

Childhood Dementia Knowledgebase

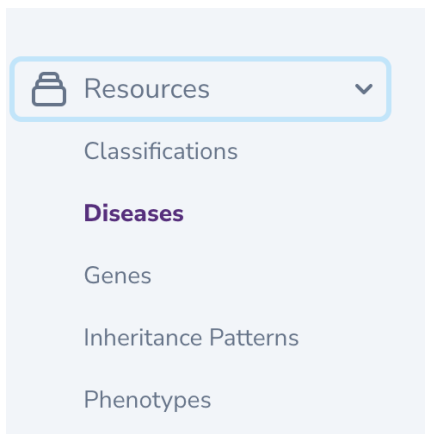
Instructions and Documentation

Thank you for your interest in the Childhood Dementia Knowledgebase. We hope it helps accelerate your research and contributes to the development of much needed treatments, cures and improvements in care and quality of life for children with dementia.

The following instructions are a guide to get you started. Please contact us if you can't find what you need:

knowledgebase@childhooddementia.org

When you log in you will see a menu on the left hand side, click on Resources, then Diseases to see the full list of childhood dementia disorders. Click to see each disorder's page. The easiest way to find a particular disorder or gene is to use the search box. This will search in all of the text fields including synonyms.



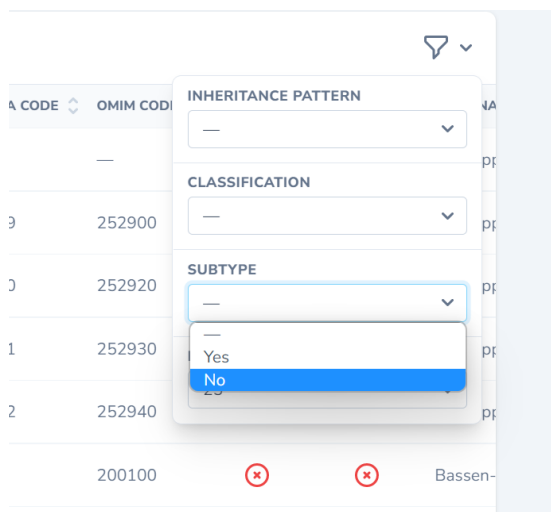
Subtypes

A field called “subtype” exists because we have some disorders that are included under both an umbrella term and individually. For example, the four subtypes of ‘MPS III (Sanfilippo Syndrome)’ (type A, B, C and D) are indicated by a tick in the subtype field and the umbrella entry ‘MPS III (Sanfilippo syndrome)’ has a red cross in the subtype field.

There are umbrella entries for 8 groups of disorders:

- MPS III (Sanfilippo Syndrome)
- Neuronal ceroid lipofuscinoses (NCLs or Batten Disease)
- Congenital disorders of glycosylation
- Mitochondrial disorders
- Urea cycle disorders
- Organic acidurias
- Amino acidopathies
- Molybdenum Cofactor Deficiency

To avoid counting disorders twice when analysing Knowledgebase data you can filter out the subtypes using the filter on the right hand side of the disease listing which looks like this:



Treatable Disorders

We have three categories relating to information about if a childhood dementia disorder is treatable:

- Treatable and usually diagnosed early

In developed countries these disorders are usually diagnosed pre-symptomatically through newborn screening and with enduring treatment compliance result in a life expectancy that is similar to the general population (e.g. phenylketonuria and maple syrup urine disease). Despite this, a small portion of children (<10%) die either in the newborn period or later because of acute metabolic crisis.

- Treatable if diagnosed early

These disorders are not widely included in newborn screening programs. However, if these conditions are detected early, existing approved treatment options can improve outcomes (E.g. X-linked adrenoleukodystrophy, cerebrotendinous xanthomatosis).

- Currently untreatable disorders

These are disorders for which there are no approved treatment options, and at most there may be clinical trials for experimental treatments. If a disorder is marked as untreatable this does NOT mean that there are no interventions to manage symptoms. For some disorders there are treatments that can slow progression of the disease and/or effectively manage some of the symptoms. Clinical care and support is extremely valuable in maximising quality of life for affected children and their families.

For each condition a link for current clinical trials and information about approved treatments (if available) is provided in the fields below.

Disclaimer: Response to treatment is variable, and individuals can have a number of symptoms and disease-associated morbidity and mortality. Some treatments e.g. HSCT also carry significant risk. The treatment landscape is constantly changing, and although we make every effort to keep the Knowledgebase up-to-date it is best to check the latest literature.

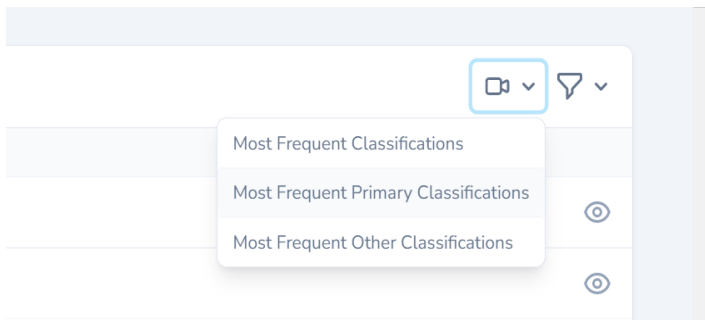
Classifications

The childhood dementia disorders have been given a 'primary classification' in the knowledgebase based on accepted pathological classification of disease. Where some conditions fit into the classification of more than one sub-group, allocation was based on the more specific aetiological category. For example, metachromatic leukodystrophy was classified as a 'lysosomal disorder of lipid metabolism and transport' instead of the more general category, leukodystrophy, describing conditions that affect the white matter of the brain. We acknowledge that many disorders can fit into more than one classification but to allow analysis of the disorders, care has been taken to assign each disorder to only one of the 14 primary classifications listed below in purple.

- Inborn Errors of Metabolism
 - Lysosomal disorders
 - Lysosomal disorders of lipid metabolism and transport
 - Lysosomal disorders of glycoproteinosis
 - Mucopolysaccharidoses
 - Other lysosomal diseases
 - Other disorders of lipid metabolism and transport
 - Disorders of amino acid and other organic acid metabolism
 - Vitamin-responsive inborn errors of metabolism
 - Disorders of mineral absorption and transport
 - Peroxisomal disease
 - Mitochondrial disorders
 - Other Inborn errors of metabolism
- Leukodystrophies not otherwise categorised
- Neurodegeneration with brain iron accumulation
- Neurodegenerative diseases not otherwise categorised

Alternative classifications have been assigned in the “other classifications” field.

To explore classifications, click on the classifications menu on the left hand side of the screen. To look at only ‘primary classifications’ apply the lens ‘most frequent primary classifications’ on the right-hand side of the screen:

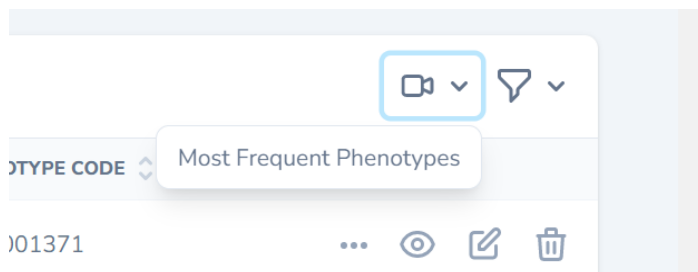


You can then click on a classification and explore which disorders are within that classification.

Phenotype

The Human Phenotype Ontology (HPO) (<https://hpo.jax.org/app/>) provides a standardised vocabulary of phenotypic abnormalities encountered in human disease. The HPO terms associated with each childhood dementia disorder have been imported into the database.

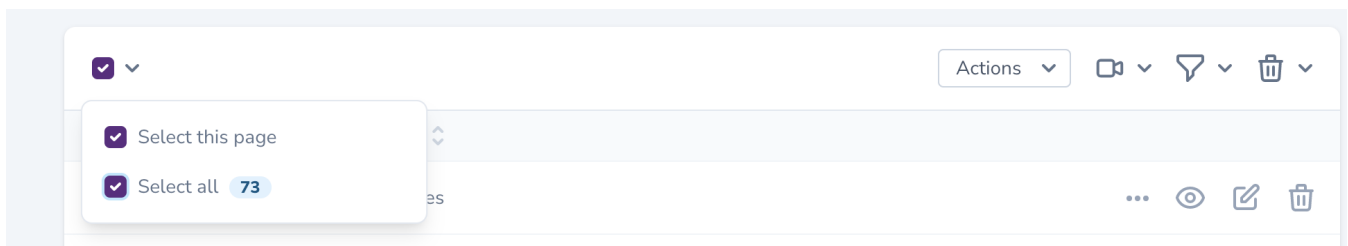
To explore the most common phenotypes click on the phenotypes menu on the left hand side of the screen. Apply the lens ‘most frequent phenotypes’ on the right-hand side of the screen:



Downloading

You can download all of the data (or a subset, for example those with a certain classification) from the Knowledgebase in excel format for your own analysis.

- 1) Select all using the check box at the top left



- 2) Select Actions - Download Excel
- 3) Run action