Personalised care of paediatric drug-resistant epilepsy in South Africa: a pilot study

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INTRODUCTION

- Sub-Saharan Africa (SSA) faces the highest burden of epilepsy worldwide, due to infections, perinatal insults, but also genetic aetiologies.
- Resources for diagnosing and managing epilepsy in SSA are limited, highlighting the need for innovative strategies.
- Personalised care or Precision medicine (PM) focuses on providing targeted, personalised care usually based on molecular, genetic or digital health data
- PM may offer a viable approach to SSA challenges, combining measurements of patients' clinical status with genetic data
- Our previous study showed feasibility of digital mobile health (mHealth) device in children with epilepsy in a low-resource setting in South Africa[1]

AIM & SAMPLE

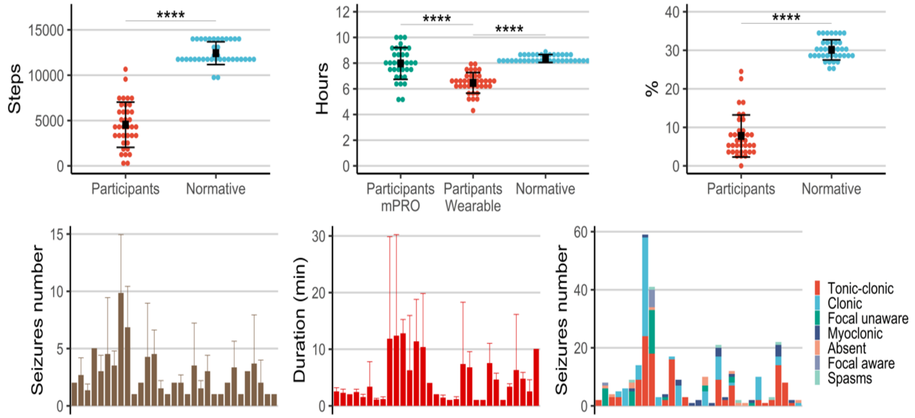
- To evaluate precision medicine initiatives, including mobile technology (mHealth) and genetic screening, in South African healthcare epilepsy service
- 40 children with drug-resistant epilepsy (ongoing seizures despite ≥2 ASMs at adequate doses), age ≥ 4 years, Red Cross Children's Hospital's epilepsy clinic

METHODOLOGY

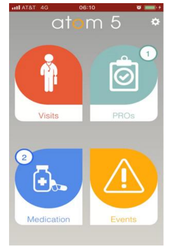
- 40 children with drug-resistant epilepsy (ongoing seizures despite ≥2 ASMs at adequate doses), age ≥ 4 years, from the epilepsy service at the Red Cross Children's Hospital
- **Next generation sequencing (NGS) gene panel:** Customised NGS panel of 78 genes used.
- **Mobile mHealth:** a customised mobile application to report seizures, events, sleep, behaviour, medication reminders, paired to a watch recording sleep, pulse, and step count
- **Pharmacogenomics:** VeriDose® Core Panel (73 target variants across 20 well-known ADME genes, incl. 68 SNPs and 5 CNVs). Design of novel custom mass array with known variants

RESULTS

- **Mobile mHealth:** Records of seizure frequency, but not duration, differed between mHealth technology and clinical records. Patients had significantly lower activity and sleep



- **Next generation sequencing (NGS) gene panel:** Epilepsy aetiology varied: structural abnormalities were most common, no aetiology for 35.9%. Five had potential genetic causes. Pathogenic variants occurred in two different probands in *SCN1A*, one likely pathogenic variant in *GRIN2A*, two variants of unknown significance in *GABRG2* & *GRIN2B*
- **Pharmacogenomics:** Pharmacogenomic analyses showed variants of interest in *CYP2D6*, *EPHX1* and *SCN1A*, but were constrained by sample size & population homogeneity.



CONCLUSIONS

- Precision medicine for drug-resistant epilepsy using mHealth and genetic testing can be utilised in a resource-limited setting.
- This study, the first to demonstrate PM in an African paediatric setting, informed establishment of diagnostic testing for epilepsy and provided novel insights into the lives of children with drug-resistant epilepsy, providing objective measurements of clinical data often missed by traditional clinical records.
- Novel genetic and pharmacogenetic insights into this population of patients

REFERENCES

Davies et al 2021 (https://doi.org/10.1002%2Fepi4.12527)

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Patients & Staff