The All Wales Psychiatric Genomics Service (AWPGS)

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Background

Individuals with schizophrenia and related neurodevelopmental disorders often experience major disruption to their lives through its impact on family and social relationships, education, employment and quality of life. Schizophrenia accounts for approximately 30% of the total expenditure on adult mental health and social care services[1].

Recent research has shown that genetic factors, particularly copy number variants (CNVs), can increase the risk of developing schizophrenia by >30 fold. Clinically relevant CNVs are seen in 2-3% of individuals with schizophrenia[2]. However, services for mental ill health lack parity with other physical health services and individuals struggle to access genetic advice and investigations.

To address this inequity, the new AWPGS was launched in June 2022. This service is the first of its kind in the UK and is provided through a partnership between the All Wales Medical Genomics Service (AWMGS), the MRC Centre for Neuropsychiatric Genetics and Genomics, the National Centre for Mental Health (NCMH) and NHS Mental Health Services.

Aims and method

To provide comprehensive multidisciplinary advice, genetic information and access to genetic testing for individuals in Wales in whom there may be concerns about a genetic predisposition to mental health disorders.

The pilot phase of this project will involve analysing DNA from 100 patients using the Illumina Infinium CytoSNP-850K platform to identify CNVs. CNVs are classified according to the latest ACMG/AMP CNV analysis guidelines[3]. Results will be fed back to the patients through genetics clinics and the impact on people and their management will be evaluated at the end of the pilot phase.

A Mental Health Genetic Service: Bringing together leading health and academic institutions

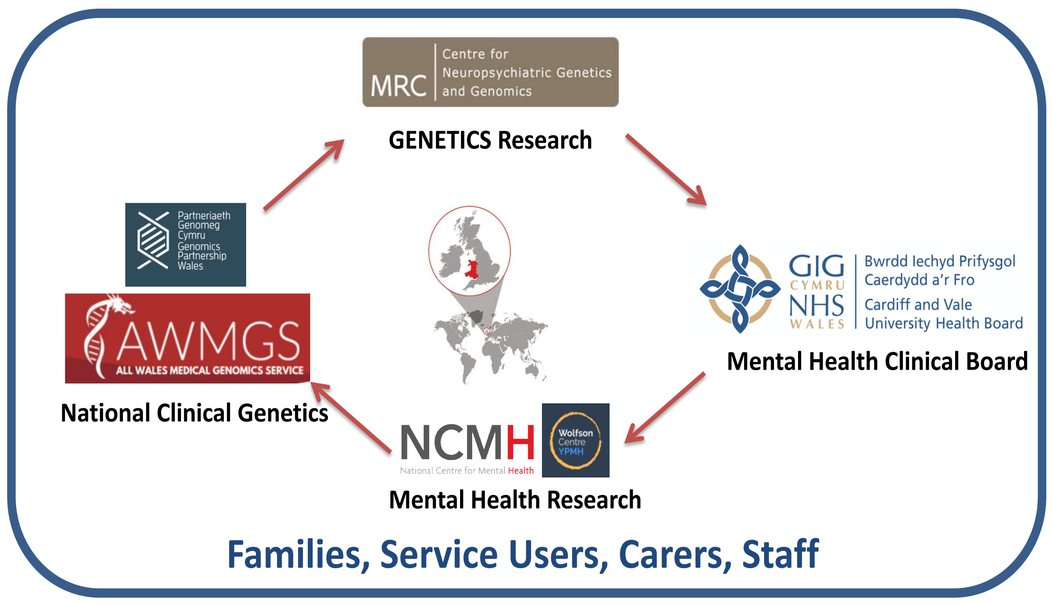
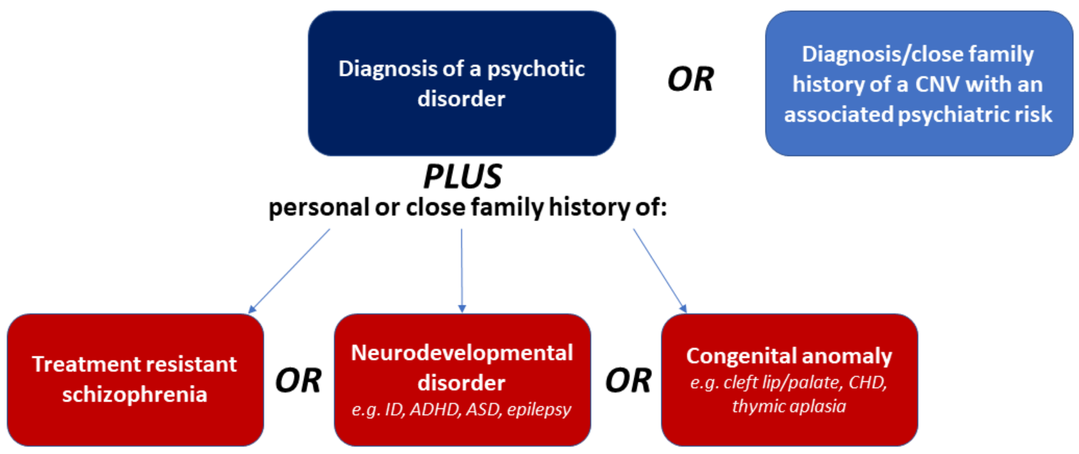


Image used with permission from Donna Duffin

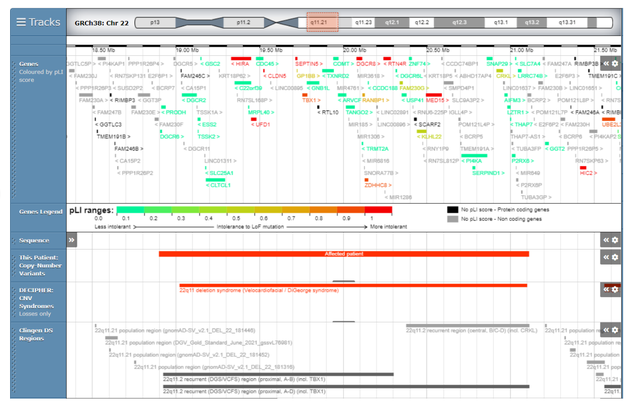
Referral criteria



Case Study 1

Clinical Features

Psychiatric: Depression, anxiety, alcohol misuse, suicide attempts
Physical: Subcutaneous granuloma, psoriasis, psoriatic arthritis, hypocalcaemia, fibromyalgia, type 2 diabetes (T2D)
Family history: T2D, attention deficit hyperactivity disorder (ADHD) and intellectual disability (ID)



Previous identification of a CNV through a research study

Result

Confirmation of a pathogenic 2.2Mb copy number loss at the 22q11.2 recurrent microdeletion syndrome (DiGeorge/Velocardiofacial syndrome) region.

Associated with a wide range of features including:
Congenital heart disease (CHD), immune deficiencies, ID, hypocalcaemia, autoimmune disorders and psychiatric illness (including anxiety and depression)[4].

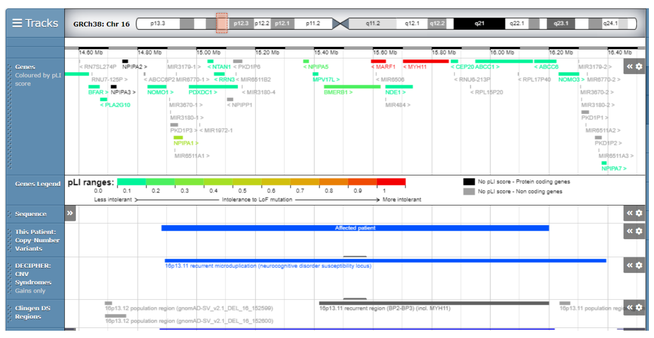
Impact on management

Offer cascade counselling and testing for family members (if desired), monitoring for CHD, immune deficiencies and other clinical features.

Case Study 2

Clinical Features

Psychiatric: Autism spectrum disorder (ASD), post-traumatic stress disorder (PTSD)
Physical: T2D, treatment-resistant hypertension, obstructive sleep apnea
Family history: ASD, pathological demand avoidance, Parkinson's



Previous identification of a CNV through a research study

Result

Confirmation of a 1.3Mb copy number gain of the 16p13.11 recurrent microduplication (neurocognitive disorder susceptibility locus).

Associated with neurodevelopmental phenotypes including ID, ADHD, ASD. Also reported to be a risk factor for thoracic aortic aneurysms and dissections[5].

But associated with incomplete penetrance and variable expressivity, with the majority being inherited from mildly affected or unaffected parents[6]. This variant has therefore been classified as a variant of uncertain significance.

Impact on management

Offer cascade counselling and testing for family members (if desired), heart monitoring and continued management of clinical features.

Summary and next steps

- The AWPGS was launched in June 2022. This new genomics service for people with mental illness is the first of its kind in the UK.
- This service will provide access to genetic testing for individuals and their families affected by mental ill health, giving parity with physical health services
- This pilot project will be used to estimate the diagnostic rate and evaluate the impact on patient management, enabling continued service improvement and monitoring.

References:

1. HQIP and RCPsych (2018) National Clinical Audit of psychosis.
2. Kirov, G., Rees, E., & Walters, J. (2015). *BJPsych Advances*, 21(3), 157-163.
3. Riggs *et al.* (2020) *Genet Med.* 22(2):245-257
4. GeneReviews: McDonald-McGinn DM, *et al.* 22q11.2 Deletion Syndrome. 1999 [Updated 2020].
5. Kuang *et al.* (2011) *PLoS Genet*:7(6)
6. El Khattabi *et al.* (2020) . *J Med Genet.* 57(5):301-307