

Introduction

Childhood dementia is characterised by global and progressive neurocognitive decline, severely impacted quality of life and shortened life expectancy.

Childhood dementia shares many similarities with the hallmark features of adult-onset dementias including memory loss, disorientation, disruptive behaviour, wandering, emotional disturbance, personality changes, sleep disturbance, loss of speech and incontinence. In addition, these children commonly suffer co-morbid disease; e.g. seizures, motor and sensory deficits, visual loss and the involvement of other organs and physiological systems.

Like the adult-onset dementias, childhood dementia has multiple causes. More than 70 monogenic, rare and ultra rare genetic disorders can be defined as causing childhood dementia. This group of disorders have received little recognition, instead, disorders are often considered individually.

Childhood dementia places a tremendous emotional, physical and financial burden on those involved in care and support. The direct healthcare and indirect societal costs of childhood dementia have not been assessed.

The objectives of this study were to:

- define and identify the population affected by childhood dementia
- quantify the current burden of childhood dementia within the Australian population
- estimate the projected financial costs of childhood dementia to the Australian economy.

Methods

Desktop research defined and identified the current and forecasted number of cases and costs associated with childhood dementia in Australia from 2021 to 2030. Case definition was restricted to childhood dementia disorders of monogenic genetic etiology. Episodic encephalopathies and epileptic encephalopathies were excluded.

Incidence and life expectancy estimates were derived for each individual condition through extensive literature research. These estimates were used to calculate an Years of Life Lost (YLL) estimate for each condition in addition to a prevalence and life expectancy estimate for childhood dementia as a whole.

A Disability Adjusted Life Year (DALY) was assigned to each condition based on an average health state weight (0.312) from the Global Health Estimate study (2015).

An average annual healthcare cost estimate of AUD\$27,900 based on three studies¹ was applied to all individual conditions (Wyatt et al., 2012; Imrie et al., 2009; Hendrie et al., 2011).

Annual indirect costs, derived from comparator literature (Imrie et al., 2009), equate to AUD\$27,433 and were equally applied to all conditions.

An estimate of AUD\$213,000 per year for the Value of a Statistical Life Year (VSLY); as recommended by the Australian Government's Office of Best Practice Regulation was applied to the YLL to measure the opportunity cost of a life year lost due to premature mortality.

An average annual cost to the National Disability Insurance Scheme (Australia) of AUD\$97,000 is applied using age-specific costs to estimate the spend over an individual's lifetime, depending on life expectancy for each condition.

Results

More than 70 individual genetic conditions were identified, including Batten disease, Sanfilippo syndrome, Niemann-Pick disease, Tay-Sachs disease, metachromatic leukodystrophy, Rett syndrome and some mitochondrial disorders.

The true number of conditions is much higher than 70 as conditions were grouped under broad disease categories, and the number of ultra-rare and novel disorders satisfying inclusion is constantly expanding.

Identified disorders, based on their cause and characteristics, were grouped into 11 broad categories. Lysosomal disease was the largest category (21%) followed by mitochondrial disorders (20%). Third most frequent is the group of "other rare neurodegenerative conditions" a disparate group of conditions such as Rett syndrome and Juvenile Huntington's disease (19%).

Less than 5% of the disorders have widely available treatments with a close-to-normal life expectancy (assuming timely diagnosis). Symptom management and palliative care are the only options for most.

The annual cost of childhood dementia to the Australian economy is more than \$389 million. The cost to the families who love these children is immeasurable.

Note: Of the 70 identified disorders, 32 were excluded from the analysis due to non-availability of incidence and life expectancy data. There is limited robust data on the costs attributed to each condition in this list, therefore, the costs attributed to childhood dementia as a whole are expected to be higher than those provided in this analysis.

Key findings

Incidence, prevalence and life expectancy:

- The collective incidence of disorders that cause childhood dementia is **1 in 2,800 births**
- An estimated **2,273 Australians** live with childhood dementia
- The average life expectancy for childhood dementia is **28 years**

Globally the impact of childhood dementia is:

- **50,000** births every year
- **700,000** individuals currently living with childhood dementia
- **48,300** premature deaths annually



Relationship with adult-onset dementia

A growing body of literature suggests that common disease mechanisms exist between adult and childhood-onset dementias e.g. neuroinflammation, mitochondrial and endolysosomal dysfunction and the accumulation of proteins and lipoproteins (e.g. P-tau, α-synuclein, cholesterol, sphingolipid) (Qureshi et al., 2020; Torres et al., 2019; Platt et al., 2018).

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. As a first step, Childhood Dementia Initiative has gained commitment from Dementia Australia and Dementia Support Australia to expand their support services to include all children with dementia. Further research is needed into the care needs of children with dementia and their families to enable systemic improvements in multidisciplinary care and support.

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.

Case Study Angelina



Angelina was like most other teenagers. She had no signs or symptoms or any abnormalities. 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.

References

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Conclusions

Dementia is typically assumed to be an aging adult disease, however, tragically, children are affected too.

This study demonstrated for the first time the burden associated with childhood dementia: the tremendous negative impact it has on affected children, families, and the community, and the resulting health and productivity costs.

The individually rare disorders which result in childhood dementia are underrepresented and often neglected in research funding and health system planning and resourcing.

The commonality of presentation and impact of childhood dementia disorders presents a powerful opportunity to collaborate to:

- achieve economies of scale and gains in efficiency in all aspects of research to accelerate therapeutic development
- improve care, support and quality of life for affected families.

The Childhood Dementia Initiative is a global organisation driving research and advocacy to urgently disrupt the impact of childhood dementia on children and families across the world.

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