

#### S4. Cox model specifications

As we included 48 variables in the model, a minimum of 480 events (10 events per covariate) were needed to avoid overfitting, although some simulation studies have suggested this criterion can be relaxed.<sup>1</sup> The equation used to model the time from index date to the first occurrence of seizure-related hospitalization is:

$$\text{Log [h (t, X)]} = \text{log [h}_0 \text{ (t)]} + \sum_1^{48} \beta_n X_n \text{ (Equation 1)}$$

Where: t represents days until the event of seizure-related hospitalization (Model), log [h (t)] represents the baseline hazard, and

X=(X<sub>1</sub>, X<sub>2</sub>, X<sub>3</sub>... X<sub>49</sub>) represents the confounders we tried to adjust for in the model.

X<sub>1</sub>: Stimulant exposure status (current, former or no use)

X<sub>2</sub>: Gender (male, female)

X<sub>3</sub>: Race (White, Black, American Indian/ Alaskan Native, Asian, Hispanic/ Latino, Native Hawaiian/ Pacific Islander, Hispanic/ Latino and ≥1 races, ≥1 race, Unknown race)

X<sub>4</sub>: Age category (3-5, 6-9, 10-14, 15-18) at baseline

X<sub>5</sub>: Epilepsy types (generalized non-convulsive, generalized convulsive, focal, unknown) at baseline

X<sub>6</sub>: Epilepsy severity (non-intractable, intractable, unspecific)

X<sub>7</sub>: Number of AEDs filled/refilled during baseline

X<sub>8</sub>: Cerebral Palsy during baseline

X<sub>9</sub>: Congenital CNS anomalies during baseline

X<sub>10</sub>: Autism during baseline during baseline

X<sub>11</sub>: Intellectual disability during baseline

X<sub>12</sub>: Head trauma during baseline

X<sub>13</sub>: Schizophrenia during baseline

X<sub>14</sub>: ADHD during baseline

X<sub>15</sub>: ODD/CD during baseline

X<sub>16</sub>: Anxiety during baseline

X<sub>17</sub>: Depression during baseline  
X<sub>18</sub>: Bipolar disorder during baseline  
X<sub>19</sub>: Sleep disorder during baseline  
X<sub>20</sub>: Foster care during baseline  
X<sub>21</sub>: Cash assistance during baseline  
X<sub>22</sub>: Poverty during baseline  
X<sub>23</sub>: Disability during baseline  
X<sub>24</sub>: State of residence at index date  
X<sub>25</sub>: Calendar year at index date  
X<sub>26</sub>: Medication possession rate during baseline  
X<sub>27</sub>: Amoxicillin during baseline  
X<sub>28</sub>: Ciprofloxacin during baseline  
X<sub>29</sub>: Desmopressin during baseline  
X<sub>30</sub>: Ofloxacin during baseline  
X<sub>31</sub>: Carbamazepine during baseline  
X<sub>32</sub>: Clonazepam during baseline  
X<sub>33</sub>: Diazepam during baseline  
X<sub>34</sub>: Valproic acid during baseline  
X<sub>35</sub>: Ethosuximide during baseline  
X<sub>36</sub>: Gabapentin during baseline  
X<sub>37</sub>: Lamotrigine during baseline  
X<sub>38</sub>: Levetiracetam during baseline  
X<sub>39</sub>: Lorazepam during baseline  
X<sub>40</sub>: Oxcarbazepine during baseline  
X<sub>41</sub>: Phenobarbital during baseline  
X<sub>42</sub>: Phenytoin during baseline  
X<sub>43</sub>: Topiramate during baseline  
X<sub>44</sub>: Zonisamide during baseline  
X<sub>45</sub>: SSRI during baseline  
X<sub>46</sub>: Non-SSRI antidepressants during baseline  
X<sub>47</sub>: Atypical antipsychotics during baseline

X<sub>48</sub>: Typical antipsychotics during baseline

After evaluating the main effects, we tested patient characteristics and stimulant interactions by adding interaction terms to the model one at a time. We selected these patient characteristics with the aim of identifying one or more subpopulations for whom the risk of seizure-related hospitalization was significantly higher for stimulant users. The information might be useful for decision making in stimulant prescribing.

Stimulant – epilepsy type interaction:

$$\text{Log [h (t, X)]} = \text{log [h}_0 \text{(t)]} + \sum_1^{48} \beta_n X_n + X_1 * X_5 \quad (\text{Equation 2})$$

Stimulant – epilepsy severity interaction:

$$\text{Log [h (t, X)]} = \text{log [h}_0 \text{(t)]} + \sum_1^{48} \beta_n X_n + X_1 * X_6 \quad (\text{Equation 3})$$

Stimulant – cerebral palsy interaction:

$$\text{Log [h (t, X)]} = \text{log [h}_0 \text{(t)]} + \sum_1^{48} \beta_n X_n + X_1 * X_8 \quad (\text{Equation 4})$$

Stimulant – Congenital CNS anomalies interaction:

$$\text{Log [h (t, X)]} = \text{log [h}_0 \text{(t)]} + \sum_1^{48} \beta_n X_n + X_1 * X_9 \quad (\text{Equation 5})$$

Stimulant – Intellectual disability interaction:

$$\text{Log [h (t, X)]} = \text{log [h}_0 \text{(t)]} + \sum_1^{48} \beta_n X_n + X_1 * X_{11} \quad (\text{Equation 6})$$