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Pre-Nusinersen Hospitalization Costs of Children With Spinal Muscular Atrophy

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Introduction

Spinal muscular atrophy (SMA) is a life-altering and life-limiting illness of infants and young children. Deletions or mutations of the *survival motor neuron 1* (*SMN1*) gene cause degeneration of spinal alpha motor neurons. Affected children become progressively weaker, including those who eventually require mechanical ventilation or expire.

Nusinersen, an antisense oligonucleotide, modifies the splicing of a "backup gene," *SMN2,* to mitigate the symptoms of SMA and has shown promise in clinical trials.[1,2] Like many treatments for orphan drugs, which must recoup investment costs from a very small population, nusinersen is very expensive. Even without accounting for the cost of in-hospital intrathecal administration, each dose is $125,000, and treatment requires six doses in the first year ($750,000) and three doses every year thereafter ($375,000).[3] These prices have, understandably, raised questions about affordability and cost-effectiveness.[3–5] Gene replacement therapy has also shown promising results in an early study[6]; its pricing structure as a potentially single-dose intervention has not yet been established but could be similarly expensive.

These high prices have, understandably, raised questions about affordability and cost-effectiveness in the medical literature and the popular media[3–5]—but these debates have focused on *list* prices. Health economists, however, evaluate the cost of a treatment using an incremental cost-effectiveness ratio (ICER). An ICER measures the incremental benefits of a new therapy like nusinersen or gene replacement not against its list price, but against its *incremental* cost—that is, the price of the new therapy minus the present cost of treatment.[7] In high-intensity chronic illnesses like SMA, the present cost of treatment can be extraordinarily high and therefore a crucial consideration. To help us understand these costs—when compared with the list price of nusinersen or future gene therapy—we used publicly available datasets from four states to estimate the present costs of inpatient care of children with SMA.

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Methods

We performed a retrospective cohort analysis of inpatient admissions of children diagnosed with severe SMA. We obtained data on every inpatient hospitalization in four states, including demographic, clinical, and cost elements. We acquired California, Florida, and New York data via the Healthcare Cost and Utilization Project (HCUP)[8] and Massachusetts data via the Center for Health Information and Analysis.[9] Combined, these four states represent 26.7% of the US population. Our proposed use of this data was reviewed and approved by the HCUP and Center for Health Information and Analysis Data Release committees, and a waiver of informed consent was obtained from the Boston Children's Hospital Committee on Clinical Investigation.

We defined children with severe SMA by collecting the unique identifiers of any child with an encounter from 2005 to 2013 carrying International Classification of Diseases, Ninth Revision (ICD-9) Clinical Modification codes (335.0 or 335.1X) for SMA in the first year of life, or any child with an encounter carrying ICD-9 Clinical Modification codes for SMA *and* a tracheostomy (V44.0, V46.1, V46.11, or V55.0) in the first 3 years of life. (Data were unavailable for New York 2005 and California 2012-2013.) We collected information from all admissions for these patients through the end of our dataset, adjusted their associated charges to 2017 US dollars, and used hospital-level cost-to-charge ratios provided by HCUP to convert charges into costs. For admissions with no information about charges (27 of 321, all in California), we used the mean daily cost of other patients with SMA at the same hospital or in the same state, adjusted for length of stay. Differences were assessed for two-tailed significance at $P = 0.05$ using the Mann-Whitney U-test in Python v3.6 (Python Software Foundation, Beaverton, OR, USA).

Results

A total of 229 children with severe SMA were identified, accounting for 950 hospitalizations and a total cost of $39,907,302 (Table). Mean annualized cost per patient was $104,197. Ninety-nine patients (32.4%) with tracheostomies accounted for 5698 (59.5%) admissions and $23,462,667 (63.0%) in costs. Mean 3-year cumulative costs in children with tracheostomies were more than double those of patients without tracheostomies ($257,279 versus $111,052, $P < 0.001$) (Fig). In our population, 53 patients (23%) expired during the hospital stay, including 41 without a tracheostomy and 12 with a tracheostomy.

TABLE.
Admissions and Costs for Patients With versus Without Tracheostomy

	Tracheostomy	No Tracheostomy
Number of Patients	99	130
Number of Admissions, (%)	569 (59.9%)	381 (40.1%)
Number of Patients with >1 admission, (%)	85 (86%)	83 (64%)
Admissions per Patient, Mean (SD)	5.6 (4.4)	2.9 (2.9)
Total Cost	$25,470,604	$14,436,697
Total Cost per Patient, Mean (SD)	$257,279 ($236,279)	$111,052 ($176,265)
Annual Cost per Patient, Mean (SD)	$115,252 ($155,012)	$89,115 ($128,903)
Expired During Hospitalization, Number (%)	12 (12%)	41 (31%)

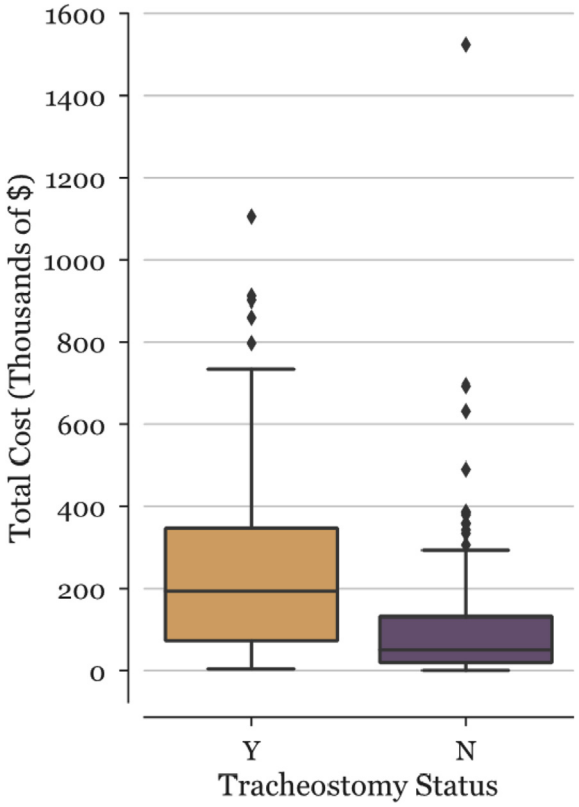

FIGURE. Cumulative costs for children diagnosed with SMA based on tracheostomy status. SMA, spinal muscular atrophy.

Discussion

We estimated the current inpatient spending of children with severe SMA as defined by our methodology. We identified 229 children with a mean annual inpatient cost of $104,197 per child. Individual costs were highly dependent on the direction of care chosen by families: mean three-year cumulative cost of care for children who received tracheostomies was $257,279, more than double that of children who did not ($111,052).

An earlier analysis by Armstrong et al. assessed spending for all children with SMA within the US Department of Defense Military Healthcare System.[10] Our study focused on a civilian population, likely more representative of the nation as a whole, and also focused on more severe cases—those children who were diagnosed either in the first year of life or who had a tracheostomy placed within the first three years of life. Although these categories likely do not perfectly capture Type I versus Type II or III SMA—where ICD-9 coding might be unreliable—they do mark the *impact* of the illness on the patients in question.

Armstrong et al. found that inpatient spending accounted for only 27% of the total health care costs in children with SMA.[10] Applying this to our population suggests that the total three-year spending is likely four times higher than inpatient spending: $952,885 in children with tracheostomies and $411,304 in children without. If, as early clinical trials suggest, nusinersen is able to improve the clinical course of children with SMA,[2] it may be able to substantially reduce these expenses. If so, its *incremental* price—the relevant economic consideration—may be considerably below its listed price of $1.5 million over three years, particularly when families select a course of tracheostomy and technology dependence.

We analyzed only one component of an ICER. Fully calculating cost-effectiveness of a given therapy would require cost data from clinical trials, which are not yet available. Furthermore, our findings underestimate the true costs of current care because of two limitations. First, we did not adjust costs for premature patient death. If all patients survived for the entire three-year interval, their costs would be substantially higher. Second, HCUP and similar administrative datasets lack patient identifiers for some encounters. If a significant number of visits were unavailable, either because of inconsistent identifiers or because they occurred in other states, the true costs of inpatient care would be higher and our calculations would underestimate the actual per-patient expenses.

Although the list price of a medication is important, both as a possible barrier to patient access and as an incentive for innovators to continue pursuing new therapies, *incremental* cost is the critical economic consideration in cost-effectiveness analysis—especially where the alternative is technology dependence. In these cases, costs can be highly sensitive to directions of care chosen by patients and families. Studies using large, more complete, real-world datasets are needed to better estimate the total medical expenses and full economic burdens faced by patients, families, and society. Our findings demonstrate how significant these burdens can be in children with high-severity illnesses like SMA and how crucial they are to our judgments around the pricing of life-improving therapies.

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