Inequity,

how to bridge the gap in care for children with a rare condition?

Liesbeth Siderius, pediatrician

Equity: fairness and justice

Introduction

- **(Dis)abled child**

Rare is common

- **The Diagnosis**

Accessibility

- **Universal Health Coverage**

Affordability and availability

- **Leave no child behind**

Universal global child health

UNIVERSAL HEALTH COVERAGE DAY

Rare is Common
Just normal People

22qdeletion

The Family

Skeletal Dysplasia

At work

Fibrodysplasia Ossificans Propressiva

Study
Animal Science

United Nations

#3 “Ensure healthy lives and promote well-being for all ages”. 2016

The United Nations has emphasized the need to:

-end preventable deaths of new-borns and children under five

-end avoidable mortality caused by non-communicable diseases

-achieve universal health coverage

-support the research and development of medicines

1 End Poverty in all its forms everywhere
3 Ensure healthy lives and promote well-being for all at all ages
4 Ensure inclusive and equitable quality education and promote lifelong learning opportunities for all
5 Achieve gender equality and empower all women and girls
#10 Reduce inequality within and among countries
#17 Revitalize the global partnership for sustainable development

NGO COMMITTEE FOR RARE DISEASES


#ADay4All
Most rare and disabling conditions manifest in early childhood
2010
EAP

NGOCommitteeRareDiseases.org

Aims to

- act as an open forum to collect, share and disseminate information and research

Training in pediatric health and social care

HOME | TOPICS | IN DEPTH | SECRETARY-GENERAL | MEDIA

Africa | Americas | Asia Pacific | Middle East | Europe | History Corner | UN Art and Gifts

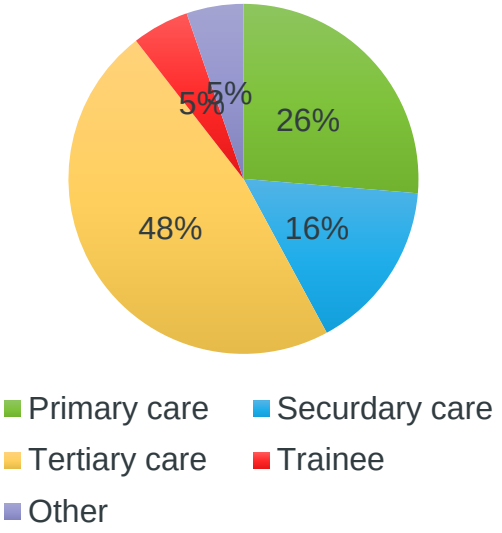
“If we are really serious about achieving universal health coverage and improving people’s lives, we must get serious about primary health care,” declared, Tedros Adhanom Ghebreyesus, WHO Director-General, at the launch of the report.

“That means providing essential health services like immunization, antenatal care, healthy lifestyle advice as close to home as possible, and **making sure people do not have to pay for this care out of their own pockets.”**

22 September 2019 UHC report United - Nations News

Universal Health Coverage, leave no child behind

Pediatricians working in:



European Pediatric Network Rare Diseases

Questionnaire
October- November 2019

Responce 38 ; 24 countries

EAP Rare Diseases

EUROPEAN PAEDIATRIC ASSOCIATION (EPA / UNEPSA)

ECPCP

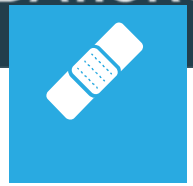
KEEP THE PROMISE:

LEAVE NO ONE BEHIND

12.12.2019 | UHCDAY.ORG

#HealthforAll

Accessible Diagnostics



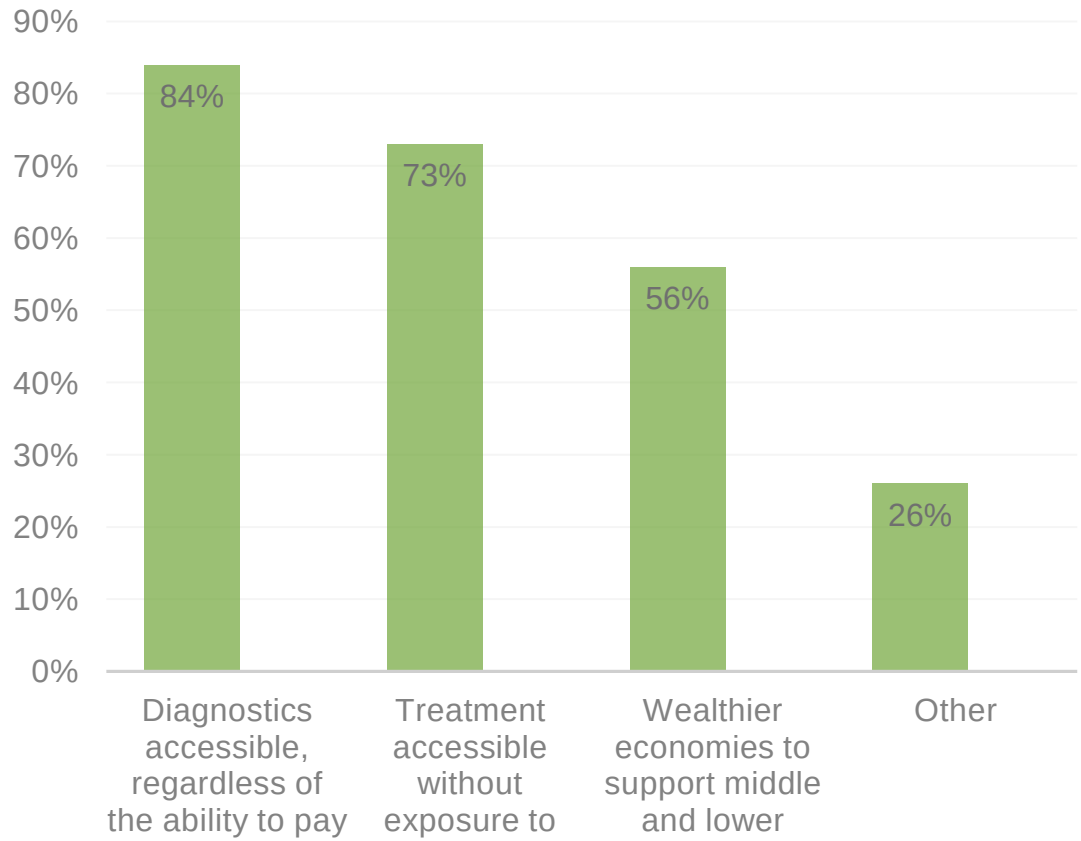
Quality Information

Training Primary Care

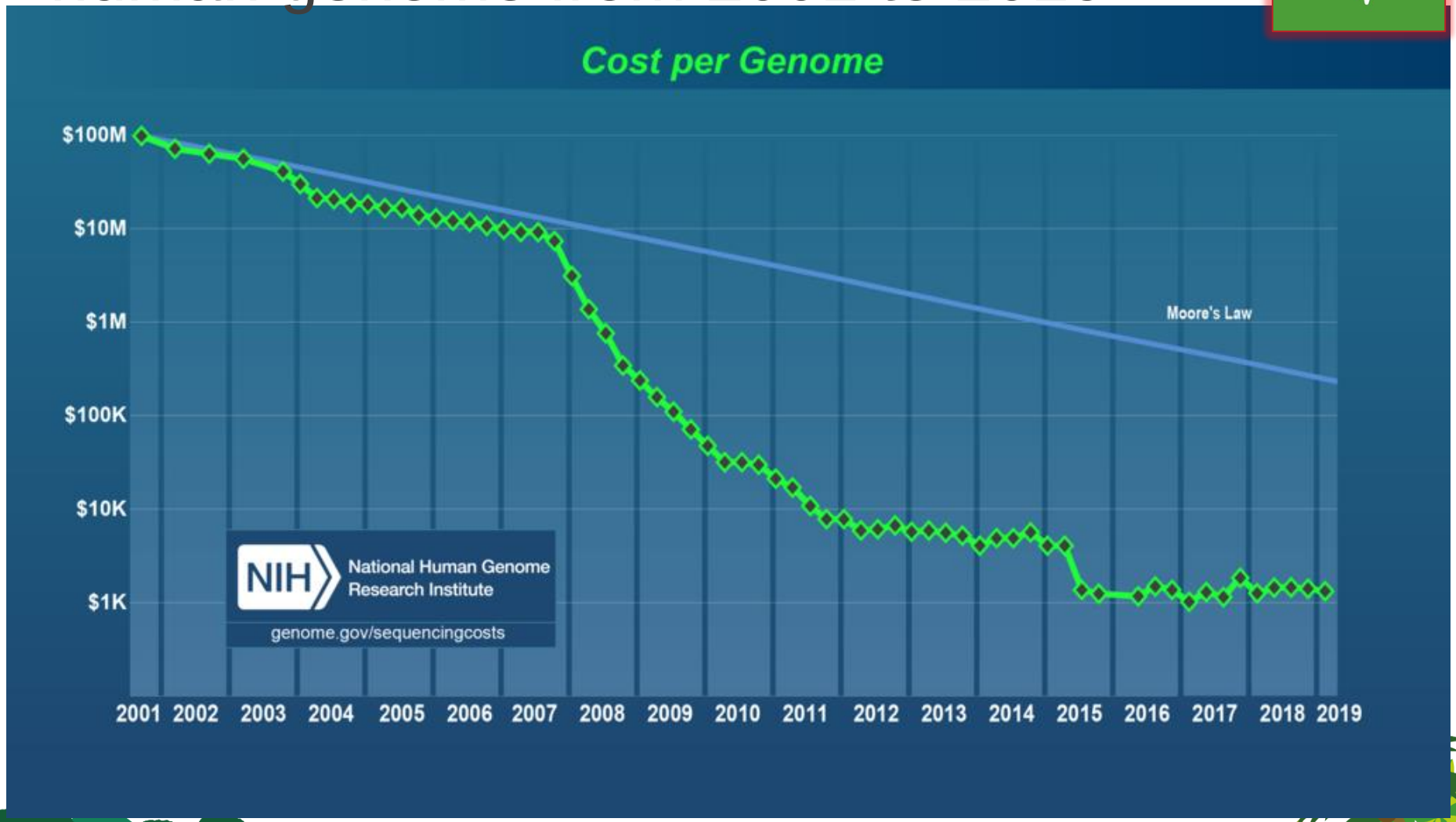
Data exchange

Strengthen efforts to address… **rare diseases** …as part of Universal Health Coverage (UHC nr 34)

What global action would be necessary?



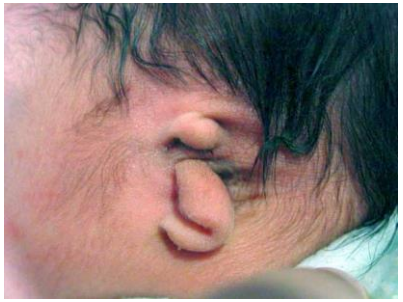
Evolution of the cost of sequencing a human genome from 2001 to 2019



Keep the promise

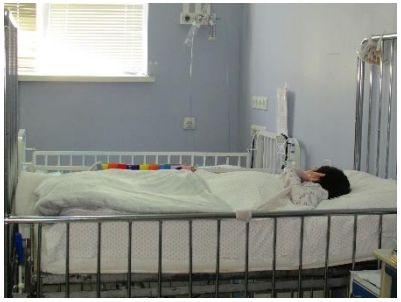
The Netherlands

Day Centre
Coffin
Lowrey
Syndrome



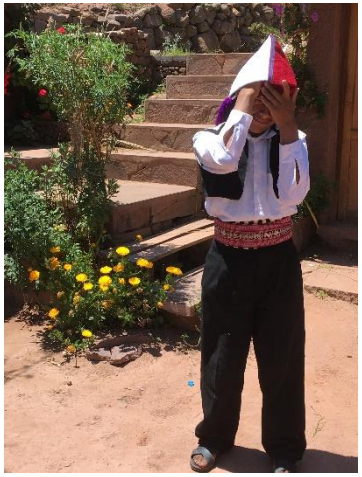
Sri Lanka

Pediatric Clinic
To be diagnosed



Georgia

Abandoned
Undiagnosed

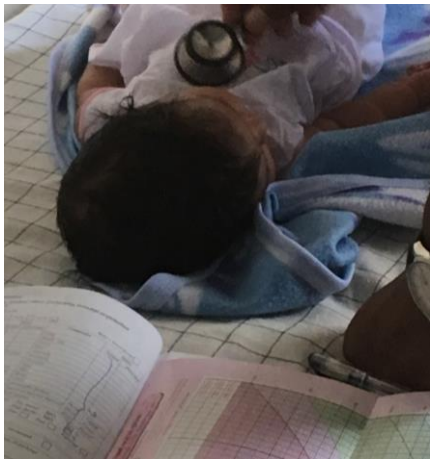


Peru

Living with family
In rural village
‘ Birth trauma’

World wide children are measured, examined, developmental screened, and vaccinated in

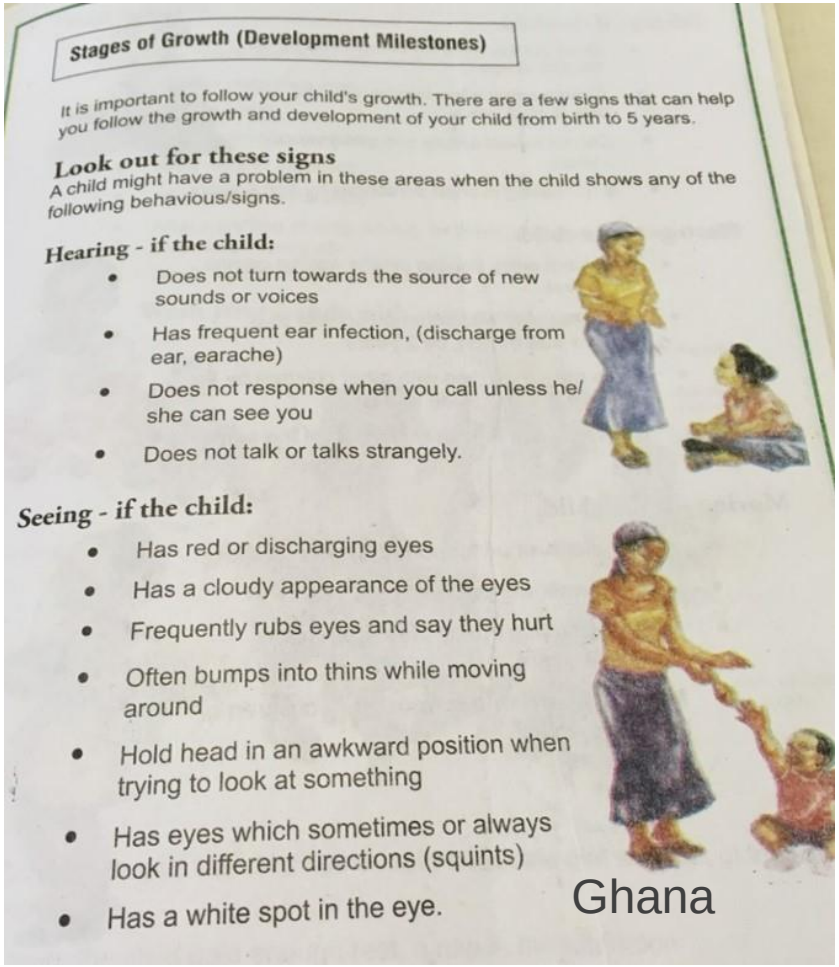
Preventive child health



World Health Organization

Home-based records

Early recognition



Disabled child

Children living with the diagnosis

- autism,
- developmental delay,
- cerebral palsy,
- epilepsy,
- hearing deficits,
- visual impairment

may very well have a

rare condition with

➢ specific health risks and treatment.

Causes of Autism

WHOLE – EXOME sequencing

In this study, we performed whole-exome sequencing on 120 Autism Spectrum Disorder cases and identified three missense mutations in coding regions of the MECP2 gene. > RETT Syndrome

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Molecular Autism

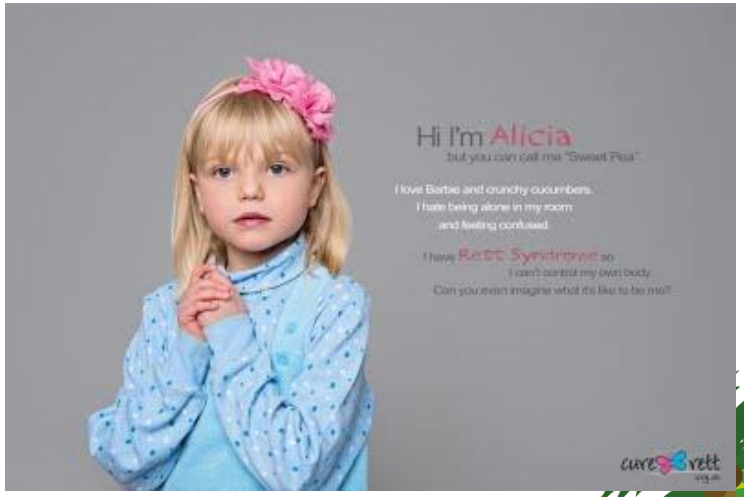
Home | About | Articles | Submission Guidelines

Abstract
Background
Methods
Results
Conclusions
Discussion
Declarations
References

Research | Open Access

Identification of autism-related *MECP2* mutations by whole-exome sequencing and functional validation

Zhu Wen, Tian-Lin Cheng, Gai-zhi Li, Shi-Bang Sun, Shun-Ying Yu, Yi Zhang, Ya-Song Du and Zilong Qiu



GENE Panels

Epilepsy (Continued)
Gene panels

☐ **Epilepsy full gene panel** (EPI00v18.1; 200 *genes)*

AARS, ACTL6B, ADSL, ALDH7A1, ALG13, AMT, ANKRD11, AP3B2, ARHGEF9, ARV1, ARX, ASAH1, ATAD1, ATP1A2, ATP1A3, ATP6AP2, ATRX, BRAT1, CACNA1A, CACNB4, CASK, CDKL5, CERS1, CHD2, CHRNA2, CHRNA4, CHRNB2, CLCN4, CLN3, CLN5, CLN6, CLN8, CNKSR2, CNTNAP2, COQ4, CPT2, CSNK2B, CTNND2, CTSD, CUL4B, DCX, DENND5A, DEPDC5, DNAJC5, DNM1, DOCK7, DYRK1A, EEF1A2, EPM2A, FGD1, FLNA, FOLR1, FOXG1, FRRS1L, GABRA1, GABRA3, GABRB3, GABRG2, GAMT, GCSH, GLDC, GLRA1, GLRB, GNAO1, GOSR2, GPC3, GPHN, GRIA3, GRIK2, GRIN1, GRIN2A, GRIN2B, GRIN2D, GRN, HCFC1, HCN1, HNRNPU, HSD17B10, HUWE1, INTS8, IQSEC2, IRF2BPL, KCNA2, KCNB1, KCNC1, KCND3, KCNH1, KCNJ10, KCNMA1, KCNQ2, KCNQ3, KCNQ5, KCNT1, KCTD7, KDM5C, KIAA2022, KMT2A, KPNA7, LGI1, MBD5, MDH2, MECP2, MED12, MEF2C, MFSD8, MOCS1, MOCS2, MTHFR, mTOR, NAPB, NBEA, NHLRC1, NPRL2, NPRL3, NRXN1, NSDHL, OFD1, OPHN1, PAK3, PCDH19, PGAP1, PHF6, PHGDH, PIGA, PIGN, PIGO, PIGT, PLCB1, PLP1, PNKP, PNPO, POLG, PPP3CA, PPT1, PQBP1, PRICKLE1, PRICKLE2, PRIMA1, PRRT2, PSAT1, PSPH, PURA, QARS, RAB39B, RAI1, RANBP2, RELN, RNASEH2A, RNASEH2B, RNASEH2C, ROGDI, RPS6KA3, SAMHD1, SCARB2, SCN1A, SCN1B, SCN2A, SCN8A, SHANK3, SIK1, SLC12A5, SLC13A5, SLC19A3, SLC1A3, SLC25A22, SLC2A1, SLC35A2, SLC6A1, SLC6A5, SLC6A8, SLC9A6, SMC1A, SMS, SNAP25, SON, SPTAN1, ST3GAL3, STX1B, STXBP1, SYN1, SYNGAP1, SYNJ1, SYP, SZT2, TBC1D24, TBCE, TBCK, TCF4, TPP1, TREX1, TRIO, UBA5, UBE2A, UBE3A, UGDH, WDR45, WWOX, YWHAG, ZDHHC9, ZEB2

MECP2

STBXP-1

☐ **Inflammatory epilepsy*** (EPI10v17.1; 3 genes)
CPT2, RANBP2, SCN1A
Copy number analysis*: ☐ SCN1A

☐ **Epilepsy with paroxysmal disorders*** (EPI08v18.1; 11 genes)
ATP1A2, ATP1A3, CACNA1A, KCNA2, KCNMA1, PRRT2, SCN1A, SCN8A, SLC1A3, SLC2A1, CTNND2
Copy number analysis*: ☐ SLC2A1

Epilepsy
Single gene | Sequence analysis

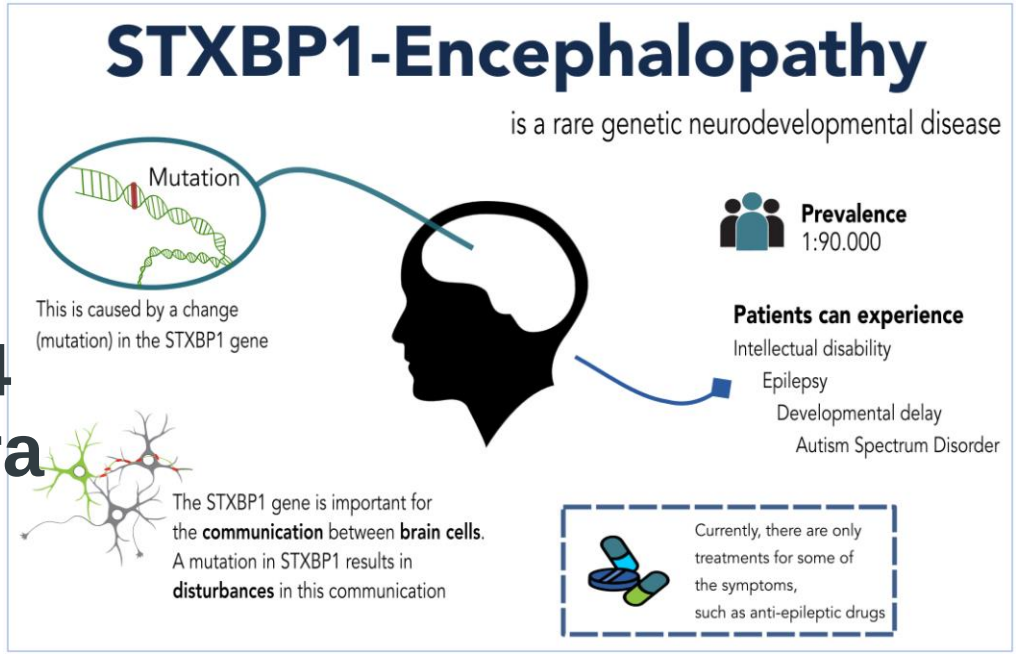
☐ Autosomal dominant lateral temporal lobe epilepsy (ADLTE)	LGI1
☐ Benign familial infantile seizures type 2 (BFIS2)	PRRT2
☐ Benign familial neonatal seizures (BFNC)$^{\delta}$	KCNQ2$^{\delta}$
☐ Benign familial neonatal seizures (BFNC)$^{\delta}$	KCNQ3$^{\delta}$
☐ Benign familial neonatal-infantile seizures (BFNIS)	SCN2A
☐ Cortical dysplasia-focal epilepsy syndrome (CDFE)	CNTNAP2
☐ Dravet syndrome (SMEI/SMEB)$^{\delta}$	SCN1A$^{\delta}$
☐ Early infantile epileptic encephalopathy type 1 (EIEE1)$^{\delta}$	ARX$^{\delta}$
☐ Early infantile epileptic encephalopathy type 2 (EIEE2)$^{\delta}$	CDKL5$^{\delta}$

At 2 month boy

Seizures : abnormal EEG generalized epilepsy

MRI normal

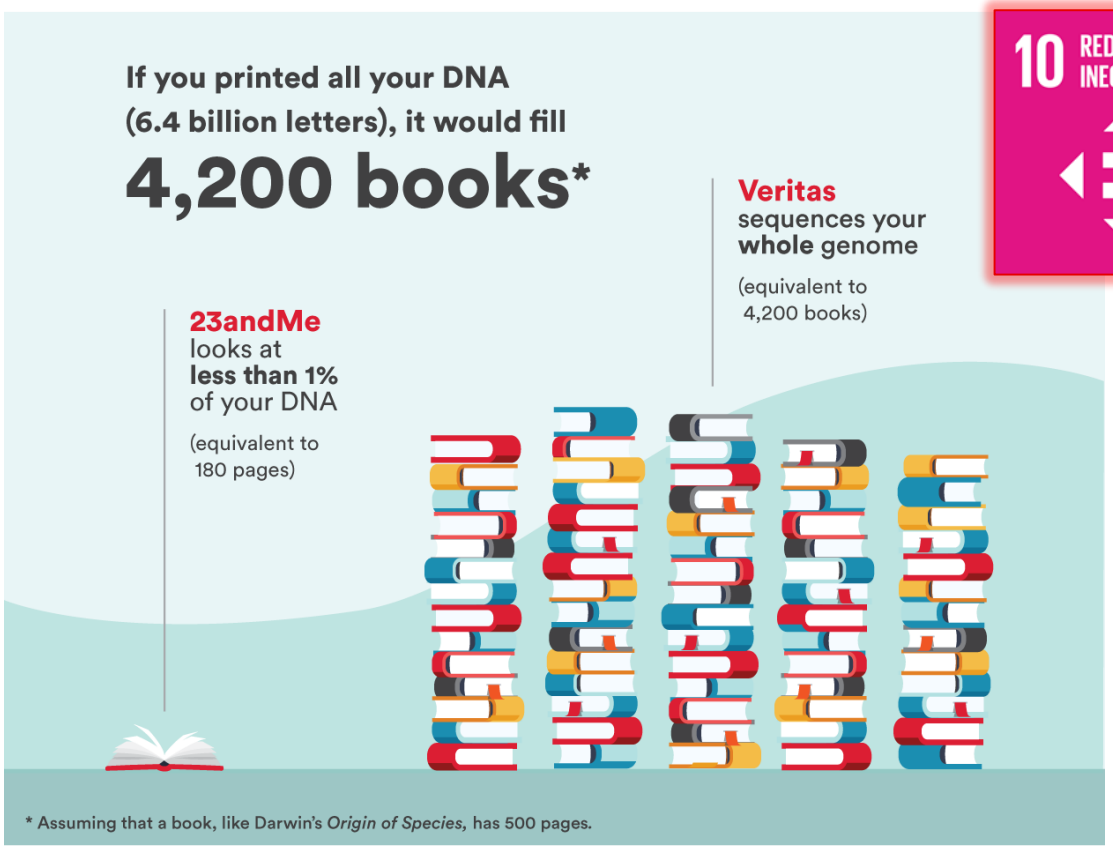
STXBP1; epileptic encephalopathy type 4 OMIM #612164/ Otahara syndrome



Vaccination risk?

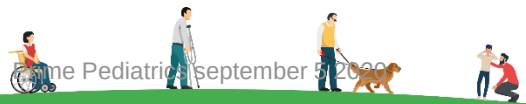
Whole Genome Sequencing, or WGS for short, is literally knowing all the letters of a person's DNA in the proper sequence. But knowing the letters is just the first part of the equation.
The tricky part is interpreting, or analyzing, what those letters mean.

www.veritasgenetics.com/myGenome



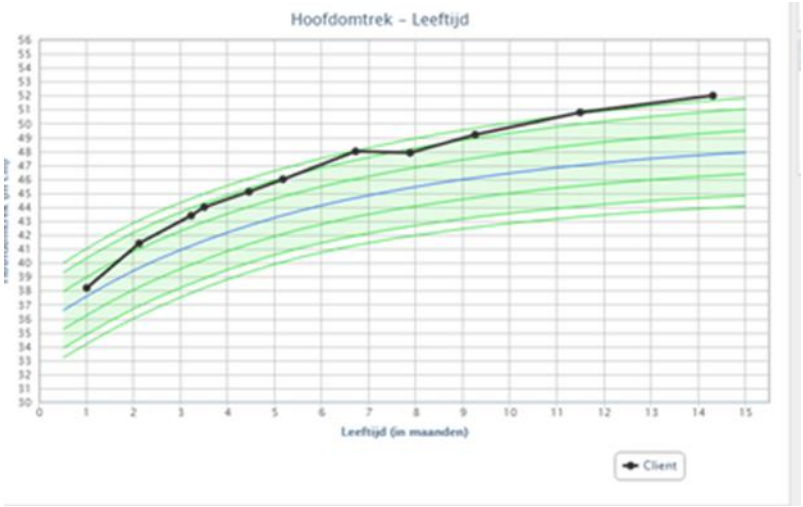
And this matters because having your **whole genome** sequenced means:

1. **More Useful Info**
   90%+ of relevant DNA is distributed across your genome
2. **More Actionable Insights**
   Make better health & lifestyle decisions with clinical-grade results
3. **A Resource for Life**
   Sequence your genome once and learn more and more as science progresses



Global Child Health

Measure
Head circumference



DCC gene mutation p.(Val1117Met) p.(Thr1339Ile) The Netherlands
Pathogenic mutation ?
DCC gene mutations are associated with congenital mirror movement disorder

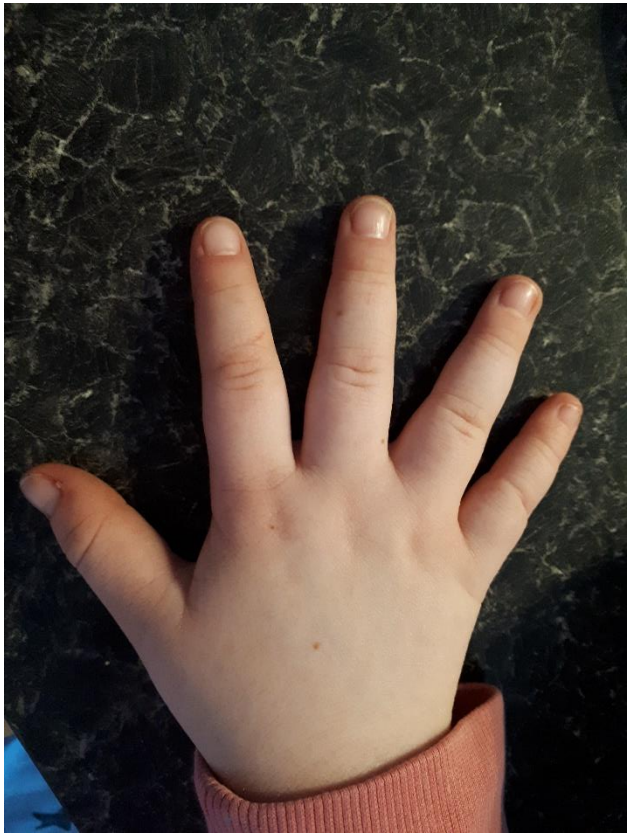
Coordinated Care

-developmental delay

-early loss of teeth

Exoom screening, genes related to developmental delay:

Gene RPSKA3: mutation c.1198C>T



Coffin Lowry Syndrome

-progressive kyphosis/scoliosis

-sensorineural hearing defect .

-cardiac evaluation

-sudden loss of muscle tone induced by unexpected tactile or auditory stimuli and epilepsy.

The Netherlands

Collaborate and improve

Diagnose

Medical guideline
- Epilepsy
- Autism
- Visual impairment

Coordinate
Medical and social support

Social Support
Co-manage with families

Register
Interoperable data

Patient Information	Primary Care	Diagnosis Collaborative care	Social Services
www.shwachman.nl https://rarecare.world	Growth retardation Recurrent infections (LOINC)	Guideline SDS (Orphanetcode; SNOMED, ATC e.a.)	Recurrent illness Fatigue, Short (ICF-CY; ISO 9999)

Stichting Shwachman syndroom Support Holland

New Diagnostics

HPO
LOINC
ICPC

Diagnosis
Hurler syndrome
PKU, Duchenne MD, FOP
Shwachman Diamond Syndrome

ICD - 10
Orphacode
OMIM
SNOMED -CT
DCOM

Sign primary care
Heelstick screening
Hearing screening
Growth; Development

Guideline
Collaborative Health Care

Interoperable data model

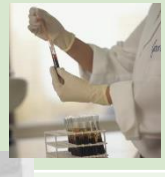
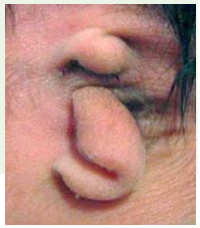
ISO 3166-1

HL7/ FHIR

ATC
New Therapeutics
ICF
ISO9999

Registry
Data collection with systematically organised computer processable collection medial terms

Guideline
Social services and rehabilitation

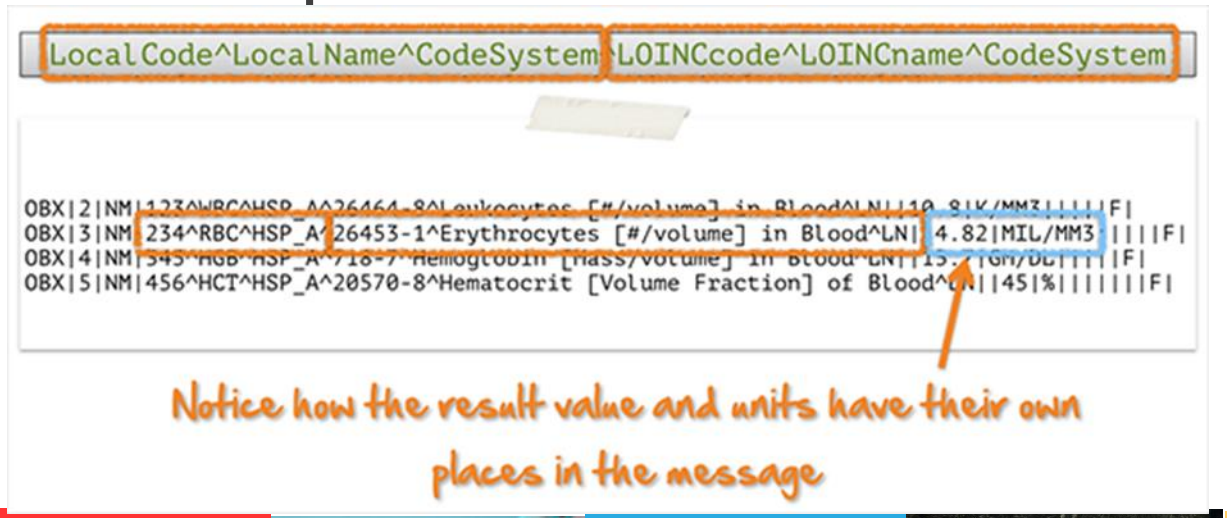
Codification	Meaning
ICD & Orpha code	International Code of Diseases / Orphanet code
ICF (-CY) 	The *International Classification of Functioning, Disability and Health for Children and Youth (ICF-CY)* is a derived vers the *International Classification of Functioning, Disability a Health* (ICF, WHO, 2001) designed to record characteris the developing child and the influence of environments surrounding the child .
LOINC 	A universal code system for tests, measurements, and observations.
ATC 	The purpose of the ATC/DDD system is to serve as a tool for drug utilization research in order to improve quality of drug use.
ISO 9999 	ISO 9999:2011 establishes a classification of assistive products, especially produced or generally available, for persons with disability.
HPO 	The Human Phenotype Ontology (HPO) provides a standardized vocabulary of phenotypic abnormalities encountered in human disease.

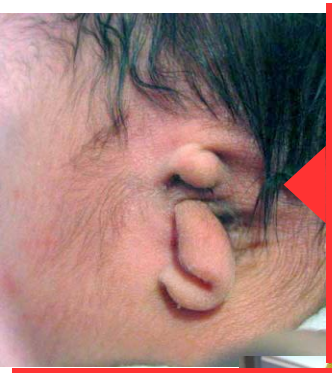
World Health Organization

LOINC

The international standard for identifying health measurements, observations, and documents.

Interoperable codes in care

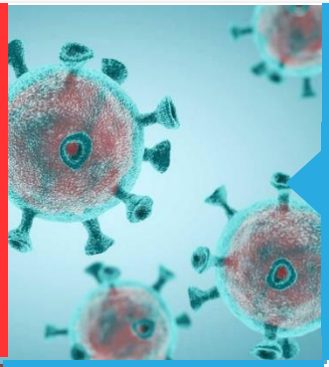




Goldenhar s
Abnormal ear

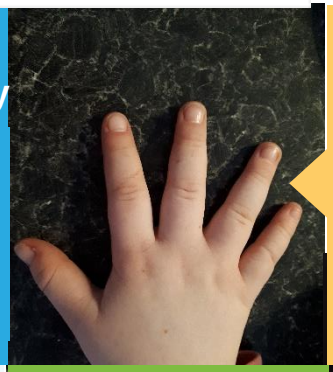
.

HP:0008551



Immunodeficiency

LOINC
94500-6
SARS

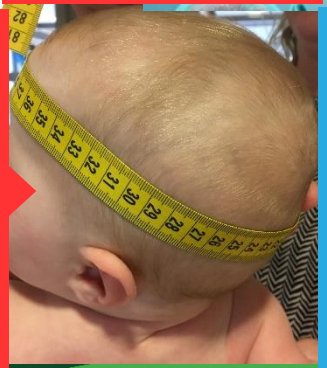


Coffin Lofry s
Tapered fingers

HP:0001182

Measuring Head Circumference

LOINC
8287-5



Neutropenia

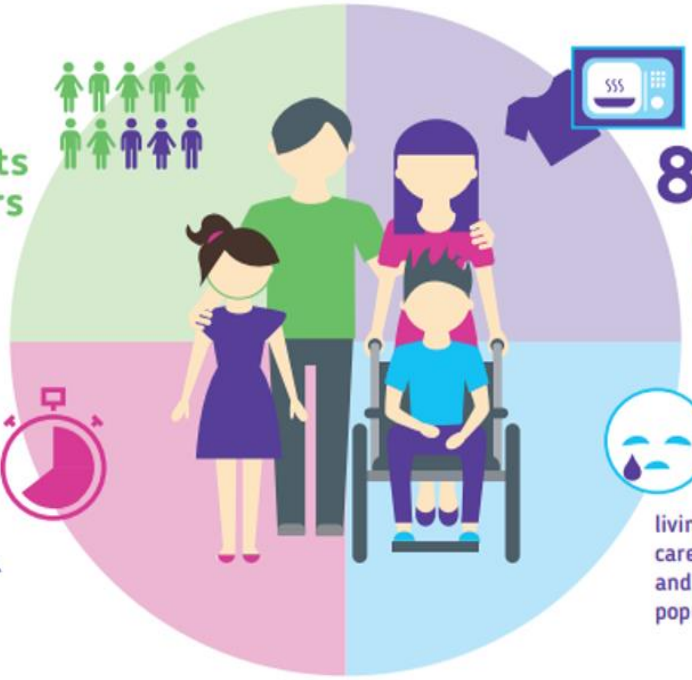
LOINC
751-8
Neutrophils

Shwachman DS

ATC

. A09AA02
Pancreatine

Rare diseases seriously impact everyday life



7 in 10 patients & carers

reduced or stopped professional activity due to their or their family member's rare disease.

8 in 10 patients & carers

have difficulties completing daily tasks (household chores, preparing meals, shopping etc.)

2/3 of carers

spend more than 2 hours a day on disease-related tasks.

3 times more people

living with a rare disease and carers report being unhappy and depressed than the general population*

* Rare Barometer Voices sample compared to International Social Survey Programme, 2011

Rare Barometer Voices

A EURORDIS INITIATIVE

Rare Barometer Voices is a EURORDIS-Rare Diseases Europe online survey initiative. It brings together over 6,000 patients, carers and family members to make the voice of the rare disease community stronger. Results are shared with policy decision makers to bring about change for people living with a rare disease.

3,071 people responded to the survey.

The survey was conducted in **23** languages across **42** countries

Thank you to all Rare Barometer Voices participants and partners!

www.eurordis.org/content/contribute-rare-barometer-programme

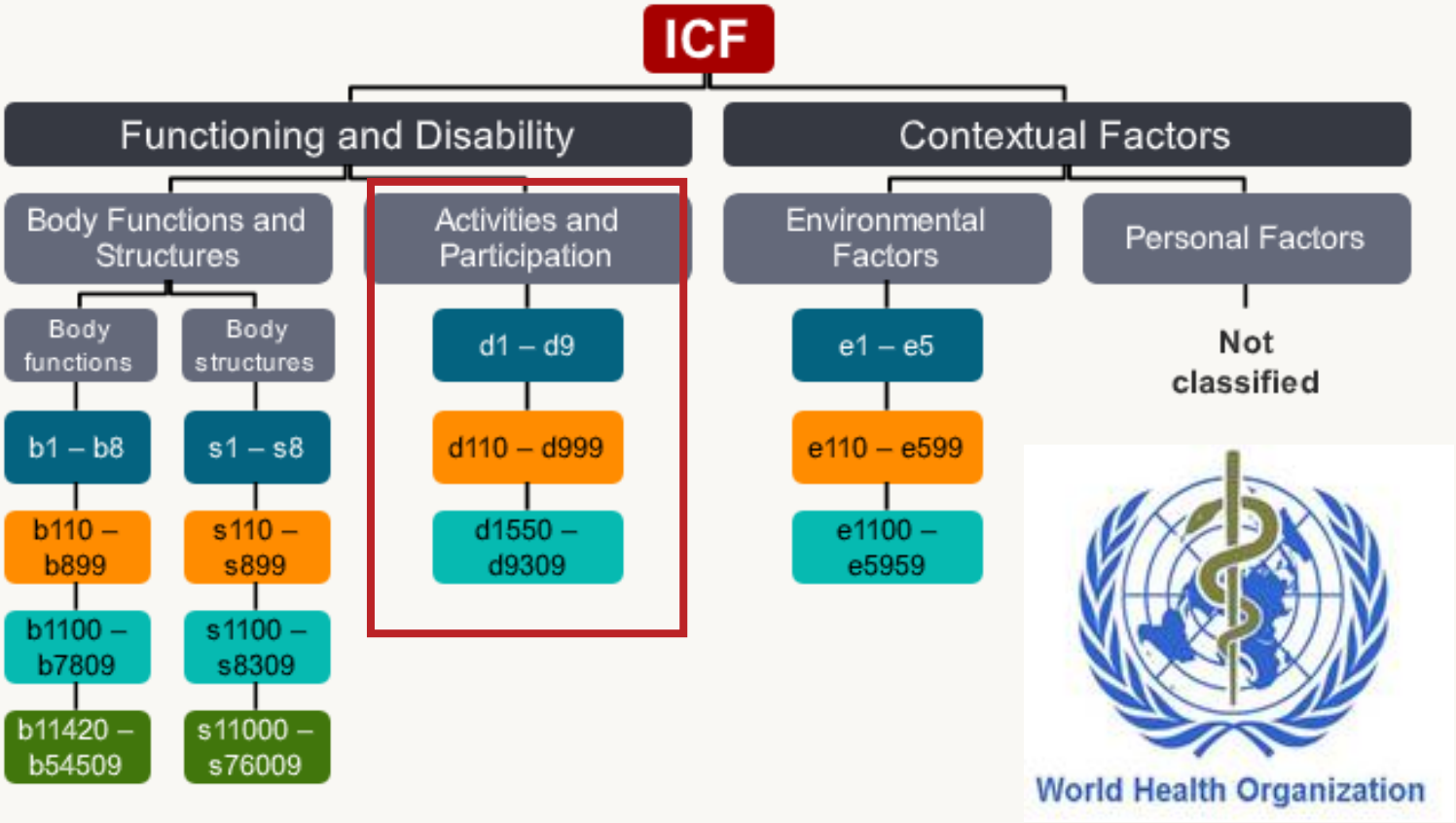
For more information visit **eurordis.org/voices** or email **rare.barometer@eurordis.org**

Global Child Health Scheme Primary Care

- Physical examination
  - Microtia
    - ICPC: H80
    - ICD 10: Q17.2
    - HPO: 0008551
  - Facial asymmetrie
    - HPO: 0000324
  - Oculo-Auriculo-Vertebral Spectrum/Goldenhar Syndrome
    - ORPHA:141132 Oculo-auriculo-vertebral spectrum
    - OMIM # 164210 HEMIFACIAL MICROSOMIA; HFM
    - Loss of hearing
      - ICF b 230
    - Listening
      - ICF d 115
- Vaccination
  - Diphteria Hemophilus Influenzae B- Pertussis- Poliomyelitis- Tetanus- Hepatitis B
    - ATC J07CA09

The structure and codes of the ICF

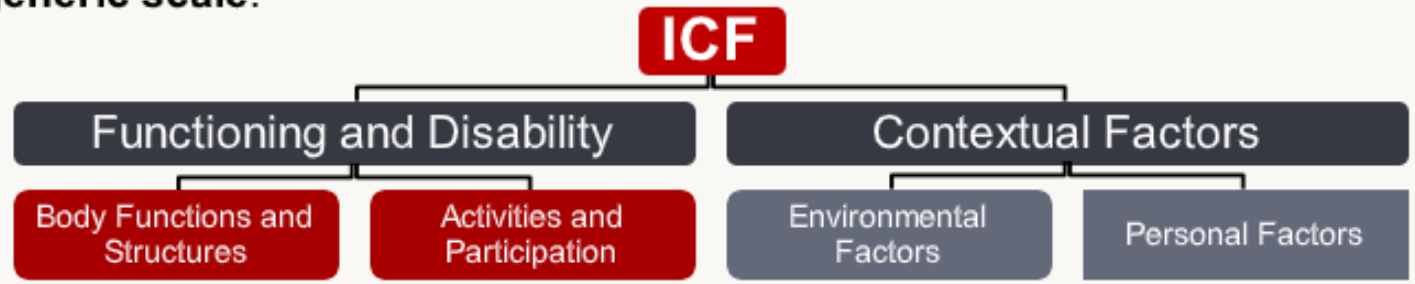
The ICF does this as well. In the ICF, ICF categories are like the geometrical objects in the previous illustration. ICF categories are placed in similar groupings of health and health-related domains and are organized in a hierarchical manner.



The following slides will explain how the ICF is structured and organized.

ICF Qualifiers

The ICF Qualifiers for the **Body Functions and Structures, Activities and Participation** components classified in the ICF are quantified using the **same generic scale**.



XXX.0 NO problem (none, absent, negligible, …)	0 – 4 %
XXX.1 MILD problem (slight, low, …)	5 – 24 %
XXX.2 MODERATE problem (medium, fair, …)	25 – 49 %
XXX.3 SEVERE problem (high, extreme, …)	50 – 95 %
XXX.4 COMPLETE problem (total, …)	96 – 100 %

XXX.8 not specified (the available information does not suffice to specify the severity of the problem, i.e. you know that it does not stand for a 0, but you have no information for deciding to apply a qualifier between 1 and 4)
XXX.9 not applicable (it is inappropriate or not possible to apply the code)

ICF d 920.0

Recreation and leisure

The structure and codes of the ICF

Categories at the 2nd level: Definition

- Activities and Participation
  - d1
  - d2
  - d3
  - d4
  - d5
  - d6
  - d7
  - d8
  - d9 Community, social and civic life
  - d910
  - d920 Recreation and leisure
  - d930
  - d940
  - d950
  - d998
  - d999

Engaging in any form of play, recreational or leisure activity, such as informal or organized play and sports, programs of physical fitness, relaxation, amusement or diversion, going to art galleries, museums, cinemas or theatres; engaging in crafts or hobbies, reading for enjoyment, playing musical instruments; sightseeing, tourism and traveling for pleasure.

28/35

Indian Mother and Childcare
Kolkata, 2020

X Linked semi dominant inheritance

The Coffin-Lowry gene (RPS6KA3) is located on the X chromosome (Xp22.2). Girls may express symptoms of CLS. Most of the persons with CLS are the...

Developmental in CLS

Developmental disability in Coffin Lowry syndrome is usually apparent at age 1-2years

Social Support

d 132 Acquiring information
d 160 Focusing attention
d 240 Handling stress and other psychological demands
d 571 Looking after one's safety
d 570 Looking after one's health
d 220 Undertaking multiple tasks
d 230 Carrying out daily routine
d 310 Communicating with - receiving - spoken messages
d 330 Speaking
d 155 Acquiring skills
d 210 Undertaking a single task
d 720 Complex interpersonal interactions

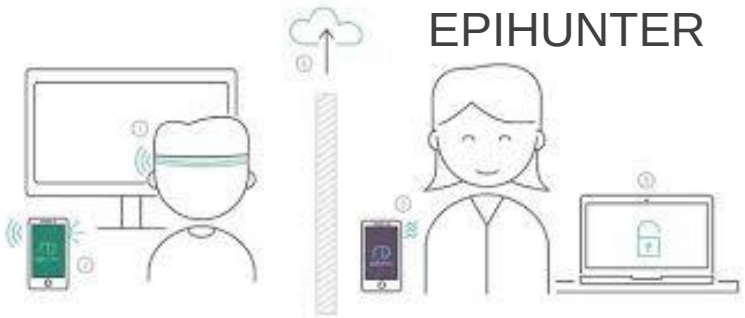
Epilepsy

ICF d132
Acquiring Information

-

Mosaic ring chromosome 20
Analyze more karyotypes !

EPIHUNTER



ICS › 11 › 11.180 › 11.180.01

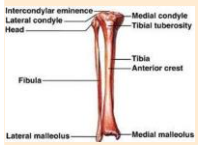
ISO 9999:2016

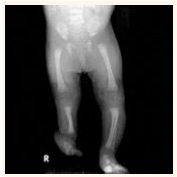
Assistive products for persons with disability — Classification and terminology

Fibula Hypoplasia

ICF International Classification, Functioning, Disability and Health

First Feature
Diagnosis Fibula Hypoplasia
Medical Guideline
ICF : Body Functions & Structures
ICF: Activity Participation





World Health Organization

ICS › 11 › 11.180 › 11.180.01

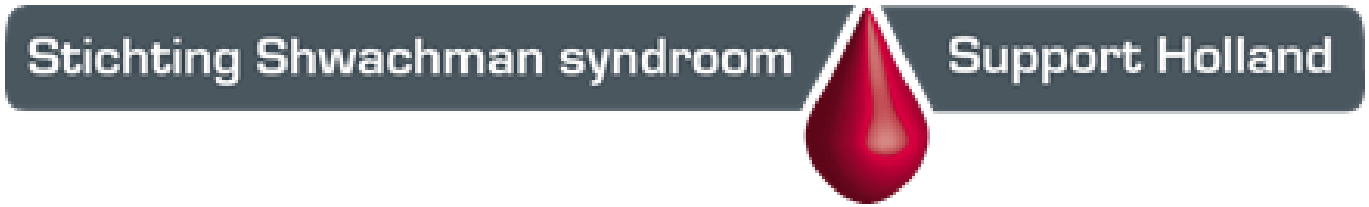
ISO 9999:2016

Assistive products for persons with disability — Classification and terminology

ISO
International Standards globally recognized guidelines and frameworks

Acknowledgement

- European Pediatric Rare Disease Network
- Consensus in Pediatrics and Child Health
- Forum Rare Diseases, Sri Lankan Pediatric Society
- Anjan Bhattacharya, Kolkata, India
- People with a rare condition and their families



https://rarecare.world/
Contact:
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Just normal people

Advocaters

Goldenhar syndrome

Thalassemia

Chromosome abnormality

Shwachman Diamond Syndrome


Thank You
For Your Attention