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Cost-Effectiveness of Nusinersen and Universal Newborn Screening for Spinal Muscular Atrophy

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Abbreviations and Acronyms: Spinal Muscular Atrophy (SMA), Willingness-to-pay (WTP), Life Year (LY), Quality-Adjusted Life Year (QALY), Incremental Cost-effectiveness Ratio (ICER), Permanent Ventilator Assistance (PVA).

Objective To evaluate the cost-effectiveness of nusinersen with and without universal newborn screening for infantile-onset spinal muscular atrophy (SMA).

Study design Markov model using data from clinical trials with U.S. epidemiologic and cost data was developed. Primary interventions studied were nusinersen treatment in a screening setting, nusinersen treatment in a non-screening setting, and standard care. Analysis was conducted from a societal perspective.

Results Relative to no screening and no treatment, the incremental cost-effectiveness ratio (ICER) for nusinersen with screening was $330,558 per event-free life year saved (LY). The ICER for nusinersen treatment without screening was $508,481 per event-free LY saved. In order for nusinersen with screening to be cost-effective at a willingness-to-pay (WTP) threshold of $50,000 per event-free LY saved, the price would need to be $23,361 per dose, less than one-fifth its current price of $125,000. Preliminary data from the NURTURE trial indicated an 85.7% improvement in expected LYs saved compared with our base results. In probabilistic sensitivity analysis, nusinersen and screening was a preferred strategy 93% of the time at a $500,000 WTP threshold.

Conclusion Universal newborn screening for SMA provides improved economic value for payers and patients when nusinersen is available.

Spinal muscular atrophy (SMA) is an neuromuscular disorder with an estimated incidence of 1 in 11,000 live births[1, 2] and is the most common fatal autosomal recessive disorder aside from cystic fibrosis.[3] SMA leads to progressive muscle atrophy and weakness, and is one of the leading genetic contributors to infant mortality.[4-6] Type 1 SMA is the most common and most severe form of the disease with onset in the first 6 months of life. Infants with type 1 SMA have rapid progression of weakness leading to complete loss of voluntary movement, severe dysphagia, and life-threatening respiratory insufficiency. Children with this condition typically do not survive the second year.[7]

Introduction of new treatments has led to the inclusion of SMA in the Recommended Uniform Screening Panel's (RUSP) list of disorders to be screened at birth. Several states in the US have already approved or are considering legislation to mandate newborn screening for SMA.[8] Recent approval of onasemnogene abeparvovec-xioi, a gene replacement therapy for SMA, provides one therapeutic option for infants with SMA.[12] Another option includes the drug nusinersen, which has been shown to improve motor function and reduce the risk of mortality among infants with Type 1 SMA.[9, 10] Data to date suggest that earlier treatment with nusinersen leads to greater improvement in outcomes.[9] Recent results with the treatment of presymptomatic patients suggest that earlier treatment is significantly more efficacious.[11] Universal screening for SMA at birth leads to earlier identification of disease and, thus, may lead to improved outcomes through earlier treatment.

Although initial efficacy studies of nusinersen demonstrate meaningfully improve health outcomes for patients with SMA, the high cost of the drug– $750,000 in the 1st year and $375,000 per year thereafter[13]–can be a barrier to access for some patients. Recent debate about the ethics of high cost therapies for rare diseases has led to a growing concern that payers may

decline to cover nusinersen or discontinue coverage if patients do not respond to therapy within arbitrary endpoints.[14-16] The high costs of nusinersen necessitate an economic evaluation of the use of the drug along with an analysis of universal screening at birth. Review of nusinersen by the Canadian Agency for Drugs and Technology in Health (CADTH) and the National Institute of Health and Care Excellence (NICE) in the United Kingdom concluded that the list price was too high to be considered cost-effective,[17, 18] even at high willingness-to-pay (WTP) thresholds – a maximum price in which healthcare consumers and private or public insurers will pay for a healthcare good or service. However, treatment in the setting of universal screening has not been examined. In this study, we examine the cost-effectiveness of nusinersen treatment for infantile-onset SMA in a universal newborn screening setting.

Methods

A decision analytic Markov model was developed to evaluate universal screening and treatment of infantile-onset SMA with periodic injections of nusinersen. Markov decision models follow a hypothetical cohort of patients through distinct health states using estimated probability parameters to evaluate a policy or compare different sets of treatment options in terms of their effectiveness and cost. We set our model with parameters based upon results of the ENDEAR trial, a 13-month randomized, multicenter, sham-controlled, phase 3 clinical trial.[9] We developed a secondary model using preliminary results (at the time of our analysis) of the phase 2 NURTURE trial (NCT02386553), which showed as of October 2018 all SMA patients alive and demonstrated a motor milestone response of 92% within the first 13 months, to supplement our main results.[11] The strategies considered in our model included: (1) nusinersen treatment with universal screening, (2) nusinersen treatment without universal screening, (3) universal screening and no treatment, and (4) no screening and no treatment.

Costs and outcomes were evaluated at one-month intervals and then extrapolated for the lifetime of the cohort. We first simulated a cohort of hypothetical patients until death or reaching 30 months of age, whichever occurred first. We limited our model's month-to-month time horizon to 30 months, because there do not exist data on the long-term survival rates of patients with type 1 SMA treated with nusinersen. Several assumptions on survival past 30 months were made due to the lack of evidence of long-term benefits of nusinersen. Because respiratory insufficiency is the primary cause of morbidity for infants with SMA, patients who responded to treatment and survived to 30 months without permanent ventilator assistance (PVA) were assigned a life expectancy equivalent to that of patients suffering from severe asthma.[19] For SMA patients who saw improvements in motor milestone response, we assigned a life expectancy halfway between that of a patient with asthma and that of the average patient from the general population from the 2015 National Vital Statistics Reports (NVSR). Life expectancy of surviving SMA infants needing PVA was based on cohort studies of Duchenne muscular dystrophy requiring nocturnal ventilation, as such persons are at risk of life-threatening respiratory disorders, exhibit muscle wasting and loss of motor skills, and have low life expectancy (25 years).[20] The set of health states in the model varied depending on the treatment arm, but consisted of the following: SMA free, untreated SMA, treated SMA, motor milestone response, PVA, and death.

Our analysis was conducted from a societal perspective by including both direct medical costs and indirect work-related income loss of a caregiver.[21] The primary outcomes of the study are the expected discounted event-free life years saved (LY) and expected discounted costs per infant. We defined event-free as patient history without need for PVA or death. Costs and outcomes were discounted at the recommended 3% discount rate where costs and outcomes are

multiplied by a discount factor ($1/(1+.03)^{year}$) applied to each year in the future; this reflects the economic principle that current health status is valued over future health status. Incremental cost-effectiveness ratios (ICERs) – the ratio between the difference in cost and the difference in effectiveness between two strategies – were calculated for each strategy following similar methodologies that have examined the cost-effectiveness of newborn screening for congenital heart disease.[22, 23] We also estimated the ICERs per quality-adjusted life years (QALYs) saved.

All infants in the nusinersen and screening arm were screened for SMA and then confirmed for type 1 in the first month after birth. If positive, 4 loading doses of nusinersen were administered. The drug is administered via lumbar puncture and therefore the associated costs in our model included both the nusinersen dose and the professional and facility payments of the procedure. These patients continued to receive periodic nusinersen injections every 4 months for the entirety of the model until death or failure to respond to treatment. Non-response was defined as patient transition to the PVA health state.

In the treatment with no screening strategy, we assumed that SMA type 1 patients would not be diagnosed until 6 months of age.[24] Similar to patients who had been diagnosed through screening, patients in this arm also received 4 loading doses of nusinersen and continued receiving administered doses until death or transitioning to PVA.

In the remaining non-treatment strategies, we modeled the natural progression of SMA based on calculations derived from the experience of the sham-control group of the ENDEAR trial. The model's Markov-state transition probabilities were then revised based on the preliminary results of the NURTURE trial and reported alongside our base model.

Model Inputs - Probabilities

The primary probability values of health-related events were based on calculations from the results of the ENDEAR trial and derived from other published literature (Table 1 and Table 2; available at www.jpeds.com). Monthly probability of death and transition probabilities to PVA between those receiving nusinersen treatment and untreated SMA are reported in Table I. The prevalence of SMA was set as the median range of rates of SMA prevalence—9.4 per 100,000.[25] Our model studied only infantile onset, type 1 SMA, which comprises 60% of all SMA diagnoses and is the most severe case.[26]

SMA-free patients in our model faced the risk of death, but no other adverse health event. Monthly death probabilities were a function of age and calculated from US neonatal and post-neonatal mortality rates from the Centers for Disease Control and Prevention's 2015 Linked Birth/Infant death records. Child mortality rates were based on the 2015 National Vital Statistics Report. We assumed that SMA patients that saw improvements in motor milestones as a result of treatment faced mortality rates at 30 months of age equivalent to the normal population.

Model Inputs – Costs

Cost inputs were derived from the literature or based on Current Procedural Terminology (CPT) codes. We included both health system and indirect medical costs. The cost of SMA screening per infant was based on the Utah Legislative increase in the total price of the newborn screening kit in 2018 from $112.16 to $115.07. This legislative increase was explicitly mentioned to accommodate the inclusion of SMA as part of the Utah Newborn-screening kit. We did not account for other costs of screening (eg, instrumentation and staff time), because utilization of these resources is likely invariant to the inclusion of SMA. The cost of a single nusinersen administration was set at $125,000 based on current pricing information.

Direct medical costs of PVA were based on estimates from Sevick et al and adjusted to 2018 dollars using personal consumption expenditures chained price index for health care services.[27, 28] Indirect medical costs of PVA consisted of average reported wage-loss of caregivers adjusted to 2018 dollars using the Bureau of Labor Statistic's employment cost index for wages and salaries.

Facility costs associated with the administration of nusinersen were based on the private payer adjustments of Medicare's average payment for injection of substance into lower or sacral spine (CPT 62311) and moderate sedation services of patient less than five years of age (CPT 99150).[29, 30] Professional costs of therapeutic injection with image guidance (CPT 62323) and moderate sedation services for children under the age of 5 (CPT 99151) were also included and adjusted to reflect a private payer's perspective.[31] Expected lifetime costs were then included as final costs in the model.[32, 33] Cost inputs are summarized in Table 2.

Model Inputs – Outcomes

QALYs, commonly used effectiveness outcomes in economic evaluations, measure the quality of life by applying utility weights for an illness. However, because there are no published utility valuations of pediatric patients suffering from SMA,[34, 35] we used utility weights based on asthma as a proxy for SMA patients surviving into adulthood without PVA. Utility weights for SMA patients are applied only after the age of 18 for surviving patient where reliable data is available.[19] The QALY results supplement our primary evaluation based on LYs.

Previous economic evaluations examining treatments for pediatric populations have used discounted LYs saved as an effectiveness outcome.[23] Our study used utilize event-free LYs saved, in which the event is defined as the need for PVA as an effectiveness outcome. We discuss the relative benefits of this effectiveness outcome in the discussion.

Sensitivity Analyses

Results from the ENDEAR trial demonstrated the benefits of early treatment of nusinersen on improved event-free survival compared with later treatment. We ran our model in a secondary scenario to account for these early and late treatment differences in survival and probability of requiring ventilator assistance. We therefore present both base case results (average patient response) and adjust our model to account for treatment time differentials in the ENDEAR trial. These adjustment factors were calculated by the authors based on results from Finkel et al and are reported in Table 1.[9] In addition, model parameters were adjusted using preliminary results of NURTURE at the time of our analysis for additional estimates. Because the outcomes of NURTURE were dependent on patients receiving treatment presymptomatically, results from the time adjusted treatment outcomes of ENDEAR were used in the nusinersen treatment without universal screening strategy.

List price of nusinersen is by far the most important component of costs and cited as the main factor in determining the cost-effectiveness of nusinersen.[36] We conducted a threshold analysis by varying the price of nusinersen from $5,000 to its current price of $125,000 to identify the price at which treatment would be cost-effective at various WTP thresholds. Finally, we performed probabilistic sensitivity analysis (PSA) to examine the impact of uncertainty in all of the parameters simultaneously. The range for long-term life expectancy and costs were defined with wide upper and lower bounds due to the lack of data on long-term healthcare utilization and benefits of nusinersen treatment (Table 2).

Results

Relative to no screening and no treatment, the ICER for nusinersen treatment without screening was $508,481 per event-free LY saved and $522,118 per event-free QALY saved.

Relative to no screening and nusinersen, ICERs for screening newborns along with treatment were $193,867 per event-free LY saved and $199,510 per event-free QALY saved. Nusinersen without screening strategy was then eliminated by extended dominance of the combined strategies of no screening and no nusinersen and screening with nusinersen. Therefore, relative to no screening and no treatment, the ICER for screening and treatment was $330,558 per event-free LY saved, which is less than a WTP of $500,000 prior proposed by the Institute for Clinical and Economic Review for evaluating ultra-rare diseases.[37] Adjusting for early and late treatment effects produced higher outcomes but at higher costs. This is due to a higher proportion of patients avoiding PVA or death and receiving the nusinersen treatment throughout life, as well as, a higher proportion of infants surviving but remaining in PVA and incurring extra costs without additional event-free LYs saved. Table 3 reports the full results and Figure 1 summarizes our main results graphically.

Sensitivity Analysis

Figure 2 depicts the results of our PSA as a cost-effectiveness acceptability curve, indicating that nusinersen with screening was a cost-effective strategy 93% of the time with a WTP of $500,000 per event-free LY saved. Figure 3 illustrates the results from our threshold analysis of the price of nusinersen. We found that at a per dose price of $23,361, universal screening and nusinersen is a cost-effective strategy given a WTP of $50,000. For higher WTP levels, $100,000 and $150,000, cost-effectiveness was achieved with per dose prices of nusinersen of $41,813 and $60,266, respectively.

When using inputs derived from the preliminary results of presymptomatically treated patients in the NURTURE trial, we found a substantial increase (85.7%) in expected LYs saved in the nusinersen treatment with newborn screening strategy. As expected, the ICERs in the

revised analysis using NURTURE data were greater than the base case analysis due to a higher proportion of patients surviving and incurring costs of annual nusinersen treatment over their lifetime. The ICERs were $254,881 per LYs saved and $261,801 per QALYs saved in the base case model for treatment in a screening setting compared with treatment alone.

Discussion

Our analysis concludes that nusinersen treatment in the setting of universal screening is a preferred strategy over treatment alone, but only cost-effective at high WTP thresholds (eg, over $300,000 per event-free LY). The clinical efficacy of medical interventions often conflict with the prospective assessment of their economic value. For rare genetic diseases such as SMA, the high price of treatment coupled with the relative rarity of the condition inevitably makes it difficult for current standards of WTP thresholds to assess treatment as cost-effective.[38] However, patients with such rare diseases have been underserved through the lack of development of viable and economically feasible treatment.[39] This historical disparity may be attributable to the low return on investment for rare diseases and therefore reduced incentives of commercial developers. Inevitably, important ethical considerations for such patients have been raised with respect to economic evaluation of costly treatment for rare diseases.[40]

Although our base-case results are in line with previous economic evaluations of nusinersen, the addition of universal newborn screening improves the economic viability of nusinersen. In our base-case analysis, relative to no screening or treatment, the combination of universal screening and treatment with nusinersen yielded an ICER below the WTP of $500,000 per LY saved, a WTP threshold that has been prior recommended for rare diseases (though later updated to $200,000 regardless of therapeutic areas) by the Institute for Clinical and Economic Review.[37]

Our methodology relied on LYs saved as our main effectiveness measure. Although QALYs were reported, there are difficulties in determining utility weights for children, as discussed earlier.[34] Nevertheless, CADTH rejected nusinersen's cost-effectiveness using this threshold.[17] A recent analysis in Sweden made similar conclusions, yet reimbursements for nusinersen has been approved in that country.[36] Coverage in the US is likely to expand as further results of clinical trials are published. Major private payer reimbursements for nusinersen require a confirmed diagnosis of SMA and observation of clinical response. In this scenario, early initiation and continued treatment of infantile-onset SMA is more likely with a policy of universal screening than treatment alone. Our study supports expansion of universal newborn screening.

The improvement seen in response to nusinersen treatment of presymptomatic patients is promising, but long-term efficacy is uncertain. Economic evaluations of this treatment should be updated in the future as follow-up studies are conducted to gauge patient outcomes over subsequent years. In addition, similar Markov models can be used to evaluate alternative treatments such as single-dose gene replacement therapy. Although preliminary studies suggest that this treatment is equally promising and with the added advantage compared with nusinersen of not requiring ongoing administrations, gene therapy has been introduced at $2.1 million.[12, 41] With such high costs, universal newborn screening will likely also play a pivotal role in improving both health outcomes and economic value of gene replacement therapy.

Our study is subject to a number of limitations. First, our focus on event-free LYs saved as our primary health outcome ignores potential emotional and psychosocial stress considerations of patient's family members.[42, 43] We included indirect costs of caregiving for SMA patients in the PVA health state, but adequate data on family members of a child with

SMA is was not available in the literature. However, this new effectiveness outcome is a conservative measure because patients progressing to the PVA health state continue to accrue costs, but do not contribute to the effectiveness of nusinersen. A utility approach with the inclusion of family spillovers will still value patients in the PVA health state, albeit at low utility values. Secondly, given the rarity of SMA, little is known about the long-term costs attributable to the disease and further research is needed to improve our understanding of expected costs of surviving SMA patients past the median survival time. In particular, the focus on respiratory symptoms influencing our assumptions on costs based on life expectancy estimates of severe asthma and Duchenne Muscular Dystrophy with ventilator support should be reconsidered in future research when new data is available. We accounted for this limitation by setting wide value range on life expectancy and age specific cost variables in probability sensitivity analysis. In addition, the sensitivity of our results by changing the long-term benefits and cost assumptions will also depend on the discount factor applied to outcome variables.

The ENDEAR trial along with preliminary results of NURTURE have demonstrated that nusinersen is an important innovation in SMA treatment. However, many have wondered whether the drug provides sufficient value to justify the high cost.[14-16] Our study examined the cost-effectiveness of nusinersen in the setting of universal newborn screening with a goal of treatment of presymptomatic infants. We demonstrated that universal newborn screening will reduce estimated ICERs compared with nusinersen alone. Our study provides additional support to the RUSP recommendations to expand universal newborn screening in all states to include SMA. Moreover, our study also provides alternative pricing recommendations based on sensitivity analysis. Using data from the ENDEAR trial, this analysis suggests that, in order to

meet a WTP threshold of $50,000 per LY saved, would require a dosage price of nusinersen that is 19% of the current price.

Studies of rare diseases, like SMA, face common constraints due to the lack of high-quality cost and outcomes data.[44] A study that examined the cost-effectiveness of prenatal screening for SMA faced similar challenges.[45] Our model parameters were an improvement on prior work, but more work is needed to fill this important gap in this literature. Continued follow-up of patients treated with nusinersen is necessary to validate further economic evaluations.

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Legends

Figure 1. ICER = incremental cost-effectiveness ratio per discounted event-free Life Year saved. The graph reports results from the base case ENDEAR trial model parameters. Effectiveness and cost outcomes are estimated per U.S. live birth.

Figure 2. Probability of cost-effectiveness based on the base case model and a list dosage price of nusinersen at $125,000.

Figure 3. ICER = incremental cost-effectiveness ratio per discounted event-free Life Year saved. Sensitivity analysis performed on the base case model. Dashed horizontal lines are set at three Willingness to pay thresholds ($50,000, $100,00, $150,000) with the corresponding nusinersen dosage price.

Table 3. LY= life year, QALY = quality-adjusted life year. ICER = incremental cost-effectiveness ratio. Adjustment probability parameters are reported in Table 1. ICERs are reported using precision to 7 decimal places.

Table 1 (online). Probability inputs.

Probability	Value	Distribution	Range	Reference
SMA prevalence	9.4 per 100,000	Beta	3.58-8.27 per 100,000	(25)
SMA type 1	60%			(26)
Death - nusinersen	1.36%	Beta	0.56%-2.77%	Monthly - Calculations based on (9)
Death - no treatment	3.73%	Beta	1.43%-7.47%	Monthly - Calculations based on (9)
Death - NURTURE	0%			(11)
Neonatal mortality rate	3.94 per 1,000			2015 CDC NCHS Linked Birth/Infant Death records
Post-neonatal mortality rate	1.96 per 1,000			2015 CDC NCHS Linked Birth/Infant Death records
Child (1-4) mortality rate	2.49 per 1,000			2015 National Vital Statistics Report Volume 66 No. 6
Death -PVA	3.19%	Beta	1.37%-6.18%	Bartlett et al. 2000
Ventilator support - nusinersen	1.94%	Beta	0.76%-4.14%	Monthly - Calculations based on (9)
Ventilator support - no treatment	2.89%	Beta	0.84%-5.94%	Monthly - Calculations based on (9)
Ventilator support - NURTURE	0%			(11)
MM Response - nusinersen	5.29%	Beta	1.55%-9.27	Monthly - Calculations based on (9)
MM Response - no treatment	0.00%			Monthly - Calculations based on (9)
Adjustment for early treatment	0.516			Adjustment factor based on (9)
Adjustment for late treatment	1.484			Adjustment factor based on (9)
MM Response – NURTURE	17.66%			≤ 13 Months (11)
MM Response – NURTURE	100%			>13 Months

Table 2 (online). Cost and outcome inputs.

Item	Value	Distribution	Range	Code	Notes
Single dose injection: nusinersen	$125,000		$5,000-125,000	J2326	Current reported Pricing
Marginal cost of SMA newborn Screening	$2.91	Gamma	$1.94-$4.45		2018 Utah legislative increase of Newborn Screening Kit.
Lumbar puncture with image guidance - professional fee	$102.60			62323	CMS
Moderate sedation service of patient <5 years - professional fee	$25.20	Gamma	$101-$232	99151	CMS
Medicare to private payer rate - professional fee	23%				(31)
Injection of substance into lower or sacral spine - facility fee	$120.06			62311	Average Medicare payment amount (2016)
Moderate sedation service of patient <5 years - facility fee	$15.22	Gamma	$141-$315	99150	Average Medicare payment amount (2016)
Medicare to private payer rate - facility fee	66%				(29, 30)
Direct monthly costs - PVA	$13,564		$8,898-$19,351		(28), PCE Health Services
Indirect monthly costs - PVA	$1,034	Gamma	$678-$1,435		(28), Bureau of Labor Statistics
Age-specific annual costs: 0-18	$4,552	Gamma	$2,936-$6,812		(32,33)
Age-specific annual costs: 19	$4,988				(32,33)
Age-specific annual costs: 20-39	$3,507		Range varied for estimating final costs by health state		(32,33)
Age-specific annual costs:40-44	$4,367	Gamma			(32,33)
Age-specific annual costs: 45-64	$6,533				(32,33)
Age-specific annual costs: >65	$16,346				(32,33)
LY - normal population	79.5 (29.91 discounted)	Gamma	17.6-44.1		(19)
LY - SMA without PVA (with presymptomatic treatment)	75 (29.48 discounted)	Gamma	19.8-44.6		(19) - Asthma used as proxy
LY – SMA with PVA	25.3 (16.4 discounted)	Gamma	10.6-22.9		(20) - Duchenne muscular dystrophy with nocturnal ventilation used as proxy
QALY - normal population	71.4				(19)
QALY - SMA without PVA	64.4				(19) - Asthma used as proxy

References (online)

Bartlett JG, Dowell SF, Mandell LA, File Jr TM, Musher DM, Fine MJ. Practice guidelines for the management of community-acquired pneumonia in adults. *Clinical infectious diseases*. 2000;31(2):347-82.

Table 3. Results of Cost-effectiveness Analysis.

Strategy	Costs per Infant	Incremental Costs	Event-free LYs	Event-free QALYs	Incremental LYs	Incremental QALYs	ICER - LY	ICER - QALY
Base Case								
No treatment / no screening	$158,397	-	32.0540	31.1517	-	-	-	-
Screening / no treatment	$158,400	$2.9	32.0540	31.1517	0	0	Dominated	Dominated
Nusinersen / no screening	$158,670	$272.8	32.0546	31.1522	0.0005	0.0005	$508,481	$522,118
Nusinersen + screening	$158,805	$135.4	32.0553	31.1529	0.0007	0.0007	$193,867	$199,510
NURTURE (preliminary)								
Nusinersen + screening	$159,005	335.5	32.0559	31.1535	0.0013	0.0013	$254,881	$261,803
Adjustment for Early and Late Treatment								
No treatment / no screening	$158,396.9		32.0540	31.1517	-	-	-	-
Screening / no treatment	$158,399.8	$2.9	32.0540	31.1517	0	0	Dominated	Dominated
Nusinersen / no Screening	$158,630.2	$233.4	32.0544	31.1521	0.0004	0.0004	$561,873	$575,144
Nusinersen + screening	$158,886.3	$256.0	32.0555	31.1532	0.0011	0.0010	$239,885	$247,492
NURTURE (preliminary)								
Nusinersen + screening	$159,005.1	$374.9	32.0559	31.1355	0.0014	0.0014	$260,833	$268,152

LY= life year, QALY = quality-adjusted life year. ICER = incremental cost-effectiveness ratio. Adjustment probability parameters are reported in Table 1. ICERs are reported using precision to 6 significant digits.

Figure 1: Cost-Effectiveness – Base Case Results: Discounted Event-Free LY Saved.

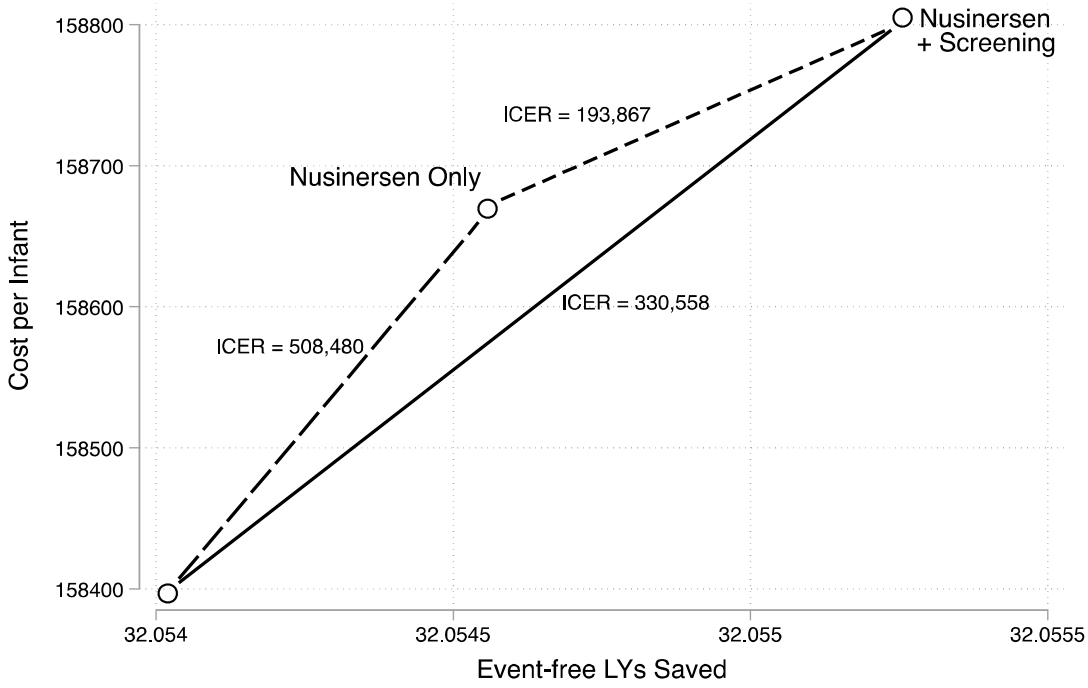

Figure 2: Cost-Effectiveness Acceptability Curve: Results from Probability Sensitivity Analysis.

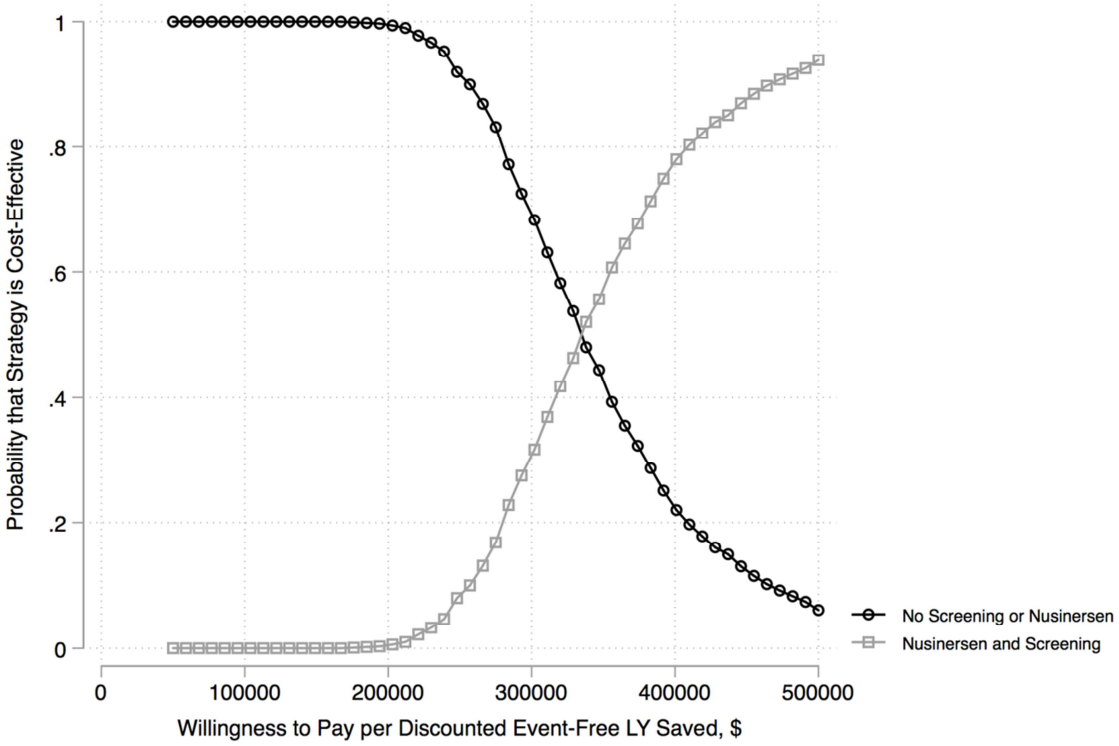

Figure 3: Threshold Analysis: Dosage Price of Nusinersen Drug Therapy.