A data-driven analysis of changes in anti-seizure medications after genetic diagnosis in 1,598 individuals with genetic epilepsies

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Introduction

- Genetic etiologies are identified in >30% of epilepsies.
- Precision medicine approaches aim to tailor medication choices to specific genetic etiologies.
- Whether recommended treatment strategies for individual genetic epilepsies are translated into clinical practice remains unknown.
- Medication prescriptions from the electronic medical records (EMR) can be leveraged to track longitudinal anti-seizure medication (ASM) use.

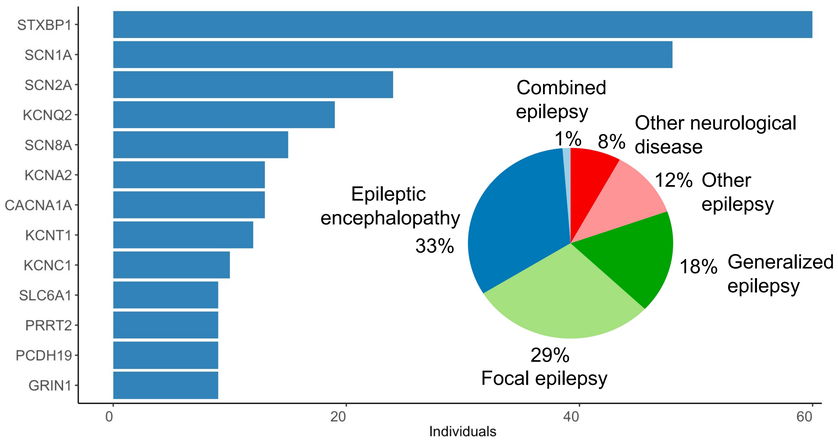


Fig 1. Overview of genetic etiologies and epilepsy phenotypes in the cohort. The most common genetic etiologies in the cohort were *STXBP1* (*n*=60), *SCN1A* (*n*=48), and *SCN2A* (*n*=24).

Methods

- ASM prescription data was extracted from 1,598 individuals with known or presumed genetic epilepsies and binned monthly.
- Longitudinal prescription patterns were assessed across 25 ASMs with a total EMR observation time of 7,872 years.
- ASMs significantly associated with individual genetic etiologies were compared to recommended guidelines.

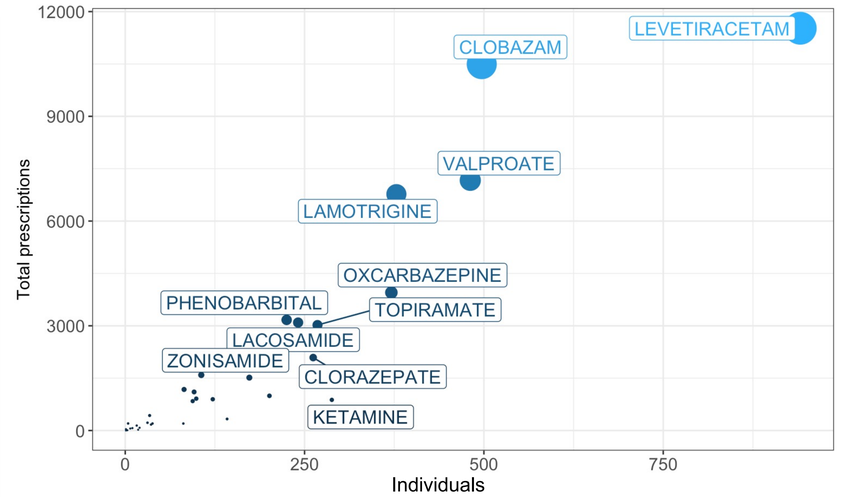


Fig 2. Distribution of ASMs in the overall cohort. Levetiracetam (*n*=11,523), clobazam (*n*=10,495), and valproate (*n*=7,167) were the most common ASMs prescribed in the cohort.

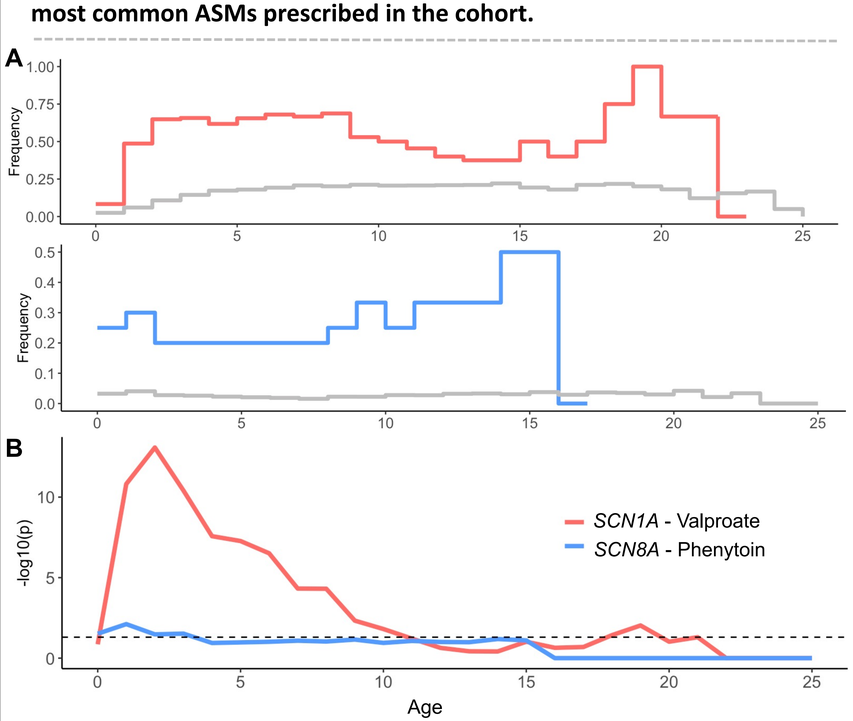
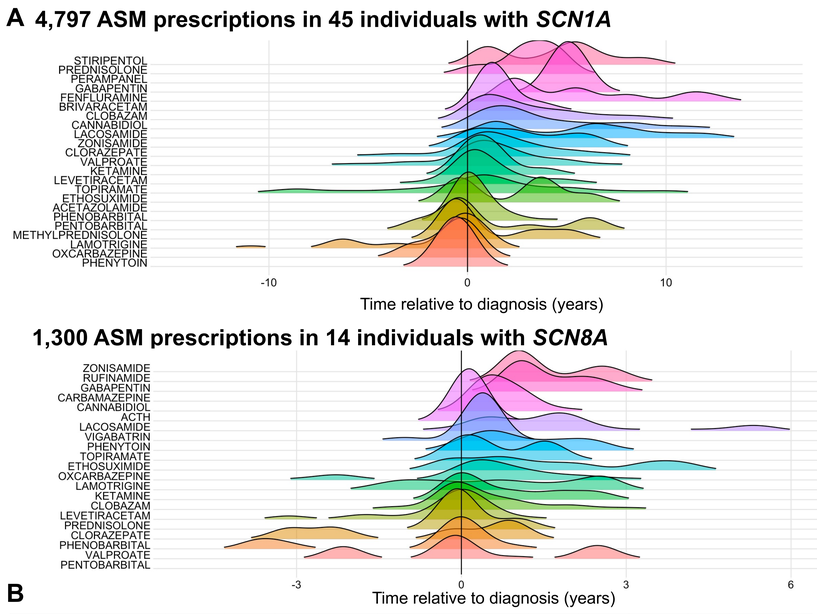


Fig 3. (A) Frequencies of two select ASMs in *SCN1A* and *SCN8A*-related epilepsies compared to the frequency in the remainder of the cohort (grey). (B) Statistical significance of the difference in frequencies by age.



	CBZ	CBD	LEV	TPM	QUIN	VPA	OXC	CZP	LCM	PRED	KET	PHB	PHT	LTG
SCN1A	107.92	81.55	4.61	0.64	-	1.14	0.14	2.51	0.00	-	3.01	3.74	0.07	0.02
PCDH19	100.00	-	10.06	0.00	-	-	-	1.85	-	-	-	0.18	-	0.67
KCNT1	10.70	100.00	0.11	1.62	100.46	0.54	0.00	0.11	0.02	-	13.81	0.36	0.00	-
KCNQ2	3.22	-	1.19	1.85	-	0.08	1.42	6.25	-	48.46	100.00	3.72	-	-
SCN2A	9.49	100.00	1.80	1.09	-	100.00	0.79	18.49	5.08	0.19	10.63	1.99	6.95	0.31
SCN8A	2.55	-	0.39	4.57	-	1.64	0.34	0.13	43.26	2.99	11.52	0.49	3.20	1.14
STXBP1	4.75	-	2.67	0.56	-	-	-	-	-	12.87	-	0.77	-	-
PRRT2	-	-	3.05	-	-	-	3.72	-	-	-	-	0.26	-	-

Fig 4. (A) Shift in ASM prescription density in *SCN1A* and *SCN8A*-related epilepsies. (B) Odds ratios for ASM changes in temporal relation to genetic diagnosis.

Discussion

- The majority of ASMs agree with known recommendations for treatment, such as the initiation of sodium channel blockers in *SCN8A*-related epilepsies.
- A learning health systems approach can be applied to assess clinical decision making in the pediatric epilepsies.

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