

# DRUG PRESCRIPTION IN AND HOSPITALIZATION OF REFRACTORY FOCAL EPILEPSY PATIENTS IN THE GERMAN NEUROTRANSDATA (NTD) NEUROLOGISTS' NETWORK – IS THERE AN UNMET NEED?

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## BACKGROUND:

Due to limited availability of cost data and underlying conditions on refractory epilepsy patients a study was conducted based on data collected by the German NeuroTransData (NTD) neurologists' network.

## OBJECTIVE:

To quantify annual drug costs and hospitalization rates (HR) of adult refractory focal epilepsy patients in Germany.

## METHODS:

### Identification of patients within the database:

We retrospectively estimated the annual hospitalization rate (HR) and medication for refractory focal epilepsy patients based on the NeuroTransData neurologists' network database (input from 79 neurologists, 34 centers, 1240 patients).

### Inclusion criteria for patients were:

- at least 1 year of disease history;
- documentation and treatment period of at least 6 months;
- treatment with at least 1 antiepileptic drug [AED] in patient history;
- at least 1 seizure during 6 months of monitoring

Data were analyzed for the 6 months between May and October 2010.

Relevant data included in the NTD-data base:

- demographic information, including work status
- seizure frequency/refractory status
- ambulatory consultation/hospitalization rate including causality and length of stay
- information on drug prescription

**Ambulatory consultation rate:** was recorded as number of visits per patient within six months.

### Dosing and cost calculation:

Dosing for all AEDs was recorded on the start and the end of the 6 months observational period. All calculations are based on the mean of this data at these points in time. We report the distribution of AEDs in the population, number of drugs per patient, the average dosing per drug (incl. 95% confidence interval). This average dosing reflects the prescribing in the real world setting (RWS) and is compared with defined daily doses<sup>1</sup> (DDD). Drug costing was based on prices to patient considering governmental clawbacks. Price level as in 2011<sup>2</sup>. Costs are reported for drugs prescribed in more than 5% of cases (with a comparison between RWS-based cost and DDD-cost) as well as per patient. Annual drug costs have been estimated by extrapolation.

**Average Hospitalization rate (HR):** was based on proportion of patients hospitalized within six months and extrapolated to one year. In addition mean duration of hospitalization and the distribution among the following reasons for hospitalization were recorded: emergency, new adjustment for medication, documentation of seizure, rehabilitation.

## RESULTS:

• **Demographics:** Mean age of 70 patients (31 male, 39 female) identified was 49.6 years. On average patients were epileptic for 21 years (median 19 years).

• **Work situation:** 21 patients were working fulltime, 5 part-time. 18 patients were retired, while 14 were incapable of working. 16 people live from pension, 26 from welfare/unemployment compensation and 7 are dependent on their relatives.

• **Information on seizure frequency/refractory status:** Of those 70 refractory patients identified in the NTD-network, 28% had one seizure (focal and secondary generalized) during the last six months of monitoring, 24% had more than 10 seizures, 16% had more than 20 seizures (see figure 1).

• **Percentage of AEDs prescribed and average drug consumption:** On average patients took 2.1 AEDs. Percentage of drugs that were prescribed in more than 5% of cases are shown in table 1. Overall patients took up to 13 different drugs in their disease history (see figure 2). Leading substances are generic: levetiracetam 43%, lamotrigine 42%, valproic acid 21% (see table 2).

• **Comparison of dosing schemes – RWS vs. DDD:** As table 3 shows in most cases real world dosing and DDD recommendation did not differ a lot. For oxcarbazepine and carbamazepine real world dosing was 28%/27% above DDD dosing but inside CI. Only for topiramate and levetiracetam with a difference between RWS and DDD of 70% and 41% respectively, DDD were outside the CI (topiramate: RWS < DDD; levetiracetam: RWS > DDD).

• **Ambulatory drug cost per day:** As table 1 shows, average daily costs per prescribed drug ranged from 0.65€ (Valproate) to 9.51€ (Lacosamid) average daily drug costs per patient (across all drugs) ranged between 7.01€ (RWS) and 6.16€ (DDD).

• **Differences in calculation basis:** Comparing cost of both settings (RWS/DDD) for 9 drugs shows that calculations based on DDDs underestimate daily cost per drug in 5 cases by 7-33% and overestimate in 4 cases by 17-25% (see table 1).

• **Average ambulatory drug cost per year:** Annual total drug costs per patient were on average 2,557.44€ (CI: 1,947.95-3,169.17€) in a RWS and 2,246.99€ calculated based on DDD.

• **Comparison of drugs with/out patent protection:** Daily drug cost of older, often generic drugs are on average 4€ cheaper than drugs still being protected by patent.

• **Reason for hospitalization:** Average HR was 44%, taking into account various reasons. Figure 3 shows causes for hospitalization stated by patients allowing for more than one per hospitalization case. Most patients were hospitalized for emergency (56%), adjustment for medication (20%) and/or documentation of seizure (18%).

• **Duration of hospitalization:** Mean duration of hospitalization was 34.9 (CI: 20.2-49.6; median 17.8) days per patient hospitalized within one year.

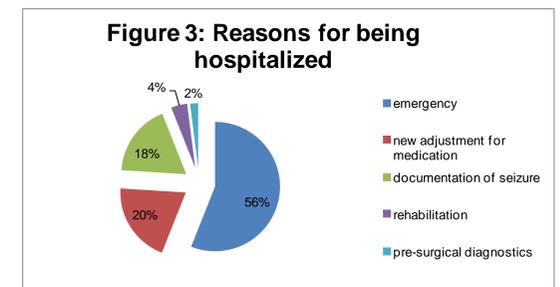
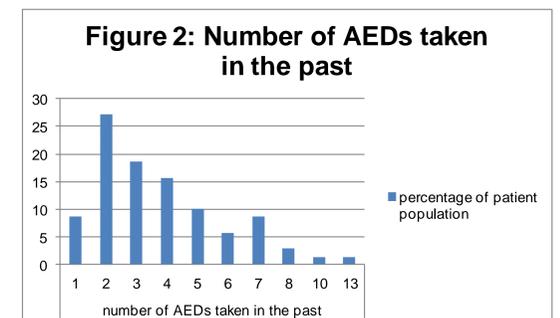
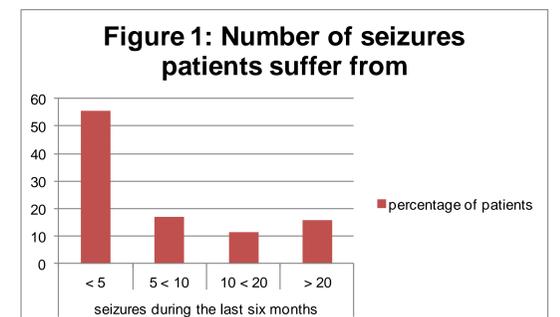


Table 1: Daily drug cost per AED per patient in €

Drug	Levetiracetam	Lamotrigine	Lacosamide	Valproic acid	Oxcarbazepine	Carbamazepine	Topiramate	Gabapentin	Phenytoin
Setting									
Real life data mean	6.68	1.25	9.51	0.65	1.96	0.77	3.37	2.62	0.26
Based on DDD	4.76	1.41	8.25	0.72	1.49	0.61	5.71	2.43	0.29

Table 2: Percentage of patients with different medication and AEDs status of patent per drug

	Levetiracetam	Lamotrigine	Lacosamide	Valproic acid	Oxcarbazepine	Carbamazepine	Topiramate	Gabapentin	Phenytoin	Clonazepam	Eslicarbazepine	Phenobarbital	Pregabalin	Zonisamide	Clobazam	Diazepam	Ethosuximide	Mesuximide	Primidone	Vigabatrin
Percentage of patients taking the following AEDs	42.9%	42.1%	17.9%	21.4%	20.0%	15.0%	10.7%	7.1%	7.1%	4.3%	2.1%	2.9%	2.9%	2.9%	1.4%	1.4%	0.7%	1.4%	1.4%	1.4%
Patent protection	no	no	yes	no	no	no	no	no	no	no	yes	no	yes	yes	no	yes	no	no	no	no

Table 3: Comparison of dosing schemes - RWS vs. DDD

	Levetiracetam	Lamotrigine	Lacosamide	Valproic acid	Oxcarbazepine	Carbamazepine	Topiramate	Gabapentin	Phenytoin
Average RWS dosing in mg	2109 (CI: 1751; 2500)	267 (CI: 203; 332)	346 (CI: 254; 438)	1360 (CI: 904; 1816)	1315 (CI: 919; 1712)	1261 (CI: 972; 1551)	177 (CI: 67; 287)	1940 (CI: 468; 3412)	265 (CI: 158; 372)
DDD dosing in mg	1500	300	300	1500	1000	1000	300	1800	300

## DISCUSSION:

• Despite multi-medication, some patients still suffer from up to 56 seizures in six months resulting in unexpectedly high hospitalization rates (44% within 1 year) and difficulties of managing their daily lives (work situation, dependency on others). Lack of adequate seizure control might be due to similar mode of actions (MOA) that most AEDs offer (effect on sodium channels/GABA receptor)<sup>3</sup>. Results from the NTD-network show, that most patients are treated with generic drugs in mono- or combination therapy (leading substances: levetiracetam 43%, lamotrigine 42%, valproic acid 21%), but new drugs are rarely used (see table 2). This could be due to the fact that new drugs are more expensive (as shown in table??). But to gain seizure freedom it might help to combine drugs with different MOA.

• DDDs seem to be a good indicator for real world prescribing of most AEDs.

• Limitations: Due to the potential selection bias and the low number of analyzed patients these results must be seen as indicative. Especially looking at DDDs the population observed might be not representative as refractory patients might be treated differently compared to other epileptic subpopulations.

## CONCLUSION:

A 44% HR and a high average number of inpatient days (~1 month) within 1 year point to an unmet need for treatment optimization in refractory focal epilepsy patients. It indicates that patients receiving combination therapy of conventional drugs are often not well controlled, supporting the consideration of using more innovative drugs.

## References:

(1) WHO Collaborating Centre for Drug Statistics Methodology [http://www.whocc.no/atc\\_ddd\\_index/](http://www.whocc.no/atc_ddd_index/) (last access: 26/11/2011)

(2) Lauer-Taxe online <http://www.lauer-fischer.de/ff/Seiten/WEBAPO-Lauer-Taxe/WEBAPO-Lauer-Taxe-demo.aspx> (latest access: 26/11/2011)

(3) Epilepsie-Netz [http://www.epilepsie-netz.de/81/Epilepsie\\_kompakt/Antikonvulsiva/Wirkmechanismen.htm](http://www.epilepsie-netz.de/81/Epilepsie_kompakt/Antikonvulsiva/Wirkmechanismen.htm)