European Reference Network for hereditary metabolic dieases

MetabERN

Allan M Lund

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital

European Reference Network

REGION The Capital Region of Denmark
Rigshospitalet

RARE INHERITED METABOLIC DISEASES: MetabERN

Coordinator
Prof. Maurizio Scarpa MD PhD
Helios Dr. Horst Schmidt Klinik Wiesbaden, Germany

69 HCPs from 18 COUNTRIES

The MetabERN is endorsed by and partners with the Society for the Study of the Inborn Errors of Metabolism (SSIEM)

European Reference Network
for rare or low prevalence complex diseases
Network
Hereditary Metabolic Disorders (MetabERN)

BE	BG	CZ	DE	DK	ES	FR	HR	HU	IT	LT	NL	NO	PL	PT	SE	SI	UK
6	1	1	10	1	5	9	1	1	11	1	5	2	1	5	2	1	6

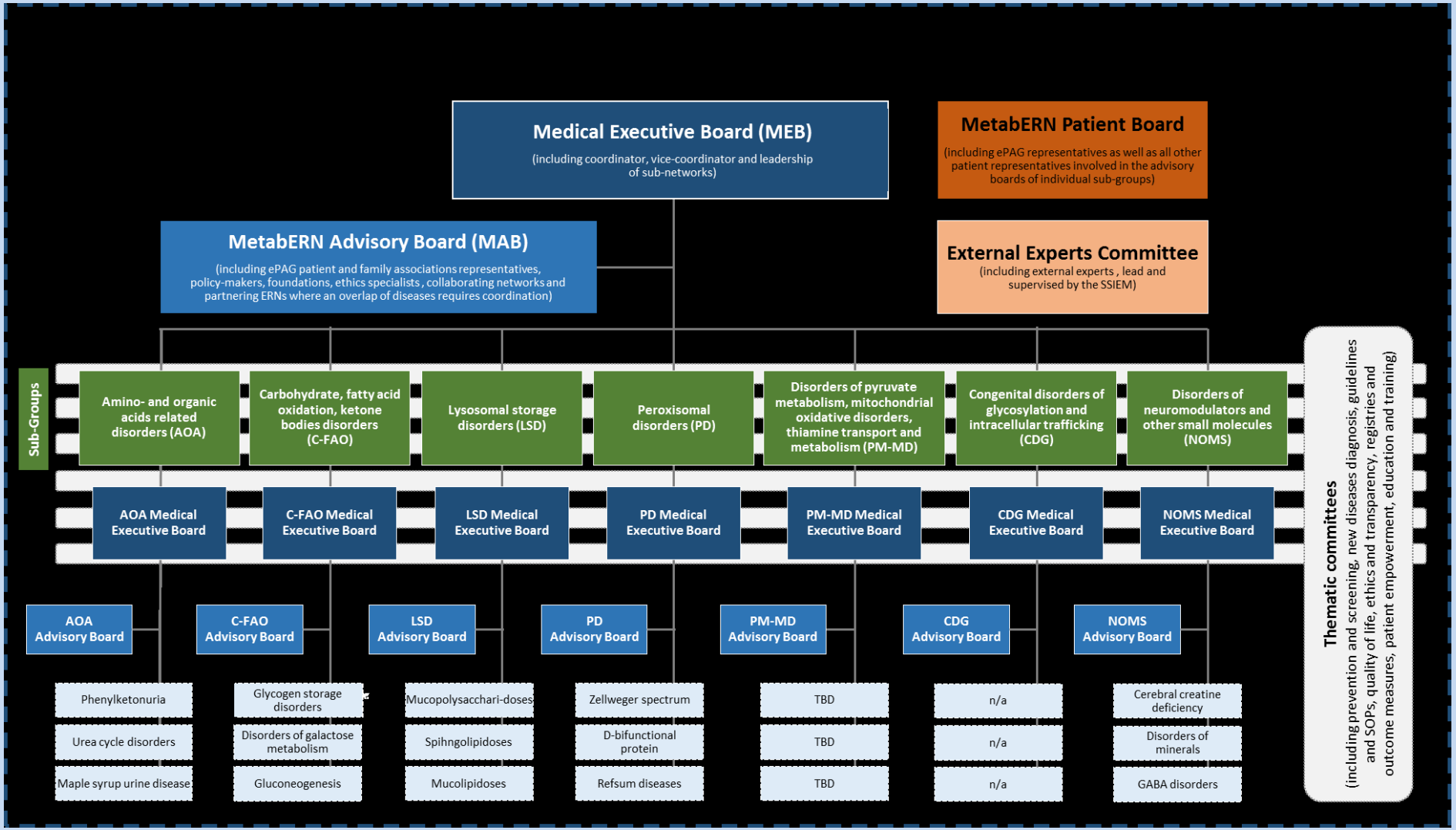
Centre Inherited Metabolic Diseases, CIMD

MetabERN

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital

European Reference Network

The Capital Region of Denmark
Rigshospitalet



CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital

European Reference Network

The Capital Region of Denmark
Rigshospitalet

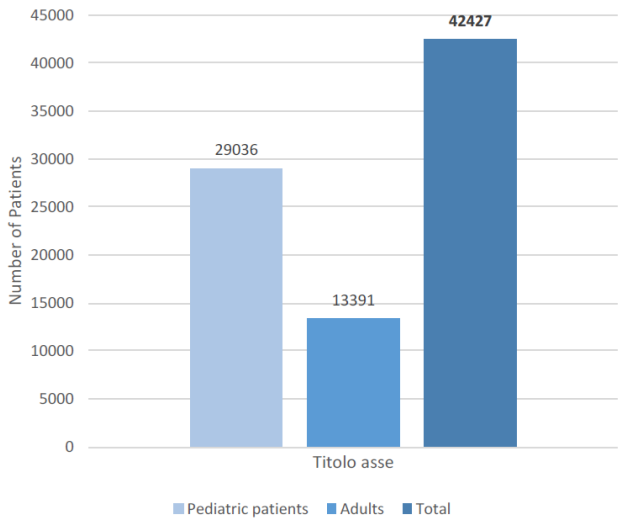
MetabERN Multidisciplinary Team (MDT)

MDT composed of

- **871** Specialized Medical Doctors
- **188** Biochemists/Biologists
- **184** Nurses
- **121** Dietician/Nutritionist
- **76** Physical therapists/Rehab
- **73** Psycologist
- **49** Social worker
- **34** Pharmacists
- **34** Coordinator/Medical Secretary
- **13** Expert in Palliative care/Pain management
- **10** PHD/student
- **28** Other

a Total of **1681** Experts

MetabERN: Patients Coverage



…. covering > 1400 different metabolic diseases

Mission

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital
European Reference Network
The Capital Region of Denmark
Rigshospitalet

- The **mission of MetabERN** is to generate a patient centered **European Reference Network for hereditary metabolic disorders** able to identify and bring the best expertise to patients to facilitate **prevention, diagnosis, management, research** and **access to therapy** to patients affected by rare inherited metabolic diseases (**IMDs**)

How our small baby was helped by MetabERN experts

ERN newsletter update 05/12/2019

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital
European Reference Network
The Capital Region of Denmark
Rigshospitalet

Having our baby girl diagnosed with the ultra-rare, chronic and very serious disease, Glycogen Storage Disease type 1b, was the hardest thing we have ever experienced. Our whole world crumbled without even having the time to mourn: we needed to get hands-on help immediately since an error could be fatal for our daughter.
We were told that GSD 1b could be treated in our respective countries (Spain and Italy). However, our daughter's case was a very severe and complex one. We had to feed Nina every 40 minutes during the day and provide continuous feeding throughout the night to avoid severe hypoglycaemias. We also had a very long list of additional nursing tasks including daily shots. Despite strict monitoring, Nina went through several unpredictable, life threatening emergency situations.
We were exhausted but found the time and energy to devour GSD guidelines, to get in touch with the best experts in the world and to raise awareness and funds for research through Nina's website and Nina's social networks (#ninalaguerrera.org).
At a certain point, Nina's health deteriorated strongly. We had already found certain potential contacts abroad during our search and **at that point we contacted MetabERN's Coordinator, Dr Maurizio Scarpa, in Italy. Dr Scarpa gave us the right guidance and confirmed that Dr Terry Derks, a member of MetabERN, was the most appropriate specialist to treat our baby**. As soon as her status stabilised, Dr Derks, MetabERN network members led by Professor Scarpa, and the Italian Health authorities, did their best to get Nina referred to the University Medical Center in Groningen (UMCG). Thanks to the use of the Directive 2011/24/EU on patients' rights in cross-border healthcare, it was possible for Nina to be cared for by Dr. Derks and his team.

MANY MORE OF THESE CASES – AND THE ERN SET-UP SEEMS TO WORK ACHIEVE IT'S MISSION

The application process and activities after that

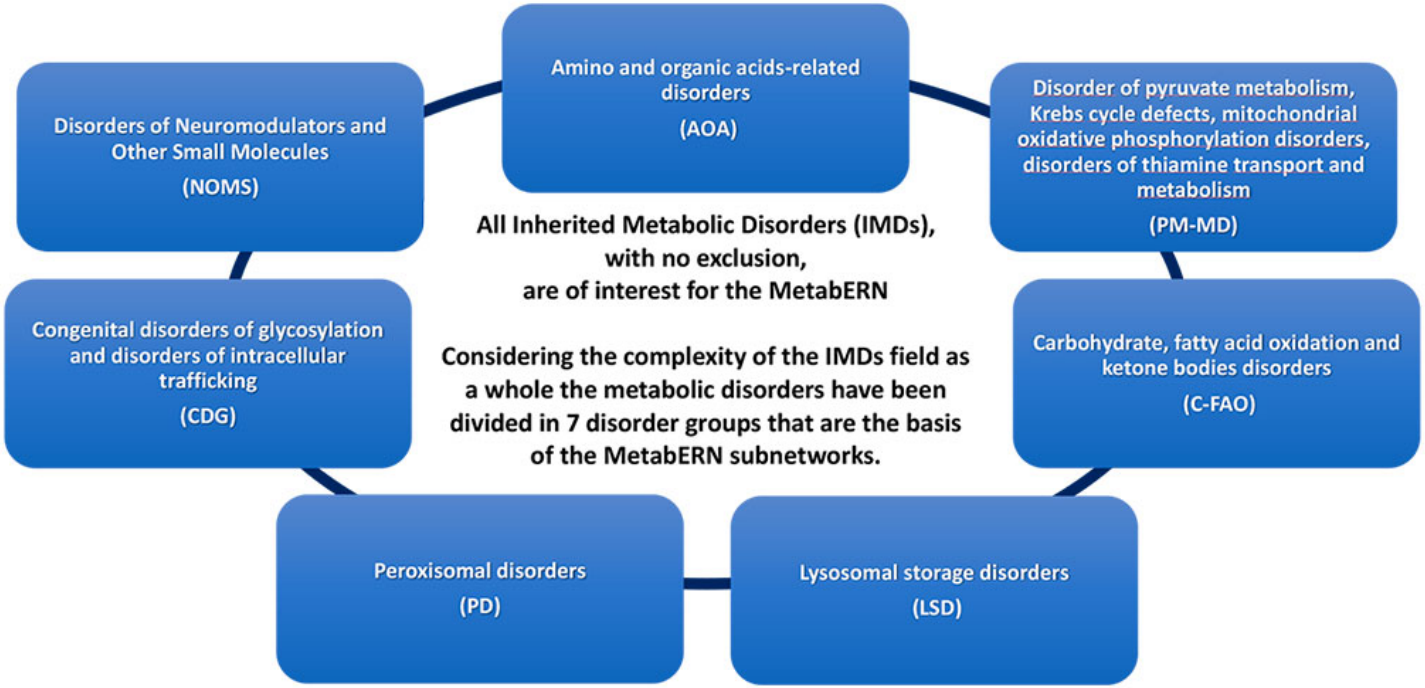
- Application and self-assesment process and first years of ERN-membership
  - **Extreme amount of paper and unparalleled over-use of words**
    - Legal, organisation, IT-infrastructure, hospital cleaning and emergency plans, medical profile, patient care ……
    - Many questionaires, organisational meetings
    - ……very little about patients

Activities on a regional level

- No regional help in the start
- 8 ERNs in Copenhagen University Hospital asked for help concerning IT, legal aspect, GDPR, consent … and more lately more functional aspects within the ERNs
  - A regional group with representation from legal, IT and finance has been formed
    - This is necessary for implementing a number of projects within the ERNs
      - Registry
      - CPMS platform
      - Other clinical platforms e.g. for biobanks
      - The reporting of ERN activities, such as patient numbers, publications etc
      - New ERN applications by other clinical entities

Activities within the ERN

- Work within the subnetworks

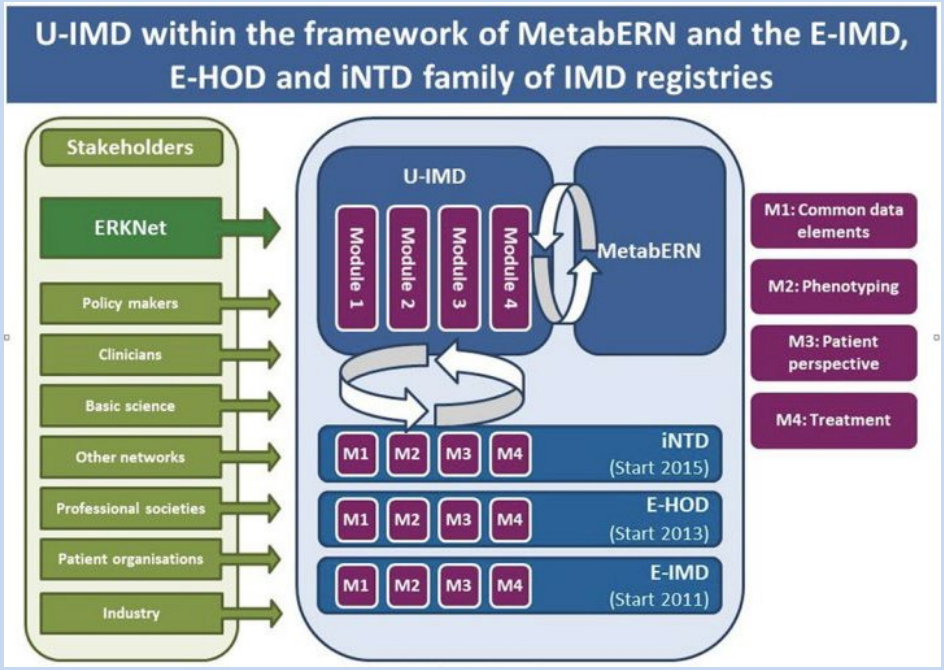


Subnetworks
Work done and in pipeline

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital
European Reference Network
The Capital Region of Denmark
Rigshospitalet

- Guideline development for specific rare disorders/situations
  - Emergency guidelines
  - Homocystinuria, Zellweger, alpha-mannosidosis, glycogen storage diseases, urea cycle disorders
    - A few published, e.g. Suggested guidelines for the diagnosis and management of **urea cycle disorders**: Häberle J et al. J Inherit Metab Dis. 2019 Nov;42(6):1192-1230. doi: 10.1002/jimd.12100. Epub 2019 May 15. Review.
- Group formed for harmonising European Newborn Screening programmes together with SSIEM, EURODIS, ISNS
- Development of educational material in collaboration with SSIEM
  - GSD
  - Alpha-mannosidosis
- Group formed for development of guidelines for child – adult transition
- Two MetabERN papers
  - Use of OMP within each HCP
    - Availability, accessibility and delivery to patients of the 28 orphan medicines approved by the European Medicine Agency for hereditary metabolic diseases in the **MetabERN** network. Heard JM et al; **MetabERN** collaboration group. Orphanet J Rare Dis. 2020 Jan 6;15(1):3. doi: 10.1186/s13023-019-1280-5.
  - Degree and kind of research activities within each HCP
    - Research activity and capability in the European reference network **MetabERN**. Heard JM et al; **MetabERN** collaboration group. Orphanet J Rare Dis. 2019 May 29;14(1):119. doi: 10.1186/s13023-019-1091-8.
- Registry

Unified EU registry for IMD building on previous EU registries

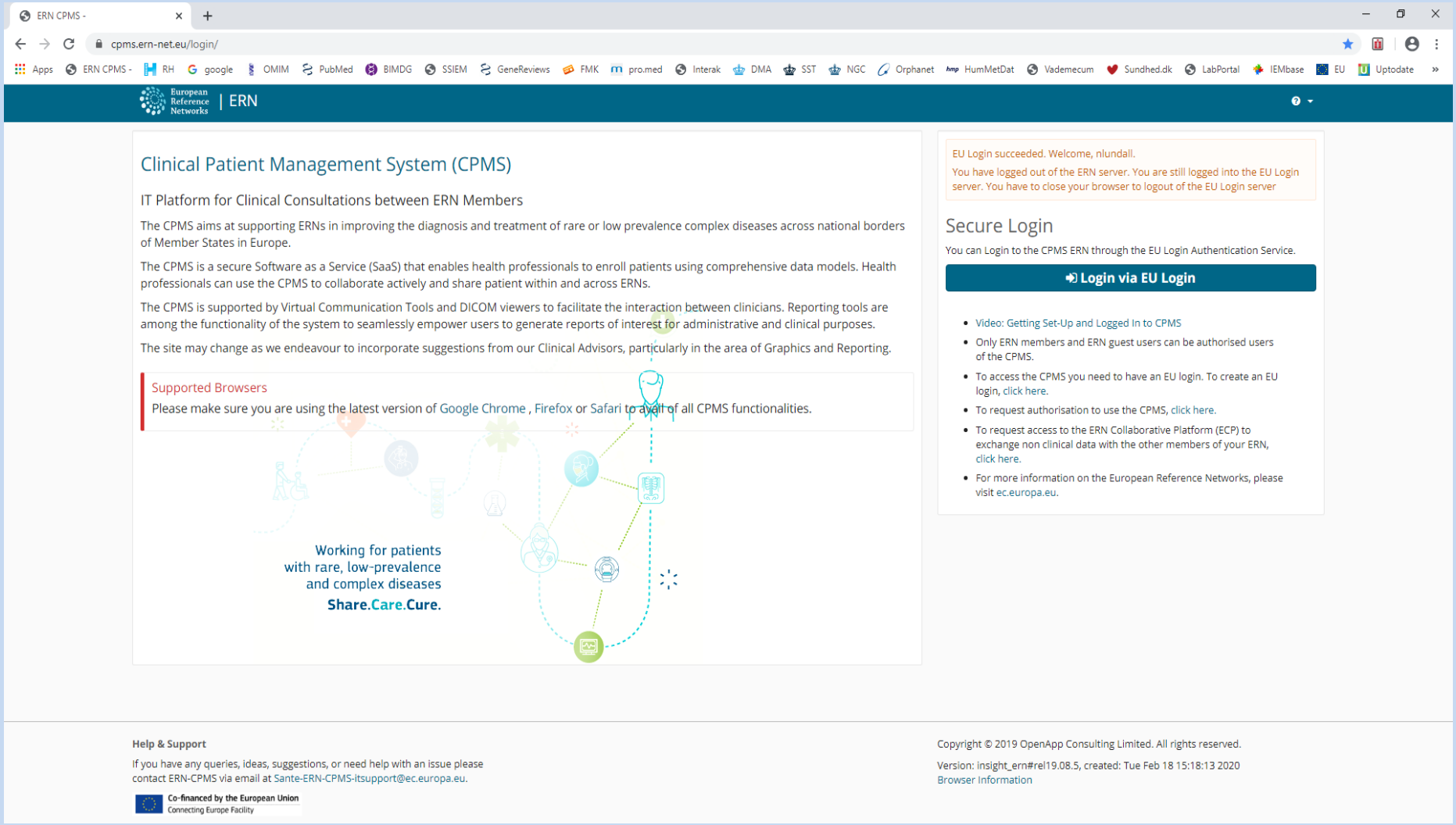


- U-IMD is now implemented
  - Aims
    - Patient registration
      - Overview of population
      - Recruitment for clinical trials/research/postmarketing surveillance
    - Guideline development, natural history studies etc
    - Only few patients still in the registry
      - Automatisation for entering is needed

CPMS platform

Clinical Patient Management System

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital
European Reference Network
The Capital Region of Denmark
Rigshospitalet



CPMS platform

Clinical Patient Management System

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital
European Reference Network
The Capital Region of Denmark
Rigshospitalet

- Clinical platform for inter HCP consultation
  - Now established
  - A very complicated, ”heavy” IT structure
    - Many critical voices within MetabERN
      - Man-power/time consuming
      - Legal/GDPR aspects – e.g. the pseudo-anonymisation process
  - Used to a limited degree, though increasingly
    - because it is a mandatory HCP performance criteria
    - …. and CPMS is not a bad idea, but developers do not understand that what we need is just a secure mail system

ERN Problems

- CPMS
  - Interface/functionality should be worked on to make it more user-friendly
  - Only for long-term management – emergency module is needed
  - CPMS needs to be incorporated into national electronic patient records
    - To ease the upload of clinical information, radiographs, clinical pictures etc.
    - Documentation of the consulting proces
    - The use of CPMS must be coded as an activity in the clinic's work
    - A start may be a new code "patient managed in collaboration with an ERN: ZDW13"
  - Practical help is needed in the clinical work with CPMS

Adoption of the ORPHA codes by ERN-Rare Liver for a more detailed patient classification and targeted financial support

ERN newsletter update

05/12/2019

The goal of the ERNs is to improve patient care when it comes to rare diseases. Thanks to our involvement in the ERN, the University Medical Center Hamburg-Eppendorf has been **making use of the ORPHA codes in addition to the mandatory ICD coding to optimise patient documentation, and consecutive treatment. An IT tool for the electronic patient chart has been developed specifically to assign an ORPHA code** to patients with rare diseases which can be accessed within the entire hospital. Unlike the ICD-coding that is usually case-specific (and also specific to the actual reason for admission), this code is patient specific, gives a more detailed classification of the rare disease and **can be evaluated by the central controlling unit. In addition, it provides future possibilities for research questions, controlling and strategic decisions within the health care provider**.

The good news is that from this year on, the University Medical Center Hamburg-Eppendorf is receiving substantial funding from health insurance companies for providing highly specialised care for patients with rare diseases in its overarching Martin-Zeitz-Centre for rare diseases. The funds will be internally distributed partly based on the number of new patients coded with an ORPHA code. This will generate additional funding exactly where the workload is, and hopefully it will motivate all sub-centres caring for rare disease patients to actually use these ORPHA codes: a real win-win situation.

Coding

- Homocystinuria (ICD E72.1) may be caused by a nutritional deficiency or by a number of inherited enzyme deficiencies
  - They have no specific ICD codes (like many other of the >1400 inborn errors) and we use instead SSIEM, ORPHA, ERNDIM, OMIN codes
    - No automatic reporting into national databases and the codes cannot in any easily searchable way be documented in electronic notes
  - ***Such codes should be incorporated in electonic health records and should be reported directly into at least our national rare disease registry (RareDis) and when possible also into more common national databases like LPR (and later U-IMD)***
  - Precise, disease specific codes are also important from practical point of view: half-yearly reporting is requested in MetabERN
    - Mandatory by the EU and included in HCP performance criteria
  - Help is needed with the above tasks – and also with the mandatory half-yearly reporting of staff, clinical trials, publications etc.

Conclusions

CIMD
Centre Inherited Metabolic Diseases
Paediatrics - Clinical Genetics
Copenhagen University Hospital
European Reference Network
The Capital Region of Denmark
Rigshospitalet

- **MetabERN** has shown its sustainability and raison d'etre
  - **Necessary network** in rare diseases, guideline development, registries, research …
- Overall a good experience to be in an ERN, though we look forward to more patient-related tasks and:
- Focus is needed on day-to-day operation to ease the full integration of ERNs into Danish Health System
  - CPMS in electronic health records
  - Incorporation of registries and specific rare disease coding into electronic health records with automatic reporting (like ICD)
  - Coding of ERN activities to be included in a clinic's performance (like coding an out-patient visit)
  - Budget for ERN activities (whether from EU or regionally)
    - The mandatory reporting of ERN activities to EU
    - Meetings, travelling
    - Work with guidelines, translations to Danish etc
- Needs formalised co-operation
  - Between Danish ERNs
  - Between the ERNs and the regional hospital administrations (like the group allready formed)
  - National Health Authorities to guide Danish ERNs concerning development in other countries (e.g. how they are implementing new codes etc.)

THANK YOU!