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# A call to introduce newborn screening for spinal muscular atrophy (SMA) in Scotland

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The recent development of three effective therapies for patients with spinal muscular atrophy (SMA) – Nusinersen (Spinraza), Onasemnogene abeparvovec (Zolgensma) and Risdiplam (Evrysdi) – arguably represents one of the great medical achievements of the 21<sup>st</sup> century.<sup>1</sup> These treatments, which all work via restoring levels of the SMN protein, have revolutionised the outlook for patients with an otherwise incurable, and mostly fatal, condition. However, all three treatments come at a significant financial cost. For example, Zolgensma (often referred to as “the world’s most expensive drug”) has a list price of nearly £1.8m per dose. Moreover, a large body of pre-clinical research, supported by emerging data from patient clinical trials, makes clear that the effectiveness of all current SMA therapies is largely determined by how early therapy can be delivered.<sup>1,2</sup> Thus, pre-symptomatic treatment of patients results in significantly better outcomes – both in terms of patient benefits and financial return on investment – than starting treatment after symptom onset.

If pre-symptomatic treatment is a key determinant of success, then it follows that any possibility to identify SMA patients before the onset of symptoms, and hence begin treatment as early as possible, should be taken advantage of. Importantly, just such an opportunity already exists: newborn screening (NBS) to identify genetic defects underlying disease. At present, NBS programmes in the UK routinely screen for conditions such as cystic fibrosis and congenital hypothyroidism, but not SMA. However, NBS for SMA has already been successfully introduced in many other countries. For example, SMA is now included in the Recommended Uniform Screening Panel (RUSP) from the US Department of Health and Human Services.<sup>3</sup> Likewise, the recent ‘Sun May Arise on SMA’ pilot NBS programme in Belgium led to the official adoption of NBS in Southern Belgium in March 2021, with Northern Belgium including SMA in their official program from 2022.<sup>4</sup> Emerging data from these real-world scenarios confirm that NBS for SMA is both robust and reliable, whilst also representing value for money.<sup>5</sup>

Recent approvals from the Scottish Medicines Consortium mean that patients with SMA in Scotland now have access to therapies. Importantly, approval has also been given (at least

for Zolgensma) for SMA patients in Scotland to receive treatment pre-symptomatically. However, while NICE has recommended use of Zolgensma for presymptomatic use in SMA, this is under a Managed Access Agreement and therefore not considered routine care. This lack of approved pre-symptomatic treatment is one reason provided by the UK National Screening Committee for not approving NBS for SMA at the UK-wide level. However, the availability of pre-symptomatic treatment for SMA in Scotland leads to a situation whereby Scottish SMA patients and their families are being denied the possibility of accessing NBS, and potentially much better clinical outcomes, due to decisions being taken and applied at the UK-wide level.

NBS does not come without important ethical, societal and financial implications.<sup>6</sup> There are myriad reasons why NBS is not suitable for many genetic conditions at present. However, as professionals involved in SMA research, diagnosis and patient care in Scotland, we believe that all of the necessary data, evidence, and therapeutic approvals are in place to justify the inclusion of SMA on NBS programmes in Scotland. The inclusion of NBS for SMA would provide the best possible quality of life for SMA patients and their families, whilst maximising the (not insignificant) return on investment that society makes in providing access to SMN-restoring therapies.<sup>7</sup>

## Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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THG has served on SMA global advisory boards for Roche. IH has served on SMA global advisory boards for Roche, Novartis and Biogen. KM has served on SMA advisory boards for Roche and Novartis.

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