Correspondence on: "Discrepancy in Spinal Muscular Atrophy Incidence findings in newborn screening programs: the influence of carrier screening?" by Kay et al

To the Editor:

We would like to congratulate Kay et al. for their article[1] on the implementation of newborn screening (NBS) for spinal muscular atrophy (SMA) in New York State (NYS), and also salute their pioneering work in NBS for SMA.[2]

In this paper, the authors review one year of NBS implementation in NYS. Of 225,093 infants, 8 were identified with SMA. All newborns were asymptomatic at diagnosis and promptly received disease-modifying treatment for the most severe forms. The authors noticed an incidence significantly lower than expected, and propose two hypotheses to explain this particularly low prevalence:

- Part of their population has been previously screened for SMA through preconceptional carrier screening, genetic counseling, cascade testing, prenatal diagnosis, or advanced reproductive technologies.
- Previous studies overestimated the incidence of SMA in the general population.

We believe it is crucial to differentiate between the two hypotheses given the public health implications and the cost of drug reimbursement, since many drug reimbursement models are linked to the exact incidence of the disease. The suggestion of a lower incidence of SMA could have considerable consequences for the reimbursement process of disease-modifying therapies in several countries, as well as for NBS funding decisions. Therefore, trying to better identify the causes of the finding is of primary importance for existing and future patients.

We could reasonably consider that the second hypothesis of a previously overestimated incidence is not valid. Indeed, other studies have demonstrated that the incidence of SMA at birth appears to be fairly comparable with that reported in the literature. Pilot studies for neonatal screening of SMA are currently underway in several countries,[3] and data of incidence are available from Germany, Belgium, and Australia. These three programs found relatively similar and close figures to the initial studies that estimated the incidence at 1 in 10,000, with higher figures in Europe. The Australian study[4] reported an incidence of 1 in 11,545, the German study[5] returned an incidence of 1 in 7096, and finally our pilot study in Belgium[6] shows an incidence of 1 in 8398. The unique studies announcing lower SMA incidence are in New York State during the pilot study (1 in 16,712) and after the first year of experience (1 in 28,137), and in Taiwan (1 in 17,181).[7]

If we consider that the low incidence reported from NYS results from a better awareness of the risks of genetic disease transmission and the concurrent implementation of carrier screening, and that a "normal" incidence would have resulted in about 22 cases in 225,093 infants, it means that about 14 potential cases of 22 (about 64%) have been avoided by carrier or prenatal screening. This heartening uptake could be the result of increased communication regarding SMA in recent years, the pioneer work conducted in NYS, the addition of SMA to the Recommended Uniform Screening Panel (RUSP) in 2018, the marketing of drugs, and polemics against the prices of these drugs in mainstream media and on social networks. All of these efforts may have encouraged future parents to ask for genetic counseling and carrier screening, which has until now remained very rare in some regions such as Southern Belgium. Nevertheless, such a lowering in incidence should normally be suggested by the number of tests carried on in the same region.

We hope that future data from NYS and from other regions in the United States and around the world will help to further reinforce and contextualize the findings of Professor Kay and her colleagues.

DISCLOSURE

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