This house believes that ALL cardiologists should be ordering ALL genetic tests-Con

Dr Sarju Mehta
Consultant in Clinical Genetics

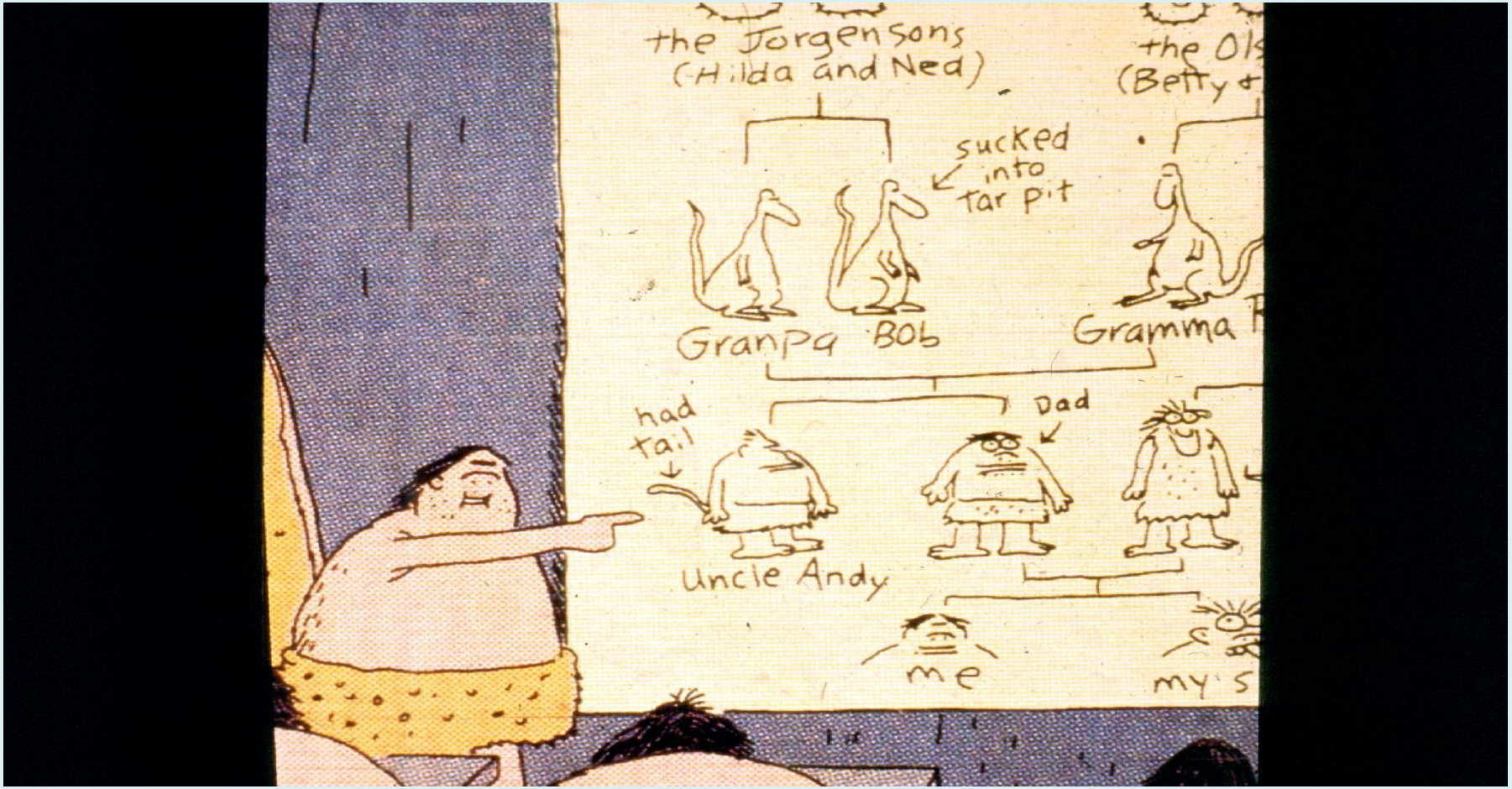
Disclaimers

- I get paid to order genetic tests

Overview

- Why is genetic testing different
- Genetic advances
- Education and training
- Infrastructure requirements

Why is Genetic testing different?



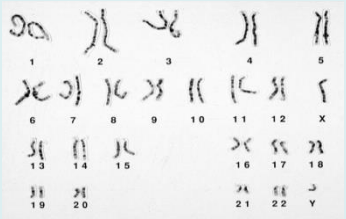
Dirk brings his family history to class

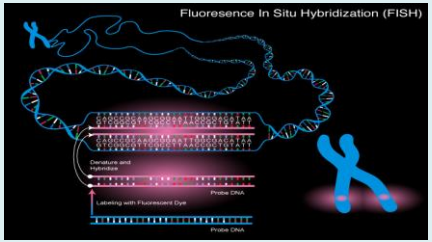
Sharing of information

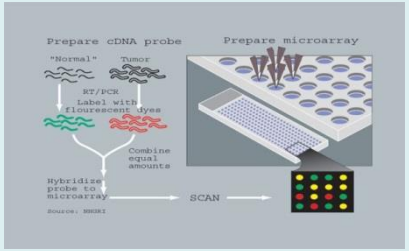
Informed Consent

Cytogenetic Advances

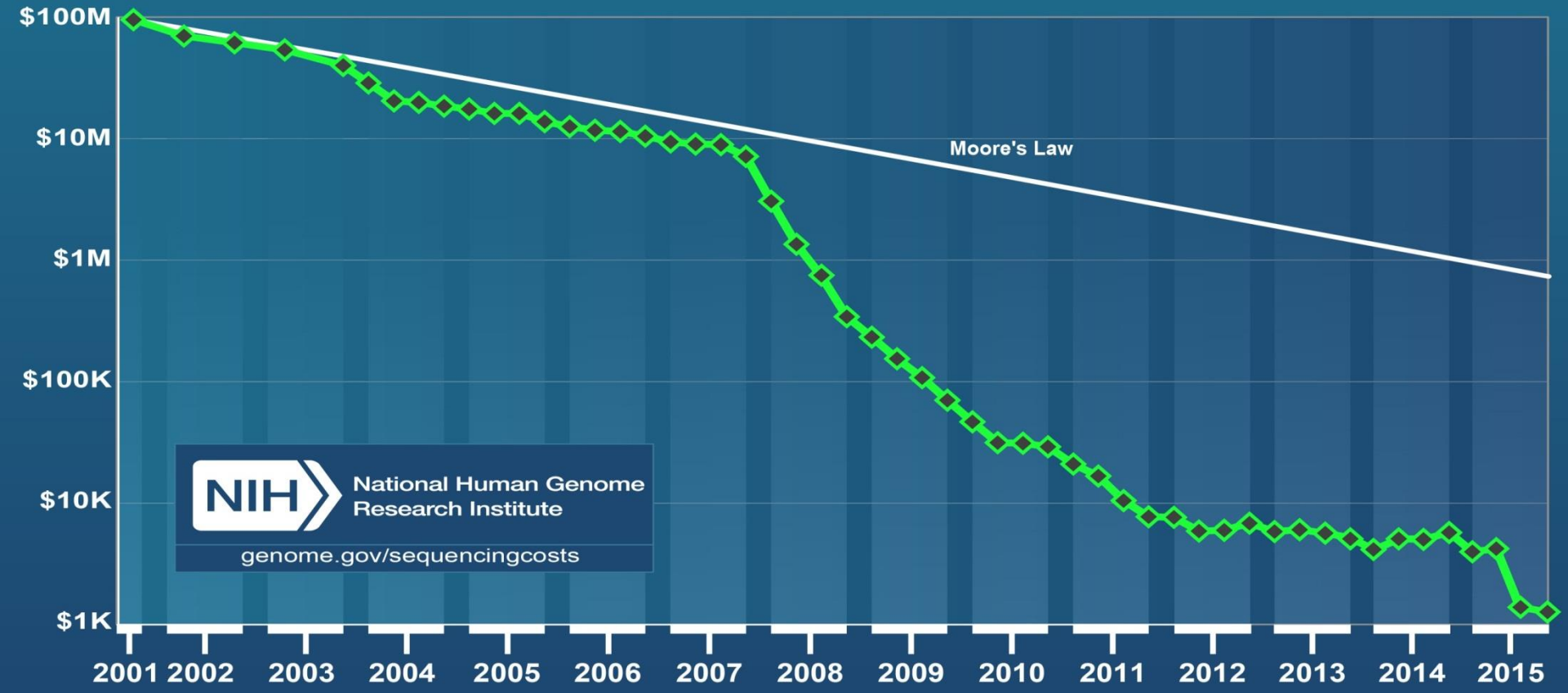
KARYOTYPE → FISH → MICROARRAY





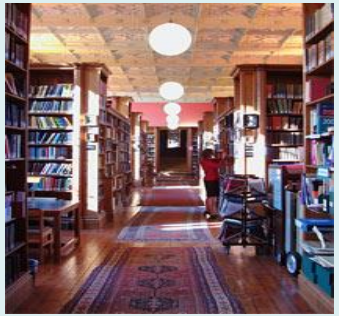


Cost per Genome



Molecular genetic advances

SINGLE GENE TESTING → GENE PANEL → EXOME

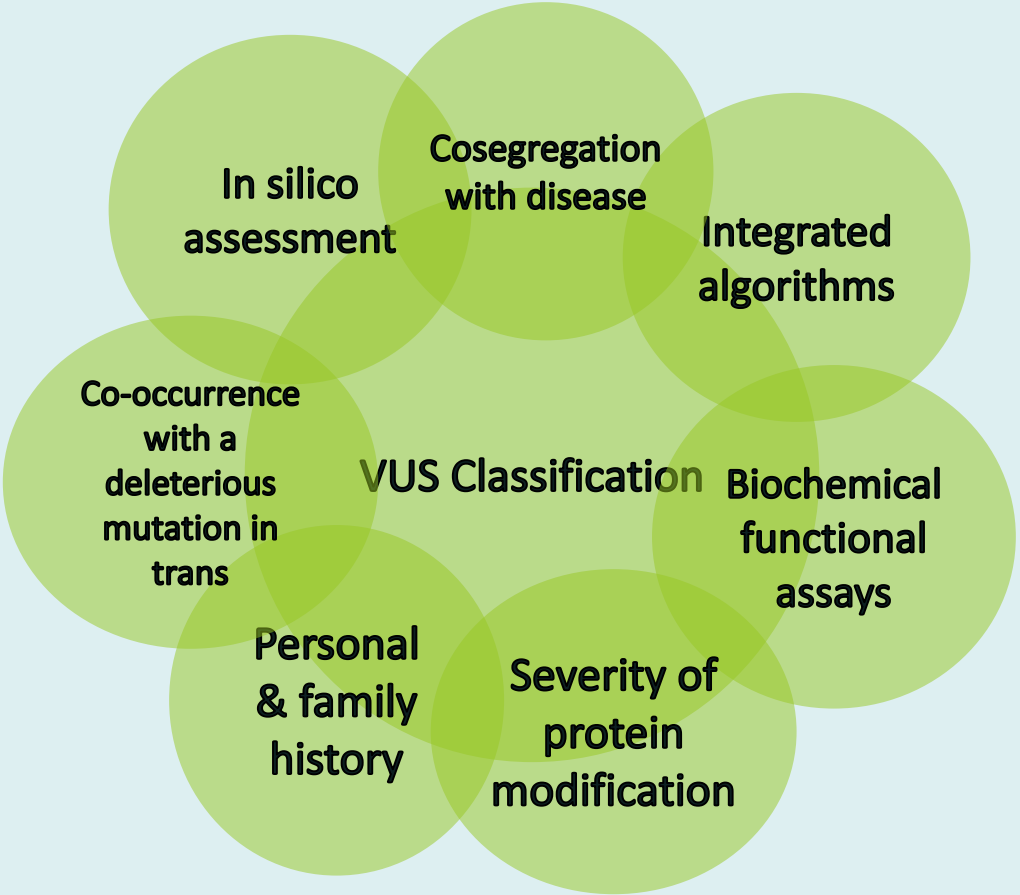


Official journal of the American College of Medical Genetics and Genomics **ORIGINAL RESEARCH ARTICLE** Genetics inMedicine

Open

Reassessment of Mendelian gene pathogenicity using 7,855 cardiomyopathy cases and 60,706 reference samples

Roddy Walsh, BSc, MSc[1,2], Kate L. Thomson, BSc, FRCPath[3,4], James S. Ware, PhD, MRCP[1,2,5], Birgit H. Funke, PhD, FACMG[6,7], Jessica Woodley, BSc[3], Karen J. McGuire, BSc[3], Francesco Mazzarotto, BSc, MSc[1,2], Edward Blair, BMSc, MRCP[8], Anneke Seller, PhD[3], Jenny C. Taylor, PhD[9,10], Eric V. Minikel,MS[11–14], Exome Aggregation Consortium[14], Daniel G. MacArthur,PhD[11,12,14,15], Martin Farrall, FRCPath[4,10], Stuart A. Cook, PhD, MRCPath[2,5,16,17] and Hugh Watkins,MD, PhD[4,10]


In silico assessment
Cosegregation with disease
Integrated algorithms
Co-occurrence with a deleterious mutation in trans
VUS Classification
Biochemical functional assays
Personal & family history
Severity of protein modification

Atlas of Cardiac Genetic Variation

The genetics of cardiomyopathy has become increasingly heterogeneous and complex in recent years, with ever more genes and variants associated with each condition. However, as our understanding of the level of rare variation in the general population has grown, it has become clear that many of these associations are not robust and may in fact represent benign, background variation unconnected to disease. The **Atlas of Cardiac Genetic Variation** utilises two substantial resources of genetic data - population data from the Exome Aggregation Consortium (ExAC) and clinical data from the Oxford Molecular Genetics Laboratory (OMGL) and the Laboratory of Molecular Medicine (LMM) - to clarify the genetics of cardiomyopathies and inform clinical decision making. Clinical geneticists and researchers can explore the overall genetic architecture of HCM, DCM or ARVC, examine the role of specific genes or check the status of individual variants identified in cardiomyopathy patients to assess the likelihood of pathogenicity. This resource was produced in conjunction with the following publication:

Reassessment of Mendelian gene pathogenicity using 7,855 cardiomyopathy cases and 60,706 reference samples.
Roddy Walsh, Kate L. Thomson, James S. Ware, Birgit H. Funke, Jessica Woodley, Karen J. McGuire, Francesco Mazzarotto, Edward Blair, Anneke Seller, Jenny C. Taylor, Eric V. Minikel, Exome Aggregation Consortium, Daniel G. MacArthur, Martin Farrall, Stuart A. Cook and Hugh Watkins. Genet. Med. 2016 doi:10.1038/gim.2016.90.

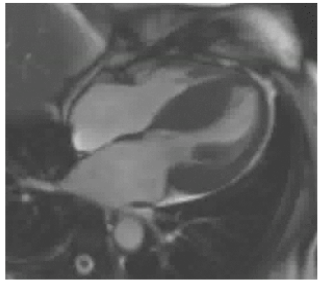
Explore by variant

Select a gene and enter a variant (HGVS format, e.g. c.1234A>T) in the form below to assess frequency in population databases (ExAC, ESP, 1000 Genomes), detection and classification by OMGL and LMM clinical labs, and the likelihood of pathogenicity for the variant in relevant cardiomyopathies.

Variant Search - Gene: Select Variant: Search Reset

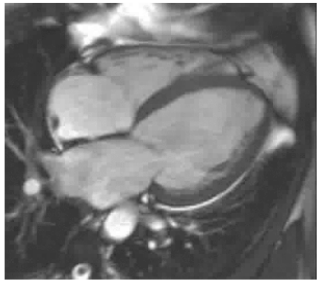
Explore by disease & gene

Hypertrophic Cardiomyopathy - HCM



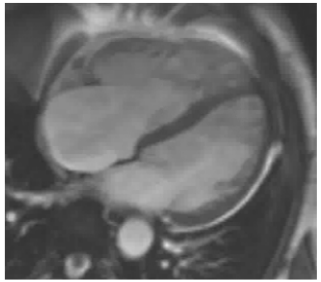
MYBPC3 - MYH7 - TNNI3 - TNNT2 - TPM1 - MYL2
FHL1 - MYL3 - GLA - PRKAG2 - NEXN - ACTC1
LAMP2 - PLN

Dilated Cardiomyopathy - DCM



TTN - DSP - MYH7 - LMNA - TNNT2 - TPM1 - VCL
TCAP - LDB3 - MYBPC3 - ABCC9 - DES - TNNI3
ACTC1 - SGCD - PLN - TAZ

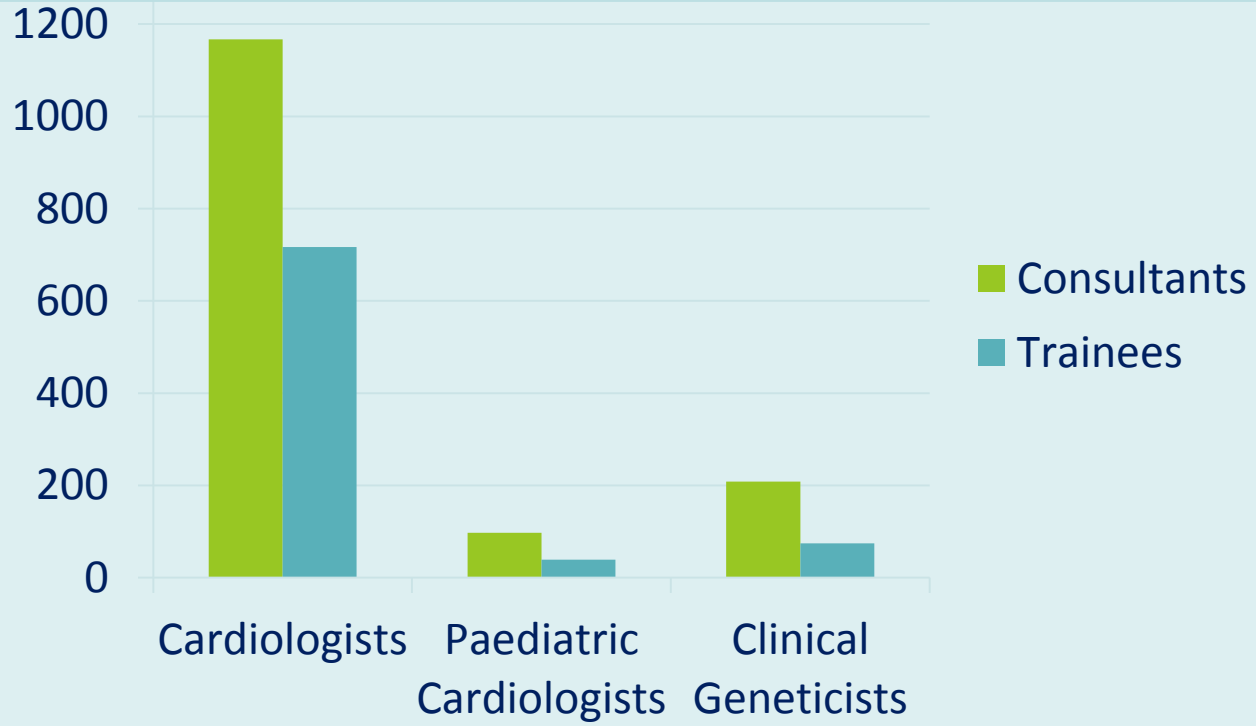
Arrhythmogenic right ventricular cardiomyopathy - ARVC



PKP2 - DSP - DSG2 - DSC2

Predictive Genetic Testing

RCP census 2014-15



Education and Training

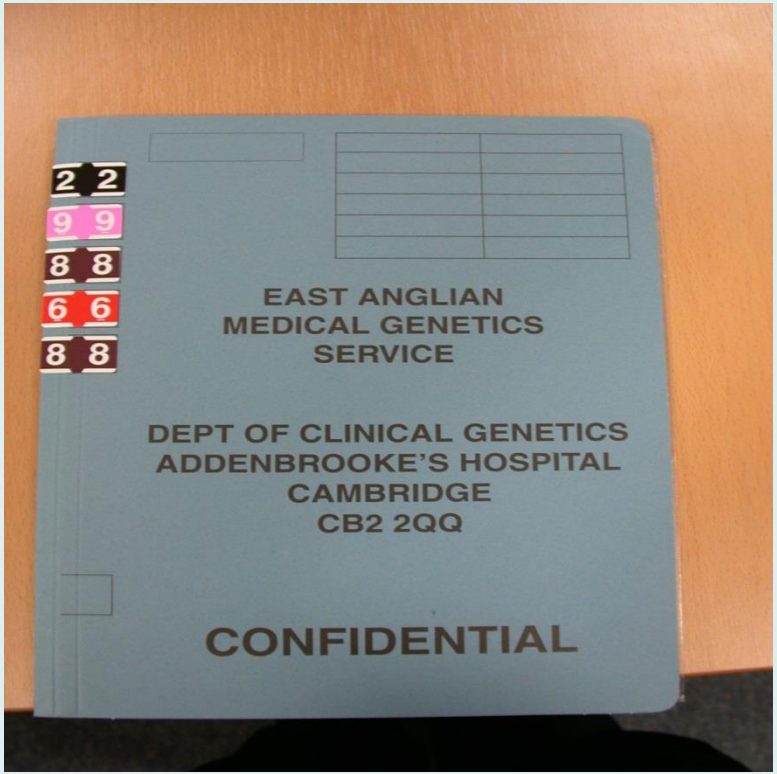
European Heart Journal (2013) **34**, 2381–2411
doi:10.1093/eurheartj/eht234

CURRENT OPINION

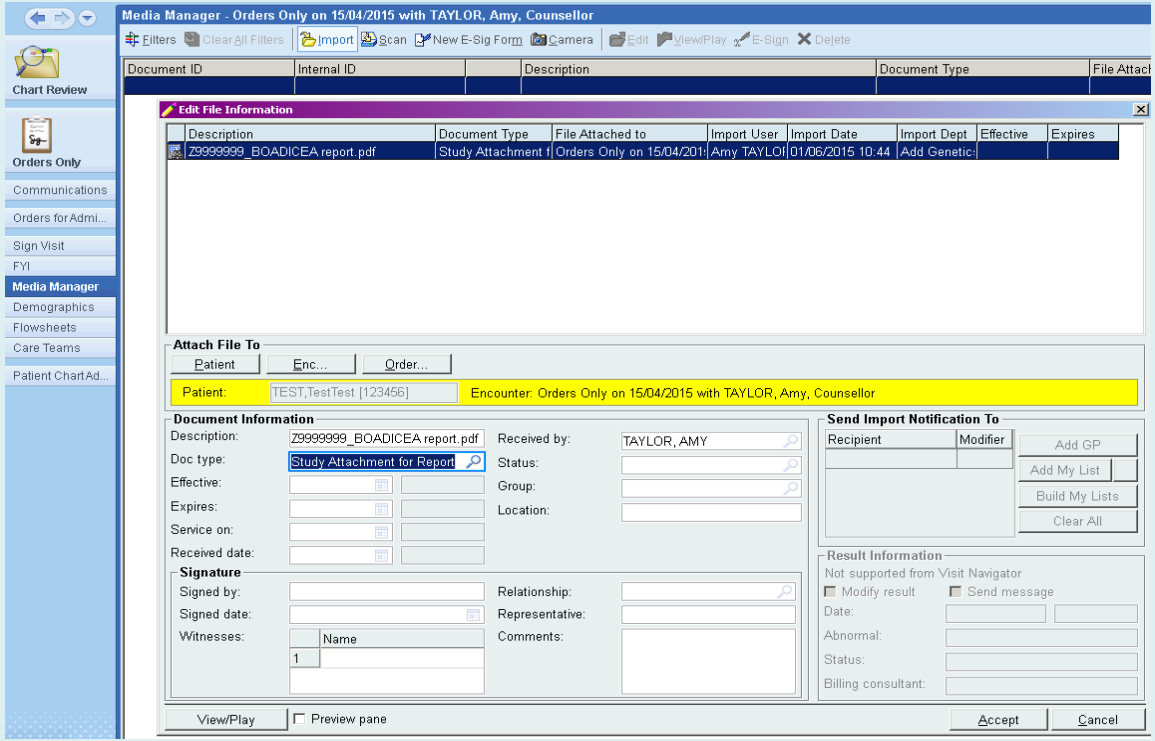
ESC Core Curriculum for the General Cardiologist (2013)

European Society of Cardiology

Hospital Infrastructure



Hospital Infrastructure



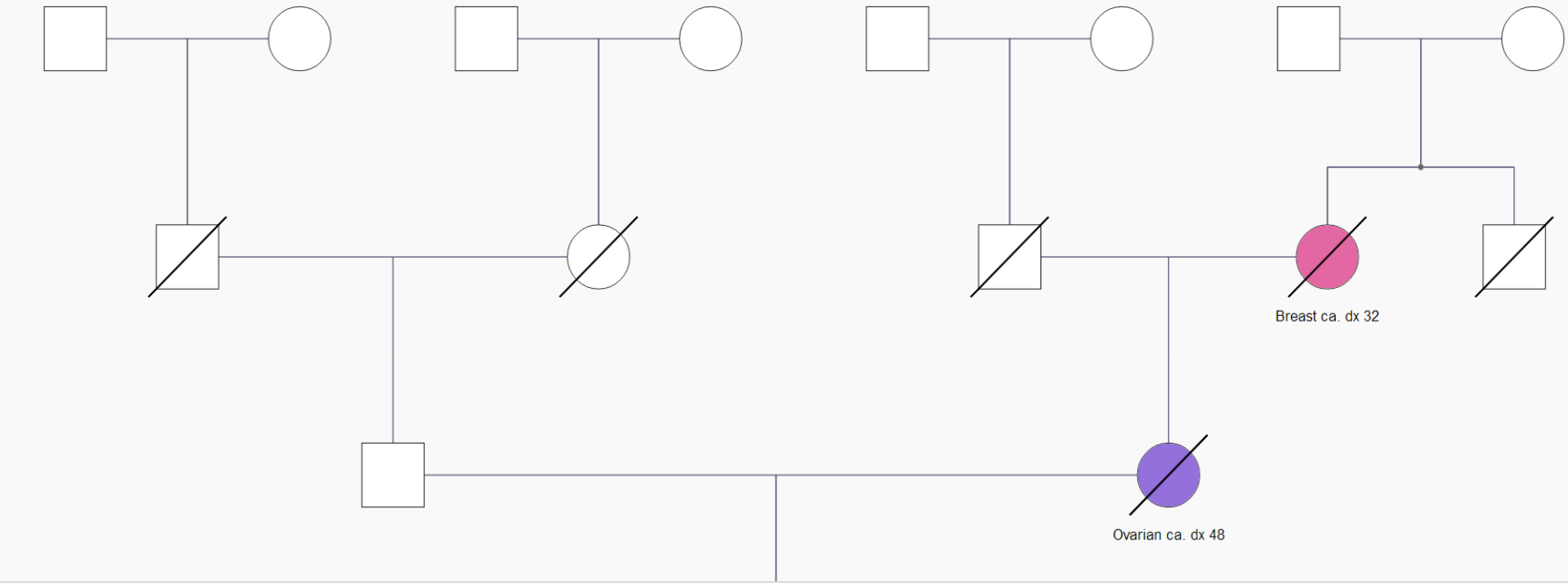
Patient information

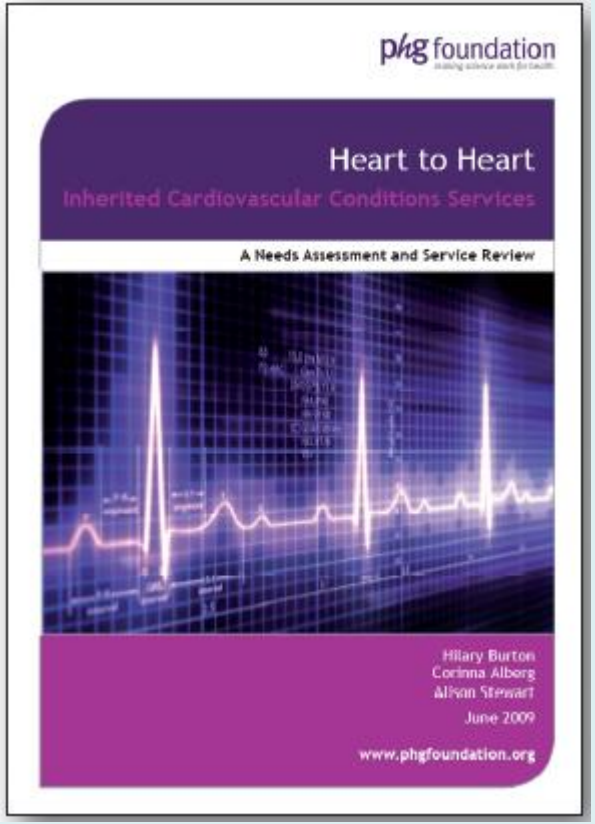
Identifier: TT test

Family history and pedigree

PEDIGREE

EDIT PEDIGREE





Every UK cardiac network should ensure that its population has access to specialised expert ICC services for children and adults, although most will not have their own service.

This house believes that ALL cardiologists should be ordering ALL genetic tests

This house believes that SOME cardiologists should be ordering SOME genetic tests

Questions?