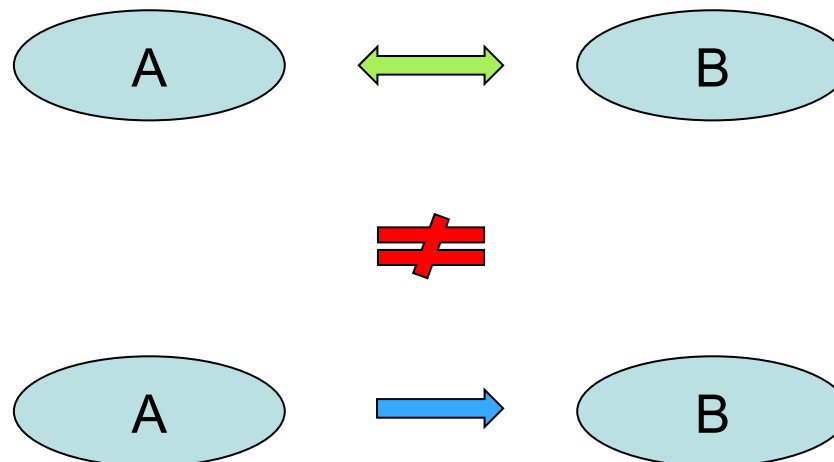
Vitamin B12 deficiency may present with serious, potentially life-threatening symptoms like spells of apneas and seizures



Nitrous oxide to the mother during labor may be a risk factor for infant B12 deficiency



Symptomatic infant B12 deficiency was missed on newborn screening in 90% of cases





Thank you for you attention!

