

Forskningsprojektet CP-EDIT Cerebral Palsy – Early Diagnosis and Intervention Trial

Topics

- ❖ CP prevention and early prediction
- ❖ Progress of the CP-EDIT trial
- ❖ Interim data
- ❖ Future implementation of an early diagnosis set-up

Disclosures

The presenter has previously or currently been involved in research contracts or advisory boards from:

Avexis

Novartis

PTC Therapeutics

Sarepta

TEVA (*dyskinetic CP*)

Quince Therapeutics

Research grants: Elsass Foundation, Rigshospitalet, Dagmar Marshalls foundation, Novo Nordisk Fonden, Danske Fysioterapeuters fond, Helsefonden, Rosalie Petersens fond, Dr. Louises børnehospitals forskningsfond, Vanførefonden

Why aim at early diagnosis of CP?

- ❖ Prevention rather than treatment

”Cure sometimes, treat often, comfort always”

- ❖ Early, precise diagnosis makes a difference

”Early diagnosis should be the standard of care because contemporary early interventions optimize neuroplasticity and functional outcomes”

- ❖ Individuals with CP should be offered the best possible treatment throughout life

Approaches vary in Denmark

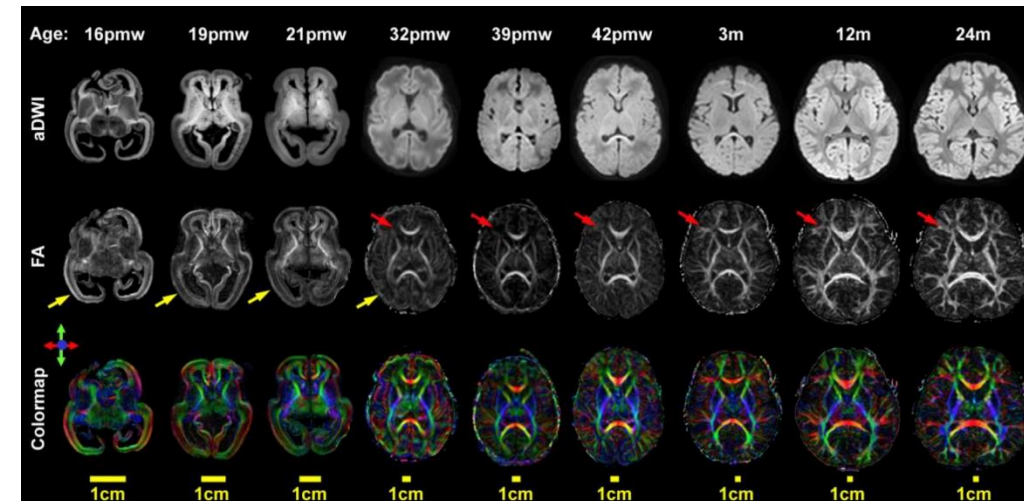
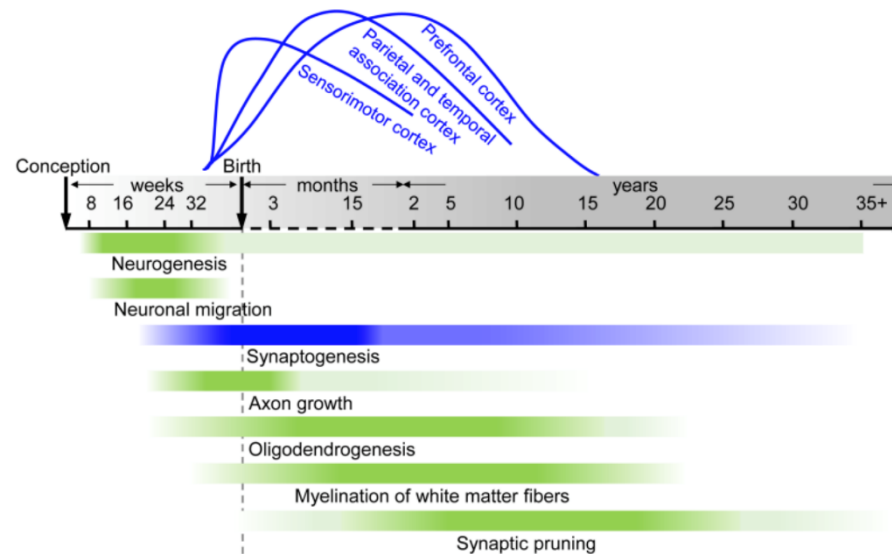
Early brain damage in children

-when do we suspect it?

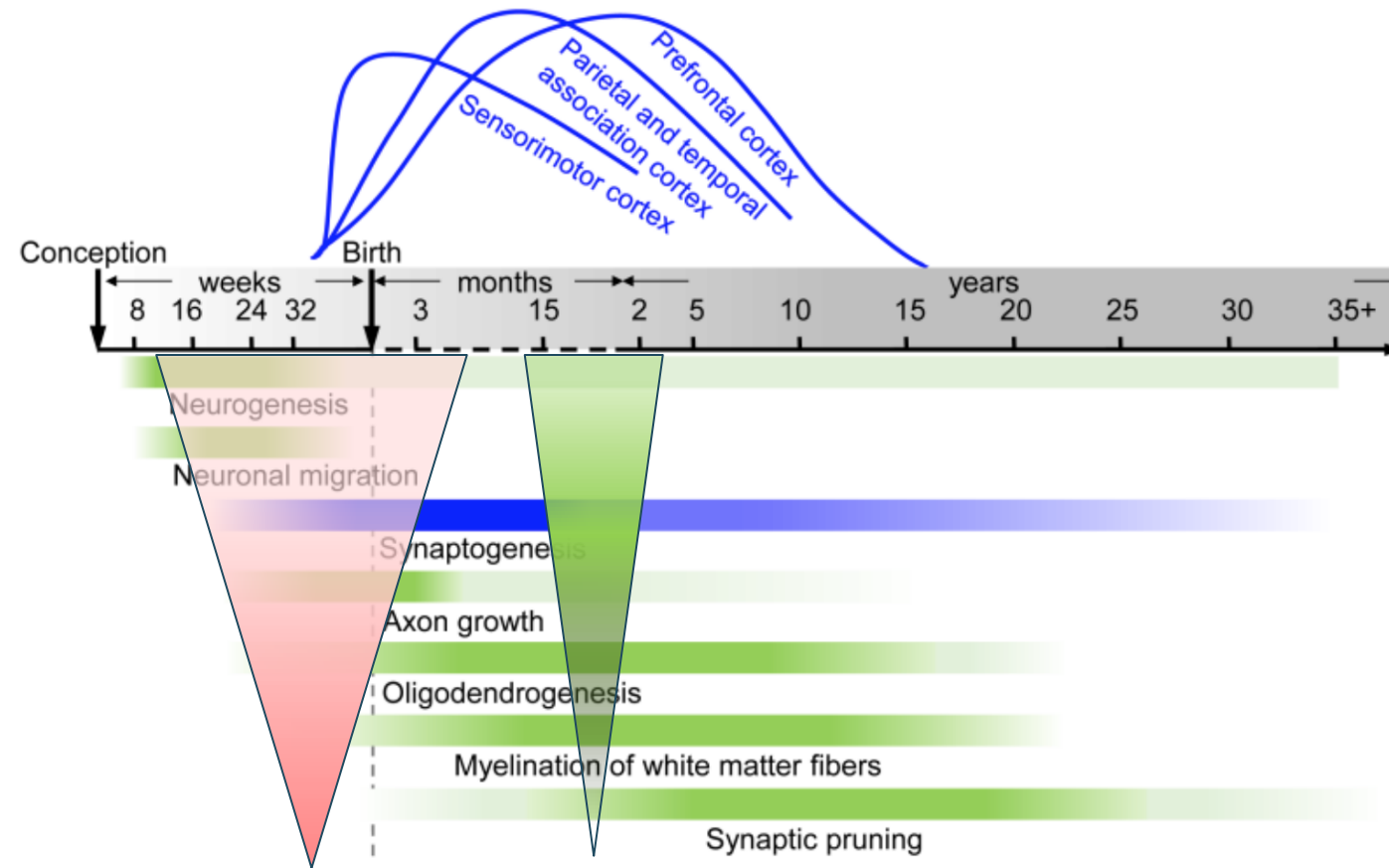
Deviation from normal development

Delayed motoric milestones

Imaging results



There is a window of opportunity for early intervention by early diagnosis



Cerebral injury CP diagnosis

Early diagnosis tools

Signs and symptoms of CP emerge and evolve before age 2 years

A combination of standardized tools should be used to predict risk in conjunction with clinical history

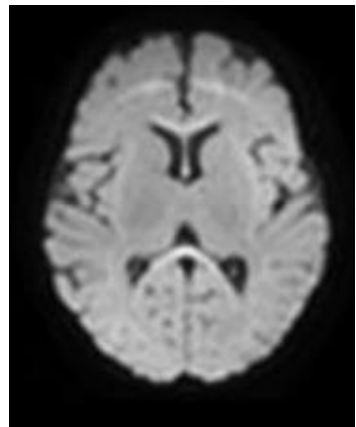
The best predictive tools vary according to age

Before age 5 months:

- Term-age MRI (86% sensitivity)
- Prectl's Qualitative Assessment of General Movements (GMA) (95% sensitivity)
- Hammersmith Infant Neurological Examination (HINE) (90% sensitivity)

After age 5 months:

- MRI (86% sensitivity)
- Parent reported Developmental Assessment of Young Children (83% sensitivity) or Alberta Infant Motor Scale (AIMS) (86% sensitivity)
- Hammersmith Infant Neurological Examination (HINE) (90% sensitivity)
- Hand assessment for infants (HAI)



Hammersmith Neonatal Neurological Examination Term and preterms at term age
Ricci D et al Early Hum Devel 2008 Page 1

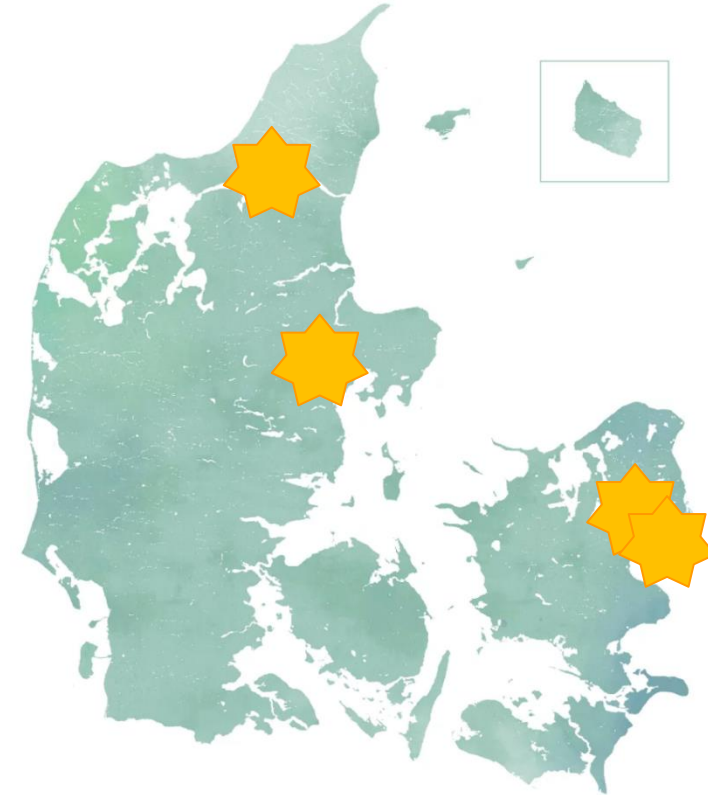
Patient Name	GA	ID	Date
DOB			
PROFICIE			
HINE REGION			
LEFT FLEXION			
LEFT EXTENSION			
RIGHT FLEXION			
RIGHT EXTENSION			
GRASP			
GRASP CONTROL			
GRASP LATER			
GRASP STRENGTH			
GRASP RELEASE			

The CP-EDIT study

- 4 sites: Rigshospitalet, Herlev, Aarhus, Aalborg
- At each site physiotherapists, occupational therapists, neonatologists, neuropaediatricians
- Three phd studies
- 500 children can be screened
- 160 children can be followed until age 2 years

Steering group

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Gija Rackauskaite
Lene Weber
Mette Johansen
Signe Vandal Pedersen



Cerebral Palsy – Early Diagnosis and Intervention Trial: protocol for the prospective multicentre CP-EDIT study with focus on diagnosis, prognostic factors, and intervention

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Abstract
Background Early diagnosis of cerebral palsy (CP) is important to enable intervention at a time when neuroplasticity is at its highest. Current mean age at diagnosis is 13 months in Denmark. Recent research has documented that an early-diagnosis set-up can lower diagnostic age in high-risk infants. The aim of the current study is to lower diagnostic age of CP regardless of neonatal risk factors. Additionally, we want to investigate if an early intervention program added to standard care is superior to standard care alone.
Methods The current multicentre study CP-EDIT (Early Diagnosis and Intervention Trial) with the GO-PLAY intervention included (Goal Oriented Parental, supported home Activity program), aims at testing the feasibility of an early diagnosis set-up and the GO-PLAY early intervention. CP-EDIT is a prospective cohort study, consecutively assessing approximately 500 infants at risk of CP. We will systematically collect data at inclusion (age 3–11 months) and follow a subset of participants (n = 300) with CP or at high risk of CP until the age of two years. The GO-PLAY early intervention will be tested in 80 infants with CP or high risk of CP.
Focus is on eight areas related to implementation and perspectives of the families: early cerebral magnetic resonance imaging (MRI), early genetic testing, implementation of the General Movements Assessment method, analysis of the GO-PLAY early intervention, parental perspective of early intervention and early diagnosis, early prediction of CP, and comparative analysis of the Hand Assessment for Infants, Hammermith Infant Neurological Examination, MRI, and the General Movements method.

The upcoming CP-EDIT study – the aims

- MRI.** To evaluate early diagnostic MR imaging of participants in cohort II. These participants may later be labelled definite CP, high risk of CP, unclear or definitely not CP.
- Genetics.** To evaluate early genomic testing of participants in cohort III, which have definite CP or high risk of CP.
- GMA implementation.** To analyse implementation of GMA.
- Prediction of CP.** To determine the clinical utility of the HINE, HAI, and GMA to predict a confirmed diagnosis of CP at 24 months
- GMA vs. HAI.** To compare diagnostic accuracy of GMA and HAI in children with hand asymmetry.
- GO-PLAY.** To analyse the effect of the GO-PLAY intervention with early family-centred set-up for children with definite or high risk of CP. For 6 months these participants will receive regular follow-up in the home of the family with physiotherapist and occupational therapist will monitor and strengthen goal-based training.
- Parents perspective on intervention.** To analyse parents' perspectives regarding barriers and facilitators involved in early intervention.
- Parents perspective on early diagnosis.** To analyse interview of parents' perspectives of gains and concerns when having an early diagnosis of high risk of CP.

The CP-EDIT study –inclusion criteria

- We aim at improving early diagnosis for both newborns and infants with risk of CP
- Inclusion period April 2023 – June 2025



CP-EDIT



Inklusionskriterier for neonatale kandidater

- GA < 32 eller FV < 1500 g samt neurologisk klinisk bekymring
- Moderat til alvorlig hjerneskade (IVH grad 3-4, PVL, neonatalt stroke, term HIE eller anden signifikant neurologisk lidelse)
- Anamnese med alvorligt forløb eller neurologiske risikofaktorer (neonatale kramper, ECMO, meningitis, kernikterus, alvorlig hypoglykæmi eller neurologiske risikofaktorer som malformation af hjerne eller øget tonus)
- Forældres bekymring og en af ovenstående

Opfylder din patient en af kriterierne? Send gerne en henvendelse til cp.rigshospitalet@regionh.dk for Østdanmark og cpedit@rn.dk for Vestdanmark



CP-EDIT

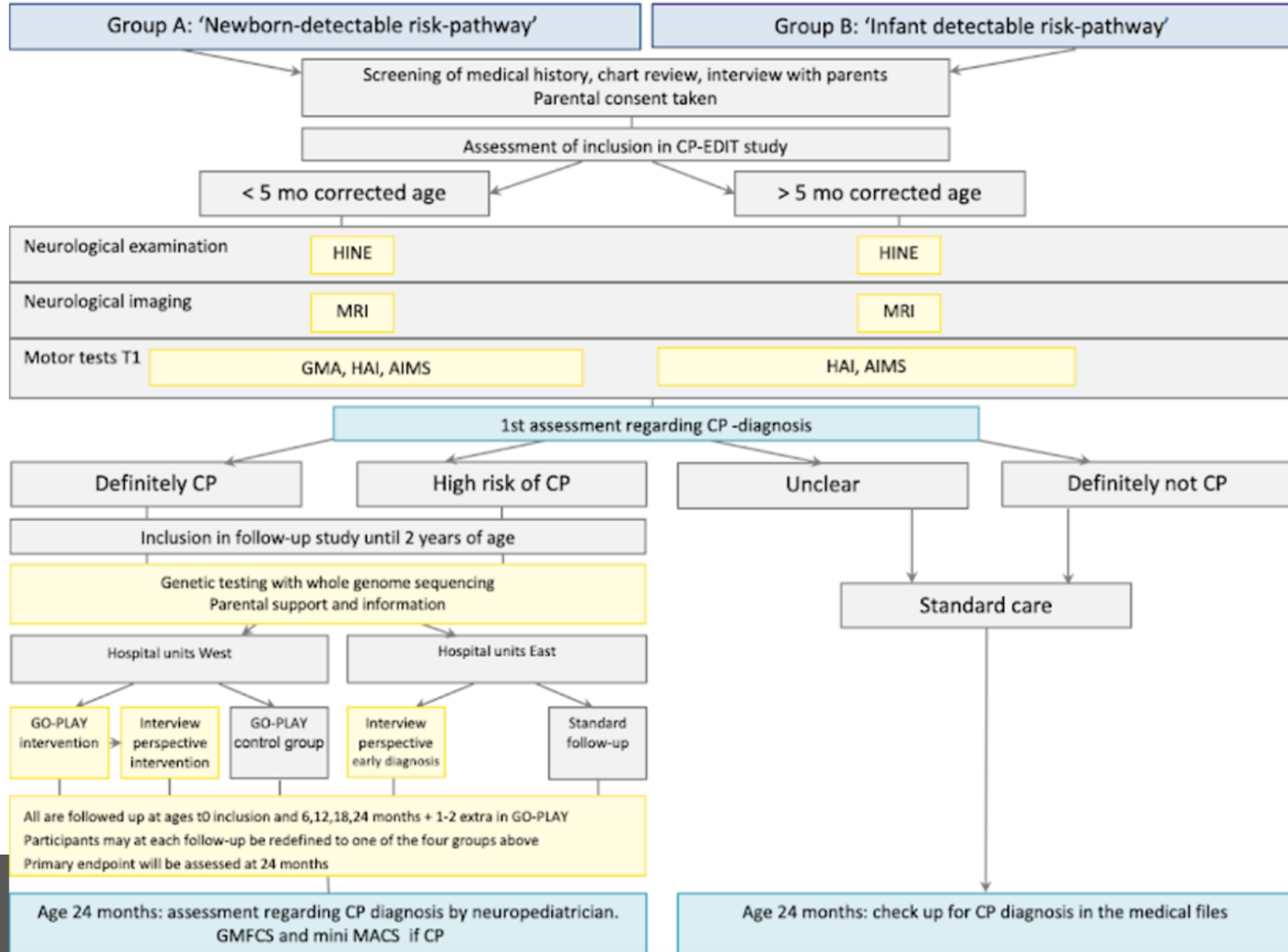


Inklusionskriterier for kandidater <12 mdr

- Asymmetrisk håndfunktion
- Kan ikke sidde selvstændigt 9 mdr gammel
- Spidsfod eller står på tæer
- Anamnese med alvorligt forløb eller neurologiske risikofaktorer (neonatale kramper, ECMO, meningitis, kernikterus, alvorlig hypoglykæmi eller neurologiske risikofaktorer som malformation af hjerne eller øget tonus)
- Forældres bekymring og en af ovenstående

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The CP-EDIT study flow



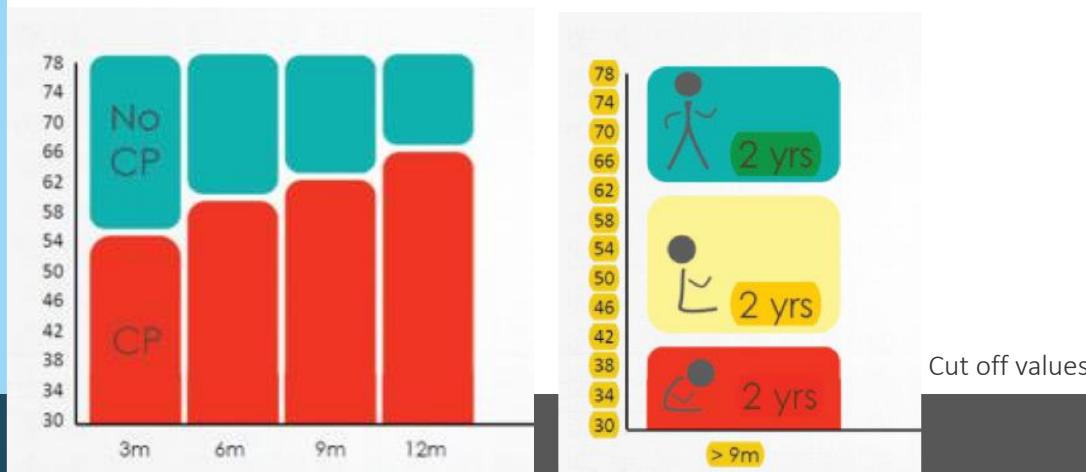
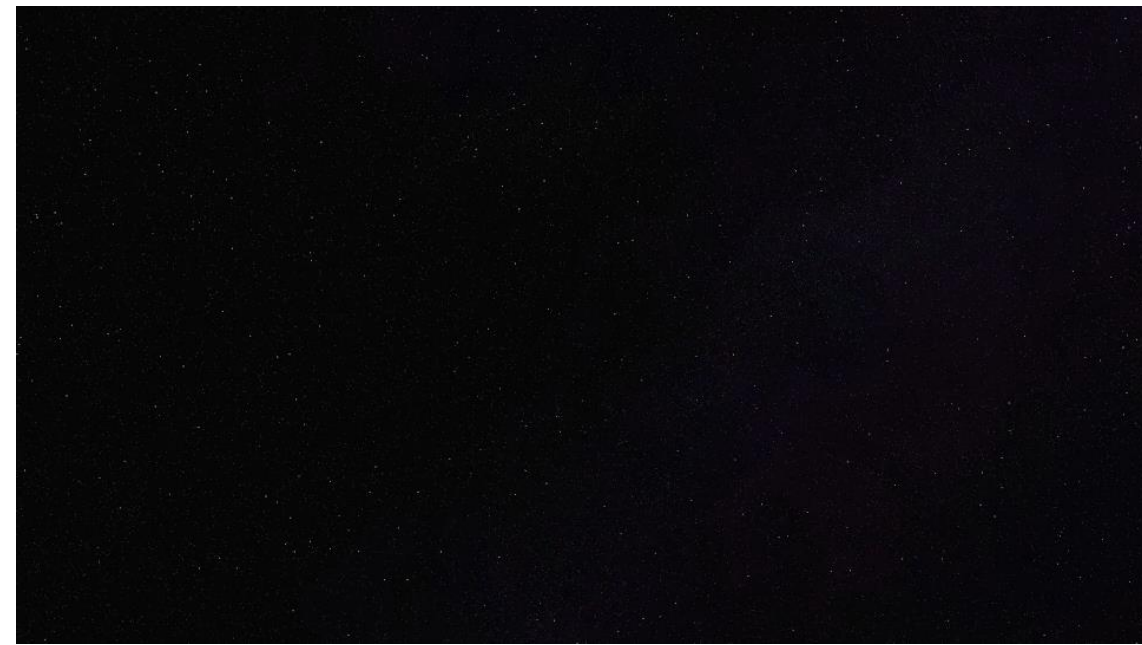
Progress – HINE experience

HINE experience in Danish neuropaediatricians and neonatologists

Sharing of standardized demonstration videos calibrated by Andrea Guzzeta

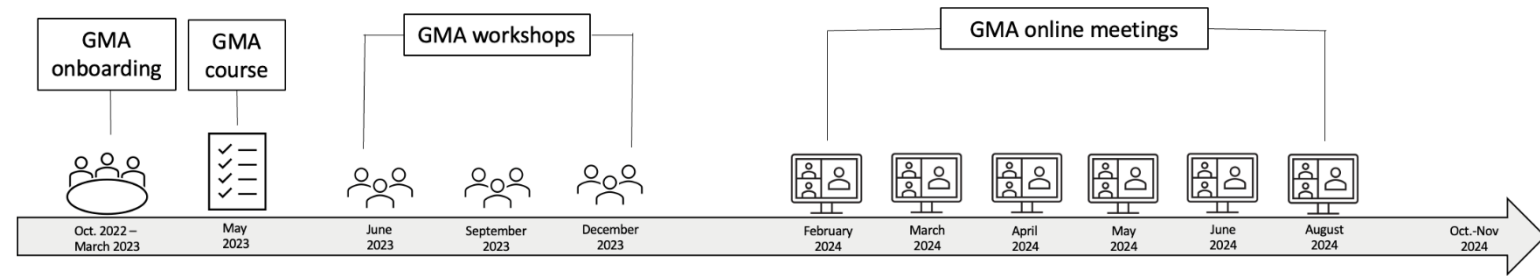
Standardized neurological examination

26 items - Children aged 3-24 mo - Takes 10-15 min



Cut off values

Progress – GMA experience



CP-EDIT GMA intervention purpose: To gain knowledge and skills in General Movement Assessment (GMA) among children's physiotherapists at 4 Danish hospitals, to support early diagnosis of cerebral palsy



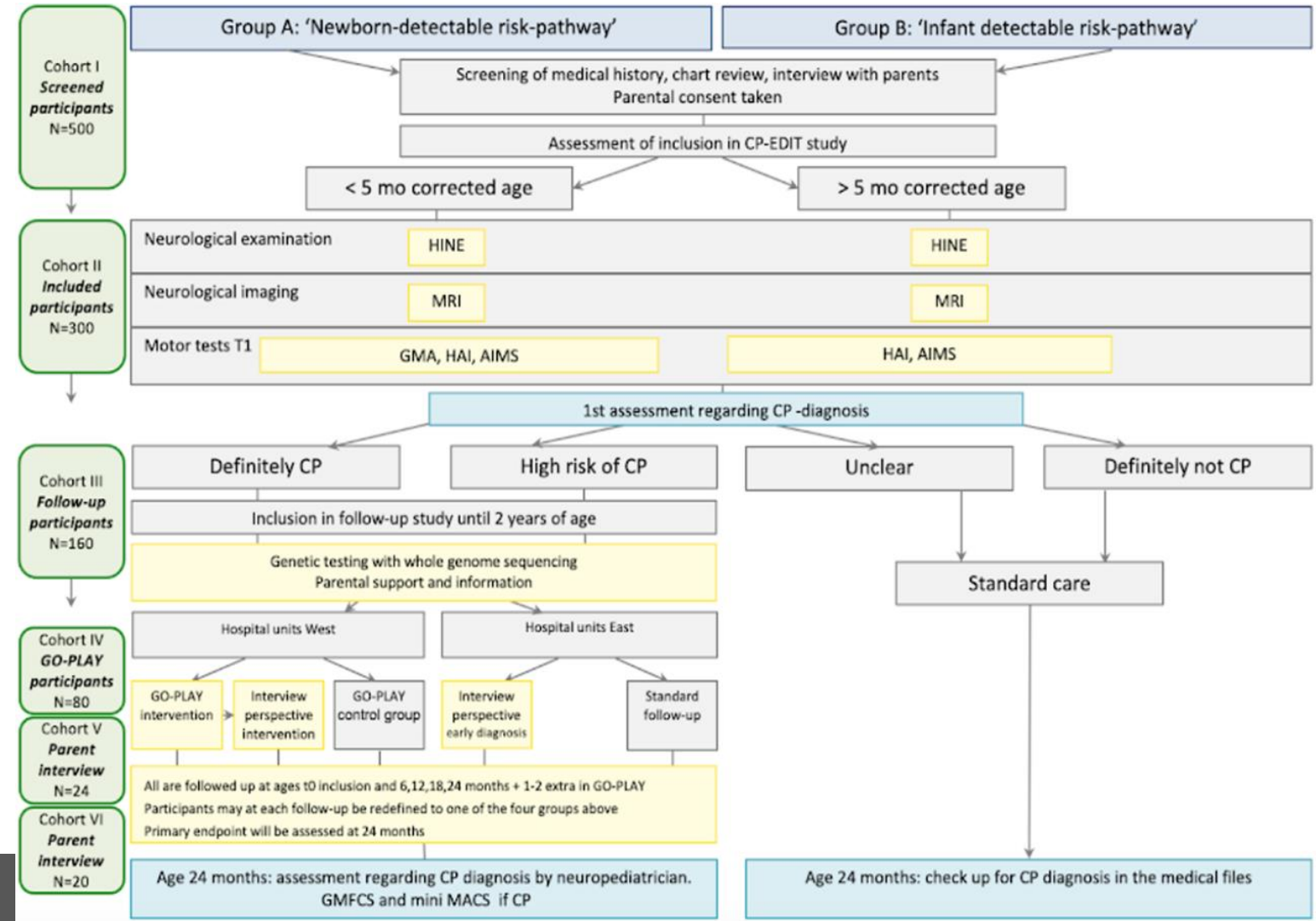
Interim data – Status on inclusion

Inclusion is ongoing

Screened children=191

Included=139

Included in follow-up=86



Future perspectives

Will there become increased awareness, lower diagnostic age?

New CP interim diagnosis

Local discussions of what the local early awareness set-up should be:

Joint evaluation at 12 weeks with physiotherapist, occupational therapist and doctor?

HINE, GMA, HAI, MRI without sedation? Genetics?

At end of CP-EDIT study we aim at:

- Implementation of a nationwide set-up for early diagnosis
- Follow-up for description of CP trajectory
- Further analyses of the simplest and AI-assisted methods
- Further knowledge-sharing of input from parents on early diagnosis and early intervention

Conclusions

Thanks to all participating infants, parents and colleagues

Inclusion is ongoing – the infant pathway is the most difficult

Early diagnosis and early intervention of CP is a large set-up requiring an extra effort and extensive collaboration

It is worthwhile



Tak til

- **Neuropædiatrisk team**, RH, Peter Born, Malene Børresen, Jeanette Tinggaard, Jakob Lorentzen, Lene Weber, øvrige tværfaglige samarbejdspartnere
- Lone Krebs (Obstretrisk klinik, Hvidovre), Gorm Greisen (GN), Gija Rackauskaite (Aarhus Univ. Hospital), Bo Mølholm (Hillerød Hospital), Mads Langager, Rebecca Fabricius, Signe Vandal, Bjarne Laursen, Susan Michelsen (Inst. for Folkesundhedsvidenskab)
- Elsebet Østergaard, Morten Dunø (Klinisk Genetisk Klinik, RH)
- Øvrige CP-EDIT samarbejdspartnere: Jan Christensen (Afdeling for Ergo- og Fysioterapi, Rigshospitalet), Jonas Kjeldbjerg Hansen og Anne-Cathrine Viuff (AUH), Gitte Hahn (GN, RH), Robin Christensen (Parker Institutet), Katrine Røhder (Inst. for psykologi, KU), Ann-Kristin Gunnes Elvrum (Norwegian University of Science and Technology), Britt Laugesen (Forskningsenhed for Klinisk Sygepleje, AUH)
- Lars Adde, Ann-Kristin Elvrum (Trondheim), Ann-Christin Eliasson (Karolinska), Cathy Morgan (Sydney)
- Cerebral parese opfølgingsprogram CPOP, Mette Johansen (AUH), CP registret, Surveillance of Cerebral Palsy in Europe
- Patricia de Liphay, Maria Willerslev-Olsen, Jens Bo Nielsen, mfl. fra Elsass Fonden
- John Vissing, Mette Ørngreen, Marie Mostue Naume (Neuromuskulær Klinik, RH / BUA)
- Julie Bindslev, Thomas Truelsen, Klaus Hansen (Neurologisk Klinik, RH / BUA)
- Karin Kok, Ghita Brekke, Sarah Sørensen, Anne Mette Raun, Christian Mølgaard, Jette Led Sørensen (Ernæringsenheden/KU)
- Vibeke Andréé, Melanie Ganz, Adam Espe Hansen, Urszula Ciochon (Radiologisk Klinik, RH)
- Kathrine Skak Madsen, Camilla Gøbel Madsen (Radiologisk Klinik, HvH)
- Nanette Mol Debes, Gitte Rønde, Jesper Johannesen, Marianne Lindblad (Herlev Hospital)

*Tak for
opmærksomheden*

*Spørgsmål
&
Kommentarer*

What follows after early diagnosis of CP?



24 recommendations when CP or possible CP is diagnosed

- Early intervention/training
- Task-specific motor training
- CIMT or bimanual therapy
- Cognitive intervention
- Face-to-face nurturing with vocalizations
- Transactional communication interventions
- Softer food consistencies
- Slightly reclined or upright positioning

Complication prevention:

- Correction of strabismus
- Visual training
- Color contrast cues
- Sleep hygiene
- Considering melatonin
- Apnea management
- Spasticity management (baclofen/botox) to improve sleep
- Comprehensive hypertonia management
- Regular use of standing equipment for positioning
- Ankle-foot orthosis

Parent support:

- mental health therapies for parents
- Cognitive behavioral therapy
- Supporting parents to carry out kangaroo care
- Musical therapy
- Attachment support and coaching

