Ageing with a rare disease

Pr Laura De Graaff, Erasmus MC, Netherlands

&

Working group of ERN-ITHACA

on ageing with intellectual disabilities

PM Anne Hugon, ERN ITHACA, France

Dorica Dan, Chair ePAGS ITHACA, Romania

European Commission

EUROPEAN REFERENCE NETWORKS

Helping patients with rare or low-prevalence complex diseases

European Reference Networks ITHACA

EURORDIS meeting Stockholm, may 25-27th 2023

AGING WITH A RARE DISEASE

Improving healthcare for adults with rare genetic syndromes

Laura de Graaff-Herder, MD, PhD
Ass. Prof. Genetic and Developmental Endocrinology
Erasmus MC Rotterdam - the Netherlands

Erasmus MC
Universitair Medisch Centrum Rotterdam

Rare
Genetic
Syndromes

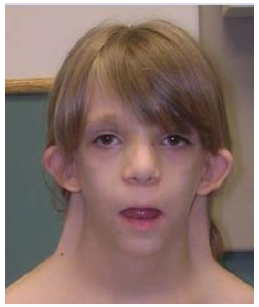
Internal Medicine
Erasmus MC Rotterdam

International Network for Research, Management & Education
Prader-Willi Syndrome

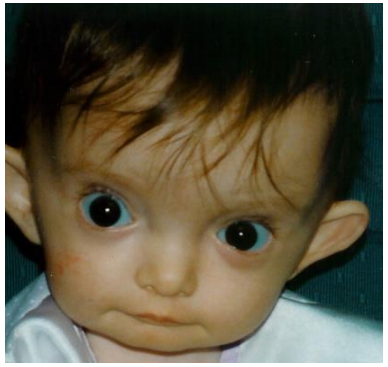
European Reference Networks

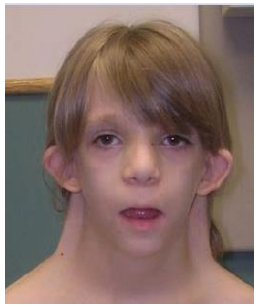
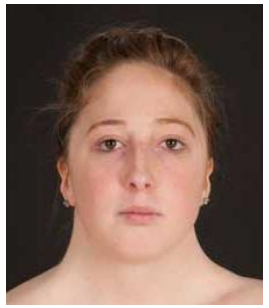
ITHACA

Endo-ERN
European Reference Network on Rare Endocrine Conditions



ESPE
European Society for
Paediatric Endocrinology

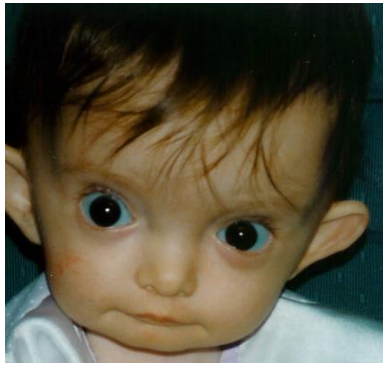






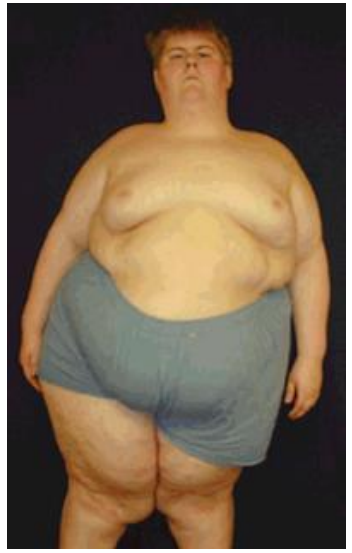


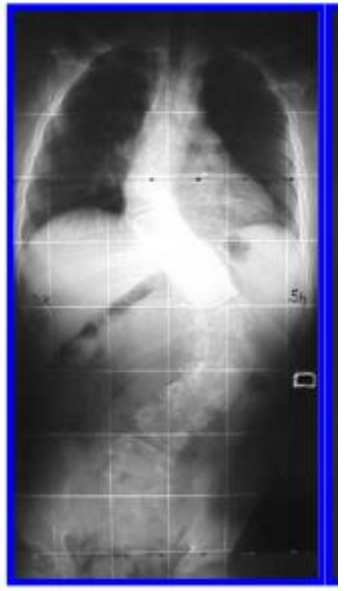


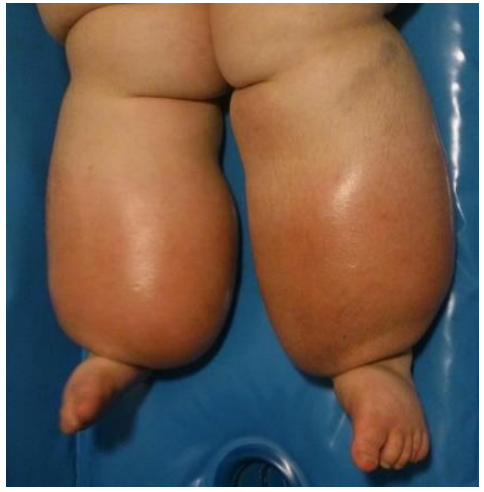



O Who is responsible for the aging adults with RD?

Improved paediatric care







Rare
Genetic
Syndromes

Internal Medicine
Erasmus MC Rotterdam

Internist-Endocrinologist

ID-dietitian

Nurse
Practitioner

ID physician
clinical geneticist

Neuro-
Psychologist

O Which disciplines should take care of aging adults with RD?

Syndrome
16p11 deletion / 16p11.2 deletion
16p13.11 deletion
17-20 desmolase deficiency and partial 17-hydroxylase deficiency
1q21 microdeletion syndrome
1q25-32 deletion
22q11 deletion
DSD
48,XXXY
Adenylsuccinasedeficiency type 1
Adrenogenital syndrome
Albright hereditary osteodystrophy
Allan-Herndon-Dudley syndrome
Alström syndrome
Angelman syndrome
Bardet-Biedl syndrome
Bloom syndrome
Borjeson-Forssman-Lehmann syndrome
CAIS
CAMK2A mutation
CHARGE syndrome
Cockayne syndrome
Cornelia de Lange syndrome
Costello (like) syndrome
Cri du chat syndrome
CTNNB1 syndrome
Dandy Walker syndrome
Trisomy 21
Sex chromosomal mosaicism (45X,46XisodicY)
Gonadal dysgenesis (46X/46XisoYp)
Jacobsen syndrome
Joubert syndrome
JS-X syndrome
Kabuki syndrome
Kallmann syndrome
Kiss1R homozygote variant
L1CAM mutation
Leydig cell hypoplasia
Ohdo syndrome
Myrhe syndroom
Neurofibromatosis type 1
Noonan syndrome
PAIS
PNPLA6 gene mutation
PTEN hamartoma tumor syndrome
Prader-Willi like
Prader-Willi syndrome
Rett syndrome
Rieger syndrome
Ringchromosome 21 syndrome
Saethre-Chotzen syndrome
Sifrim-Hitz-Weis syndrome
Silver-Russel syndrome
Smith-Lemli-Optiz syndrome
Smith Magenis syndrome
Sotos-like syndrome
SRY+XX male
Klinefelter syndrome
Tatton Brown Rahman syndrome
TBLX1 mutation
Tetra-X syndrome
Triple-X syndrome
TRPV4 mutation
Tuberous sclerosis complex
Turner syndrome
Williams-Beuren syndrome
XXYY-syndrome
Unknown syndrome
Total

Since 2015:

>1100 patients

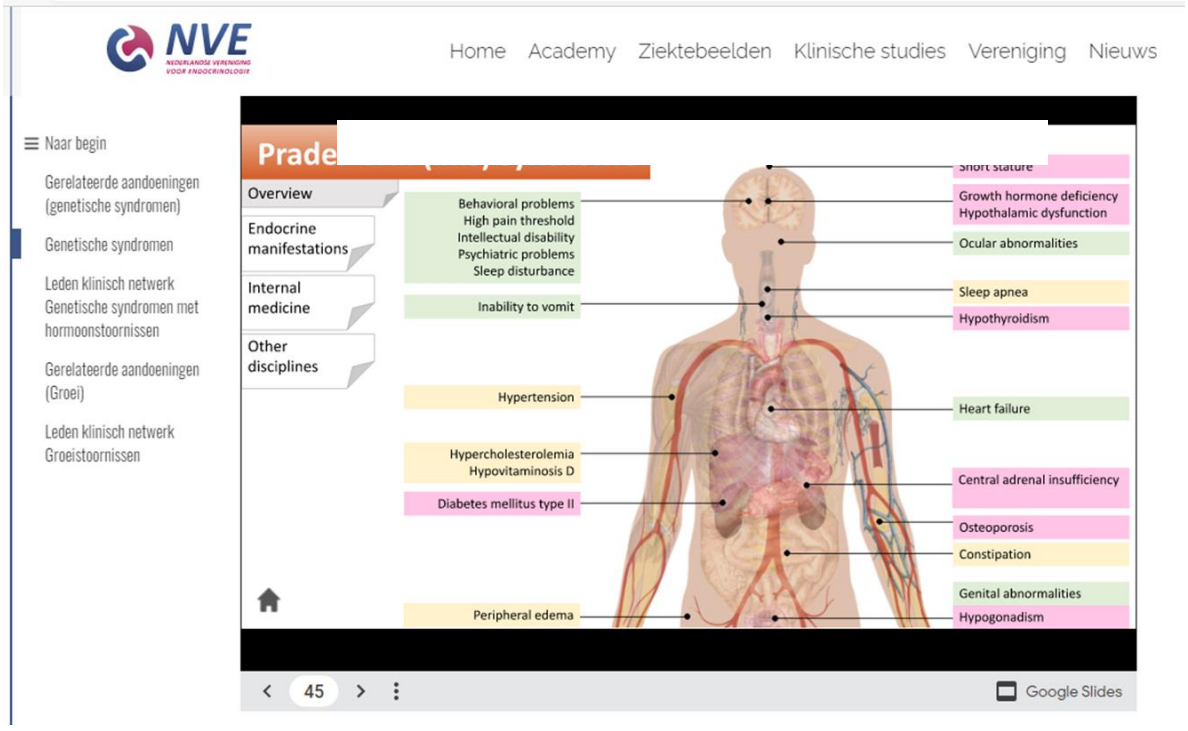
>90 syndromes

16 x

O do the needs of aging adults depend on the type of RD ?

- who is responsible for making guidelines?

NVE (Dutch Association of Endocrinology): New network ‘Genetic and Developmental Endocrinology’



Article

What Every Internist-Endocrinologist Should Know about Rare Genetic Syndromes in Order to Prevent Needless Diagnostics, Missed Diagnoses and Medical Complications: Five Years of ‘Internal Medicine for Rare Genetic Syndromes’

Anna G. W. Rosenberg [1,2], Minke R. A. Pater [1], Karlijn Pellikaan [1,2], Kirsten Davidse [1,2], Anja A. Kattentidt-Mouravieva [3], Rogier Kersseboom [3], Anja G. Bos-Roubos [4], Agnies van Eeghen [5,6,7], José M. C. Veen [8], Jiske J. van der Meulen [8], Nina van Aalst-van Wieringen [9], Franciska M. E. Hoekstra [1,10], Aart J. van der Lely [1,†] and Laura C. G. de Graaff [1,2,7,11,12,13,*,†]

Bardet-Biedl syndrome [30,31,32,33,34]	KG, M, ID		
Bloom syndrome [35]			ID
Börjeson-Forssman-Lehmann syndrome [36,37]	KG		ID
CAMK2A variants [38,39]			ID
CHARGE syndrome [40,41,42,43,44,45,46,47,48,49,50,51]			ID
CHD8 syndrome [52,53,54]			ID
Chromosome 1q21 deletion syndrome [55,56,57]			ID
Chromosome 1q25-32 deletion [58,59]			ID
Chromosome 16p11.2 deletion syndrome [60,61,62]	KG		ID
Chromosome 16p13.11 deletion syndrome [63,64,65]			ID

INfoRMEd-PWS

International Network for Research, Management & Education on adul

Dr Assumpta Caixas Pedragos *(adult endocrinologist)*
Hospital de Sabadell, Sabadell, Spain

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Italian Auxological Institute, Verbania, Italy

Dr. Antonino Crinò *(adult and pediatric endocrinologist)*
Bambino Gesù Hospital, Palidoro (Rome), Italy

Ass. Prof. Charlotte Höybye *(adult endocrinologist)*
Karolinska University Hospital, Stockholm, Sweden

Ass. Prof. Tania Markovic *(adult endocrinologist)*
Royal Prince Alfred Hospital, Camperdown, Australia

Prof. Christine Poitou-Bernert (adult endocrinologist)
Pitié-Salpêtrière Hospital, Paris, France

Dr. Muriel Coupaye (adult endocrinologist)
Pitié-Salpêtrière Hospital, Paris, France

Dr. Tony Goldstone (adult endocrinologist)
Imperial College, London, United Kingdom

Dr. Laura de Graaff-Herder (adult endocrinologist)
Erasmus University Medical Center, Rotterdam, The Netherlands

Specialized care for adults with Rare Genetic Syndromes

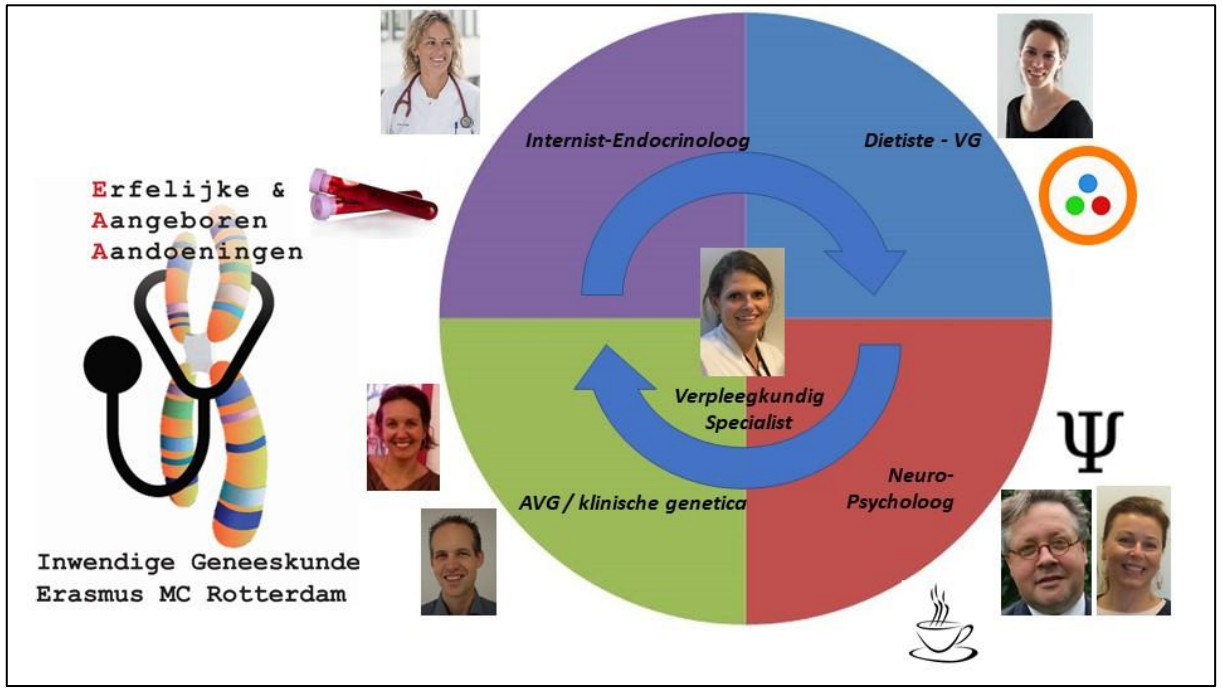
Improve patient care through

1. *Multidisciplinary approach*
2. *Scientific research*
3. *Registration of medical problem at adult age*

Prevent

1. *Missed diagnoses*
2. *Complications, mortality*
3. *Overtreatment*
4. *Undertreatment*

➔ *Improve medical care (guidelines!)*
➔ *Reduce healthcare costs*
➔ *Improve quality of life*







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ERN-ITHACA

European Reference Network for Rare Malformation Syndromes, Intellectual and Other Neurodevelopmental Disorders

WHO WE ARE

Subnetwork: adults with intellectual disabilities

EuroNDD @Amsterdam, April 20-21, 2023

The EU Reference Network ITHACA announces the first 2-day European workshop on the multifaceted care and research of rare genetic neurodevelopmental disorders. This meeting will be fully supported by the European Union to enhance cross-border and multidisciplinary knowledge exchange and collaboration.

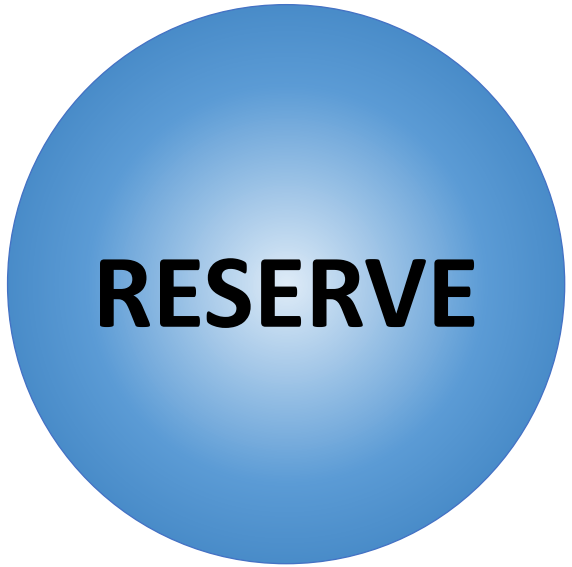
+ INFOS

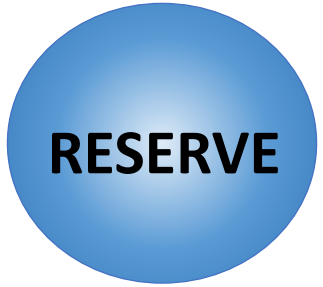
Guidelines for adults with intellectual disabilities (Williams-Beuren syndrome, PWS, Down syndrome)

Geriatric principles

Dr. Stéphanie Miot, MD,PhD, geriatrician and psychiatrist, Montpellier, France

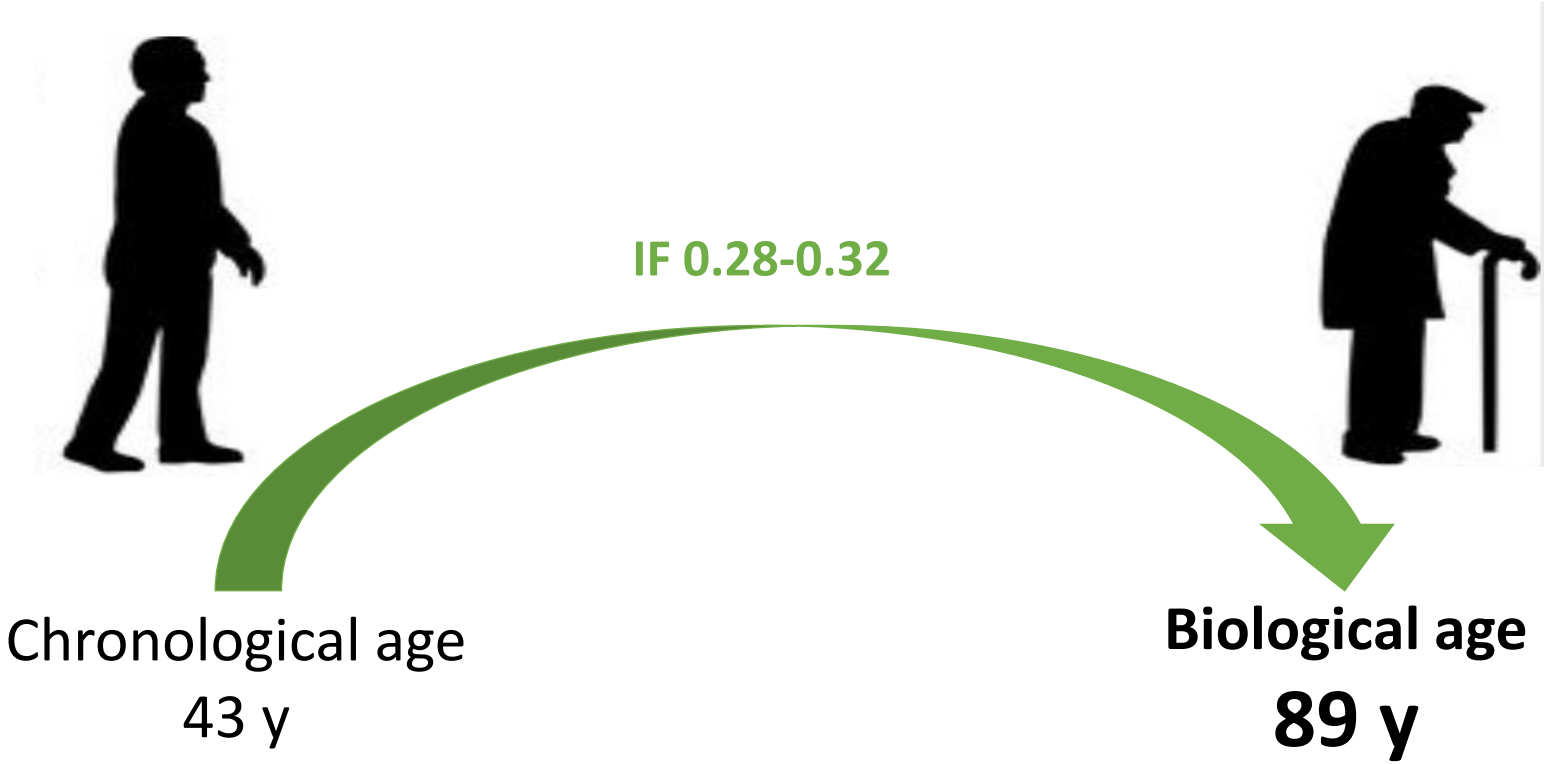
- Normal vs pathological = **spectrum**





Fragility in neurodevelopment disorders (NDD)

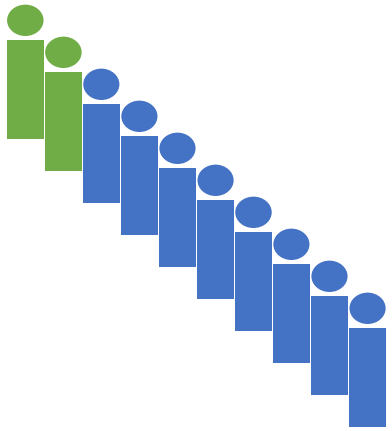
- ↗ biological age in Autism spectrum disorder (ASD) & Intellectual disability (ID)



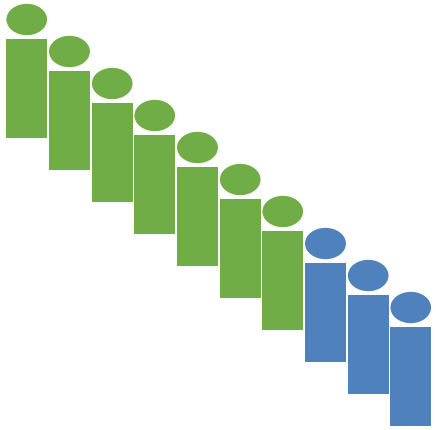
Miot, in preparation

Aging / Multimorbidity in NDD

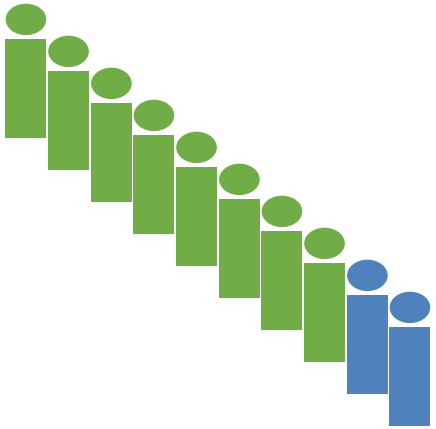
- ↗ accumulation of chronic diseases
- multimorbidité in Autism spectrum disorder (ASD) and Intellectual disability (ID)
  - **Earlier and higher** *(Cooper, 2015; Miot, 2022)*



23.2%
General population
Barnett, 2012



71-79.8%
ID
Mc Carron, 2013 ; Hermans, 2014



84.1%
ASD-ID
Miot, 2022

Comprehensive Geriatric Assessment (CGA)

- ↗ geriatric syndrome prevalence
- ↗ comorbidities burden
- ↗ multimorbidity
- ↗ polypharmacy
- ↗ biological age

Pathological ? earlier aging ?

Need Earlier CGA+++

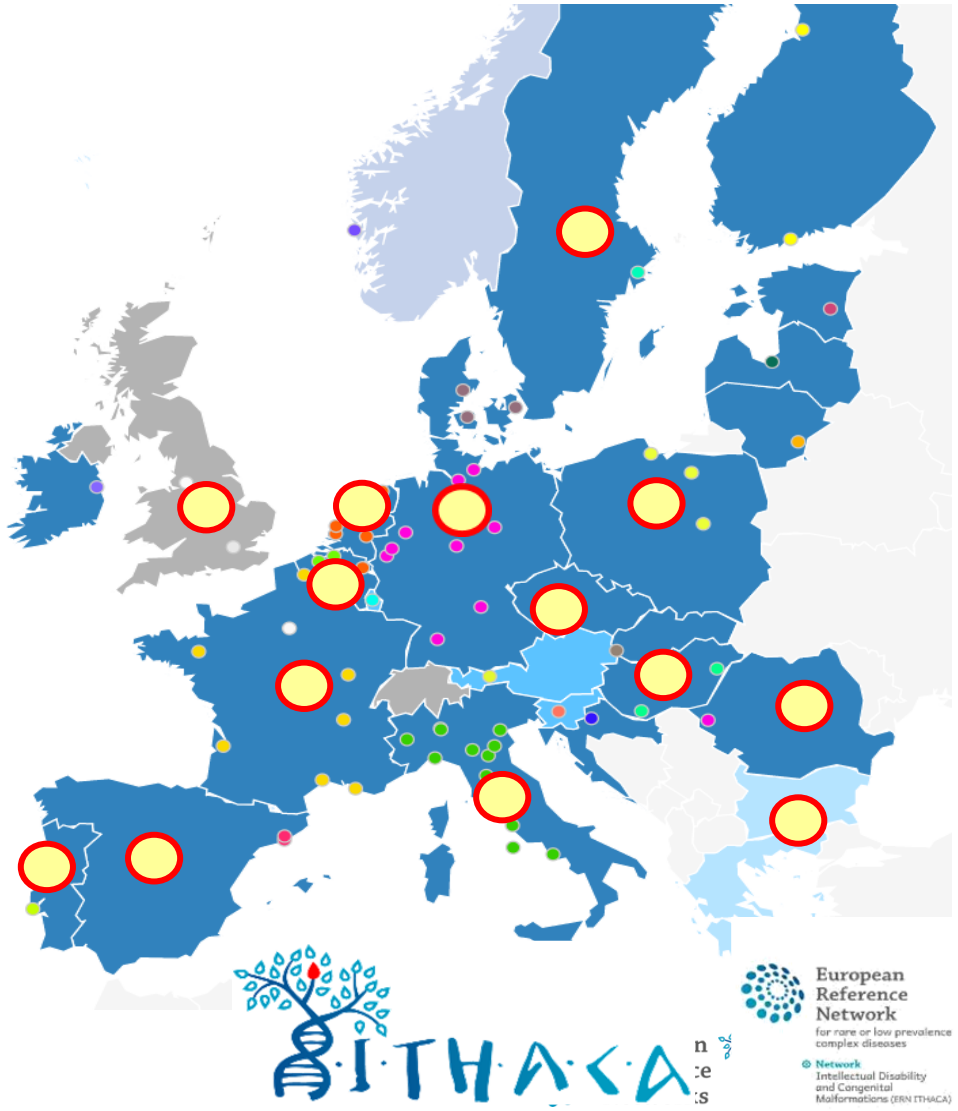
☑ **Pathological aging**
☑ **Specific needs & holistic approach**
☑ **Helpers and HCW training**

European Reference Network - ERN ITHACA

Intellectual disabilities, **T**ele**H**ealth, **A**utism and **C**ongenital **A**nomalies

- Pr A. Verloes, Coordination Paris (post-Brexit)
- 71 from 25+1 countries
- HCP : expert genetics centers in teaching hospitals
- Over 5000 RD genetics
- Axes
  - Develomental anomalies
  - Neurodevelopmental disorders NDD (ID, ASD,PIMD SyNDD gene data base)
  - + specific Genetic, multifactorial (e.a. spina bifida) or environmental
- A growing Patient Community, ePAGS

The Patient Community



07/06/2023

Working Group NDD
Neurodevelopmental disorders

ITHACA

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+ INFOS

Guidelines for adults with intellectual disabilities (Williams-Beuren syndrome, PWS, Down syndrome) …

Task Force (WG) ID Adult “care for adults with ID ”

Work group Chairs

- Miot S. et De Graaff L.
- Hugon A

- **Delivrables : European good practices**
  - Down, Williams-Buren, and Prader-Willi syndromes
  - Generalisations for NDD adults

  ⇨2023 – 24 Practical Recommendations, accessible to all caregivers Publish at least one paper in 2023 (transition) and one in 2024 (comorbidities)

  ⇨2024 -27 Toolbox to be deployed (dedicated website, testimonials, webinars, etc.)

- **General objectives**
  - To establish a medical care management for ID adults and older adults, provide best practice, to be used in daily life
  - Improve collaboration & communication between clinician and adult patient’s caregivers / Medical homes

Experts welcome!

Pr. Laura de Graaff, MD,PhD, genetic and developmental endocrinologist, Rotterdam, the Netherlands

Dr. Stéphanie Miot, MD,PhD, geriatrician and psychiatrist, Montpellier, France

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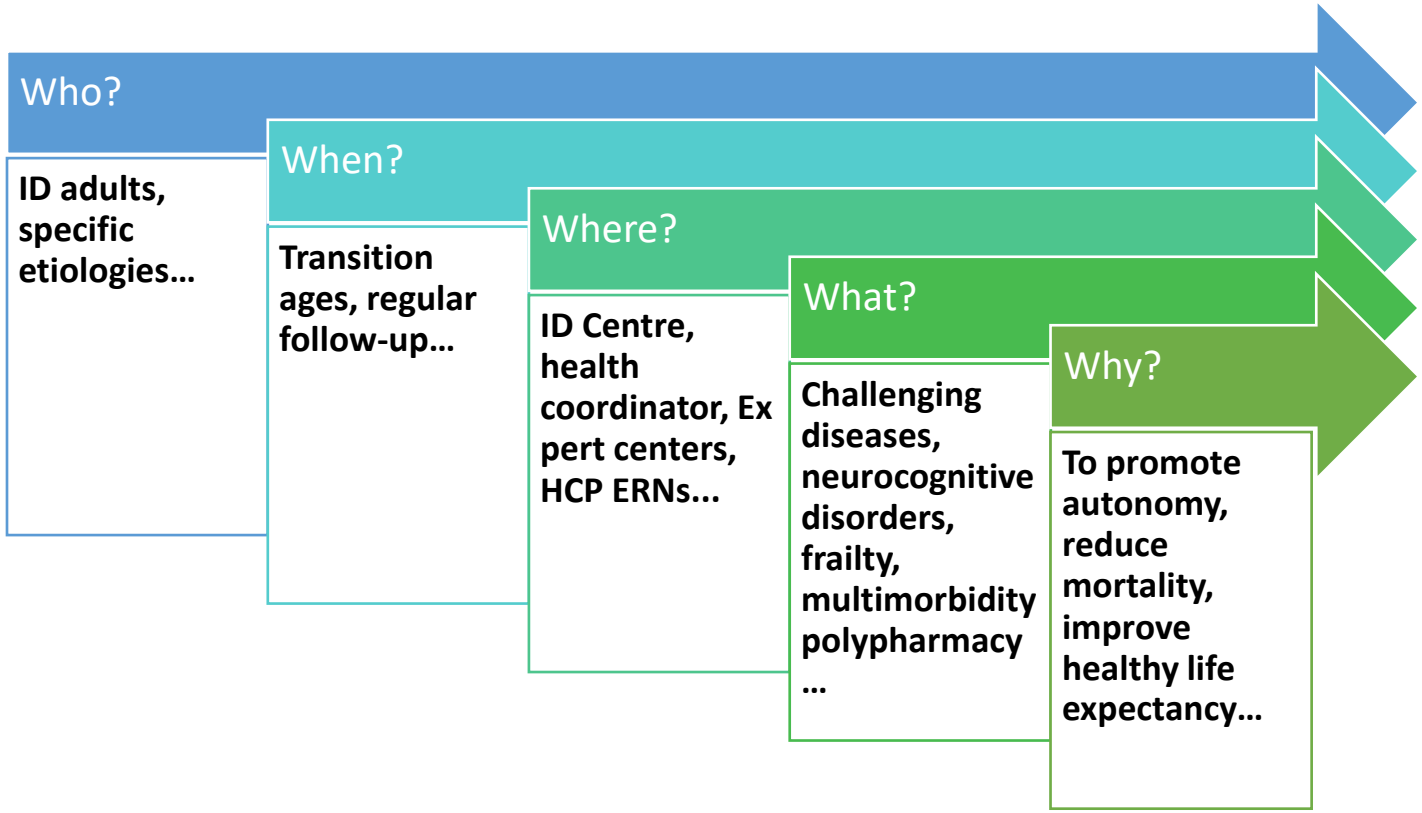
Task Force (WG) ID Adult “care for adults with ID ”

- Define : best practices ’healthcare for adults with ID’ based on expert panel & literature
- Provide : Assessment tools, Recommendations of good practice for the management of mentally disabled adults with ID

Medical care management for ID adults



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Why work on “care for ID and ageing adults ” ?

- In summary
  - A growing population that has been little studied, yet a literature exists
  - Advancing age is little considered, even more so when it is complex
  - Reassure, remove prejudices " obstacle “
  - Recognise the "preserved" capacities of people
  - Need for support for patients and their carers

It’s important to Raise awareness and understanding of the complexity of clinical management difficulties in order to improve management and quality of life over the long term

Transmit and share knowledge Be facilitators

Holistics care such as Medical + Social + Psychological

Thanks you for your attention

https://ern-ithaca