



# **Proposal of a Priority List of Rare Diseases Needing a Specific ICD Code**

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# Criteria for Selection

- Diseases listed in a rare disease patient **registry**
- Diseases having a **diagnostic test**
- Diseases having a dedicated **patient organisation**
- Diseases included in the priority list of the Orphanet **Emergency** guidelines project
- Diseases having an **orphan designation/drug**

# Emergency Criteria

## « A » criteria

- particular caution in transporting the patient
- particular caution for tracheal intubation
- particular caution in administering anaesthesia
- need for transfusion
- drug interactions
- hemorrhagic syndrome
- ischemic syndrome
- deep thrombophlebitis
- metabolic decompensation
- dehydration – electrolytic decompensation
- hypoglycemia – hyperglycemia
- status epilepticus
- unconsciousness / malaise / confusion / coma
- acute psychiatric trouble
- acute palsy
- arrhythmia – Heart conduction trouble
- respiratory distress
- heart failure
- sepsis (severe)
- toxic epidermal necrolysis

## « B » criteria

- seizures - epilepsy
- acute headache
- muscular weakness or deficit
- syncope
- arterial hypertension – hypertensive crisis
- acute renal failure
- hepatic failure
- acute visual troubles
- vertigo
- severe acute pain
- fractures
- acute infection
- acute cutaneous eruption
- fever
- acute abdominal pain
- vomiting - diarrhea
- counterindication to organ donation

# Sources Cross-linked

- Veneto registry of rare diseases
- 1348 Orphanet disease entries with a diagnostic test
- 2751 Orphanet disease entries with a patient organisation
- 114 priority diseases for emergency guidelines
- 217 diseases linked to an orphan designation /drug (excluding infectious diseases)
- 1706 diseases with prevalence data

# Resulting Classification of 921 Priority Diseases - extract

- **Rare cardiac disease**
  - ❖ **Heart malformation, congenital**
    - Tetralogy of Fallot
    - Atrioventricular canal, complete
    - **VATER association**
    - **Monosomy 22q11**
    - **CHARGE association**
  - ❖ **Cardiac disease, genetic**
    - Cardiomyopathy, familial dilated
    - Cardiomyopathy, hypertrophic, primary or idiopathic
    - **Barth syndrome**
  - ❖ **Cardiac disease, acquired, rare**
    - Peripartum cardiomyopathy
- **Gastroenterologic disease, rare**
  - Achalasia, primary
  - Gastric cancer
  - Hirschsprung disease
- **Pancreatic disease, rare**
  - **Cystic fibrosis**
  - Shwachman-Diamond syndrome
- **Esophageal malformation**
  - **VATER association**
- **Anorectal malformation syndrome**
  - Anorectal malformation
  - **VATER association**
  - **Monosomy 22q11**
- **Hepatic disease, rare**
  - Budd-Chiari syndrome
  - **Alpha-1 antitrypsin deficiency**
- **Respiratory disease, rare**
  - **Cystic fibrosis**
  - **Alpha-1 antitrypsin deficiency**
  - Diaphragmatic hernia, congenital
  - Laryngo-tracheo-esophageal cleft
- **Skin disease, rare**
  - Lamellar ichthyosis
  - **Ehlers-Danlos syndrome, classic type**
  - Pseudoxanthoma elasticum
  - Ataxia telangiectasia
  - **Melanoma, familial**
- **Eye disease, rare**
  - Anophthalmia - Microphthalmia, isolated
  - Aniridia
  - **WAGR syndrome**
  - **Melanoma, familial**
- **Renal disease, rare**
  - Renal agenesis, bilateral
  - **CHARGE association**
  - **WAGR syndrome**
  - Nephrotic syndrome, idiopathic, steroid-sensitive
  - **Cystinosis**
- **Metabolic disease, rare**
  - **Barth syndrome**
  - Citrullinemia
  - **Cystinosis**
- **Systemic and rheumatologic disease**
  - **Ehlers-Danlos syndrome, classic type**
  - Marfan syndrome
  - Amyloidosis

# ICD-10 and Priority List of Diseases

- 400 diseases had no specific code
- 259 diseases are listed under an existing code
- 262 diseases had a specific ICD-10 code

... BUT there are several miscodings

# Priority List: Validation Process

Submission to:

- Orphanet Scientific Advisory Board?
- Learned societies?
- WHO collaborating centre?
- Patient organisations?
- Network of EU competent authorities?
- Other?

Timetable?



# **Coding rare diseases with ICD-10**

Problems and Questions

# • Cross-matching ICD-10 coding systems: Outcome typologies

- ICD-10 codes that do not match (no specific code)
  - Mistake in one of data sets
  - Different interpretations are possible
- ICD-10 codes that match
  - RD is correctly coded in ICD-10 (specific code, RD mentioned)
  - RD is coded in a wrong ICD-10 category (specific code, RD mentioned)
  - Coincidental interpretations (no specific code)

## In other words...

- There is no specific code for the RD nor is the RD mentioned under a category
  - Coding needs interpretation
- There is a specific code for the RD or it is mentioned under a category
  - Correct
  - Incorrect

# Mismatch due to different interpretations

- CADASIL (OMIM 125310)
  - UKGTN 177.8
    - Other specified disorders of arteries and arterioles
  - Orphanet F01.1
    - Multi-infarct dementia (In: vascular dementia)

# Match due to coincidental interpretations

- Pulmonary lymphangiectasia, congenital
  - CINEAS Q34.8
  - Orphanet Q34.8
    - Other specified congenital malformations of respiratory system

There is no code for congenital lung malformations of vascular origin

# Matching categories, however...

- Gastric cancer
  - CINEAS: C16.9
    - Stomach, unspecified - Gastric cancer NOS
  - Orphanet: C16
    - Malignant neoplasm of stomach

Ambiguity of the ICD-10 ?

# Matching incorrect specific codes

- Marfan syndrome
  - Q87.4
    - In: Q87 Other specified **congenital malformation** syndromes affecting multiple systems


Could have been included in

- M30-M36 Systemic connective tissue disorders

# • Matching codes included in inappropriate categories

- VATER association
  - Q87.2 Congenital malformation syndromes predominantly involving limbs
    - Holt-Oram
    - Klippel-Trenauney-Weber
    - ...
    - VATER

VATER = **V**ertebral defects, **A**nal atresia, **T**racheo**E**sophageal fistula with esophageal atresia and **R**adial dysplasia

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**Some problems,  
some questions...**

# • Coding according to the cause or the consequence?

- Leigh syndrome
  - **G 31.8**: Other specified degenerative diseases of nervous system
    - Sub-acute necrotizing encephalopathy [Leigh]
  - **Orphanet classification**
    - Neurometabolic diseases
    - Metabolic diseases
      - Mitochondrial diseases

There is no mitochondrial diseases category in ICD-10

# • Coding according to the cause or the consequence?

- Kearns-Sayre syndrome
  - **H 49.8**: Other paralytic strabismus
    - ...
    - Kearns-Sayre syndrome
  - **Orphanet classification**
    - Neurometabolic diseases
    - Neuromuscular diseases
    - Metabolic diseases
      - Mitochondrial diseases
    - Deafness, genetic
    - Rare eye diseases:
      - Corneal dystrophies
      - Syndromic retinitis pigmentosa
      - Symptomatic strabismus

# • Coding according to the cause or the consequence?

- Alkaptonuria E70.2
- Tyrosinemia type 1 E70.2
  - **E 70.2**: Disorders of tyrosine metabolism
    - Alkaptonuria
    - Tyrosinemia
    - ...
  - **Both diseases are coded to the cause but phenotypes are quite different**
    - Alkaptonuria: pigmentation disorders, muscular-skeletal symptoms, arthropathy... or asymptomatic
    - Tyrosinemia: severe hepatocellular necrosis (early onset form), renal tubulopathy (late onset form)

# How to code hereditary forms of diseases?

- Melanoma, familial
  - C43 Melanoma, malignant
    - A Z80 code should be added to familial forms of cancers?
- What about familial forms of not rare diseases?
  - Parkinson disease, familial form
    - G20 Parkinson disease

# Problematic groups of diseases

- Systemic diseases (Internal medicine)
  - Marfan disease in Q87.4 (malformations)
  - Amyloidosis in E85 (metabolic disorders)
  - Mastocytosis in:
    - Q82 (Other congenital malformations of skin)
    - C96.2 (Malignant mast cell tumour)
  - Mediterranean fever
    - E85.0 (Non-neuropathic heredofamilial amyloidosis) in Metabolic disorders

# Problematic groups of diseases

- Metabolic diseases
  - Some categories lacking:
    - Mitochondrial diseases
    - Lysosomal diseases
    - Peroxysomal diseases
    - *etc.*
- Some metabolic diseases are coded according to their consequences because they are not identified as metabolic in ICD-10

# Problematic groups of diseases

- Skin diseases
  - Some skin diseases are coded as malformations
    - Q80 Congenital ichthyosis
    - Q81 Epidermolysis bullosa
    - Q82.1 Xeroderma pigmentosum
    - *etc.*

# Problematic groups of diseases

- Mental retardation
  - ICD-10 codes for MR are based on QI
    - Coding can only be done on an individual basis
    - Coding for syndromes with MR it is, therefore, not possible

# Problematic groups of diseases

- Polymalformative syndromes, sequences, associations.
  - There is no specific category for them, so one of the malformations present should be highlighted
  - Monosomy 22q.11 (Di George syndrome)
    - D82.1 DiGeorge's syndrome – Pharyngeal pouch syndrome – Thymic: aplasia or hypoplasia with immunodeficiency (in: Immunodeficiency associated with other major defects)

Immunodeficiency is not constant in DiGeorge syndrome.

# Problematic groups of diseases

- Rare cancers
  - ICD-10 codification is only anatomical
  - Coding rare cancers with ICD-O?
    - Needs to be tested for rare cancers.