Supplementary table 1. Most prevalent diseases amongst cases (N = 459)

Name of the disease	**n***
Marfan's syndrome	42 (14.7%)
Sjögren's syndrome	39 (13.7%)
Alpha-1-antitrypsin deficiency	28 (9.8%)
Prader-Willi	26 (9.1%)
Phelan-McDermid	19 (6.7%)
Becker and Duchenne's diseases	16 (5.6%)
Gilles de la Tourette	15 (5.3%)
Rett	14 (4.9%)
Cornelia de Lange	10 (3.5%)
Steinert	10 (3.5%)
Primary Biliary Cirrhosis	10 (3.5%)
Addison's syndrome	9 (3.2%)
Smith-Magenis	7 (2.5%)
Williams	7 (2.5%)
Succinic semialdehyde dehydrogenase (ssadh) deficiency	7 (2.5%)
Wilson	7 (2.5%)
Neurofibromatosis	7 (2.5%)
Fragile X syndrome	6 (2.1%)
Friedreich's ataxia	6 (2.1%)

*Number of patients and percentage.

Supplementary table 2.

GENETIC AND NEUROGENETIC SYNDROMES (n=299)			
Genetic syndromes (n=156)	**Number of patients (1)**	**Prevalence (2)**	**Expected number of patients (3)**

Marfan syndrome	42	1-5/10,000	0,09-0,45 in 905 participants
Prader-Willi syndrome	26	1-9/100,000	0,009-0,08
Phelan McDermid syndrome	19	4x10-4/10,000	0,36
Cornelia de Lange	11	Unknown	
Smith-Magenis syndrome	7	1-9/100,000	0,009-0,08
Williams syndrome	6	1/7,500	0,12
Fragile x syndrome	6	1-5/10,000	0,09-0,45
Klinefelter syndrome	5	No data	
22q11 syndrome	5	1-5/100,000	0,009-0,045
Angelman syndrome	4	1-9/100,000	0,009-0,08
Rubinstein-Taybi syndrome	4	1-9/100,000	0,009-0,08
Camurati Engelmann syndrome	3	Unknown	
Dystrophic epidermolysis bullosa	3	1-9/1,000,000	0,0009-0,008
Algrove syndrome	2	No data	
Loeys Dietz syndrome	2	Unknown	
Osteogenesis imperfecta	2	1-5/10,000	0,09-0,45
Castellman	1	No data	
Ectodermic dysplasia	1	No data	
13q microdelition	1	<1/1,000,000	<0,0009
Scleroderma	1	1-5/10,000	0,09-0,45
Xp22.12 microduplication	1	No data	
Autosomal dominant polycystic kidney disease	1	1-5/10,000	0,09-0,45
Sotos syndrome	1	1-9/100,000	0,009-0,08
Multiple congenital artrogriposis	1	No data	

Mowat Wilson syndrome	1	Unknown	
Neuromuscular diseases (n=60)			
Duchènne muscular dystrophy	16	1-9/100,000	0,009-0,08
Steinert myotonic dystrophy	10	1-5/10,000	0,09-0,45
Becker muscular dystrophy	5	1-9/100,000	0,009-0,08
Charcot Marie Tooth syndrome	5	1-5/10,000	0,09-0,45
Merosin deficient muscular dystrophy	4	1-9/1,000,000	0,0009-0,008
Spinal muscular atrophy	4	Unknown	
Facioscapulohumeral muscular dystrophy	3	1-9/100,000	0,009-0,08
Miastenia gravis	3	No data	
Miotubular myopathy	2	No data	
Non-specified sensitivomotor neuropathy	2	No data	
RYR1 deficiency	1	Unknown	
Congenital muscular dystrophy laminin deficiency	1	Unknown	
Non-specified muscular dystrophy	1	No data	
Inclusion body myositis	1	1-9/1,000,000	0,0009-0,008
Non-specified congenital myopathy	1	No data	
Bethlem myopathy	1	<1/1,000,000	<0,0009
Neurologic/Psychiatric syndromes (n=57)			
Tourette syndrome	15	No data	
Rett syndrome	14	1-9/100,000	0,009-0,08
Neurodegeneration with brain iron accumulation (NBIA)	6	Unknown	
GRIN2B mutation	4	Unknown	

Spastic paraparesis	4	1-9/100,000	0,009-0,08
Amyotrophic lateral sclerosis	4	1-9/100,000	0,009-0,08
Narcolepsy	1	1-5/10,000	0,09-0,45
Joubert syndrome	1	1-9/100,000	0,009-0,08
GRIN1 mutation	1	No data	
Lisencephly type 1	1	No data	
Sd Helsmoortel-Van Der Aa (ADNP)	1	1-9/100,000	0,009-0,08
Juvenile parkinsonism	1	<1/1,000,000	<0,0009
Generalized dystonia	1	No data	
Bainbridge Ropers syndrome	1	<1/1,000,000	<0,0009
CDKL5 mutation	1	Unknown	
Siringomielia	1	No data	
Ataxia (n=18)			
Machado-joseph disease/spinocerebellar ataxia type 3	7	1-9/100,000	0,009-0,08
Friedreich ataxia	6	1-9/100,000	0,009-0,08
Charlevoix-saguenay spastic ataxia	2	Unknown	
Ataxia telangiectasia	2	1-9/1,000,000	0,0009-0,008
Cerebellar ataxia	1	1-9/100,000	0,009-0,08
Neuroectodermic syndromes (n=8)			
Neurofibromatosis type 1	7	1-5/10,000	0,09-0,45
Tuberous sclerosis complex	1	Unknown	
INHERITED METABOLIC DISORDERS (n=53)			
Mitochondrial syndrome	12	1-9/100,000	0,009-0,08

SSADH	7	Unknown	
Wilson disease	7	1-9/100,000	0,009-0,08
Lysosomal acid lipase deficiency	4	1-9/100,000	0,009-0,08
Fabry disease	4	1-5/10,000	0,09-0,45
Very long-chain acyl-coa dehydrogenase deficiency (VLCAD)	3	1-9/100,000	0,009-0,08
Mucopolysaccharidosis type 2	2	1-9/1,000,000	0,0009-0,008
Glutaric aciduria type 1	2	Unknown	
X-linked adrenoleukodystrophy	2	Unknown	
Dopamine transporter deficiency	1	No data	
Smith-Lemli-Opitz syndrome	1	Unknown	
Trimethylaminuria	1	Unknown	
2-hydroxyglutaric aciduria	1	Unknown	
Ornithine transcarbamylase deficiency (OTC) deficiency	1	1-9/100,000	0,009-0,08
Carnitine palmitoyltransferase II (CPT II) deficiency	1	1-9/100,000	0,009-0,08
Congenital hypertriglyceridemia	1	<1/1,000,000	<0,0009
Citrullinemia	1	Unknown	
Mucopolysaccharidosis type 1	1	1-9/1,000,000	0,0009-0,008
Classic galactosemia	1	Unknown	
OTHERS (n=107)			
Endocrinologic syndromes	5	No data	
Haemophilia	2	1-9/100,000	0,009-0,08
Autoimmune syndromes (n=55)			
Sjögren syndrome	35	1-5/10,000	0,09-0,45

Addison disease	10	1-5/10,000	0,09-0,45
Systemic lupus erythematosus	5	1-5/10,000	0,09-0,45
Dermatomyositis	3	1-9/100,000	0,009-0,08
Autoimmune polyendocrinopathy type 1	1	1-9/1,000,000	0,0009-0,008
Autoimmune polyendocrinopathy type 2	1	Unknown	
Pulmonary syndromes (n=28)			
Alpha-1 antitrypsin deficiency	28	1-5/10,000	0,09-0,45
Digestive syndromes (n=17)			
Primary biliary cholangitis	10	1-5/10,000	0,09-0,45
Autoimmune hepatitis	4	1-5/10,000	0,09-0,45
Hirschsprung disease	1	Unknown	
Cowden syndrome	1	1-9/1,000,000	0,0009-0,008
Caroli disease	1	Unknown	

(1) Number of patients that participated in the study

(2) Data from www.orpha.net

(3) Expected number of cases in Spain

Unkown: the term was found in Orphanet, but with no data available

No data: the disease/term was no found in Orphanet