Incorporating epilepsy genetics into clinical practice: utility and cost saving

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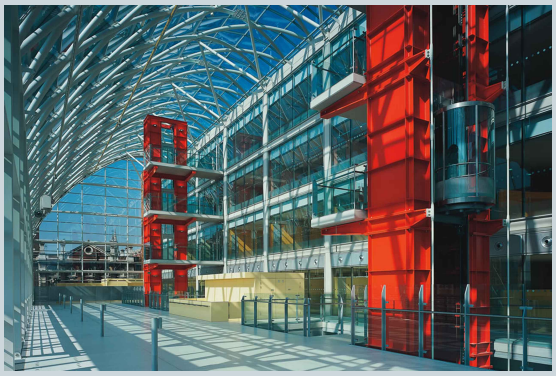
Introduction

We established a regional epilepsy genetics service:
- southeast **England**
- serving a population of **3.5 million**.

The service has two components:
- a specialist outpatient **clinic**
- a **molecular diagnostic** service.

We evaluated:
- the **effectiveness** and **utility** of NGS
- investigation **costs**
- the patient/referrer **experience**



Evelina London Children's Hospital

Methods

- **Prospective** observational design over 18 months
- **N=96 consecutive** patients with primary Dx suspected genetic epilepsy
- Educational workshop for paediatricians

We used:
- Amplexa epilepsy **NGS gene panels**: 46 – 102 genes
- **ACMG** variant classification
- MDT clinical interpretation
- ILAE definition of AED resistance

We assessed:
- **Diagnostic yield** by age group
- Family and referrer **satisfaction** survey
- Investigational **costs** in neonatal epilepsy (n=16)
  - video EEG, MRI, metabolic, single genes

Results

Effectiveness and Utility

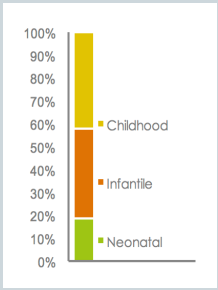


Figure 1. Demographic breakdown of tested patients

- 60% of patients had ≥ 1 variants
  - 19 benign
  - 16 VUS
  - **23 likely pathogenic**

Pathogenic variants: *SCN8A, SCN2A, SCN1A, KCNQ2, HNRNPU, GRIN2A, SYNGAP1, STXBP1, STX1B, CDKL5, CHRNA4, PCDH19, PIGT*

- **SCN8a** (n =4) and **SCN2a** (n=3) most common
- **Turnaround Time: 21 DAYS**
- Overall diagnostic **yield 29%** amongst **AED resistant** cases
- Treatment **implications for 63%** with pathogenic variants

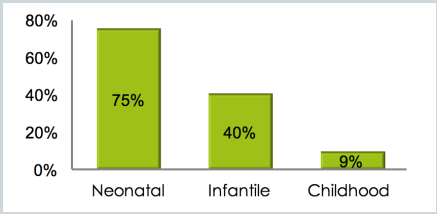


Figure 2. Diagnostic yield by age of seizure onset

Cost

- Actual investigation costs neonatal epilepsy **€10,171** (range: €5,534 – €16,972).
- Theoretical costs if gene panel first line**: €3,083**

Patient/Referrer Experience

- **100%** families would **recommend** to friends and family
- **50%** referrers think gene panel **reduces investigations**

Conclusions

1. NGS panel has high utility and effectiveness if seizure **onset <2 years**
2. Earlier diagnostic use of gene panel could **cut** investigation **costs by 70% or €7,000**
3. Turnaround time is **world leading** 21 days vs. median diagnostic delay 3 years
4. Enthusiastic **acceptance of genomic medicine** by referrers and families