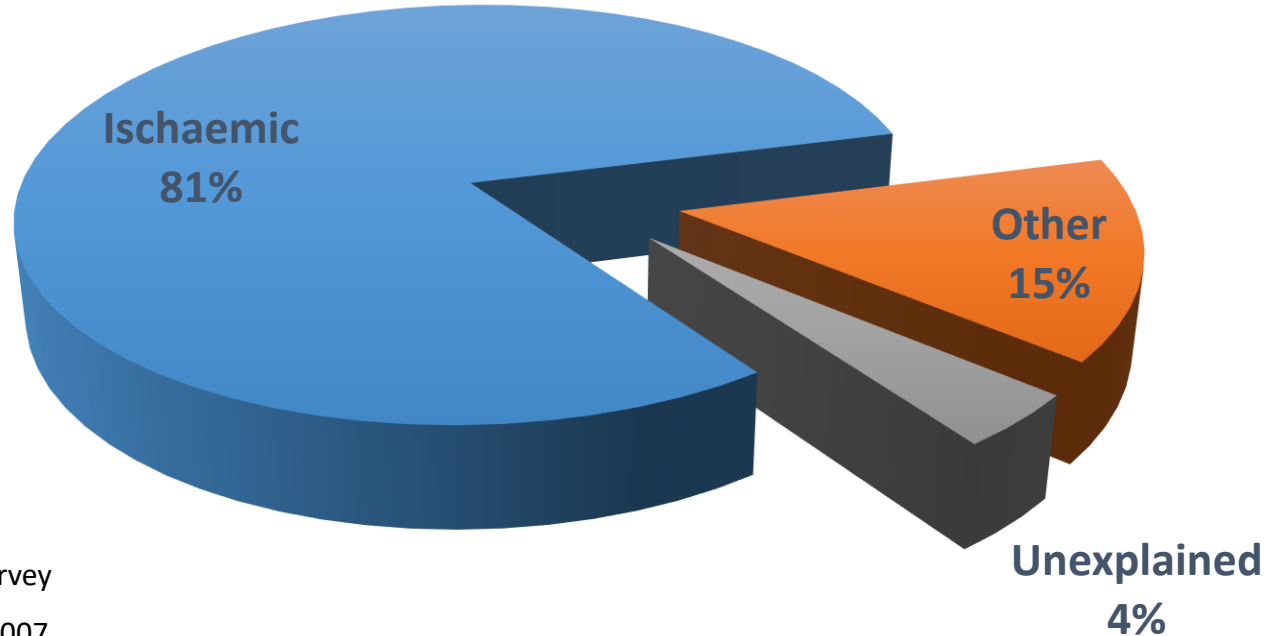


BHF-NHSE Sudden Unexpected Death Pathway Pilot and National Roll-Out

Elijah R Behr MA MBBS MD FRCP FESC

Sudden Cardiac Death

50-100,000 p.a. in the UK



1-64 age group

Coronial Autopsy Survey

Bowker et al, QJM 2007

Epidemiology of Young SCD: 1-35 yrs old

European annual incidence

2.8 per 100,000 (Denmark)

2.9 per 100,000 (Ireland)

1.8 per 100,000 (England/Wales)

1.0 per 100,000 (Veneto, Italy)

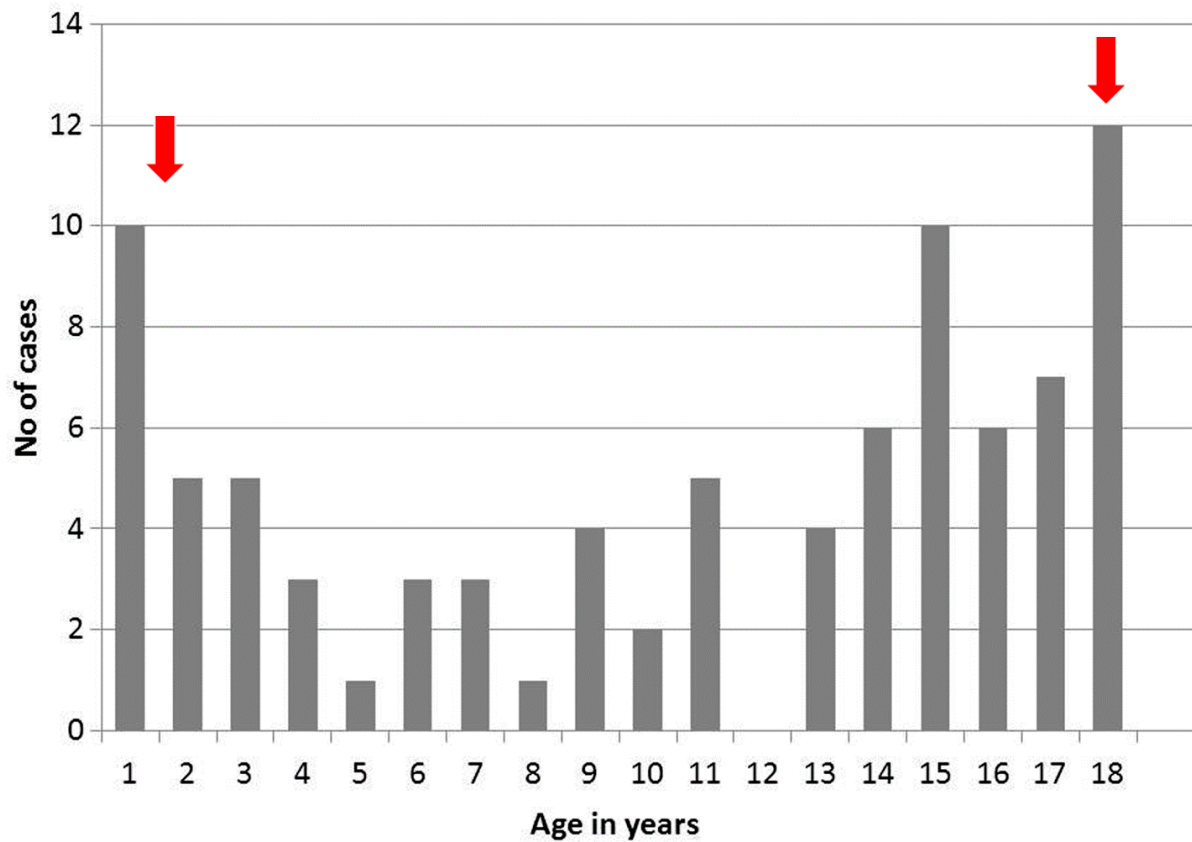
Incidence rates 1–18 years

Denmark 2000–2006

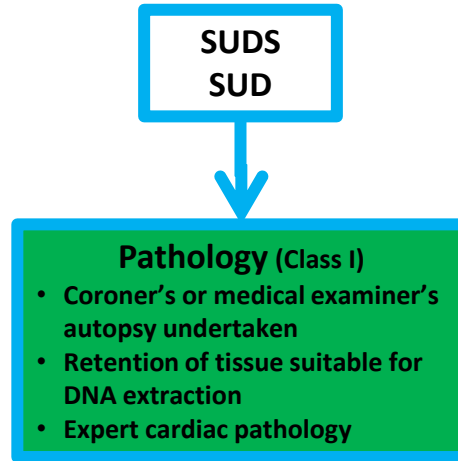
Incidence rates (per 100 000 person-years)

Sudden unexpected death	1.5
Sudden cardiac death	1.1 (70%)

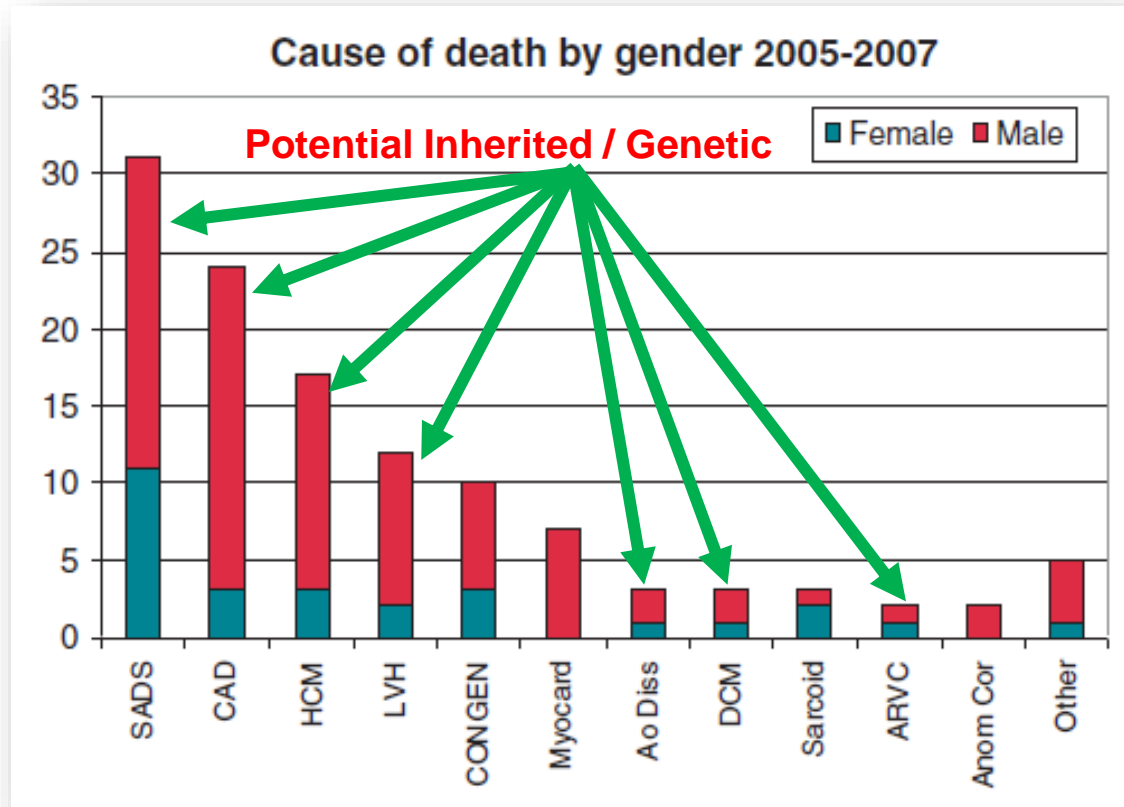
Age Distribution



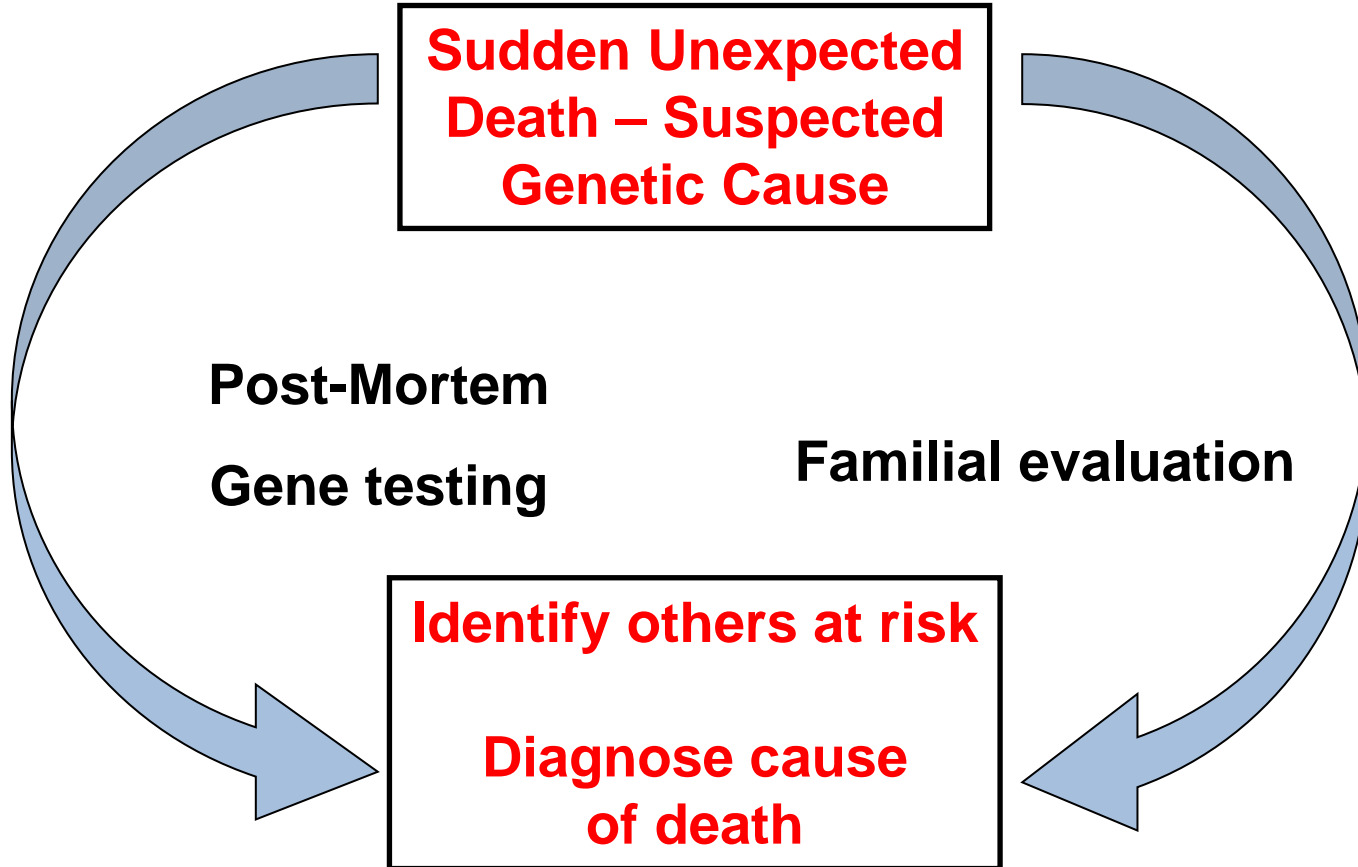
First step is
Autopsy



Causes of Young Sudden Death: 1-35 years



Approaches



Sudden Unexpected Death

```
graph TD; A[Sudden Unexpected Death] --> B[Pathology]; B --> C[Cause Explained];
```

Pathology

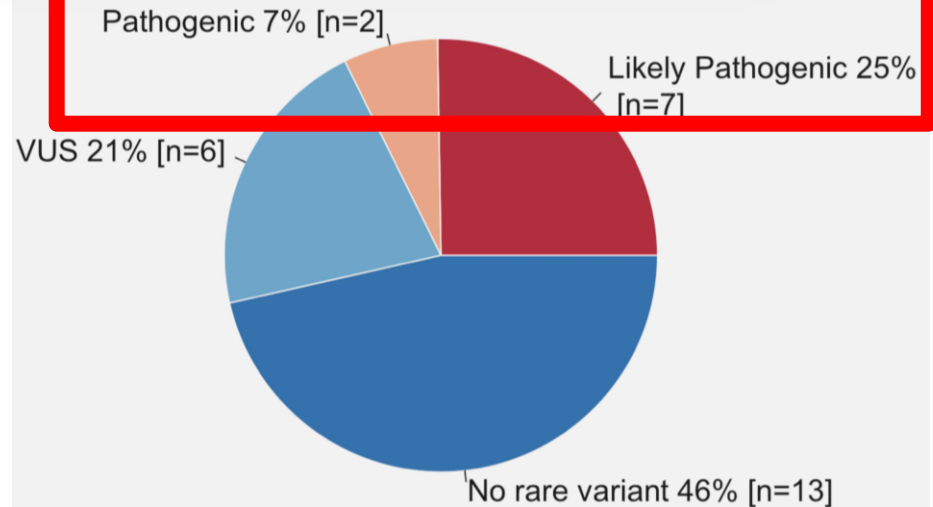
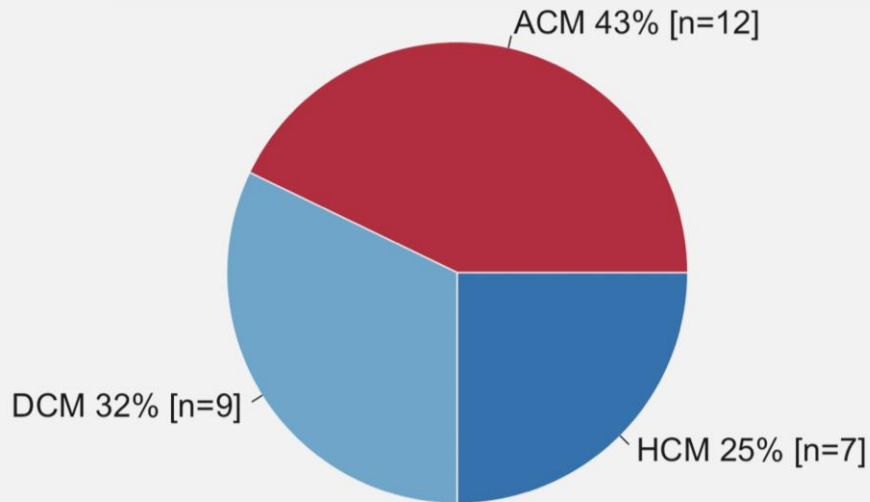
- Coroner's or medical examiner's autopsy undertaken
- Retention of tissue suitable for DNA extraction
- Expert cardiac pathology

Cause Explained

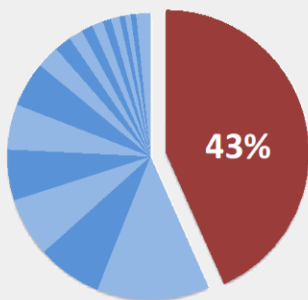
- If disease is likely to be inherited (e.g. HCM, ARVC) then instigate:
1. appropriate evaluation in ICC clinic;
 2. post-mortem genetic testing targeted to phenotype



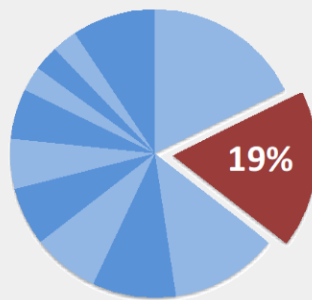
The yield of postmortem genetic testing in sudden death cases with structural findings at autopsy



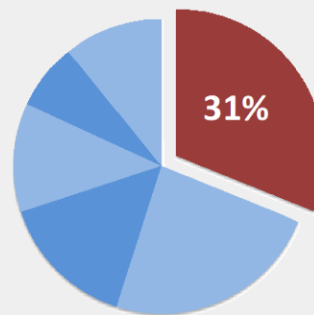
The 'normal heart' is common in most series of young SCD – SADS and SUDIC



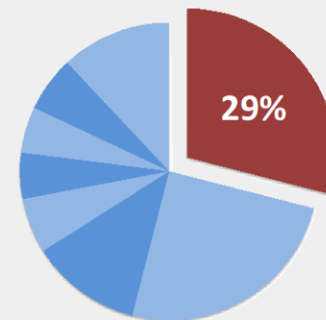
Winkel et. al. 2011



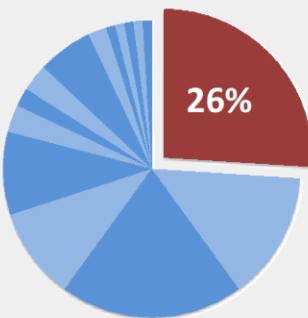
Morentin et. al. 2003



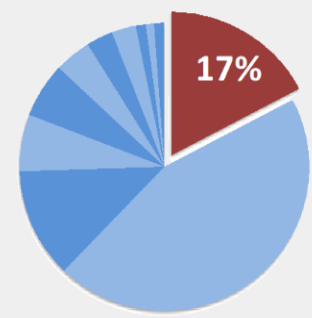
Doolan et. al. 2004



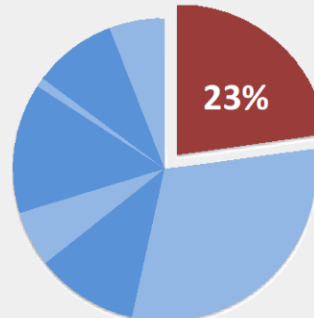
Puranik et. al. 2005



Margey et. al. 2011



Corrado et. al. 2001



de Noronha et. al.

**Sudden Unexpected
Death**

Pathology

- Coroner's or medical examiner's autopsy undertaken
- Retention of tissue suitable for DNA extraction
- Expert cardiac pathology

SADS / SUDIC

- Normal autopsy
- Negative toxicology
- Normal expert pathologist's assessment ‡

**Post-mortem gene testing:
R138 and R441**

Pathogenic variant present

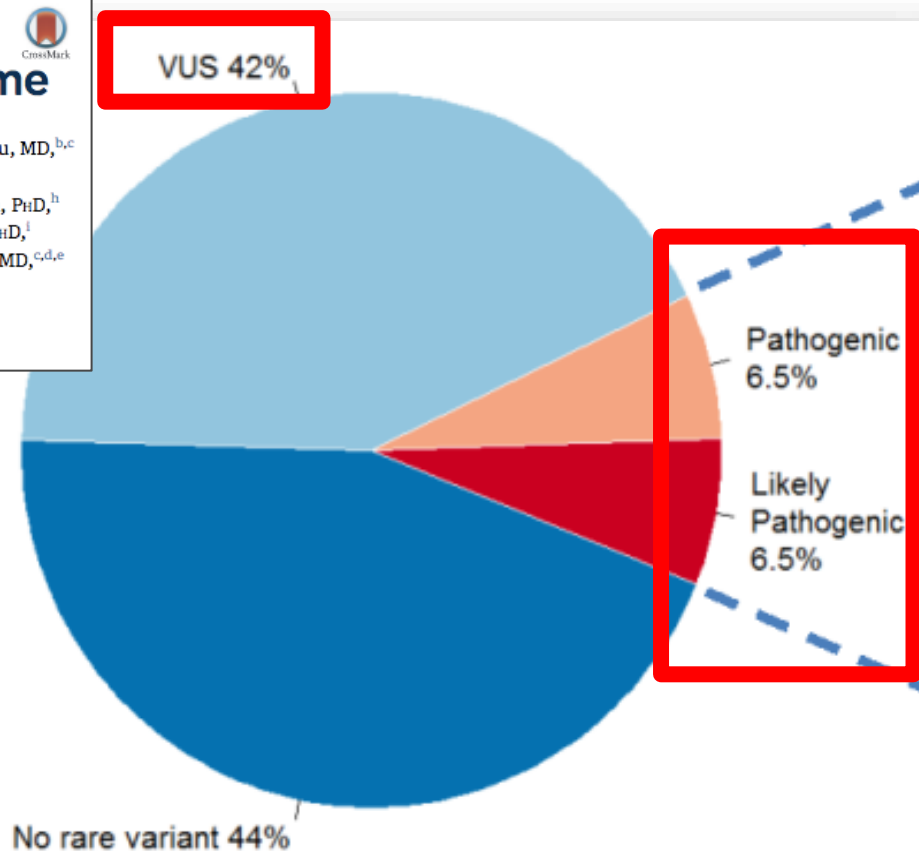
Cascade testing of relatives

Utility of Post-Mortem Genetic Testing in Cases of Sudden Arrhythmic Death Syndrome



Najim Lahrouchi, MD,^a Hariharan Raju, MBChB, PhD,^{b,c} Elisabeth M. Lodder, PhD,^a Efstathios Papatheodorou, MD,^{b,c} James S. Ware, PhD,^{d,e} Michael Papadakis, MBBS, MD,^{b,c} Rafik Tadros, MD, PhD,^{a,f} Della Cole, BSc,^{b,c} Jonathan R. Skinner, MBChB, MD,^g Jackie Crawford,^g Donald R. Love, PhD,^g Chee J. Pua, PhD,^h Bee Y. Soh, PhD,^h Jaydutt D. Bhalshankar, PhD,^h Risha Govind, MSc,^{d,e} Jacob Tfelt-Hansen, MD, DMSc,ⁱ Bo G. Winkel, MD, PhD,ⁱ Christian van der Werf, MD, PhD,^a Yanushi D. Wijeyeratne, BMBS,^{b,c} Greg Mellor, MBChB, MD,^{b,c} Jan Till, MD,^{c,d,e} Marta C. Cohen, MD, DMJ (PATHOL),^j Maria Tome-Esteban, MD, PhD,^{b,c} Sanjay Sharma, MBChB, MD,^{b,c} Arthur A.M. Wilde, MD, PhD,^{a,k} Stuart A. Cook, MD, PhD,^{d,h,l} Connie R. Bezzina, PhD,^a Mary N. Sheppard, MB, BCH, BAO, MD,^{b,c} Elijah R. Behr, MBBS, MD^{b,c}

Overall immediate 'diagnostic' yield of post-mortem genetic testing is 13%



Familial Evaluation

First degree relatives
(Obligate carriers
Symptomatic relatives)



Initial Evaluation

Personal and family history
Physical examination
Resting ECG (high leads)
Exercise ECG
Echocardiogram



Additional tests

24 hour ECG, CMR and ajmaline test

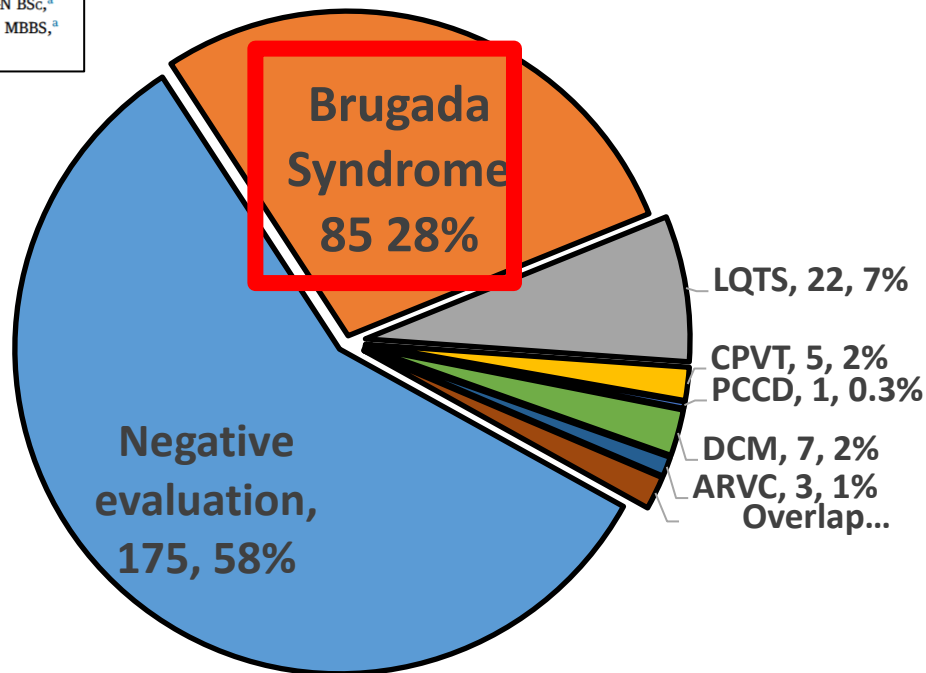
The Diagnostic Yield of Brugada Syndrome After Sudden Death With Normal Autopsy



Michael Papadakis, MBBS, MD,^{a,b} Efstathios Papatheodorou, MD,^{a,b} Greg Mellor, MBChB, MD,^{a,b} Hariharan Raju, MBChB, PhD,^{a,b} Rachel Bastiaenen, PhD,^a Yanushi Wijeyeratne, MBBS,^a Sara Wasim, BSc,^a Bode Ensam, MBChB,^{a,b} Gherardo Finocchiaro, MD,^{a,b} Belinda Gray, BSc(MEd), MBBS, PhD,^a Aneil Malhotra, MBChB, MA, MSC, PhD,^{a,b} Andrew D'Silva, MBBS,^{a,b} Nina Edwards, BSc,^a Della Cole, RGN BSc,^a Virginia Attard, MSc,^a Velislav N. Batchvarov, MD, PhD,^a Maria Tome-Esteban, MD, PhD,^a Tessa Homfray, MBBS,^a Mary N. Sheppard, MB, BCh, BAO, MD,^a Sanjay Sharma, MBChB, MD,^{a,b} Elijah R. Behr, MBBS, MD^a

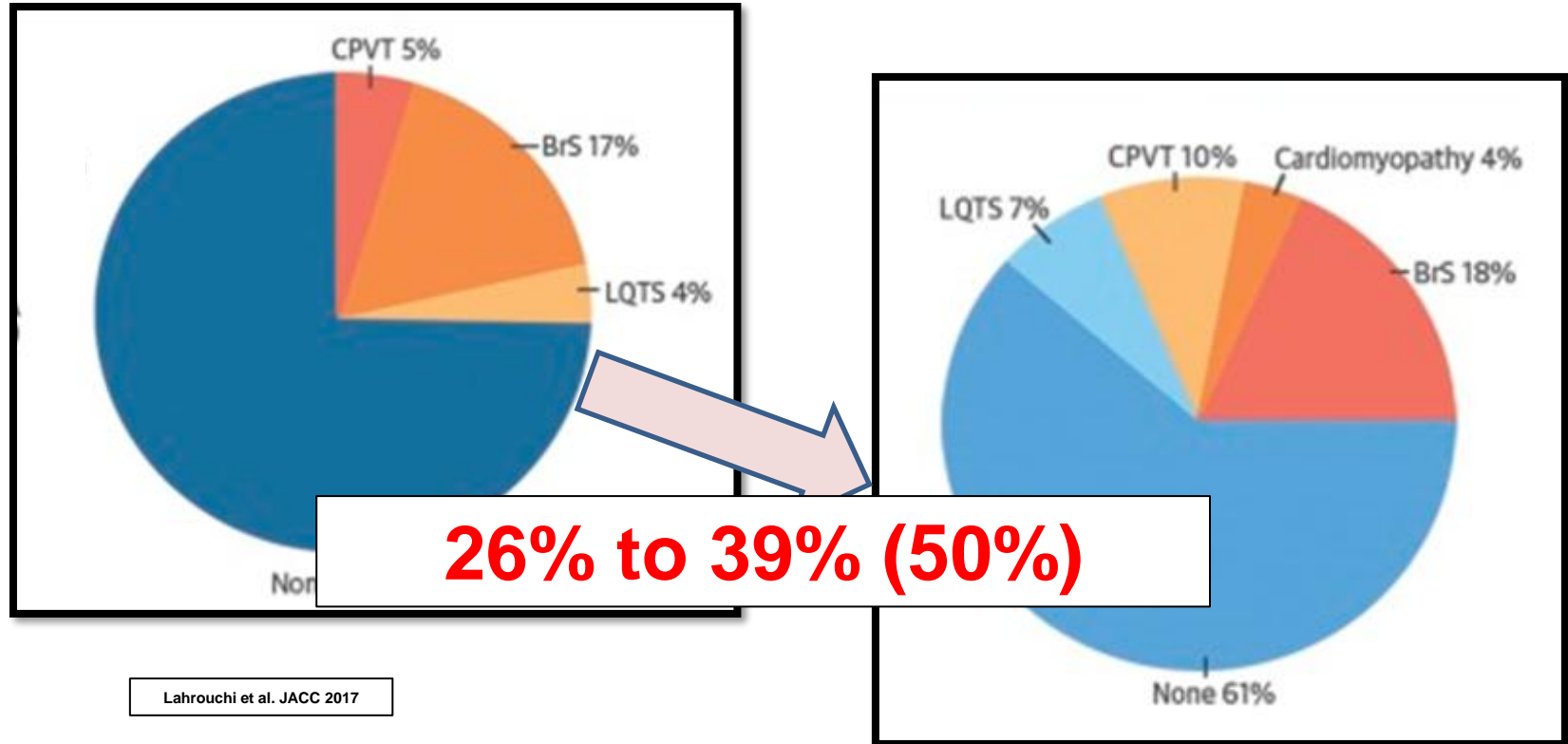
SADS Cohort

- Negative evaluation
- BrS
- LQTS
- CPVT

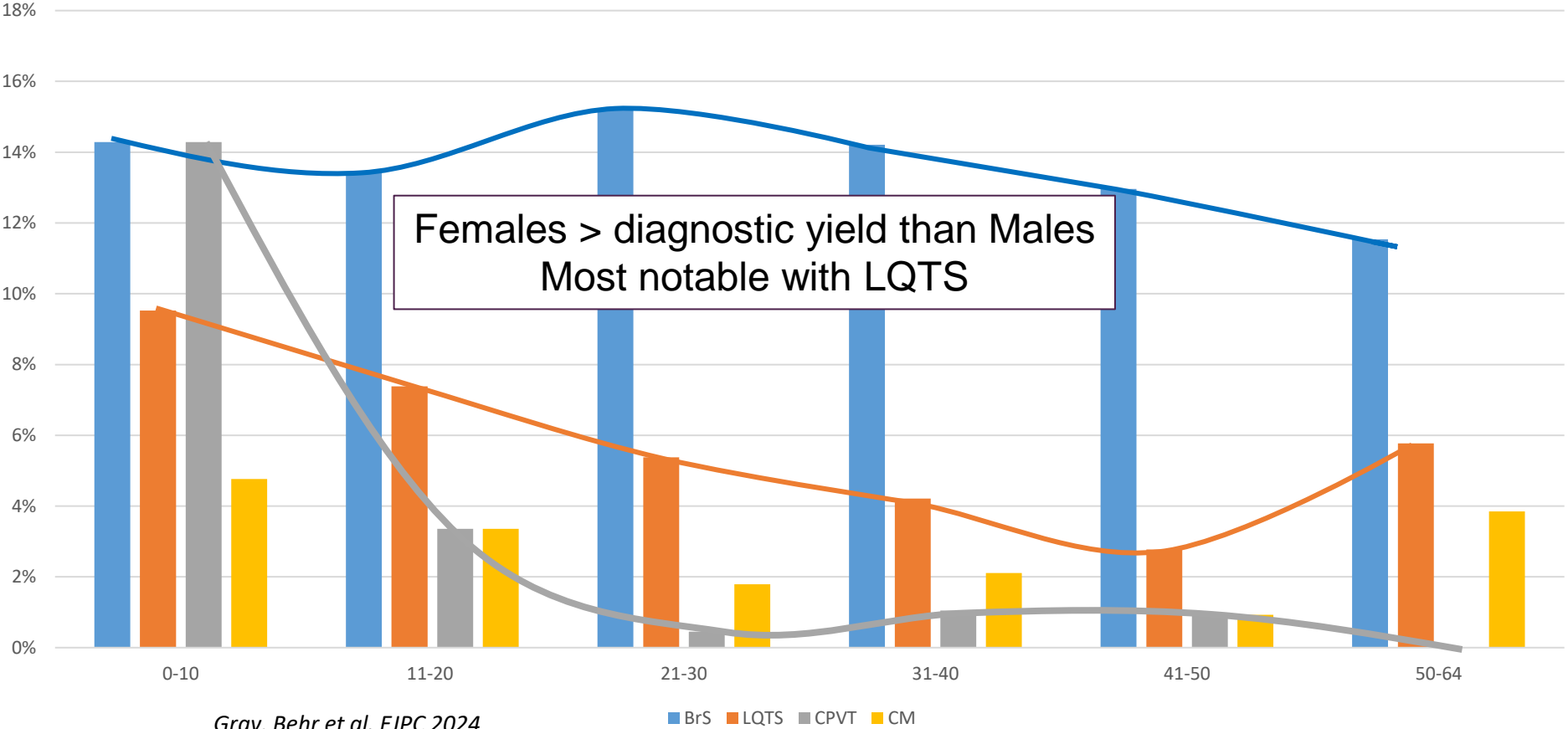


N= 303 families

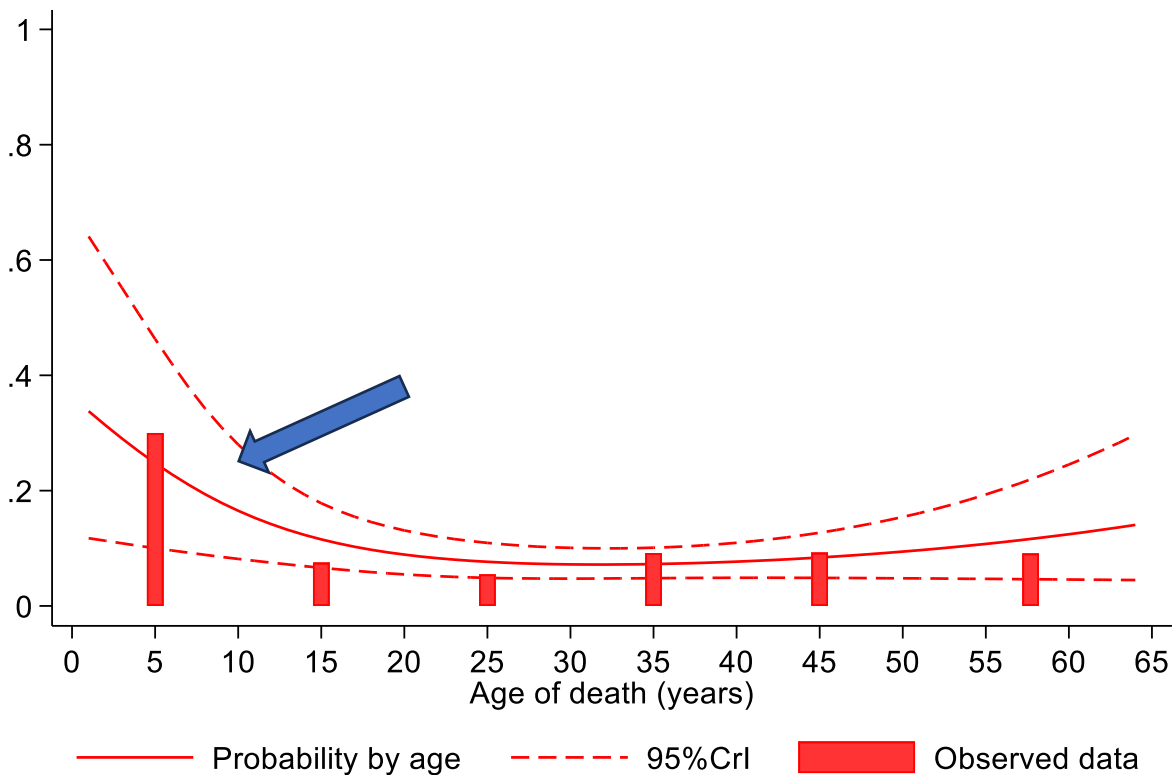
Combining Family Evaluation with Molecular Autopsy increases Yield



SADS Age-Related Diagnostic Yields (760 cases) Family (407) and Molecular Diagnoses (424)



Age-related Diagnostic Yield by Molecular Autopsy

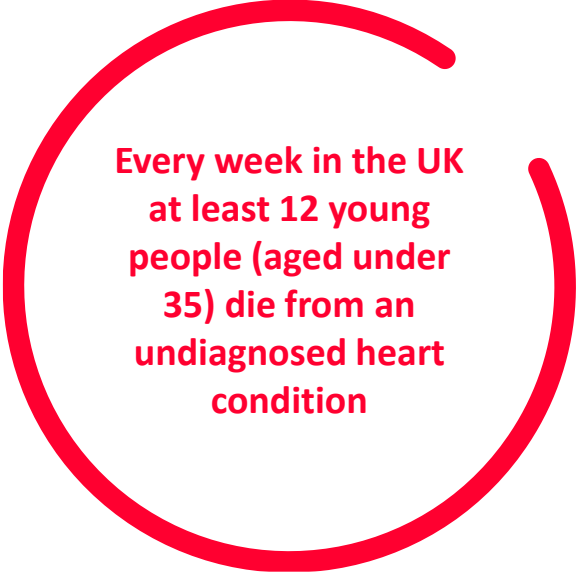


Applying Research & Guidelines to Improving the Pathway for Sudden Unexpected Death (SUD)

An estimated **750+** SUD per annum due to ICC

Aims:

- Early identification
- Assessment of the surviving family members
- Early treatment
- Reduce the risk of premature death



**Every week in the UK
at least 12 young
people (aged under
35) die from an
undiagnosed heart
condition**

Transformation Project: National referral pathway for post-mortem genetic testing

What:

- Development and testing of the pathways between the Coroner and the NHS
- To improve systematic access to a genomics driven clinical service
- Centred on the needs of families after SUD

How:

- MDT of:
 - Coroners, coroners' officers, pathologists
 - Cardiologists, geneticists, cardiac genetic nurse and/or counsellors
 - Genetic scientists
 - Seven pilot sites across England



CHIEF CORONER



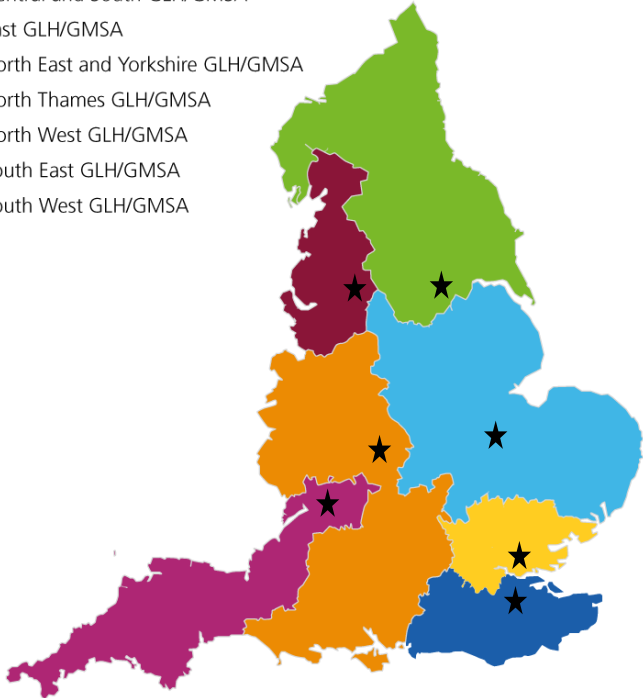
The Royal College of Pathologists
Pathology: the science behind the cure



**Powerful coalition working
together to save lives**

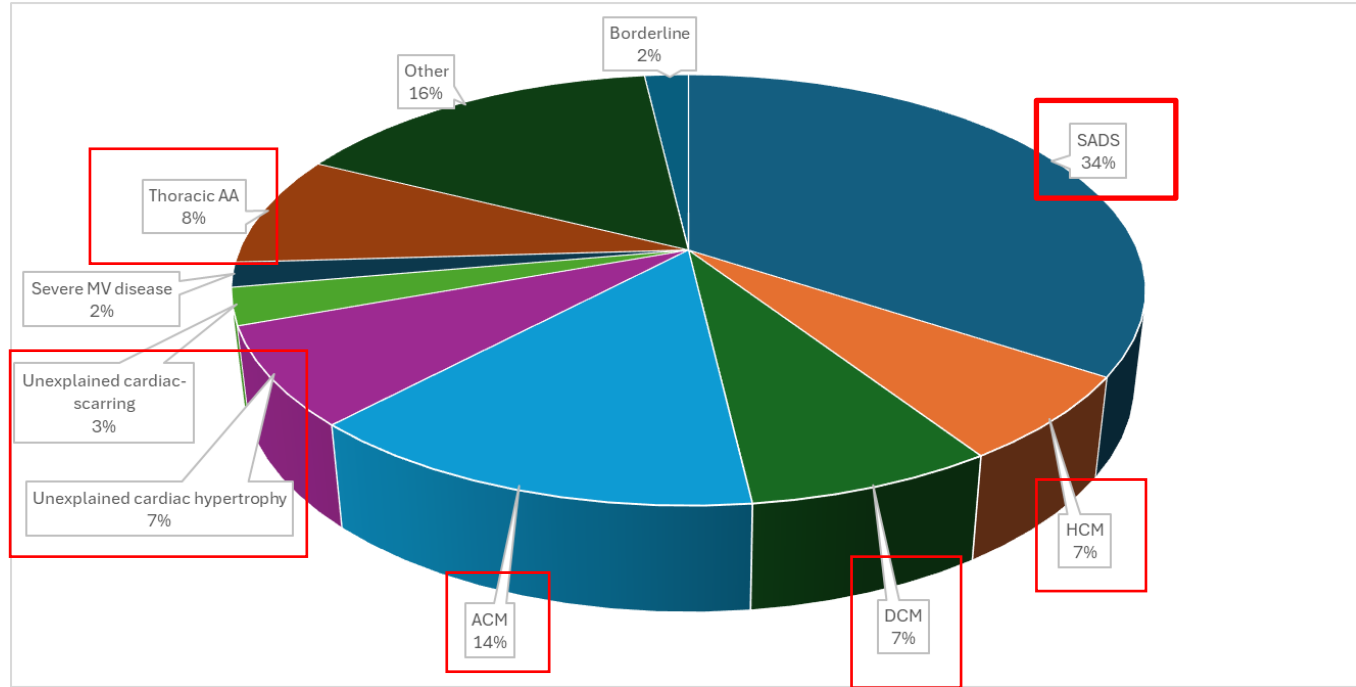
Pilot sites and programme objectives

- Central and South GLH/GMSA
- East GLH/GMSA
- North East and Yorkshire GLH/GMSA
- North Thames GLH/GMSA
- North West GLH/GMSA
- South East GLH/GMSA
- South West GLH/GMSA

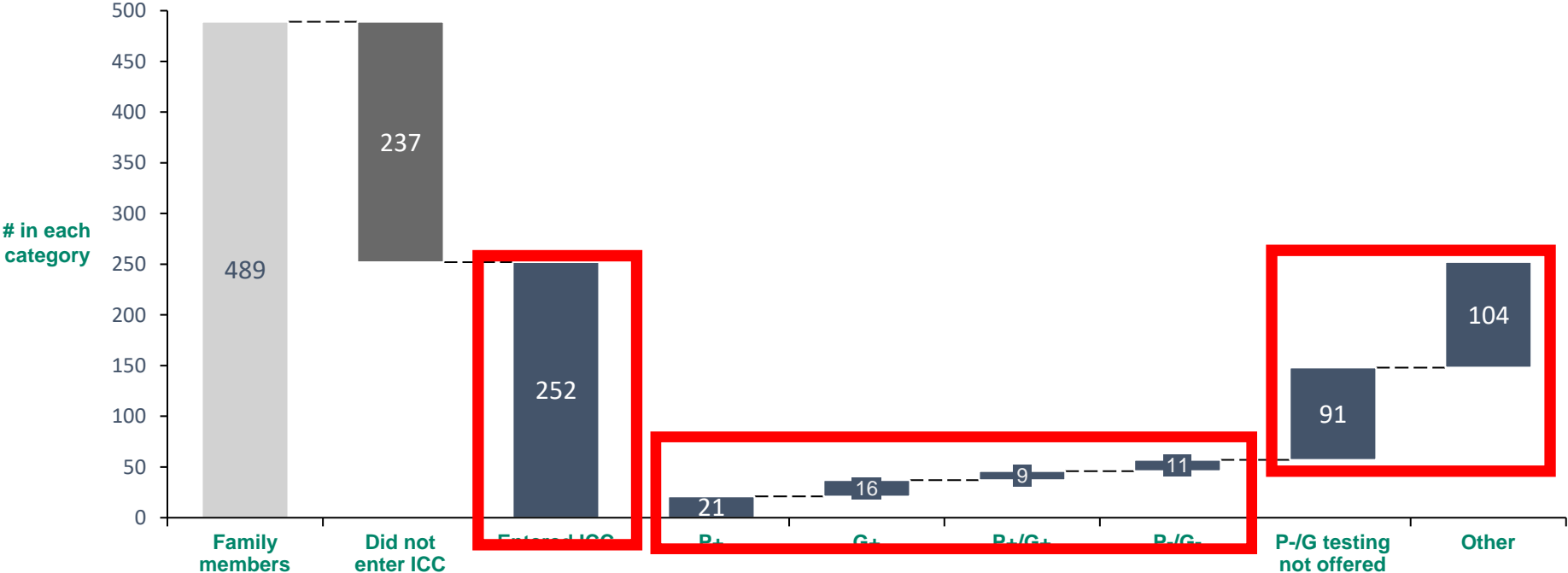


1. Establish consistent pathology practice for SUD including expert pathology
2. Routine tissue retention for DNA extraction
3. Establish coronial and NHS pathways for family for genetic testing and clinical evaluation.
4. Establish mechanism for standardised post-mortem genetic testing via NHS GLH – R138 and R441
5. Develop and disseminate best practice nationally for adoption of pathway within NHS
6. Engagement and input of patient and support groups linked to inherited cardiac disorders
7. Develop evidence base for a proposed national roll out

Aetiologies of SUD (N = 108) – Interim – final data awaited



Relatives and the ICC Service – Interim – final data awaited



P+ Phenotype positive, where genotype is either negative or unknown; G+ Genotype positive where phenotype is either negative or not documented
 Other includes those lost to follow up or where screening was ongoing

Final Evaluation Report: Key Findings

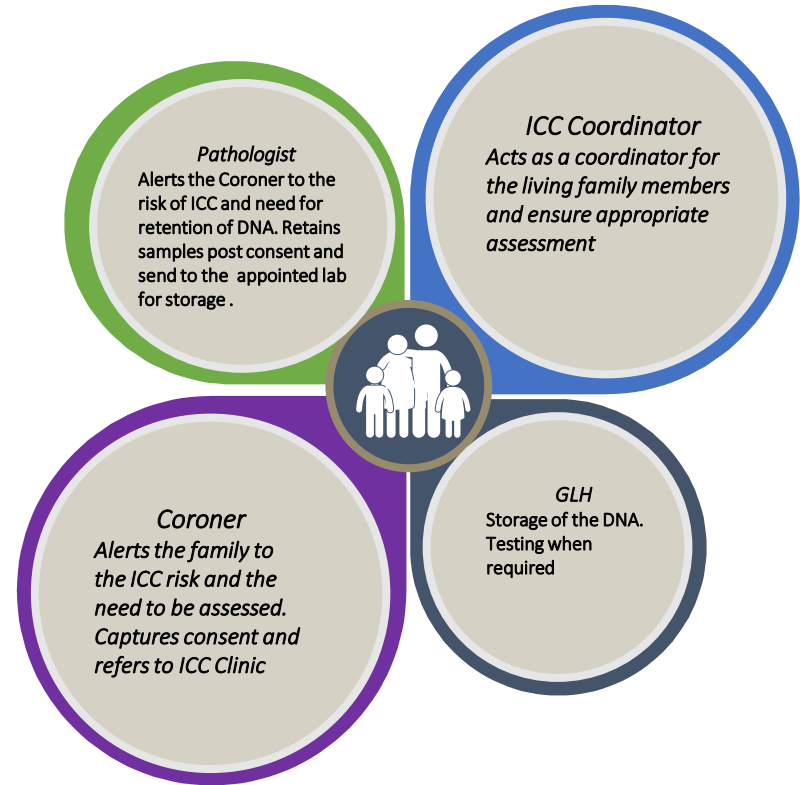
Key findings:

- The pathway was effective and achieved the intended outcomes
- Implementation of the pathway was cost neutral and labour light for Coroners
- The ICC Coordinator role was vital to both implementation and service delivery, and will be vital to roll out
- Good communication and teamwork between the different disciplines across the pathway was essential

Final Evaluation Report: Family Experience

- Seamless process that brought them into ICC services swiftly and without them having to take action
 - Single point of contact was valued
 - Knowledge of the case history and family dynamics
 - Trust and rapport
 - Confidence that someone is holding all the threads
- Family members felt supported in a way that felt personalised to their needs
- Family members received the information they needed
- Support was mostly well-paced, but getting index case genomic test results felt slow

National Adoption of the Sudden Unexpected Death and Sudden Cardiac Arrest Pathways



The Vision for National Adoption

Every index case, where cardiac genetic disease is the suspected cause of an out-of-hospital cardiac arrest or sudden death, will be appropriately identified so that all living index cases, first-degree and at-risk relatives receive appropriate and timely follow up and genetic testing in a specialist ICC service.

Inclusion criteria for SUD cases

1. SUD Cases reported to HM Coroner
2. Include cardiac arrest where resuscitation has failed or no recovery despite initially successful resuscitation notified to Coroner
3. Age >1 years old
4. Suspected cardiac genetic cause of death
OR
5. Unexplained despite full coronial and expert cardiac autopsy and pathological testing = SADS/SUDIC



In Practice

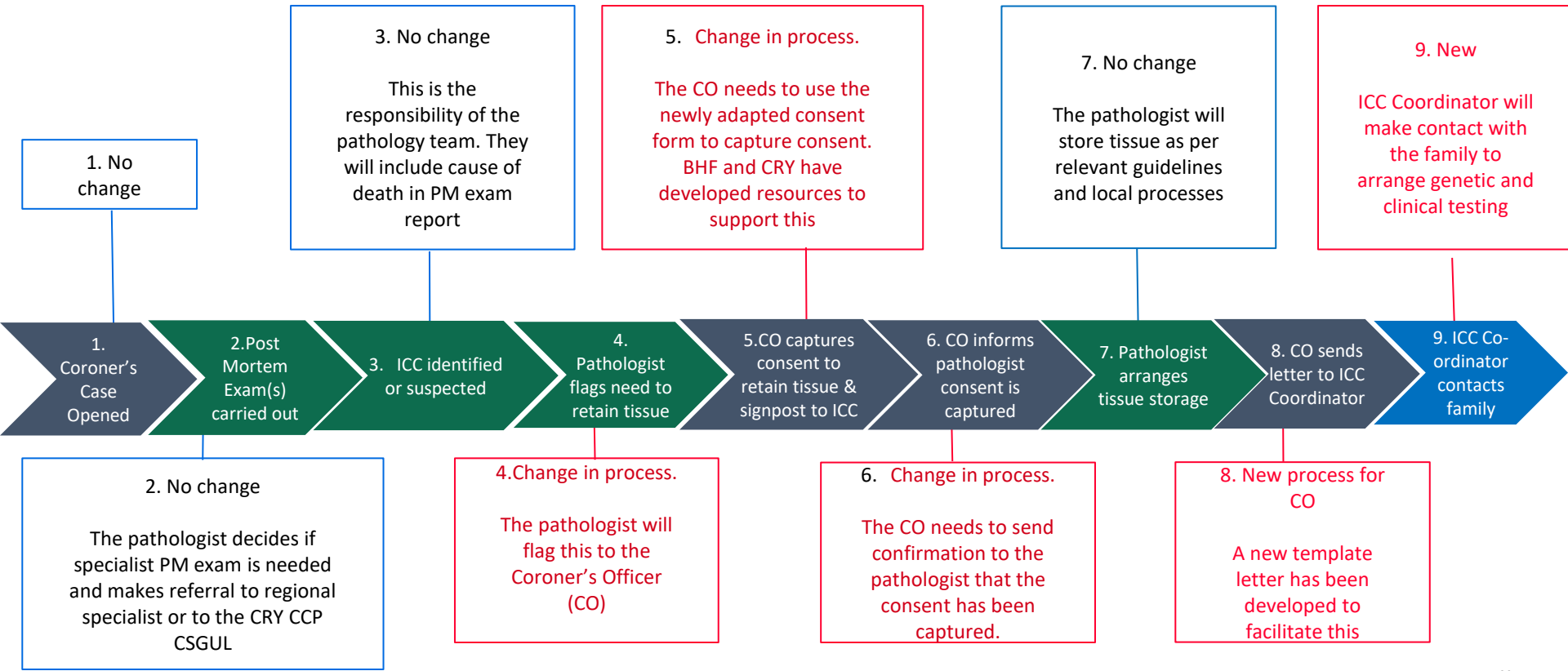
In practice, the pathway will be initiated by the:

- Coroner where the index case dies without being admitted to hospital following an out-of-hospital cardiac arrest (OHCA) or sudden death
- Coroner where the index case dies in hospital following an admission post an OHCA and is notified to the coroner

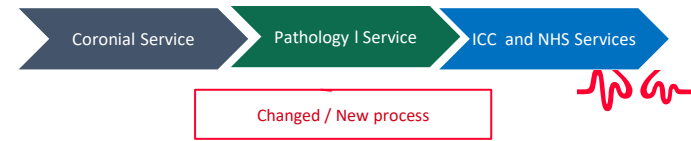
The step by step process



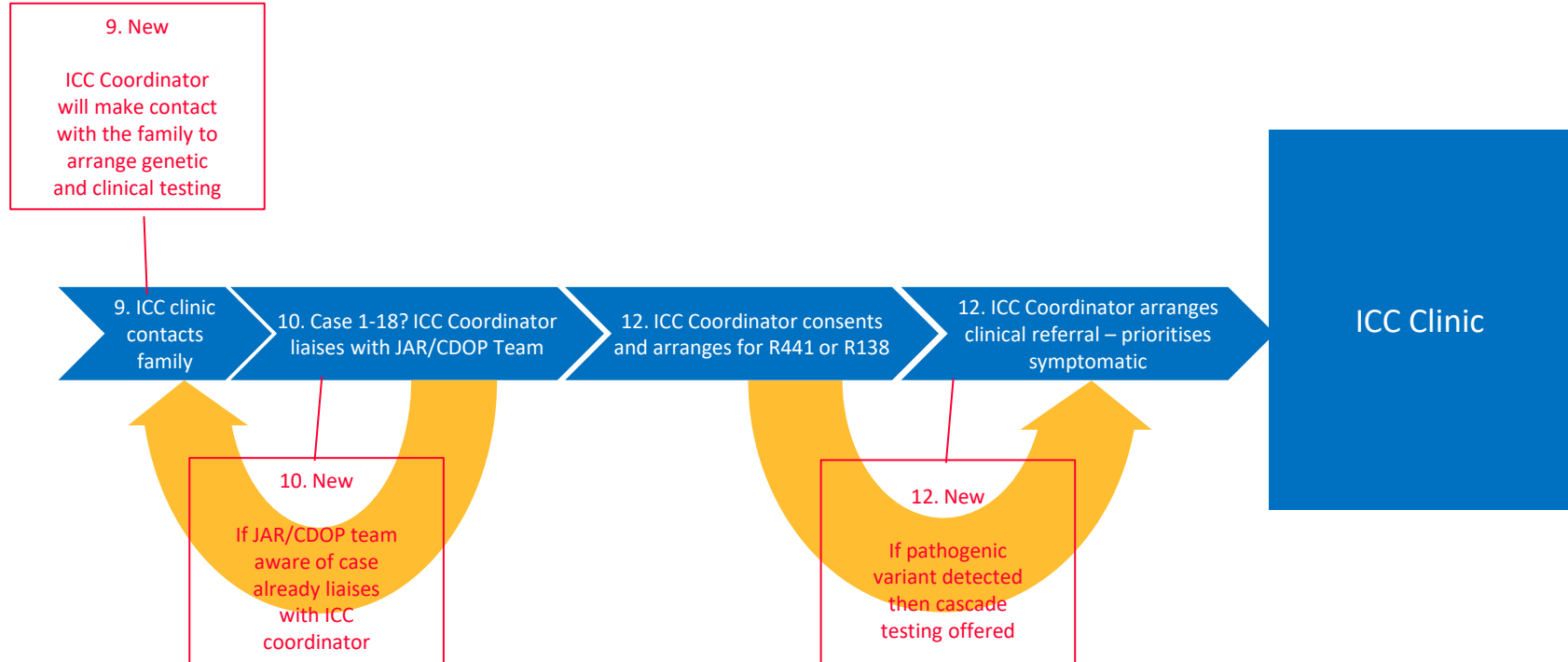
Changed / New process



The step by step process



This high-level process highlights the steps in the process .



Reminder of key learning from programme

*'The role of the ICC Coordinator within existing ICC services is critical to the success of the pathway.
The relationship between the local ICC Coordinator and the Coroners' Officers is particularly important to ensure that appropriate cases were referred to the NHS'*

**Evaluation Report 2024
Bright Purpose**

Liaison and collaboration between ICC Coordinator and JAR/CDOP team is vital