FILE E-1. INPUT PARAMETERS

The effectiveness parameters for the model were based on: 1) two different meta-analyses with two different methodologies on the effectiveness of non-intravenous benzodiazepines ^{1, 2}. and 2) two different meta-analyses with two different methodologies on the effectiveness of nonbenzodiazepine antiseizure medications ^{3, 4}. Within each treatment category (non-intravenous benzodiazepines and non-benzodiazepine antiseizure medications) we considered a loweffectiveness choice and a high-effectiveness choice. For non-intravenous benzodiazepines, the low-effectiveness choice was based on the current estimates of effectiveness of rectal diazepam and the high-effectiveness choice was based on the current estimates of effectiveness of intranasal midazolam. For non-benzodiazepine antiseizure medications, the low-effectiveness choice was based on the current estimates of effectiveness of intravenous phenytoin and the high-effectiveness choice was based on the current estimates of effectiveness of intravenous phenobarbital. As a sensitivity analysis, we also compared within each category the loweffectiveness choice with a medium-effectiveness choice. For non-intravenous benzodiazepine, the medium effectiveness choice was intranasal lorazepam. For non-benzodiazepine antiseizure medication, the medium effectiveness choice was intravenous valproate. The costs of these treatment choices were estimated in 2019 based on data from Lexicomp and corroborated with retail pharmacies ⁵.

Cost of different treatment choices.

| Rectal diazepam | | | | |
|---|---------------------|--|--|--|
| Rectal diazepam 2.5 mg | \$306.90-\$347.86 | | | |
| Rectal diazepam 10 mg | \$364.06-\$412.64 | | | |
| Rectal diazepam 20 mg | \$364.06-\$412.64 | | | |
| Intranasal midazolam | | | | |
| Intranasal midazolam 5 mg | \$330 | | | |
| Intranasal midazolam 10 mg | \$660 | | | |
| Intranasal lorazepam | | | | |
| Intranasal lorazepam 2mg | \$0.62-\$4.06 | | | |
| Intranasal lorazepam 4mg | \$2.05-\$3.92 | | | |
| Intravenous fosphenytoin | | | | |
| Intravenous fosphenytoin 500 mg | \$2.7-\$9.5 | | | |
| Intravenous fosphenytoin 1000 mg | \$5.4-\$19 | | | |
| Intravenous fosphenytoin 1500 mg | \$8.1-\$28.5 | | | |
| Intravenous fosphenytoin 2000 mg | \$10.8-\$38 | | | |
| Intravenous phenobarbital | | | | |
| Intravenous phenobarbital 500 mg | \$201.39-\$261.39 | | | |
| Intravenous phenobarbital 1000 mg | \$402.78-\$522.78 | | | |
| Intravenous phenobarbital 1500 mg | \$604.17-\$784.17 | | | |
| Intravenous phenobarbital 2000 mg | \$805.56-\$1,045.56 | | | |
| Intravenous valproate | | | | |
| Intravenous valproate 500 mg \$40.15-\$ | | | | |
| Intravenous valproate 1000 mg \$80.3-\$257.6 | | | | |
| Intravenous valproate 1500 mg \$120.45-\$386. | | | | |
| Intravenous valproate 2000 mg \$160.6-\$515. | | | | |

The costs of emergency department visits, hospital admissions for status epilepticus, and intensive care unit for status epilepticus were estimated based on prior literature on costs in the USA ⁶⁻⁸. When the estimates were from prior years, we transformed them in 2019 USA dollars using the USA Bureau of Labor Statitics Consumer Price Index ⁹.

Cost of hospital visits. All values are presented as median $(p_{25}-p_{75})$

| | Original values pediatric | Original values adult patients | 2019 USA dollars values | 2019 USA dollars values |
|--------------------------|---------------------------|--------------------------------|----------------------------|----------------------------|
| | patients | | for pediatric patients | for adult patients |
| Cost of | Estimated in | Estimated in | \$2,081 (\$1,079 | \$2,081 (\$1,079 |
| emergency | 2016 USA | 2016 USA | to \$4,119) | to \$4,119) |
| department | dollars: | dollars: | | |
| visits ⁶ | \$1,959 (\$1,016 | \$1,959 (\$1,016 | | |
| | to \$3,877) | to \$3,877) | | |
| Cost of hospital | Estimated in | Estimated in | \$7,039 (\$3,908 | \$9,697 (\$6,072 |
| admission for | 2016 USA | 2016 USA | to \$14,869) | to 18,284) |
| status | dollars: | dollars: | | |
| epilepticus ⁷ | \$6,625 (\$3,678 | \$9,127 (\$5,715 | | |
| | to \$13,995) | to \$17,209) | | |
| Cost of hospital | Estimated in | Estimated in | \$14,116 (\$8,916 | \$18,252 (\$10,275 |
| admission for | 2016 USA | 2016 USA | to \$23,664) | to \$30,065) |
| refractory | dollars: | dollars: | | |
| status | \$13,286 (\$8,392 | \$17,179 (\$9,671 | | |
| epilepticus ⁷ | to \$22,273) | to \$28,298) | | |
| Cost of hospital | Estimated in | Estimated in | \$148,520 | \$57,993 (\$41,583 |
| admission for | 2016 USA | 2016 USA | (\$69,154 to | to \$83,161) |
| super- | dollars: | dollars: | \$244,843) | |
| refractory | \$139,790 | \$54,584 | | |
| status | (\$65,089 to | (\$39,139 to | | |
| epilepticus ⁷ | \$230,451) | \$78,273) | | |

Legend: N/A: Not applicable.

REFERENCES

- 1. Arya R, Kothari H, Zhang Z, Han B, Horn PS, Glauser TA. Efficacy of nonvenous medications for acute convulsive seizures: A network meta-analysis. Neurology 2015;85:1859-1868.
- 2. Sánchez Fernández I, Gainza-Lein M, Loddenkemper T. Nonintravenous rescue medications for pediatric status epilepticus: A cost-effectiveness analysis. Epilepsia 2017;58:1349-1359.
- 3. Sánchez Fernández I, Gainza-Lein M, Lamb N, Loddenkemper T. Meta-analysis and cost-effectiveness of second-line antiepileptic drugs for status epilepticus. Neurology 2019;92:e2339-e2348.
- 4. Yasiry Z, Shorvon SD. The relative effectiveness of five antiepileptic drugs in treatment of benzodiazepine-resistant convulsive status epilepticus: a meta-analysis of published studies. Seizure 2014;23:167-174.
- 5. Lexicomp. Lexicomp. URL: http://online.lexi.com [online]. Available at: http://online.lexi.com. Accessed October, 9, 2019.
- 6. Lane BH, Mallow PJ, Hooker MB, Hooker E. Trends in United States emergency department visits and associated charges from 2010 to 2016. The American journal of emergency medicine 2019:158423.
- 7. Sánchez Fernández I, Amengual-Gual M, Barcia Aguilar C, Loddenkemper T. Estimating the cost of status epilepticus admissions in the United States of America using ICD-10 codes. Seizure 2019;71:295-303.
- 8. Sánchez Fernández I, Loddenkemper T. Estimating the cost of admissions related to convulsive status epilepticus in the United States of America. Seizure 2018;61:186-198.
- 9. United States Department of Labor. Bureau of Labor Statistics. Consumer Price Index. URL: https://www.bls.gov/cpi/ [online]. Available at: https://www.bls.gov/cpi/. Accessed October, 25, 2019.