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Genetically informed phenotyping enables population research into rare developmental disorders in childhood

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Background

We currently lack large-scale population and genomic data linkages for rare childhood conditions. Genetically informed phenotypes have the potential to identify affected children within existing population datasets to explore how genetic risk interacts with social and environmental factors to shape outcomes.

Methods

We used linked national hospital and education records for England (ECHILD) to identify children with rare developmental disorders using a clinical rule-based phenotyping algorithm developed from the 100,000 Genomes Project. We compared affected children with the general population on sociodemographic and birth characteristics and examined outpatient referral patterns (including to clinical genetics service), ICD-10 diagnostic phenotype and complexity, and age at first clinical genetics referral.

Results

We identified 25,204 children with phenotypes indicative of developmental disorders (0.5% of 5 million births), of whom 33% were referred to clinical geneticists. Boys predominated, especially in the autism group. Nearly a quarter of children with a developmental disorder lived in the 10% most deprived areas and had lower gestational age, maternal age at birth, and birthweight. Paediatric neurology was the most common specialist referral after general paediatrics. The proportion of children with a clinical genetics referral increased with phenotypic complexity (15% with one phenotype vs 54% with five).

Conclusion

In the absence of genomic data, rule-based phenotyping enables large-scale identification of children with rare developmental disorders in linked population datasets. It reveals social gradients in vulnerability and variation in referral pathways by phenotypic complexity, providing a foundation for equity-focused research and child outcome evaluation where linked genomic data are unavailable.

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