# Childhood dementia: the collective impact and opportunities for intervention

Kristina L. Elvidge (1), John Christodoulou (2,3), Michelle A. Farrar (4,5), Dominic Tilden (6), Megan Maack(1), Madeline Valeri (6), Magda Ellis(6), Nicholas J.C Smith (7,8)

1. Childhood Dementia Initiative, NSW 2. Murdoch Children's Research Institute, Royal Children's Hospital, Victoria. 3. University of Melbourne, Victoria 4. Sydney Children's Hospital, Randwick, NSW. 5. UNSW Sydney, NSW 6. THEMA Consulting Pty Ltd, NSW 7. University of Adelaide, Adelaide, South Australia. 8. Women's and Children's Health Network, South Australia.

childhood dementia INITIATIVE

## What is childhood dementia?

Childhood dementia is a devastating group of disorders with a high level of unmet need. Typically monogenic in origin, this collective of individual neurodegenerative conditions are defined by a progressive impairment of neurocognitive function, presenting in childhood and adolescence.

In contrast to adult-onset dementia, childhood dementia has received little recognition in the medical literature and the lay media. This is due to the individual rare and ultra-rare disorders being considered individually based on their pathology rather than as a broader clinical phenotype as the adult dementias are.

## Methods

A literature review and Human Phenotype Ontology database search identified conditions that met the case definition for primary monogenic childhood dementia disorders:

- progressive neurocognitive decline;
- presenting before 18 years of age;
- multiple losses of prior attained development skills;
- generalised (not focally restricted) brain dysfunction; and
- monogenic aetiology.

This study focused on the primary monogenic causes as they constitute the greatest burden of childhood dementia in developed countries and for the purposes of modelling, they have a more predictable incidence than acquired diseases such as subacute sclerosing panencephalitis (SSPE). It is important to acknowledge that SSPE, caused by the persistence of the measles virus in the CNS, is a significant cause of childhood dementia in countries where immunisation rates are low

An expert clinical working group reviewed and ratified inclusion. Epidemiological data were extracted from published literature and collective burden modelled. The characteristics of the childhood dementia disorders were analysed based on accepted pathological classification of disease.

Key statistics for each of the childhood dementia disorders have been deposited in the Childhood Dementia Knowledgebase - a relational database. It allows identification of disorders with a particular symptom or which are amenable to a certain treatment approach, encouraging the concurrent study of multiple childhood dementia disorders. You can access it here: childhooddementia.org/knowledgebase

**For a PDF of this poster, to view the Childhood Dementia Knowledgebase, and to join the Childhood Dementia Research Alliance, scan the QR code or visit: childhooddementia.org/for-researchers**

## Results

**170+** childhood dementia conditions

Babies born with currently untreatable childhood dementia: **1 in 2,900**

**2.5 years:** Mean onset age

Median life expectancy: **9 years**

**Figure 1: Overall survival of the cohort born with a currently untreatable childhood dementia**

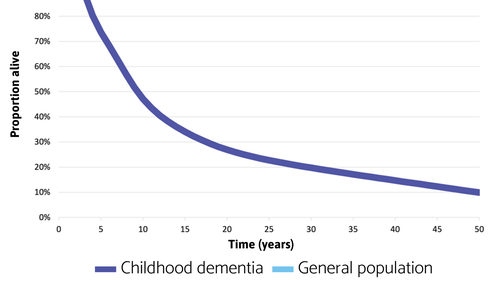
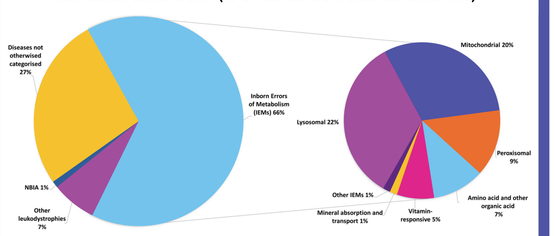



**Figure 2: Aetiopathological classifications of childhood dementia conditions (% of childhood dementia births)**




## Relationship with adult-onset dementia

A growing body of literature suggests that common disease mechanisms exist between adult and childhood-onset dementias (Qureshi et al., 2020; Torres et al., 2019; Platt et al., 2018), for example:

- neuroinflammation,
- mitochondrial dysfunction
- endolysosomal dysfunction and
- the accumulation of proteins and lipoproteins (e.g. P-tau, α-synuclein, cholesterol, sphingolipid)

Relatively recently it was discovered that carriers of some childhood dementia gene mutations (previously thought to be asymptomatic), have an increased risk of developing dementia and/or Parkinson's disease later in life (e.g.GBA, MCOLN1 and SMPD1 genes) (Clark et al., 2015). This further cements the link between childhood and adult-onset dementia.

Like the adult-onset dementias, care needs for children with dementia are high and progressively increase. Families report that care and support is inadequate, poorly coordinated and inconsistently delivered. Childhood Dementia Initiative is working with national dementia organisations to expand their support services to include children with dementia. Further research is underway to understand care and support needs to enable systemic improvements.

Cross pollination and collaboration between childhood and adult-onset dementia research and clinical care systems will lead to advancement in therapeutic development and improvements in care and quality of life for affected families.

## Conclusion

Dementia is typically assumed to be a condition of older adults, however, it can occur throughout the lifespan, even in children. This study highlights the importance of grouping the childhood dementia conditions as a phenotypic syndrome, rather than individually rare diseases, in keeping with the approach to adult dementia.

Collectively addressing childhood dementia is a world-first approach being led by the Childhood Dementia Initiative. It provides opportunities for greater scale, impact and improvement of policy, services and therapeutic development. It represents a paradigm shift in how these children are viewed, cared for and treated.

**References**

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## Case study: Angelina

**Angelina was like most other teenagers. She had no signs or symptoms. She was extremely social, self-motivated, goal-driven, academic and had big dreams for her future. She was in school musicals and attending acting classes and wanted to become a makeup artist and business owner.**

**In September 2018, 14-year-old Angelina, was found unconscious in a corridor at her school. One year later, Angelina was diagnosed with childhood dementia caused by a rare genetic disorder called Lafora disease. Symptoms include seizures, muscle spasms, difficulty walking, behavioural changes, confusion and cognitive decline. Within just a few years from the onset of symptoms, children typically find it hard to complete daily activities. Most only live for around 10 years from those first symptoms.**

**Sadly, Angelina's condition declined in the year following her diagnosis. At times Angelina started to find it difficult to speak, swallow or walk unassisted. By June 2020, Angelina's behaviour started to change. For Angelina, this made her irritable and impacted her mental health. She started to refuse to eat, co-operate with self-care, get out of bed, or take her medications. Angelina's short and long-term memory and cognitive abilities significantly declined too.**