impact that caring for someone with SMA has on caregivers. This understanding is crucial as new therapeutic options become available that may change the standard of care and prognosis for individuals diagnosed with SMA.

http://dx.doi.org/10.1016/j.nmd.2020.08.186

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A population-based study examining the epidemiologic burden, healthcare resource utilization and costs of spinal muscular atrophy in Alberta, Canada

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Spinal muscular atrophy (SMA) is a rare neurodegenerative disease that affects one in 10,000 live births. This study describes the epidemiology, healthcare resource utilization (HRU), and costs for children with SMA in Alberta, Canada. This retrospective study identified pediatric patients with SMA between April 2012 – March 2017 by linking several Alberta administrative datasets (health services, vital statistics, and pharmacy data) utilizing a published algorithm based on diagnostic codes. Age at the first SMA diagnostic code date was used as a proxy for SMA type based on the following cut-offs: type I (<6 months), type II (6-18 months), and type III (18 months to <18 years). Five-year incidence and prevalence estimates were calculated for SMA cases identified between 2012-2016 divided by the total person-years/persons at risk. All-cause and SMA-specific (SMA as a primary diagnosis) HRU and per-patient costs were examined in the first year post-SMA diagnosis for hospitalizations, length of stay (LOS), physician visits, ambulatory care visits, SMA-related medication expenses and long-term care. All costs were inflated to 2020 Canadian dollars (CAD) using the Statistics Canada health and personal care consumer price index. 49 children with SMA were identified (median age 4.1 (interquartile range [IQR] 0.6-8.4) years; type I n=10, type II n=7, type III n=32). The overall five-year incidence and prevalence of SMA in Alberta was 1.0 (confidence interval [CI] 0.8-1.4) per 100,000 person-years and 10.0 (CI 9.3-10.6) per 100,000 persons, respectively. In the first year post-SMA diagnosis, 51.0% of patients had ≥1 hospitalization (SMA-specific: 24.5%) with a mean LOS of 29.8 (standard deviation [SD] 41.6) days (SMA-specific: 14.0 [SD 12.6]); the mean number of all-cause specialist visits was 48.4 (SD 70.1) (SMA-specific: 12.6 [SD 29.9]), while fewer than five individuals were dispensed medication. The mean all-cause costs were $29,776 (SD 38,405) (SMA-specific: $7,132 [SD 12,930]), whereas, among type I, type II, and type III patients, all-cause costs were $47,713 (SD 32,495), $52,209 (SD 34,440), and $19,263 (SD 37,632), respectively. This study highlights the economic burden of SMA. While SMA is rare, the HRU and costs were substantial, particularly among those with type I and II disease in Alberta.

http://dx.doi.org/10.1016/j.nmd.2020.08.187

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"Registre-SMA France": a national registry of patients with spinal muscular atrophy (SMA)

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Changes in standards of care and the emergence of innovative targeted therapies have changed the natural history of SMA. This new landscape shows the need of real-life registries to answer to clinical, economic and ethical issues. We present the French registry of SMA treated and untreated patients followed in reference centers of the national network (FILNEMUS). The registry will provide information about SMA patients in real-life conditions at the moment in France. It will also be a robust baseline for a prospective register, as it will longitudinally follow these patients and the newly diagnosed ones over the next 5 years. This observational registry collects data on epidemiology, personal and family history, genetics, clinical features, motor and respiratory function, nutrition, rehabilitation, drug therapies, adverse events, quality of life and survival. It will include genetically confirmed SMA types 1, 2, 3 and 4 followed in France from September 2016 with an estimated population of 1000 patients (50% children). Enrolment started in January 2020. As of 1 April 2020, 47 patients (33 children, 16 adults). have been registered in four centers (9 SMA1; 21 SMA2; 9 SMA3). 42 centers will take part in the project (26 pediatric, 13 adults). Preliminary results of the retrospective study from 2016 to 2019 (R-SMA) will be showed at the meeting. The French registry is currently operative and will spread in the following months to complete the national territory. Characterization of treated and not treated SMA patients will allow improving the understanding of the disease, and developing better therapeutic strategies and follow-up tools.

http://dx.doi.org/10.1016/j.nmd.2020.08.188

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Systematic literature review of the economic burden and economic evaluations in spinal muscular atrophy

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New treatments in spinal muscular atrophy (SMA) have led to a complete change in the pattern in the use of health care resources in this disease. Through all over the world, the very high cost of innovative medication has led to public debates largely expressed in mainstream medias. We have systematically reviewed studies evaluating the cost of SMA and economic evaluations of spinal muscular atrophy. The review was conducted according to PRISMA guidelines and included original articles published between January 1, 1998 and March 2020. Seven studies reporting the cost of SMA were identified. The average annual costs of untreated SMA1 (including early onset and SMA before one year), were relatively similar across the different studies, ranging from $106,000 to $140,000 per year. On the other hand, the costs for SMA 2, 3 and 4 were mainly presented together (ranging from $23,000 to $115,000), despite a high heterogenicity in clinical conditions leading to very different health care resource consumption. Five economic evaluations were published between 2017 and 2020 and included innovative disease modifying medications. Three assessed the cost-effectiveness of nusinersen against standards of care, one of them two treatments (nusinersen and zolgensma) against standards of care and one compared Nusinersen and Zolgensma. All studies used a decision-analytic model to assess the cost-effectiveness and are based on same clinical trials involving a limited number of patients. Due to the extremely high cost of treatment, the incremental cost-effectiveness ratio of drugs versus no treatment is generally above $200,000, leading to no cost-effective results. In conclusion, all studies converge to demonstrate the significant economic cost of SMA, especially SMA1, but a better evaluation of the cost related to other forms is needed. A few economic evaluations suggest that drugs delivered in post-symptomatic phase at current prices are actually not cost-effective at commonly accepted

cost-effectiveness threshold. No economic evaluation of newborn screening has yet been conducted.

http://dx.doi.org/10.1016/j.nmd.2020.08.189

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ATEND: Development of a wheelchair based motor assessment

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Individuals with chronic SMA have a heterogenous presentation. The only scale validated for weak individuals is the CHOPINTEND designed for SMA1 infants. For weaker individuals who have severe contractures, motor assessments are a challenge due to limitations in the ability to transfer or lie prone. With recent developments in treatment for SMA, there is a growing need for a wheelchair based scale for non-sitters. Here, we describe the initial development of a new scale, Adult Test of Neuromuscular Disorders (ATEND), a wheelchair based assessment for older and weaker individuals with SMA. This scale was based on a review of multiple assessments for weaker individuals including: CHOPINTEND, MFM32, RHS, NSAA, PUL2.0, and EK2. Initial review of the HFMSE, RULM and CHOPATEND revealed a floor effect for both the HFMSE and RULM in SMA confirming the need for a more sensitive scale. CHOPATEND items was performed with qualitative item review of experienced administration/scoring challenges and clinical reasoning associated with testing of non-infants was interrogated to determine themes. We reviewed 27 CHOPATEND assessments performed in the wheelchair and found items that were not feasible including rolling, side lying reaching, suspended hip and knee flexion and head and pelvic extension in prone suspension. Review of items that have been developed and validated in other scales emerged as relevant to assess motor function in the wheelchair including RHS items Hook lying, sitting, lifts head, EK2 items trunk control, arm movement, joystick controls, PUL2.0 item lift small weight, and MFM32 item on finger diagram. The final ATEND has 15 items ranging from head control to hand function based on contractures and the emerging phenotype from older, weaker individuals with SMA who have been treated with SpinrazaÒ. Test construct is based on a total score of 47. The ATEND is a collaborative effort based on clinical need to assess individuals with SMA having the greatest limitations in strength, range of motion and positioning. Initial trial of the ATEND is feasible and may be more sensitive to detect motor function in non-sitters. We are actively collecting data on the ATEND with future plans for modern psychometric analysis to understand reliability, validity and item fit for individuals with SMA who are unable to sit and transfer out of their wheelchairs.

http://dx.doi.org/10.1016/j.nmd.2020.08.190

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Diverse cohort of spinraza-treated spinal muscular atrophy patients at Mayo Clinic Rochester for theranostic biomarker discovery

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Spinal muscular atrophy (SMA) is a neurodegenerative disease caused by a deletion of the SMN1 gene. The SMN2 gene differs from the SMN1 gene by a C to T transition that causes exon skipping of exon 7, which leads to a truncated SMN protein that is rapidly degraded. Spinraza works by binding downstream of exon 7 on SMN2 pre-mRNA and promoting the inclusion of exon 7, thereby increasing the amount of full-length SMN protein. The discovery of SMA biomarkers for the monitoring of response to therapy is now a priority with the introduction of Spinraza and the rapid development of other therapeutics. We have currently enrolled a diverse cohort of 17 Spinraza-treated SMA patients at Mayo Clinic Rochester and the Mayo Clinic Health System into our biomarker study, collecting blood and CSF from these patients over time as they receive Spinraza. Our patients include 2 Type 1, 8 Type 2, and 7 Type 3 SMA patients, ages ranging from 6 weeks to 53 years old. Pathogenic point mutations included siblings, a 34 year old man and 33 year old woman, with a missense mutation in exon 1 (c.5C>G) in SMN1 as well as a 10 year old boy, with a frameshift mutation in exon 2 (c.91dupT) in SMN2. None of the 17 patients have reported progression of disease since receiving Spinraza. As consistent with prior reports, younger patients that were treated earlier in life had the highest relative increases in motor function scores. The patient with the greatest increase in scores, a 26 month old boy with Type 1 disease, exhibited a 61% increase in CHOP intend score at day 373 of treatment. His first injection was given at 3 months of age. Of note, 2 patients were still having improvements in North Star Ambulatory Assessments at day 511, a 7 year old girl and 5 year old boy, both with Type 3 disease, exhibiting increases of 15% and 11% respectively. This cohort is diverse and well suited for the discovery of theranostic biomarkers of Spinraza-treated SMA disease.

http://dx.doi.org/10.1016/j.nmd.2020.08.191

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Investigating temporal changes in percent predicted FVC and RULM score in non-ambulant SMA type III children

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Spinal muscular atrophy (SMA) type III is a relatively mild form of SMA, however these patients still gradually deteriorate, and a significant proportion of cases lose ambulation during childhood. There are a lack of studies investigating changes in respiratory and upper limb function in this population after loss of ambulation (LOA). The aim of this study is to investigate the change in the percentage of predicted forced vital capacity (FVC) and the change in the revised upper limb (RULM) score in these patients across a 24-month period after LOA. Retrospective analyses were performed on a total of 23 non-ambulant SMA III patients on clinical data collected as part of routine biannual appointments at two UK centres. Mean age at baseline was 10.2 years (range 4 to 14). The mean and median FVC percentage predicted score at baseline were both 95.0%. We observed a progressive deterioration in FVC over the 24-month period. The mean decrease in FVC percentage predicted score was 17.2% with a standard deviation of 15.3. Of these 23 patients 11 had a scoliosis, 1 of these had previously had spinal surgery and 5 had spinal surgery during the study period. Data on RULM was available in 16/23 patients with mean age at baseline of 11.5 years (6.2 to 15.7). The mean and median RULM score at baseline were 30.3 and 30.0 respectively. We observed a progressive deterioration in upper limb function over the 24 months. The mean decrease in RULM score was 3 with a standard deviation of 3 and a range from -8 to +1. Using a Wilcoxon signed rank test both results were significant. ($p<0.05$). This study highlights that SMA type III patients demonstrate progressive deterioration in their upper limb and respiratory function after LOA. Combining correlative data from these assessments may provide insight into clinical progression within this patient population and ultimately be used to generate a predictive model.

http://dx.doi.org/10.1016/j.nmd.2020.08.192