Presentation, diagnosis and management of SMA: Multidisciplinary perspectives
What are the causes and consequences of diagnostic delay in SMA?

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SMA, spinal muscular atrophy.
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**SMA and prevalence**

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<tr>
<th>SMA carrier prevalence:</th>
<th>~1/40–1/50 individuals</th>
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<td>25% chance of SMA in the child of two carriers</td>
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<td>SMA prevalence:</td>
<td>~1/11,000 live births</td>
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**SMA**

- A progressive neuromuscular disorder resulting from mutations or deletions of the *SMN1* gene
- *SMN2* is a back-up for *SMN1*, but only produces small amounts of functional SMN protein
- Lack of SMN predominantly affects motor neurons, but other organ systems are also involved

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SMA, spinal muscular atrophy; SMN, survival motor neuron.
SMA symptoms

**Infantile-onset SMA before 6 months**

- The majority of cases of SMA have onset in infancy
- Poor head control
- Slow feeding leads to failure to thrive
- Hypotonia and progressive proximal muscle weakness with respiratory failure typical before 2 years old
- ‘Bell-shaped’ chest and paradoxical breathing pattern, with respiratory failure typical before 2 years old
- Tongue fasciculations
- Absent or reduced muscle stretch reflexes
- Less severe SMA is usually associated with higher numbers of copies of SMN2 and later onset of symptoms

SMA, spinal muscular atrophy; SMN, survival motor neuron.
SMA symptoms and severity

SMA onset between 6 and 18 months
- Patients can usually sit unsupported but are never able to stand or walk

SMA onset after 18 months
- Patients with later-onset SMA are independent walkers (may have a waddling gait)
- Proximal muscle weakness, with the legs more severely affected than the arms, may cause frequent falls or difficulty walking on stairs and running
- Muscle stretch reflexes (such as the patellar reflex) may be lost
- Fine tremor may also be present in the fingers and hands

SMA, spinal muscular atrophy.
Differential diagnoses and SMA

- Early identification of SMA without newborn screening is a considerable challenge
  - Healthy children reach developmental milestones at different rates, making it difficult to know when to initiate clinical investigation\(^1\)
  - Many systemic illnesses, CNS conditions and infections have symptoms of low muscle tone and drive\(^2\)
  - Non-thriving hypotonic infants can have a broad range of underlying morbidity besides SMA\(^2\)

CNS, central nervous system; SMA, spinal muscular atrophy.
Newborn screening for SMA

- Earlier treatment is associated with better outcomes\(^1\)–\(^5\)
- Effort to identify SMA and enable treatment before symptoms develop\(^6\)
- Now part of the Recommended Uniform Screening Panel for newborns in the USA, with implementation decided on a state-by-state basis\(^6\)

SMA, spinal muscular atrophy.