Young onset dementia - increasing awareness and opportunities for genetic testing. Memory clinics and the NHS Genomic Medicine Service.

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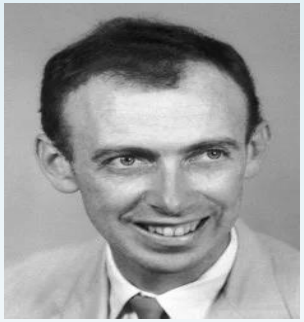
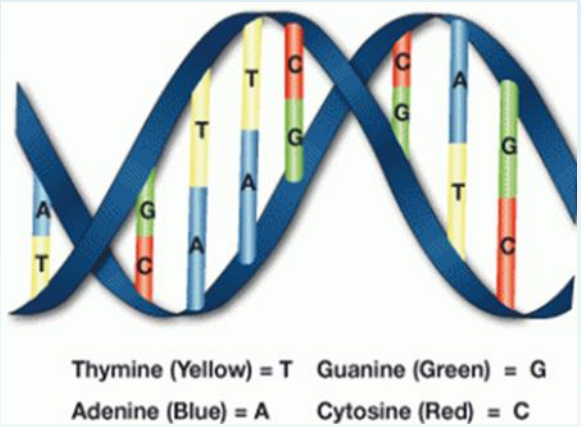
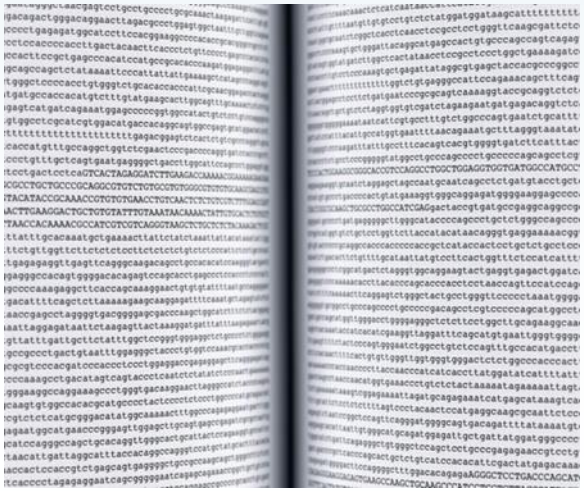
NHS East London NHS Foundation Trust

NHS North Thames NHS Genomic Medicine Service Alliance

DNA: Structure and sequence







Genetic Forms of Dementia

- Aetiological sequence changes
- Rare
  <1% Alzheimer's Disease
  v. rare in Vascular Dementia
  v. rare in Lewy Body Dementia
  > 25% Frontotemporal dementia
  and in some rare dementias
- Usually young onset....but not always
- Young onset dementia usually not genetic
- Usually family history….but not always

Tower Hamlets Diagnostic Memory Clinic

Genetic testing in the memory clinic in the old days

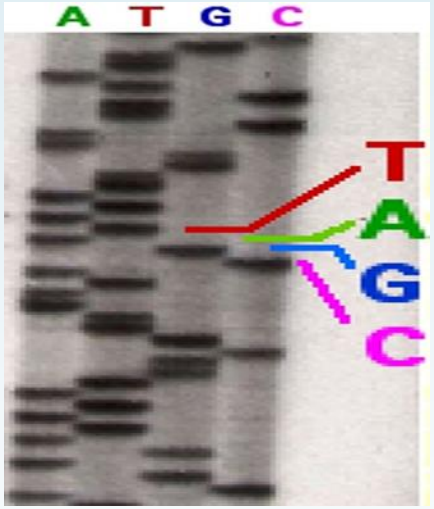
Theoretically possible, practically impossible

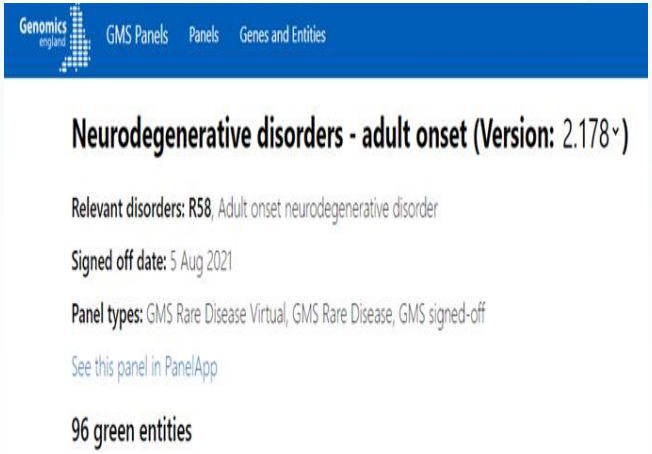
- Diagnostic testing possible for some variants in APP, PSEN1, PSEN2, TAU, GRN, NOTCH3, maybe some others
- One gene at a time, different labs
- Funding

Onwards referral, long diagnostic journey

- Young onset
- More complex presentation
- Comprehensive local assessment
- NHNN, Queen Square
- Comprehensive assessment
- Genetic diagnosis at end of journey

Change 1: Next generation sequencing and comprehensive testing

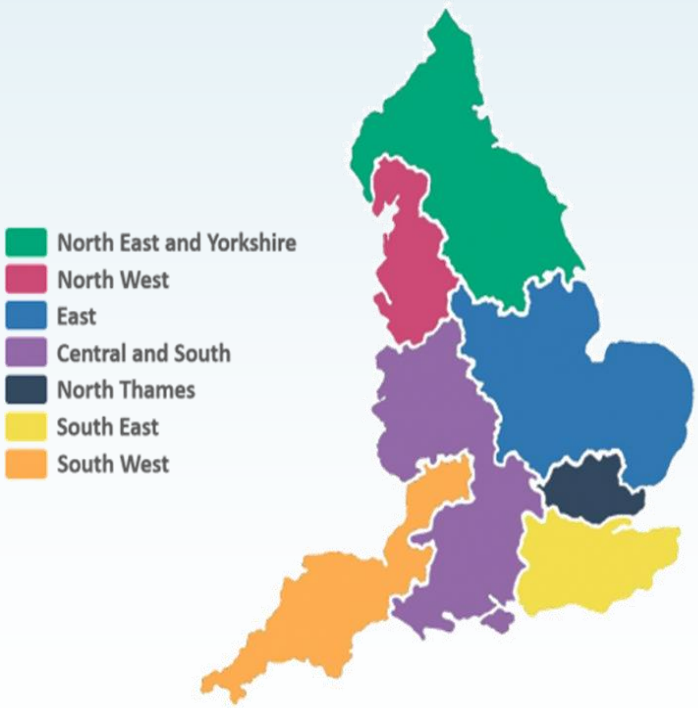




1986-2001

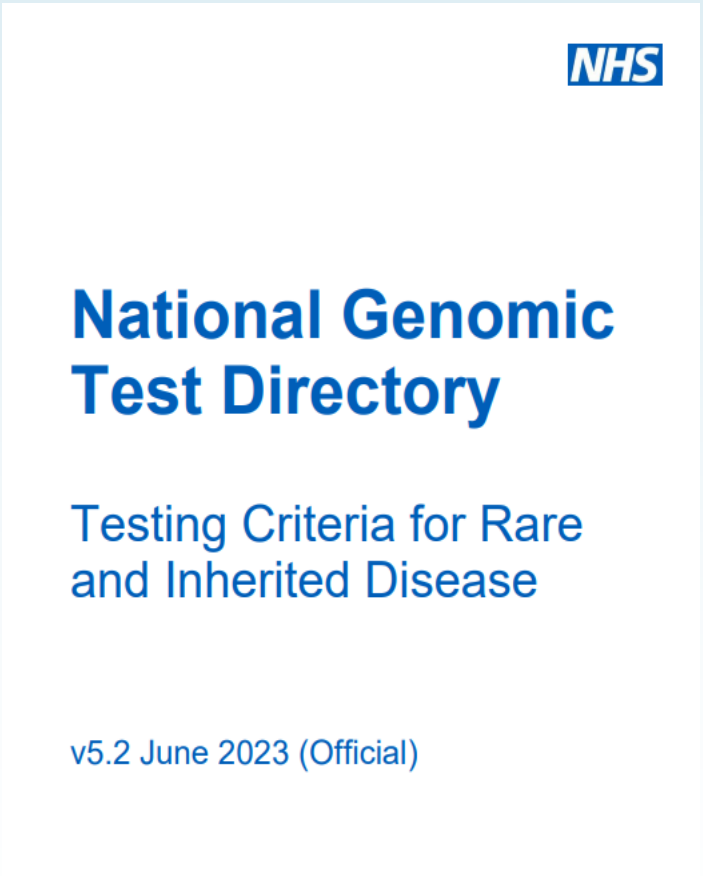
$3 billion

Change 2: NHS England Genomic Medicine Service 2018



- **NHS Genomic Laboratory Hubs (GLHs)**
- **The National Genomic Test Directory**
- **NHS Genomic Medicine Service Alliances (GMSAs)**

Central funding and the National Genomic Test Directory



R58 Adult onset neurodegenerative disorder

Testing Criteria

Young onset or familial neurodegeneration starting in adulthood with a likely monogenic cause, including:

1. Unexplained dementia
   a. Age at onset <55 years where acquired causes (e.g. stroke, tumour) have been excluded, OR
   b. Family history of dementia of the same type and/or family history of MND in a first / second degree relative

Requesting Specialties

- Clinical Genetics
- Neurology
- Psychiatry

https://www.england.nhs.uk/wp-content/uploads/2018/08/Rare-and-inherited-disease-eligibility-criteria-version-5.2.pdf

Mainstreaming of genomic investigation and NHS Genomic Medicine Service Alliances

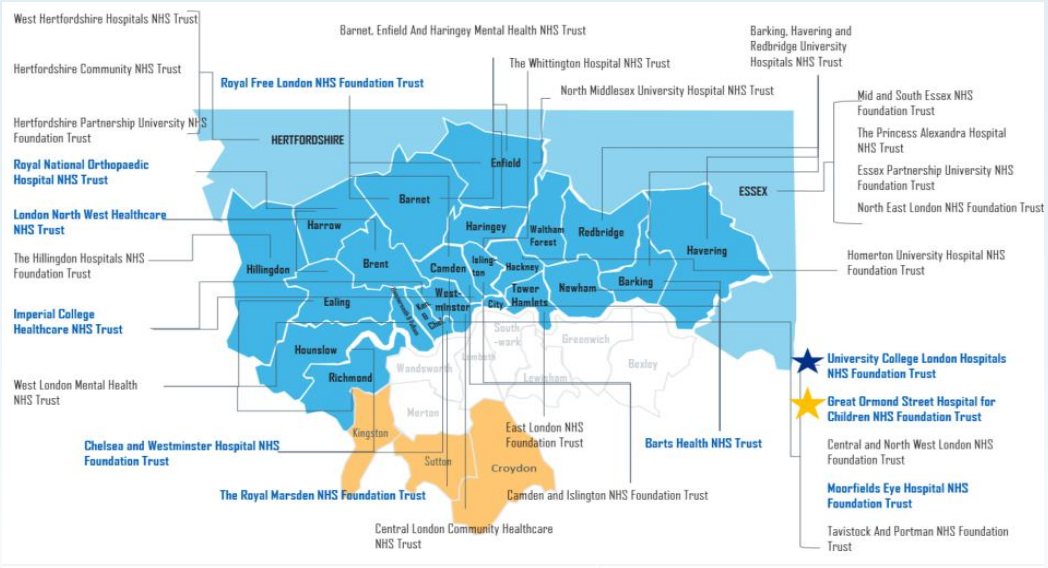
NHS North Thames Genomic Medicine Service (GMS) Alliance

The NHS North Thames Genomic Medicine Service (GMS) Alliance is one of seven alliances launched by NHS England in January 2021, created to support the systematic implementation of genomic medicine into the mainstream healthcare system and harness the power of genomics to improve the health of our population.

NTGMSA local transformation project: Embedding genomic testing in memory clinics and intellectual disability services

- **Mapping** mental health and genomic medicine working in North Thames region
- **Consultation** on improving access to and ensuring equity in genomic investigation
- Creation of **model genomic testing pathways** with provision of appropriate **educational resources**

Mapping use of genomic investigations by memory clinics in North Thames



Request data extracted from North Thames GLH

Test indication	Requests from the 10 NT Mental Health Trusts, 18 months 2021-2022
Adult with ID	9 (6/2155 microarray)
Dementia	0/660

Consultation on improving access and equity in genomic investigation in memory clinics

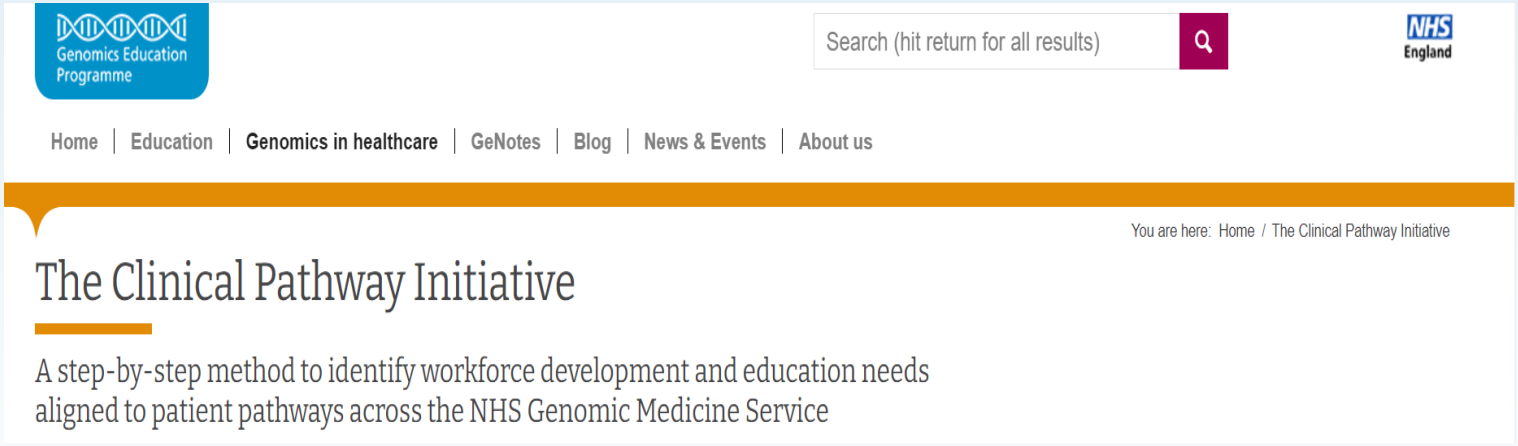
Patients and carers

- Lack of discussion of genetics
- Post diagnostic support

Health Care Professionals

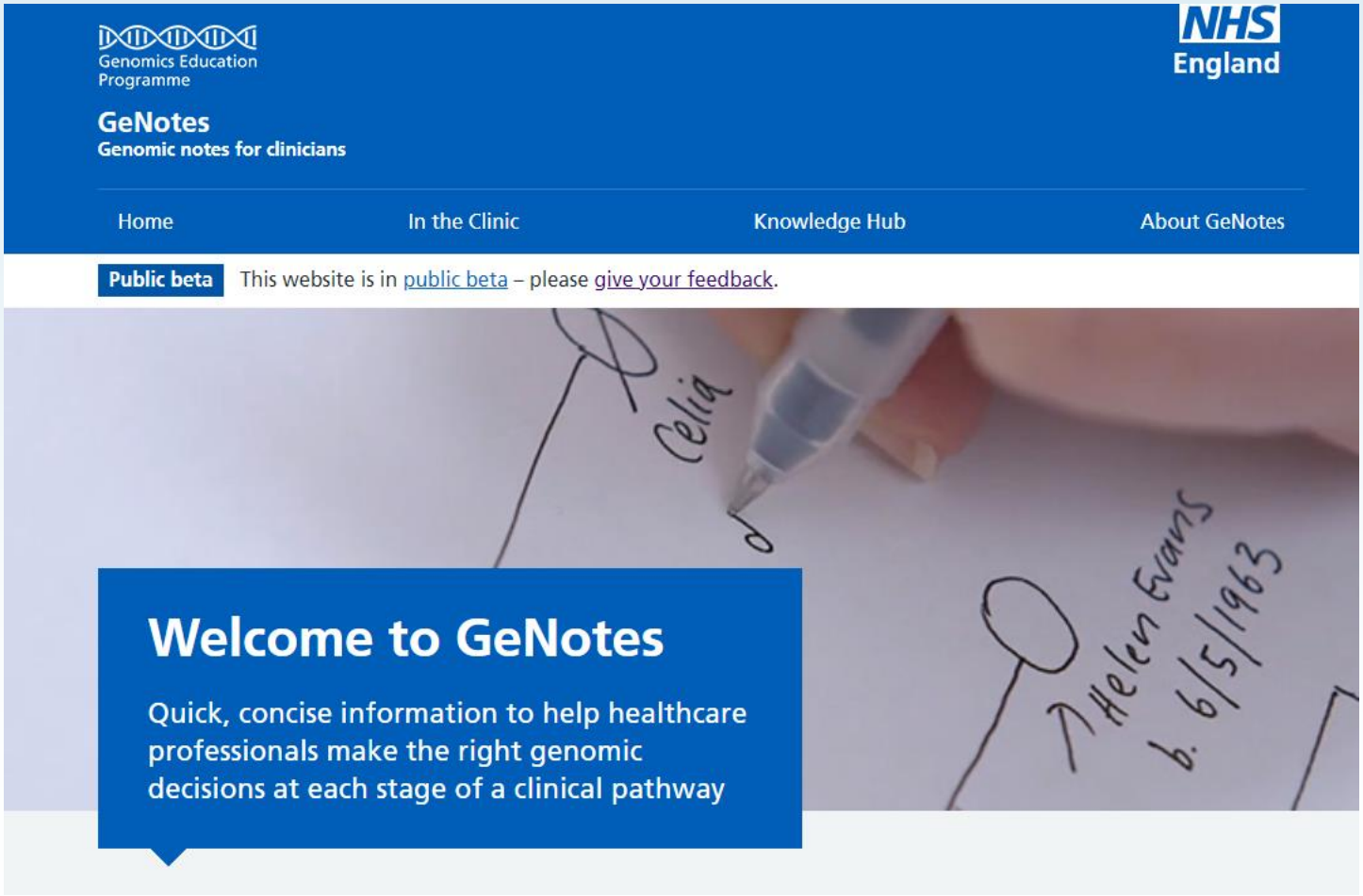
- Lack of awareness
- Practicalities of testing
- Relevance to practice

Embedding genomics into dementia assessment (and care) pathways



https://www.genomicseducation.hee.nhs.uk/the-clinical-pathway-initiative/

Resources to support clinicians with testing



https://www.genomicseducation.hee.nhs.uk/genotes/

Change 3: Guidelines around testing

Dementia: assessment, management and support for people living with dementia and their carers

NICE guideline
Published: 20 June 2018
www.nice.org.uk/guidance/ng97

1.2.18 Do not use Apolipoprotein E genotyping or electroencephalography to diagnose Alzheimer's disease.

1.2.19 Be aware that young-onset Alzheimer's disease has a genetic cause in some people.

1.2.25 Be aware that frontotemporal dementia has a genetic cause in some people.

1.2.28 Be aware that young-onset vascular dementia has a genetic cause in some people.

MSNAP CCQI
MEMORY SERVICES NATIONAL ACCREDITATION PROGRAMME

RC PSYCH
ROYAL COLLEGE OF PSYCHIATRISTS

152.	2	The service has access to specialist post-diagnostic counselling provided by a psychologist or other appropriately qualified professional for people with specific needs *Guidance: E.g. genetic and rarer disorders, and severe adjustment reactions to the diagnosis*	19
165.	3	The service is able to refer to genetic counselling for patients and their unaffected relatives (where there is likely to be a genetic cause for their dementia)	3

Old Age Psychiatry

Royal College of Psychiatrists Higher Specialty Curriculum (ST4 – ST6)

Version 1.0

August 2022

Royal College of Psychiatrists Report

https://www.rcpsych.ac.uk/improving-care/campaigning-for-better-mental-health-policy/college-reports/2023-college-reports/the-role-of-genetic-testing-in-mental-health-settings-(cr237)

Dementia related recommendations

Consider genetic investigation for people with any the following:

- suspected frontotemporal dementia
- dementia onset <55 years of age
- a family history compatible with a dementia-causing genetic variant
- clinical features suggestive of Down Syndrome (mosaic cases)
- clinical features compatible with rare single-gene forms of dementia

Develop local pathways for genetic investigation of dementia to ensure equitable access to appropriate genetic testing.

- We recommend the establishment of multidisciplinary meetings that include clinical genetics and genetic counselling

Nurses and Genomics

Nursing and genomic medicine

NHS 75

St George's University Hospitals
NHS Foundation Trust

Neurogenetics Clinic is a nurse-led service with an aim to improve the diagnosis and health outcomes of patients with rare genetic neurological diseases, with a focus on young adults with complex epilepsies and neuromuscular disorders.

Implementation and sustainability: MDT approach

Key role of nurses in the Tower Hamlets Diagnostic Memory Clinic

- ✓ Pre-diagnostic counselling
- ✓ History + collateral information
- ✓ MSE + standardised cognitive assessment tool
- ✓ ECG + neuro examination
- ✓ Referral for **routine** investigations – blood tests, structural neuroimaging
- ✓ Referrals for **specialist** investigations – neuropsychology, functional OT assessment, functional neuroimaging, CSF biomarkers, genetic testing
- ✓ Clinical formulation with MDT
- ✓ Maintaining contact with patients and families/carers
- ✓ Post-diagnostic support

CNS role in ELFT memory services

Funding – North Thames GMSA
Time - 1 day a week
Task – to work across East London NHS Foundation Trust dementia services

TRAINING

- ⇨Development & delivery of training
- ⇨Link with genomic services
- ⇨Network of genomic practitioners
- ⇨Specialist placements for nursing students

CLINICAL ROLE

- ⇨Nurse-led clinic
- ⇨Drawing family history
- ⇨Consent
- ⇨Ongoing support for patients & families
- ⇨Point of contact

Training with MDT teams

Discussing genetics and genetic testing

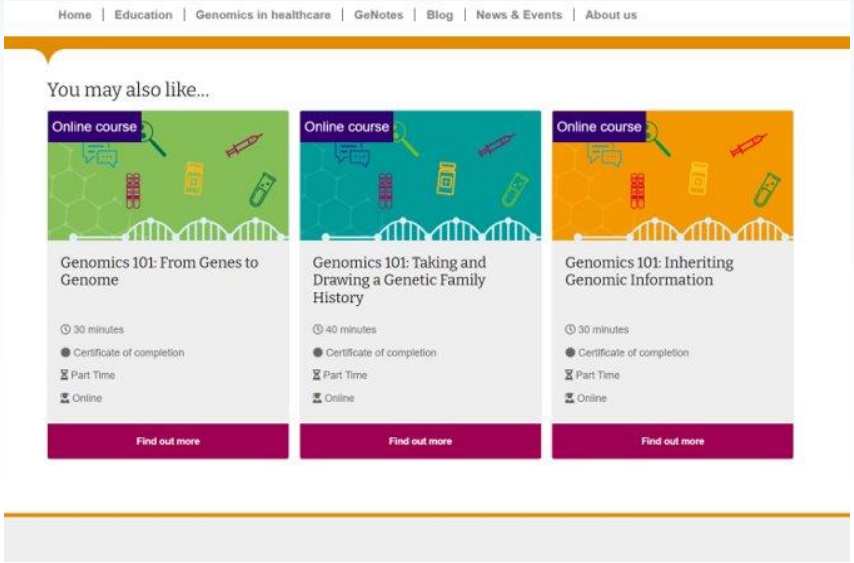
- General conceptual understanding
- Disentangling patient choice from family motivation
- Explaining remit and process (diagnostic not predictive testing)
- Capacity/consent issues
- Implications for family/Involving family

KNOWLEDGE

⇨ Genomics & genetics

⇨ Eligibility criteria for testing

⇨ Bespoke training



Training with MDT team

Obtaining an accurate family history

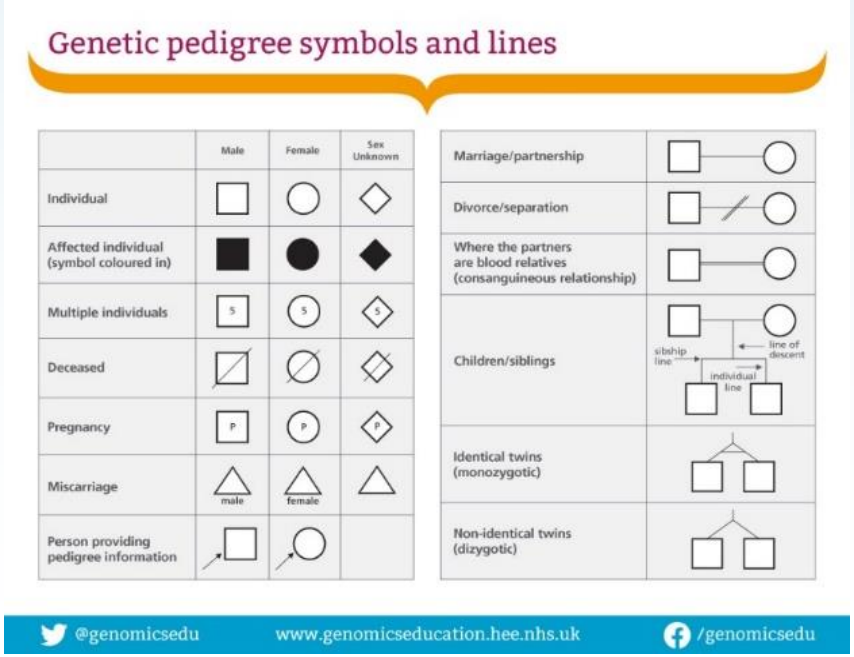
- General lack of information
- Concealed family history (early death of parent)
- Phenotypic spectrum (particularly FTD)

SKILLS

⇨ Consent & capacity

⇨ Pre-diagnostic counselling

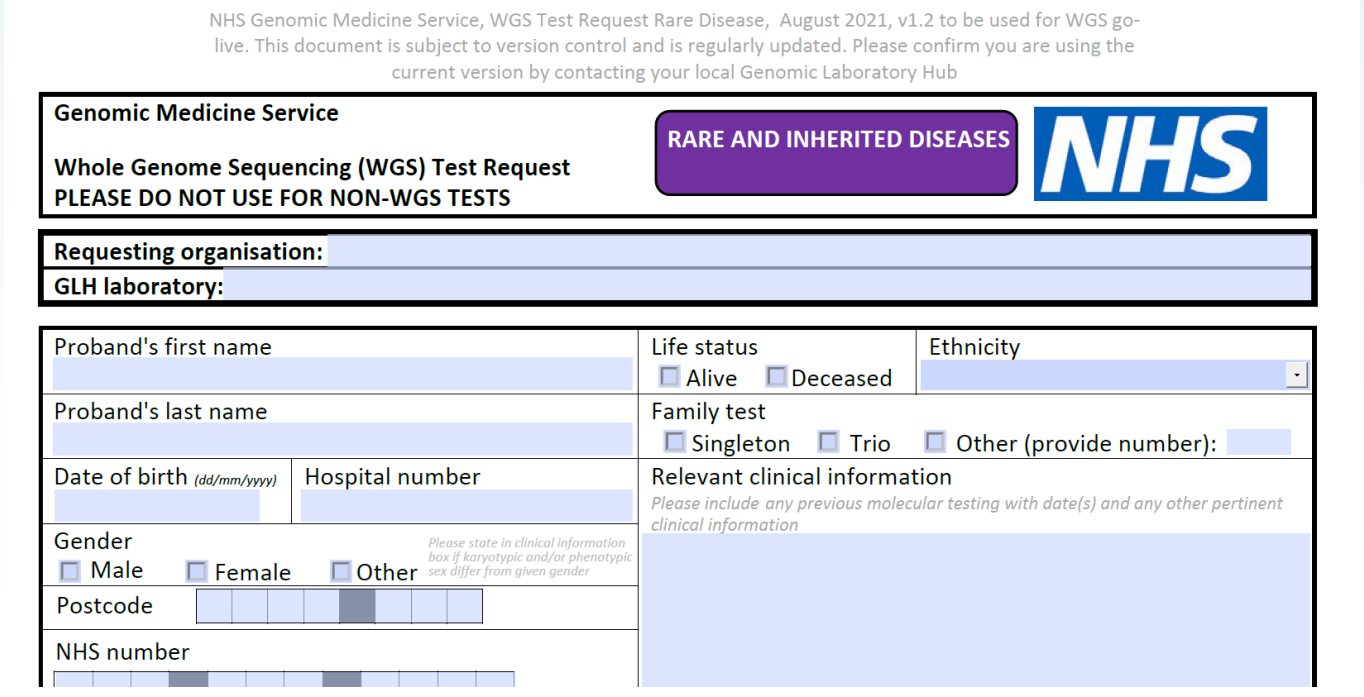
⇨ Taking family history



Training with MDT team

Organising testing itself

- Forms
- Blood test
- Getting blood from arm to lab



NHS Genomic Medicine Service, WGS Test Request Rare Disease, August 2021, v1.2 to be used for WGS go-live. This document is subject to version control and is regularly updated. Please confirm you are using the current version by contacting your local Genomic Laboratory Hub

Genomic Medicine Service

Whole Genome Sequencing (WGS) Test Request
PLEASE DO NOT USE FOR NON-WGS TESTS

RARE AND INHERITED DISEASES

NHS

Requesting organisation:
GLH laboratory:

Proband's first name

Proband's last name

Date of birth *(dd/mm/yyyy)*

Hospital number

Gender
☐ Male ☐ Female ☐ Other
Please state in clinical information box if karyotypic and/or phenotypic sex differ from given gender

Postcode

NHS number

Life status
☐ Alive ☐ Deceased

Ethnicity

Family test
☐ Singleton ☐ Trio ☐ Other (provide number):

Relevant clinical information
Please include any previous molecular testing with date(s) and any other pertinent clinical information

Experience of testing over last 12 months: diagnostic accuracy

- 7 requests: 4 positive, 3 negative
- 9 pending
- 2 change of subtype diagnosis AD -> FTD, and FTD -> AD
- 2 families requested referral to GMS
- Same variants in Bangladeshi and Somali ancestry

Can genetic testing accelerate diagnosis?

- Recent onset of symptoms
- Strong family history of dementia
- symptomatic MCI level
- Genetic testing as part of standard memory clinic ax…
- Has capacity, can make informed decision
- Can hold the information and discuss with wider family

QI project

- Quality improvement methodology
- Measure the impact of awareness raising and training

Thank you

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