



# Mowat-Wilson Syndrome

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## First description and alternative names

Mowat et al. (1998) first delineated the syndrome and suggested it was caused by a microdeletion in chromosome 2q22-2q23 or by a de novo mutation of a gene within this region. In 2001, Cacheux et al. (2001) and Wakamatsu et al. (2001) independently identified the cause of the syndrome to be deletions or intragenic mutations of the ZEB2 gene. Zweier et al. (2002) later proposed the name “Mowat-Wilson syndrome”, abbreviated to MWS.

## Incidence/prevalence

MWS has an estimated prevalence of 1 in 50,000 – 70,000 live births (Mowat; Wilson, 2010), though several authors suggest it may be more common than originally thought (Adam et al., 2006; Engenheiro et al., 2008; Garavelli, Cerruti-Mainardi, 2007; Mowat, Wilson, & Goossens, 2003). While early publications reported more males than females due to the ascertainment bias of hypospadias and Hirschsprung disease (HSCR), more recent reports suggest MWS affects both genders equally (Garavelli & Cerruti-Mainardi, 2007; Zweier et al., 2005).

## Genetics

Mowat-Wilson syndrome is caused by mutation or deletion of the ZEB2 gene, previously known as the Zinc Finger Homeobox 1 B gene (ZFHX1B) located on chromosome 2 at the location 2q22 (Cacheux et al., 2001; Mowat et al., 2003; Wakamatsu et al., 2001). Over 110 different mutations have been reported (Dastot-Le Moal et al., 2007), the majority of which result in premature stop codons. However, in recent years, cases with a milder phenotype resulting from missense mutations and partial loss of ZEB2 function have been reported (Ghoumid et al., 2013; Yoneda et al., 2002; Zweier, Horn, Kraus, Rauch, 2006).

While most cases of MWS occur de novo, germline mosaicism is possible and the recurrence rate is estimated at around 2.3% (Cecconi et al., 2008). Physical features and natural history Mowat-Wilson syndrome is characterised by a distinct constellation of facial features in association with variable congenital anomalies. Medical complications can include seizures (in around 80% of cases), Hirschsprung disease (40-50%), severe constipation in those without Hirschsprung disease, agenesis of the corpus callosum (around 45% of cases), congenital heart defects (around 50%), kidney and urogenital anomalies (around 50%). Microcephaly occurs in over 80% of cases (Garavelli & Cerruti-Mainardi, 2007; Mowat; Wilson, 2010). Structural eye anomalies and strabismus have been noted in some people with MWS (Mowat; Wilson 2010), and one case of MWS with bilateral sensorineural hearing loss has been reported (Abdalla, Zayed, 2013).

The facial characteristics of Mowat-Wilson syndrome change with age (Garavelli et al., 2009). Babies generally have a square face with a prominent, triangular-shaped chin, and a broad, saddle nose. With age, the face lengthens, and adults with MWS have a very long chin, with prognathism. By adulthood, the nose has lengthened, has a convex profile and overhangs the philtrum. MWS specific information and growth charts are now available from: <https://mowat-wilson.org/new-diagnosis/welcome-package/> and <https://mowat-wilson.org/2020/10/27/mowat-wilson-syndrome-growth-charts/>,

Other facial features include:

- Hypertelorism (wide set eyes)

- Deep set but large eyes
- Open mouth
- M shaped upper lip
- High arched palate
- Full or everted lower lip
- Fine, sparse hair
- Large uplifted ear lobes with a central depression – arguably the most recognisable feature of MWS. The uplifted lobes remain with age but the depression becomes less marked.
- Flat feet and long, tapering fingers and toes are common, as is short stature.

### **Behavioural characteristics**

A recent study (Evans et al., 2012) reported that the behaviours associated with MWS include a very high rate of oral behaviours (in particular, chewing or mouthing objects or body parts and grinding teeth), an increased rate of repetitive behaviours (such as switching lights on and off; flicking, tapping or twirling objects), and an under-reaction to pain. Other aspects of the MWS behavioural phenotype are suggestive of a happy affect and sociable demeanour. Despite this, those with MWS displayed similarly high levels of behavioural problems as a control group with a similar level of intellectual disability from other causes, with over 30% showing clinically significant levels of behavioural or emotional disturbance.

There are some reports of sleep disturbance in people with MWS (Evans, 2009).

### **Neuropsychological characteristics**

Most people with MWS show a severe-profound level of intellectual disability (ID). However, as the syndrome was identified relatively recently, it is possible that more cases with milder phenotypes will be identified in the future. Motor skills are typically very delayed. While in many individuals, speech is absent or limited to a few words, some have greater success with signing or augmented and alternative communication systems (Evans, 2009). A study found that receptive language was superior to expressive on two measures of communication skills, though the difference in terms of age equivalents was only a few months (Evans, 2009).

### **Useful websites/associations for more information**

- **Website and international registry for families affected by MWS:** [www.mowatwilson.org](http://www.mowatwilson.org)
- **Australian 'Mowilsi' site:** <http://www.mowatwilsonsupport.org/>
- **French forum for families:** <http://smwf.forumactif.org/>
- **UK Support group:** <http://www.mowatwilsonsyndrome.org.uk/>
- **Italian support group:** <http://www.mowatwilson.it/>

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## **Fact sheet updated by David Mowat, 2021**

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