

# Pathway to diagnosis in Sanfilippo disease (MPS III) – results from an international caregiver survey

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## Background

- Patients with MPS III (mucopolysaccharidosis III) usually appear normal at birth, with developmental delay becoming evident by the age of 2–5 years (1)
- Definitive diagnosis often occurs after the point when development has plateaued or moved into rapid decline (2)
- Earlier diagnosis is essential for optimum outcomes of future treatments (2)
- Early symptoms are often non-specific, such as recurrent ear, nose and throat infections and diarrhoea, and behavioural issues that may be mistaken for variants of normal childhood behaviour (3)

## Study aims

- To understand further the early presenting symptoms of MPS III
- To identify those healthcare professionals (HCPs) that see individuals with MPS III at an early age

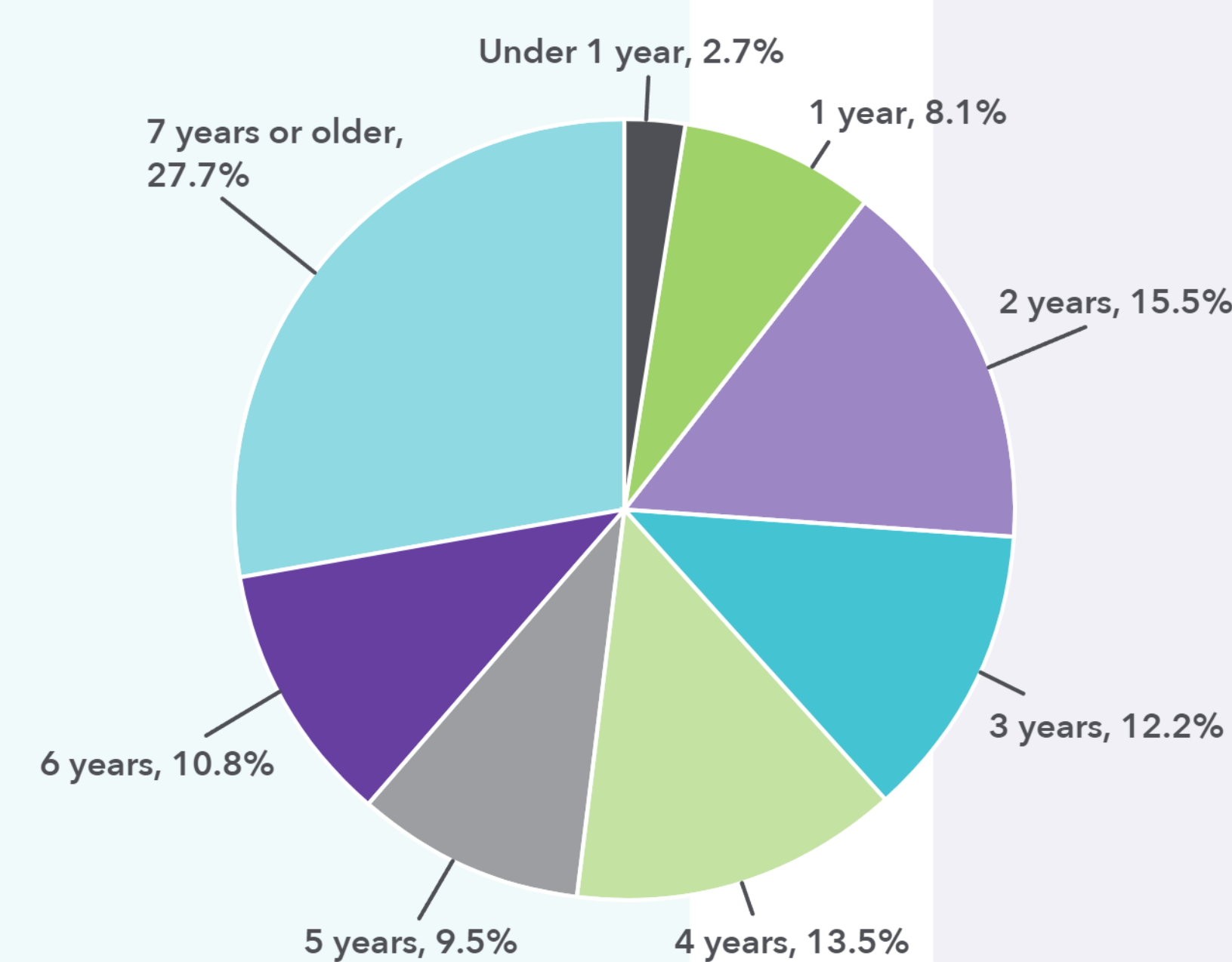
## Methods

- We developed a questionnaire to determine the pathway to diagnosis and burden of illness
- Only diagnostic pathway results are presented here (see poster LB-02 for burden of illness results)
- Patient organisations distributed the questionnaire and conducted parent/caregiver interviews in their own countries
- Parents or caregivers of individuals with MPS III were eligible to take part and provided informed consent
- Questionnaires were completed via face to face or telephone interview, by post or online

## Results

- A total of 174 responses were received of which 149 were suitable for analysis
- Of the 40 countries approached, responses were received from 13: Australia, Austria, Bosnia, Canada, Germany, India, Indonesia, Japan, Serbia, Spain, Switzerland, Turkey and UK
- MPS III individuals were aged between 1 and 48 years (mean 18 years); male (47.7%), female (47.0%)

Figure 1. Age at diagnosis (N=148)



## Diagnostic delay

- Mean age at diagnosis was 6.3 years (range 0.5–42 years, SD 6.0 years)
- Just over one quarter were diagnosed before the age of 3 years (Figure 1)
- The delay between first concerns and diagnosis of MPS III was a mean of 3.8 years (range 0–41 years, SD 5.7 years)

## First symptoms of concern

- The mean age at first concern was 2.6 years (range 0–22 years, SD 2.5 years)
- 36.8% of responders noticed something unusual when their child was born: breathing difficulties (5.6%), large head, hernia or excess body hair (all 3.5%)
- Parents/guardians were usually the first to suspect that 'something was wrong' with the child (75.9%), however, for 13.1% it was a primary care physician who first had concerns
- Different symptoms raised concern in parents/guardians vs primary care physicians (Table 1)

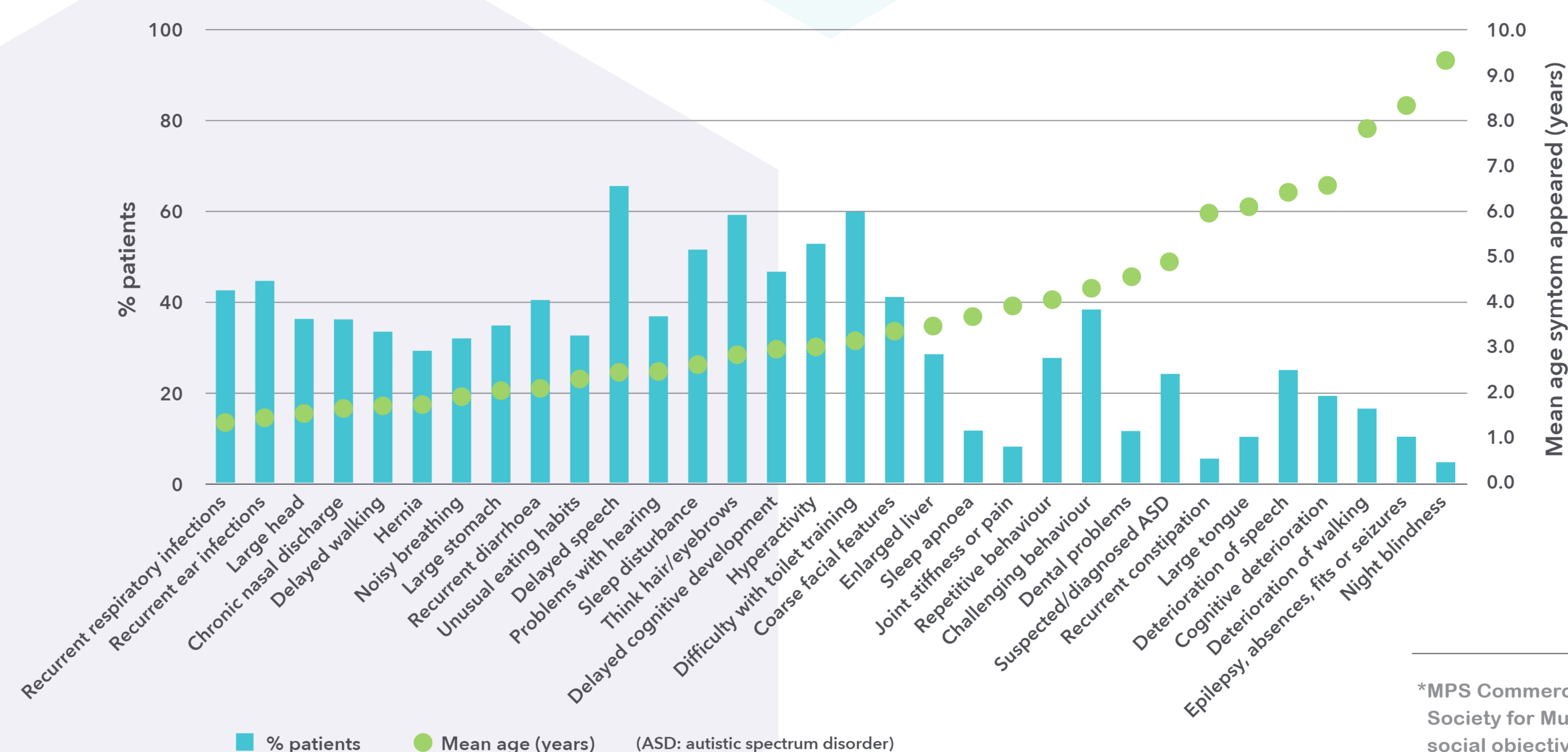
Table 1. Most common symptoms of first concern

Parent / guardian (% patients)	Primary care physician (% patients)
Delayed speech (37.2%)	Facial features (6.9%)
Sleep disturbance (28.3%)	Large head (6.9%)
Delayed cognitive development (20.0%)	Recurrent ear infections (4.8%)
Recurrent respiratory infections (20.0%)	Recurrent respiratory infection (4.1%)

## Symptoms present before diagnosis

- Overall, the most common symptoms pre-diagnosis were delayed speech (65.7%), difficulty with toilet training (60.1%) and thick hair/eyebrows (59.4%), (Figure 2)

Figure 2. Symptoms present before diagnosis of MPS III



- Early symptoms were often non-specific including recurrent respiratory and ear infections, and delayed walking
- Symptoms most likely to raise a suspicion of MPS, thick hair/eyebrows (43.1%) and coarse facial features (43.1%), did not present until a mean age of 2.8 years and 3.4 years, respectively

## Healthcare professionals seen before diagnosis

- Patients were often seen by several different HCPs before a diagnosis was reached
- 50.7% had seen at least five HCPs before diagnosis and 27.1% had seen at least seven HCPs
- Repeated visits to a primary care physician were common: 58.7% reported visiting their primary care physician >10 times before being referred to a specialist
- 38.6% had been referred to an ear, nose and throat (ENT) specialist – at a mean age of 3.0 years
- Mean age when seen by a:
  - Hospital paediatrician – 3.4 years
  - Paediatrician specialising in metabolic disease – 5.6 years
  - Geneticist – 6.8 years

## Diagnosis

- The first to suspect MPS were:
  - Hospital paediatrician (22.1%)
  - Paediatrician specialising in metabolic diseases (11.7%)
  - Primary care doctor (8.3%)
  - Community/developmental paediatrician (8.3%)
- MPS III had been previously diagnosed as:
  - Developmental delay (30.1%)
  - Attention deficit hyperactivity disorder (ADHD) (11.2%)
  - Autistic spectrum disorder (10.5%)

## Conclusions

This study illustrates the significant delays that occur in the diagnosis of MPS III. While hospital paediatricians were the most likely to suspect MPS, they were only identifying 22.1% of cases and were unlikely to see a child before the age of 3 years.

The non-specific nature of early symptoms, coupled with a lack of awareness of MPS III means that the early signs of disease are often not recognised and may be mis-diagnosed. Future disease modifying therapies will rely on early diagnosis to allow for intervention before the steep decline in cognitive function begins.

This points to both the importance of newborn screening and need for targeted education of HCPs likely to see children in the early stages of disease, including community and primary care HCPs and ENT specialists.

## References

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